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IMMUNOHISTOCHEMICAL PROPERTIES OF THE LIVER OF INFANTS WHO DIED IN THE NEONATAL PERIOD BORN WITH PREECLAMATION

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Abstract. *In order to examine the changes in the liver of infants who died in the early neonatal period due to preeclampsia, immunohistochemistry was used to detect active changes in hepatocytes, to determine whether or not the characteristics of hepatocytes change, and to interpret the changes in the antigenic structure. It should be noted that through immunohistochemical examination, we were able to detect necrosis, pre-necrosis, proliferative indicators, and then to determine the activity of blood cells in the liver.*

Keywords. *Morphology, immunohistochemistry, liver, preeclampsia, infant.*

The urgency of the problem. It has been determined that the number of pregnant women with preeclampsia in the world has increased by 2.1 times in the last 10 years. At least 10-30% of them have signs of liver damage due to microangiopathy as part of a general disorder of blood vessels. This leads to a sharp deterioration in the metabolism between the mother and the fetus, the elimination of toxic substances. In the USA and European countries, this type of pathology accounts for an average of 2.1-5.7% of all pregnancies, while in the CIS countries this figure is 10.5-18.2%. In Central Asia, the number of deaths from preeclampsia and eclampsia in 2020 was about 8.9-12.7% of all pregnant women.

Signs of liver damage appear at the end of the II-III trimesters of pregnancy, usually against the background of a detailed clinical picture of hypertensive disorders. In the absence of arterial hypertension or proteinuria, an atypical course of preeclampsia can be observed. Liver damage can manifest itself only with laboratory changes (increased AST/ALT, mild thrombocytopenia), without jaundice and other complications, including the development of HELLP syndrome. It is precisely in these changes in the third trimester of pregnancy that sharp changes in fetal development occur, the inability to fully utilize harmful substances secreted by the fetus through the placenta, and lead to morphofunctional stress of the fetal liver.

Objective. To study the morphological and immunohistochemical changes that occur in the pathomorphological characteristics of the liver of infants whose mothers have preeclampsia.

Materials and methods. Liver tissue was obtained from 66 infants born to mothers with preeclampsia who were brought to the Republican Center for Pathological Anatomy from the RIPIATM for autopsy. Morphological, immunohistochemical and statistical research methods were used to improve the assessment of morphological changes characteristic of the liver of infants who died in the neonatal period due to preeclampsia.

Results and discussion. In order to examine the changes in the liver of infants who died in the early neonatal period due to preeclampsia, immunohistochemical studies were performed to identify active changes in hepatocytes, to determine whether there were any changes in the characteristics characteristic of hepatocytes, and to interpret changes in the antigenic structure. Let's remind, through

immunohistochemical examination, we examined the liver necrosis, pre-necrosis process, proliferative indicators, and then the activity of blood vessels in the liver.

Immunohistochemical studies were performed using monoclonal antibodies and a systemic imaging system (Ventana Ultra USA):

1. CD 31 (PECAM-1)
2. CK 34 (vascular growth factor, indicating neoangiogenesis)
3. P 53 is a factor indicating increased apoptosis of hepatocytes.
4. Ki 67 is a factor determining the proliferative index.

The Ki-67 marker is expressed mainly in the perinuclear region of any cells and is a marker determining proliferative activity. This plays an important role in assessing the proliferative index of fibroblasts. The significance of the markers used in immunohistochemical examination is as follows: the Ki-67 marker is a marker that determines cell proliferation and is expressed in different levels (light, medium and strong liver color) in all active phases of the cell: G1, S, G2, M. This marker is highly expressed from the initial phase of cell activation, from the G1 to the M phase, and is clearly visible in the metaphase of mitosis. In the initial phase of G1, the Ki-67 marker is located at the centromere of satellite DNA and at the telomere of the chromosome.

In the intermediate phases of cell activation, the Ki-67 marker is detected intranuclearly in the nucleolus, but by the G2 phase, it is expressed in the nucleolus and karyoplasm. When the cell enters the post-mitotic G0 phase, the Ki-67 marker is degraded by proteosomes and undergoes complete catabolism and is not expressed in cells in interphase. This is important in the evaluation of the proliferative index of fibroblasts, which are proliferatively active in hypotocytes.

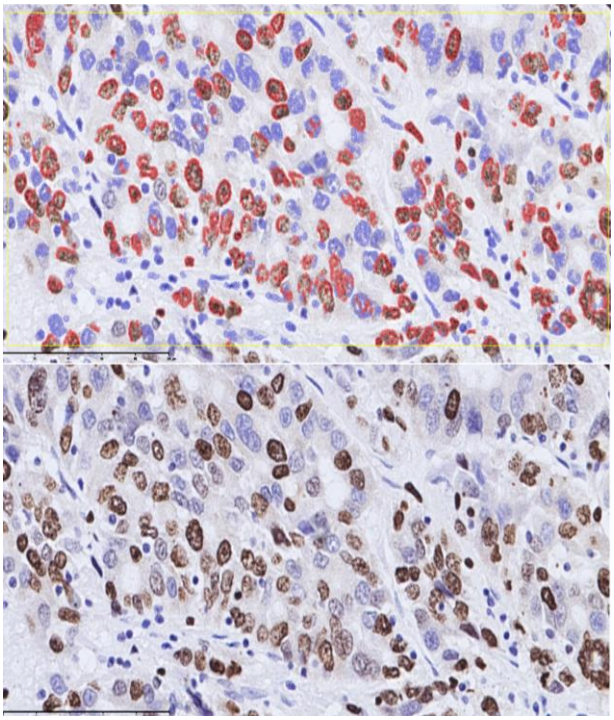

Fig. 1. An infant born with preeclampsia and dying in the early neonatal period. Protocol 46-D. High positive expression of the Ki-67 marker. Scanned and the level of expression was determined using the QuPath-0.4.0.ink. program. Expressed cells are dark red. Stain Dab chromogen. Size 10X10.

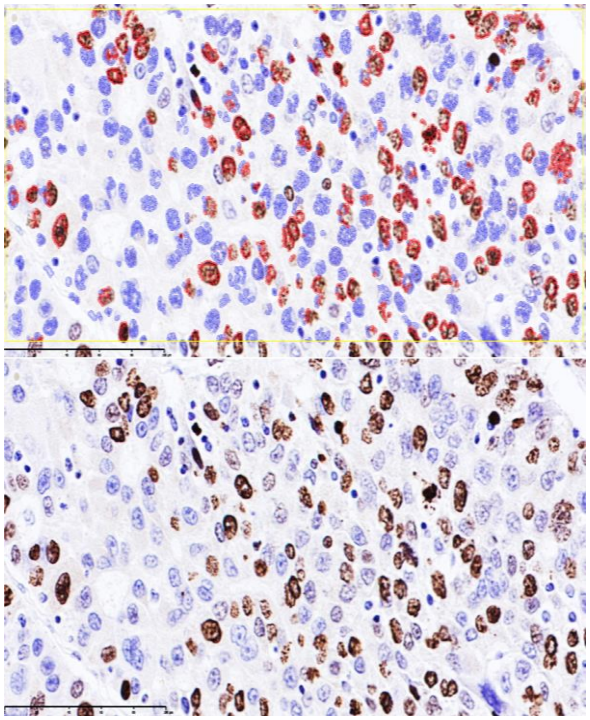

Fig. 2. An infant born with preeclampsia and dying in the late neonatal period. Protocol 17-DI. High positive expression of the Ki-67 marker. Scanned and the level of expression was determined using the QuPath-0.4.0.ink. program. Expressed cells are dark red. Stain Dab chromogen. Size 10X10.

In our study, high positive expression of the Ki-67 marker was detected in 63.1% of the subjects, mainly in hepatocytes, with very low expression in mesenchymal cells. This indicates that compensatory regenerative indicators are high in the liver parenchyma in infants, which indicates a high level and diversity of factors affecting the proliferative type of liver in preeclampsia. The high number of hepatocytes still undergoing 2 and 3 nuclear mitosis phases in the liver, the high number of hepatocytes that completely occupy the liver in terms of volume, the adaptation mechanism aimed at eliminating tissues and cells specific to the fetus in the early neonatal period, is directly related to the detoxification activity of the liver, and it is precisely in preeclampsia that the immunohistochemical aspects of these morphofunctional indicators in hepatocytes lag behind the norm.

In our study, moderate positive expression was detected in 29.9% of the subjects. The remaining 6.8% had a negative reaction, mainly expressed. This, in turn, led to the fact that in the early neonatal period, the positive expression of the Ki-67 marker in the liver of infants was high, and according to the proliferative index, by index, it was found that 38.23±1.42% The proliferative index in mesenchymal cells was 11.01±1.02%, and this indicator was not statistically different from the indicators in the control group, so it was not included in our study.

In the late neonatal period, the expression of the Ki-67 marker was mainly expressed in hepatocytes, with nuclear expression, heterogeneously expressed in the nuclear, subnuclear and perinuclear areas, and was lower than in the early neonatal period, indicating a decrease in the proliferative resources of the liver and a decrease in the self-repair function of the liver, as well as an increase in the process of fibrosis in the liver. This was revealed by the fact that the Ki-67 marker reacted mainly in hepatocytes, with relatively low values of about 10% in the late neonatal period. While in the early neonatal period, the highest rate of proliferation in the liver of infants was 48.9% (see Figure 4.1), in the late neonatal period this rate was 34.23% (see Figure 4.2). This also confirms the direct relationship between the duration of the influencing factors, the decrease in the liver's intracellular and extracellular matrix resources, and the increase in mesenchymal tissue.

The proliferative index of the Ki-67 marker in the late neonatal period of infants born against the background of preeclampsia was 25.38±1.05%, while the proliferative index in mesenchymal cells was mainly 14.78±1.66%, confirming the increase in the stromal components of the liver in this process.

In the next immunohistochemical study, the mutant protein transcription factor is studied by studying the reaction of the P-53 marker.

The P-53 protein is a proapoptotic factor, which, as a result of the accumulation of abnormal proteins, onoproteins, and various foreign mutant proteins in the cytoplasm of cells, triggers the apoptosis mechanism in the cell, which leads to organ failure, depending on the duration of this process and the level of influencing factors. This may lead to misunderstandings in our studies, since high positive expression of the P-53 marker indicates a high probability of tumor progression. It should be noted that this marker is characterized by high reactivity in stress, strong ionizing radiation, infectious diseases, infectious toxic shock, chemical toxic poisoning, chromosome and gene mutations. However, in our study, it was found that the ontogenesis of the liver is lagging behind in the background of preeclampsia, as well as the presence of secondary infectious factors, which is manifested by a high positive reaction of the P-53 marker. If the genetic apparatus of the cell is not damaged, then P-53 also occurs with a low positive reaction, and if DNA is damaged, P-53 is also activated. Thus, P-53 is activated when damaging factors accumulate in DNA. As a result of P-53 activation, the cell cycle stops and apoptosis occurs. The significance of the increased concentration of P-53 is that it rapidly replicates with DNA and damages the genetic apparatus, and this condition is considered to be the readiness of the cell to DNA damage. In well-differentiated cells with intact maturation, the latent P-53 protein is located in the cytoplasm of the cell. When the cell's proliferative activity increases, this P-53 protein translocates to the nucleus, and in the absence of stress on the cells, this protein is degraded within 5-20 minutes.

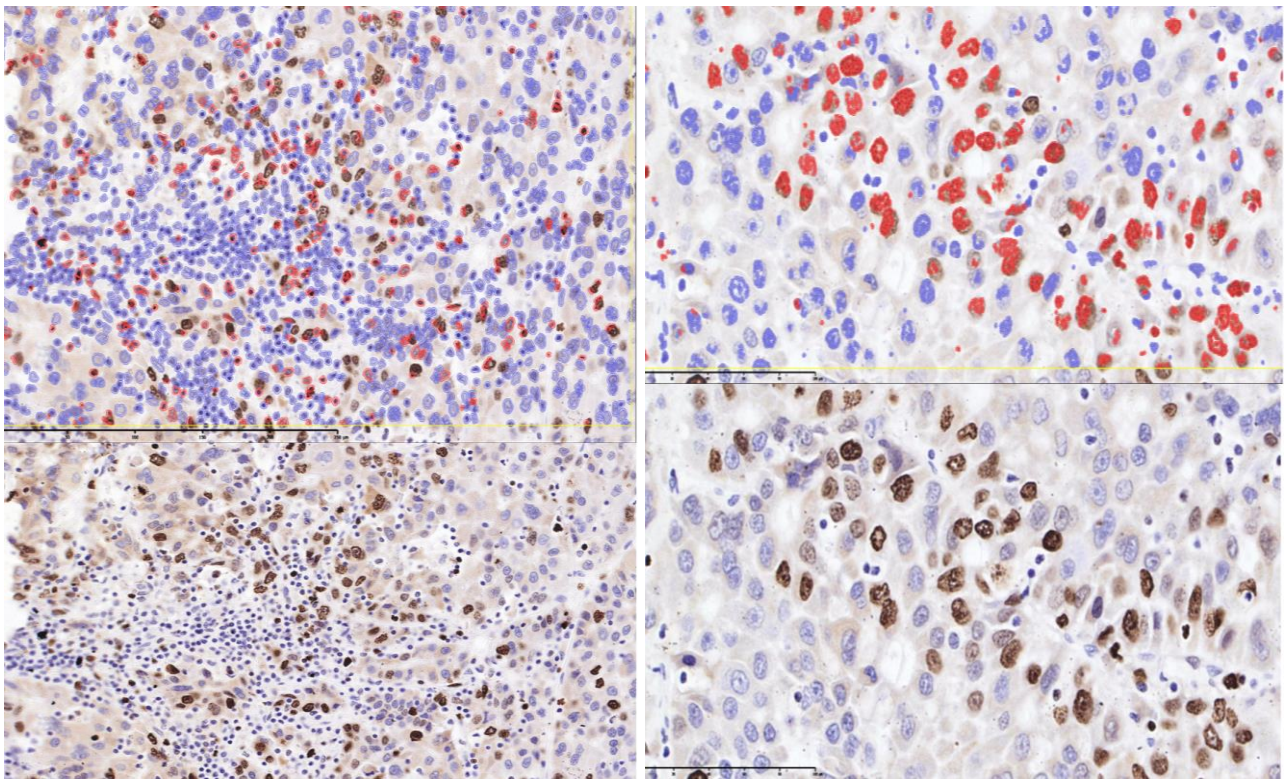

Fig. 3. A baby born with preeclampsia and died in the late neonatal period. Protocol 17-DI. High positive expression of R-53 marker. QuPath-0.4.0.ink. was scanned in the program and the level of expression was determined. Expressed cells are dark red. Paint Dab chromogenic.
The size is 10X10.

In our study, 71.1% of the subjects had high positive expression of the P-53 marker, indicating that the liver injury process is ongoing, and that the liver of infants born against the background of preeclampsia, as a result of toxic effects, causes damage to the nuclear structures of hepatocytes, which leads to the activation of this gene. In the early neonatal period, the highest level of positive expression of the P-53 marker was 26.8%, the lowest was 16.5%, and the average positive reaction was 19.3%, confirming the high level of liver injury. In the liver of infants born in the late neonatal period against the background of preeclampsia and living up to 8-28 days, the lack of tolerance to toxic substances, excessive accumulation of metabolites, manifested in the form of fatty and protein inclusions in the cytoplasm of hepatocytes, was manifested by the occurrence of cell decomposition, necrobiosis and induced apoptosis. Recall that in previous morphological studies, we have shown that in hematoxylin and eosin staining, apoptosis and necrosis processes occurred in parallel in hepatocytes. This, in turn, confirmed the fact that in IGH studies, in the late neonatal period, the P-53 marker was significantly lower than in the early neonatal period, confirming the fact that the damage process was proceeding rapidly.

Thus, in the late neonatal period, the positive rate of the P-53 marker is on average 22.9%, which leads to the clinical morphological manifestation of liver failure and hepatic coma.

CD-34 is a membrane protein expressed in cells of many tissues and is an intercellular adhesion molecule (adhesion between cells) involved in the early stages of hematopoiesis.

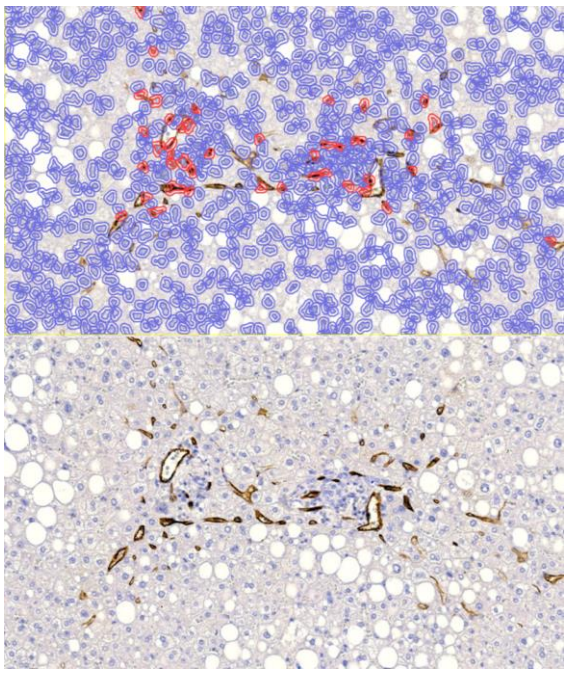

Fig. 4. Infant born with preeclampsia and dying in the early neonatal period. Protocol 17-DI. Low positive expression of the CD-34 marker. Scanned and the level of expression was determined using the QuPath-0.4.0.ink. program. Expressed cells are dark red. Staining Dab chromogen. Size 10X10.

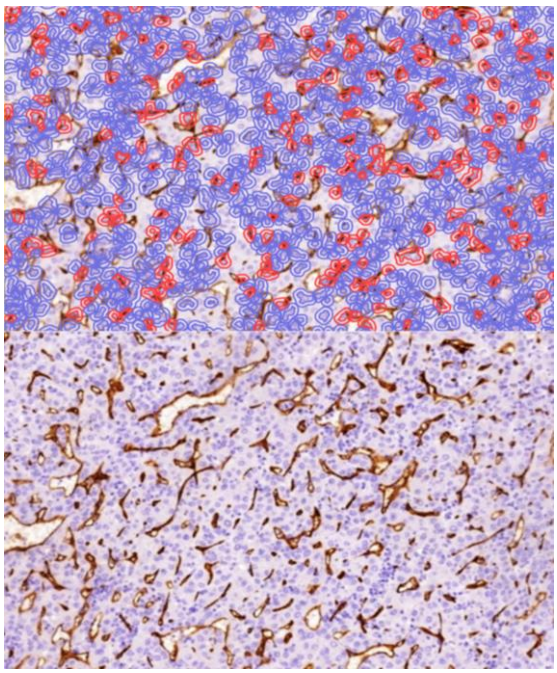

Fig. 5. Infant born with preeclampsia and dying in the late neonatal period. Protocol 17-DI. Low positive expression of the CD-34 marker. Scanned and the level of expression was determined using the QuPath-0.4.0.ink. program. Expressed cells are dark red. Staining Dab chromogen. Size 10X10.

It is a marker of vascular endothelium and is tested to assess the level of neoangiogenesis. Studying the processes of neoangiogenesis in benign and malignant tumors is an important promising direction in assessing tumor progression and developing antiangiogenic therapies.

The CD-34 marker was examined to assess the level of angiogenesis in reparative regeneration of liver damage in preeclampsia.

Low positive expression of the CD-34 marker in hemocapillaries in the liver confirms that in most cases, in areas of damage and secondary inflammation, fibroblasts, mainly from mesenchymal cells, are proliferating, and sparse fibrous connective tissue is formed in place of the lost vascular components.

Thus, in the early neonatal period, in most infants born against the background of preeclampsia, the number of cells undergoing necrosis and apoptosis in the liver under the influence of secondary infectious factors, and in areas where the stroma of the damaged segments is exposed, the transformation of endothelial cells into fibroblasts or the process of mesenchymal metaplasia is confirmed, confirming the proliferation of connective tissue in the liver.

In the late neonatal period, the intensification of this process and the parallel increase in the CD-34 marker by 5-6%, morphologically, in the damaged segments of the liver, small-caliber blood vessels are redeveloped mainly in the perilobular and periportal areas, which, as a result, confirms the slowing of blood circulation in the microcirculatory system in the liver.

CD-31 (PECAM-1) - PECAM-1 is involved in transendothelial migration of leukocytes, angiogenesis and integrin activation. In addition to the functions listed above, PECAM-1 serves as a mechanosensor of the cell. The purpose of the study is to determine that the protein molecules in the PECAM-1 marker are in a homophilic dimer state, and the molecule of one cell binds to the molecule of a neighboring cell, ensuring its stability and forming intercellular contacts. If mechanical stress is

observed between the cells and their separation from each other, this protein is synthesized in large quantities to bind them to each other. As a result, it ensures the stability of the state. In this case, the cytosolic state of the protein is associated with the actin filaments of the cell. Mechanical dilation of a vessel, for example due to increased blood flow, leads to the elongation of two interacting proteins relative to the actin filament within the cell.

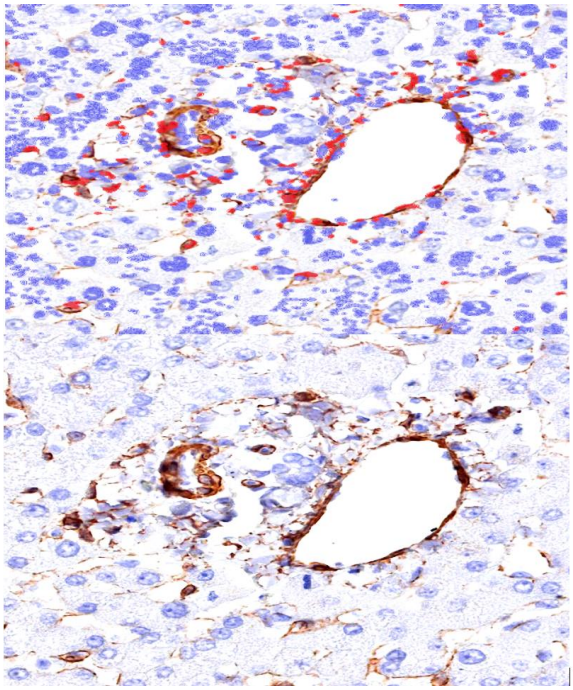

Fig. 6. Infant born with preeclampsia and dying in the early neonatal period. Protocol 17-DI. type. Low positive expression of the CD-31 PECAM marker. Scanned and the level of expression was determined using the QuPath-0.4.0.ink. program. Expressed cells are dark red. Staining Dab chromogen. Size 10X10.

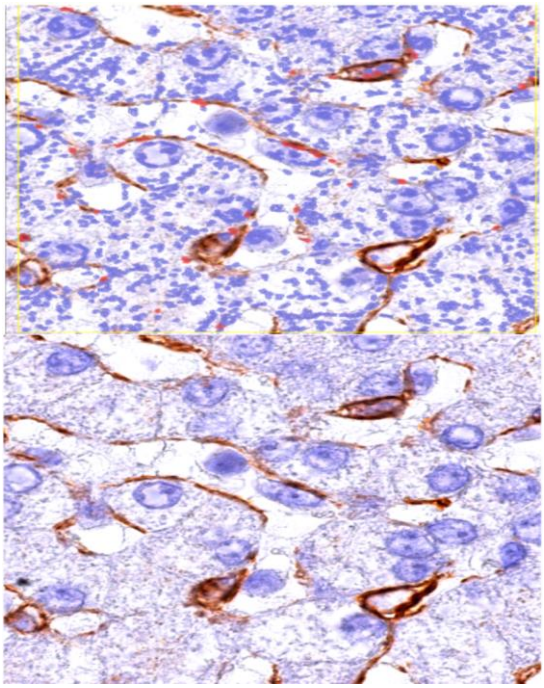

Fig. 7. Infant born with preeclampsia and dying in the late neonatal period. Protocol 17-DI. Low positive expression of the CD-31 PECAM marker. Scanned and the level of expression was determined using the QuPath-0.4.0.ink. program. Expressed cells are dark red. Staining Dab chromogen. Size 10X10.

This stretching leads to the action of tyrosines and their phosphorylation by tyrosine kinase, which activates the corresponding signaling pathway. Thus, the cellular response to changes in blood flow is morphologically manifested. In our study, these changes include a decrease in the number of hemocapillaries, compression of small-caliber vessels (recall that in preeclampsia, venous congestion and massive dystrophic processes in hepatocytes, varying degrees of expansion of sinusoids, parallel expansion of the spaces of Disse, leading to a pronounced violation of microcirculation, increased necrosis and apoptosis in hepatocytes, and the formation of sparse and coarse fibrous connective tissue). As a result, a sharp decrease in the positive reaction of this marker, clinically morphologically, leads to liver failure, and those born against the background of preeclampsia and die in the neonatal period mainly from liver failure. This is important in revealing the essence of our study and in interpreting the morphological basis of the resulting immunohistochemical changes.

In immunohistochemical studies, the CD-31 marker is a morphological marker of damage mainly to endothelial cells.

Specifically, it is confirmed that in the liver, it causes vasodilation of small vessels and simultaneously leads to functional tension of the active filament, a glycoprotein transmembrane protein, both extracellular and intracellular. It should be noted that the high positive expression of the

CD-31 (PECAM-1) marker by external factors is characterized by the binding of the membrane glycoprotein involved in the role of the active filament on the endothelial surface and the functional tension of endothelial cells, and in our study, the lack of a factor stimulating this process led to low positive expression.

In our study, in 76.8% of infants who died in the early neonatal period, low positive expression of the CD-31 (PECAM-1) marker was found, with a negative reaction in 23.2%.

In the late neonatal period, this indicator was expressed in 82.6% with low positive expression, and in 17.3 with a negative reaction. This, in turn, allows us to predict that in severe cases of hepatic preeclampsia, the process of damage begins during fetal development, mainly in dystrophic, necrobiotic forms, with a sharp narrowing of the sinusoids.

Thus, the lack of significant statistical differences in the low positive expression of the CD-31 (PECAM-1) marker in the early neonatal and late neonatal periods, characterized by a low positive reaction to this marker, and in clinically morphologically, in infants born against the background of preeclampsia, in assessing the morphofunctional indicators of the liver, of course, in the liver tissue, vascular endothelial growth factor in advance, and the use of angioprotective drugs, serves as one of the main criteria for diagnosing, saving the lives of infants and determining the economic and social effectiveness of treatment.

Conclusions. In infants born against the background of preeclampsia and dying in the early neonatal period, it was found that the predominance of the Ki-67 marker reaction of proliferative indicators occurred mainly in hepatocytes, while in the late neonatal period, the predominance of the P-53 marker was observed, which increased the apoptosis process and reduced the proliferative properties of hepatocytes, and the proliferation of fibrous connective tissue instead of vascular tissue was detected by the CD-31 and CD-34 markers.

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A CLINICAL CASE OF LOBULAR CAPILLARY HAEMANGIOMA OF THE NASAL CAVITY DURING PREGNANCY

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Abstract. *A benign lesion called a lobular capillary haemangioma originates in the vascular tissue of the skin, mucosa, muscles, glands, and bones. These lesions spread quickly. Rarely occurs nasal localization. Pregnancy and microtrauma are the two most frequently suggested aetiological reasons. Pregnancy-related incidence has been reported to range from less than 2% to roughly 5%. Depending on the severity of the symptoms and the stage of the pregnancy, the treatment of a pregnant woman with such a lesion may be complicated. The preferred course of treatment is complete surgical excision, either with or without pre-operative embolization.*

Keywords: *capillary hemangioma, nasal septum, nose bleeds, nasal cavity, pregnancy, pathology.*

Introduction. Hemangiomas are benign tumors that arise in the vascular tissue of the skin, mucous membranes, muscles, glands, or bones [1,4,7,9]. Lobular capillary hemangioma (LCH), also known as pyogenic granuloma or pregnancy granuloma, is a rapidly growing lesion with extensive endothelial proliferation [2,5,12]. This lesion typically appears in the oral cavity and is rarely found in the nasal region. The etiology of LCH during pregnancy remains unclear [3,6,8]. The most widely accepted hypothesis suggests that this lesion may result from an interaction between local irritants and subsequent tissue inflammation, amplified by female sex hormones produced during pregnancy [2,5]. LCH generally resolves after childbirth, and endoscopic endonasal total excision is usually the definitive solution.

Clinical case. A 30-year-old pregnant woman at 32 weeks of gestation was admitted in September 2022 with complaints of nasal congestion, anosmia, periodic nasal bleeding from the left side, severe left-sided nasal dyspnea, and dry mouth. These symptoms had been present since August 2023. The patient's history revealed that the first left-sided nasal bleeding occurred at 30 weeks of pregnancy, accompanied by a rise in systemic arterial blood pressure to 140/80 mm Hg. The bleeding was stopped with soft anterior nasal packing. The patient noted that the intensity and duration of the nasal bleeding increased with each subsequent episode. Hemostasis test results and the patient's hemoglobin levels were within acceptable ranges. Two weeks before admission, an ENT specialist performed an outpatient endoscopy of the nasal cavity and found a polyp-like neoplasm on the left side of the nose, which bled upon palpation. An MRI of the nose and sinuses (without contrast) revealed a round tissue mass in the left nasal cavity, filling the posterior part of the nasal cavity from the middle of the left middle nasal concha to the left choana, with axial dimensions of 2.5x2.0 cm and vertical dimensions of no more than 3.0-3.5 cm. The neoplasm was partially displaced, leading to the destruction of the nasal septum. A biopsy of the neoplasm was accompanied by massive bleeding. Histological examination (capillary hemangioma) revealed that the tumor consisted of small, dense capillaries (Fig. 1). Complete blood count: Hb - 80; erythrocytes – 3.0; CP – 0.9; leukocytes – 10.8; ESR – 23 mm/s; Coagulation (Sukhorev's test): initial – 2.4; final – 3.8; platelets – 188; eosinophils – 6; neutrophils (banded) – 5; segmented neutrophils – 82; lymphocytes – 53; monocytes – 11. ECG: No abnormalities

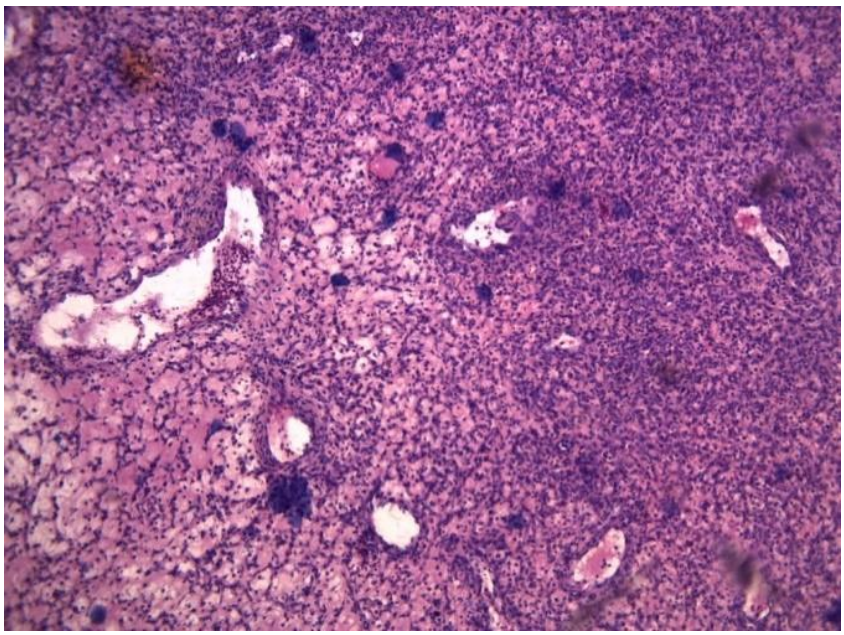

Fig. 1. Capillary hemangioma, hematoxylin-eosin staining (x120)

During the five-day hospitalization, preoperative hemostatic therapy was administered to prevent intraoperative bleeding, using 5 ml of 5% tranexamic acid solution, intramuscularly once a day. Under local anesthesia of the nasal mucosa (2 ml of 10% lidocaine solution), an endonasal excision was performed. Hemostatic tampons were used to control bleeding on both sides of the nasal cavity. In the postoperative period, the patient received preventive hemostatic therapy and systemic antibacterial treatment under the supervision of an obstetrician. On the second postoperative day, the tampon was removed from the nasal cavity, and a cotton tampon with antiseptic ointment was placed. Further nasal irrigation with saline solution was recommended for a month. The nasal mucosa appeared pink, the nasal passages were unchanged, there was no discharge, and nasal breathing was unobstructed. During a follow-up examination on the 21st day (November 15, 2022), the patient complained of nasal congestion and dryness of the nasal mucosa.

The postoperative period proceeded without complications. The nasal passages were irrigated daily (twice a day). The patient was discharged on the 5th day in satisfactory condition. The biopsy results remained unchanged compared to the preoperative findings (final diagnosis: capillary hemangioma of the nasal septum with erosions).

One month after surgery, the patient continued anticancer therapy with tamoxifen (20 mg/day). During a scheduled follow-up anterior rhinoscopy, thickening of the nasal mucosa was found at the upper edge of the nasal septal perforation. This thickening was excised on February 11, 2023, under local anesthesia using a high-frequency scalpel. The biopsy confirmed that the thickening was a hemangioma. No postoperative complications were observed. The patient is under outpatient observation.

Three months after discharge, the patient returned to the hospital due to nasal bleeding and a headache. A repeat CT scan showed no signs of mass formation. At the 6-month follow-up after surgery, the patient reported no complaints and no signs of recurrence. Microbiological analysis was negative. Thus, functional disorders and nasal bleeding did not completely resolve with conventional treatment.

Conclusion. Lobular capillary hemangioma during pregnancy is a benign condition that typically manifests in the third trimester. The most common clinical presentation is nasal bleeding. Nasal LCH can be treated surgically with a relatively low risk of recurrence.

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DIAGNOSIS AND TREATMENT OF SUDDEN SENSORINEURAL HEARING LOSS: LITERATURE REVIEW AND RESEARCH METHODS

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Abstract: *A distinguishing feature of sudden sensorineural hearing loss (SSNHL) is a rapid onset of sensorineural hearing impairment occurring within 72 hours, which is almost always unilateral. Most cases are idiopathic, and the degree of hearing loss significantly affects the prognosis for recovery. The aim of this study was to evaluate the effectiveness of steroid and antiviral therapy in the treatment of idiopathic sudden sensorineural hearing loss. We conducted a retrospective study of patients who presented to a tertiary academic specialty medical center. A total of 51 patients were examined. All patients received a standardized treatment regimen. Our treatment protocol resulted in a hearing recovery rate that exceeded the rate of spontaneous recovery. Antiviral therapy and extended steroid treatment duration may contribute to improved recovery outcomes.*

Keywords: *sudden sensorineural hearing loss, treatment, diagnosis.*

Introduction. The diagnosis and treatment of sudden sensorineural hearing loss (SSNHL) have remained challenging for clinicians for decades. SSNHL is believed to affect approximately 1 in 10,000 people annually [2,5,8]. Although SSNHL is a well-recognized condition, there is no universally accepted definition or treatment protocol. Furthermore, despite extensive evaluation, the etiology can only be determined in 10–15% of cases [1,3,10]. Viral infections, vascular disorders, and ruptures of cochlear membranes are among the factors associated with SSNHL or are suspected to be possible causes [4,9,11].

Numerous factors hinder the development of standardized definitions and treatment protocols for SSNHL [12,15]. Limited understanding of the pathophysiology of the disease contributes to the lack of effective treatment. It has become evident that this disorder does not result from a single disease process. An additional complicating factor is the high rate of spontaneous recovery [5,6,7,13]. According to most studies, spontaneous recovery occurs in 45% to 65% of patients. In this study, we present the treatment of idiopathic SSNHL using a combination of steroid and antiviral therapy.

Methods. A retrospective chart review was conducted to identify patients treated for idiopathic sudden sensorineural hearing loss (SSNHL). Only patients who presented with a complaint of sudden hearing loss were included. The term "sudden" was limited to cases where hearing loss occurred instantly or developed within no more than three days. SSNHL was defined as a hearing loss of 30 dB or more affecting at least three frequencies. All patients were examined within seven days of the onset of hearing loss.

The medical records of all patients diagnosed with SSNHL from 2023 to the present were reviewed at the Department of Otorhinolaryngology of Samarkand Medical University. Patients in whom no identifiable cause of SSNHL was found were considered to have idiopathic SSNHL. Medical records of patients who underwent evaluation for idiopathic SSNHL were selected. Records lacking follow-up audiometric testing were excluded. The remaining 51 medical records were thoroughly analyzed. Demographic data, including age and gender, were recorded. The course of the illness, consultations with other specialists, and use of medications prior to presentation were documented. Attention was paid to any history of otologic, vascular, or autoimmune diseases prior to presentation. The charts were also reviewed for smoking, alcohol use, and other chronic illnesses. All patients provided a full medical history and details about the current condition during the initial visit. The presence of tinnitus or vertigo was also noted. A comprehensive neurotological examination was included in the physical assessment.

Each patient presenting with sudden hearing loss underwent audiological evaluation within 12 hours of the initial visit, with the majority being tested within 2 hours.

Following the diagnosis of idiopathic SSNHL, the treatment protocol was initiated. Most patients began treatment within 6 hours of the first visit. The treatment regimen was the same for all patients and none had received prior treatment. All patients diagnosed with idiopathic SSNHL were prescribed a three-week course of steroids (see Table 1). In addition, they received a one-week course of valacyclovir (500 mg three times daily) and a three-week course of famotidine (20 mg twice daily) to prevent gastrointestinal complications.

Table 1.

Three-week steroid course with dose reduction.

DAYS	DEXAMETHASONE (MG)	DOSAGE SCHEDULE
0-14	4	4 times a day
15-16	1	3 times a day
17-18	0.5	3 times a day
19-20	0.5	2 times a day
21	0.5	1 time a day

Follow-up Visits Patients were scheduled for follow-up visits two weeks after the start of treatment, with an audiogram performed on the same day as the visit. Subjective changes in hearing were recorded during the second visit. The course of treatment and repeat audiograms were reviewed. All patients diagnosed with idiopathic SSNHL underwent magnetic resonance imaging (MRI) of the internal auditory canal to rule out retrocochlear damage within one month of diagnosis. After the second visit, patients were asked to return one month later for a follow-up audiogram.

Variables Analysis Variables that may influence recovery in SSNHL were analyzed. These included the patient's age, time since the onset of symptoms, dizziness, tinnitus, gender, lateralization, and audiogram type. Patients were divided into two groups: those under 40 years of age and those over 40 years. The time since the onset of symptoms was classified as within 3 days or later. A history of subjective movement occurring simultaneously with hearing loss was used to determine the presence of dizziness.

Audiograms were classified into 4 types of sensorineural hearing loss: ascending (13 patients, 25%), descending (27 patients, 53%), mid-frequency (4 patients, 8%), and profound hearing loss (7 patients, 14%). Descending audiograms showed a greater loss at 8 kHz compared to 4 kHz. Ascending audiograms showed the opposite. Mid-frequency loss was displayed as a "U-shaped" pattern on the audiogram. Finally, sensorineural hearing loss greater than 90 dB at all frequencies was considered profound hearing loss.

Follow-up Audiograms Follow-up audiograms were performed two weeks after the start of treatment in most cases. In four of the selected medical records, post-treatment audiograms were conducted more than six months after the treatment course ended. These cases were included in the study; however, analysis of the data without these patients did not show significant differences in outcomes. Due to the lack of pre-treatment audiograms before the onset of SSNHL, hearing in the unaffected ear was used as the normal comparison. A recovery was defined as the return of half of the difference between the affected and unaffected ears.

Results. Out of 51 patients, 30 (59%) were male and 21 (41%) were female. The right ear was affected in 20 (39%) patients, and the left ear in 31 (61%) patients. Gender and the side of the affected ear did not have a statistically significant impact on recovery ($P > 0.05$).

37 (73%) patients reported hearing recovery at follow-up, and repeat audiograms confirmed the improvement in results. No deterioration in hearing, tinnitus, or dizziness was reported after treatment. Additionally, no complications related to the treatment protocol were observed.

The average age of participants was 49 years, with a range from 19 to 81 years. A statistically significant ($P < 0.05$) increase in recovery levels was noted in the younger age group (Figure 1). All patients were evaluated and received treatment within 7 days of sudden sensorineural hearing loss onset. Each patient developed the maximum hearing loss within less than 8 hours. A statistically significant ($P < 0.05$) increase in recovery levels was observed in patients who received treatment within 3 days.

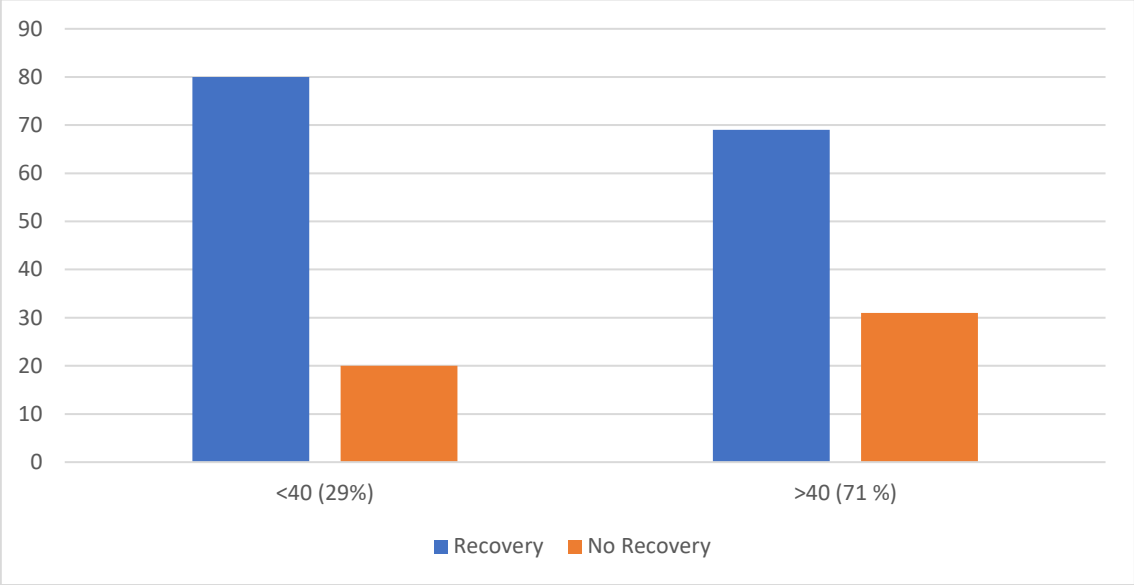

Fig. 1. Recovery and Age.

Dizziness and tinnitus did not have a statistically significant impact on recovery ($P > 0.05$) (Fig. 2). Treatment of patients with hearing loss in the mid frequencies, as well as those with descending and ascending audiogram types, resulted in a statistically significant level of recovery ($P < 0.05$) (Fig. 3).

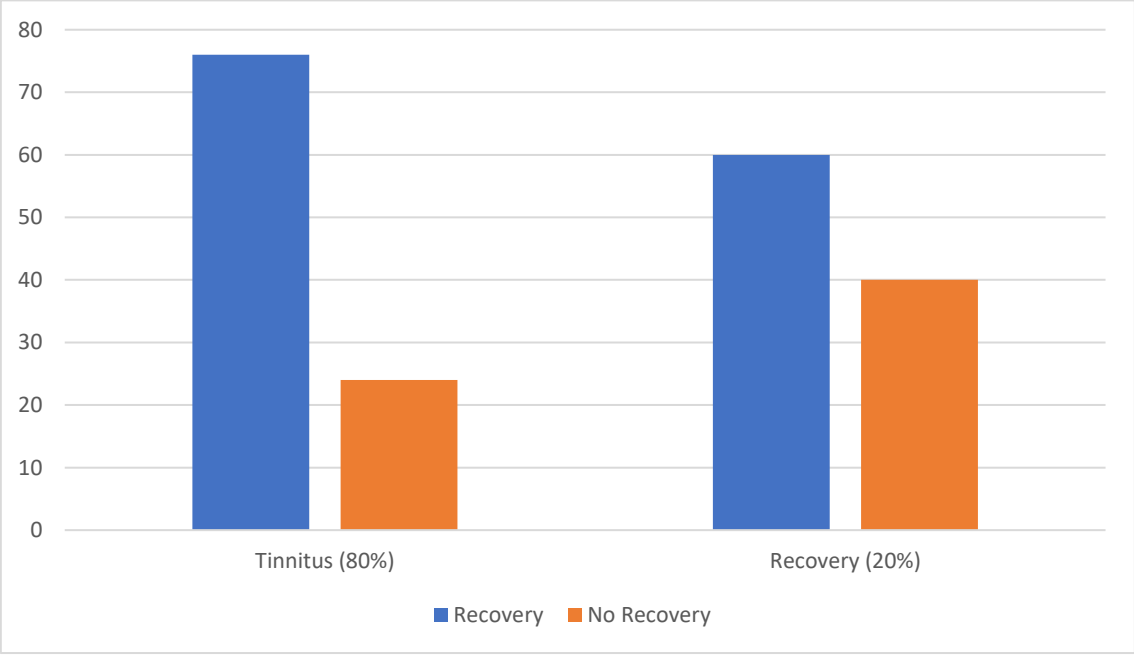

Fig. 2. Recovery and Tinnitus.

As mentioned earlier, the data were treated as dichotomous, non-parametric variables, with the exception of the age variable. A non-parametric analysis of repeated measures was conducted, resulting in a chi-square value of 194.23 (df = 6) ($P < 0.001$). Post-hoc Tukey's multiple comparisons test revealed that the outcome was significantly influenced by age, the time of onset of hearing loss, and the type of audiogram. However, the outcome was not influenced by gender, dizziness, tinnitus, or the side of the affected ear ($P > 0.05$).

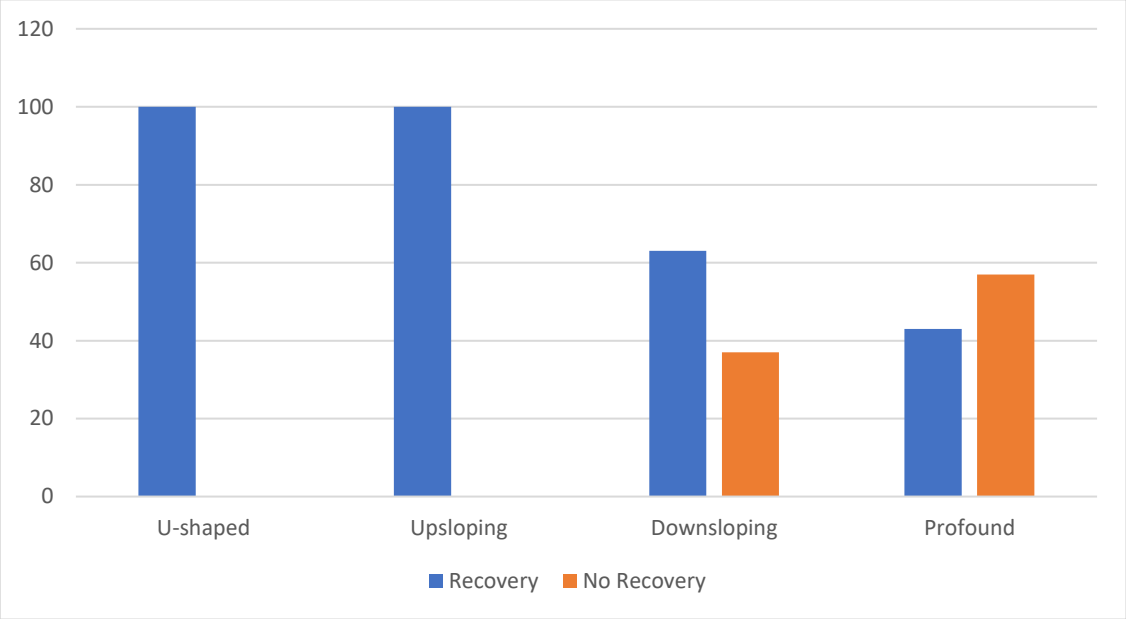

Fig. 3. Recovery and Audiogram Type.

Discussion. Research on idiopathic sudden sensorineural hearing loss (SSHL) has had limited success in establishing a standard definition and treatment protocols. This is primarily due to the rarity of the condition in otological practice, the lack of precise etiological classification, and the high rate of spontaneous hearing recovery. In this case series, we presented a group of patients who presented with complaints of sudden hearing loss and were diagnosed with idiopathic SSHL. We defined SSHL as a hearing loss of at least 30 dB across three adjacent frequencies within 3 days or less, according to the description by Wilson and colleagues. In our study, all patients experienced the maximum hearing loss within 8 hours.

Overall, our treatment protocol resulted in a recovery rate of 73%, which is higher than the rate of spontaneous recovery. We also showed that patients younger than 40 years old had a statistically significantly higher recovery rate ($P < 0.05$). Therefore, age is an important prognostic factor for recovery in our study.

The time from the onset of hearing loss to seeking medical help also proved to be a significant prognostic factor. In our study, all patients were examined within 7 days. Most other studies have shown that seeking help later than 7–10 days is associated with worse outcomes. It is suggested that this is related to the effect of self-selection—patients with rapid spontaneous remission do not seek medical attention. In our study, treatment started within 3 days of symptom onset resulted in significantly better outcomes.

The frequency of dizziness and tinnitus in our study was comparable to that reported by other authors. Contrary to previous reports, dizziness in our study was not a prognostic indicator of a poor outcome. The reasons for this remain unclear—possibly due to differences in patient selection criteria, patient population, or the specifics of the treatment protocol.

We achieved 100% hearing recovery in patients with mid-frequency hearing loss. In patients with profound hearing loss, no treatment benefit was observed—the recovery rate was similar to the spontaneous recovery rate.

Ascending audiograms were previously associated with a more favorable prognosis. All patients with ascending hearing loss in our study recovered after treatment. In our study, patients received a steroid course with gradual dose reduction over 3 weeks. It is possible that the longer steroid course explains the better outcome compared to placebo.

Furthermore, a recent randomized double-blind placebo-controlled multicenter study showed that antiviral medications did not provide additional benefits over steroids alone in the treatment of idiopathic SSHL. However, viral infections are believed to play a significant role in the etiology of SSHL. It is possible that certain viral strains, prevalent in our region, are more responsive to the proposed treatment, while results may differ in other regions. Additionally, that study was conducted in a multicenter setting with multiple doctors, which complicates ensuring the same level of care for all SSHL patients.

We obtained a better overall hearing recovery rate compared to spontaneous recovery. However, in our study, all patients with ascending and mid-frequency hearing loss recovered after treatment, and 91% of patients with dizziness also had a positive outcome.

The treatment protocol in our study included a three-week steroid course with gradual dose reduction only in the last week. It is possible that the longer course of therapy explains the differences in recovery outcomes in our patients. The improved results may also be linked to the use of antiviral therapy alongside steroids, as most of the studies we analyzed did not use antiviral medications. Given that drugs such as acyclovir have an extremely low risk of side effects, we recommend treating patients with idiopathic SSHL using a combination of steroid and antiviral therapy.

Conclusion. We presented a clinical case series involving 51 patients with idiopathic sudden sensorineural hearing loss (SSHL), who were treated with steroids and antiviral medications. It was demonstrated that age, the time between the onset of symptoms and the initiation of treatment, as well as the type of audiogram, were statistically significantly associated with treatment outcomes. Gender, the presence of dizziness, tinnitus, and the side of the affected ear did not have a statistically significant impact on the degree of hearing recovery.

Furthermore, we showed that, contrary to previous studies, our treatment protocol was effective in all patients with ascending and mid-frequency types of SSHL. Additionally, according to our data, the presence of dizziness is no longer a sign of poor prognosis.

Further prospective studies are needed to evaluate the effectiveness of each component of the treatment regimen, as well as the impact of changes in steroid dosage and duration of treatment. As knowledge about the etiology of SSHL accumulates, more targeted treatment methods may be applied, replacing the current empirical approaches.

Until then, we recommend treating patients with idiopathic SSHL using steroid and antiviral therapy, as our study showed improved outcomes with this regimen.

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DEXAMETHASONE INJECTION INTRATYMPANIC FOR REFRACTORY SUDDEN SENSORINEURAL HEARING LOSS

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Abstract. *The purpose of this case-control study was to examine the impact of intratympanic dexamethasone injection (ITDI) as a therapeutic alternative for individuals with SSNHL who did not respond to traditional oral steroid therapy. This study comprised sixty-six SSNHL patients who had not responded to an oral steroid treatment regimen. Pure-tone average (PTA) improvement was defined as more than 10 dB. Two (6.1%) of the 33 patients in the control group and 13 (39.4%) of the 33 patients who received ITDI showed improvements in their hearing. Eleven out of twenty patients who did not exhibit any improvement in PTA by ITDI demonstrated improvement over 10 dB in certain frequencies, whereas five out of thirteen patients represented hearing improvement above 20 dB in PTA. There were no definite prognostic factors between the patients who responded to ITDI and those who did not.*

Key words: *dexamethasone, sudden sensorineural HL, tympanum, injection.*

Introduction. Sudden sensorineural hearing loss (SSNHL), typically described as an acute, one-time decline in hearing accompanied by tinnitus and vertigo, occurs in 5-20 individuals per 100,000 population according to research. The etiology of SSNHL remains idiopathic, but potential causes include viral infections, vascular disorders, cochlear membrane rupture, immunological diseases, and otological tumors. Treatment for SSNHL includes steroids, vasodilators, antiviral agents, diuretics, and low-salt diets. The spontaneous recovery rate without treatment ranges from 30% to 60%, with most cases recovering within 2 weeks after onset. It is also known that this recovery rate increases with several treatment methods, including steroids. High-dose systemic steroid therapy is currently the primary treatment for SSNHL due to its strong anti-inflammatory effects, particularly in cases of moderate and severe hearing loss. Despite the use of oral steroids for 2 weeks, either alone or in combination with other medications, the prognosis for patients with refractory hearing loss remains poor. Around 30%-50% of patients show no response to treatment. For these patients, high-dose steroid therapy over a prolonged period may sometimes be applied, but it is not easily used due to side effects such as facial flushing, edema, rash, nasal bleeding, digestive disorders, liver dysfunction, and glucose intolerance. Additionally, no alternative treatments have been reported to date. Intratympanic steroid injection involves administering steroids through the tympanic membrane, which reduces the systemic toxicity of steroids and increases the steroid concentration in the cochlear perilymph. Pärns et al. reported a recovery rate of 53% in 13 patients with SSNHL, and there are other reports showing a 38%-72% success rate with intratympanic steroid injections. However, in most of these reports, intratympanic steroid injection was used as first-line therapy for SSNHL, not as second-line therapy for refractory SSNHL. The aim of this study is to evaluate the effectiveness of intratympanic steroid injections in patients with SSNHL who poorly responded to systemic steroid treatment.

Materials and methods. A controlled study was conducted from March 2021 to January 2025, including 66 patients with idiopathic SSNHL who did not show a successful response to combined treatment, including oral steroids. We collected data on the dexamethasone intratympanic injection (ITDI) group from August 2021 to January 2025. During this period, we treated 33 patients (34 ears) with ITDI. All patients underwent medical history, physical and audiological examination, serology for syphilis, autoimmune antibody tests, and magnetic resonance imaging. We excluded patients with

SSNHL potentially caused by trauma, syphilis, Meniere's disease, tumors, or autoimmune diseases. For all 66 participants, standard treatment was provided, including oral steroid administration for 10 days, rest, smoking cessation, a low-salt diet, and other medications. The oral steroid prednisone was used for 10 days according to the following scheme: 60 mg per day for 5 days, 40 mg per day for 2 days, 20 mg per day for 2 days, and 10 mg per day for 1 day. Intravenous antiviral agent acyclovir and hydrochlorothiazide were sometimes used in combination with the oral steroid. ITDI injections were performed 4 weeks after the initial conservative treatment. After confirming the integrity of the tympanic membrane, local anesthesia was applied using 10% lidocaine spray. The procedure was performed with the patient in a supine position under a microscope. A 25-gauge spinal needle and 1 mL syringe were used to make one puncture at the upper anterior part for ventilation and another puncture at the middle anterior part for perfusion. Dexamethasone was administered through this site in a volume of 0.3-0.4 mL. The patient was instructed to avoid swallowing or movement while lying with the head tilted at a 45˚ angle towards the healthy ear for 40 minutes. ITDI injections were performed twice a week for 2 consecutive weeks. Pure-tone audiometry was conducted immediately before each injection and 1 week after the last injection. Speech discrimination testing (SDT) was also performed 1 week after the last injection. In the control group, pure-tone audiometry was performed at 4 and 8 weeks after the initial conservative treatment, and speech discrimination testing was also performed at that time. However, some patients did not undergo SDT at 8 weeks, and they were excluded from this analysis.Hearing improvement was defined as a decrease in the average pure-tone audiometric threshold at 4 frequencies (0.5, 1, 2, and 3 kHz) by 10 dB or an increase in the speech discrimination score (SDS) by 15% or more. Additionally, the difference in thresholds at each frequency on pure-tone audiometry was analyzed. Side effects and subjective symptoms were also analyzed. Statistical analysis was performed using independent t-tests, paired t-tests, and chi-square tests. Statistical significance was determined at a confidence level of $P < 0.05$.

Results. The average age of patients in the ITDI group was 39.4 years, while in the control group, it was 42.8 years. The male-to-female ratio in the ITDI group was 13:20, and in the control group, it was 14:19. The average time from the onset of the disease to the start of treatment in the ITDI group was 5.2 days, and in the control group, it was 6.5 days. The baseline hearing level in the ITDI group was 72.0 ± 23.4 dB PTA, while in the control group, it was 76.5 ± 28.7 dB. There were no statistically significant differences between the two groups in terms of age ($P = 0.096$), sex ratio ($P = 0.977$), time from disease onset to treatment ($P = 0.831$), and baseline hearing level ($P = 0.221$) (Table I).

Table I.

Comparison of the Characteristics between the Group Receiving Intratympanic Dexamethasone Injection (ITDI) and the Control Group

Variable	Itdi group* (n = 33; 34 ears)	Control group (n = 33)	P value
Age (years)	39.3	42.8	.096
Sex (male: female)	13:20	14:19	.977
Duration from onset to initial treatment (days)	5.2	6.5	.831
Pure-tone average (db)	72.0 ± 23.4	76.5 ± 28.7	.221

** Patients who were treated with a course of ITDI therapy. χ^2 test and independent t-test.*

Objective Hearing Improvement. When comparing clinical outcomes between the two groups, improvement of 10 dB or more in PTA was observed in 13 (38.2%) of the 34 ears in the ITDI group, while no improvement was noted in the remaining 21 ears. In the control group, hearing improvement was recorded in only two ears (6.1%), while no changes in hearing thresholds were observed in 29 ears (87.8%), and two ears (6.1%) showed worsening.

In the ITDI group, the average PTA before and after ITDI treatment was 72.0 ± 23.4 dB and 62.9 ± 22.5 dB, respectively, resulting in an improvement of 9.1 dB in average PTA, which was statistically significant (P = 0.001). In the control group, the average PTA at 4 and 8 weeks after treatment was 76.5 ± 28.7 dB and 74.1 ± 25.7 dB, respectively, resulting in an improvement of 2.4 dB. This difference was not statistically significant.

In the ITDI group, five ears showed hearing improvement of more than 20 dB, eight ears showed improvement of 10-20 dB, and eleven ears showed improvement of more than 10 dB at certain frequencies without a significant change in PTA.

Table II shows hearing improvement in patients treated with ITDI, depending on their response to initial treatment, including oral steroids. No statistically significant differences (P = 0.127) were found between seven patients (43.8%) who showed a partial response and six patients (33.3%) who showed no response. Additionally, Table III shows hearing improvement in ITDI-treated patients based on PTA prior to ITDI treatment.

When analyzing hearing improvement by frequency in the ITDI group (34 ears), improvement of 10 dB or more was observed at low frequencies (0.25, 0.5, and 1 kHz) in 17 ears (50.0%), at mid frequencies (2, 3 kHz) in 12 ears (35.3%), and at high frequencies (4, 6, and 8 kHz) in 13 ears (38.2%). These results showed that hearing improvement most commonly occurred at low frequencies.

In the ITDI group, the number of patients showing improvement in hearing after each injection was as follows: 12 ears (35.3%) after the first injection, 5 ears (14.7%) after the second injection, 4 ears (11.8%) after the third injection, and 7 ears (20.6%) after the fourth injection. The average number of injections needed for hearing improvement was 2.2.

Subjective Hearing Improvement. Among 20 patients in the ITDI group who did not show hearing changes after ITDI, three patients experienced subjective hearing improvement, and 10 patients reported a reduction in tinnitus. Additionally, three patients reported that the sound became clearer. In the control group, only three of the 31 patients who showed no hearing improvement reported a reduction in tinnitus.

Factors Affecting Hearing Improvement in the Intratympanic Dexamethasone Injection Group. We analyzed several prognostic factors between 13 patients (positive response group) who experienced hearing improvement after ITDI and 20 patients (non-response group) who showed no improvement. The average age in the positive response group was 41.5 years, while in the non-response group, it was 37.7 years. The male-to-female ratio in the positive response group was 2:10 and in the non-response group, it was 10:11. The period from the onset of hearing loss to the start of initial treatment was 6.5 days in the positive response group and 4.7 days in the non-response group. The period from disease onset to the start of dexamethasone injections was 31.8 days in the positive response group and 35.1 days in the non-response group. No statistically significant differences were found.

Discussion. Sudden sensorineural hearing loss (SSNHL) is typically characterized by a rapid onset of hearing loss, usually within 3 days, with a hearing loss greater than 30 dB at three consecutive frequencies. The etiology of SSNHL remains undetermined in otolaryngology, although various causes have been proposed, such as vascular lesions, membrane ruptures, and viral infections. Therefore, treatment for SSNHL may aim to eliminate these etiological factors or create conditions in the middle ear that promote hearing restoration.

Table II.

Hearing Improvement in Patients Treated with Intratympanic Dexamethasone Injection (ITDI) According to the Response to Initial Treatment Including Oral Steroids

Initial response	>20 db hearing gain	10–20 db hearing gain	No gain
Partial response* (n = 16)	1 (6.3%)	6 (37.5%)	9 (56.3%)
No response (n = 18)	4 (22.2%)	2 (11.1%)	12 (66.7%)

** Patients who showed hearing improvement of 10 dB or more at initial treatment, including oral steroids, and were subsequently treated with a course of ITDI therapy.*

Steroid therapy has long been considered the primary treatment for SSNHL.

Table III.

Hearing Improvement in Patients Treated with Intratympanic Dexamethasone Injection (ITDI) According to Pure-Tone Averages Before ITDI

Pta range before itdi (db)	>20 db hearing gain	10–20 db hearing gain	No gain
26–40 (N = 2)	2	–	–
41–55 (N = 10)	2	1	7
56–70 (N = 3)	3	–	–
71–90 (N = 11)	1	6	4
91–110 (N = 8)	2	1	5

On the other hand, 10 patients showed hearing improvement of more than 10 dB at certain frequencies among the 20 patients whose average pure-tone threshold (PTA) values did not improve. These 20 patients reported changes in subjective symptoms, such as improved hearing, reduced tinnitus, or clearer sound perception. These subjective symptoms may be associated with hearing improvement at specific frequencies, despite the lack of improvement in overall PTA. In conclusion, the ITDI group demonstrated significantly greater hearing improvement (9.1 dB) compared to the control group (2.4 dB), as well as a greater improvement in subjective symptoms. This effect is most likely due to ITDI rather than the natural course of the disease.

Since steroids administered through the tympanic membrane penetrate the perilymph of the cochlea via the round window, the steroid may have a greater effect on the basal turn than the apical turn. Therefore, we expected hearing improvement to be more pronounced at high frequencies (basal turn) than at low frequencies (apical turn). However, in this study, 50% of hearing improvements (average 11.0 dB) occurred at low frequencies, whereas 34%–38% of improvements (average 5.2–7.5 dB) occurred at mid and high frequencies. These results suggest that ITDI may be more effective in patients with low-frequency hearing loss. It is hypothesized that once a certain concentration of steroid is achieved in the cochlea, hearing recovery may occur more easily at low frequencies than at high frequencies. This phenomenon may be explained by differences in the damage threshold or reversibility of hair cell recovery depending on their location. Some support for this hypothesis can be found in the fact that hearing loss caused by noise, ototoxic drugs, or trauma more frequently affects the high-frequency (basal) region of the cochlea than the apical region.

ITDI is a procedure performed under microscopic visualization with local anesthesia, requiring the patient to remain in a specific position for 40 minutes. It demands space and additional time for the procedure. Therefore, determining the optimal number of injections and the interval between them is essential, although such data have not yet been published. We also evaluated hearing changes by performing pure-tone audiometry immediately before each injection. In the ITDI group, the number of ears showing hearing improvement was as follows: 12 ears (35.3%) after the first injection, 5 ears

(14.7%) after the second injection, 4 ears (11.8%) after the third injection, and 7 ears (20.6%) after the fourth injection. Based on these results, we cannot definitively determine the optimal number of injections, but we believe that at least four may be required.

Known disadvantages of intratympanic steroid injections include temporary dizziness, tympanic membrane perforation, and otitis media caused by stimulation of the middle ear mucosa. In this study, only three patients experienced temporary dizziness, which appeared to result from the caloric effect of the medication and may be preventable by warming the dexamethasone solution.

Conclusion. ITDI may be a simple and effective treatment method for patients with SSNHL who do not respond to initial treatment, including systemic steroid therapy.

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WHAT ARE THE EFFECTS OF TITANIUM DIOXIDE AND ALUMINUM ON THE BRAIN?

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Abstract. *Synthetic food colorants are organic compounds that do not occur naturally, meaning they are artificially produced. Most of them have been used in the global food industry for decades. Many of these colorants form insoluble complexes (lakes) with metal ions and, in this form, serve as pigments for coloring powdered products, dragees, tablets, and chewing gum. Unlike natural food colorants, synthetic ones do not exhibit biological activity and do not contain flavoring compounds or vitamins. However, they offer significant technological advantages over natural colorants, as they are less sensitive to processing and storage conditions while providing bright, easily reproducible colors [7], [8], [9].*

Key words: *E 171, titanium dioxide, nanomaterials, E173, aluminum, natural brain barrier, cumulation.*

Inrtoduction. Like other fine-particle food additives, titanium dioxide is mainly found in food products. It is found in large quantities in carbonated drinks, various colored sweets, packaged salty and fatty crackers, potato chips, paper candies, pastries, dairy and cheese products, and sausage products.[1]

Titanium dioxide is actively used not only in the food industry, but also in the pharmaceutical industry, in the production of personal hygiene products, and cosmetics as a bleaching agent. Titanium dioxide is a water-insoluble substance with low toxicity. [2]

In the body, titanium accumulates in the form of proteins. Enterally administered titanium dioxide interacts with the aggressive environment of the stomach significantly affecting the properties of proteins and enzymes changes.

In a laboratory study, chronic (90 days) enteral administration of titanium dioxide to rats resulted in spleen damage, thrombocytopenia, lymphopenia, decreased hemoglobin levels, and decreased immunoglobulin levels. [4]

In another laboratory study, administration of titanium dioxide at a dose of 10 mg/kg resulted in severe liver damage, nephron apoptosis, and impaired immunoregulation.

When titanium dioxide was administered enterally at a dose of 100 mg/kg for 10 days, it was found that CD4 lymphocytes increased in all areas of the intestine, and the secretion of cytokines IL-4, IL-12, IL-23, and TNF increased mainly in the colon wall. [5]

Many studies have been devoted to the effects of titanium dioxide on the body, especially on the lungs, and the changes that occur in it. In this, solutions were sought to the questions related to the entry of small-sized titanium dioxide through the respiratory tract in the workplace and the development of pathological processes. Experiments conducted on rats with high doses of titanium dioxide for two years showed that tumors developed in the lungs of the rats, which indicated the carcinogenic properties of titanium dioxide. [6]

Fine-particle titanium dioxide, which enters the body through the intratracheal route, damages the cellular structure of alveolar macrophages and leads to impaired function. In addition, it reduces the chemotoxic properties of alveolar macrophages. Small amounts of titanium dioxide increase the phagocytic properties of macrophages, while large amounts reduce this property. With an increase in the amount of fine-particle titanium dioxide, the production of NO and TNF increased, since more

pro-inflammatory mediators were synthesized under the influence of fine-particle titanium dioxide than with conventional titanium dioxide. [7] Small amounts of titanium dioxide increased the sensitivity of the upper respiratory tract by twofold, and the number of cells responsible for inflammation increased by up to threefold. Histological examination revealed edema, epithelial destruction, and inflammation [8].

Free titanium dioxide causes denaturation of cytoplasmic proteins [9].

E 173 Aluminum is one of the most common elements on Earth, ranking third after oxygen and silicon. Aluminum compounds occur in nature in a variety of forms. Aluminum compounds are part of more than 280 minerals and are actively used in various fields of human activity. Despite the widespread use of aluminum compounds, their negative consequences remain one of the most important and necessary problems of modern medicine. In particular, its complications related to the brain are the cause of much discussion. There is still much debate about whether Alzheimer's disease, autism, Parkinson's disease, multiple sclerosis, and similar profound changes in the brain are caused by aluminum and its compounds. (11) Aluminum in drinking water, inhalation and food products despite entering in large quantities through mucous membranes in small quantities reabsorption occurs. luminum is not essential for the human body and metabolic processes (13). This element has a strong toxic effect on the body and the brain. The many ways in which aluminum enters the body and its widespread use further emphasize its toxic properties. [11,12,13].

This toxic effect is especially pronounced in Alzheimer's disease, autism, progressive sclerosis, and other brain dysfunctions. The attention of international scientific journals has been focused on aluminum and the above-mentioned neurological diseases. [12]

The main part of aluminum enters the body through water, food dyes and used in packaging, preparation, and storage of food products enters through the details. Unprocessed food products the amount of aluminum in its composition is less than 5-7 mg/g. Aluminum entering the body with water is 0.3%, and with food - 0.1%. The daily intake of aluminum is 15 mg / day [14].

E 171 and E 173 are used as food dyes and give the product a white color. The fact that these dyes can change the analeptic properties of the product is very useful for entrepreneurs. But there is another side to the matter. All food additives, including food dyes that give color, can cause various pathological reactions in the body. processes are developing[6].

This article aims to demonstrate the effects and accumulation of the bleaching dyes E 171 and E 173 (when taken in large quantities) on the brain. The active substances of these dyes are: titanium dioxide (171) and aluminum (E 173). The effects of titanium dioxide and aluminum substances on the nervous system, including the brain, have been proven in numerous experiments. For example, titanium dioxide powder was given to experimental rats for a long time and changes in the brain were observed. When the EEG of the rat brain was performed, it was observed that active epileptic foci appeared in the brain and the rats became very aggressive. [1], [2], [3]. Aluminum is believed to be one of the main causes of neurodegenerative diseases: Alzheimer's disease, Parkinson's disease, autism [4], [5].

The purpose of the study: To determine the accumulation of titanium and aluminum elements in the brain.

Material and methods of research. We will study the extent to which titanium and aluminum accumulate in the brain, and how this accumulation is related to changes in the brain. White, inbred rats selected (the number of rats 40) for the experiment will be divided into 4 groups:

1. Control group-10
2. Group that received E171-10
3. Group that received E173-10
4. The group that received E171 and E173-10

The above group of rats was given enteral titanium dioxide and aluminum in the form of powder.

The standard for determining the mass amounts of macro- and microelements in the researched samples is carried out in relation to samples with known amounts of elements.

Instrumental neutron activation analysis It was shown that for 90 days, laboratory white rats were fed with food dyes E171 (TiO ₂- titanium dioxide) and E173 (Al, aluminum) and the following results were obtained. The rats that received food dyes as an experiment were divided into 3 groups:

Group I E171 (titanium dioxide) was given 500 mg/kg orally per day for 90 days as an experiment. Our instrumental neutron activation analysis revealed that the test sample contained an average of 3.63 mg of titanium dioxide in the dry mass of the brain trace amount of titanium (Ti) was detected. In the brains of rats selected for control, this amount was 0.28 mg.

Group II was also given 500 mg/kg of food dye E173 (Al – aluminum) to laboratory white rats for 90 days as an experiment. In our instrumental neutron activation analysis, the test sample contained an average of 4.21 mg of aluminum in the dry mass of the brain. Element aluminum (Al) was detected in the amount of 0.53 mg/kg in the control group rats.

Group III E171 (titanium dioxide) 500 mg/kg and 500 mg/kg of E173 (Al – aluminum) food dyes orally for 90 days as an experiment. Our instrumental neutron activation analysis showed that the study sample contained an average of 3.7 μg / g of titanium (Ti) and 4.5 μg/g of titanium (Ti) in the dry mass of the brain traces of aluminum (Al) elements were detected.

Groups	Used substance	Average amount of substance in dry mass of brain after 90 days feeding	How much increased
E171 intaked	TiO_2	3.63 mg	13 fold
E173 intaked	Al	4.21mg	8 fold
E171+E173 intaked	TiO_2+ Al	TiO_2-3.7mg Al-4.5 mg	13.2 fold 8.5fold

Group	TiO_2	Al
Control	0.27mg	0.56mg

Results and discussion. The result obtained in the above experimental groups, compared with the control group, revealed differences in titanium: an average of 3.63/0.27 μg/g, 13 times more, and aluminum: an average of 4.21/0.56 μg/g, 8 times more. In addition, in the group given aluminum and titanium at the same time, compared with the control group, it was found that: titanium increased by 3.7/0.27 μg/g, 13.2 times, and aluminum increased by 4.5/0.56 μg/g, 8.5 times.

Conclusion. Around the worldl it is known that the brain has a natural blood-brain barrier, and the peculiarity of this barrier is its selective permeability. Accordingly, various toxic substances, poisonous products and many types of drugs circulating in the blood cannot pass through this barrier. However, there are exceptions, and there are 3 types of entry mechanisms for substances that have the property of crossing the barrier: 1) slow diffusion 2) active transport mechanism 3) endocytosis. The ability of the two food dyes titanium dioxide and aluminum shown in the experiment to cross the brain barrier has been proven in many experiments. If aluminum crosses the barrier by binding to proteins through the active transport pathway, then the physical properties of titanium dioxide help it in this way. Small particles (nanoparticles) of size 5-100 nm can easily pass through the brain barrier and show the property of accumulation. However, the question of how titanium enters the brain is a matter of much debate among scientists. During the 90 days of possible entry, it is shown that the active substances in the enterally administered dyes (E 171 and E 173): aluminum and titanium, accumulate in the brain to a high degree, and changes in the brain may be associated with the degree of this accumulation.

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THE ROLE OF ULTRASOUND EXAMINATION IN THE DIAGNOSIS OF ATOPIC DERMATITIS IN CHILDREN

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Abstract. *Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by impaired skin barrier function, immune dysregulation, and vascular changes, posing significant diagnostic and monitoring challenges. Recent advancements in high-frequency ultrasound imaging, Doppler ultrasonography, and shear-wave elastography have positioned ultrasound as a promising non-invasive tool for assessing structural and functional skin changes in AD. This article reviews the diagnostic value of ultrasound in evaluating epidermal and dermal alterations, vascularization, and tissue elasticity in pediatric AD patients. By analyzing data from clinical studies, we highlight how ultrasound complements traditional diagnostic methods, such as the SCORAD index, and supports personalized treatment strategies. The integration of ultrasound modalities enhances the understanding of AD pathogenesis and aids in monitoring disease progression and therapeutic efficacy.*

Key words: *Atopic dermatitis,SCORAD, Ultrasound examination,Doppler,SLEB.*

Introduction. Atopic dermatitis (AD) is a prevalent chronic inflammatory skin disease, particularly affecting children, with a significant impact on quality of life due to its association with other allergic conditions, such as bronchial asthma and allergic rhinitis [1]. The complexity of AD pathogenesis, involving immune dysregulation, skin barrier defects, and vascular changes, necessitates advanced diagnostic tools to assess disease severity and guide treatment [2]. While clinical scoring systems like SCORAD provide a standardized measure of disease severity, they rely on subjective evaluations of skin manifestations, which can introduce variability [1]. Non-invasive imaging techniques, such as dermoscopy and high-frequency ultrasound, have emerged as objective methods to visualize skin structures in vivo, offering quantitative data to support clinical assessments [5].

Ultrasound examination, utilizing high-frequency transducers (20–100 MHz), Doppler ultrasonography, and shear-wave elastography, enables detailed visualization of the epidermis, dermis, and subcutaneous tissues [2, 4]. These modalities provide insights into structural changes, inflammatory processes, and tissue elasticity, which are critical for understanding AD pathogenesis and evaluating treatment outcomes. This article synthesizes findings from recent studies to elucidate the diagnostic and monitoring potential of ultrasound in pediatric AD, with a focus on its ability to differentiate acute and chronic disease phases and guide therapeutic decisions.

Materials and Methods. The reviewed studies involved pediatric patients with AD, ranging from 0 to 18 years, diagnosed based on clinical criteria and the SCORAD index [1, 3]. Ultrasound examinations were conducted using high-frequency linear transducers (20–100 MHz) on devices such as Aplio 500 and SkinScanner DUB TPM, operating in B-mode, Doppler, and elastography modes [2, 3]. Key parameters measured included:

- Epidermal and dermal thickness (in micrometers, μm).
- Echogenicity (acoustic density, in arbitrary units, 0–255).
- Subepidermal low echogenic band (SLEB) thickness and echogenicity.
- Vascular density via Doppler ultrasonography.
- Tissue elasticity via shear-wave elastography.

Studies compared ultrasound findings in AD-affected skin with adjacent healthy skin, using a ratio coefficient (RC) to quantify differences [3]. Statistical analyses employed multivariate analysis of variance (MANOVA) and Student's t-test, with significance set at $p < 0.05$ [1, 3]. Data were collected from 128 AD patients and 40 healthy controls in one study [1], and 22 AD patients in another [3], alongside a cohort evaluated for innovative ultrasound techniques [2, 6].

Results.

Ultrasound Findings in Acute AD.

In acute AD, ultrasound revealed significant epidermal and dermal thickening, attributed to keratinocyte hyperplasia and edema [2]. The mean dermal thickness in active AD was increased by 20–40% compared to healthy controls [2]. Doppler ultrasonography demonstrated enhanced vascular density in affected areas, indicative of active inflammation and angiogenesis [2]. Shear-wave elastography showed reduced skin elasticity due to inflammatory edema, correlating with higher SCORAD scores [2]. The subepidermal low echogenic band (SLEB), a hallmark of inflammation, was consistently observed in affected areas, with thicknesses ranging from 89.3 to 125.87 μm and low echogenicity (2 arbitrary units) [3].

Ultrasound Findings in Chronic AD.

In chronic AD, ultrasound images displayed heterogeneous dermal structures with fibrotic zones and epidermal thinning due to prolonged inflammation and skin atrophy [2]. Doppler studies indicated reduced vascularization, reflecting diminished inflammatory activity [2]. Elastography revealed increased skin stiffness due to fibrotic remodeling, with reduced elasticity correlating with chronicity [2]. These findings distinguished chronic AD from acute phases, aiding in tailored treatment approaches, such as barrier repair versus anti-inflammatory therapies [2].

Therapeutic Monitoring.

Ultrasound proved valuable in assessing treatment efficacy. In a study of 22 children treated with a combination of 0.1% methylprednisolone aceponate cream, 0.03% tacrolimus ointment, and emollients, ultrasound scans after 4 weeks showed reduced epidermal thickness, increased dermal echogenicity, and diminished SLEB thickness, aligning with clinical improvement (SCORAD reduction from 58.6 to 21.3 in severe cases) [3]. The ratio coefficient (RC) approached 1, indicating normalization of skin structure [3]. Persistent SLEB in severe cases suggested residual inflammation, guiding extended therapy [3].

Clinical Correlations.

Ultrasound parameters correlated with SCORAD scores, with thicker epidermis and dermis, lower echogenicity, and increased vascularity corresponding to higher disease severity [1, 2]. The presence of SLEB in 62–100% of scans (depending on severity) highlighted its role as a marker of inflammation [3]. Elastography data indicated progressive elasticity loss in patients with frequent exacerbations, signaling a risk of chronic tissue remodeling [2].

Discussion. Ultrasound examination offers a non-invasive, repeatable method to assess ADrelated skin changes in real-time, overcoming the subjectivity of clinical evaluations [1, 5]. High-frequency ultrasound (20–100 MHz) provides high-resolution imaging (16–72 μm), enabling differentiation of epidermal and dermal layers, as well as subcutaneous structures [4]. The ability to quantify thickness, echogenicity, and vascularity enhances diagnostic precision, particularly in distinguishing acute inflammation (edema-driven) from chronic remodeling (fibrosis-driven) [2].

The SLEB, observed in both affected and adjacent healthy skin, is a critical indicator of subclinical inflammation, potentially predicting exacerbation risks [3]. Doppler ultrasonography and elastography further refine the assessment by quantifying vascular changes and tissue stiffness, respectively, which are pivotal in tailoring therapies [2]. For instance, increased vascularity in acute AD supports the use of anti-inflammatory agents, while fibrotic changes in chronic AD necessitate barrier-enhancing treatments [2].

Compared to dermoscopy, which visualizes superficial epidermal and papillary dermal structures [1], ultrasound provides deeper tissue insights, making it complementary in AD diagnostics [5]. Its non-invasive nature, lack of radiation, and ability to monitor dynamic changes position ultrasound as a superior tool for longitudinal studies [4, 3]. However, limitations include operator dependency and the need for specialized high-frequency equipment, which may restrict accessibility [4, 6].

Conclusion. High-frequency ultrasound, Doppler ultrasonography, and shear-wave elastography are transformative tools in the diagnosis and management of atopic dermatitis in children. These modalities provide objective, quantitative data on skin structure, inflammation, and tissue elasticity, enhancing the understanding of AD pathogenesis and supporting personalized treatment strategies. By correlating ultrasound findings with clinical severity (SCORAD) and monitoring therapeutic responses, clinicians can optimize patient outcomes. Future research should focus on standardizing ultrasound protocols and integrating these findings with immunological and histological data to further refine AD management.

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WHEN ALGORITHMS MEET ANATOMY: UZBEKISTAN'S MEDICAL EDUCATION IN THE AGE OF TECHNOLOGY

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***Abstract**: In the context of rapid digital transformation, medical education in the Republic of Uzbekistan is experiencing significant qualitative shifts.This article examines the growing role of information technologies — including artificial intelligence — in shaping the professional training of future healthcare providers. Particular attention is paid to interdisciplinary approaches, the enhancement of analytical and diagnostic skills, and the integration of digital responsibility and medical ethics into the learning process.*

Using the example of the Tashkent Medical Academy, the article highlights how modern platforms and simulation technologies facilitate the development of competent, practice-ready specialists. The study aims to underscore the pedagogical significance of digital innovations in fostering both professional competence and a deep sense of humanism and ethical responsibility among medical students.

***Keywords:** pedagogy, medical education, technology, artificial intelligence, Uzbekistan, digitalization, simulation, distance learning, e-learning, telemedicine, medical training, virtual reality, blended learning, educational innovation, healthcare system, medical curriculum, clinical skills, interactive learning, digital transformation, future of education, AI in medicine, smart education, continuing medical education (CME), teacher development, academic reform, ICT in education.*

Digital transformation is encompassing all areas of life, and medicine is no exception. In recent years, Uzbekistan has demonstrated rapid progress in the digitalization of healthcare: electronic medical records are being implemented, telemedicine is being introduced, and unified medical databases are being created. These developments necessitate a reevaluation of the approach to training doctors—not only as specialists in biology and medicine but also as confident users of digital technologies. In this context, pedagogy plays a crucial role, as it must ensure high-quality, innovative, and ethically-oriented training for future medical professionals. To advance the development of artificial intelligence technologies in healthcare, the Republic of Uzbekistan adopted the Presidential Decree No. PP-4996 dated February 17, 2021, "On Measures to Create Conditions for the Accelerated Implementation of Artificial Intelligence Technologies."

Furthermore, the strategy outlined in the Presidential Decree No. UP-6079 dated October 5, 2020, "On the Approval of the Strategy ‘Digital Uzbekistan – 2030’ and Measures for Its Effective Implementation," includes the adoption of targeted programs for scientific research and innovative projects aimed at developing the country's digital economy.

A priority of these targeted programs is expected to be scientific research in areas such as the study and practical application of technologies like virtual and augmented reality, artificial intelligence, cryptography, machine learning, big data analysis, and cloud computing in various sectors of the economy.

Moreover, in light of the Presidential Decree of the Republic of Uzbekistan No. PP-4996 dated February 17, 2021, “On Measures to Create Conditions for the Accelerated Implementation of Artificial Intelligence Technologies,” the use of AI technologies in healthcare is reaching a new level. The decree highlights several key areas where AI technologies are planned to be developed and implemented as priorities in medicine and healthcare. These include early diagnosis of pneumonia based on the analysis of CT scan images and early detection of breast cancer using mammography

images. To support these initiatives, the creation of national big data repositories is planned. These datasets will be made publicly available, as the active development and implementation of AI technologies is impossible without such open-access data. The decree also includes provisions for supporting educational and research projects in the field of artificial intelligence, which is essential for progress in this area.

Technology has become an indispensable tool in modern medical education, providing access to interactive learning materials, simulations, online communications, and knowledge assessment systems.

Modern medical education in Uzbekistan is increasingly adopting digital solutions:

At the Tashkent Medical Academy, the Tashkent Pediatric Medical Institute, and the Samarkand Medical Academies, virtual simulators are already being implemented to model clinical situations.

The use of virtual and augmented reality (VR/AR) helps students study anatomy and physiology at a new level, with greater clarity and depth.

Distance learning platforms such as ZiyoNET, Moodle, and specialized modules provided by the Ministry of Health of Uzbekistan enable expanded access to knowledge, even in remote regions.

In Uzbekistan, the legal framework permits the use of blended learning in medical universities, allowing a significant portion of the educational program to be delivered remotely. The Law of the Republic of Uzbekistan “On Education” dated September 23, 2020, No. 2 ZRU-637, defines distance education as a form of learning that does not require separation from employment. This law also refers to “distance education technologies,” which may be used by educational institutions in experimental and innovative activities.The decision to develop distance education was supported by a resolution of the Cabinet of Ministers of the Republic of Uzbekistan titled “On the Program for the Development of the Service Sector for 2016–2020.”. “As a result of this program, several universities have implemented the Moodle distance learning system, which is used in combination with traditional education methods”.

The COVID-19 pandemic and related restrictive epidemiological measures created the need to implement distance technologies and e-learning in medical universities, whose faculty were primarily focused on in-person teaching methods, particularly bedside learning. The urgent shift to distance education within a short timeframe created a demand for ready-to-use digital educational resources in the medical field. Developing such resources is a labor-intensive process that requires instructors to be proficient in information technologies, the presence of a well-developed university website, and support from IT specialists.

During the COVID-19 pandemic and the period of self-isolation, the Moodle platform proved to be the most practical tool at the Tashkent Medical Academy. It effectively facilitated the organization of remote learning, ensured access to educational materials, and maintained interaction between instructors and students.

It is worth noting that Moodle has become a central component of the medical educational environment: instructors use it to upload materials, conduct tests, and discuss topics with student groups. Video lectures, clinical case simulators, and even elements of augmented reality are also widely used, allowing students to practice skills without any risk to patients. All of this makes education more flexible, convenient, and aligned with modern demands.

Digital technologies are the key to effective and accessible medical education.

Let us now briefly look at artificial intelligence as an active element in the system of training medical personnel.

AI systems are already being actively used in educational processes in various countries and are beginning to be introduced in Uzbekistan as well. These systems can analyze a student's progress, adapt content to individual needs, suggest additional tasks, and even assess knowledge. For instance, in a medical university, AI can help students better understand complex topics in anatomy through 3D visualization or simulate clinical cases to develop practical skills. Such technologies allow

instructors to focus on deeper engagement with students, while routine tasks are automated. However, it is important to remember that AI is a tool, not a replacement for the educator.

Application of AI in Diagnostics: At the Tashkent Oncology Center, AI algorithms are used to analyze medical images such as X-rays and MRIs for the early detection of oncological diseases. These systems assist doctors in identifying tumors at early stages, increasing diagnostic accuracy and reducing the number of errors. In the Uzbekistan Cardiology Center, AI technologies have been implemented to analyze ECGs and other cardiological tests, which helps in the rapid and accurate diagnosis of heart diseases such as arrhythmia and ischemic heart disease. This reduces waiting time for results and improves the quality of medical care.

Educational Potential of AI in the Republic of Uzbekistan:

In medical universities across Uzbekistan, discussions are underway about integrating AI into the educational process to create personalized learning programs for students. For example, AI systems can adapt learning materials based on a student's mastery of various medical subjects. The use of AI in simulators for future doctors allows for the modeling of clinical cases, enabling students to practice their skills in a safe, controlled environment.

AI-based scenarios allow students to analyze clinical cases and receive immediate feedback.

The use of chatbots and AI models in the learning process helps automate knowledge assessments, provide personalized recommendations, and engage in dialogue with learners.

Developing Uzbek-specific medical AI modules has become a promising objective for local universities and IT companies.

From a pedagogical standpoint, using AI helps students develop key analytical and diagnostic skills by providing a safe environment for making and learning from mistakes, which contributes to effective learning.

Interdisciplinary Training of Future Doctors in Uzbekistan:

Today's physician is a specialist who interacts with software, digital platforms, and electronic databases. In this regard:

Courses on digital literacy, medical informatics, and data analysis are gradually being integrated into the curricula of Uzbekistan's medical universities.

Collaboration with the IT industry is beginning: students are undertaking internships at companies involved in developing medical platforms.

Work is being carried out to incorporate digital ethics and legal foundations of data handling into academic courses.

At the Tashkent Medical Academy (TMA), interdisciplinary training of future doctors is implemented through the integration of theoretical knowledge with practical skills, promoting a comprehensive approach to education.

The academy actively utilizes modern educational technologies such as digital platforms for remote learning, enabling students to study various disciplines in a flexible format.

Moreover, TMA organizes international symposiums and conferences where students can exchange experiences with peers from other countries, broadening their professional horizons.

Thus, interdisciplinary training at the Tashkent Medical Academy aims to equip students with a wide range of knowledge and skills essential for a successful medical career.

A medical professional cannot be limited to a narrow field of knowledge, as the complexity of real-world situations requires a multidisciplinary approach. Therefore, interdisciplinary education plays a key role in preparing specialists who are ready to face modern challenges.

We would like to emphasize that all technologies and their applications in medical education offer new opportunities for teaching and learning. However, they also present an important challenge — fostering digital responsibility and medical ethics among future professionals. In the context of rapid technological advancement, it is crucial that students not only master new tools but also develop the skills to use digital resources responsibly and ethically in their practice. This includes understanding the confidentiality of medical information, respecting patients' rights, and being

accountable for using artificial intelligence and other technologies in decision-making processes.Thus, cultivating digital responsibility becomes an integral part of training modern medical specialists, ensuring a balance between innovation and ethical standards.

This approach highlights the importance not only of students' technical training but also of instilling ethical and responsible habits in using new technologies — a particularly vital concern in medicine, where patient trust and safety come first.

In the era of technology, it is especially important not to forget the core value of medicine — the human being. The pedagogical mission is to teach students the ethically grounded use of technology:

Awareness of the responsibility behind decisions made with the help of AI.

Ensuring patient data confidentiality and legal compliance when working with electronic medical records.

Building a culture of communication in digital environments — both with patients and colleagues.

Medical university faculty face the crucial task of shaping professional responsibility and humanistic values, which are essential components of the educational process.

Conclusion. Thus, technologies serve not just as auxiliary tools, but as integral instruments in training medical personnel. The key lies in learning to use them wisely and effectively while maintaining a balance between digital opportunities and the hands-on, practical experience that remains the foundation of medicine.

The digitalization of medical education in Uzbekistan opens up new possibilities but also requires a comprehensive approach — modernizing technical infrastructure, training educators in new teaching methods, and integrating technology into clinical practice. It is essential that digital tools do not replace real-life interactions between students and patients, but rather complement and enhance the process of preparing qualified specialists.

Uzbekistan is confidently moving forward on the path of healthcare digitalization, and the role of pedagogy in this process is more significant than ever. The integration of technology into medical education demands thoughtful methodological solutions, a new role for educators, and the nurturing of digitally literate and ethically grounded professionals. A computer in a white coat is already a reality — and pedagogy must prepare future doctors to interact with this reality effectively and responsibly.

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MOLECULAR IDENTIFICATION OF NEW LOCAL STRAINS OF BIFIDOBACTERIA AND LACTOBACILLI USING 16S RRNA

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Abstract. *In light of the growing interest in using probiotic microorganisms in medicine and the food industry, there is an increasing need to develop effective methods for their identification and characterization. This study presents the results of molecular genetic analysis of newly isolated local strains of bacteria from the genera Bifidobacterium and Lactobacillus, obtained from samples collected in Uzbekistan. For identification purposes, methods of amplification and sequencing of the 16S rRNA gene were used, along with species-specific primers when necessary. The obtained nucleotide sequences were compared with NCBI databases, allowing for precise determination of the taxonomic position of the studied isolates. The research revealed the presence of both widely distributed and unique strains with potential for further application in the development of probiotic preparations. The acquired data contribute to expanding knowledge about the biodiversity of probiotic microflora and highlight the significance of local microbiological resources.*

Key words: *Identification of strains, local strains, bifidobacteria, lactobacteria, 16S rRNA, molecular genetic identification, probiotics, gene amplification.*

Introduction. In recent decades, there has been growing interest in studying the human microbiota as a key factor influencing health and organism development. Special attention is given to the intestinal microbiota of newborns, as it is during this period that the primary colonization of the intestines by microorganisms occurs, forming the metabolic and immune foundation for the entire lifespan. Among the most important representatives of the early microflora are bacteria of the genera Bifidobacterium and Lactobacillus, which possess pronounced probiotic potential. Strains of *Bifidobacterium* and *Lactobacillus* promote the fermentation of oligosaccharides, the synthesis of organic acids and B vitamins, and exhibit antagonistic activity against pathogenic and opportunistic microorganisms. Their metabolites modulate the immune response, reduce inflammation, and stimulate the maturation of the immune system in infants. Given these properties, they are widely used in the production of probiotic preparations, particularly for young children [6;8;9;10].

Nevertheless, the effectiveness of probiotics may depend on strain-specific properties, as well as the geographical and ethnic background that shapes the microbiota. In this context, the isolation and identification of local probiotic bacterial strains adapted to the biological characteristics of a specific region's population is becoming increasingly relevant. Studying the microbiota of newborns is particularly important, as it is at this age that the primary interaction between the immune system and microbes occurs.

In recent years, molecular genetic methods based on the amplification and sequencing of the 16S rRNA gene have gained widespread use in microbiological research, including the identification of probiotic bacteria of the Bifidobacterium and Lactobacillus genera. This approach enables a high degree of accuracy and reproducibility in determining the taxonomic position of bacterial isolates [1;3;5]. Furthermore, the use of 16S rRNA analysis facilitates comparison of the obtained data with extensive databases such as EzBioCloud and NCBI, which significantly simplifies the interpretation of results. This highly specific method allows for determining the taxonomic affiliation of microorganisms even in cases where cultivation is difficult or morphological characteristics are similar between different species.

In the present study, molecular genetic identification of two local strains isolated from the feces of healthy newborns in the Tashkent region was conducted to assess their belonging to probiotically significant species of Bifidobacterium and Lactobacillus.

Purpose of the study. To conduct molecular genetic identification of newly isolated local *Bifidobacterium* and *Lactobacillus* strains obtained from the feces of healthy newborns using 16S rRNA gene sequence analysis.

Materials and research methods. For the amplification of the 16S rRNA gene, validated universal primers were used:

[Forward Primer (Bifidobacterium) /5'-TGAAGGGTGGGGATGACGT-3',
Reverse Primer (Bifidobacterium): /5'-ACGGGCGGTGTGTACAAAG-3',
Forward Primer (Lactobacillus) /5'-GGGTGGTAATGCCGGATG-3',
Reverse Primer (Lactobacillus): /5'-CCACCGTTACACCGGGAA-3'].

These primers are widely used in studies for the identification of *Bifidobacterium* and *Lactobacillus* species. The choice of primers was based on publications by Jin et al. [4] and Matsuki et al. [7], which demonstrated high specificity and sensitivity of the respective primer pairs in detecting and differentiating target bacterial taxa. The study involved two strains: one representative of the genus Bifidobacterium and the other of the genus Lactobacillus. The strains were isolated from the feces of healthy 5-day-old newborns hospitalized in the maternity ward of the Zangiata District Medical Association in the Tashkent region. Molecular genetic identification was carried out using 16S rRNA gene sequencing. The nucleotide sequences were amplified using universal primers, followed by sequencing and comparison with reference databases (NCBI BLAST) to determine their taxonomic affiliation.

Results and discussion. The obtained results demonstrate the effectiveness of 16S rRNA profiling for the identification of newly isolated *Bifidobacterium* and *Lactobacillus* strains. However, it should be noted that factors such as sample processing method, DNA extraction technique, and primer selection for PCR can influence the accuracy of the results. These observations are consistent with the findings of Fouhy et al. [2], who showed that even minor variations in the protocol can significantly alter the composition of the detected microbiota. This highlights the importance of standardizing methodological approaches in microbiological and metagenomic studies.

During the molecular genetic identification of isolates obtained from local samples, the following data were obtained (Table 1). All isolated strains showed a high degree of similarity to specific reference strains, confirming their identity and affiliation with particular bacterial species.

1. *Bifidobacterium bifidum* CNCM I-4319 – The isolate identified as *Bifidobacterium bifidum* showed 100% identity with the reference strain, confirming the accuracy of molecular identification for this species. B. bifidum is well known for its important role in maintaining gut microbiota health and fermenting complex carbohydrates.
2. *Bifidobacterium animalis subsp.lactis* DSM 10140 – This strain showed 99% identity with the reference strain *B.animalis subsp.lactis*. This subspecies is commonly used in the production of probiotic supplements due to its ability to improve gut microbiota and support the immune system.
3. *Limosilactobacillus fermentum* EFEL6800 – Identified as *Limosilactobacillus fermentum*, with 98% identity to the reference strain. *L.fermentum* is known for its probiotic properties, including the ability to suppress pathogenic microorganisms and help maintain gut flora balance.
4. *Lactobacillus helveticus* DS3_8 – The isolate identified as *Lactobacillus helveticus* showed 100% identity with the reference strain. This species is used in cheese and other dairy product manufacturing and exhibits antimicrobial activity as well as the ability to support gastrointestinal health.
5. *Lacticaseibacillus rhamnosus* 1.0320 – Identified as *Lacticaseibacillus rhamnosus*, with 99% identity to the reference strain. This species is a well-known probiotic used for the prevention and treatment of diarrheal diseases and for enhancing the immune system.

The results of molecular identification confirm the high accuracy of the methods used for determining bacterial species and subspecies. All isolated strains demonstrated a high level of identity with reference strains, supporting their classification within the stated species. Notably, species such as Bifidobacterium bifidum and Lactobacillus helveticus, which showed 100% identity, exhibit strong potential for use in probiotic formulations, as evidenced by their well-documented beneficial properties. For instance, B. bifidum plays a crucial role in maintaining intestinal balance and may be used for the prevention of dysbiosis and other gastrointestinal disorders.

The isolate Bifidobacterium animalis subsp. lactis also showed a high level of identity and is a well-studied probiotic frequently used in the production of functional food products. This strain holds significant potential for improving gut microbiota and enhancing immune protection. The identification results of Limosilactobacillus fermentum and Lacticaseibacillus rhamnosus highlight the considerable diversity of local strains, which may possess unique probiotic properties. L. fermentum, with its antibacterial activity, and L. rhamnosus, with its proven immunomodulatory effects, could be utilized in the prevention and treatment of disorders associated with gut microbiota imbalance.

Thus, all isolated strains represent substantial interest for further research and the development of probiotic products. The obtained data may serve as a foundation for the creation of novel biotherapeutic strategies and functional foods based on local bacterial strains.

Table 1

BLAST analysis results of isolated strains of Bifidobacteria and Lactobacilli

Isolate	Closest Reference Strain	Species Identified	Sequence Identity (%)
1	*Bifidobacterium bifidum* CNCM I-4319	*Bifidobacterium bifidum*	100%
2	*Bifidobacterium animalis* DSM 10140	*B. animalis* subsp. *lactis*	99%
3	*Limosilactobacillus fermentum* EFEL6800	*Limosilactobacillus fermentum*	98%
4	*Lactobacillus helveticus* DS3_8	*Lactobacillus helveticus*	100%
5	*Lacticaseibacillus rhamnosus* 1.0320	*Lacticaseibacillus rhamnosus*	99%

The isolation of such strains from the intestines of healthy infants indicates their potential safety and physiological compatibility, which is especially important when developing probiotics for newborns.

It is important to note that the isolated strains were obtained from the feces of newborns in a maternity ward who had not received antibiotic therapy and were in satisfactory clinical condition. This points to natural colonization of the gut by potentially beneficial microorganisms and emphasizes the physiological relevance of the identified bacteria. From a practical perspective, local strains isolated from members of the regional population may be more effective when used in microbiota-targeted interventions, as they are adapted to the specific dietary habits, environmental conditions, and immune status of the population. Moreover, the confirmed taxonomic identity with industrial reference strains broadens the potential for their further use as probiotic agents.

Conclusions:

1. Molecular genetic identification of two newly isolated local strains obtained from the feces of healthy newborns was performed using 16S rRNA gene analysis.

2. All isolates were identified as *Bifidobacterium animalis subsp.lactis* with a 99% identity level, *Bifidobacterium bifidum* with 100% identity level, *Lactobacillus helveticus* with 100% identity level, *Lacticaseibacillus rhamnosus* with 99% identity level, and the last as *Limosilactobacillus fermentum* with a 98% identity level.

3. The obtained results indicate the presence of naturally occurring probiotic strains in the intestines of newborns from the Tashkent region, showing high similarity to industrially applied cultures.

4. The identified strains may be considered promising candidates for the development of regionally adapted probiotic formulations.

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EVALUATION OF BRAIN TUMORS USING MAGNETIC RESONANCE IMAGING IN ADULT PATIENTS

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Abstract. *This descriptive and analytical study was carried out at the Republican Specialized Scientific-Practical Center of Neurosurgery between January 2023 and September 2023 to assess brain tumors using Magnetic Resonance Imaging (MRI). The study included a sample of 30 patients, both male and female, aged between 20 and 80 years, who were suspected of having brain tumors. The results indicated that the most affected age group was 40 to 60 years, accounting for 46.7% of cases, whereas the 60 to 80-year age group had the lowest prevalence at 16.7%. Female patients were more commonly affected than males, making up 53% of cases compared to 47% for males. Non-malignant tumors were the most prevalent, comprising 57% of cases. Among malignant tumors, 84.7% were classified as primary, while 15.3% were secondary. Meningioma was the most frequently observed tumor type on MRI, accounting for 43.3% of cases in both male and female patients.*

Keywords: *brain tumors, MRI, non-malignant tumors, meningioma.*

Introduction. A brain tumor is defined as a pathological proliferation of cells forming a mass within the intracranial compartment. These neoplasms can be categorized based on their biological behavior into benign (non-invasive, non-metastatic) and malignant (invasive, potentially metastatic) types. Brain tumors may arise de novo from neural or supporting tissues within the central nervous system, termed primary brain tumors, or they may represent secondary involvement due to hematogenous dissemination from extracranial primary malignancies, known as metastatic brain tumors. The growth rate of brain tumors varies significantly, and both the size and location of a tumor influence its impact on the nervous system, potentially leading to dysfunction in affected areas. Treatment options depend on several factors, including the tumor's type, location, and size [5].

Brain tumors represent a significant medical and societal challenge due to their complex nature and high morbidity. Malignant brain neoplasms, in particular, are associated with unfavorable clinical outcomes, exhibiting a five-year survival rate of approximately 35%. According to global cancer statistics, in 2020, there were an estimated 308,102 newly diagnosed cases of primary brain and central nervous system (CNS) tumors, resulting in 251,329 cancer-related deaths, underscoring their substantial global mortality burden [7].

The 2021 World Health Organization (WHO) Classification of CNS Tumors introduced significant changes in the diagnostic approach to brain tumors. This classification now integrates both histological and genetic factors, providing deeper insights into tumor prognosis and treatment strategies. However, these advancements also present challenges in diagnosing specific tumor subtypes [6,4].

Brain tumors are diagnosed using imaging techniques such as positron emission tomography (PET), computed tomography (CT), and magnetic resonance imaging (MRI), with MRI offering distinct advantages over other modalities. MRI provides detailed anatomical information, helping to determine the location, size, shape, and type of a tumor. However, manual interpretation by radiologists can be subjective, time-consuming, and prone to errors. Therefore, automated tumor

detection methods using machine learning and advanced image processing are being explored to enhance early diagnosis [2].

Timely detection of brain tumors is essential for enhancing therapeutic efficacy and improving patient prognosis. A variety of imaging modalities—including positron emission tomography (PET), single-photon emission computed tomography (SPECT), computed tomography (CT), magnetic resonance imaging (MRI), and magnetic resonance spectroscopy (MRS)—offer critical diagnostic information. Among these techniques, MRI is regarded as the gold standard owing to its exceptional soft tissue contrast and broad clinical accessibility. Utilizing radiofrequency pulses in conjunction with a strong magnetic field, MRI enables high-resolution visualization of intracranial structures, making it particularly effective for detecting and characterizing brain abnormalities [8].

From a general perspective, T2-weighted (T2w) and FLAIR MRI sequences are essential for detecting brain lesions of various origins. In brain tumor assessment, these sequences help identify tumors and provide insight into their characteristics. T2w signal intensity reflects tissue density and cellularity, with highly cellular tumors often appearing hypointense. However, a hyperintense signal on T2w/FLAIR does not always indicate a tumor, as it may also represent peritumoral edema or infiltrative tumor tissue, particularly in gliomas [1].

Diffusion-weighted imaging (DWI) is an advanced MRI technique that quantifies the random thermal (Brownian) motion of water molecules within biological tissues. In isotropic diffusion, water molecules exhibit unrestricted movement in all directions, whereas anisotropic diffusion indicates directional restriction, often due to structural barriers such as cell membranes or fiber tracts. DWI allows for the derivation of the apparent diffusion coefficient (ADC), a quantitative parameter reflecting the degree of water diffusion. Since ADC values are closely associated with tissue cellularity and integrity, DWI offers critical insights into tumor microstructure in vivo. As a result, DWI has become an indispensable tool in oncologic neuroimaging, aiding in tumor detection, characterization, and treatment response assessment [3].

Materials and methods of research. This study was conducted at the Republican Specialized Scientific-Practical Center of Neurosurgery from January 2023 to September 2023. It included 30 patients (both male and female), aged between 20 and 80 years, who were suspected of having brain tumors and underwent MRI scans in the radiology department. Patients were selected through a convenient sampling method.

MRI scans can detect tumors in any lobe of the brain, allowing for an initial assessment of whether a tumor is benign or malignant. To enhance tumor visualization, Gadolinium contrast media is administered intravenously, with the dosage adjusted according to the patient's weight. For a definitive diagnosis and to differentiate between benign and malignant tumors, biopsy procedures may be performed.

Results and discussion. All collected data analyzed and tabulated in tables and graphs as follows:

Table 1

Frequency distribution of the patients by gender and age

Patients' distribution		Count	%
Gender	Female	16	53,3%
	Male	14	46,7%
Age	20 to 40 years old	11	36,7%
	40 to 60 years old	14	46,7%
	60 to 80 years old	5	16,7%

In table 1, showed that 53,3% of patients were females, with only 46,7% for males. However, some specific types of brain tumors, such as meningioma, are more common in women. Most patients had 40 to 60 years with 46.7%, then 36,7% for those who have 20 to 40 years old, and 16.7% from patients had 60 to 80 years old. Compared with other studies indicated that the number has been increased during the last past decayed and most of them are between age 50 to 70.

Table 2

Frequency distribution of the tumors by histological type

Nature of the tumor	Type of the tumor	Count	%
Benign	Meningioma	13	43,3%
	Pituatry adenoma	4	13,3%
Malignant	Anaplastic astrocytoma	8	26,6%
	Glioblastoma	3	10%
	Metastasis	2	6,6%

Table 2 displays the frequency distribution of brain tumors according to their histopathological classification, distinguishing between benign and malignant types. Among the benign tumors, **meningiomas** are the most common, accounting for **43.3% (n=13)** of cases, followed by **pituitary adenomas** at **13.3% (n=4)**. On the malignant side, **anaplastic astrocytomas** represent the highest proportion, comprising **26.6% (n=8)** of cases, while **glioblastomas** account for **10% (n=3)**. Additionally, **metastatic tumors** contribute to **6.6% (n=2)** of the total cases. This distribution highlights the predominance of benign tumors in the studied cohort, with meningiomas being the most frequently observed histological type.

Fig. no 1: A bar graph displays the frequency of malignancy type

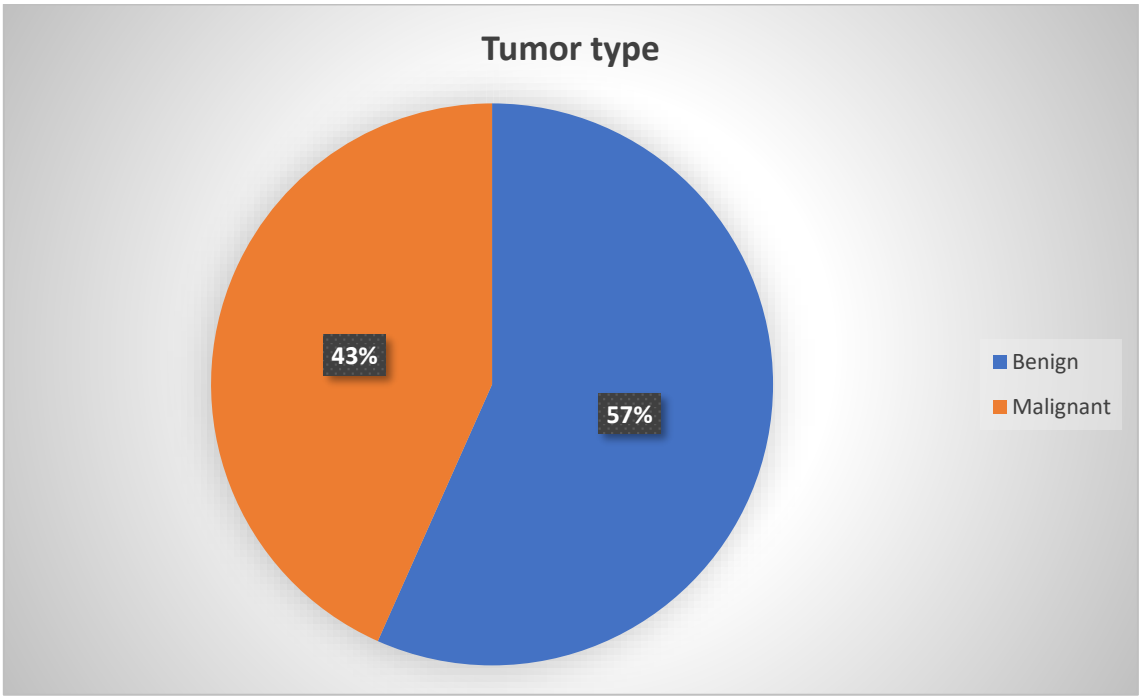

Fig. 1. Illustrates a bar graph depicting the frequency distribution of malignant tumor types. The graph visually emphasizes the variation in occurrence of tumors.

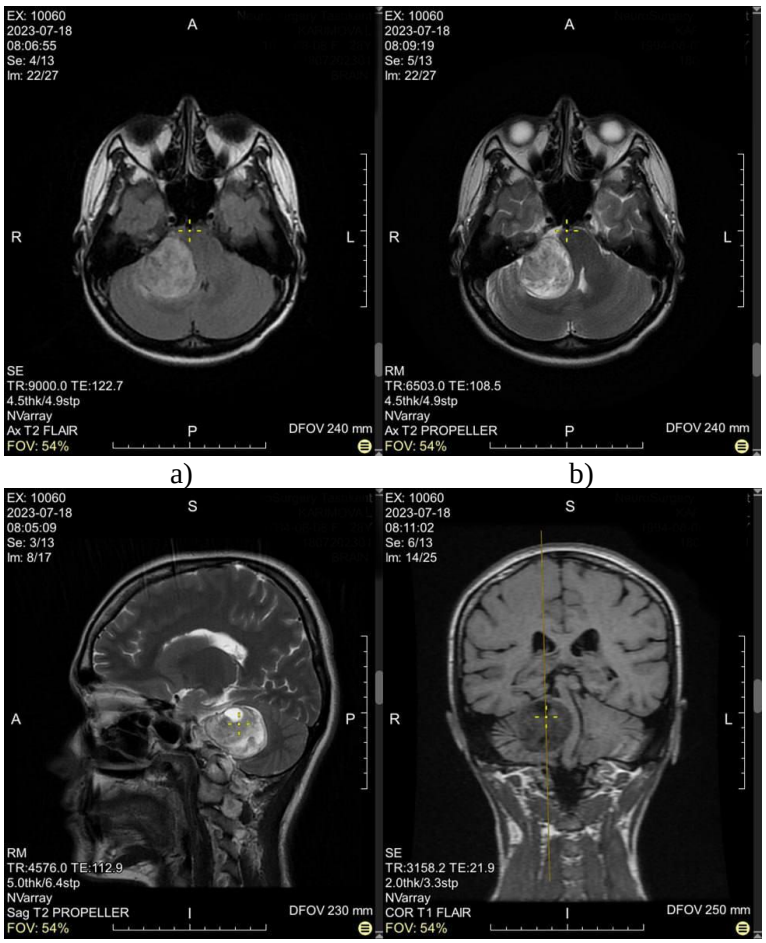

Fig. 2. Illustrating MRI images of an extracerebral mass in the posterior cranial fossa meningioma in a 40-year-old patient:
a) T2-FLAIR image Axial; b) T2-weighted image Axial; c) T2-weighted image Saggital
d) T2-FLAIR image Coronal

In the projection of the right cerebellopontine angle, extending caudally to the level of the foramen magnum, an irregularly shaped mass is visualized, measuring 39.5 × 35 × 38 mm, with well-defined but uneven contours, a heterogeneous solid structure, mixed signal characteristics on T2 and FLAIR, hypointense on T1, causing compression of the brainstem and adjacent parts of the right cerebellar hemisphere.

Meningiomas are the most common **primary intracranial tumors**, arising from the **arachnoid mater**. MRI is the preferred imaging modality for their **detection, characterization, and differentiation** from other brain tumors.

Key MRI Features of Meningiomas:

T1-Weighted Imaging (T1WI): Typically, **isointense or slightly hypointense** compared to gray matter.

T2-Weighted Imaging (T2WI): Often **isointense to hyperintense**; may show cystic changes or peritumoral edema.

FLAIR (Fluid-Attenuated Inversion Recovery): Highlights peritumoral edema if present.

Contrast-Enhanced T1WI (with Gadolinium): **Strong, homogeneous enhancement** (hallmark feature). **Dural tail sign** – tapering enhancement along the dura, indicating meningeal involvement.

Diffusion-Weighted Imaging (DWI) & Apparent Diffusion Coefficient (ADC): **Low diffusion restriction**, distinguishing it from more aggressive tumors.

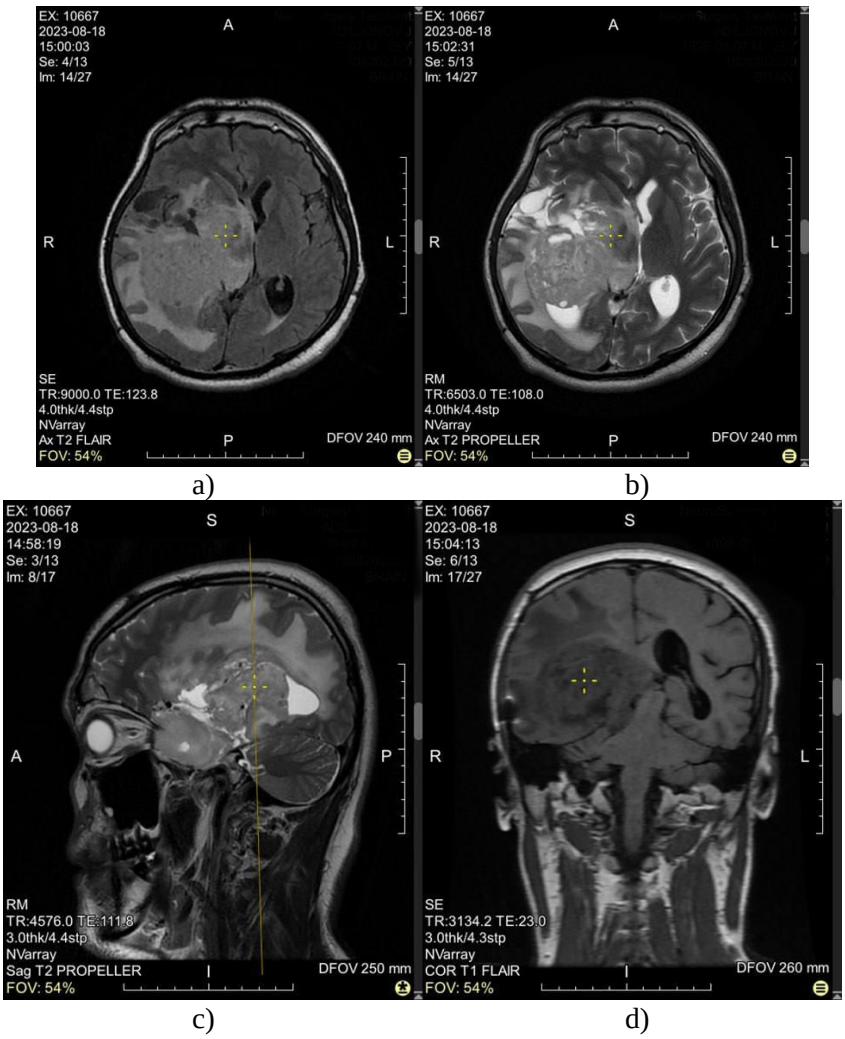

Fig. 3. Illustrating MRI images of a right temporal lobe anaplastic astrocytoma in a 56-year-old patient:
a) T2-FLAIR image Axial; b) T2-weighted image Axial; c) T2-weighted image Saggital
d) T2-FLAIR image Coronal

In the right frontoparietotemporal region, an irregularly shaped mass is visualized, measuring **87.1 × 84.3 × 77.6 mm**, with a heterogeneous cystic-solid structure. It extends into the **suprasellar and prepontine cisterns on the right**, as well as the **right cavernous sinus**, encasing the **M1 segment of the right internal carotid artery in a cuff-like manner**. The mass causes **compression of adjacent brain structures**. There is **marked peritumoral edema**.

Astrocytomas are a type of **glioma** arising from **astrocytes**, the star-shaped glial cells in the brain. MRI is the gold standard for diagnosing and classifying astrocytomas based on their **location, size, grade, and infiltration**.

Key MRI Features of Astrocytomas:

T1-Weighted Imaging (T1WI): **Low-grade astrocytomas** appear **hypointense or isointense** compared to gray matter.**High-grade astrocytomas (e.g., glioblastomas)** may have **necrotic** areas with heterogeneous signals.

T2-Weighted Imaging (T2WI) & FLAIR: Hyperintense lesions with poorly defined margins are commonly seen in low-grade astrocytomas. In higher-grade tumors, peritumoral edema is more prominent.

Contrast-Enhanced T1-Weighted Imaging (with Gadolinium): Low-grade astrocytomas typically exhibit minimal or no contrast enhancement. High-grade astrocytomas (Grade III–IV) often demonstrate irregular, ring-like enhancement due to necrosis and neovascularization.

Diffusion-Weighted Imaging (DWI) & Apparent Diffusion Coefficient (ADC): High-grade astrocytomas frequently show restricted diffusion, which is attributed to increased cellularity.

Conclusion. The primary aim of this study is to investigate the prevalence of brain tumors among both male and female populations and to evaluate the differential impact based on sex. Our analysis reveals a higher incidence of brain tumors in females compared to males. Furthermore, the age group most commonly affected falls between 40 and 60 years, a trend that aligns with our data. A key objective of this research is to assess the diagnostic value of Magnetic Resonance Imaging (MRI) in brain tumor evaluation. The results underscore the high diagnostic accuracy of MRI, highlighting its critical role in the detection, characterization, and comprehensive assessment of brain tumors.

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ANALYSIS OF INFLAMMATORY DISEASES OF THE UPPER RESPIRATORY TRACT AND ANTIBIOTIC DRUGS USED IN THEM

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Annotation. The purpose of the study*: to identify cases of infection with inflammation of the upper respiratory tract and their sensitivity to antibiotics of the population of the Republic of Uzbekistan for the period 2023-2024 in administrative regions (by cross section of Regions).* ***Materials and methods:*** *in the bacteriological Lobaratorium of the Tashkent Medical Academy of the Republic of Uzbekistan, infections detected in patients with nasal infections from the second half of 2023 to the beginning of 2024, as well as microorganisms detected in them, their sensitivity to antibiotics were analyzed. Bacteriological, statistical methods were used.* ***Results analysis and discussion.*** *During this 6-month period, 148 patients (30 men, 118 women) had complaints of inflammatory diseases in the nasal cavity. Samples from them were collected in 145 of the total patients when the laboratory was diagnosed with 160 different bacteria (Streptococcus ssp.-25%, Staphylacocus aureus-30%, Candida ssp.-20%, Proteus mirabilis -10%, Pseudomonas auriginosa-10% and Klebsiella ssp.-5%). Microorganisms were not detected in 3 patients.* ***Conclusion:*** *as a result of the analyzes, we can see more (80%) women with inflammation of the nose get sick (the average age was 30-35). The bacterium that causes the most inflammation is Staphylacococcus aureus (30%), as well as the bacteria from the most effective antibiotics: sulfamethoxazole, Levofloxocin, amoxicillin and ampicillin, gave a good result.*

Keywords: *inflammation of the upper respiratory tract, bacteria, antibiotics, microorganisms*

Relevance. Acute upper respiratory tract infections are a global health problem according to the World Health Organization (15). RS is an inflammation of the nasal and paranasal sinuses (2). Allergic rhinitis (AR) is a common disorder that afflicts 400 million people worldwide and it represents a global concern as its prevalence has increased over the years (8). Respiratory tract infections are defined as inflammation and damage to the upper respiratory tract caused by viruses and bacteria (6). Respiratory tract infections are a leading cause of morbidity and mortality worldwide (3). They can also be inhaled into the lungs during travel (13). The health consequences of these conditions are related to the activity of infectious agents, and the intensity of their occurrence is directly related to social (level of urban development and sanitary culture of the population) and natural and climatic conditions (15). They are caused by mucosal inflammation, which inhibits mucociliary function of the nose and paranasal sinuses (9). Several gram-positive and gram-negative bacteria are the main causative agents of upper respiratory tract infections, with Pseudomonas aeruginosa, Staphylococcus aureus, and Streptococcus pneumoniae species being the main causative agents (10). Resistance to antibiotics is currently a global threat to the establishment of a safe and effective treatment. If no action is taken, the estimated annual death toll of 700,000 is expected to rise to 10 million by 2050 (4). In the Republic of Uzbekistan, many efforts have been made to combat the disease, with some epidemics being eradicated. The diversity of infectious agents has led to the development of new drugs. The most important thing in doing so is to make the right diagnosis and provide the right treatment. Incorrect prescriptions remain a major problem, especially for primary health care providers and for the population as a whole (12).

Research objective: Incidence of upper respiratory tract infections and their sensitivity to antibiotics in the population of Tashkent city during 2023-2024.

Inspection material and methods: In the Bacteriological Laboratory of the Tashkent Medical Academy of Tashkent city, infections detected in patients with nasal infections from the second half

of 2023 to the beginning of 2024, as well as microorganisms identified in them, and their antibiotic sensitivity were analyzed. Samples of patients were cultured on Endo, Blood agar, Saburo, VSA, JSA, Muller Hilton nutrient media and we observed daily microbial colonies on agar media, and we evaluated the grown colonies according to their cultural, tinctorial, and morphological characteristics to determine the pure culture of bacteria. The isolated colonies were cultured on neutral agar and the disk diffusion method was used to determine antibiotic sensitivity. Bacteriological and statistical methods were also used. **Analysis and discussion of results.** During this 6-month period, 148 patients (30 men, 118 women) complained of inflammatory diseases of the nasal cavity. When samples taken from them were subjected to laboratory diagnosis, 160 different bacteria were detected in 145 of the patients (Streptococcus ssp.-25%, Staphylococcus aureus-30%, Proteus mirabilis-10%, Candida ssp.-20%, Pseudomonas auriginosa-10% and Klebsiella ssp.-5%). No microorganisms were detected in 3 patients. The following antibiotics were found to be highly sensitive to the above-identified bacteria: Streptococcus - amoxicillin, ampicillin, ceftriaxone, azithromycin, levofloxacin and clindamycin, Staphylococcus aureus - sulfamethoxazole, ampicillin, vancomycin, Candida ssp. - nystatin, amphotericin-b, fluconazole, Pseudomonas auriginosa - gentamicin, meropenem, cefepime, levofloxacin, Klebsiella ssp. - ceftriaxone, meropenem, gentamicin, sulfamethoxazole. The type and dose of these drugs are selected depending on the type of infectious agent and its amount in the body.

In this diagram, we have determined the level of infection by gender: in men and women.

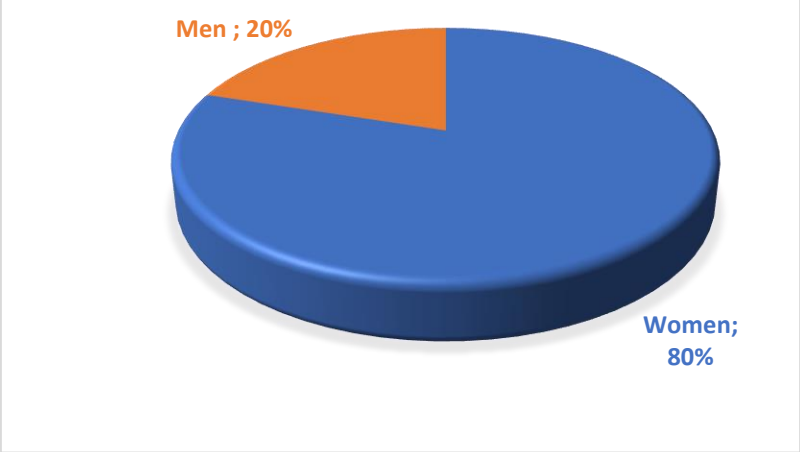

Fig 1. Distribution of patients by gender.

As you can see from the table, we can see that women are 4 times more likely to suffer from nasal infections than men.

Table 1.

Bacteria isolated from patients with throat infections, comparative analysis CFU/ml 1g (M±m)

Isolated microorganisms	KHQB/ml 1g
Staphylococcus aureus	4,11±0,3
Klebsiella spp.	4,5±0,3
Klebsiella pneumoniae	4,5±0,1
Escherichia coli	3±0,2
Pseudomonas aeruginosa	4,5±0,1
Streptokokk ssp.	4,25±0,2
Candida ssp.	4,44± 0,6
Proteus mirabilis	3,83±0,2

Note: **-; **- significant difference compared to group 1 (P<0.05, P<0.01).*

As a result of our investigation (Table 1), it was found that not only one bacteria, but also different bacteria, develop the disease in patients with nasal infections. We distributed the quantitative indicators of the bacteria according to the results of the analysis of each patient. We also calculated the percentage of their disease-causing bacteria in the patients and presented them in the form of a diagram (Fig 2).

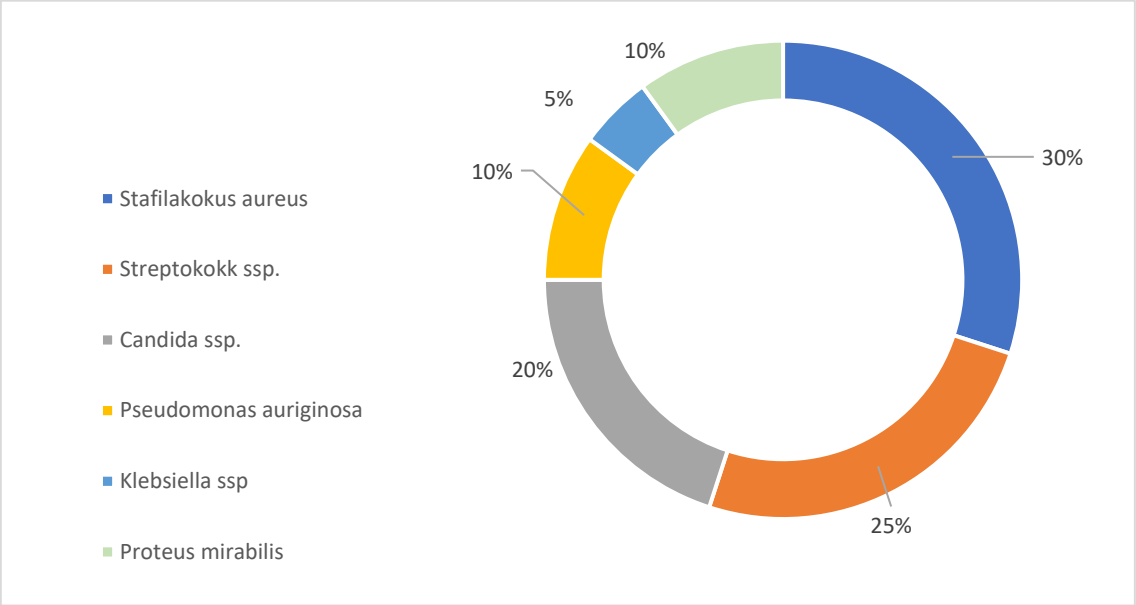

Fig 2. Percentage of bacteria causing disease

Our study also revealed that (diag.2), in patients (Streptococcus ssp.-25%, Staphylococcus aureus-30%, Candida ssp.-20%) caused 3 times more diseases than other bacteria. Also, cases of monoinfection and diinfection were observed among patients. We calculated the results of the conducted studies and presented these cases in the form of a diagram.

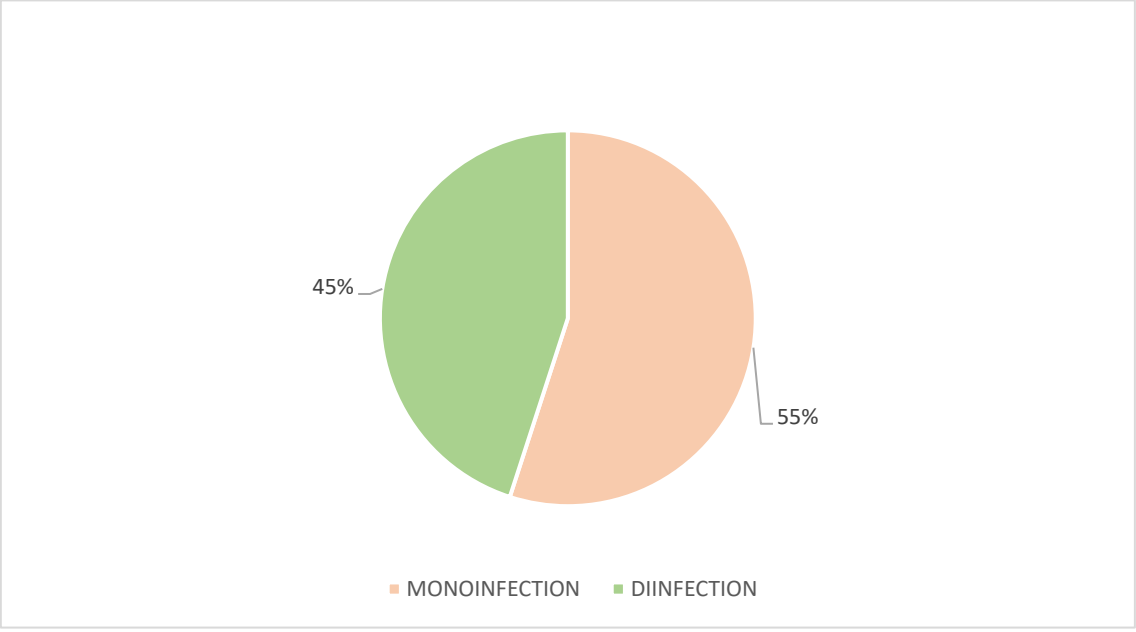

Fig 3. Occurrence of mono and di infections in patients.

This diagram shows that patients with dual infection are 1.22 times more likely to be infected than patients with mono infection. In the treatment of diseases caused by these bacteria, antibiotics sensitive to each bacterium were used, and patients were cured within 1-2 weeks, and in some cases up to 1 month.

During our research, we used and studied many foreign literatures, below we present the results of some of these articles for comparison:

The oral microbiota acts as the primary barrier against the invasion of respiratory viruses into the human body. Disruptions in the local airway microbiota caused by respiratory viral infections might initially occur in the oral cavity and subsequently affect distant microbial com munities at sites connected through the oral-lung or oral-gut axes. The dual interaction between the oral microbiome, inflammation, and the immune system during the disease suggests that changes in the oral microbiota could potentially serve as non-invasive biomarkers for ecological disturbances in the lung microbiome or the invasion of po tential pathogens into the lungs, thus giving early warning of disease severity. Microbiome ecological imbalances can facilitate the invasion of respiratory viruses and the inflammatory environment necessary for virus replication. Therefore, we believe that patients with oral micro biome imbalances might face significantly increased risks of disease complications and mortality during seasonal outbreaks of respiratory viruses and sporadic epidemics. Consequently, during periods of epidemic outbreaks, conducting oral microbiome testing for patients with compromised oral environments and promptly implementing oral microbiome interventions is of paramount importance to prevent the occurrence of uncontrolled inflammation or to mitigate its severity(15).

Baseline characteristics.

There were 280 patients diagnosed as URTI with fever for screening from March 2016 to December 2019. A total of 278 patients meeting the inclusion criteria were enrolled finally. The eligible patients were randomly assigned to the CQQNC group and the QKLC group. During this trial, 5 subjects in the CQQNC group and 4 subjects in the QKLC group dropped out. Finally, 134 subjects in the CQQNC group and 135 subjects in the QKLC group were analyzed summarizes the demographic and baseline characteristics. There were no significant differences in demographic characteristics and vital signs between the two groups, except for the diastolic blood pressure. Fig. 4. Flow diagram.

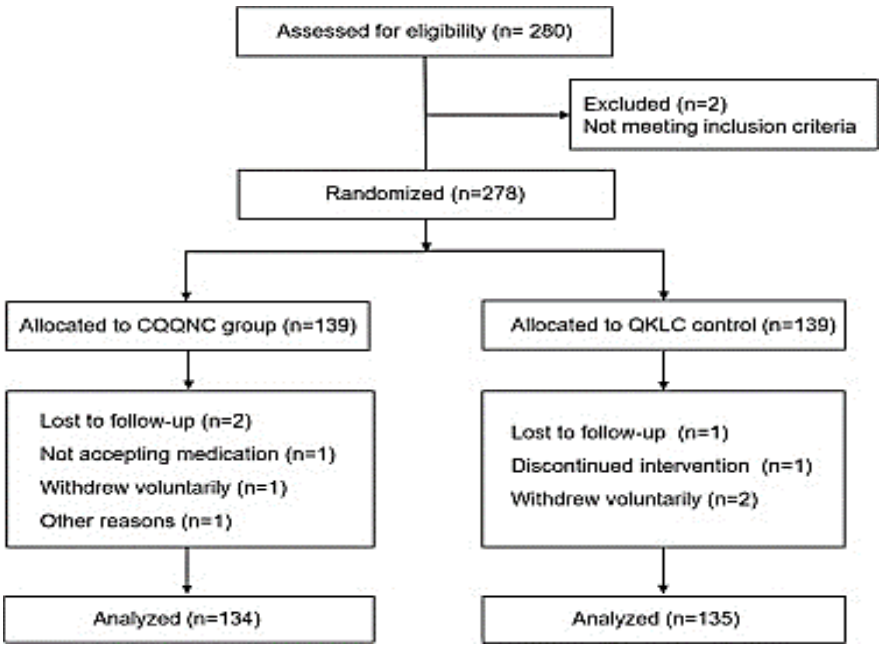

Fig. 4. Flow diagram.

Table 2.

Demographic and baseline characteristics.

Empty Cell	Total (N = 269)	QKLC group (N = 135)	CQQNC group (N = 134)	*P value*
Age, Mean ± Sd, y	43.14 ± 12.66	43.08 ± 12.76	43.19 ± 12.60	0.939
Sex, No.%				0.303
Male	108 (38.71)	50 (35.71)	58 (41.73)	
Female	171 (61.29)	90 (64.29)	81 (58.27)	
BMI, Mean ± Sd, kg/m^2	23.00 ± 2.71	23.01 ± 2.64	23.00 ± 2.78	0.993
Course, Mean ± Sd, h	17.39 ± 7.78	17.55 ± 7.92	17.23 ± 7.67	0.772
Vital signs				
Temperature, Mean ± Sd, ℃	38.37 ± 0.31	38.34 ± 0.32	38.41 ± 0.30	0.061
Respiratory rate, Mean ± Sd, bpm	19.28 ± 1.88	19.21 ± 1.90	19.34 ± 1.87	0.583
Heart rate, Mean ± Sd, bpm	80.76 ± 12.97	80.51 ± 13.06	81.01 ± 12.93	0.752
Systolic blood pressure, Mean ± Sd, mmHg	121.46 ± 9.89	122.48 ± 10.34	120.44 ± 9.33	0.085
Diastolic blood pressure, Mean ± Sd, mmHg	76.81 ± 7.93	77.79 ± 8.44	75.83 ± 7.28	0.038

Abbreviations: *BMI, body mass index; bpm, beats per minute; SD, standard deviation; CQQNC, Chaiqin Qingning Capsules; QKLC, Qingkailing Capsules (14).*

Primary outcome

The body temperature of patients in both treatment groups decreased after 3 days of medication. The median antipyretic onset time was 5 h (IQR: 5, 6) in the CQQNC group and 10 h (IQR: 10, 12) in the QKLC group. The between-group differences [0.19 (95%CI: 0.14–0.26); $P < 0.0001$] in the proportion of antipyretic onset during the observation period were given in. The median temperature recovery time was 19 h (IQR: 15, 20) in the CQQNC group and 27 h (IQR: 23, 28) in the QKLC group. illustrated the between-group difference in the proportion of temperature recovery [0.57 (95%CI: 0.45–0.7); $P < 0.0001$] (14).

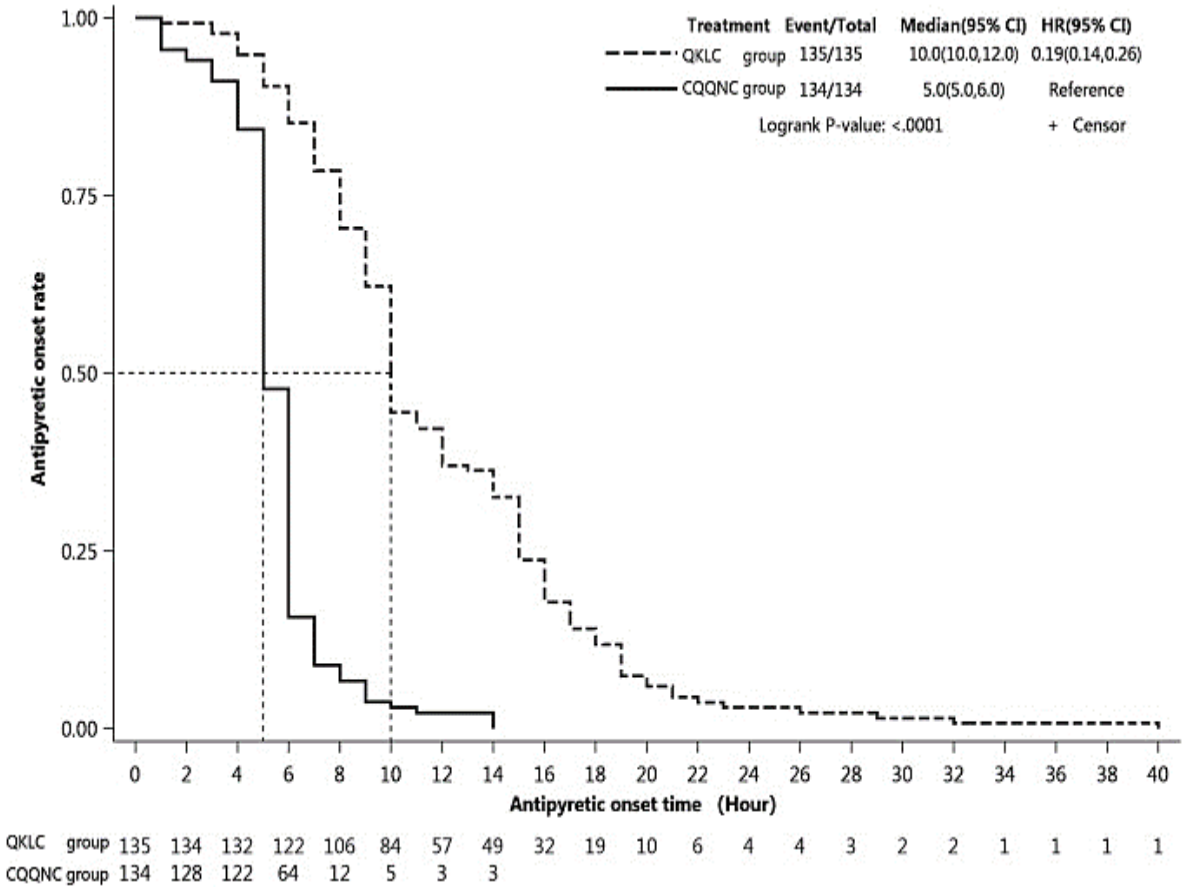

Fig. 5. Kaplan-Meier curves of antipyretic onset rate after medication.

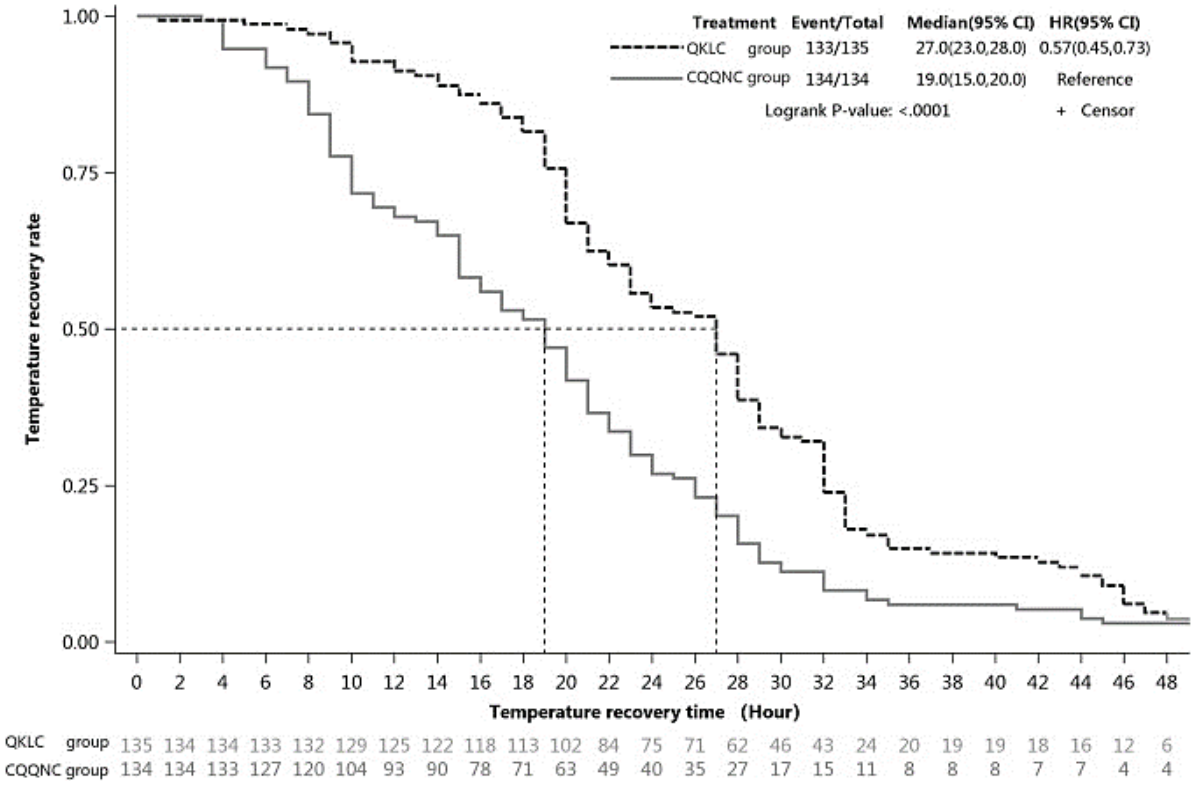

Fig. 6. Kaplan-Meier curves of temperature recovery rate after medication.

Local administration of antibiotics can combat pre-systemic meta bolism, alleviate systemic adverse effects, mitigate deactivation by metabolic enzymes, improve drug bioavailability, and enable the commencement of remedial activity. However, regarding antibiotics applied to manage bacterial CF, administering the medication directly to the lungs via the respiratory tract encounters various challenges as well. Along with complications revealed by cells, organelles, and bacterial biofilms, delivering drugs locally to the lungs needs to circumvent the biological obstacles posed by the unique configurations and actions of the respiratory tract [71,85]. The lungs possess robust natural defences and physical hurdles that create challenges for inhalable medications to effectively target their intended site of action. Even when inhaled medications successfully penetrate deep into the lungs, they are swiftly eliminated or rendered ineffective by body's defence mechanisms. As a result, achieving drug delivery to specific pulmonary targets is a com plex undertaking.

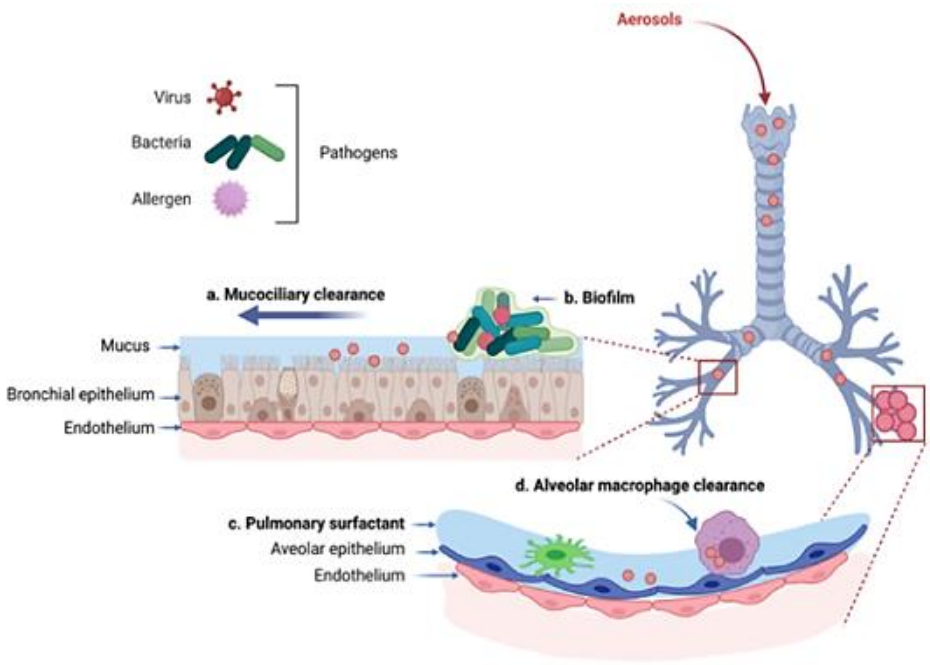

Fig. 7. Barriers in the pulmonary delivery of antibiotics. Reproduced with permission and without modification from Ref.

To achieve precise drug delivery to the lungs, there are three vital hurdles to overcome. The first barrier is anatomical in nature. The lungs comprise an intricate bronchial network with ciliary cells, responsible for pulmonary mucociliary clearance to eliminate particles that accu mulate in the airways. These activities represent a mechanical obstacle that hinders drug delivery to the lungs. The second hurdle entails the mucous layer. The respiratory mucus that lines the airways, from the nose to the smaller bronchial tubes, aids in capturing and expelling external substances, encompassing xenobiotic compounds like antibi otics. Moreover, this mucous barrier operates synergistically with anatomical obstacles, enhancing the efficacy of lung mechanical barriers through airway narrowing due to inflammation and excessive mucus production (13).

Nasal and oral microbiomes of infants with fewer early-life respiratory tract infections are enriched with *Prevotella* spp

We performed differential abundance analysis to examine niche-specific taxa across health states. At the genus level, we did not identify significant differences in abundance of nasal taxa between those with or without early-life LRTI or >4/y URIs, including *Dolosigranulum,* which has been implicated in respiratory health. Examination at the species level identified 6 nasal species and 7 oral species that were differentially abundant between those with or without a history of LRTI.

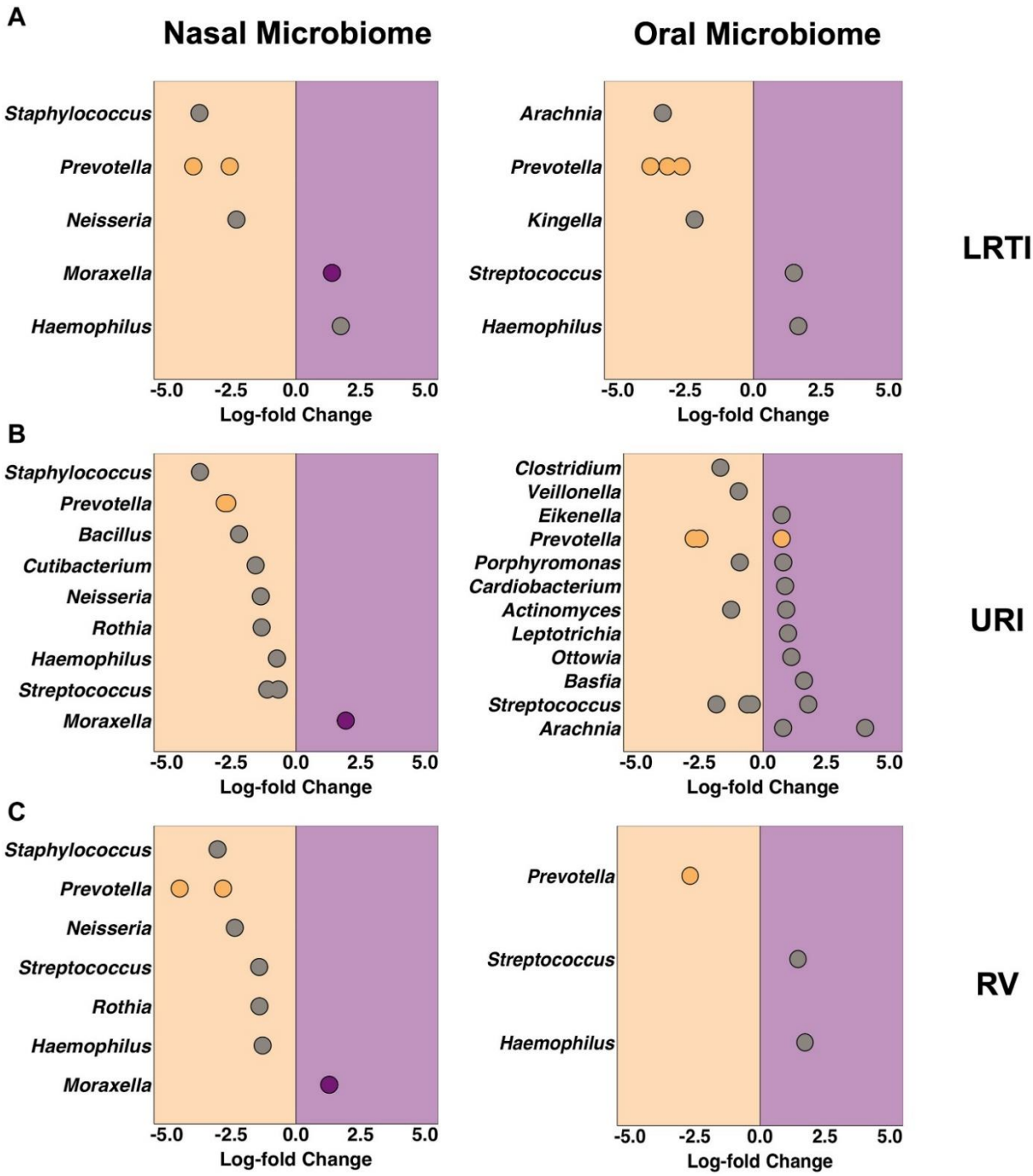

Fig 8. Nasal and oral microbiomes of infants with early-life respiratory tract infections are depleted of *Prevotella* spp. Differential abundance analyses via edge R of nasal *(left)* and oral *(right)* bacteria demonstrate lower abundance of several *Prevotella* spp *(yellow points)*, as well as higher nasal abundance of *M catarrhalis (purple points)* among participants with (A) ≥1 episode of LRTI, (B) >4/y URIs, and (C) >4/y symptomatic RV infections from birth to age 24 months *(purple shading)* relative to healthy participants *(yellow shading)*. Individual points represent species grouped by genus, with taxa of interest colored. Taxa with false discovery rate (FDR)-corrected *P* <.05 is shown (12).

A total of 2,858 records were identified through database searching and an additional 14 were identified through other sources. After duplicates were removed, 1,990 records remained. These records were screened and 1,926 were excluded. The remaining 64 full-text studies were assessed for eligibility with 35 records excluded for not reporting barriers (n=14), respiratory POCT (n=12),

primary care (n=3), other reasons (n=3), abstract-only (n=2) and a review (n=1). Of the 29 remaining studies, one was removed as it related to nursing homes only. The key barriers and facilitators were then identified from the 28 included studies (10).

After exclusion of 298,775 RTI episodes (24.8%) with codes of low specificity (i.e., not specific enough to differentiate between lower and upper RTI), a total of 905,964 lower or upper RTI episodes with at least one antibiotic prescription were identified. Almost half of all RTI episodes concerned adults consulting their GP for upper RTI (48.6%) and – in general – the main class of initial antibiotic prescription was an oral penicillin (66–90%). Among adults, individuals with lower RTI were older (median age 62 years) and more likely to have a history of comorbidities such as COPD, asthma and pneumonia, compared to those with upper RTI (median age 37 years). In children, 89.9% of episodes were related to upper RTI.

Within-episode antibiotic repeat prescription rates, stratified by age and RTI type, as well as rates per GP are illustrated in. The overall proportion of within-episode repeat prescriptions was 12.7% (95% CI 12.5–12.9%), but with considerable variability between individual GPs. Among adults, within-episode repeat rates were higher for lower RTI (19.9%, 95% CI 19.3–20.5%) than for upper RTI (10.5%, 95% CI 10.3–10.8%). In children, rates were similar for lower RTI (10.5%, 95% CI 9.4–11.5%) and upper RTI (10.0%, 95% CI 9.7–10.4%). Pre- and intra-pandemic within-episode prescription proportions did not change in most groups, except for upper RTIs in adults, which increased during the pandemic (4).

Meta-analysis: effect of vitamin D supplementation on immune markers.

We undertook a statistical pooling of estimates across 13 studies, to quantify the difference in the levels of various immunological markers (CRP, IL-6, IL-10, INF gamma) and vitamin D levels after vitamin D supplementation in the intervention group as compared to the control group, through a meta-analysis. At least three studies with common immune markers were subjected to meta-analysis.

Five studies (n = 788) were included to assess the difference in CRP levels after vitamin D supplementation. The standard mean difference of −0.25 with low heterogeneity among studies (I^2 = 0.0 %). There was a significant decrease in CRP levels after intervention with an overall effect of Z = 3.47 (P < 0.00) (fig.9).

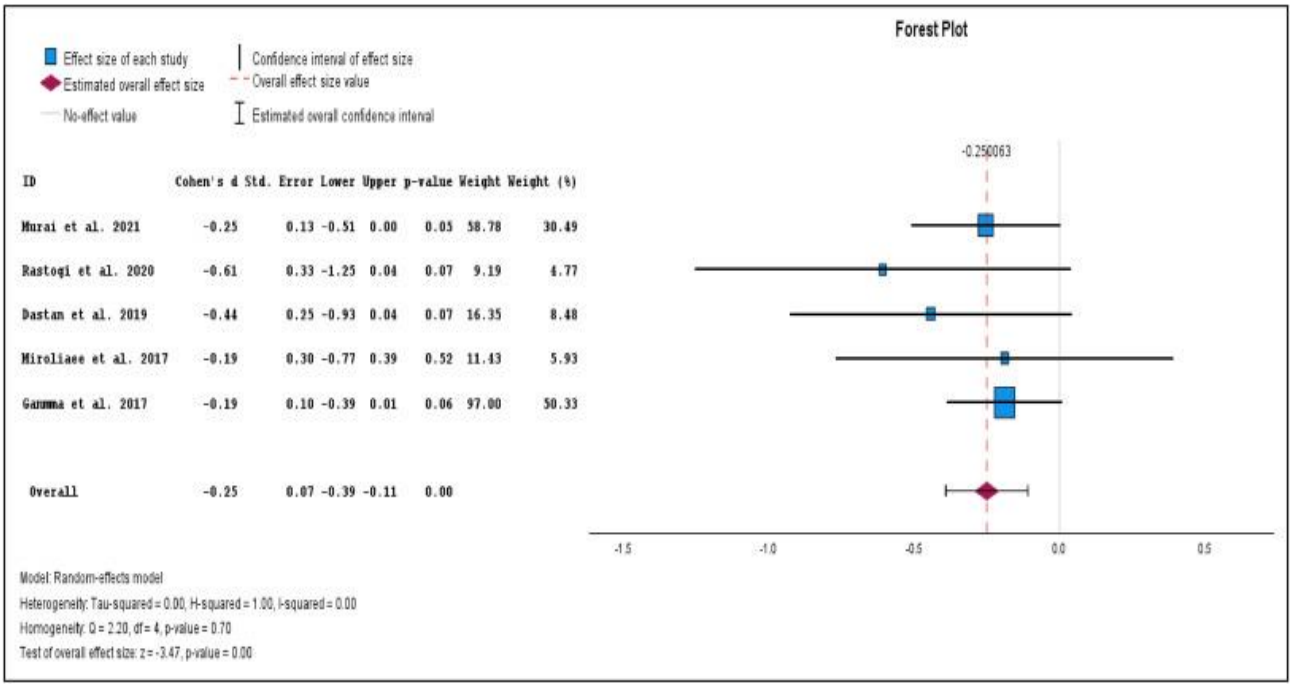

Fig. 9. Forest plot for the difference in CRP levels after the intervention (3).

Conclusion. The results of the analysis showed that nasal diseases are mainly manifested as an additional symptom in seasonal infectious diseases. In addition, in a smaller percentage, the infectious agent itself causes the disease independently. As a result of the analysis, we can see that women (80%) are more likely to suffer from nasal inflammation (average age 30-35). The most common cause of inflammation is Staphylococcus aureus (30%), and the most effective antibiotics for the bacteria: Sulfamethoxazole, Levofloxacin, Amoxicillin and Ampicillin gave good results. The use of correct treatment methods for patients with this infection helps to cure the disease faster.

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CHANGES IN THE CELLULAR COMPOSITION AND BIOCHEMICAL INDICATORS OF SYNOVIAL FLUID IN CHRONIC SYNOVITIS

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Abstract. *The article presents the results of a study of the cellular composition and physicochemical properties of synovial fluid (SF) in patients with acute and chronic synovitis of the knee joint. It was found that chronic synovitis is accompanied by more pronounced changes in cellularity and inflammatory markers in the SF compared to the acute process. An analysis of cytological parameters was performed, including the number of leukocytes, erythrocytes, the presence of polynuclear cells, rhagocytes, histiocytes, macrophages and crystals, using a modified formula for the inflammatory activity index. A direct relationship was found between the degree of turbidity of the SF, the number of leukocytes and the severity of degenerative changes in the joint. The data obtained confirm the diagnostic significance of a comprehensive analysis of the SF in assessing the severity of the inflammatory process and predicting the course of chronic synovitis of the knee joint.*

Keywords: *Chronic synovitis, synovial fluid cellularity, biochemical changes in synovial fluid.*

In 2020, there were approximately 654.1 million people worldwide aged 40 and older with knee osteoarthritis (Aiyong Cui, Huizi Li. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. EClinicalMedicine. 2930 (2020) 100587). By 2024, the burden of osteoarthritis continued to grow globally, affecting about 7.6% of the world's population, with projections indicating an increase of 60% to 100% by 2050 (Osteoarthritis year in review 2024: Epidemiology and therapy. Alice Courties, Inès Kouki, Nadine Soliman, Sylvain Mathieu, Jérémie Sellam. Osteoarthritis and Cartilage, Vol. 32, Issue 11, Nov 2024, pp. 1397–1404). Notably, osteoarthritis ranks seventh among leading causes of disability worldwide after age 70, primarily affecting the knee joints.

The overall annual incidence of soft tissue knee injuries was 718 per 100,000 people (672 per 100,000 in women and 766 per 100,000 in men) (Charlotte Bergknut, George Peat. Population incidence of soft tissue knee injury: estimates from a Swedish healthcare register. Abstract #916. American College of Rheumatology, 2012 Annual Meeting, November 9–14, 2012, Washington). The most common injuries diagnosed were knee contusions (31.3%), followed by ligament sprains (27.7%), damage to various knee structures (22.3%), meniscal tears (11.3%), collateral ligament injuries (10.7%), and cruciate ligament injuries (9.9%).

Among the various manifestations of chronic joint diseases, synovitis holds a leading position. The inflammatory process developing in the synovial membrane determines the key clinical features and drives disease progression. It represents the body's response to a pathogenic stimulus, manifested either as primary synovial inflammation in chronic arthritis or secondary synovitis in osteoarthritis. According to current understanding, a critical step in chronic arthritis development is the recognition of an unidentified pathogenic factor by an antigen-presenting cell.

Since the progression of joint pathology through arthritis and synovitis involves inflammation—and the nature of the disease depends on the ratio of specific cellular elements in the synovial fluid—we attempted to develop a method for objectively evaluating the course of the pathological process and predicting chronic synovitis.

Synovial fluid (SF) originates from three main sources:1. Blood transudate containing water, electrolytes, and proteins;2. Secretions from synovial lining cells—hyaluronic acid and proteolytic enzymes;3. Waste products from cell turnover and matrix components—mainly proteoglycans and glycoproteins—continuously entering the joint cavity during its normal functioning.

The primary functions of SF include: - Metabolic: exchange between the joint cavity and the bloodstream, and elimination of foreign and certain autoantigens; - Locomotor: production of biological joint “lubrication” to ensure smooth movement of joint surfaces; - Trophic: transportation of key energy substances to cartilage tissue.

SF reflects processes occurring in the cartilage and synovial membrane, responding sensitively to even minor disruptions with changes in physicochemical characteristics and cellular composition. Thus, laboratory analysis of SF is of fundamental importance in diagnosing joint diseases and chronic synovitis. It is especially important to emphasize that typical changes in SF often appear before clinical signs develop. Therefore, comprehensive laboratory analysis of SF—the synovial environment of the joint—is essential to understanding the nature of intra-articular changes. Cytosis is one of the most sensitive criteria in differential diagnosis. In addition to the total number of cellular elements, their qualitative composition is also significant for diagnosing joint pathology. While the cellular composition of SF is well studied under normal and autoimmune inflammatory conditions, research on acute and chronic synovitis is limited and inconsistent.

Objective: to investigate the cellular composition of synovial fluid in acute and chronic synovitis of the knee joint.

Materials and Methods

The study included 50 patients with knee synovitis admitted to the trauma department of the 2nd clinic of TMA. Of these, 24 (48%) had acute synovitis and 26 (52%) had chronic synovitis.

Among all patients, 28 (56%) were men and 22 (44%) were women. Patient ages ranged from 25 to 69 years. The average age in the acute group was 42.42±2.15 years, and in the chronic group, 49.46±2.60 years. Distribution by age and sex was conducted following WHO (2018) guidelines. Most were of young and middle age. In the acute group, there were 14 (58.3%) men (41.7% young and 16.7% middle-aged) and 10 (41.7%) women (middle-aged). In the chronic group, 14 (53.8%) were men (15.4% young, 23.1% middle-aged, and 15.4% elderly) and 12 (46.2%) women (7.7% young, 23.1% middle-aged, and 15.4% elderly). Acute synovitis was more common in middle-aged men, while chronic synovitis occurred in men of all age groups and in middle-aged and elderly women.

The study recorded the duration of chronic synovitis, previous joint trauma, and genetic predisposition to osteoarthritis. Diagnoses were established jointly with traumatologists based on clinical history, MRI, and arthroscopy, assessing intra-articular pathology. The Bauer-Jackson classification was used for cartilage condition; ISAKOS classification for meniscal damage.

Synovial fluid collected during arthroscopy was used as the material for research. Physicochemical properties and cellular composition were determined via microscopy. Both native and stained samples were examined. Native preparations provided an estimate of cell content, while stained samples allowed cell type differentiation. CRP levels were determined using a biochemical analyzer and LAHEM biotests. As synovial fluid cannot be collected from healthy individuals, literature data was used for comparison. Statistical analysis was conducted using Statistica software.

The conducted research revealed certain differences in the studied indicators depending on the course of synovitis. For instance, a change in the color of synovial fluid (SF) to red in cases of acute synovitis of the knee joint was observed in 50% of the subjects and was associated with mechanical trauma and the development of hemosynovitis. In contrast, during the chronic course, the SF was red in 30.8% of cases, milky in 7.7%, and straw-yellow in 61.5%. Furthermore, while in acute synovitis the SF was cloudy in 33.3% of cases, during the chronic course this figure increased to 46.2%. Normally, SF should be light yellow and transparent.

It should be noted that the observed changes in the physical properties of synovial fluid (SF) in cases of acute knee synovitis were mainly associated with mechanical trauma, which led to varying degrees of hemorrhage. In chronic synovitis of the knee joint, cloudiness of SF samples was more frequently observed, along with the presence of lipid droplets and a creamy consistency. This was likely related to the presence of knee osteoarthritis in most patients with chronic synovitis. In this group, arthroscopy more often revealed old meniscal injuries, patellofemoral osteoarthritis, increasing pain syndrome, and degenerative changes. Duplex scanning also revealed varicose veins of the lower limbs, inguinal lymphadenopathy, and secondary lymphedema of the lower limbs.

The creamy appearance of SF in two female patients was associated with disability despite their young age, as well as high cholesterol levels. Charcot-Leyden crystals and elevated cellularity were also found.

Cellularity of the synovial fluid plays an important role in evaluating the degree of inflammation in the knee joint. Normally, SF should not contain red blood cells. In patients with acute knee synovitis, the number of erythrocytes in the SF ranged from 3 to 364 per μL, with an average of 84.33 ± 25.37 per μL. In 58.3% of cases, the count did not exceed 20 per μL, in 16.7% it reached up to 100, and in 25.0% it exceeded that, indicating the presence of hemosynovitis. In patients with chronic synovitis, the erythrocyte count ranged from 4 to 3200 per μL, with an average of 376.23 ± 181.07 per μL. In 69.2% of cases, the count did not exceed 20 per μL; in 15.4% it reached up to 100, and in 15.4% it exceeded that.

Counting cellular elements and determining their ratios is one of the most important components of laboratory examination in joint pathology. In addition to the total number of cellular elements, the qualitative composition of SF is critically important in diagnosing joint disorders. It is known that an increased presence of polymorphonuclear cells, ragocytes, histiocytes, macrophages, and crystals indicates an inflammatory nature of joint changes.

Under normal conditions, the leukocyte count in SF should not exceed 200 cells per μL. In our study, among patients with acute knee synovitis, the leukocyte count varied widely—from 120 to 16,840 per μL—with an average of 4006.58 ± 1244.10 per μL. In 8.3% of cases, the count did not exceed 200 per μL; in 58.4% of patients, it ranged from 200 to 2000 per μL, indicating a non-inflammatory origin; in 33.3%, it exceeded 2000 per μL, suggesting an inflammatory process.In chronic synovitis, the leukocyte count ranged from 320 to 21,200 per μL, with an average of 8346.92 ± 1574.61 cells per μL. In 42.2% of patients, the count ranged from 200 to 2000 per μL; in 53.8%, it exceeded 2000 per μL. It should be noted that a significant increase in leukocyte count coincided with high cloudiness of the SF and the presence of degenerative joint changes.

Table 1.

Indicators	Acute, n=24	Chronic, n=26
Total cellularity, cells in 1 μl	4095,42±1254,97	8727,15±1595,81
Leukocytes, cells in 1 μl	4006,58±1244,10	8346,92±1574,61
Erythrocytes, cells in 1 μl	84,33±25,37	376,23±181,07
Polynuclears, %	25,0	38,5
Rhagocytes, %	25,0	57,7
Histiocytes, %	33,3	46,1
Macrophages, %	16,7	38,5
Inflammatory activity index	2,45±0,66	4,75±0,80

In patients with acute knee synovitis, synovial fluid (SF) showed isolated occurrences of polymorphonuclear cells (25%), ragocytes (25%), histiocytes (33.3%), and macrophages (16.7%). In contrast, during the chronic course, these elements were detected more frequently—polymorphonuclear cells, ragocytes, histiocytes, and macrophages were observed in 38.5%, 57.7%, 46.1%, and 38.5% of cases, respectively—and in significantly higher quantities.

The total cellularity was 4095.42 ± 1254.97 cells per μL in the acute phase, and 8727.15 ± 1595.81 cells per μL during the chronic phase. To evaluate the activity level of the inflammatory process based on cytological data, a formula proposed by P. Stiehl (1981) was used, with modifications to include erythrocytes, polymorphonuclear cells, ragocytes, histiocytes, and macrophages. The calculated index of inflammatory activity (A) was interpreted as follows:

- A < 1.0 – no activity (Grade 0),
- A from 1.0 to 5.0 – low activity (Grade 1),
- A from 5 to 10 – moderate activity (Grade 2),
- A > 10 – high activity (Grade 3).

The results showed that 66.7% of patients with acute synovitis had an activity index of 0. Grade 1 inflammatory activity was identified in 12.5% of patients, and Grade 2 in 20.8%. Among patients with chronic synovitis, 46.1% had an activity index of 0, 7.7% showed Grade 1 activity, 30.8% Grade 2, and 15.4% Grade 3. These findings indicate that the inflammatory process was more pronounced in chronic synovitis.

Various types of crystals were also detected. In acute cases, crystals were found in 83.3% of patients—oxalates in 16.7% and uric acid crystals in 66.7%. In chronic cases, crystals were present in 100% of patients—oxalates in 7.7%, uric acid crystals in 84.6%, and Charcot-Leyden crystals in 7.7%.

According to several authors, in some cases, cytological examination of SF may be limited to the leukocyte formula (...). They recommend counting both viable and destroyed cells, as a significant number of destroyed cells is considered normal. These cells can be differentiated using supravital staining with neutral red.

Based on the conducted research, the following conclusions can be drawn:

1. In patients with acute knee synovitis, hemosynovitis was observed in 50% of cases. In chronic synovitis, the SF was red in 30.8% of cases, milky in 7.7%, straw-yellow in 61.5%, and cloudy in 46.2% of cases.

2. The leukocyte count varied widely: on average, it was 4006.58 ± 1244.10 per μL in acute cases and 8346.92 ± 1574.61 per μL in chronic synovitis, which correlated with increased cloudiness of the synovial fluid.

3. In patients with chronic synovitis, polymorphonuclear cells, ragocytes, histiocytes, macrophages, and various crystals were detected more frequently and in greater quantities than in acute synovitis.

An index for assessing inflammatory activity based on cytological data was proposed. Among patients with acute synovitis, Grade 1 and Grade 2 activity were found in 12.5% and 20.8% of cases, respectively. In chronic synovitis, Grade 1, 2, and 3 activity were found in 7.7%, 30.8%, and 15.4% of cases, respectively.

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DIFFERENTIAL CLINICAL INDICATORS IN CHILDREN WITH ASPERGER'S AND KANNER'S SYNDROMES

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Abstract. *Autism spectrum disorder (ASD) encompasses a wide range of neurodevelopmental syndromes, most notably Asperger's syndrome (AS) and Kanner's syndrome (KS). Despite overlapping characteristics, key clinical differences exist between these syndromes. This study investigates differential clinical indicators in 240 children aged 3–11 years, categorized into AS and KS groups. Emphasis was placed on speech development, cognitive functioning, comorbidity profiles, and social behaviors. The results support the necessity for a refined diagnostic approach and tailored therapeutic strategies.*

Keywords: *autism spectrum disorder, Asperger's syndrome, Kanner's syndrome, differential diagnosis, children, neurodevelopment.*

Introduction. Autism Spectrum Disorder (ASD) refers to a heterogeneous group of neurodevelopmental conditions characterized by difficulties in social communication, restricted interests, and repetitive behaviors. The global prevalence of ASD has increased significantly over the past two decades, currently estimated at 1 in 100 children worldwide [1]. Among the most recognized clinical subtypes of ASD are Kanner's Syndrome (KS), also referred to as classic autism or infantile autism, and Asperger's Syndrome (AS), which is considered a higher-functioning variant of ASD [2,3].

Although AS and KS share core autistic features, they differ significantly in terms of developmental milestones, intellectual functioning, language abilities, and social behaviors. KS typically manifests before age 3 with severe speech delay, global cognitive deficits, pronounced social withdrawal, and stereotypic behavior patterns [4]. In contrast, AS is usually identified later, around 5–6 years of age, and is marked by preserved or even advanced vocabulary, average to above-average intelligence, yet profound deficits in pragmatic communication, empathy, and social reciprocity [5,6]. These distinctions are clinically relevant, as they influence not only diagnostic precision but also the choice of educational, psychological, and medical interventions.

A challenge persists in differentiating AS from KS, especially in early childhood, where overlapping features may confound clinicians [7]. Modern diagnostic systems, including the DSM-5, have merged both syndromes under the umbrella of ASD, which, while improving diagnostic sensitivity, may obscure critical phenotypic distinctions [8]. Recent studies underscore the necessity of maintaining a sub-categorical understanding to tailor treatment plans more effectively and understand neurobiological underpinnings [9,10].

This study aims to provide a comprehensive clinical comparison between AS and KS in children aged 3 to 11 years, analyzing multiple domains including language development, cognitive function, behavioral symptoms, and comorbid neurological conditions. A total of 240 children were assessed using standardized diagnostic instruments to identify statistically significant clinical differentials. Our hypothesis posits that children with KS will exhibit more profound developmental impairments and neurological comorbidities, while children with AS will demonstrate higher verbal and intellectual performance but more pronounced social communication difficulties.

Results

Table 1.

Demographic Distribution

Age (years)	AS Group (n=120)	KS Group (n=120)
3–5	42 (35.0%)	56 (46.7%)
6–8	48 (40.0%)	41 (34.2%)
9–11	30 (25.0%)	23 (19.1%)

***Male/Female ratio**: AS – 4:1; KS – 5:1.*

The distribution by age suggests that children with KS are diagnosed earlier than those with AS, which is consistent with clinical observations that KS symptoms manifest more severely and earlier in development. A higher proportion of KS cases fall in the 3–5 year group, while AS cases are more evenly spread across age ranges, indicating possible underdiagnosis or late recognition in AS due to subtler symptoms. The male predominance in both groups reflects established epidemiological trends, supporting a male-to-female ratio of approximately 4–5:1 across ASD subtypes [1,6].

Table 2.

Language and Cognitive Profile

Parameter	AS Group (mean±SD)	KS Group (mean±SD)	*p* value
Age of first words (months)	24.3 ± 3.1	39.5 ± 4.6	<0.001
IQ (WISC-IV full-scale)	98.2 ± 11.7	68.7 ± 14.5	<0.001
Verbal Expression (ADOS-2 score)	3.2 ± 0.8	6.4 ± 1.1	<0.001

The findings confirm significant differences in speech and cognitive development. Children with KS show delayed language acquisition, with the average age of first words well beyond the expected developmental milestone. Their IQ scores fall within the mild intellectual disability range, consistent with previous research [4,10]. In contrast, children with AS demonstrate near-average to average cognitive functioning and significantly earlier speech onset. ADOS-2 scores reflect milder impairments in verbal expression among AS children, emphasizing their relatively preserved linguistic abilities despite pragmatic challenges.

Table 4.

Comorbid Conditions

Condition	AS group (%)	KS Group (%)	p Value
Epilepsy	4.2%	!9.2%	<0.001
Sleep disturbances	30.8%	58.3%	<0.001
ADHD symptoms	52.5%	45.0%	0.28

Comorbidity patterns differ significantly. Children with KS are more prone to epilepsy and sleep disorders, likely due to underlying neurobiological vulnerability and structural abnormalities in the brain [14]. The comparatively low epilepsy rate in AS children is consistent with their higher cognitive functioning. ADHD-like symptoms are common in both groups, though slightly more prevalent in AS, reinforcing the clinical need for comprehensive neuropsychological screening in all ASD subtypes [15].

Discussion. Our findings highlight pronounced distinctions in clinical presentation between AS and KS. Children with KS demonstrated greater severity in language delays, cognitive impairment, and stereotypic behaviors, aligning with previous reports [9,10]. In contrast, children with AS

exhibited relatively preserved cognitive and verbal profiles, but profound social difficulties consistent with prior studies [11–13].

The higher prevalence of epilepsy in KS corroborates literature linking early neurodevelopmental insults with increased seizure risk [14]. The presence of ADHD symptoms in both groups suggests overlapping attentional deficits, although more prominent in AS [15].

These results support the need for tailored diagnostic criteria and intervention strategies targeting syndrome-specific needs.

Conclusion. Differential diagnosis between Asperger's and Kanner's syndromes in ASD is essential for individualized clinical management. Our findings reveal distinct neurocognitive and behavioral markers that can aid clinicians in early and accurate identification of ASD subtypes.

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MODERN APPROACHES TO THE TREATMENT OF TYPE 2 DIABETES MELLITUS WITH CHRONIC HEART FAILURE

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Abstract. *Type 2 diabetes mellitus (DM2) and chronic heart failure (CHF) often occur together, exacerbating each other's course and worsening the patient's prognosis. The relationship between these diseases is determined by pathophysiological mechanisms, including insulin resistance, inflammation, and endothelial dysfunction.*

Diabetes mellitus, a widespread socially significant disease with numerous micro- and macrovascular complications, acts both as a risk factor for heart failure and as a condition that significantly exacerbates its course.

The relationship between diabetes and CHF is complex and is caused by several mechanisms. Diabetes contributes to the development of cardiomyopathy, impaired diastolic function of the heart and the progression of coronary artery atherosclerosis, which eventually leads to the development or worsening of CHF [9].

Keywords: *SGLT-2 inhibitors, chronic heart failure, type 2 diabetes mellitus, ejection fraction, NT-proBNP.*

Introduction. Studies confirm the high prevalence of CHF among patients with T2DM. According to a multicenter study, CHF is detected in 39.2% of patients with T2DM [13]. In a Russian study, concomitant DM2 was recorded in 20.2% of patients with CHF, which significantly increased the risk of heart attacks, strokes, and chronic renal failure [2].

According to scientific research, the cost of treating T2DM is about 569 billion rubles per year, of which 34.7% is due to complications from the cardiovascular system [1].

Patients with a combination of type 2 diabetes mellitus (DM2) and chronic heart failure (CHF), especially those with reduced ejection fraction (EEF), are at high risk of adverse clinical outcomes. The presence of T2DM worsens the course of CHF, enhances myocardial remodeling, promotes the progression of renal dysfunction, and significantly increases mortality from cardiovascular causes.

According to large cohort studies and meta-analyses, 5-year mortality in combination with DM2 and CHF exceeds 50% [5,8]. The prognosis is particularly unfavorable in patients with an uncontrolled glycemic profile, decreased renal function (GFR <60 ml/min/1.73 m2) and elevated levels of NT-proBNP.

DM2 increases the risk of hospitalization for CHF decompensation by about 1.5–2 times compared with patients without diabetes [10]. This is due both to the direct negative effect of hyperglycemia and insulin resistance on the myocardium, and to a more pronounced activation of neurohumoral mechanisms (RAAS, sympathetic system).

As is known, patients with type 2 diabetes have insulin resistance, in which tissues, including the myocardium, lose sensitivity to insulin. This reduces glucose utilization and increases the dependence of the heart muscle on free fatty acids (FFA), the metabolism of which is less efficient and leads to excess oxygen consumption [7].

Chronic hyperglycemia and protein glycation. Chronic hyperglycemia and protein glycation. Constantly elevated glucose levels lead to protein glycation and the formation of glycation end products (AGEs), which cause oxidative stress, inflammation, and myocardial fibrosis, contributing to the progression of CHF [3].

Activation of the renin-angiotensin-aldosterone system (RAAS). In patients with CHF and T2DM, hyperactivation of the RAAS is observed, which leads to vasoconstriction, sodium and water retention, myocardial hypertrophy, and deterioration of the pumping function of the heart [12].

Inflammation and oxidative stress. DM2 is accompanied by chronic low-level inflammation. Cytokines (for example, TNF-α, IL-6) damage the endothelium, increase fibrosis, impair diastolic function, and promote cardiac remodeling [15].

Diabetic cardiomyopathy. Even without severe atherosclerosis, patients with DM2 may develop diabetic cardiomyopathy characterized by diastolic dysfunction, left ventricular hypertrophy, and increased myocardial stiffness [4].

Microangiopathy and deterioration of myocardial perfusion. DM2 causes microvascular lesions, including capillary reduction and thickening of the basement membranes, which impairs myocardial perfusion and promotes the development of ischemia even in the absence of stenosing atherosclerosis [16].

In recent years, SGLT-2 inhibitors have attracted special attention, which demonstrate a pronounced cardioprotective effect, regardless of the presence of diabetes. Large RCTs, including DAPA-HF [11] and EMPEROR-Reduced [14], have shown a reduced risk of cardiovascular death and hospitalization for CHF in patients with SFV, including patients with T2DM.

The main risk factors for worsening the prognosis in patients with DM2 and CHF are: High levels of NT-proBNP (> 2000 pg/ml); Decreased LVEF <30%

• Chronic kidney disease (GFR <45 ml/min/1.73 m2)
• Elderly (>70 years old)
• A history of frequent hospitalizations
• Glycosylated hemoglobin (HbA1c) >8.5%
• Concomitant diseases: anemia, atrial fibrillation, obesity

Adequate management of such patients requires a multidisciplinary approach with an emphasis on optimizing drug therapy (SGLT-2 inhibitors, beta blockers, ace inhibitors/ACE inhibitors, mineralocorticoid antagonists), correction of glycemia, control of blood pressure and kidney function.

Treatment and modern approaches: the combination of DM2 and CHF requires an integrated approach combining glycemic control and correction of cardiovascular risk. In recent years, the treatment paradigm has undergone significant changes, especially due to the introduction of drugs with both hypoglycemic and cardioprotective effects.

The current ESC (2021) and AHA (2022) guidelines identify four key classes of drugs that are proven to improve prognosis.:

• RAAS inhibitors: ACE inhibitors (enalapril, ramipril) or angiotensin II / neprilysin receptor antagonists (ARNI – sacubitril/valsartan).

Beta blockers: bisoprolol, carvedilol, nebivolol or metoprolol succinate.

• Mineralocorticoid antagonists (MPas): spironolactone, eplerenone.
• SGLT-2 inhibitors: dapagliflozin, empagliflozin — regardless of the presence of diabetes.

Prescribing all four classes of drugs significantly reduces mortality and the frequency of hospitalizations [1].

SGLT-2 inhibitors are a new therapeutic strategy. Sodium-glucose cotransporter type 2 (SGLT-2) inhibitors were initially used as hypoglycemic agents, but numerous RCTs have proven their powerful cardioprotective and nephroprotective effects.

Basic drugs:

• Dapagliflozin — DAPA-HF study: reducing the risk of death or hospitalization due to CHF by 26% [2].

• Empagliflozin — EMPEROR-Reduced study: similar results, especially in the population with T2DM [6].

SGLT-2 inhibitors also reduce the progression of CKD, reduce edema, improve quality of life, and have a diuretic effect without significantly lowering blood pressure.

Glycemic control. The target HbA1c level in patients with CHF should be individualized (usually in the range of 6.5–7.5%), avoiding both hypoglycemia and severe hyperglycemia. Metformin remains the drug of choice with preserved renal function, however, in CHF, a combination with SGLT-2 inhibitors is preferred.

Thiazolidinediones (pioglitazone), which can cause fluid retention and worsen CHF, should be avoided [4].

Other important aspects: Diuretics — for signs of fluid retention, in the lowest effective doses. Statins are used in the presence of atherosclerotic CC disease. Blood pressure control — target level <130/80 mmHg (if tolerated). Assessment of kidney function is mandatory monitoring of GFR and potassium levels. Lifestyle modification — weight control, salt restriction, physical activity within tolerance limits.

Modern approaches to the treatment of DM2 in patients with CHF are based on the principles of individualization, organoprotection and evidence-based medicine. The use of drugs with proven effects on cardiovascular outcomes (primarily SGLT-2 inhibitors) has become a major achievement in recent years. An integrated and personalized approach significantly improves the prognosis and quality of life of such patients.

The aim of the study. Based on the above, we set ourselves the goal of conducting a comparative analysis of the effectiveness of dapagliflozin and empagliflozin therapy in patients with chronic heart failure with reduced ejection fraction and concomitant type 2 diabetes mellitus. We focused on assessing changes in the level of NT-proBNP, left ventricular ejection fraction, quality of life (KCCQ), and the frequency of hospitalizations for CHF decompensation during the six-month follow-up period.

Materials and methods. The study included 34 patients with a diagnosis of chronic heart failure (CHF) with reduced ejection fraction (LVEF < 40%) and concomitant type 2 diabetes mellitus (DM2). The inclusion criteria were stable CHF (NYHA class II–III), NT-proBNP level > 1000 pg/ml, age from 45 to 75 years, as well as stable glycemic therapy for ≥3 months prior to the start of the study. The patients were randomized into two therapeutic groups (17 people each): 1. The dapagliflozin group received the drug at a dose of 10 mg/day orally; 2. The empagliflozin group received the drug at a dose of 10 mg / day orally. Gender composition: 14 women and 20 men, distributed proportionally between the groups. The patients were followed up for 6 months. All participants continued to receive standard CHF therapy (beta blockers, ace inhibitors/ARNI, MRA, and diuretics, if necessary), which remained unchanged throughout the follow-up period.

Assessment of clinical outcomes:

• Functional status was assessed using the KCCQ scale (Kansas City Cardiomyopathy Questionnaire), with the change in score recorded by the 6th month.

• Hemodynamic parameters — NT-proBNP and left ventricular ejection fraction (LVEF) — were determined upon activation and after 6 months.

• The frequency of hospitalizations for CHF decompensation was recorded during follow-up.

• Side effects were monitored on each visit.

For statistical analysis, descriptive statistics methods, Student's t-test for comparing averages, and the $\chi 2$-test for categorical variables were used. The p value < 0.05 was considered statistically significant.

Results. During the six-month follow-up, we noted positive dynamics of clinical parameters in patients of both study groups. However, statistically significant differences in a number of key parameters were recorded between the groups receiving dapagliflozin and empagliflozin.

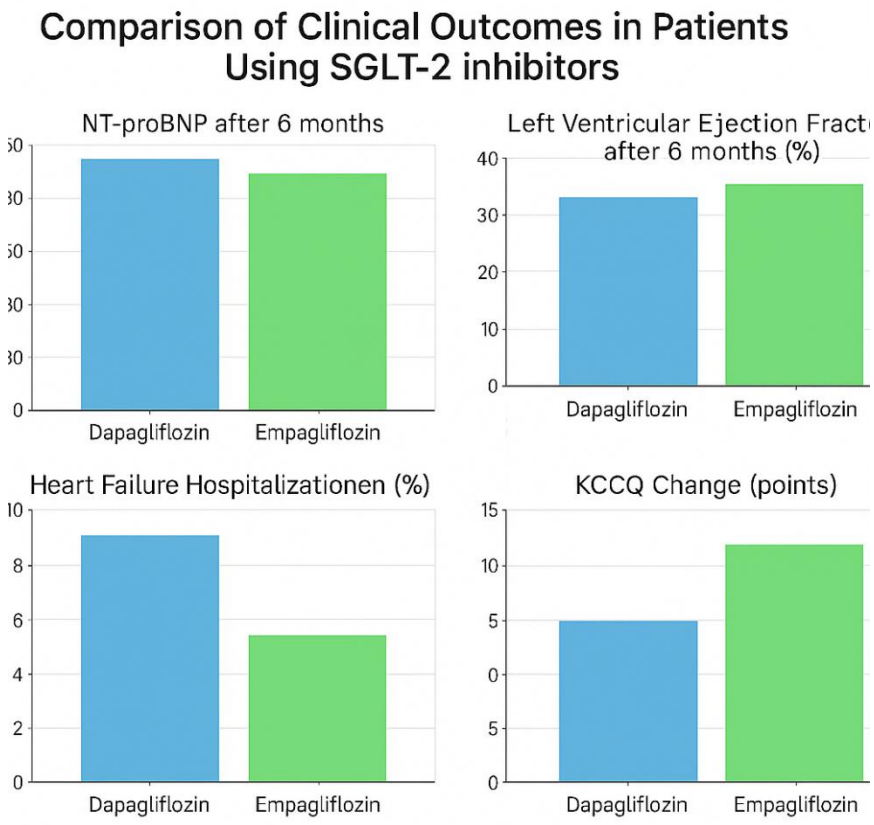
Table.

Comparison of clinical outcomes in patients treated with dapagliflozin and empagliflozin (n=34)

Indicator	Dapagliflozin (n=17)	Empagliflozin (n=17)	p-value
Average age, years	64 ± 7	63 ± 6	0.71
Men / Women	10 / 7	10 / 7	1.00
NT-proBNP, baseline (pg/ml)	2300 ± 480	2250 ± 450	0.66
NT-proBNP, after 6 months (pg/ml)	1800 ± 400	**1500 ± 350**	**0.02**
LV ejection fraction, % (initial)	31 ± 4	32 ± 5	0.53
LV ejection fraction, % (after 6 months)	35 ± 5	**39 ± 4**	**0.01**
CHF hospitalizations, n (%)	5 (29%)	**2 (12%)**	**0.04**
Δ KCCQ score (quality of life)	+8 ± 2	**+12 ± 3**	**0.01**
Side effects, n (%)	2 (11.8%)	1 (5.9%)	0.55

Note:

- The p-values were calculated using ANOVA and χ2-test.
- The best results among the groups are highlighted in bold.
- Δ KCCQ — change from baseline



We found that the level of NT-proBNP decreased in both groups, but the decrease was more pronounced in the empagliflozin group, from an average of 2,250 ± 450 to 1,500 ± 350 pg/ml, compared with 2,300 ± 480 to 1,800 ± 400 pg/ml in the dapagliflozin group (p = 0.02).

Ejection fraction The left ventricle in patients treated with empagliflozin increased from 32 ± 5% to 39 ± 4%, whereas in the dapagliflozin group the increase was from 31 ± 4% to 35 ± 5% (p = 0.01). We regard this as a more pronounced restoration of systolic function during empagliflozin therapy.

The frequency of hospitalizations for CHF decompensation during the observed period was 5 cases (29%) in the dapagliflozin group and 2 cases (12%) in the empagliflozin group (p = 0.04), which, in our opinion, indicates a more stable clinical course with the use of empagliflozin.

We also recorded an improvement in quality of life on the KCCQ scale: in the empagliflozin group, the increase was 12 ± 3 points, while in the dapagliflozin group it was 8 ± 2 points (p = 0.01).

Side effects were rare and had no serious clinical consequences. We registered adverse reactions in 2 (11.8%) patients in the dapagliflozin group and in 1 (5.9%) patient in the empagliflozin group (p = 0.55), the differences were statistically insignificant.

Thus, according to the results of our analysis, empagliflozin demonstrated a more pronounced positive effect on functional and biomarker parameters in patients with CHF and T2DM, with a similar safety profile with dapagliflozin.

Conclusion. Thus, the presence of diabetes in patients with CHF requires special attention and an integrated approach to treatment aimed at both glycemic control and optimizing therapy for heart failure.

SGLT-2 inhibitors are an effective component of CHF therapy with reduced ejection fraction. Empagliflozin may have a more pronounced beneficial effect on cardiovascular outcomes in this population.

Thus, our data allow us to recommend empagliflozin as the preferred drug in the combination therapy of CHF in patients with concomitant DM2, subject to individual tolerability and compliance with treatment standards.

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MORPHO-FUNCTIONAL CHANGES IN THE ENDOCRINE PANCREAS OF WHITE RATS UNDER METABOLIC SYNDROME CONDITIONS

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Abstract. *To assess the morphological characteristics of the pancreas in experimental metabolic syndrome. Materials and Methods: White laboratory rats under hypokinetic conditions were used in the experiment. To achieve the research goal, the pancreases of 51 sexually mature white laboratory rats were examined. The animals were divided into two groups. The first group consisted of intact adult rats (control). In the second group, the rats were placed in a special cage with an area of 150 cm² to induce an experimental metabolic syndrome model. Results: In experimental metabolic syndrome, vacuolization of the cytoplasm, irregular nuclear shape, and nucleolar segmentation were observed in the β-cells of the endocrine part of the pancreas. These changes may be associated with impaired intracellular transport and reduced secretory activity. In α-cells located at the periphery of the islets, increased glucagon expression, chromatin condensation, and indistinct cell boundaries were detected, indicating a disruption of hormonal balance. Conclusion: Under metabolic syndrome conditions, a decrease in the number and size of pancreatic islets, structural abnormalities in β-cells, and mild edema and vascular changes in the surrounding connective tissue were observed. These changes were accompanied by reduced hormonal activity of the gland.*

Keywords: *metabolic syndrome, pancreas, endocrine cells, pancreatic lobule, insulin, glucagon.*

Introduction. In recent years, it has been reported that nearly 60% of the global population has insufficient physical activity to maintain a healthy lifestyle [1]. According to literature sources, physical inactivity is responsible for the deaths of approximately 1.9 million people [5]. Reduced physical activity leads to disruptions in the body's overall metabolism [7]. Over time, changes begin to occur in the cardiovascular, respiratory, musculoskeletal, and endocrine systems [9]. Many sources highlight that hypodynamia is one of the leading causes of metabolic syndrome [15]. Metabolic syndrome leads to multiple metabolic disturbances, increasing the risk of cardiovascular diseases and diabetes mellitus. The pathogenesis of metabolic syndrome involves complex mechanisms and remains a subject with many unresolved issues [2, 6, 11, 14, 18].

Metabolic syndrome (MS) is a complex pathological condition characterized by disturbances in carbohydrate, fat, and protein metabolism, insulin resistance, abdominal obesity, hypertension, and dyslipidemia. It is considered one of the most pressing issues in modern medicine. In recent years, the prevalence of MS has increased significantly. According to the World Health Organization, signs of metabolic syndrome are observed in approximately one-third of adults globally. In the United States, this rate reaches around 35%, while in European countries it ranges between 25–30%. In Uzbekistan, some studies have reported that metabolic syndrome is present in 20–25% of the population [3, 8, 10, 13, 20].

One of the most important factors in the development of metabolic syndrome is hormonal imbalance, particularly the morpho-functional changes occurring in the endocrine part of the pancreas—the islets of Langerhans. Dysfunction of β-cells results in decreased insulin secretion, while overproduction of glucagon by α-cells disrupts glucose metabolism. This leads to hyperglycemia, cellular stress, and inflammatory processes in the body [4, 12, 16, 17, 19, 21].

Today, under conditions of metabolic syndrome, not only hormonal changes but also morphological and histological alterations in the pancreatic islet apparatus, as well as the condition of β- and α-cells, have become a critical focus of research. Understanding the morpho-structural and functional changes in these cells can help in early diagnosis, prevention, and treatment strategies for MS.

Therefore, studying the morphological and functional changes in the endocrine part of the pancreas in an experimental model of metabolic syndrome holds significant scientific and practical value.

Purpose of the Research. Evaluation of the Morphological Characteristics of the Pancreas in Experimental Metabolic Syndrome.

Materials and Methods. The study focused on evaluating the morpho-functional changes occurring in the endocrine part of the pancreas under conditions of metabolic syndrome.

To achieve this goal, 51 sexually mature male white laboratory rats were selected. The rats were divided into two groups: Group 1 — control (intact) rats; Group 2 - experimental group, in which a model of metabolic syndrome was induced over 30 days using a special high-fat diet.

The rats in the experimental group were fed a high-calorie, fat-rich diet, containing up to 65% fat daily. During the experiment, the rats were kept under the same temperature and lighting conditions in the vivarium. Both groups were housed in cages that allowed free movement throughout the experiment.

At the end of the 30-day experiment, the rats were euthanized by decapitation in accordance with the “European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes” (Strasbourg, 1985). Both control and experimental groups were kept in identical vivarium conditions.

For morphometric examination, the NanoZoomer (REF C13140-21.S/N000198/ HAMAMATSU PHOTONICS/431-3196 JAPAN) Hamamatsu system and QuPath-0.4.0 (NanoZoomer Digital Pathology Image) morphometric software were used. The obtained data were statistically processed using the Microsoft Excel 2010 statistical package to calculate the arithmetic mean (M), the standard error (m), and the reliability coefficient (t). Histological images were captured using a CX40 model microscope equipped with an OD400 camera.

Results. In white laboratory rats, the pancreas has an average weight of 208.3 ± 5.8 g and appears pink or pinkish-yellow in color. Anatomically, the pancreas in rats is located in the abdominal cavity, positioned above the lesser curvature of the stomach and along the proximal part of the duodenum. The organ has a trilobed shape, comprising the left lobe - lobus sinister or the gastrosplenic (tail) portion — cauda pancreatis, the middle lobe - lobus medius or the head - caput pancreatis, and the right lobe - lobus dexter.

Our anatomical studies on the rat pancreas revealed three distinct macroscopic parts. The first part - the duodenal portion - is situated within the U-shaped curve of the duodenum, caudal to the opening of the common bile duct. The second part consists of numerous isolated lobules aligned along the bile duct. The third part - the gastrosplenic portion - is located to the left of the first two parts, within the duplication of the gastrosplenic ligament. The main bulk of the pancreas lies adjacent to the stomach, while its lateral region reaches toward the splenic hilum, encasing the main splenic vein through its small penetrating vessels.

In the control group, the organ parenchyma consisted of lobules separated by fine connective tissue, within which blood vessels and ducts were present. The exocrine portion of the pancreas was composed of typical acini. The acini consisted of conical exocrinocytes, which exhibited basophilia at the basal part and acidophilia at the apical portion. The nuclei were round with clearly visible nucleoli. The cytoplasm appeared granular in structure.

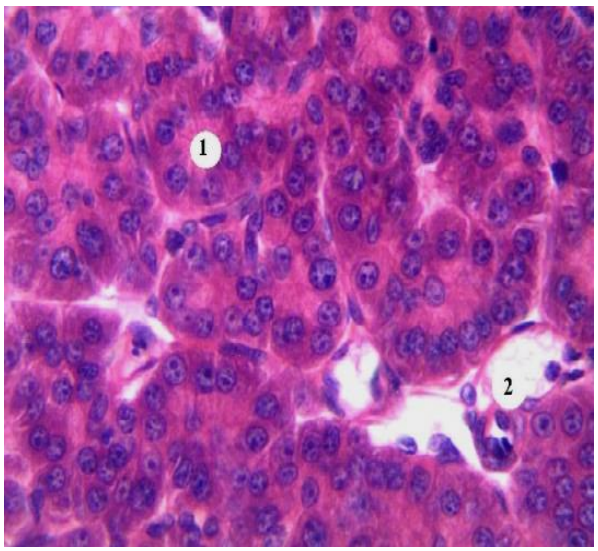

Fig. 1. Histological structure of the pancreas in the control group of rats.
1 – Pancreatic acinar cells, 2 – Blood vessels.
Hematoxylin and eosin staining.
Magnification: 40x10.

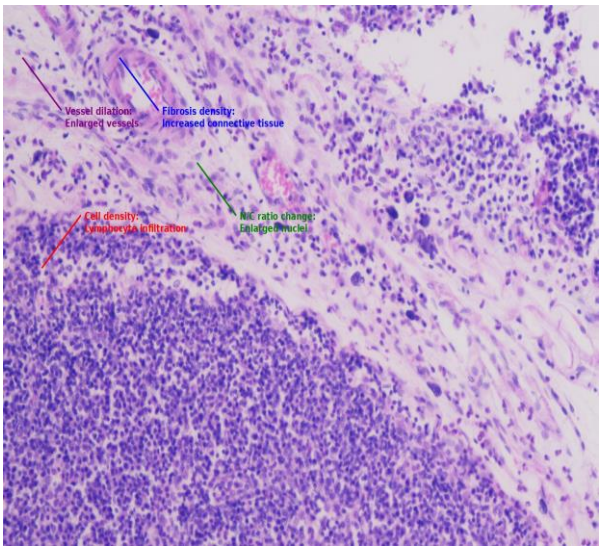

Fig. 2. Histological structure of the pancreas in the experimental group of rats.
Islet structure disruption (blue) – Disorganization of normal architecture and uneven distribution of cells.
Increased fibrosis (green) – Proliferation of connective tissue around the islets.
Lymphocytic infiltration (red) – Development of an inflammatory process.
Vascular dilation (purple) – Impaired microcirculation and ischemic changes.
Hematoxylin and eosin staining.
Magnification: 20x10.

In the experimental group (metabolic syndrome model), significant morphological changes were observed in the pancreas. The shape and arrangement of exocrine acini appeared irregular, with cytoplasmic vacuolization in exocrinocytes, nuclear deformation, and, in some cases, nuclear segmentation. Basal basophilia was reduced, while apical acidophilia was weakened. Most acini were surrounded by slightly edematous connective tissue. The number of endocrine islets was reduced, and their size decreased as well. In β-cells, vacuolization and chromatin condensation were detected. In

α-cells, enhanced glucagon expression was accompanied by nuclear shape irregularities and indistinct cell contours.

Furthermore, the architecture of the pancreatic tissue was significantly disrupted under metabolic syndrome conditions. The borders between lobules became indistinct, and in some areas, an expansion and densification of connective tissue were observed. Dilation of interlobular excretory ducts and blood-filled vessels surrounding them indicated microcirculatory disorders characteristic of metabolic syndrome.

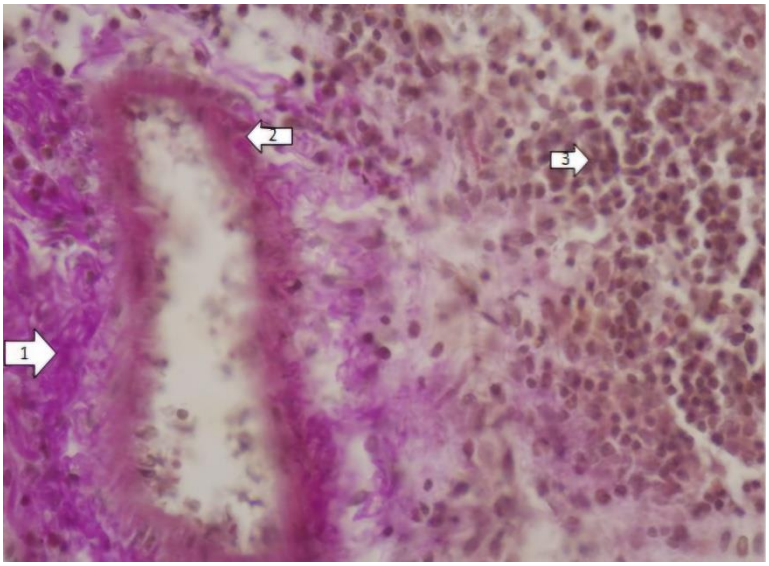

Fig. 3. Histological structure of the pancreas in the experimental group of rats.
Degenerative changes were observed in the pancreatic tissue stained using the Weigert method.Fragmentation of elastic fibers and structural disorganization (1).
Increased cellular infiltration in the connective tissue (2).
Under the influence of metabolic syndrome, increased cellular density and structural changes in the pancreatic parenchyma (3).
Image stained with Weigert method, magnification: 40×10.

Mild edema was observed between the acini, indicating the accumulation of interstitial fluid and disruption of the secretory process. Dilated intralobular ducts were lined with cuboidal or flattened epithelium, and secretory cells were detected in their stroma. These findings suggest pathological alterations in exocrine activity.

Mild edema was observed between the acini, indicating the accumulation of interstitial fluid and disruption of the secretory process. Dilated intralobular ducts were lined with cuboidal or flattened epithelium, and secretory cells were detected in their stroma. These findings suggest pathological alterations in exocrine activity.

In the endocrine regions, β-cells displayed nuclear shrinkage and signs of karyopyknosis, indicating reduced cellular activity. The area of α-cells decreased by 8.5% compared to the control group, with enlarged nuclei, increased vacuole number, and reduced electron density. Although the total area of secretory granules in α-cells increased, their diameter decreased from 22.7 ± 0.9 nm to 18.4 ± 0.5 nm, reflecting a diminished capacity for hormone production.

According to morphometric measurements, the average diameter of pancreatic acini was 11.4 ± 0.3 μm, and their height was 2.15 ± 0.18 μm. In the experimental group, the diameter decreased by up to 3%, and height by up to 12%. These changes suggest a regressive state of the exocrine component of the pancreas under metabolic syndrome conditions.

Conclusion. The results of the 30-day experimental study demonstrated significant morpho-functional alterations in the pancreas of white laboratory rats under metabolic syndrome conditions. Notably, there was expansion of interlobular connective tissue within the stroma, edema and inflammatory infiltrates in blood vessels, and morphological changes in the excretory ducts. In the exocrine portion, a reduction in the diameter and height of acinar cells, decreased secretory activity, and a decline in morphometric parameters were observed, indicating impaired digestive function of the pancreas.

In the endocrine portion, structural changes in the islets of Langerhans were detected, particularly karyopyknosis and nuclear shrinkage in β-cells, and nuclear deformation along with altered morphometric parameters of secretory granules in α-cells. These findings indicate dysregulation in insulin and glucagon secretion.

Overall, the morpho-functional changes occurring in the exocrine and endocrine components of the pancreas under metabolic syndrome provide a significant experimental foundation for understanding the pathogenesis and complications of this condition.

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OROPHARYNGEAL CANDIDIASIS: COMPARISON OF CLINICAL CHARACTERISTICS OF ACUTE AND CHRONIC COURSE

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Abstract. *Oropharyngeal candidiasis (OPC) is one of the most common fungal infections of the oral mucosa, pharynx and larynx caused by yeast-like fungi of the genus Candida. Candida albicans remains the most common pathogen, but the clinical significance of other species (C. glabrata, C. tropicalis, C. parapsilosis) is increasing. The aim of this review is to summarize current data on the clinical characteristics of acute and chronic course of OFC, analysis of risk factors, diagnostic methods and approaches to therapy. The importance of immune status, background diseases and iatrogenic factors in the pathogenesis of the disease is considered, and modern classification approaches, differential diagnostics and therapeutic strategies are presented. The need for an individualized approach and preventive measures to prevent relapses is substantiated.*

Key words: *oropharyngeal candidiasis, Candida albicans, acute course, chronic course, mycoses, clinical forms, antifungal therapy.*

Introduction. Fungal infections of humans remain an important problem of clinical mycology, especially in the context of the growth of iatrogenic conditions, chronic diseases and immunodeficiencies. The genus Candida unites about 200 species of yeast-like fungi, of which about 20 are capable of causing diseases in humans. Oropharyngeal candidiasis occupies a significant place among mycoses of the mucous membrane, especially in children, elderly and immunocompromised patients [1, 2, 6, 7, 11].

Candida albicans is the most common pathogen, possessing high adhesive capacity, pronounced virulence factors and the ability to form biofilms. However, in recent decades, the clinical significance of other Candida species resistant to traditional antifungals has increased, especially in patients receiving long-term antibacterial or immunosuppressive therapy.

OPC can occur in both acute and chronic forms, differing in pathogenesis, clinical picture and treatment approaches. Against the background of a decrease in the immune status, the disease acquires a recurrent or persistent nature, requiring complex diagnostics and therapy [3, 8, 10, 12].

Epidemiology and risk factors. The incidence of OFC varies depending on age and concomitant conditions. In adults, it can reach 42.9%, in newborns - about 5%, in infants - up to 10%, and in the elderly - about 10% [4, 13, 17]. The high-risk group includes patients with carbohydrate metabolism disorders (in particular, diabetes), immunodeficiencies, oncohematological and endocrine diseases.

Risk factors for the development of oral candidiasis also include:

– metabolic disorders (diabetes mellitus, hypovitaminosis);
– long-term antibacterial therapy;
– hormonal drugs (GCS, cytostatics);
– dysbacteriosis and immunodeficiency states;
– wearing dentures (especially with poor hygiene);
– artificial feeding in children and morphofunctional immaturity of the mucosa.

In hospitalized patients, especially in intensive care units, candidiasis carriage can reach 88% [5, 14, 18].

Clinical features of acute and chronic oropharyngeal candidiasis. Oropharyngeal candidiasis is a common fungal disease caused by yeast-like fungi of the genus Candida, mainly Candida albicans, affecting the mucous membrane of the oral cavity and pharynx. Depending on the nature of the clinical course, acute and chronic forms of the disease are distinguished, each of which has its own characteristics of clinical manifestations, pathogenetic mechanisms and approaches to therapy [6, 15, 19].

Acute oropharyngeal candidiasis. The acute form of the disease is characterized by a sudden onset, a pronounced inflammatory reaction from the mucous membrane and the presence of general symptoms of intoxication. Most often, acute oropharyngeal candidiasis develops in patients with weakened immunity, after courses of antibacterial or hormonal therapy, as well as in the presence of metabolic or chronic somatic diseases.

The main clinical manifestations of acute candidiasis include:

– Plaques on the mucous membrane: white, cheesy or filmy formations localized on the tongue, cheeks, gums, soft palate. Plaques are easily removed, revealing a hyperemic or eroded surface underneath, often with pinpoint hemorrhages.

– Hyperemia and edema of the mucous membrane: inflamed areas become painful upon palpation and may be accompanied by maceration and the formation of erosions.

Sensory disturbances: burning sensation, itching and pain, which intensifies when eating food, especially hot and spicy food; taste disturbances are possible.

– Symptoms of general intoxication: subfebrile body temperature, weakness, fatigue, malaise, especially pronounced in children and elderly patients.

According to clinical classification, acute oropharyngeal candidiasis can occur in two forms:

1. Limited form – characterized by localized damage to the mucous membrane (tongue, soft palate, inner surface of the cheeks) and usually occurs in mild cases of the disease, without pronounced immune disorders.

2. Diffuse form – accompanied by damage to large areas of the mucous membrane of the oral cavity and pharynx. It is more often observed in patients with immunodeficiencies (including HIV infection, oncohematological diseases), after long-term treatment with antibiotics or with severe systemic disorders. It is characterized by more pronounced symptoms and requires systemic antifungal therapy [7, 9, 16, 20, 25].

Thus, acute oropharyngeal candidiasis requires timely detection, clinical assessment of severity and selection of adequate therapy taking into account the general condition of the patient and the course of the disease.

Chronic oropharyngeal candidiasis. Chronic oropharyngeal candidiasis is a long-term pathological condition characterized by less pronounced general symptoms, but a tendency to relapse, resistance of the pathogen to therapy and association with chronic somatic diseases. From a clinical point of view, chronic candidiasis manifests itself in several forms, among which the most common are hyperplastic and atrophic forms, as well as recurrent and persistent course of the disease.

The hyperplastic form is characterized by the formation of dense, grayish-white plaques, tightly attached to the surface of the mucous membrane. The plaques are difficult to remove, and may cause injury to the mucous membrane and the appearance of pinpoint hemorrhages. This form is characterized by persistent inflammation, and in the presence of background pathology of the mucous membrane (leukoplakia, chronic glossitis) can be considered a precancerous condition.

The atrophic form is manifested by thinning of the mucous membrane, pronounced hyperemia, dryness and smoothness of the relief. The tongue, palate and inner surface of the cheeks are most often affected. Patients complain of constant burning, which intensifies when talking, eating or when exposed to temperature irritants. This form is especially characteristic of the elderly, as well as people who have been using dentures for a long time.

According to the nature of the course, chronic candidiasis is divided into:

– Relapsing form, characterized by periods of clinical remission, alternating with exacerbations. Relapses are provoked by the persistence of forms by predisposing factors, such as immunodeficiency states, microbiota disorders (dysbacteriosis), the need for or repeated use of antibiotics, glucocorticosteroids and other immunosuppressants. Patients periodically note the appearance of plaque, burning and discomfort in the oral cavity.

– Persistent form, in which clinical manifestations persist constantly, without periods of significant improvement. The course is characterized by low efficiency of standard therapy and requires a comprehensive diagnostic examination, assessment of the sensitivity of the fungal flora and the immunological status of the patient. There is often a need to correct background pathology and prescribe systemic therapy [8, 21, 24].

Chronic forms of the disease require an individualized and comprehensive approach to treatment, including not only the prescription of antifungal drugs, but also the elimination or correction of predisposing factors. Thus, a clear distinction between acute and chronic oropharyngeal candidiasis is of great practical importance. Understanding the clinical and pathogenetic differences allows for timely diagnosis of the disease, selection of optimal therapeutic tactics and implementation of measures to prevent relapses and complications, especially in patients from risk groups.

4. **Differential diagnostics**

OPC must be distinguished from:

– Streptococcal and staphylococcal tonsillitis;

– Herpetic stomatitis;

– Leukoplakia, lichen planus, Behcet's syndrome, etc.

Clinical examination should be supplemented by:

– Microscopy of smears to detect pseudomycelium;

– Cultural examination on nutrient media;

– If necessary, tests for sensitivity to antimycotics.

Principles of therapy and prevention of oropharyngeal candidiasis. Treatment of oropharyngeal candidiasis should be based on the individual characteristics of the clinical picture, the form of the disease (acute or chronic), the degree of expression of inflammatory changes, as well as the general condition of the patient and the presence of concomitant pathologies. A comprehensive therapeutic approach allows for clinical recovery, reduces the risk of chronicity of the process and prevents relapses.

Local therapy. It is the first stage of treatment, especially in mild and limited cases of the disease. It involves the use of antifungal drugs in the form of:

– Solutions, gels and lozenges with antifungal agents, the most commonly used are nystatin, clotrimazole and capsamycin. These drugs provide a direct effect on the lesions.

– Antiseptic solutions for treating the oral mucosa (for example, chlorhexidine, miramistin), which help reduce bacterial and fungal contamination and prevent secondary infection.

Systemic therapy. It is indicated for moderate and severe cases of the disease, diffuse and chronic forms of candidiasis, as well as in patients with a weakened immune status.

The most commonly used are:

– Fluconazole is the most commonly prescribed systemic antifungal agent, effective against most strains of Candida albicans.

– Itraconazole is used in the presence of resistance to fluconazole or for lesions caused by other types of Candida. The duration of systemic therapy is determined by clinical dynamics, but usually ranges from 10 to 21 days with subsequent observation [12, 13, 22].

Supportive and corrective measures. Effective treatment is impossible without eliminating predisposing factors. Important:

– Correct background conditions, including hypovitaminosis, iron deficiency, hormonal and metabolic disorders.

– Normalize the intestinal microbiota, which is achieved by using probiotics and prebiotics, especially in the presence of dysbacteriosis.

– Ensure thorough oral hygiene, especially for patients with dentures. Dentures must be treated daily, not left overnight, and regularly professionally cleaned.

– Strengthen the patient's immune status - through a balanced diet, sanitation of foci of chronic infection, correction of immunodeficiency states if necessary.

Prevention. Prevention of oropharyngeal candidiasis is aimed at preventing primary infection, relapses of the disease and complications. The main preventive measures include:

– Control and limitation of the unjustified use of antibacterial drugs, especially broad-spectrum ones, in order to preserve the normal microflora of the mucous membrane.

– Conducting regular sanitation of the oral cavity, especially for patients using dentures, suffering from caries, periodontal disease and other dental diseases.

– Timely detection and treatment of underlying chronic pathologies, such as diabetes mellitus, gastrointestinal diseases, immunodeficiency states.

– Preventive examinations by a dentist and therapist, especially for patients from risk groups (the elderly, newborns, oncohematological patients, patients on long-term drug therapy) [3, 13, 23].

Early detection of oropharyngeal candidiasis signs and timely treatment can significantly reduce the risk of complications, prevent chronicity of the process and improve the quality of life of patients. Effective prevention plays a key role in reducing the prevalence of the disease, especially in the context of the growth of immunocompromised states and iatrogenic factors.

Conclusion. Oropharyngeal candidiasis is a heterogeneous group of fungal infections that require a differentiated approach to diagnosis and treatment. Distinguishing between acute and chronic course is of fundamental importance for choosing effective therapy and preventing relapses. An integrated approach, including correction of background conditions, use of antifungal agents and restoration of microbiota, allows achieving stable remission and preventing the development of complications, especially in risk groups. In the context of growing antibiotic resistance and an increase in the number of immunocompromised patients, the problem of OPC remains clinically relevant.

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EVALUATION OF THE EFFECTIVENESS OF SURGICAL TREATMENT IN CLINICAL FORMS OF TRANSIENT ACUTE PARAPROCTITIS

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Annotation. ***Research objective:*** *To study the methods used in Uzbekistan to quickly and without complications treat patients with acute acute paraproctitis by correctly diagnosing them and applying the right treatment measures.* ***Materials and methods:*** *In the purulent surgery department of the Rustamov's clinic of Mirzo Ulugbek district of Tashkent city, 45 patients with paraproctitis were admitted in October-November 2024 and divided into 20 control groups and 25 patients into main groups. The medical history of the patients was studied and a retrospective analysis was conducted. Paraproctitis with aerobic flora was observed in all patients. Also, additional examinations, including: a sharp increase in the leukocyte and erythrocyte sedimentation rate in the blood test, were observed.* ***Analysis and discussion of results:*** *Additional tests, including: a sharp increase in the leukocyte and erythrocyte sedimentation rate in blood tests, were also observed. After the operation, the patients were administered detoxification, antibiotic, analgesic, antihypoxic, and tissue metabolism-improving drugs.* ***Conclusion:*** *One of the main aspects is correct and early diagnosis of the disease and successful surgery, which allows the process to be uncomplicated.*

Keywords: *acute paraproctitis, leukocytes, ESR, purulent cavity, antibiotics, analgesics.*

Relevance. Anorectal abscesses and fistulas are potentially debilitating but rarely life-threatening conditions. They usually originate from an infection in the cryptoglandular epithelium and, based on their location, are classified into perianal, ischiorectal, intersphincteric and supralevator. According to the literature, perianal and ischiorectal abscesses are the most common (1). Supralevator abscesses are the least common, occurring in 1% to 9% of patients, and they present with nonspecific anal pain and fever while redness or swelling of the buttocks may be absent. Spread across specific anatomic spaces is a very rare complication but may potentially lead to sepsis and death (9). Acute paraproctitis is one of the most common purulent surgical diseases, accounting for 0.5-4% of all surgical diseases and 24-50% of urgent proctological diseases. Acute paraproctitis is observed in severe form (ischiorectal, pelviorectal, retrorectal, horseshoe-shaped) in 5-58% of cases, in 4.0% of cases, pus ruptures into the abdominal cavity, and in 1.2% of cases, it spreads to the groin and genital areas (7,10). Postoperatively, recurrent paraproctitis or rectal fistula occurs in 24-88% of cases, anal sphincter insufficiency occurs in 6-27.9% of cases, and posterior anal discomfort occurs in 17-36% of cases (4,6). Complex anal fistulas are difficult to manage. The success rate of most procedures is not satisfactory as the recurrence rates are very high in these fistulas. Depending on the location and severity of paraproctitis, radical and 2-stage operations are performed. In radical operations, the purulent cavity is opened, cleaned, and the purulent duct and internal opening are closed. This method is used in mild forms of paraproctitis. 2-stage operations: 1) the purulent cavity is opened, cleaned, and the internal opening is drained with a ligature. In the 2nd stage, the fistula is cut. These methods are used in severe forms of paraproctitis(5,7,10). After surgery, treating patients with antibiotic therapy, analgesics, detoxification, and drugs that improve regeneration and hemodynamics helps the disease to progress more quickly and without complications.

Research objective: To study the methods used in Uzbekistan to quickly and without complications treat patients with acute acute paraproctitis by correctly diagnosing them and applying the right treatment measures.

Inspection material and methods: A retrospective analysis was conducted of the medical history of 25 patients who were included in the main group and who were diagnosed with paraproctitis in October-November 2024 at the Department of Purulent Surgery of the Rustamov Clinic of the Mirzo Ulugbek District of Tashkent. Paraproctitis with aerobic flora was observed in all patients.

Analysis and discussion of results. We studied the condition of 25 patients with acute paraproctitis, who were included in the main group and visited our clinic in October-November 2024, before and after treatment. 20 of the patients were men and 5 were women (**Fig 1**.).

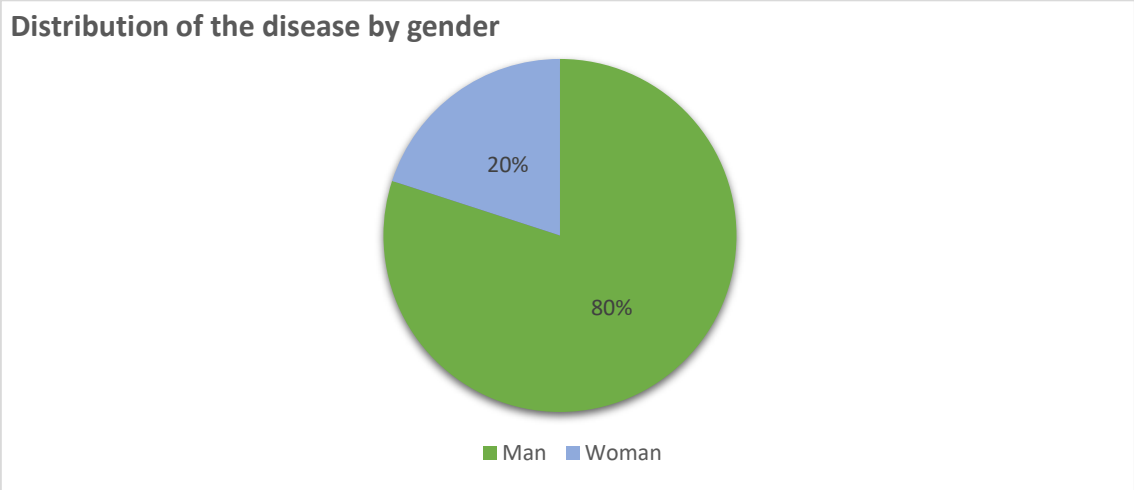

Fig 1. Distribution of patients by gender.

As you can see from the diagram, men are 4 times more likely to get sick than women.

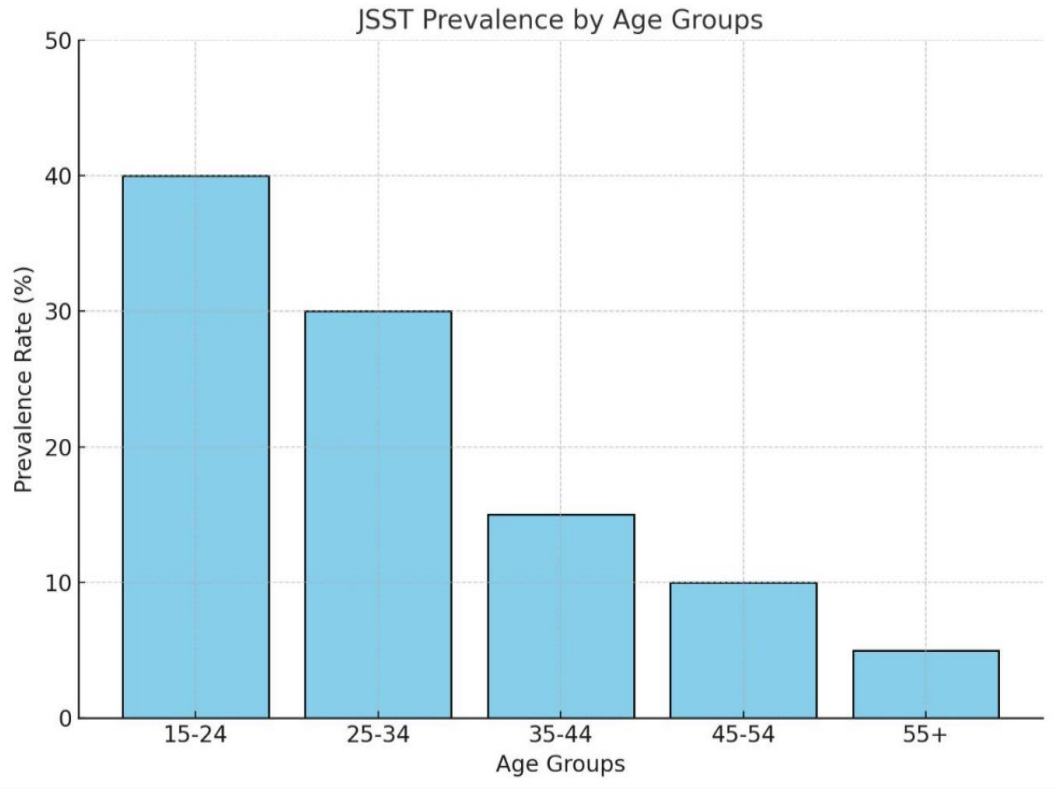

Fig 2. Average age of those affected by the disease

Also, the average age of our patients was 43 years for men and 44 years for women (**Fig 2**.). Blood tests, ECG, and ultrasound examinations were performed, the patient's life and medical history were studied, and a local examination was performed. The results showed that the patients' blood tests showed a significant increase in the number of leukocytes (**Table 1.**), an increase in the level of ESR, and during local examination, when palpating the affected area with a hand, we can see redness and swelling, as well as pain in that area, and increased sphincter tone.

Table 1.

Analysis of blood samples taken from patients

General blood test results		
Analysis indicator	**Standard**	**In patients**
Hemoglobin	Men: 130-170 gr/l	Norm
	Women: 120-150 gr/l	Norm
Red blood cell (erythrocyte) count	Men: 4,0-5,0·10^{12}/l	Norm
	Women: 3,5-4,7·10^{12}/l	Norm
Leykocyte count	Price range 4,0-9,0 x10^{9}/l	Increased (±15,0 x10^{9}/l)
Platelet count	Price range 180-320·10^{9}/l	Norm
Erythrocyte sedimentation rate (ESR)	Men: 3 — 10 mm/ hour	Increased ±12 mm/ hour
	Women: 5 — 15 mm/ hour	Increased ±18 mm/ hour

In addition, in some patients, during ultrasound examination, we observed infiltrates of various sizes in the affected area. We also observed that the patients had used various ointments, antibiotic tablets, and painkillers for 3-4 days without any effect. Based on the data obtained, these patients were diagnosed with acute paraproctitis and were referred for the operation "Opening the purulent cavity and liquidation of the internal opening" as a treatment procedure.

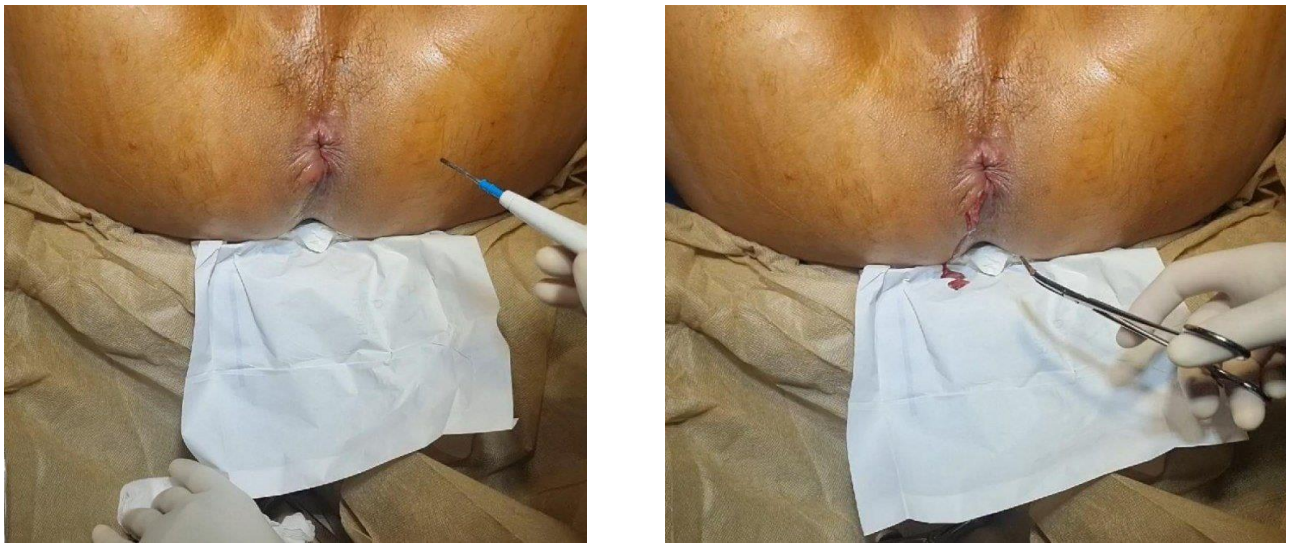

Fig 3,4. "Opening of the purulent cavity and liquidation of the internal hole" operation

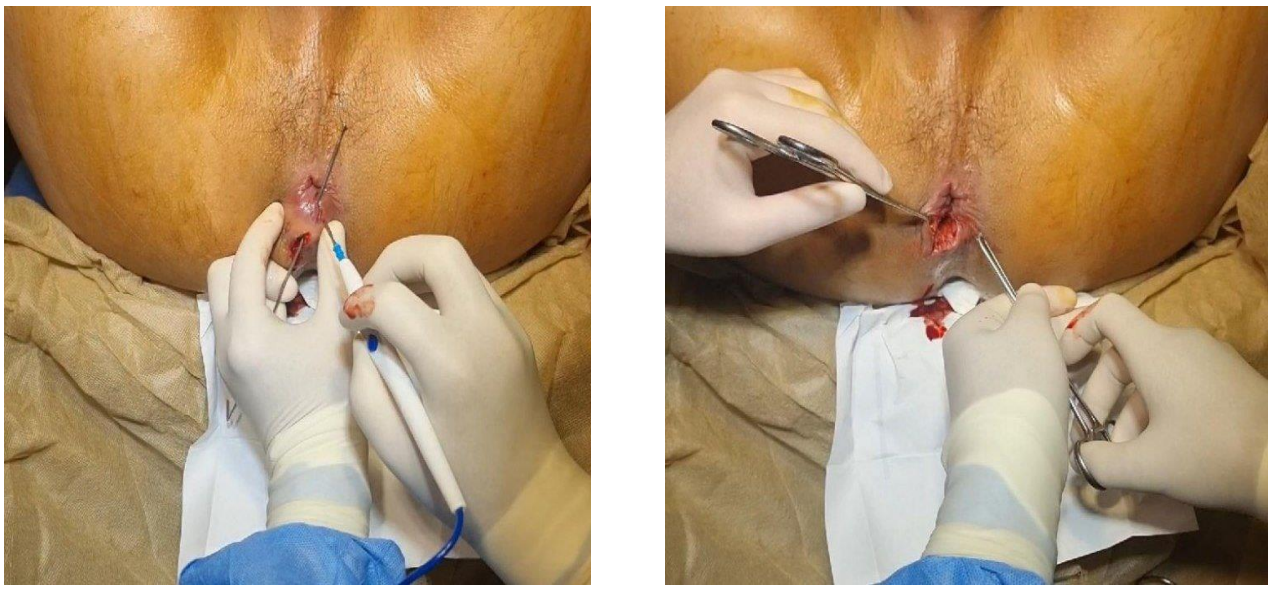

Fig 5,6. "Opening of the purulent cavity and liquidation of the internal hole" operation

The patients were prepared for the operation in accordance with the established standards. After that, the patients underwent the operation "Opening the purulent cavity and liquidating the internal hole" under spinal anesthesia. The patients were treated in the hospital for 2-9 days. In the postoperative period, local antiseptic treatment (hydrogen peroxide, betadine) was carried out 1-2 times a day.

Patients received antibiotic (ceftriaxone, levofloxacin, metrogil) and analgesic (blokium, ketonal) treatments based on daily standards, and some patients additionally received infusions of detoxification (Nacl-0.9%, reosorbilact) and antihypoxic drugs.

In these patients, the process of clearing postoperative pus and necrotic tissue took an average of 3-5 days. In some patients, the process was even faster.

During our research, we used and studied many foreign literatures, below we present the results of some of these articles for comparison:

An otherwise healthy 52-year-old male patient was admitted to our surgical department from a public hospital with sepsis following multiple drainage procedures of a perianal abscess. He presented with fever, cramping lower abdominal pain and severe pain around the area of the buttocks. The physical examination revealed tenderness upon deep palpation of the right lower abdominal quadrant with no evidence of peritoneal irritation. An extensive perianal surgical wound was revealed, indicating the previous drainage procedures were performed through bilateral ischioanal incisions. No pathology of the scrotum and groin was observed. The digital rectal examination provoked severe pain and was not diagnostic. The laboratory studies showed leukocytosis (white blood cells number, 18.000/μL; neutrophils, 97%) and an increased level of C-reactive protein (CRP, 30 mg/L). The computed tomography (CT) scan, which was performed 5 days prior to presentation, demonstrated a posterior horseshoe abscess and inflammation of the right pararectal space. Due to the patient’s indolent clinical presentation, the complex perianal surgical wound and the persistent fever despite the multiple drainage procedures, a magnetic resonance imaging (MRI) of the lower abdomen and pelvis was performed. As a new finding, an abscess cavity was revealed in the right supralevator space. Fluid collections and air were detected in the retropubic area and anterolateral extraperitoneal compartments which extended to the anterior abdominal wall.

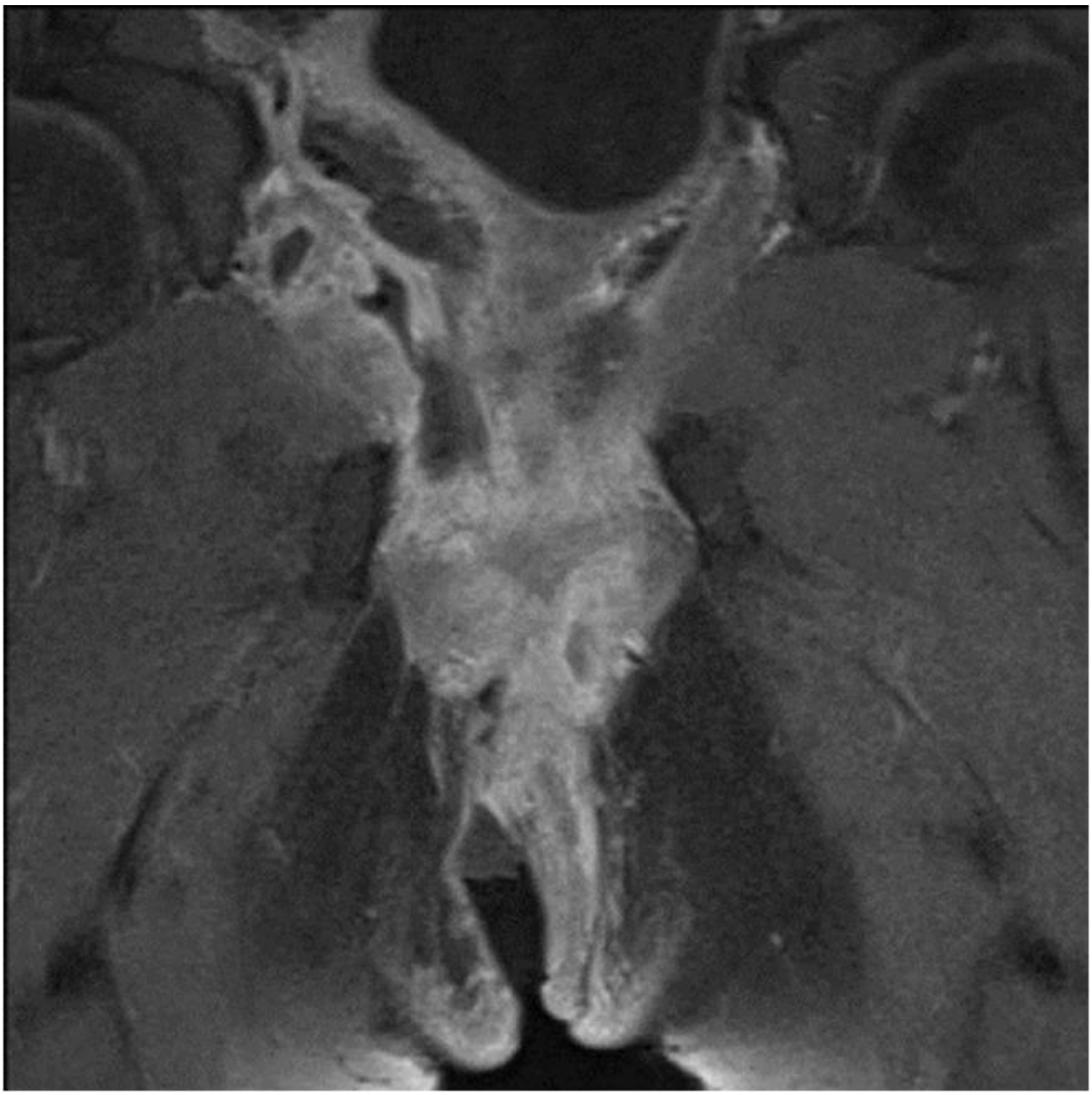

Fig. 7. Horseshoe abscess cavity involving the bilateral ischioanal spaces.

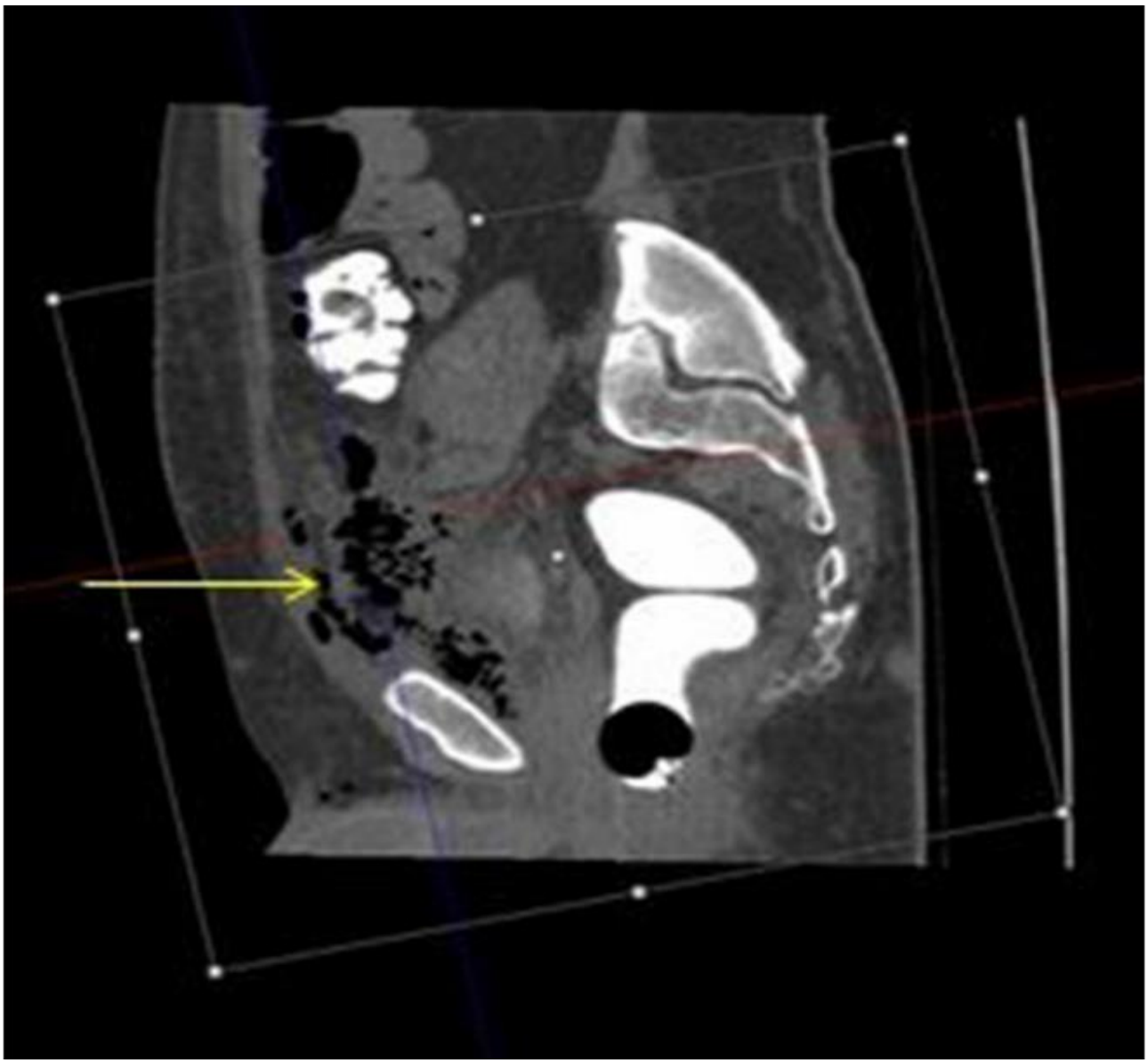

Fig. 8. Air and fluid (arrow) in the anterolateral extraperitoneal compartments.

Initial resuscitation with crystalloids and intravenous broad-spectrum antibiotics was followed by an examination under general anaesthesia. Prior to induction of general anesthesia, the patient received counsel regarding the emergency procedure, and written informed consent was obtained. Our institution's policy is that a case report does not meet the criteria of research that must be approved by the Health Sciences Institutional Review Board (IRB) therefore it is exempt from IRB review. In the operating room, thorough inspection and wash-out of the bilateral ischioanal spaces were possible through the previous incisions. Neither an additional surgical wound to the perineum nor a posterior midline sphincterotomy were performed. The anoscopic examination revealed the internal opening of a fistulous tract in the posterior midline (6 o'clock in lithotomy position). A malleable probe was placed through the internal opening to the right deep postanal cavity, excluding any other potential limbs of the fistula. A vessel loop was placed as a loose seton drainage in the fistula tract.

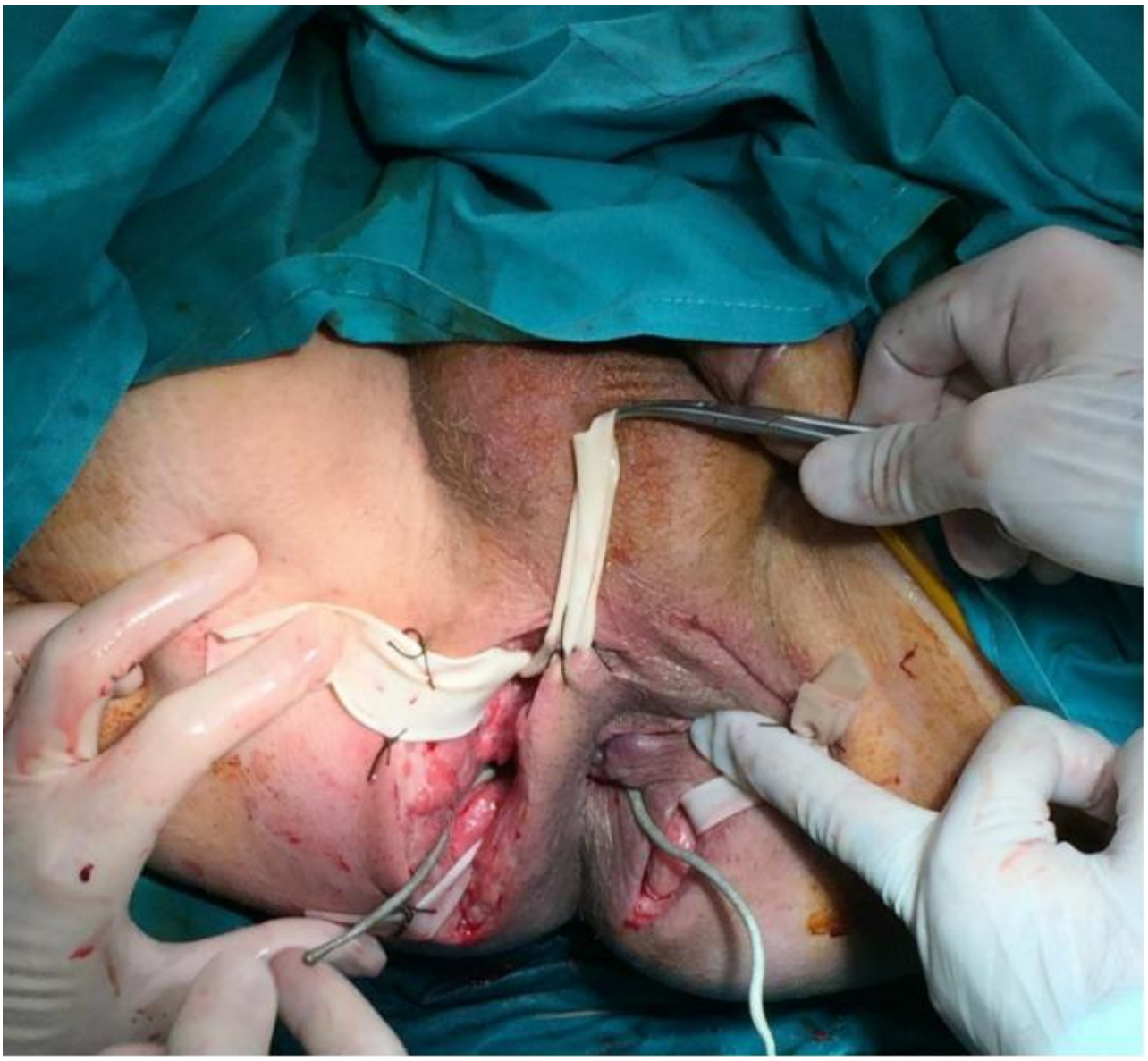

Fig 9. Drainage of the ischioanal abscesses using drainages.

The patient remained hospitalized for eight days. The fever receded on the second postoperative day. Serial irrigations through the Foley catheter and digital examinations separating the wound edges were performed. Considering the patient's progressive clinical and laboratory improvement, no further surgical exploration was performed. The patient was discharged on the eighth postoperative day in good condition. He was encouraged to clean his wounds with tap water twice a day. The drains were removed five days later. One week after the drainage procedure, a CT scan confirmed the radiologic amelioration. The inflammatory process was limited, and no abscess cavities were detected. The surgical wounds were kept open to heal by secondary intention and were found to be completely healed 8 weeks later. The seton drainage remained, tracking a transphincteric fistula-in-ano. A ligation of intersphincteric fistula tract (LIFT procedure) was performed. The patient was placed in the prone position. The vessel loop as a seton drainage was removed, and a metallic probe was inserted inside the tract. An incision was made at the intersphincteric groove. Identification and suture ligation of the tract were achieved. The wound was closed with nonabsorbable sutures. The postoperative course was uneventful. Four weeks later, closure of the loop sigmoidostomy was

performed with no postoperative complications. No recurrence was observed during a follow-up of twenty months. Neither sphincteric dysfunction nor degree of incontinence was encountered(1).

A 57-year-old male presented to the ED with diffuse pain vaguely located at the lower abdomen over the previous 24 hours. He was awake and alert and did not complain of pain in any other site. His past medical history included type 2 diabetes mellitus (DM), gout, myocardial infarction and chronic obstructive pulmonary disease. There was no history of constipation or perianal inflammation. He was a heavy smoker, his body mass index was 45 kg/m^2, and he admitted poor compliance with all of his medications. On admission he was febrile (body temperature, 39.5°C), hypertensive (blood pressure, 160/90 mmHg), slightly tachycardic (heart rate, 88 beats/minute), and hyperglycemic (blood glucose, 250 mg/dL). Physical examination revealed pain with deep palpation, no rebound tenderness, negative Giordano sign, and no signs of deep vein thrombosis in the extremities. The scrotum and groin were normal. The digital rectal examination was negative for blood but revealed mild nonspecific pain. A plain abdominal radiograph was normal, and laboratory findings consisted of elevated white blood cell count and C-reactive protein (white blood cells, 26,000/μL; neutrophils, 85%; C-reactive protein, 21.58 mg/L).

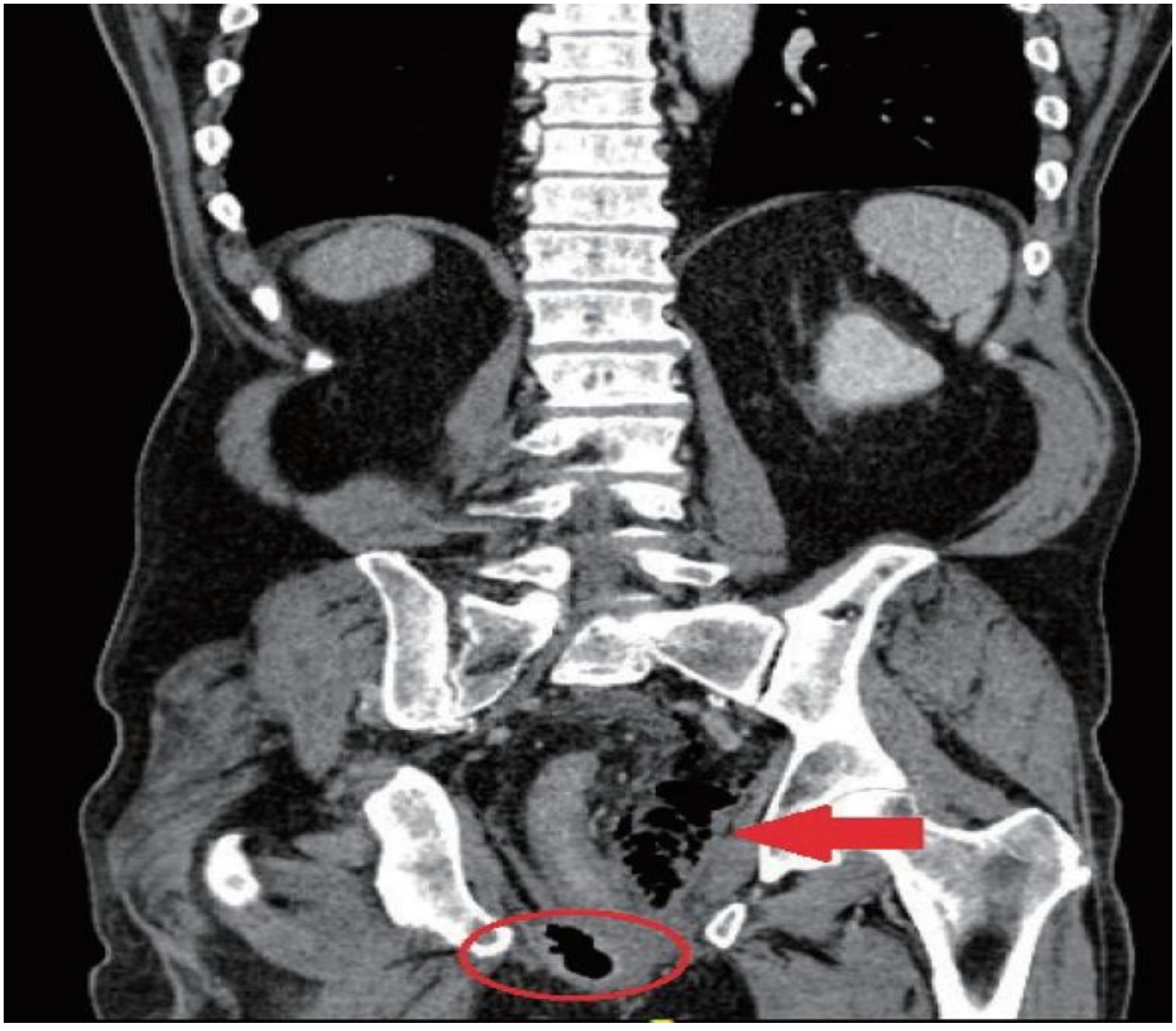

Fig. 10. Frontal view of the abscess cavity on the right side (circle) with contralateral extension to the left suprasphincteric space (arrow).

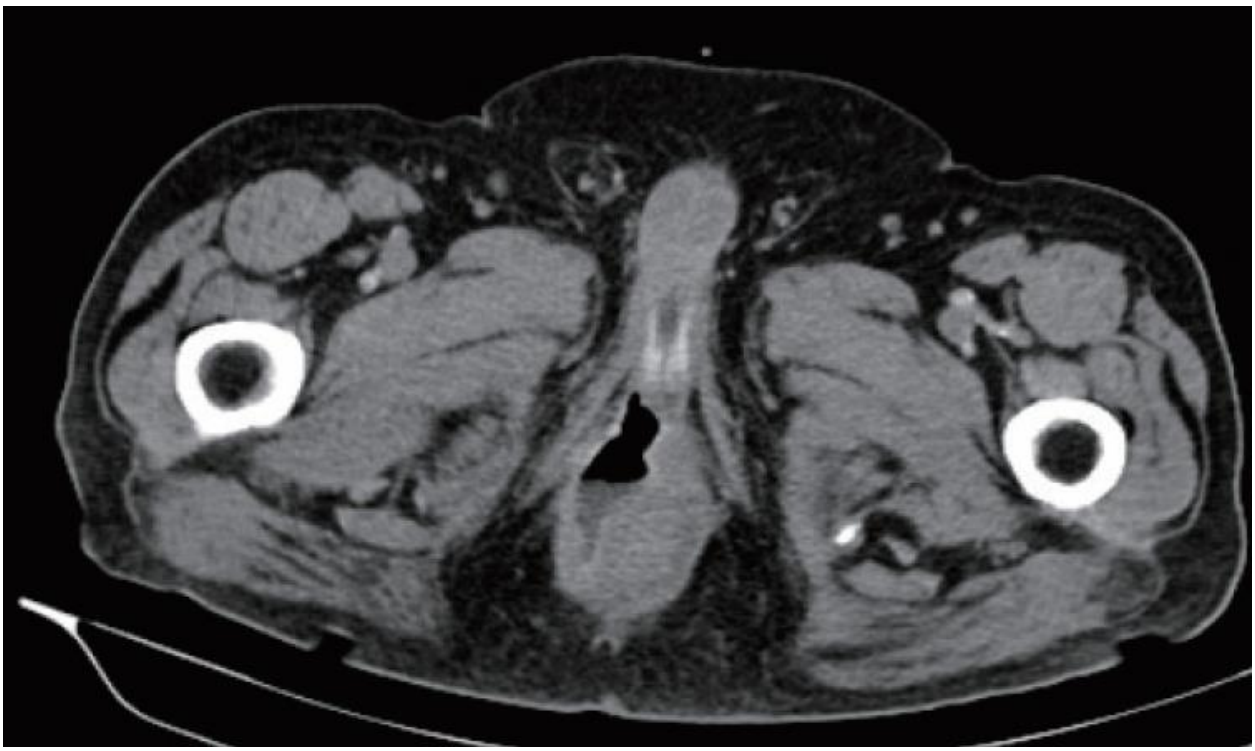

Fig. 11. Fluid-filled cavity with air in axial view.

Deep spreading perianal abscesses represent one of the most morbid entities in anorectal disease. Their rarity and insidious clinical manifestations can lead to delayed diagnosis, severe sepsis, and death. Comorbidities, such as IBD, heart disease, obesity, or DM, raise the risk of complications, and the absence of typical signs along with abdominal pain can confuse the physician in search of abdominal pathology.

Retroperitoneal abscesses usually originate from the genitourinary tract, may be idiopathic or postoperative, and infrequently involve other organs like the colon, duodenum, and pancreas. Traditionally, lumbar incision was proposed for treatment, with the transperitoneal approach being the least successful, in an overall mortality background of 26% highly associated with critically ill patients and delayed diagnoses (9).

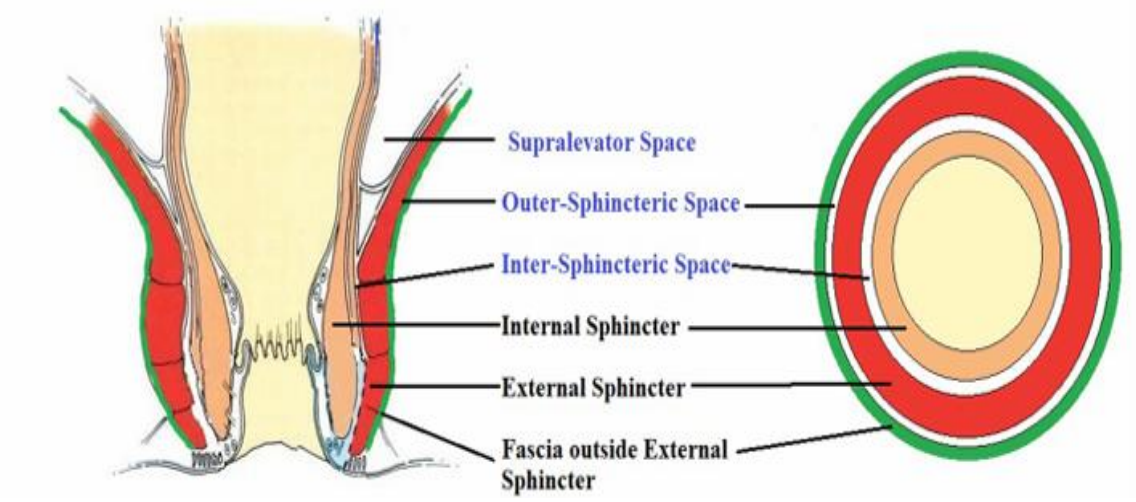

Fig. 11. Schematic diagram showing intersphincteric and outer-sphincteric spaces (8).

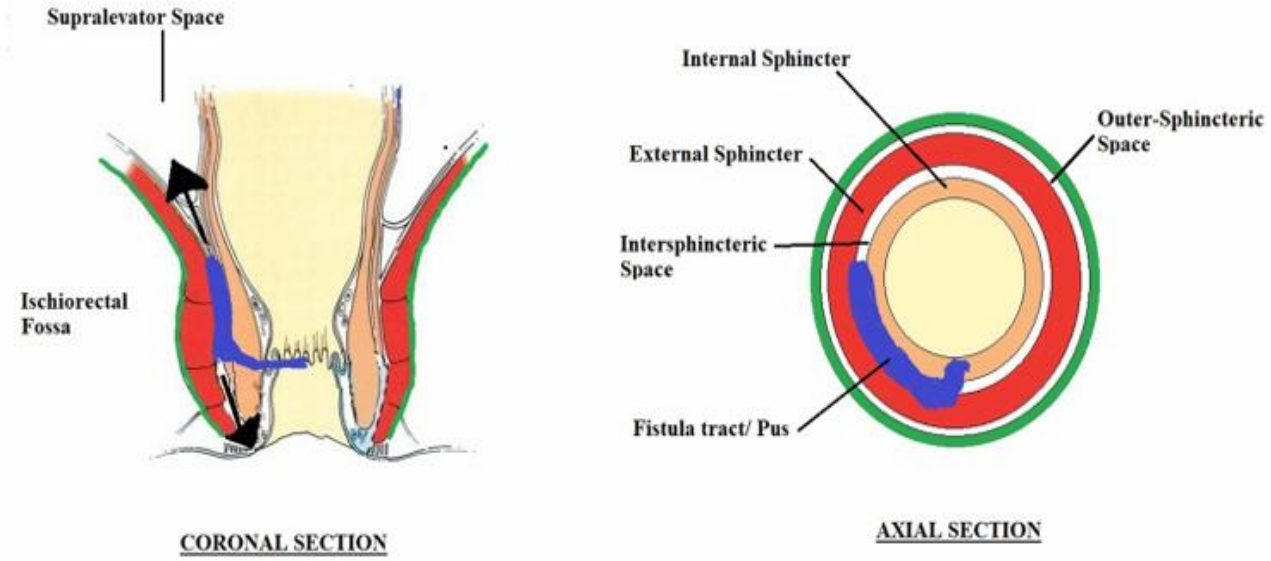

Fig 12. Schematic diagram highlighting abscess/fistula tract in the intersphincteric space and its propensity to spread to supralevator space (8).

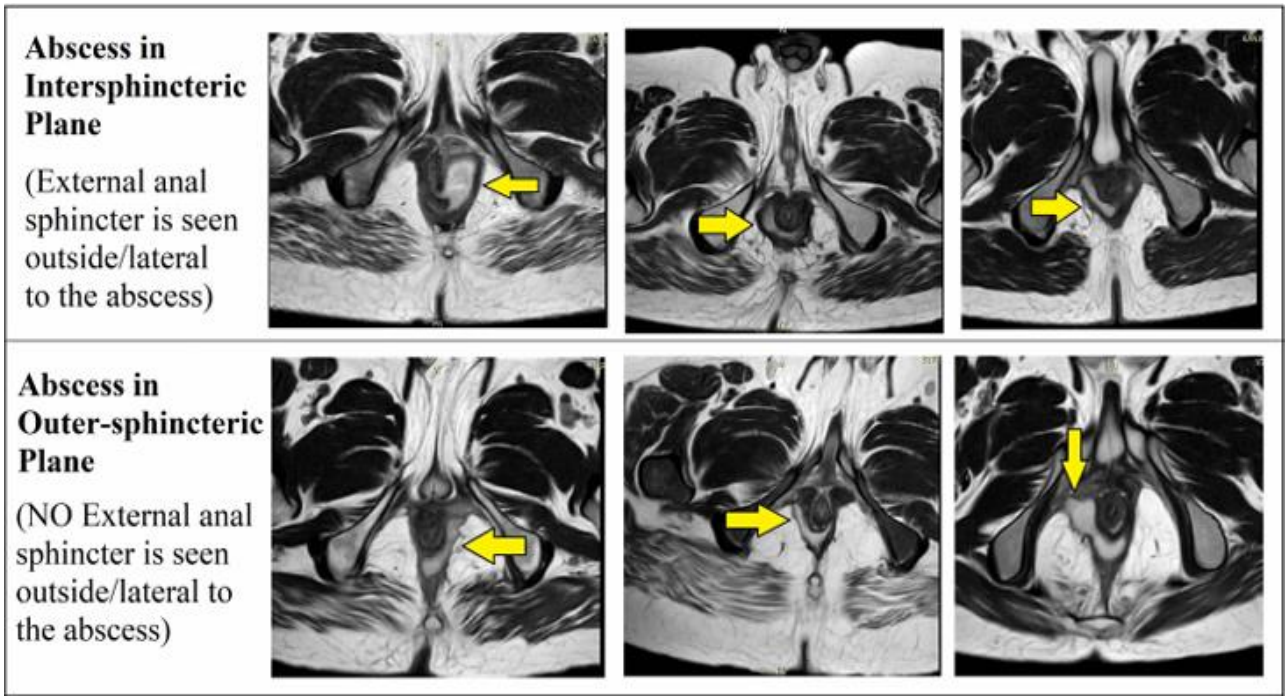

Fig 2. Upper panel: Abscess in the intersphincteric space (external sphincter muscle can be seen lateral to the abscess). Lower panel: Abscess in the outer-sphincteric space (external sphincter muscle cannot be seen lateral to the abscess and the abscess is juxtaposed to the fat in ischiorectal fossa) (8).

Conclusion. In patients with acute paraproctitis, in addition to local antiseptic and general antibacterial therapy, the use of detoxification, antihypoxic, and tissue metabolism-improving drugs further increases the effectiveness of treatment. One of the main aspects is the correct and early diagnosis of the disease and successful surgery, which allows the process to be uncomplicated.

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COMPARISON OF THE EFFECTIVENESS OF TRADITIONAL AND DIFFERENTIATED CONSERVATIVE TREATMENT METHODS FOR AVASCULAR NECROSIS OF THE FEMORAL HEAD FOLLOWING COVID-19 INFECTION

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Abstract. *Background: Avascular necrosis (AVN) of the femoral head is an ischemic bone disease that can progress to joint destruction. Post-COVID-19 patients are increasingly being diagnosed with AVN due to virus-induced vascular damage. Traditional treatments often fail to target the altered microvascular environment caused by COVID-19. Objective: To evaluate the clinical and radiological outcomes of a new combination treatment for AVN in post-COVID patients. Methods: A retrospective cohort study was conducted with 198 patients diagnosed with MRI-confirmed Stage 1–3 AVN of the femoral head post-COVID infection. Patients were divided into two groups: conventional therapy (n = 90) and novel combination therapy (n = 108). Clinical, radiographic, and quality-of-life outcomes were assessed over 6 to 18 months. Results: The main group had lower femoral head collapse (10.2% vs. 37.8%), reduced surgical intervention (2.8% vs. 6.7%), and significantly improved SF-36 quality of life scores. MRI scans indicated better structural preservation, and VAS scores for pain improved more markedly in the main group. Conclusion: This novel multimodal treatment combining bisphosphonates and hirudotherapy significantly improves outcomes in AVN following COVID-19, offering a promising non-surgical alternative for early-stage disease.*

Keywords: *Avascular necrosis, COVID-19, bisphosphonates, hirudotherapy, femoral head, osteonecrosis, vascular injury.*

Introduction. Avascular necrosis (AVN), also known as osteonecrosis, is a condition marked by the progressive death of bone tissue due to impaired blood supply to the bone tissue. The femoral head is the most common site affected, leading to joint degeneration and disability if left untreated [2, 4, 6]. AVN is often associated with conditions like long-term corticosteroid use, alcohol abuse, trauma, and systemic diseases such as sickle cell anemia and lupus [3, 7, 9]. However, the recent surge in AVN cases following COVID-19 infection has raised new concerns among clinicians [1, 13, 18].

Unlike the traditional AVN pathogenesis, which frequently involves long-term corticosteroid use, post-COVID AVN has been observed even in patients with minimal to no corticosteroid exposure [11, 19]. This suggests that the SARS-CoV-2 virus itself might play a critical role in AVN's development, likely through mechanisms like endothelial dysfunction, hypercoagulability, microthrombosis, and direct vascular injury [5, 21, 25]. The COVID-19 virus induces endothelial inflammation, which disrupts vascular integrity, leading to microvascular thrombosis, ischemia, and subsequent bone necrosis [21, 24].

As AVN is becoming more common in post-COVID patients, the traditional treatments, i.e., corticosteroids, NSAIDs, bisphosphonates, and rehabilitation, are ineffective [15, 19, 22]. As bisphosphonates inhibit osteoclastic activity and stop bone loss by not functioning at microvascular damage at the fundamental level, they have also failed in most cases [17, 19, 21]. Medicinal leech therapy, or hirudotherapy, has been suggested as a novel method of improving microcirculation, removing venous congestion, and inducing neovascularization. These actions are all significant in the advancement of bone healing as the reestablishment of blood supply is critical in the fight against ischemia [18, 23]. The objective of the current research is to assess the effect of new multimodal

treatment using bisphosphonates and hirudotherapy on the AVN treatment in post-COVID patients [2, 23].

We hypothesize that this treatment will be more effective than standard treatment in clinical, radiological, and quality-of-life scores by affecting bone metabolism as well as vascular damage.

Materials and methods.

Study Design and Setting

This retrospective cohort study was conducted at Tashkent Medical Academy between January 2021 and December 2024. Data were collected from orthopedic, radiology, and rehabilitation departments. Patients diagnosed with post-COVID AVN of the femoral head were enrolled after ethical approval from the Institutional Review Board.

Inclusion Criteria:

‣ Age between 18 and 75 years
‣ SARS-CoV-2 IgG positive (confirmed history of COVID-19)
‣ MRI-confirmed AVN of the femoral head (Ficat-Arlet Stage I–III)

Exclusion Criteria:

‣ Previous hip surgery or joint replacement
‣ Severe systemic illness or contraindications to bisphosphonates
‣ Incomplete follow-up data or inability to attend follow-up visits

Patient Groups

Control Group (n=90): Standard care consisting of NSAIDs for pain management, corticosteroids (if indicated), systemic anticoagulants, and vitamin D3 supplementation.

Main Group (n=108): Bisphosphonates (oral alendronate 70 mg weekly), vitamin D3 supplementation, Hirudotherapy at the hip 3 times every 10 days, Nutritional and anti-inflammatory support

Outcome Measure

• Radiological assessment: MRI (T1 and STIR sequences) at baseline and at 6, 12, and 18 months
• Pain: Visual Analogue Scale (VAS)
• Function: Timed Up and Go (TUG) test
• Quality of life: SF-36 questionnaire
• Need for surgical intervention: Necessity for hip replacement

Results.

a. Radiological Outcomes (refer to table 1)

Femoral head collapse: Main group: 10.2%, Control group: 37.8%

Progression to Stage 3 AVN:

Main group: 19.4%

Control group: 51.1%

Table 1.

Radiologic outcomes

Stages according to ficat and arlet classification	Total (N)	Number of patients showing Radiographic Progress (%)	Number of patients showing Radiographic collapse (%)	Number of patients undergoing surgery (%)
Main Group (n=108)	108	21 (19.4%)	11 (10.2%)	3 (2.8%)
Stage 1	16	9 (56.3%)	1 (6.3%)	0
Stage 2	81	10 (12.3%)	10 (12.3%)	0
Stage 3	11	2 (18.2%)	0	3 (27.3%)

Control group (n=90)	90	15 (16.7%)	34 (37.8%)	6 (6.7%)
Stage 1	14	7 (50%)	2 (14.3%)	0
Stage 2	67	7 (10.4%)	26 (38.8%)	0
Stage 3	9	1 (11.1%)	6 (66.7%)	6 (66.7%)

b. Pain and Function

VAS Score

Main group: 7.2 → 1.6 (improvement of 5.6 points)

Control group: 7.1 → 3.9 (improvement of 3.2 points)

c. SF-36 Quality of Life Score

Main group showed significant improvements in all domains, especially in physical functioning and pain reduction.

d. Surgical Outcome

Main group: 3 patients (2.8%) required surgery

Control group: 6 patients (6.7%) required surgery

Discussion. There is ample evidence in this research supporting the therapeutic benefits of the combination of bisphosphonates and hirudotherapy in the treatment of AVN following COVID-19 infection. The results indicate that this multimodal treatment not only preserves femoral head structure but also improves pain, function, and quality of life compared to conventional therapy [6, 9, 15]. The significantly reduced incidence of collapse of the femoral head and advancement to later phases of AVN in the main group suggests that bisphosphonates, being inhibitors of osteoclast-mediated bone resorption, play a pivotal role in stabilizing the dead bone [22].

Apart from bisphosphonates, hirudotherapy offers extra benefit with the improvement in blood supply and ischemic injury prevention to bone tissue. The application of medicinal leeches to the injured region enhances venous return, prevents thrombosis, and stimulates the development of new blood vessels, essential for healing the tissue [17, 23, 25]. This new combination therapy targets both the bone and vascular aspects of post-COVID AVN, treating the pathophysiology of the condition instead of symptomatic improvement.

The significant improvement in VAS and TUG scores signifies that patients on the combination therapy exhibit amazing reduction in pain and functional impairment, leading to increased mobility and independence. The quality of life improvement, as reflected by SF-36, is also the global benefits of this therapeutic modality, which emphasize the need for addressing physical as well as psychological recovery issues [13, 19]. These are consistent with recent studies reporting that post-COVID complications, particularly vascular and musculoskeletal, have to be addressed by managing them through protocols for the ischemic and inflammatory components of the disease. Our study builds on the hypothesis that early use of bisphosphonates and hirudotherapy may be a non-surgical procedure of joint replacement in the treatment of post-COVID AVN.

Conclusion. This study proves the effectiveness of a combination of bisphosphonates and hirudotherapy for the treatment of avascular necrosis of the femoral head due to COVID-19 infection. With combined therapy of the ischemic and metabolic aspects of the disease, this new multimodal therapy significantly improves radiological, functional, and quality-of-life parameters, offering a promising new alternative to conventional therapy. This association can diminish demands for early surgery and improve late patient outcomes if started early enough, providing perhaps a new post-COVID AVN standard of care.

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COMPARATIVE EFFECTIVENESS OF A LOCALLY ADAPTED SALINE-BASED DEL NIDO CARDIOPLEGIA IN PEDIATRIC SEPTAL DEFECT REPAIR

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Abstract. Background: *In pediatric cardiac surgery, the prevention of ischemic myocardial injury remains a key factor in ensuring favorable outcomes. The cardioplegia technique selected during surgery plays a decisive role in protecting the immature myocardium in infants and toddlers undergoing correction of congenital heart defects (CHDs).*

Aim: *To evaluate and compare the incidence of early postoperative myocardial injury in children aged 12 to 36 months who underwent open surgical repair of septal congenital heart defects, depending on the type of cardioplegic solution applied-crystalloid versus a locally adapted blood-based del Nido cardioplegia.*

Study Design and Methods:

This single-center, prospective, comparative clinical study was carried out at the National Children's Medical Center (Uzbekistan) from February 2021 to December 2024. Ninety-one pediatric patients with atrial or ventricular septal defects were assigned to two treatment arms: 44 children received traditional cold crystalloid cardioplegia, while 57 were treated using a modified del Nido solution containing oxygenated blood in a 4:1 ratio. The main outcome measure was a persistent >10-fold elevation in plasma troponin I within 6 hours postoperatively and at the 24-hour mark. Additional parameters included left ventricular ejection fraction (LVEF) changes and need for inotropic support.

Findings:*The rate of significant troponin I elevation was considerably lower in the del Nido group (31.3%) than in the crystalloid group (62.5%; $p < 0.001$). Although both groups demonstrated a postoperative decline in LVEF, the reduction was markedly less in the del Nido group (18% vs. 30.7%), suggesting more efficient myocardial protection.*

Conclusions:*The use of a blood-enhanced del Nido cardioplegia formulation demonstrated clear clinical advantages over crystalloid cardioplegia in pediatric patients undergoing septal defect repair, resulting in reduced biochemical markers of myocardial injury and better preservation of ventricular contractility in the early postoperative period.*

Keywords: *Myocardial protection, pediatric heart surgery, del Nido cardioplegia, ischemia-reperfusion injury, congenital heart disease.*

Introduction. Myocardial protection during pediatric cardiac surgery remains one of the most critically discussed challenges in contemporary cardiac practice. The diversity of cardioplegic strategies and the continuous development of modified solutions reflect the ongoing search for optimal methods to minimize ischemia-reperfusion injury during procedures requiring cardiopulmonary bypass (CPB). As the complexity and duration of congenital heart defect (CHD) repairs increase, so does the need for cardioplegic formulations capable of maintaining myocardial integrity during prolonged periods of asystole and ischemia [3].

Effective intraoperative myocardial protection significantly impacts not only perioperative stability but also the long-term cardiac function and survival of pediatric patients undergoing open-heart surgery [1,2]. Current global trends show that approximately 84% of pediatric cardiac surgeons perform procedures under cardioplegic arrest, while only 16% operate on a fibrillating heart. Among those using cardioplegia, blood-based techniques remain predominant (83.5%) over crystalloid-based methods (16.5%) [7]. A previous survey by Jacob S. (2008) also revealed that 56% of surgeons preferred cold blood cardioplegia, 14% used normothermic blood cardioplegia, 14% used crystalloid

cardioplegia, 21% employed retrograde perfusion, and 16% performed surgery without any cardioplegic strategy [6].

In response to the unique metabolic characteristics of immature myocardium, researchers at the University of Pittsburgh introduced a specialized cardioplegic solution in the early 1990s, targeting intracellular calcium control, energy preservation, lactate minimization, and enhanced buffering capacity. This formula, later refined by Dr. Pedro del Nido, became widely used in pediatric settings. However, its base component—Plasma-Lyte A—is not consistently available in several Asian healthcare systems, including Uzbekistan.

To address this limitation, we developed a modified version of the del Nido solution, substituting Plasma-Lyte A with 0.9% normal saline and tailoring the composition using locally available pharmacological agents. Despite the growing clinical use of del Nido cardioplegia worldwide, there is still limited evidence linking postoperative biomarker levels, such as high-sensitivity troponin I, with echocardiographic parameters of myocardial function in young children [2-3].

This study, therefore, was designed to evaluate the clinical efficacy of our adapted del Nido formulation by analyzing a comprehensive set of metabolic and functional indicators, including serum troponin and CK-MB levels, lactate and glucose trends, CPB and aortic cross-clamp times, incidence of arrhythmias, duration of mechanical ventilation, ICU stay, and the need for inotropic support.

Objective. To assess the incidence and severity of myocardial ischemic injury in children aged 1 to 3 years undergoing open-heart surgery for septal congenital heart defects, comparing the outcomes of blood-based modified del Nido cardioplegia versus conventional crystalloid cardioplegia.

Materials and Methods. A prospective, comparative clinical study was conducted at the National Children's Medical Center in Tashkent, Republic of Uzbekistan, from February 2021 to December 2024. The objective was to assess the effectiveness of intraoperative myocardial protection in children undergoing open-heart surgery for congenital heart defects (CHDs), using either cold crystalloid cardioplegia or a modified blood-based del Nido solution.

Study Population:

The study enrolled 106 pediatric patients aged 1 to 3 years with isolated septal defects—atrial septal defect (ASD) or ventricular septal defect (VSD). All patients underwent elective surgical correction under cardiopulmonary bypass (CPB) with cardioplegic arrest.

Group Allocation:

- **Control Group (n = 45):** Received standard cold crystalloid cardioplegia.
- **Intervention Group (n = 61):** Received a modified del Nido cardioplegia composed of pharmacological agents and oxygenated blood in a 4:1 ratio.

Inclusion Criteria:

- Age between 12 and 36 months;
- Diagnosis of isolated ASD or VSD indicated for primary radical repair;
- Preoperative high-sensitivity troponin I (hs-TnI) ≤ 0.034 ng/mL;
- Absence of ischemic changes on preoperative electrocardiogram (ECG);
- No associated genetic or comorbid systemic pathology;
- Signed informed consent obtained from parents or legal guardians.

Exclusion Criteria:

- History of prior palliative CHD surgery;
- Presence of complex or non-septal congenital heart anomalies;
- Lack of parental/legal consent for study participation.

Surgical Protocol:

All procedures were performed under standardized general anesthesia. The operative technique included a median sternotomy, harvesting and tailoring of an autologous pericardial patch, and initiation of CPB through arterial cannulation of the ascending aorta and bicaval venous cannulation (superior and inferior vena cava).

Myocardial arrest was induced via antegrade administration of the cardioplegic solution through a cannula placed in the aortic root after application of the aortic cross-clamp. The target systemic temperature was maintained between 32°C and 33°C. Cardioplegic solutions were prepared by trained nursing personnel according to a standardized digital calculator protocol, maintaining strict aseptic conditions. Solutions were cooled to 2–4°C prior to administration. In the intervention group, oxygenated blood was added to the base solution following the initiation of CPB.

Post-Bypass Management:

After restoration of spontaneous cardiac rhythm and successful weaning from CPB, all patients underwent modified ultrafiltration to optimize fluid balance and hemodynamics.

The detailed composition and formulation of the cardioplegic solutions utilized in each group are provided in Tables 1 and 2.

Table 1.

Original Del Nido Cardioplegia Formulation

Ingredient	Volume (mL)	Function
Plasma-Lyte A	1000.0	Base solution: Na 140 mEq/L; K 5 mEq/L; Mg 3 mEq/L; pH 7.4
Potassium chloride (KCl)	13.0	Myocardial depolarization
Sodium bicarbonate 8.4% ($NaHCO_3$)	13.0	pH buffer
Magnesium sulfate 50% ($MgSO_4$)	4.0	Calcium channel blocker, enhances myocardial recovery
Lidocaine 1%	13.0	Sodium channel blocker, hyperpolarizing agent
Mannitol 20%	16.3	Osmotic agent, scavenger of free radicals

Table 2.

Composition of Cardioplegic Solutions Used in the Study

Ingredient	Crystalloid Cardioplegia (CC)	Modified del Nido Solution	Function
Sodium chloride 0.9% (NaCl)	500.0 mL	500.0 mL	Base solution
Potassium chloride 4% (KCl)	32.5 mL	32.6 mL	Myocardial depolarization
Sodium bicarbonate 4% ($NaHCO_3$)	13.8 mL	14.4 mL	pH buffer
Magnesium sulfate 25%	4.0 mL	4.2 mL	Calcium channel blocker
Lidocaine 2%	3.25 mL	3.4 mL	Sodium channel blocker, stabilizes membrane potential
Mannitol 15%	11.5 mL	11.5 mL	Osmotic diuretic, free radical scavenger
Glucose 40%	2.5 mL	—	Energy substrate (present only in CC solution)
Oxygenated autologous blood	—	142.0 mL	Oxygen carrier, added in a 1:4 ratio (blood:solution)

We also developed a custom electronic calculator for cardioplegic solution formulation, which enables rapid and precise computation of the required drug volumes. This tool minimizes reagent overuse and allows for individualized volume adjustment based on the patient's body weight.

Table 3.

Electronic Calculator for Modified Del Nido Cardioplegia Composition

Component	Concentration (mg/mL)	Volume (mL)
Sodium chloride 0.9%	7.947	**200.0**
Mannitol 15% (150 mg/mL)	3.044	4.6
Lidocaine 2% (20 mg/mL)	0.122	1.4
Magnesium sulfate 25% (250 mg/mL)	1.867	1.7
Sodium bicarbonate 4% (40 mg/mL)	1.020	5.8
Potassium chloride 4%	2.304	13.0
Mix the prepared volume by shaking 3 times	4 parts	226.5
Add oxygenated blood (mL)	1 part	57.0
Administer cold (6–8°C) at a dosage of 20 mL/kg, not exceeding 100 mmHg	Total: 5 parts	283.0

Specify volume of NaCl 0.9% for final solution preparation

Endpoints and Outcome Measurements

Primary Endpoint:

The primary clinical endpoint was defined as a >10-fold increase in serum troponin I concentration at 6 hours following surgery that persisted through the 24-hour mark. This biochemical finding was interpreted in conjunction with the diagnosis of **myocardial injury syndrome**, which was established based on the following criteria:

- Sustained elevation of troponin I (>10× upper reference limit) at both 6 and 24 hours postoperatively;
- Emergence of pathological Q waves or complete left bundle branch block (LBBB) on the postoperative electrocardiogram;
- At least a 50% reduction in global longitudinal strain (GLS) of the left ventricle, as assessed via transthoracic echocardiography (TTE), relative to baseline preoperative values.

Biomarker Assessment:

Cardiac-specific biomarkers—including high-sensitivity troponin I and creatine kinase–MB (CK-MB)—were quantified using immunofluorescence-based assays (NT-proBNP, Finecare) processed on the WONDFO Finecare III Plus analyzer. Measurements were obtained at four time points: preoperatively, and at 6 hours, 24 hours, and 72 hours (day 3) following surgery.

Reference Ranges:

- Troponin I: 0.00–0.10 ng/mL
- CK-MB: 0.00–5.00 ng/mL

Echocardiographic Monitoring:

Transthoracic echocardiography was performed using a Vivid T8 ultrasound system (General Electric Healthcare, USA). Examinations were conducted at baseline (preoperatively), and postoperatively at 6 hours, 24 hours, and on postoperative day 10. Left ventricular function was assessed, with specific focus on global longitudinal strain (GLS) and ejection fraction.

Statistical Analysis

All tabulated data are presented as mean ± standard deviation (M ± σ), where *M* represents the arithmetic mean and *σ*denotes the standard deviation. The analysis of differences between groups was conducted using **nonparametric statistical methods**, considering the non-normal distribution of several variables.

Group comparisons for independent samples were performed using the **Mann–Whitney U-test**. The Wilcoxon–Mann–Whitney *W*-statistic was calculated according to the formula:

W=min⁡(∑Ri,∑Si)W=min(∑Ri,∑Si)

where:

• Ri- denotes the ranks of the sample with the lower rank sum,
• Si- denotes the ranks of the sample with the higher rank sum.

Statistical significance was determined by comparing the smaller rank sum to critical *W*-values from standard reference tables. A *p*-value < 0.05 was considered statistically significant.

Correlation between independent variables was assessed using the **Spearman rank-order correlation coefficient (r_s)**, calculated as follows:

rs=1−6∑(r1−r2)2n(n2−1)rs=1−n(n2−1)6∑(r1−r2)2

where ∑(r1−r2)2∑(r1−r2)2 is the sum of squared differences between paired ranks.

The strength of association was interpreted as follows:

• r>0.7r>0.7: strong correlation,
• 0.3<r≤0.70.3<r≤0.7: moderate correlation,
• r≤0.3r≤0.3: weak correlation.

All statistical computations were performed using **Microsoft Excel 2019** and **IBM SPSS Statistics version 26**. The methodology and interpretation principles were guided by Rebrova O.Yu., *Statistical Analysis of Medical Data*, 3rd ed., Moscow: Media Sfera, 2006

Table 4.

Preoperative Clinical and Demographic Characteristics of Patients (M ± SD)

Parameter	Crystalloid Group (n=45)	Del Nido Group (n=61)	p-value
Length of hospital stay, days	25.8 ± 11.5	13.3 ± 5.1 ***	< 0.001
Mechanical ventilation time (hrs)	26.8 ± 10.7	20.3 ± 8.3 ***	< 0.001
Age, years	2.2 ± 0.9	1.69 ± 0.69 ***	< 0.001
Height, cm	86.3 ± 8.5	81.6 ± 7.1 ***	< 0.001
Weight, kg	11.7 ± 2.5	10.6 ± 3.3 **	< 0.01
Body surface area (BSA), m²	0.53 ± 0.08	0.49 ± 0.08 **	< 0.01
Body mass index (BMI), kg/m²	23.8 ± 6.9	25.9 ± 8.0	n.s.

Table 5.

Intraoperative Parameters in Study Groups (M ± SD)

Parameter	Crystalloid Group (n=45)	Del Nido Group (n=61)	p-value
Total anesthesia time, hours:min	3:50 ± 0:53	3:02 ± 0:32 ***	< 0.001
Surgical time, hours:min	2:56 ± 0:44	2:09 ± 0:29 ***	< 0.001
Cardiopulmonary bypass duration (CPB), minutes (t IK)	67.9 ± 32.5	50.1 ± 18.6 ***	< 0.001
Aortic cross-clamp time, minutes (t Ao SS)	43.1 ± 24.4	31.8 ± 15.5 **	< 0.01
CPB duration after aortic unclamping, minutes	13.5 ± 5.1	9.53 ± 4.19 ***	< 0.001

Table 6.

Cardioplegia Delivery Parameters in Study Groups (M ± SD)

Parameter	Crystalloid Group (n=45)	Del Nido Group (n=61)	p-value
Volume of first cardioplegia dose, mL (V_1)	251.9 ± 60.7	229.1 ± 58.1 *	< 0.05

Volume of second (repeat) dose, mL (V_2)	114.4 ± 24.1	101.0 ± 26.1	n.s.
Total volume of solution administered, mL (*V_total*)	295.1 ± 79.9	235.7 ± 61.5 ***	< 0.001
Volume per kilogram of body weight, mL/kg (*V/weight*)	25.6 ± 6.1	23.0 ± 5.5 *	< 0.05
Volume per minute of CPB duration, mL/min (*V/t_CPB*)	5.1 ± 2.37	5.3 ± 2.3	n.s.
Volume per kg and CPB time, mL/kg·min (*V/(weight × t_CPB)*)	0.44 ± 0.18	0.51 ± 0.20 **	< 0.01
Frequency of cardioplegia administration (*number of doses*)	1.43 ± 0.64	1.07 ± 0.25 ***	< 0.001

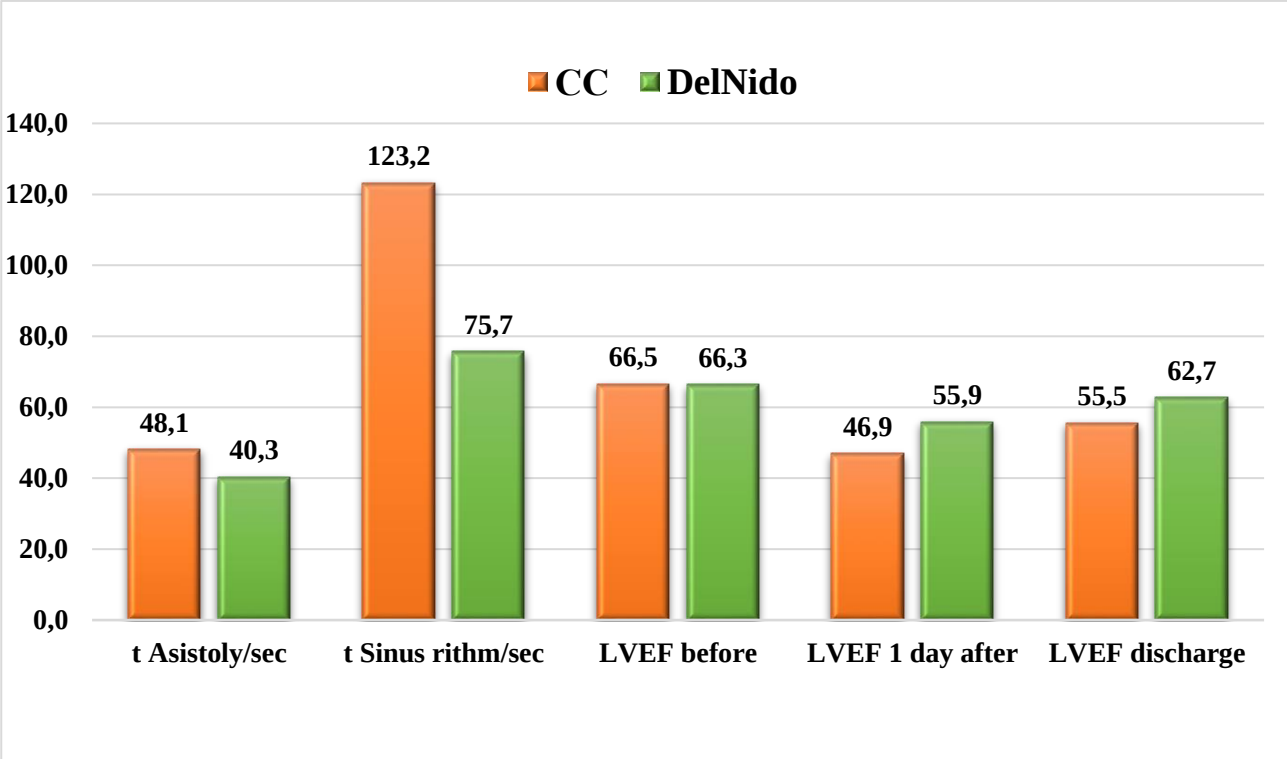

Fig. 1. Comparison of results in the CC and Del Nido Groups

Results. Baseline preoperative plasma troponin I concentrations were within the normal reference range in both the crystalloid cardioplegia (CC) and modified del Nido groups. Preoperative transthoracic echocardiography demonstrated no statistically significant differences between the groups in terms of left ventricular longitudinal mechanics or overall cardiac function.

Likewise, no significant intergroup differences were observed in intraoperative parameters such as cardiopulmonary bypass (CPB) duration, aortic cross-clamp time (myocardial ischemia period), duration of postoperative mechanical ventilation, or length of stay in the intensive care unit (ICU).

Importantly, no in-hospital mortality occurred in either group.

Troponin I Kinetics: Postoperative monitoring revealed a significant elevation in serum troponin I at 6 hours in all patients. However, the magnitude of increase was significantly greater in the CC group compared to the del Nido group (9.03 ± 1.02 ng/mL vs. 7.09 ± 0.01 ng/mL, $p < 0.001$). Notably:

- In the del Nido group, 16 patients (28%) exhibited a >10-fold elevation in troponin I at 6 hours, which persisted through 24 hours.
- In the CC group, this pattern was observed in 25 patients (56.8%).

Thus, the **primary endpoint**—defined as sustained troponin I elevation >10× upper reference limit at both 6 and 24 hours—was reached significantly more frequently in the CC group ($p < 0.001$).

By postoperative day 3, troponin I levels declined in both cohorts, with no statistically significant difference in the **rate of decline** between the groups.

Left Ventricular Function (LVEF): Postoperative echocardiographic assessment revealed marked differences in LVEF preservation:

- At 24 hours post-surgery, LVEF declined by **30.7%** from baseline in the crystalloid group.
- In contrast, LVEF in the del Nido group declined by only **18%**, indicating superior myocardial functional preservation ($p < 0.01$).

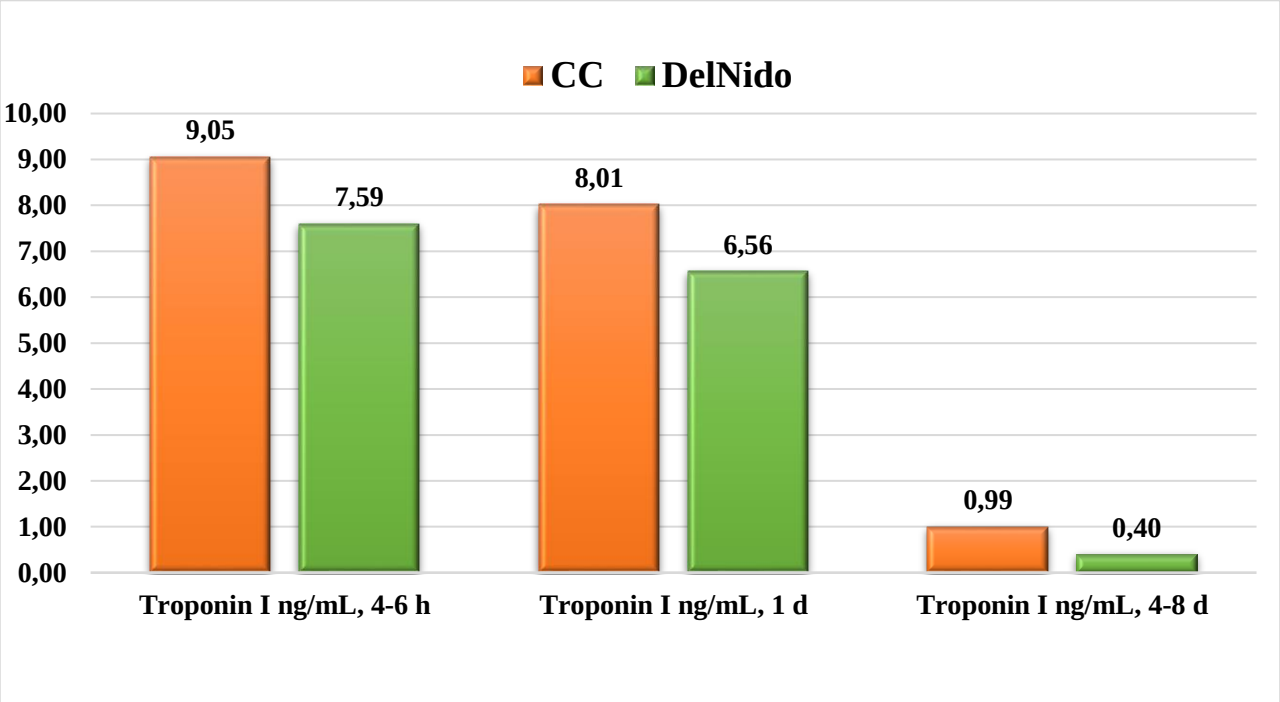

Fig. 2. Postoperative Troponin I Dynamics in the CC and Del Nido Groups

Additional Observations. No statistically significant differences were noted between the study groups in terms of postoperative serum lactate and glucose dynamics. Both groups exhibited similar metabolic responses across all monitored time points. Furthermore, no instances of new-onset complete left bundle branch block (LBBB) or clinically significant arrhythmias were observed during the postoperative period in any patient.

Discussion. This prospective clinical study compared two widely utilized cardioplegic strategies in pediatric patients undergoing surgical correction of atrial and ventricular septal defects: conventional cold crystalloid cardioplegia and a locally modified, blood-enriched del Nido solution.

Children in the del Nido group demonstrated:

- significantly lower postoperative elevations in cardiac-specific troponin I,
- more favorable preservation of left ventricular longitudinal function (assessed by echocardiography),
- and a reduced need for postoperative inotropic support compared to those who received crystalloid cardioplegia.

These findings suggest superior myocardial protection conferred by the del Nido solution in this pediatric cohort.

Although cardioplegia is a routine component of pediatric open-heart surgery, the literature continues to reflect a lack of consensus regarding the optimal formulation for young patients [11,12]. Among the proposed intraoperative markers of myocardial injury, **dynamic changes in troponin I**

have emerged as a sensitive and reliable indicator, even in pediatric populations [11]. However, pediatric-specific thresholds for prognostic interpretation remain undefined.

A study by J.A. Su et al. (2019) found that 93% of infants under one year of age exhibited elevated troponin I levels at 8 hours following CHD repair. Interestingly, only 14% of these children had persistent or rising troponin levels thereafter. This subgroup experienced a disproportionately high incidence of postoperative complications such as low cardiac output syndrome, ischemic stroke, and acute kidney injury. Although a troponin I concentration of 8.44 ng/mL at 12 hours post-surgery showed a trend toward prognostic significance ($p = 0.1$; AUC = 0.53), no definitive cutoff value was established [10].

In the present study, **21 patients (23.1%)** exhibited sustained elevation of troponin I at 24 hours, which was accompanied by pathological ECG findings and increased inotropic requirements—criteria consistent with **postoperative myocardial injury syndrome**. These outcomes are likely multifactorial, reflecting the cumulative effects of direct surgical trauma, ischemia–reperfusion injury, and systemic inflammatory responses induced by cardiopulmonary bypass (CPB).

Conclusion:

1. **Myocardial injury syndrome** was observed in **26% of pediatric patients** during the early postoperative period following surgical repair of atrial and ventricular septal defects. This syndrome was characterized by sustained elevation of troponin I levels beyond 24 hours, ischemic electrocardiographic changes, and the need for increased inotropic support, reflecting significant perioperative myocardial stress.

2. The application of **blood-based del Nido cardioplegia** in young children was associated with a **lower incidence and reduced severity of myocardial injury** when compared to conventional cold crystalloid cardioplegia. These findings suggest that the modified del Nido protocol may offer superior myocardial protection and should be considered a favorable strategy in the surgical management of congenital septal heart defects in early childhood.

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BALANCED AMINO ACID NUTRITION IN SEPSIS WITH ORGAN FAILURE

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Abstract. Background: *Sepsis complicated by multiple organ failure (MOF) remains a critical challenge in intensive care. Adequate nutritional support plays a key role in modulating the metabolic response and improving clinical outcomes.****Objective:*** *To evaluate the clinical efficacy of parenteral nutrition enriched with balanced amino acid solutions in patients with sepsis and MOF compared to standard formulations.****Methods:*** *A total of 80 postoperative patients with sepsis and MOF were enrolled. The intervention group (n=43) received parenteral nutrition with balanced amino acids (Gepa, Nefro), while the control group (n=37) received standard amino acid solutions. Biochemical, hemodynamic, and clinical parameters were assessed over 14 days.****Results:*** *Patients receiving balanced amino acids showed earlier reductions in catabolism, improved protein metabolism (albumin, transferrin levels), lower inflammatory markers (CRP, fibrinogen), and better SOFA/APACHE II scores by day 14. Duration of mechanical ventilation and time to gastrointestinal recovery were shorter.****Conclusion:*** *The inclusion of balanced amino acids in parenteral nutrition significantly improved clinical outcomes in septic patients with MOF, emphasizing the value of personalized metabolic support in critical care.*

Keywords: *sepsis, multiple organ failure, balanced amino acids, parenteral nutrition, intensive care, inflammatory markers, metabolic support.*

1. Introduction.

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection, often culminating in multiple organ failure (MOF) [19]. Despite advances in critical care, the morbidity and mortality associated with sepsis remain high, with MOF accounting for a significant portion of ICU-related deaths [20]. This necessitates a multidisciplinary therapeutic strategy, where nutritional support plays a central role [15].

Parenteral nutrition (PN) is essential for patients with severe gastrointestinal dysfunction or hypercatabolic states, where enteral feeding is not feasible [5]. Conventional PN often relies on standard amino acid solutions. However, critically ill patients exhibit complex metabolic derangements, including increased protein catabolism and impaired immune function [22]. Therefore, balanced amino acid solutions enriched with functional amino acids such as glutamine, arginine, and branched-chain amino acids (BCAAs) are being investigated for their potential benefits [17][4].

These amino acids play critical roles: glutamine supports gut integrity and immune defense [21]; arginine promotes nitric oxide synthesis and wound healing [13]; BCAAs regulate muscle protein synthesis and immune responses [6]. Formulations like Gepa and Nefro are designed to correct these metabolic imbalances, potentially improving nitrogen retention, modulating inflammatory responses, and accelerating recovery.

Despite promising biochemical profiles, data on their clinical effectiveness in septic patients with MOF are limited. This study aims to assess the impact of balanced amino acid-based PN on clinical and laboratory outcomes compared to standard formulations.

2. Materials and methods.

Study Design and Population: This prospective, comparative study was conducted in the Department of Anesthesiology and Reanimatology at Tashkent Medical Academy. Eighty adult patients with postoperative sepsis and multiple organ failure were enrolled between 2023 and 2024. Patients were randomly assigned into two groups: the intervention group (Group A, n=43) received

parenteral nutrition enriched with balanced amino acids (Gepa, Nefro), while the control group (Group B, n=37) received conventional amino acid-based nutrition.

Inclusion Criteria:

- Age ≥ 18 years
- Diagnosed sepsis according to Sepsis-3 criteria
- Postoperative status with evidence of MOF (≥2 organ dysfunctions)
- Expected ICU stay > 7 days

Exclusion Criteria:

- Terminal illness or expected survival < 48 hours
- Parenteral nutrition contraindications (e.g., severe hemodynamic instability)
- Pregnancy

Nutritional Protocol: Both groups received isocaloric parenteral nutrition tailored to energy needs calculated via predictive equations. Group A was administered balanced amino acid formulations (Akumin Gepa, Akumin-Nefro) for 7–14 days. Group B received standard amino acid solutions. Glucose and lipid emulsions were adjusted to maintain euglycemia and adequate energy intake.

Data Collection: Clinical data were collected at baseline and on days 1, 5, 7, 10, and 14. The following parameters were assessed:

- Hemodynamic variables (MAP, HR)
- SOFA and APACHE II scores
- Inflammatory markers (CRP, ESR, leukocyte count)
- Protein metabolism (serum albumin, transferrin, total protein)
- Energy expenditure and nitrogen balance
- Glycemic control
- Duration of mechanical ventilation and ICU stay
- Gastrointestinal recovery (bowel movement, enteral feeding initiation)

Statistical Analysis: Data were analyzed using SPSS version 26.0. Results are presented as mean ± standard deviation (SD). Differences between groups were assessed using Student's t-test or Mann-Whitney U test for continuous variables, and chi-square test for categorical data. A p-value < 0.05 was considered statistically significant.

Ethical approval was obtained from the institutional review board of Tashkent Medical Academy. Written informed consent was obtained from all participants or their legal representatives.

3. Results.

The baseline characteristics of both groups were comparable. The analysis revealed significant differences favoring Group A across multiple parameters.

3.1 Hemodynamic and Clinical Stability Group A patients had more stable mean arterial pressure (MAP) and heart rate (HR) by day 5. Systolic blood pressure improved with fewer vasopressor requirements.

3.2 Protein Metabolism and Nutritional Markers Total protein, albumin, and transferrin levels improved more significantly in Group A. By day 7, albumin levels reached 33.28 ± 0.8 g/L in Group A vs. 30.27 ± 1.2 g/L in Group B ($p < 0.05$).

3.3 Inflammatory ResponseC-reactive protein (CRP) levels decreased earlier in Group A, with values declining from 123.25 ± 14.54 mg/L to 80.65 ± 23.12 mg/L by day 14. Fibrinogen and leukocytosis also showed significant reductions.

3.4 Metabolic Expenditure and Nitrogen Balance Group A demonstrated a more rapid normalization of energy expenditure and nitrogen loss. On day 5, nitrogen loss was 22.9 ± 1.1 g/day in Group A vs. 20.9 ± 1.3 g/day in Group B.

3.5 Glycemic Control Fasting glucose levels remained within normal range in both groups, but the incidence of hyperglycemia (>8 mmol/L) was lower in Group A after day 7.

3.6 SOFA and APACHE II Scores By day 14, APACHE II scores decreased to 18.4 ± 0.54 in Group A and 20.12 ± 0.62 in Group B. SOFA scores dropped to 4.75 ± 1.6 in Group A compared to 4.91 ± 1.8 in Group B.

3.7 Gastrointestinal Function Return of bowel movements occurred earlier in Group A (3.37 ± 0.68 days) than in Group B (5.0 ± 1.02 days). Diarrhea incidence was lower in Group A (26.6% vs. 34.2%).

3.8 Length of Mechanical Ventilation and ICU Stay Duration of mechanical ventilation was shorter in Group A (10.88 ± 9.17 days) vs. Group B (11.83 ± 8.66 days). Total ICU stay followed a similar trend.

Visual representations of key comparisons are provided in Figures 1–6 and Tables 1–5 (to be inserted).

4. Discussion.

The results of this study demonstrate that balanced amino acid-based parenteral nutrition provides significant clinical advantages in patients with sepsis and multiple organ failure. Group A, receiving balanced amino acids, showed more rapid improvements in protein metabolism, inflammatory markers, and clinical severity scores compared to the control group.

Earlier normalization of serum albumin and transferrin levels suggests a faster correction of protein-energy malnutrition, which plays a critical role in sepsis prognosis. Inflammatory markers such as CRP and fibrinogen also declined more efficiently, indicating a favorable immunometabolic modulation. This is consistent with literature highlighting the immunomodulatory potential of amino acids such as glutamine and arginine [17][21][13].

Additionally, patients in the intervention group exhibited faster gastrointestinal recovery, reduced duration of mechanical ventilation, and shortened ICU stays—key outcomes associated with lower healthcare burden and mortality risk. These results support prior findings on the benefit of metabolic resuscitation strategies in sepsis [15][22].

Importantly, the lower incidence of hyperglycemia observed in Group A may reflect improved metabolic homeostasis and reduced insulin resistance, a common complication in critically ill patients receiving PN.

While both groups received isocaloric nutrition, the tailored amino acid composition in the intervention group likely enhanced nitrogen retention and facilitated faster recovery from catabolic states. Despite some overlapping trends, the earlier and more pronounced improvements in Group A emphasize the therapeutic value of balanced amino acids.

Limitations of this study include a single-center design and short follow-up period. Larger multicenter trials with extended observation are needed to confirm these results and assess long-term outcomes.

5. Conclusion.

The use of balanced amino acid-based parenteral nutrition in the complex management of patients with sepsis and multiple organ failure significantly improved clinical, metabolic, and inflammatory parameters compared to standard amino acid formulations. These findings support the implementation of metabolically targeted nutritional strategies in critical care settings.

Further research should explore long-term outcomes and cost-effectiveness of such interventions in broader patient populations.

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PATHOMORPHOLOGICAL CHANGES IN THE STRUCTURAL COMPONENTS OF PANCREATIC TISSUE IN THE OFFSPRING OF DIABETIC MOTHER RATS (LITERATURE REVIEW)

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Annotation. *In recent years, diabetes mellitus has become a widespread endocrine disorder and a significant medical and social problem for many countries. This is often associated with the high frequency of various complications of the disease (blindness, small intestine insufficiency, myocardial infarction, gastrointestinal system disorders, gangrene of the limbs, etc.). These complications, in turn, lead to loss of working capacity and disability in patients. Although damage to various organs in diabetes mellitus has been extensively studied, unfortunately, the morphofunctional condition of organs, particularly the vascular and tissue structures of the stomach, has not yet been sufficiently explored in depth. To date, the morphofunctional features and pathogenesis mechanisms of organ damage in diabetes mellitus, especially the ante- and postnatal morphogenesis of internal organs and the pathomorphological mechanisms of damage in offspring born to diabetic mothers, have not been adequately investigated. However, an in-depth study of this disease opens up opportunities to influence the outcome of complications, and to improve the quality and effectiveness of treatment.Thus, the search for solutions to these issues highlights the relevance and significance of problems in this field.*

Keywords: *Diabetes mellitus, morphology, morphometry, stomach, postnatal ontogenesis, intact rats.*

According to the World Health Organization, in 2010 the number of patients with diabetes mellitus (DM) worldwide reached 285 million, and according to expert forecasts, this number is expected to rise to 435 million by 2030. In Russia, the prevalence of DM was recorded in 3.36 million patients in 2011, fluctuating between 1.5% and 3.5% of the total population [15]. In Moscow, the incidence of DM increases by 6–8% annually, primarily due to type 2 diabetes, reflecting global trends. A notable increase in the number of pregnant women suffering from gestational diabetes mellitus (GDM) has been observed globally, ranging from 1% to 14% (average 7%), with the figure in Moscow reaching up to 4% [13]. According to official statistics, over the last decade, the incidence of DM among pregnant women in the Russian Federation increased by 20% [14]. Despite GDM being a transient condition, it significantly affects the health of both mother and fetus during pregnancy. GDM is associated with complications such as severe gestosis, preterm birth, polyhydramnios, and placental insufficiency, which in turn may cause fetal hypoxia, delivery asphyxia, trauma, asymmetric macrosomia, and impaired fetal nutrition [7,8]. Even with intensive treatment and screening, the rate of complications among newborns from GDM mothers varies between 12% and 28% [10,11]. Studies show that infants born to GDM mothers are prone to respiratory and metabolic disorders, central nervous system lesions, and a high incidence of macrosomia [12]. These complications are often linked to hormonal imbalances in the mother-fetus-newborn system. According to [2], placental insufficiency and specific features of the fetoplacental complex in GDM may disrupt the fetal hormonal profile. Chronic intrauterine hypoxia along with dishormonogenesis impairs the

differentiation and formation of fetal organs and tissues, as well as the postnatal onset of their functions. It is also known that children born to GDM mothers may exhibit health disturbances not only at birth but also later in life [7]. Although long-term consequences of GDM for future generations are understudied, reports indicate increasing cases of adolescent obesity and early onset of insulin-dependent diabetes [8]. Timely diagnosis and appropriate treatment of GDM significantly reduce pregnancy and delivery complications, and decrease the incidence of diabetic fetopathy (DF), increasing the likelihood of a healthy birth to 97–98% [5,6]. Therefore, GDM mothers and their newborns are currently under close supervision by obstetricians, endocrinologists, and neonatologists [1,3,4]. DF remains the leading cause of neonatal disorders among children born to mothers with GDM. According to [9], in infants born to women with type 1 diabetes, 71.65% exhibit early childhood hypoglycemia and hypoproteinemia, while DF-positive infants also show elevated triglycerides (TG) and low-density lipoproteins (LDL). In their first year of life, these infants present significantly higher average glycemia levels than control groups, and during the second half of the year, TG, LDL, and cholesterol levels increase markedly. An inverse correlation was observed between breastfeeding duration and cholesterol levels: the earlier breastfeeding is stopped, the higher the cholesterol level ($r = –0.44$, $p = 0.049$). According to [7], diabetes during pregnancy leads to specific fetal changes, such as increased abdominal diameter and shortened femur length. These features are more pronounced in fetuses of mothers with diabetic nephropathy. The presence of DM in pregnant women leads to a 96.6% chance of syndrome development in their offspring, and this rate rises to 100% in cases of diabetic nephropathy. Insulin deficiency reduces glucose delivery to insulin-dependent tissues, resulting in chronic hyperglycemia, glucosuria, osmotic diuresis, and dehydration. Enhanced gluconeogenesis and lipolysis lead to metabolic acidosis and weight loss. In early infancy, the high demand for insulin and unique water-salt metabolism make infants prone to rapid dehydration, while acidosis may develop slowly or remain unmanifested. Aplasia or hypoplasia of the pancreas disrupts its exocrine function, although malabsorption syndrome usually appears after DM manifests clinically.

Conclusion. Our research indicates that diabetes mellitus is a globally prevalent disease. While its clinical-functional features, pathogenesis, and pathophysiology are well-studied, the pathomorphology and morphofunctional changes it induces—especially in offspring born to diabetic parents—remain insufficiently explored. These include the morphological alterations in internal organs caused by the disease, which require further investigation.

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FEATURES OF THE ORIGIN OF FATTY LIVER DYSTROPHY IN ADOLESCENTS

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Annotation. *In this article, the influence of clinical-metabolic risk factors on the development of fatty hepatosis and the role of this disease in the deepening of obesity in the conditions of simple (exogenous-constitutional) obesity in 93 adolescents aged 17-30 years were determined. According to the results of the study, it was determined that abdominal obesity, insulin resistance, and stress are the most sensitive risk factors for the development of fatty hepatosis in adolescents. However, high specific risk factors include atherogenic dyslipidemia, hypertriglyceridemia, insulin resistance, inflammatory and prothrombotic conditions, and microalbuminuria. The frequency of fatty hepatosis among teenagers was 22%. We found out that the causes of fatty hepatosis in this age group are lack of energy, poor nutrition, and high consumption of energy products. Thus, taking into account the individual risk factors of adolescents in the early stages of fatty hepatosis, it is recommended to include drugs with hypolipidemic and hepatoprotective properties in the complex therapy for the prevention of fatty hepatosis.*

Keywords: *fatty hepatosis, body mass index, obesity, adolescents, clinical and metabolic risk factors.*

Nonalcoholic fatty liver disease **(**NAJBP)– is a disease characterized by the accumulation of triglycerides in liver cells, which progresses through three stages: fatty hepatosis, steatohepatitis, and cirrhosis. Fatty hepatosis (fatty liver) is a common disease worldwide, affecting approximately one-quarter of the general population. It is caused by poor diet, physical inactivity, diabetes, hormonal imbalances, and genetic factors. This condition can lead to liver inflammation and dysfunction [2,6].

There are no accurate statistics on the incidence of fatty liver disease among young people. However, in connection with the increase in obesity among children and adolescents, the incidence of fatty liver disease is also increasing in this age group. Factors such as obesity, poor diet, and lack of physical activity contribute to the development of fatty liver disease among young people. The prevalence of this disease has increased dramatically in recent decades. Worldwide obesity epidemic This is causing the disease to spread widely not only in adults but also in adolescents. Today, the NAJBP is based on various clinical recommendations part of metabolic syndrome is being considered as [1,8].

NAJBP has several codes (K74.6, K76.0, K73.9, K73.0) according to the International Classification of Diseases (ICD-10), which makes it difficult to account for this disease. There is no single standard for the treatment of this disease in the practice of adolescent medicine. This is mainly due to the lack of scientific studies assessing the effectiveness of drugs in the treatment of NAJBP in children and adolescents [4,10]. The use of modern ultrasound technologies is recommended for the detection of the early stages of NAJBP in adolescents [11,12], and the use of metabolic therapy in treatment is advisable [9,13].

Research objective:

The aim of this study is to determine the frequency of fatty hepatosis in young people, assess the role and influence of the main clinical-metabolic risk factors on its development, and determine its role in the development of obesity.

Research methodology and materials:

The study included 93 adolescents (18–30 years old). The study was conducted in 2024–2025 in an inpatient setting at the Central Polyclinic of the Student Campus, Tashkent city. The average age of the participants was 22 years old. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The study participants were evaluated based on the following criteria:

Age 17–30 years old

Obesity grade 1–2 (Body Mass Index (BMI): +2.0 SDS – +3.0 SDS)

Fatty liver levels

Absence of acute or congenital diseases

Not taking medication in the past month

The diagnosis of steatohepatosis was made based on the following criteria:

During an ultrasound examinationsigns of fatty liver Exogenous-constitutional obesity of I–II degree No signs of liver cell damage

Exclusion of other liver diseases

TMI (kg/m²) and waist circumference (OT, cm) measured, ultrasound examination.

Statistical analysis and discussion of results.

Statistical analysis of the results was performed using Statistica 6.0 (StatSoft, USA) and Microsoft Excel 2007 (USA). Proportion rates between groups were compared using Fisher's exact test and χ^2 (chi-square) test. Correlation was assessed using Pearson's coefficient. Relative risks, their sensitivity and specificity, and reliability ratios (LR+) were also calculated. Results were considered statistically significant at $p<0.05$.

Results and discussion.

Of the 93 young people studied, 22%, or 21, were diagnosed with fatty liver disease. Of the 22 patients with fatty liver disease, 12 had grade 1 fatty liver disease, and 9 had grade 2 fatty liver disease. In the analysis of young people by gender, 46 were men and 47 were women. Of the 46 men, 11 had fatty liver disease, or 5 had grade 1 fatty liver disease, and 6 had grade 2 fatty liver disease. Of the 47 women, 10 had fatty liver disease, or 7 had grade 1 fatty liver disease, and 3 had grade 2 fatty liver disease.

Table 1

Analysis of adolescents by gender

Gender ratio	Sex ratio of adolescents studied	Gender ratio of patients with fatty hepatosis	
		1-degree	Level 2
Male	46	5	6
Woman	47	7	3
Total	93	12	9

Of the 93 adolescents studied, 10 had grade 1 obesity and 8 had grade 2 obesity when their body mass index was measured. Of the adolescents with grade 1 obesity, 9 had grade 1 fatty liver and 1 had grade 2 fatty liver. Of the adolescents with grade 2 obesity, 8 had grade 2 fatty liver.

Table 2

Body mass index	Number	Number of people diagnosed with fatty liver disease	
		Level 1	Level 2
Underweight	13	1	0
Normal body weight	49	0	0
Excess body weight	13	2	0
Obesity level 1	10	9	1
Grade 2 obesity	8	0	8

Note: *1. The risk of developing fatty heptoses is hypertriglyceridemia, low LDL cholesterol, oxidative stress. It is associated with early risk factors such as obesity and late risk factors such as abdominal obesity, insulin resistance, and inflammatory processes.*

2. The risk of insulin resistance is 3.48 times higher, the risk of hypertriglyceridemia is 8.36 times higher, and the risk of inflammation is 3.62 times higher It turned out.

3. Ultrasound and metabolic marker evaluation are important for early detection of NAJBP.

4. Risk factors for the development of obesity-related fatty hepatosis in young children were assessed as follows: factors with high sensitivity (≥0.6), abdominal obesity, insulin resistance, stress, factors with high specificity (≥0.8). Atherogenic dyslipidemia Hypertriglyceridemia Insulin resistance Proinflammatory state Prothrombotic state Microalbuminuria

Research analysis.

The results of the analysis show that: there is a direct relationship between metabolic syndrome markers and liver density. The high relative risks of developing fatty liver disease confirm that these factors lead to liver damage. Insulin resistance, stress and proinflammatory processes are the main pathological mechanisms in fatty liver disease. The liver is a central organ of metabolic diseases and is closely related to these pathological processes. The results confirm the "interrelationship between fatty liver disease and metabolic syndrome."

Treatment and prevention measures.

To prevent fatty hepatosis, it is recommended to take the following measures:

1. Eat a healthy diet: Choose foods that are low in fat, high in unsaturated fats, and high in fiber. Limit sugar and carbohydrates. Eat fruits, vegetables, whole grains, and lean proteins.

2. Physical activity: Get at least 150 minutes of moderate or 75 minutes of vigorous physical activity per week.

3. Avoiding excess weight: Exercise regularly and eat healthily to keep your weight under control or lose excess weight.

4. Avoid alcohol: It is recommended to limit or not drink alcohol at all, as it puts an additional burden on the liver.

5. Take medications with caution: Some medications can have negative effects on the liver, so do not take medications without your doctor's advice.

6. Medical checkups: Get regular medical checkups and monitor your blood fat levels, diabetes, or symptoms of metabolic syndrome.

7. Stress Management: Use relaxation techniques to reduce stress, as excessive stress can increase fat accumulation in the body.

Conclusion:

1. Early risk factors for the development of fatty hepatosis in young people: hypertriglyceridemia, malnutrition, lack of physical activity, atherogenic dyslipidemia (decreased levels of LDL cholesterol, stress

2. Later-stage risk factors: abdominal obesity, insulin resistance, proinflammatory state.

3. In young children, markers of metabolic syndrome (hypertriglyceridemia, insulin resistance, proinflammatory process) are associated with fatty hepatosis, and it is necessary to prescribe hypolipidemic and hepatoprotective drugs in the early stages.

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CANDIDIASIS: A COMPREHENSIVE REVIEW

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Candidiasis is an opportunistic infection due to Candida, which can affect the oral cavity, vagina, penis, or other parts of the body. Identify the etiology of candidiasis medical conditions and emergencies. Untreated Candida infection carries the risk of leading to a systemic infection in which other organs can become involved and may lead to sepsis. This activity covers the presentation, examination, diagnosis, treatment, and management of this condition to enable healthcare practitioners to achieve optimal patient outcomes.

Keywords: *Candida, kandidoz, vagina, Saburo, sepsis, diagnosis, treatment.*

Introduction. Candidiasis is an opportunistic infection caused by Candida, a type of fungi. Fungi are eukaryotic organisms found in the form of yeasts, molds, or dimorphic fungi. Candida is a form of yeast. Candidiasis occurs most commonly as a secondary infection in immunocompromised individuals. Synonyms of candidiasis include candidiasis, moniliasis, and thrush. These are common inhabitants in the oral cavity, gastrointestinal tract, vagina penis, or other parts. They become pathogenic only when favorable conditions arise. It can affect the oral cavity, vagina, penis, or other parts of the body. Candidiasis affecting the mouth is commonly called thrush. It presents as white patches on the tongue, throat, and other mouth areas. Soreness and difficulty in swallowing include other symptoms associated with thrush. The vagina, when affected with Candida, is called a yeast infection [1].

Oral candidiasis can be pseudomembranous, erythematous, and chronic hyperplastic candidiasis. Pseudomembranous candidiasis is common in chronically ill patients and infants. It is presented as white, soft, slightly elevated plaques most commonly on the tongue and buccal mucosa. Plaques resemble curd and consist of tangled masses of fungal hyphae with intermingled desquamated epithelium, necrotic debris, keratin, leukocyte, fibrin, and bacteria. This white plaque, when wiped away, leaves an erythematous area.

Erythematous candidiasis is also known as antibiotic sore mouth. It occurs as a sequel to the use of broad-spectrum antibiotics or corticosteroids. The lesions present as consistently painful erythematous areas along with central papillary atrophy of the tongue. It is also known as a kissing lesion when the palate is involved and exhibits erythema due to contact with the tongue.

Chronic hyperplastic candidiasis, also known as candidal leukoplakia, presents with firm white persistent plaques on lips, tongue, and buccal mucosa. These plaques may be homogenous or nodular and persist for years. It has premalignant potential.

Candida associated lesions include denture stomatitis, angular cheilitis, and median rhomboid glossitis. Secondary oral candidiasis can also occur, which include chronic mucocutaneous candidiasis, chronic familial candidiasis, chronic localized mucocutaneous candidiasis, chronic diffuse mucocutaneous candidiasis, and candidiasis endocrinopathy syndrome.

Vaginal candidiasis presents with genital itching, burning, and a white “cottage cheese-like” discharge from the vagina. The penis is less commonly affected by a yeast infection and may present with an itchy rash. Yeast infections may spread to other parts of the body resulting in fevers along with other symptoms and become invasive rarely.

Oral candidiasis is one of the most common fungal infections, affecting the oral mucosa. The yeast Candida albicans cause these lesions. Candida albicans are among the components of normal oral microflora, and around 30% to 50% of people carry this organism. The rate of carriage increases

with the age of the patient. Candida albicans are recovered from 60% of dentate patients' mouths over the age of 60 years.

There are many forms of Candida species, which present in the oral cavity. Species of oral Candida include C. albicans, C. glabrata, C. krusei, C. parapsilosis, C.pseudotropicalis, C. stellatoidea, and C. tropicalis. Oral candidiasis may present as a variety of disease entities in both normal hosts and the immunocompromised. These include hyperplastic or atrophic (denture) candidiasis, pseudomembranous candidiasis (thrush), linear gingival erythema, median rhomboid glossitis, and angular cheilitis. It can result in a broad range of clinical manifestations ranging from mild acute superficial infections to fatal disseminated disease. Disseminated candidiasis is almost exclusively in acquired or inherited immuno-deficiencies. Superficial candidiasis is the most common form.

Etiology. Candidiasis is an opportunistic infection. Candida albicans is present in healthy persons colonizing the oropharyngeal, esophageal, and gastrointestinal mucosa. Candida albicans can cause mucosal candidiasis in these areas where they usually are present in an immunocompromised host. In patients who have leukemia, lymphoma because of the consumption of corticosteroids or cytotoxic drugs, their immunity is compromised, leading to candidal infection.

Antibiotic usage is commonly associated with candidiasis. Cancer cytotoxic chemotherapy may result in fungemia caused by Candida albicans, which develop from fungal translocation through compromised mucosal barriers. Fungal commensals in the upper and lower GI tract can transform into opportunistic pathogens due to changes in endogenous bacterial population size or composition, as well as changes in the host environment.[2] Vaginal colonization increases in diabetes mellitus, pregnancy, and the use of oral contraceptives. Oral candidiasis is very closely associated with HIV patients. More than 90% of patients with HIV present with candidiasis.

Other predisposing factors of candidiasis include TB, myxedema, hypoparathyroidism, Addison’s disease, nutritional deficiency (vitamin A, B6, Iron), smoking, poorly maintained dentures, IV tubes, catheters, heart valves, old age, infancy, and pregnancy. Xerostomia is also a predisposing factor due to the absence of protective antifungal proteins, histatin, and calprotectin.

Epidemiology. Candidiasis is more prevalent in old age and infancy. In the US, about 37% of newly born babies may be affected by thrush during the first few months of life. Children using inhaled steroids also have a higher incidence of oral candidiasis. In women, it is common during pregnancy. Thrush may be the first indication of HIV infection. Thrush is universal and is more frequent in populations with poorly nourishment. Thrush occurs equally in males and females.

Although Candida albicans is the most prevalent etiology of candidiasis, there has been a significant increase in non-Candida species in recent times. It is important to know about non-albicans species as the treatment depends on that, and certain medications like commonly used Non-albicans Candida may be resistant to fluconazole. Among the Candida species, C. albicans was the most common species (42/95; 44.21%), followed by C. lusitaniae (18/95; 18.95%), C. parapsilosis (13/95;

13.69%), C. glabrata (8/95; 8.42%), C. kefyr (6/95; 6.31%), C. famata (5/95; 5.26%), C. Africana (2/95; 2.11%), and C. orthopsilosis (1/95; 1.05%), respectively [3]. The incidence of invasive and disseminative candidiasis has been on the rise globally, and people with an impaired immune system are the most vulnerable [4].

Pathophysiology. Candida albicans cause thrush when normal host immunity is disturbed. The organism may overgrow on the oral mucosa causing desquamation of epithelial cells and accumulation of keratin, bacteria, and necrotic tissue. This debris forms a pseudo-membrane, which adheres closely to the mucosa. This membrane may rarely involve extensive areas of edema, ulceration, and necrosis of underlying mucosa.

Neonates affected with thrush are usually colonized by C. albicans during passage through the affected vagina; with an active vaginal yeast infection, the chances of development of thrush in the neonate increase.

There are three major routes by which Candida reaches the bloodstream: the most frequent route is via the gastrointestinal tract mucosal barrier, others being through an intravascular catheter and from a localized infection. Candida can pass into the bloodstream in neutropenic patients as well as in intensive care unit patients. They are also a part of the normal gut microflora, and any condition that may make a person immunocompromised can lead to candidiasis in the bloodstream. Candida growth of indwelling catheters, especially central lines, can occur at either the implantation site or the hub and lead to the next infection with Candida. Bloodstream invasion is not common from a localized infection but frequent with ascending Candida urinary tract infection associated with either intrinsic obstruction or extrinsic compression.

Vulvovaginal candidiasis may be triggered by the use of local or systemic antimicrobial therapy, and it may also precipitate recurrent episodes of disease. The exact mechanism by which antibiotics cause candidal vulvovaginitis is still unknown. Hypothetically, the pathophysiology of vulvovaginitis may be due to reduction or change of normal vaginal flora, restraints of yeast colonization, and proliferation [5].

Histopathology. Candidiasis sections present spongiotic changes in the epidermis with irregular acanthosis, mild spongiosis, and inflammatory changes. The distinguishing feature of the superficial epidermis is the presence of neutrophils in the stratum corneum and upper layers of the epidermis. A small collection of neutrophils (spongiform pustulation) may form, which resembles impetigo or psoriasis [6].

Candida albicans is a pathogenic yeast-like fungus, that grows partly as yeast and partly as elongated cells resembling hyphae which form pseudo mycelium. Candida albicans can be identified from other candida species by growth characteristics, sugar assimilation, and fermentation tests. It produces germ tubes within two hours when incubated in human serum at 37-degree celsius.

History and Physical. The patient with vulvovaginitis may present with intense itching and irritation in the vagina and vulva, a burning sensation with urination which can be mistaken for urinary tract infection, vaginal soreness, or pain, a dry erythematous rash, and a thick white cottage cheese-like discharge.

Candida also presents as an oral infection called thrush, which is a white or yellow non-scrapable rash on the tongue and mucous membranes of the mouth, or redness and soreness with cracking at the corners of the mouth. It causes pain with swallowing when it extends into the oral pharynx. It is common in infants, the elderly, and patients with a compromised immune system. Systemic candidemia causes fever, chills, hypotension, and confusion.

Laryngeal Candida infection is a rare condition. It predominantly presents in females. They usually complain of dysphonia. It largely correlates with gastroesophageal reflux or a history of usage of inhaled corticosteroids. Glottis may be affected by the presence of leukoplastic lesions [7].

Evaluation. A vaginal discharge sample can help to diagnose vaginal candidiasis by examining it under a microscope or by fungal culture in a laboratory. Under the microscope, budding yeast is visible. Oral thrush is mostly a clinical diagnosis but can also be confirmed by looking at the scrapings of the rash under the microscope. For systemic candidiasis, a blood culture is a diagnostic tool [7].

Treatment / Management. Candida infections are treated with antifungal medications such as nystatin, clotrimazole, amphotericin B, miconazole. Mild or moderate genital Candida infections can have treatment with antifungal vaginal cream. The antifungal creams come in 1, 3, or 7-day treatment. Econazole or fluconazole 150 mg orally one-time dose can also be prescribed [8].

Oral and topical treatments have similar efficacy, but oral medications are more expensive. Clinicians should avoid prescribing fluconazole in the first trimester of pregnancy [9]. For recurrent vaginal candida infections, fluconazole dosing is on days 1, 4, and 7, and then weekly for six months is given. Similar treatment can be used for oral thrush, with oral lozenges as a substitute dose form. Systemic candidiasis requires treatment with oral or intravenous antifungal medications, including caspofungin, fluconazole, and amphotericin B.

In cases of denture stomatitis, the patient should refrain from using their denture for at least two weeks along with the topical application of antifungal medication. Angular cheilitis occurs due to loss of vertical dimension. Thus, after the infection subsides fabrication of new denture prostheses with proper vertical dimensions is essential. Oral application of probiotics can serve as an adjuvant in treating oral candidiasis [10].

Differential Diagnosis. Spongiform pustulation can also present in pustular psoriasis, subcorneal pustulosis, acute generalized subcorneal pustulosis conditions. Hence, special stains should be used to exclude fungal etiology in psoriasis.

Impetigo also shows spongiform pustulation. Bacterial colonies in impetigo may be seen by using Gram stain, which GMS and PAS stains will not stain fungal forms.

Spongiform pustulation is a characteristic of tinea cruris and corporis. Special stains reveal septate hyphae without the budding yeasts of candida. The distinction can occasionally be challenging. Candida usually infiltrates the keratinized epithelium, whereas dermatophytosis usually involves only the stratum corneum.

The correct diagnosis of laryngeal candidiasis is difficult for the otolaryngologist, and a high level of suspicion is in order. This condition should also be part of the differential diagnosis in patients with predisposing factors presenting with suspected lesions [7].

Prognosis. Vaginal and skin infections, although the most common Candida infections are localized. Therefore, these can be treated with antifungal drugs to obtain complete recovery and excellent prognosis and outcomes. An untreated Candida infection can affect other organs and may lead to a systemic infection. The long-term prognosis with systemic candidiasis depends on the severity and location of the Candida infection, the general health of the infected person, and the timing of diagnosis and treatment.

Almost one-third of the patients with candidemia develop septic shock according to host factors such as age and source of the infection than intrinsic virulence factors of organisms [11].

Complications. Pregnant women have higher chances of colonizing Candida in the vagina during pregnancy [12], Vaginal candidiasis is among the common forms of fungal diseases frequently occurring in pregnant women which may lead to systemic infections in neonates, especially with low birth weight (LBW) and prematurity after delivery.

Intertrigo is a common inflammatory dermatosis affecting opposing skin surfaces that can result from Candida, under the effect of mechanical and environmental factors. It presents with pain and itching, which decreases the quality of life, leading to high morbidity. Predisposing factors, such as obesity, diabetes mellitus, and immunosuppressive conditions, facilitate both the incidence and recurrence of the disease. Candidal intertrigo is usually treated with topical application of nystatin and azole group antifungals [13].

Untreated Candida infection carries the risk of leading to a systemic infection in which other organs can become involved and may lead to sepsis. Intestinal candidiasis can occur as a sequel to oral antibiotic therapy. Bronchopulmonary candidiasis is a rare complication of pre-existing pulmonary disease. Septicemia, endocarditis, and meningitis occur as terminal complications in immunosuppressive and leukemic patients. In leukemia patients, systemic candidiasis presents as prolonged neutropenia and fever refractory to the antibiotic.

Deterrence and Patient Education. Symptoms of a yeast infection may mimic other conditions. Hence physical examination and laboratory testing are very important. The risk factors that may increase the chances of developing a yeast infection include antibiotic usage, diabetes mellitus, pregnancy, hormonal birth control, and immunocompromised conditions such as HIV, chemotherapy, or some medications. It is essential to test and diagnose accurately when symptoms are bothersome and before starting any treatment.

Enhancing Healthcare Team Outcomes. A primary care physician can easily diagnose candidiasis, but it can pose a problem when it recurs or is present in immunocompromised individuals.

For the care of such individuals, it is important to have the help of the pharmacist who will be vital in guiding the treatment of resistant or recurrent infections. Obstetrics/gynecology may also be helpful in pregnant females along with nurses who can educate them on lifestyle modification. Oral candidiasis usually occurs beneath denture-bearing areas. Thus, diagnosis and treatment of oral candidiasis are often done by the dentist. Proper oral hygiene instructions should be given to denture patients to prevent the development of oral candidiasis. The dentist should consult with the physician to find out any underlying immunocompromising situation. Nanomaterial incorporated dentures can be given to patients who are susceptible to oral candidiasis.[14]

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GENDER-SPECIFIC FUNCTIONAL PROFILES IN OUTPATIENT GERIATRIC REHABILITATION: TOWARDS A PERSONALIZED MULTICOMPONENT MODEL

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Abstract. *The article presents the results of an outpatient study on functional deficits in elderly patients, with a focus on gender differences and personalized approaches to rehabilitation. The research was conducted using a structured clinical-functional evaluation of 247 geriatric patients (135 women and 112 men) aged 60 and older. Validated scales were applied, including MMSE, MoCA, BDI, MNA, TUG, Barthel Index, and SF-36. The study included analysis of physical, cognitive, emotional, nutritional, and social impairments, stratified by sex and age. The findings revealed significant gender-related differences: women were more likely to experience depression, malnutrition, and loneliness, while men demonstrated higher rates of sarcopenia, cognitive decline, and mobility disorders. Implementation of a gender-sensitive rehabilitation model resulted in significant improvement across multiple indicators ($p < 0.05$), emphasizing the need for differentiated ambulatory care strategies.*

Keywords: *geriatric rehabilitation, outpatient care, gender differences, functional decline, sarcopenia, cognitive impairment, nutritional deficits, quality of life.*

Introduction. Modern demographic trends, characterized by increasing life expectancy and a growing elderly population, require a healthcare system shift towards preserving functional health and preventing disability. In this context, the role of outpatient services becomes particularly significant, as they serve as the first line of contact with patients and play a key role in the implementation of active aging programs.

According to the European Union Geriatric Medicine Society (EUGMS) and the World Health Organization (WHO), geriatric care should shift its focus from disease treatment to the maintenance of functional autonomy and quality of life, with special attention to the outpatient and community-based levels of care [3, 9].

Geriatric rehabilitation, as an integral part of continuous medical and social support, must consider the wide spectrum of age-related deficits and the individual characteristics of each patient [1, 6]. Ignoring gender-based differences in clinical and functional status may reduce the effectiveness of interventions, limit adherence to treatment, and diminish the preventive potential of rehabilitation programs.

This study explores the functional health profiles of older patients undergoing outpatient rehabilitation, with an emphasis on gender stratification. The goal is to identify stable patterns of functional impairment and provide a rationale for developing a personalized rehabilitation model adapted to the capabilities of outpatient care and the objectives of healthy aging.

The aim of the study. To assess gender-specific clinical and functional characteristics of elderly patients undergoing outpatient rehabilitation and to substantiate the need for a personalized approach to the prevention of age-related functional decline in ambulatory care.

Materials and Methods. The second stage of this multicenter study was aimed at profiling the clinical and functional status of elderly patients to individualize rehabilitation strategies and justify the need for gender-specific stratification in outpatient practice. The sample included 247 older adults

aged 60 to 84 years who underwent comprehensive clinical and functional assessments at the Research Institute of Rehabilitology and Sports Medicine, Samarkand State Medical University, during 2024.

Functional stratification of patients was based on integrated assessment using validated tools. The following scales were applied: Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) [7], Beck Depression Inventory-II (BDI-II) [4], and Mini Nutritional Assessment (MNA) [8]. Additionally, the Hospital Anxiety and Depression Scale (HADS), Timed Up and Go (TUG), Barthel Index, and SF-36 were used. Patient grouping was based on the principle of descriptive clustering, reflecting similarity in deficit severity. Although formal factor or algorithmic clustering methods were not applied, the identified profiles formed the basis for developing a modular rehabilitation model.

In addition to clinical scales, questionnaire data were collected to assess subjective health perceptions, motivation, and barriers to rehabilitation participation.

Statistical analysis included descriptive statistics, Student's *t*-test, Pearson's chi-square test, and correlation analysis. A significance level of $p < 0.05$ was considered statistically significant. The analysis enabled comparison of the severity and structure of functional deficits between male and female patients, identification of typical combinations of impairments, and formulation of individualized rehabilitation pathways for outpatient settings.

Results. The analysis of data obtained during the second stage of the study revealed distinct gender-specific characteristics in the clinical and functional profiles of geriatric patients undergoing outpatient rehabilitation. The structural-functional stratification conducted on a sample of 247 patients (135 women and 112 men) demonstrated marked differences in the type and combination of functional deficits between males and females.

A significant proportion of female patients exhibited an emotional-nutritional profile, characterized by moderate depressive symptoms, reduced nutritional status, and lower scores in the psychoemotional domains of quality of life. In contrast, male patients more frequently showed cognitive and somatic impairments, including reduced physical activity, spatial disorientation, and delayed motor performance.

Comparative analysis using validated scales (MMSE, MoCA, BDI, MNA, TUG, Barthel Index, SF-36) revealed statistically significant gender differences ($p < 0.05$) in cognitive functioning, nutritional condition, motor performance, and emotional state. These differences were systematic and observed both in average group values and in the frequency of extreme scores within the distributions.

Significant interscale correlations ($p < 0.05$) were found, reflecting functional links between cognitive, psychoemotional, and somatic domains. In men, a positive correlation was observed between cognitive scores (MMSE, MoCA) and physical autonomy (Barthel Index, TUG), particularly in those with chronic cerebrovascular insufficiency and hypertension. This finding suggests a synergistic progression of cognitive and somatic deficits. Among women, an inverse correlation was found between depression (BDI) and nutritional status (MNA), especially in those with osteoarthritis, type 2 diabetes, and chronic gastrointestinal disorders. These relationships underscore the gender-specific pathogenesis of aging-related impairments and highlight the need for multidisciplinary, individualized approaches.

The analysis of deficit combinations showed a high prevalence of multi-component impairments, primarily in the form of cognitive-somatic or emotional-nutritional clusters. These profiles provided a basis for patient stratification and informed the preliminary framework for a gender-sensitive, modular rehabilitation model tailored to outpatient settings.

The results supported the empirical identification of consistent functional patterns and established the foundation for designing personalized, gender-oriented strategies in age-related preventive care.

Table 1.
Associations between functional deficits and clinical conditions in geriatric patients by gender

Type of Deficit	Associated Condition(s)	Predominant Gender	Comments
Cognitive impairments	Cerebrovascular disease, hypertension	Men	Decline in MMSE and MoCA scores combined with TUG > 20 sec and low Barthel Index
Hypomobility	Ischemic heart disease, osteoarthritis	Men > Women	Motor dysfunction closely related to cardiac and orthopedic comorbidities
Depressive symptoms	Osteoarthritis, type 2 diabetes, chronic stress	Women	High BDI scores, frequent complaints of insomnia and fatigue
Nutritional deficit	Chronic gastritis, pancreatic insufficiency	Women	MNA < 17, often associated with anxiety and low vitality
Multi-deficit (cognitive-somatic)	Combination of cerebrovascular disease and hypodynamia	Men	Stable correlation between MMSE and TUG in patients with cerebrovascular disorders
Multi-deficit (emotional-nutritional)	Type 2 diabetes, gastrointestinal pathology	Women	BDI > 14 and MNA < 17 combined with low SF-36 quality of life scores

Discussion. The findings of this study underscore the importance of clinical and functional stratification of older patients as a key tool for enhancing the precision and effectiveness of outpatient rehabilitation. The identified gender differences in the prevalence and structure of functional deficits indicate the existence of stable patterns that necessitate a personalized approach during both assessment and intervention planning.

These differences are particularly relevant in outpatient care, where limited resources, brief consultations, and the high level of patient autonomy require rational and flexible intervention strategies. The impossibility of applying a universal rehabilitation template for all geriatric patients highlights the value of a modular model, in which core components are adapted according to sex, age, and dominant types of deficits.

The observed correlations between cognitive and motor impairments in men, as well as between depression and nutritional deficits in women, point to the need for integrating multidisciplinary approaches in outpatient rehabilitation programs. These gender-specific functional profiles are consistent with international findings. For example, Collerton et al. (2009) observed that women more frequently exhibit emotional-nutritional and psychosocial profiles, whereas men tend to experience cognitive and somatic impairments [2]. Similarly, Meskers et al. (2019) emphasized the importance of early detection of combined deficits and the implementation of gender-specific interventions in outpatient care settings [5].

Neglecting these gender differences may reduce the effectiveness of rehabilitation, especially in outpatient environments where continuous monitoring is often lacking. Therefore, personalized strategies based on clinical-functional profiles and gender stratification can not only improve rehabilitation outcomes but also enhance patient adherence to treatment.

The results also highlight the crucial role of outpatient facilities as primary agents in promoting active aging and preventing disability. Early identification of functional impairments, stratified assessments, and the creation of individualized rehabilitation pathways at the primary care level reduce the need for costly inpatient care and contribute to improved quality of life for older adults.

The scientific novelty of this study lies in the implementation of clinical-functional stratification of geriatric patients through descriptive clustering based on gender and disease associations. This approach enabled the identification of multi-deficit profiles and laid the groundwork for the

development of a personalized, gender-sensitive outpatient rehabilitation model suited to the realities of resource-limited healthcare systems.

Conclusion:

1. The clinical and functional stratification of geriatric patients in outpatient settings revealed consistent gender-based differences in the structure of age-associated deficits, supporting the need for individualized rehabilitation approaches.
2. It was established that men predominantly exhibit a cognitive-somatic profile characterized by reduced mobility and autonomy, while women are more likely to present with emotional and nutritional deficiencies associated with lower quality of life and depressive symptoms.
3. Identified interscale correlations and links with specific comorbidities suggest the existence of multi-deficit patterns that require comprehensive multidisciplinary management within outpatient rehabilitation programs.
4. The structural and functional profiles obtained through descriptive clustering formed the foundation for developing a personalized, gender-sensitive outpatient rehabilitation model adapted to the limited resources of primary care and the goals of active aging.
5. The findings have strong practical implications for optimizing outpatient care for older adults and can inform the design of regional disability prevention programs and health promotion strategies.

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TOXICITY ASSESSMENT OF STEM CELLS IN SOFT TISSUE DEFECTS IN EXPERIMENTAL ANIMALS

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Abstract. *The article presents an experimental analysis of cytoxicity of stem cells application in deep soft tissue defects in experimental animals (rats). The dynamics of animal weight and relative weight of internal organs also did not undergo statistically significant deviations in comparison with control and reference values, which indicates the safety of the used stem cells for the organism of experimental animals.*

Introduction. The study of stem cell properties and their influence on reparative processes in the body is one of the most urgent tasks of modern cell biology. Currently, much attention is paid to cell technologies based on transplants derived from the patient himself. The advantage is the availability of suitable non-immunogenic cellular material [1,2]. autologous mesenchymal stem cells isolated from bone marrow, adipose tissue, skin, umbilical cord and placenta have found clinical application. A large experience of their use, with positive effects, is represented by tens of millions of transplants in various diseases [3,4,5]. Mesenchymal stem cells can be isolated from various tissues - muscular, embryonic, connective [6,10]. However, obtaining mesenchymal stem cells from adipose tissue in almost any quantity from people of different constitution is considered the most promising [7,8,9].

Purpose of the study. To evaluate the cytoxicity of mesenchymal stem cells when injected in the treatment of deep soft tissue defect in experimental animals

Material and methods of research. Experimental studies were performed in accordance with the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986), in accordance with the "Rules for Conducting Work Using Experimental Animals". Preclinical studies of methods of treatment of deep soft tissue defects using stem cells to optimize regeneration were carried out.

Determination of biochemical and hematological indices of peripheral blood of experimental animals was made on the basis of accredited research laboratory (NIL) of Tashkent Research Institute of Vaccines and Sera on the basis of normative and methodological documents of the State System of the Republic of Uzbekistan.

Obtaining primary culture of rat stem cells. Primary culture of rat stem cells was obtained from adipose tissue of white mongrel rats. Laboratory rats were euthanized by decapitation after sedation with inhalation gas mixture containing isoflurane supplied through Mindray V60 ISOFLURANE anesthesia-breathing apparatus.

The removed organs and soft tissue defect areas of the animals were fixed in 10% buffered formalin solution for 24 hours. The organs after fixation were run in a histoprocessor of automatic carousel type "Thermo Fisher STP 120" (TFS, USA) for dehydration, impregnation and

paraffinization. Slices obtained on a 3-4 μm rotary microtome NM 325 (TFS, USA) were stained with hematoxylin and eosin and examined at different magnifications with an Axio Lab.A1 microscope (Carl Zeiss, Germany) and photographed with a SDPTOP digital video camera. with a SDPTOP digital video camera.

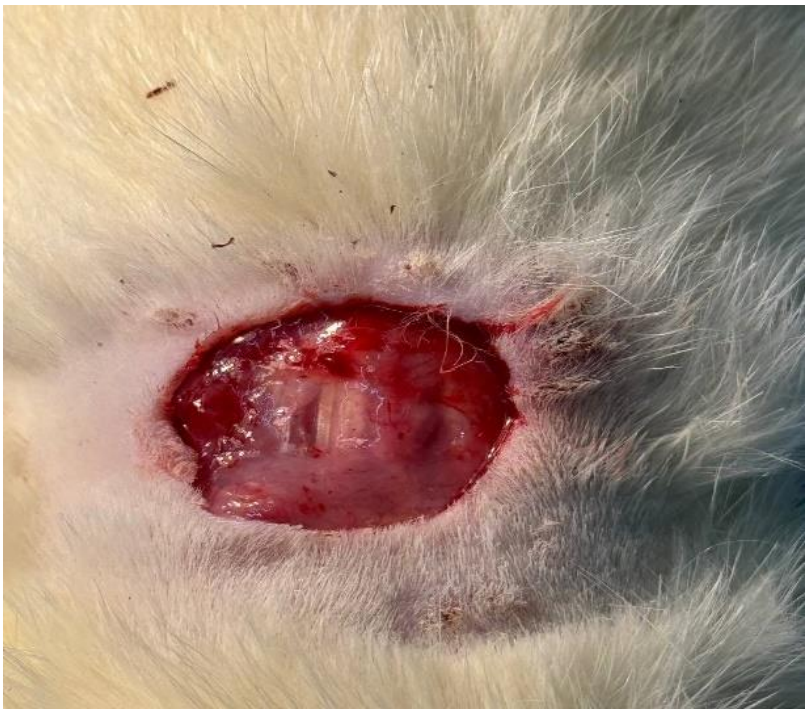

Fig. 1. Model of a deep defect on the back of the rat

Creation of a model of an experimental deep soft tissue defect was carried out by forming a round defect with a diameter of 2 x 2 cm on the back using a scalpel, after preliminary treatment of the surgical field (Fig.1). After creation of the defect model, injection treatment with stem cells was carried out, accordingly to the groups of experimental animals. After 28 days, animals were slaughtered and organs were taken for study: brain, heart, lung, liver, spleen, kidney, stomach, duodenum, small intestine, large intestine, lymph node and mucosa section.

Results and discussion. Observation in dynamics was carried out during the 1st, 3rd, 5th, 7th, 7th, 14th, 28th days. The general condition of animals and clinical signs of possible intoxication were evaluated: general condition of animals, feed and water consumption, change of body weight, peculiarities of their behavior, intensity and character of motor activity. Local status was also evaluated. Biopsies and blood for biochemical analysis were taken on the 3rd and 7th day.

The obtained results indicate that the application of stem cells does not cause intoxication of the organism of experimental animals. The obtained clinical and experimental data on the absence of endogenous intoxication, as well as the absence of complications during the observation period testified to the effectiveness and safety of the developed method of treatment of deep soft tissue defects using cell therapy.

Conclusion. The obtained experimental data (absence of endogenous intoxication), as well as the absence of complications during the observation period testified to the effectiveness and safety of the developed method of treatment. The use of cell products based on stem cells and tissue-engineered constructs created on their basis is reasonable to use as a regulator of the wound process for better graft engraftment in the treatment of oral cavity defects of various genesis, as well as in the preparation of the surgical field in patients undergoing elective surgery.

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УДК: 614.2:616.31

OUR EXPERIENCE WITH SURGICAL TREATMENT OF ROTATOR CUFF INJURIES OF THE SHOULDER JOINT

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Abstract. *CSJ injuries occur in 63-84% of shoulder injuries. The rotator cuff ranks third (16%) after spinal (23%) and knee (19%) disorders in terms of frequency of rotator cuff injuries. The frequency of tears varies from 5 to 37% (A. DePalma), of which about 15-20% in 60-year-olds, 26-30% in 70-year-olds, and 36-80% in 80-year-olds. Such a high incidence of pathology is predetermined by regular degenerative changes in the tendinous and muscular tissues of the rotator cuff of the shoulder, which develop in people with age and are caused by anatomical features of the shoulder joint structure. In the tendon part of the rotator cuff of the shoulder there is a so-called 'load cable' or 'sickle-shaped area', within which blood flow is reduced, and there the tear formation occurs. Magnetic resonance imaging (MRI) is highly informative in the diagnosis of pathological changes of the rotator cuff of the shoulder. T2-VI with signal suppression from fatty tissue in the oblique coronal projection is considered to be the most informative.*

Key words: *shoulder joint, rotator cuff, injury, treatment.*

Introduction. The scapula muscles and their function have been known for about five centuries. For the first time determined the role of the suprasternal, substernal, and subscapular muscles in the functioning of the upper limb was studied by A. Vesalius as early as the 16th century. He gave them the name "shoulder rotators and those who play a role in raising the shoulder." Smith in 1834 drew attention to the damage to a group of scapulae Jarjavay J was the first to describe subsacromial bursitis in 1867. Condition that develops in the shoulder joint immediately or after some time after an acute injury, he described and introduced the term brachiocephalic periarthritis. Duplay in 1872. He believed this condition was related to destruction or adhesion of the shoulder joint capsule [2,8]. During other researchers of the nineteenth century Duronea, Pinguad and Charvot (1879) tried to refute his theory, believing that the cause pathologies should be considered as rheumatic or neurogenic. Most cuff injuries, can be repaired classical reinsertation proposed by E.A. Codman. Even with extensive damage, recovery is usually possible with a satisfactory with a distant result [1,4,13]. At the same time, there is no universal,effective method that can be used in operational interventions aimed at restoring anatomical relationships and functions of the shoulder joint. Unfortunately, one-third of patients with extensive with rotator cuff injuries, surgical treatment presents certain difficulties. The reason for this is secondary degenerative changes and retraction of displaced individuals attachment of short shoulder rotators. In such cases, alternative surgical methods are being considered (Figure -1).

Open and arthroscopic degenerative removal was proposed. altered and functionally unstable tissues, however, while some authors believed this contributed to a significant decrease pain intensity, restoration of active movements were not observed. In addition, the reduction of pain syndrome is short-lived and such the scope of the operation is preferable for elderly patients with the prevailing symptom is pain. [6,11]. McLaughlin H.L. did not consider it necessary to achieve anatomical restoration, considering it possible to insert the tendon where it can to be brought in without tension and fixed with a transossal cord but this did not contribute to the restoration of the shoulder joint function due to a violation of biomechanics [5,7].

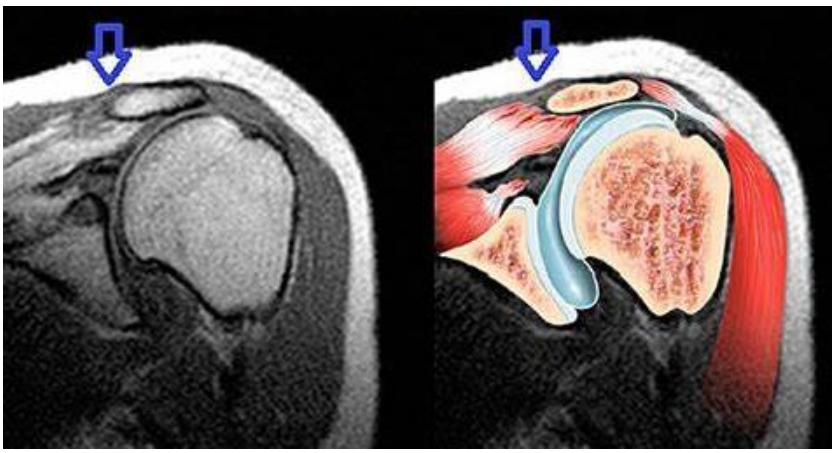


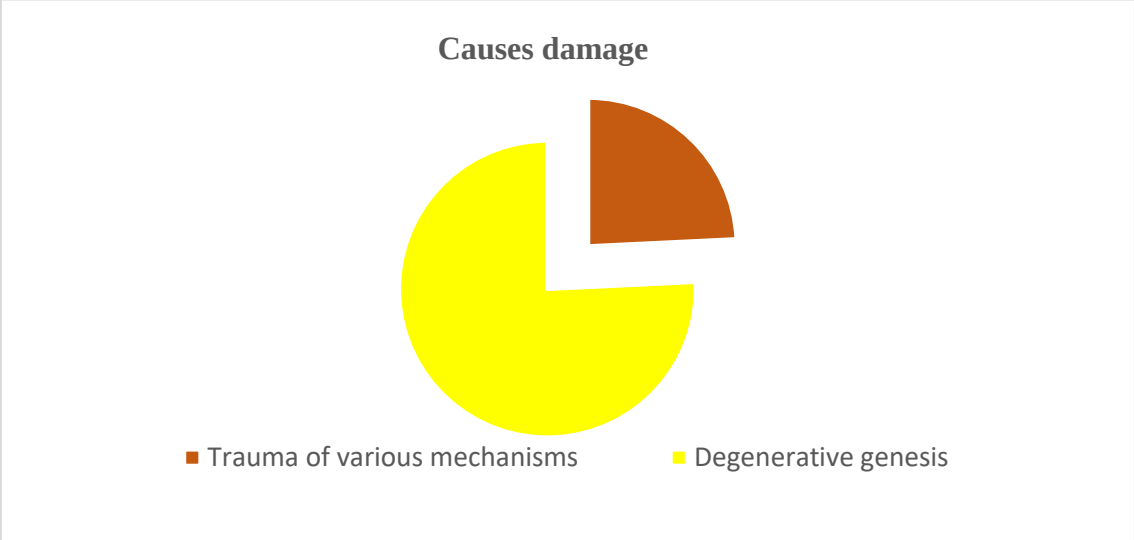
Fig. 1. Rotator cuff injuries of the shoulder joint.

Therefore, choosing a treatment method for extensive injuries of the rotary shoulder cuff, presents significant difficulties. This is due to the diversity of the coverage of the pathological process by anatomical structures, muscle retraction and their degeneration, lower surfaces of the acromial process of the scapula, with changes in the acromial clavicular joint, pain syndrome, synovitis, bursitis, impaired mobility of the shoulder joint, genesis of injury, duration pathology and age of the patients. Presence of a significant number of points views and contradictions in views on the methods and possibilities of operational restoration of cuff integrity indicates their insufficiency effectiveness, lack of justified criteria for selecting rational methods of surgical interventions and requires further study [9,14].

Material and methods of research.

66 patients (41 men, 25 women) with the diagnosis of chronic damage of shoulder rotator cuff tendons, combined contracture of the shoulder joint were operated openly (from 2022 to 2025) at the Samarkand Branch of the Republican Specialised Scientificand Practical Medical Centre for Traumatology and orthopedics. The average age of the patients was 58 years. In 16 patients (24.2%) the causes of rotator cuff damage were traumas of various mechanisms, and in 50 patients (75.8%) they were of degenerative genesis In all patients with degenerative tears were accompanied by subacromial impingement syndromes. And in 6 patients besides impingement there was adhesive capsulitis of the shoulder joint. According to our observation, the average period of patients' visits to a specialised consultation was 2-5 months.

Diagram-1.



MRI of the shoulder joint showed signs of rupture of the tendon part of the supraspinous and subscapularis muscles of the shoulder rotator cuff with diastasis between the fixation point to the greater tubercle and the flotation edge of the tendon of more than 2.0 cm and retraction into the subacromial space. Objective examination data combined with clinical examination allowed us to confirm the absolute signs of rotator cuff injury, determine its localisation and the degree of tendon rupture.

Surgical technique: Under general intubation anaesthesia, the patient's position is 'on the side'. The patient is fixed with stops. The operated limb is placed in the position of 20-30 degrees of abduction, 20 degrees of flexion. Extension of the operated limb along the axis with a load of 4-5 kg. The arthroscope is inserted into the shoulder joint through standard posterior and anterior ports. The shoulder joint is visualised with an optic inserted through the posterior port. Diagnostic arthroscopy revealed the nature of the rotator cuff injury. According to the size of the tear: small, medium, large and according to the shape of the tear: 'L' and 'U' shaped. The astroscope was also used to identify pathologies of the subacromial space. Subacromial decompression was performed in patients with impingement syndrome after determination of rotator cuff injury. The subacromial bursa was dissected for optimal visualisation of the rotator cuff tendon. If necessary, acromionoplasty was performed using a shaver and bone drill.

The patient was then transferred to the back. Patients with adhesive capsulitis underwent closed joint redressing. After repeated treatment of the operating field in the upper extremity, the subacromial cavity was opened through the deltoid access: a skin incision was made from the anterior-upper corner of the acromion to the big tubercle of the humerus. The deltoid muscle was divided bluntly.

The zone of the bone-tendon defect from the natural fixation point in the projection of the greater tubercle of the humerus to the flotation and retrapped edge of the tendons of the supraspinous and plantar muscles more than 3.0 cm was determined, after which the edges of the damaged tendons of the shoulder rotator cuff were refreshed and adapted to the maternal bed of the humerus by mobilisation. A perceptive bone bed was prepared in the place of natural fixation of the tendon of the supraspinous muscle by removing scar tissue and a part of the cortical layer of the greater tubercle of the humerus. After that, the refreshed edges of the flotating tendons of the supraorbital and subscapularis muscles were sutured with Polyester№ 6 thread.Next, percutaneous sutures were performed in the head of the humerus using a hook-shaped spoke with an exit on the cortical plate distal to the greater tubercle of the humerus. After that, thread tensioning and adaptation of the flotating tendon edge in the natural fixation point were performed. After fixation of the percutaneous sutures, we checked the volume of movements in the shoulder joint and the stiffness of the adapted tendons of the shoulder rotator cuff. The wound was haemostasis and sutured layer by layer. The operated upper limb was fixed with a withdrawal splint (30° abduction and 20° anterior deviation) for 4 weeks.

Results and discussion. Results of surgical treatment was performed by follow-up examination at 3, 6 months and 1 year with clinical examination of the patient (tests for shoulder rotator cuff function, range of motion; VAS pain (0 - no pain, 10 - severe pain) and completion of the standardised UCLA shoulder functional assessment scale (adapted to the daily life of patients: 34-35 points - excellent score, 28-33 points - good, 21-27 points - satisfactory, less than 20 points - poor), pain syndrome, joint function and muscle strength during labour and daily activities of the patient were evaluated.

Table-1

Treatment results

Treatment results	Number of patients	Percentage
Great results	38	57,5%
Good result	25	37,8%
Unsatisfactory results	3	4,7 %
Total	66	100%

An excellent result was obtained in 38 patients (57.5%). A good result was obtained in 25 patients (37.8%). 3 patients (4.7%) had an unsatisfactory result. The reasons for unsatisfactory results were extensive defect and late conversion of patients (2), and concomitant diabetes mellitus in patient (1) resulted in ligature fistula. After removal of the ligature, a good result was obtained.

Conclusion:

1. Despite the traumatic nature of the surgical intervention, reinsertion of the rupture of the rotating cuff tendon is a choice operation that provides the maximum prospects for restoring patients' working capacity.

2. According to the research results, the increase in the proportion of good results showed the effectiveness of the applied surgical method.

3. It also prevents decreased work capacity and various complications that may occur in patients, returning them to an active lifestyle.

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STUDY OF P-SELECTIN LEVELS AND HEMOSTASIS GENES GENETIC POLYMORPHISMS AMONG PATIENTS WITH GOUT

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Abstract. *Gout is a metabolic and inflammatory disorder characterized by hyperuricemia and crystal-induced arthritis, often accompanied by an elevated risk of cardiovascular events and thrombosis. P-selectin, a marker of platelet activation and endothelial dysfunction, has been implicated in thrombotic processes. Genetic polymorphisms in hemostasis-related genes may contribute to both hyperuricemia-related inflammation and thrombogenic potential. The objective of this study was to investigate P-selectin levels and common genetic polymorphisms in MTHFR, F5, F2, and PAI-1 genes among 80 patients with gout and 20 healthy controls to assess their combined role in increasing thrombotic risk. Plasma P-selectin levels and genotypic variations in MTHFR C677T, F5 G1691A, F2 G20210A, and PAI-1 675 4G/5G were analyzed in a cohort of gout patients (n = 80) and healthy controls (n = 20). Enzyme-linked immunosorbent assay (ELISA) was used to quantify P-selectin. Genotyping was conducted using TaqMan PCR. Statistical correlation analyses were performed to determine the relationship between elevated P-selectin levels and the presence of high-risk genotypes. Gout patients exhibited significantly elevated P-selectin levels (range: 0.01–3.58 ng/mL), with many exceeding the normal threshold (0.30 ng/mL), compared to controls (0.02–0.18 ng/mL). High-risk genotypes were notably more frequent among gout patients: MTHFR TT (13%), F5 AA (5%), F2 AA (22%), and PAI-1 4G/4G (62%). Correlation analysis showed a moderate positive relationship between P-selectin levels and genetic polymorphisms ($r = 0.378$, $p = 0.00036$), with $R^2 = 0.143$. Elevated P-selectin levels in gout patients are moderately associated with thrombosis-related genetic polymorphisms, suggesting an interplay between genetic predisposition and thrombo-inflammatory processes in gout.*

Keywords. *Gout, P-selectin, Hemostasis, Gene polymorphism, MTHFR C677T, F5 G1691A, F2 G20210A, PAI-1 4G/5G, Thrombosis, Endothelial dysfunction, Platelet activation, Hyperuricemia.*

Introduction. Gout is a chronic inflammatory arthritis resulting from monosodium urate crystal deposition in joints, arising due to prolonged hyperuricemia. Besides joint involvement, gout is increasingly recognized as a systemic disease with implications for cardiovascular health. Thrombotic complications, particularly venous thromboembolism, have been observed at higher rates among gout patients [1, 5]. P-selectin, a glycoprotein expressed on activated platelets and endothelial cells, mediates leukocyte adhesion and platelet aggregation, playing a crucial role in the pathogenesis of thrombosis [2, 3]. Elevated P-selectin levels serve as biomarkers for vascular inflammation and prothrombotic states [4]. The potential genetic basis of thrombosis in gout patients includes polymorphisms in key hemostasis genes such as MTHFR C677T, F5 G1691A (Leiden mutation), F2 G20210A, and PAI-1 675 4G/5G [6, 7]. This study explores the relationship between P-selectin levels and these genetic polymorphisms in gout patients.

Materials and Methods. 80 patients diagnosed with gout and 20 healthy controls were included. Plasma P-selectin levels were measured using ELISA. Genotyping for MTHFR C677T, F5 G1691A, F2 G20210A, and PAI-1 675 4G/5G was performed using TaqMan Real-Time PCR. Pearson correlation was used for statistical analysis.

Results. P-selectin levels were significantly elevated in the gout patient group compared to the control group. Specifically, P-selectin levels in patients ranged from 0.01 to 3.58 ng/mL, with many patients displaying levels exceeding the normal threshold of 0.30 ng/mL. The majority of patient values clustered between 0.5 and 1.5 ng/mL. In contrast, the control group exhibited P-selectin levels ranging from 0.02 to 0.18 ng/mL, all within or below the normal range, indicating a statistically significant difference between the two groups ($p < 0.001$).

Regarding genetic polymorphisms, the distribution of high-risk genotypes in gout patients was notable. For MTHFR C677T, 13% of patients were homozygous for the TT genotype, which is considered a high-risk variant for thrombosis, while 24% were heterozygous (CT), and 63% were homozygous for the normal CC genotype. In the control group, no individuals were found with the TT genotype; most were either CC or CT.

For F5 G1691A (Factor V Leiden), 5% of patients had the AA genotype, 8% were GA, and 87% were GG. In the control group, the majority were GG, with no AA genotypes detected.

For F2 G20210A (Prothrombin gene), 22% of patients exhibited the high-risk AA genotype, 30% were GA, and 48% were GG. The control group had only 3 individuals with the GA genotype and none with the AA genotype.

The PAI-1 675 4G/5G polymorphism showed that 62% of patients had the 4G/4G genotype, which is associated with higher thrombosis risk due to reduced fibrinolysis. 19% were 4G/5G, and 19% were 5G/5G. In the control group, most individuals were either 5G/5G or 4G/5G, with very few exhibiting the 4G/4G genotype.

Correlation analysis between P-selectin levels and genetic polymorphisms revealed a moderate positive correlation with a Pearson correlation coefficient of $r = 0.378$, and the p-value was 0.00036, indicating statistical significance. The coefficient of determination, R^2, was 0.143, suggesting that approximately 14.3% of the variation in P-selectin levels could be explained by the presence of these genetic polymorphisms.

These findings collectively suggest that gout patients have high genetic and biochemical predisposition of increased thrombotic risk.

Discussion. The findings of this study demonstrate a significant elevation in P-selectin levels among gout patients, which correlates moderately with the presence of high-risk genetic polymorphisms in hemostasis-related genes. Elevated P-selectin levels reflect increased platelet activation and endothelial dysfunction, both of which are known contributors to thrombotic events. The high prevalence of the PAI-1 4G/4G genotype among patients suggests a potential mechanism for impaired fibrinolysis, contributing to a prothrombotic state. This genotype has been widely reported to be associated with elevated PAI-1 levels, reducing the breakdown of fibrin clots and enhancing clot stability.

The association of MTHFR TT genotype with increased P-selectin levels may be linked to hyperhomocysteinemia, which is a known result of MTHFR enzyme deficiency. Elevated homocysteine levels can lead to endothelial damage, increased oxidative stress, and subsequent platelet activation, all of which contribute to elevated P-selectin levels. Similarly, F5 G1691A and F2 G20210A mutations, both associated with increased thrombin generation, could amplify platelet activation, thereby increasing P-selectin expression.

While the correlation coefficient ($r = 0.378$) indicates a moderate relationship, the relatively low R^2 value (0.143) suggests that genetic polymorphisms explain only part of the variation in P-selectin levels. This implies that other factors such as systemic inflammation, renal function, lifestyle, and additional genetic variants may also influence P-selectin levels and thrombotic risk in gout patients. The multifactorial nature of thrombotic risk underscores the complexity of its management in gout, necessitating a comprehensive approach that includes genetic screening, inflammatory marker monitoring, and cardiovascular risk assessment.

These results are consistent with previous studies highlighting the role of endothelial dysfunction and prothrombotic states in gout pathogenesis. The observed genetic predispositions provide insight into the underlying mechanisms linking gout to cardiovascular morbidity and mortality. Identification of high-risk genotypes in gout patients could enable personalized therapeutic strategies aimed at reducing thrombotic complications, including the use of antiplatelet or anticoagulant therapy in selected individuals.

Limitations of this study include the sample size, which may not capture the full genetic diversity of the population. Further studies with larger cohorts and inclusion of additional polymorphisms are warranted to confirm these findings and explore the interaction between genetic and environmental factors in the regulation of P-selectin and thrombotic risk.

Conclusion. Gout patients have high level of P-selectin levels, which means platelet activation and endothelial inflammation. Also, genetic polymorphisms of hemostasis genes contribute to increased thrombosis risk. Patients with gout should have multidisciplinary approach, in order to prevent serious complications of coagulation system.

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LIVER MORPHOMETRIC CHANGES DURING FETAL DEVELOPMENT IN EXPERIMENTAL KIDNEY DISEASE: A COMPARATIVE ANALYSIS

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Abstract. *For the first time, a systematic investigation was conducted on white fetal rats with experimentally induced chronic kidney disease (CKD) to assess morphological changes in different regions of liver tissue. The study evaluated the effects of Juizar water treatment by analyzing morphometric parameters of the liver to determine its therapeutic efficacy. Additionally, the research aimed to establish early diagnostic criteria for liver cell damage based on experimental findings. The results were used to develop examination protocols for treating women with CKD, with a focus on predicting and preventing liver complications. Further studies were conducted to prepare reproductive age women particularly pregnant women for healthy fetal development by enabling early detection and prevention of liver cell damage. In Uzbekistan, work is carried out to improve the social protection of the population and the quality of medical services. Steps are taken towards the elimination of chronic liver diseases, prevention of their consequences, as well as the introduction of early diagnosis and effective treatment methods. In this regard, it is important to improve the skills of medical personnel, introduce modern diagnostic tools and provide the population with the right health information. In the Prevention of liver diseases, the formation of the right lifestyle and regular medical examinations are central. The reforms carried out in this way in our country serve to improve the quality of prevention and treatment of diseases.*

Keywords: *Chronic kidney disease, prevention of liver diseases, biochemical parameters, diagnostic criteria.*

Introduction A study investigated the effects of administering high doses of zidovudine, lamivudine, and ritonavir to pregnant rats, revealing structural and dimensional alterations in the maternal liver and kidneys. However, no such changes were observed in the fetal organs. *(Morphological and morphometric analysis of the liver and kidneys of pregnant rats and their fetuses treated with zidovudine, lamivudine, and ritonavir throughout pregnancy.* Physiological changes that occur in the body during pregnancy, especially their impact on liver and kidney functions, occupy a significant place in the field of Medicine. In fetuses with chronic maturation diseases, it is necessary to identify changes in the morphological and morphometric indicators of these organs, better understand clinical results and develop the right methods of treatment [1,5].

Another study found a strong link between a high-fat diet in white rats and kidney damage, including reduced glomerular density, structural abnormalities, enlarged renal vessels and tubules, glomerular necrosis and atrophy, and thickening of the basement membrane.Embryonic cell injection offers an efficient method for promoting epithelial differentiation and tubule formation, facilitating key developmental processes such as complex structure formation and basement membrane assembly. Additionally, grafting techniques enable research into embryonic kidney vascularization and the influence of endothelial cells on developing embryonic cells. [6,7].

The study of morphological and morphometric indicators of the liver and kidneys in the context of fetal and maturational diseases makes it possible to improve the methods of diagnosis and treatment of yanchi in clinical practice. New research in this area is necessary, especially through these methods, it is possible to understand the main mechanisms of the development of mattresses and develop new treatment strategies.

Additional studies have investigated the impact of experimentally induced kidney disease on fetal liver development. Through a comparative assessment, researchers analyzed morphometric alterations in the liver, assessing possible changes in its architecture and dimensions in fetuses with impaired kidney function. These results enhance our knowledge of the relationship between kidney dysfunction and liver maturation during gestation, offering valuable perspectives on interorgan interactions in fetal development and disease. [2,4].**The main purpose of the study of post-chronic kidney disease changes in morphological and morphometric indicators of the liver of white-breed fetal rats.**

Material and methods of research. A study involving 150 white rats modeled chronic maturation failure, followed by histological examination of liver tissue after one month. Microscopic analysis was conducted on the liver cell structure of fetal-stage rats. The research was carried out at the Bukhara branch of the Bukhara State Medical Institute and the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health, with statistical analysis performed using Fisher's exact test (or Student's t-test, depending on the context).

Results and discussion. The embryology, morphology and histology of the normal human liver - the only largest organ in the human body - are described. It has been argued that liver biopsy samples must be processed with special care to obtain optimal sections. Morphological studies of liver tissue have the potential to obtain more information than electron microscopy. Some histological changes may be noticeable in surgical liver samples, but they are often insignificant. On the other hand, some morphological changes, especially in needle biopsy samples, are often subtle but may have diagnostic significance.

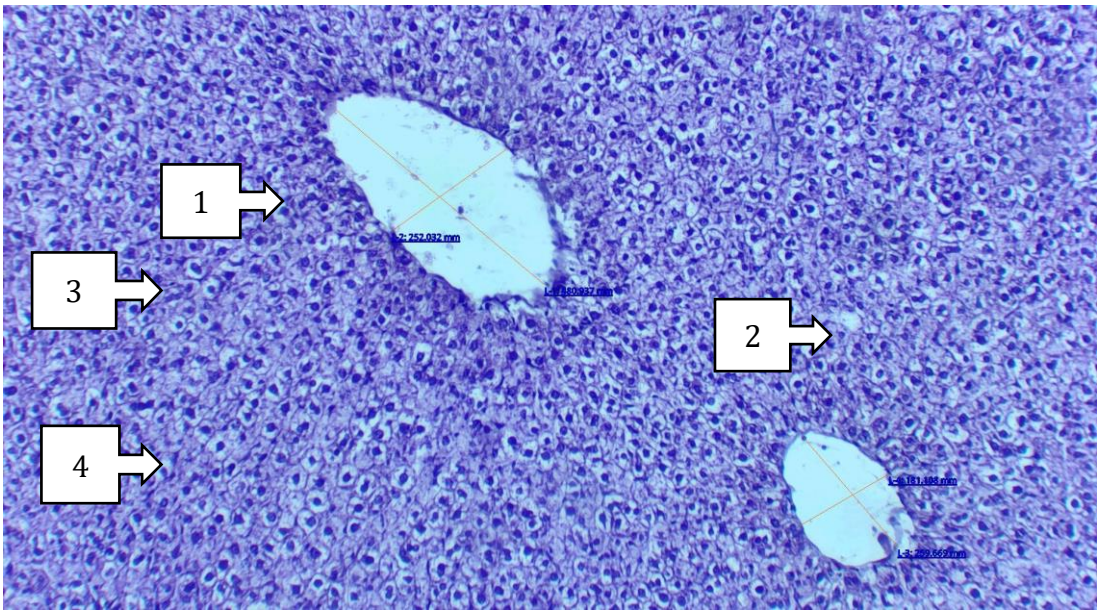

Fig. 1. Morphometry structure of liver tissue. Paint G-E. size 10x10

1.Deformation and cavity of the central vein wall in dimensions.

2. Small volumetric vacuoles (droplets. the nucleus of hepatocytes is in the center, basaphilically painted.

3. The sinusoid space and the pericinusoid area (Disse) space are narrowed.

4. The Kupfer cell and the bi-nuclear hepatocytes are numerically abundant.

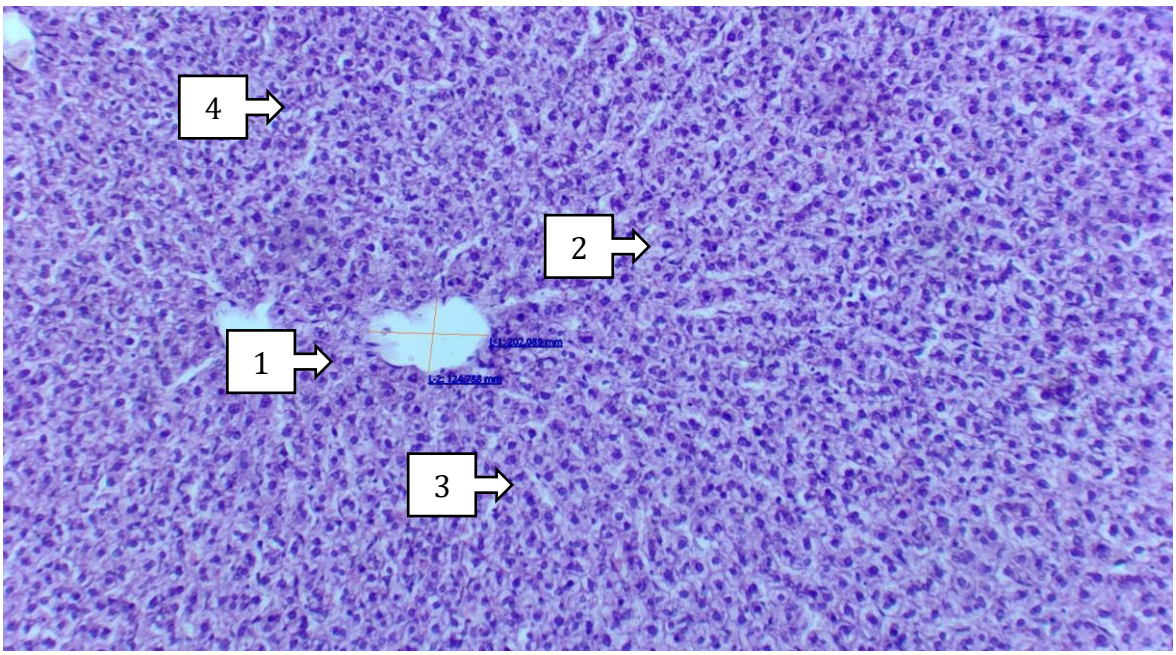

Fig. 2. Morphometry of liver tissue. Paint G-E. paint 10x10.

1.Deformation and cavity of the central vein wall in dimensions.
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3.The sinusoid space and the pericinusoid area (Disse) space are narrowed.
4.The Kupfer cell and the bi-nuclear hepatocytes are numerically abundant.

The study investigated morphological and functional changes in hepatocytes of the liver in conditions of chronic maturation failure, as well as the pathogenetic mechanisms that affect them. The results show that kidney dysfunction has a very strong effect on the structure of the liver, leading to metabolic and structural disorders in it. These assignments not only made it possible to more deeply understand the physiology of the digestive system, but also helped to understand the complex organ-aralic interactions that arise during pregnancy [1,3].

Morphometric indicators of the liver of healthy white-breed rats (M±m)

Histological indicators	Min	Max	Avarage
Hepatocyte	1 mm²-3	1 mm²-7	1 mm²-7
Nucleus	1 mm²-4	1 mm²-8	1 mm²-6
Sinusoid width	5mkm	15mkm	10mkmv
Cytoplasm size	average for each cell-210mkm3	average for each cell-650mkm3	average for each cell-420mkm3
Number of mitochondria	1 hepatocyte-100	1 hepatocyte-300	1 hepatocyte-200
Blood vessel diameter			
Hepatic artery	50mkm	150mkm	100mkm
Portal vein diameter	100mkm	300mkm	200mkm
Biliar capillaries	10mkm	30mkm	20mkm

Conclusion. The study investigated morphological and functional changes in hepatocytes of the liver in conditions of chronic maturation failure, as well as the pathogenetic mechanisms that affect them. The results show that kidney dysfunction has a very strong effect on the structure of the liver, leading to metabolic and structural disorders in it. These assignments not only made it possible

to more deeply understand the physiology of the digestive system, but also helped to understand the complex organ-aralic interactions that arise during pregnancy.

When morphometric indicators of the liver of healthy white-breed rats were studied, the following results were obtained: the size of hepatocytes ranges from 1 mm2-3 to 1 mm2-7 on average 1 mm2-7; the size of the nuclei ranges from 1 mm2-4 to 1 mm2-8 on average 1 mm2-6; the width of the sinusoids ranges from 5mkm to 15mkm on average 10mkmv; the size of the cytoplasm averages-210mkm3 to-650mkm3 on average-420mkmkm3; the number of mitochondria -300 to 1 hepatocyte-200 on average; hepatic artery size ranges from 50 μm to 150 μm on average 100 μm; portal vein diameter ranges from 100 μm to 300 μm on average 200 μm; biliary capillaries ranged in diameter from 10 μm to 30 μm, averaging 20 μm.

Hepatocytes are the main cell of the liver. The structure of the hepatocyte cell is cuboid or polygonal. The nucleus is in the center of the cell, round in shape-in most cases it is bicellular. The cytoplasm is stained eosinophilic. In its cytoplasm, it is rich in an endoplasmic lattice (organelle synthesizing blood plasma proteins) and a large amount of granular endoplasmic lattice (organelle synthesizing toxins, bilirubin and bile fluid). In hepatocytes, the following surfaces are differentiated. Sinusoidal surface of hepatocytes. The Sinusoid has a surface facing the capillaries, carries out the exchange of substances, the synthesis of proteins. Biliary surface-bile fluid synthesis occurs. The apical surfaces of the two adjacent hepatocytes, which have pits on the membrane, fuse to form the wall of the bile duct.

Hepatocytes are surrounded by fine connective-reticulin fibers, forming a stroma. Hepatocytes combine to form the liver plate. The plates also form a cross-anastamosis, between which sinusoid capillaries are located, which are considered branches of the portal vein and hepatic artery. The wall of Sinusoid capillaries will contain Kupfer cells of phenestrated endothelium and star-shaped reticulo-endotheliocytes. The basal membrane consists of incomplete fenesters. Kupfer cells perform the following tasks; phagocytosis of antigens that come through the blood. By breaking down aging erythrocytes, the iron is bound to ferritin protein, stored as a reserve and involved in the formation of erythrocytes at the required time is EET. Between sinusoids and hepatocytes is the pericinusoid space, this space is called the Disse space. In the processes of metabolism, manashu space is the main one. There is another HSC star-shaped cell in the Disse cavity. The function of the HSC cell is to accumulate vitamin A and fat-soluble vitamins. Synthesis of extrasellular matrix i.e. is converted to myofibroblasts in the wound Mahal.Liver slices are the structural functional unit of the liver. In the middle of each blotch is the central vein (Vena centralis). The Sinusoid capillaries and liver plate are radially oriented to the central vein. The liver fragments are separated by Inter-hepatic intercostal connective tissue,and in this area the hepatic triad (artery, vein, and bile ducts) settles.

We studied morphological and morphometric indicators of the liver of pregnant white-breed rats in our experiment. In the central vein, we can see a general venous wave, deformation of the central venous wall as a result of a slowdown in the circulation of venous blood, a fullness with an enlarged cavity. The consequence of this is the expansion of the Sinusoid space, fullness and narrowing of the cavity in the pericinusoid area (Disse). The narrowing of the Disse cavity directly affects the processes of metabolism, slowing down these processes. Processes such as slowing down the exchange of substances in the liver,hypoxia are obvious evidence of uneven thickening of light pink collagen fibers around the central vein.Hypoxia has a direct effect on the functional state of hepatocyte - cell structures. Small volumetric vacuoles(droplets) appeared in the cytoplasm of hepatocytes. This process has led to a mild disruption of the water-electrolyte balance inside and outside the cell. It was found that fluid in the form of vacuole drops passed into the hepatocytes. In this, hepatocytes - the nucleus is in the center, basafil is painted. The cytoplasm is eosinophilic stained, wide in size. The dimming of the blood increases the agglutination of erythrocytes, and this led to an increase in the Kupfer cells (the function of which was described above) in the sinusoid wall. We can see that regenerative regeneration processes are enhanced when the body's capacitor processes are increased and the number of dual-core hepatocytes among hepatocytes increases.

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MORPHOMETRIC CHARACTERISTICS OF THE LIVER DURING PREGNANCY IN EXPERIMENTAL CHRONIC RENAL FAILURE

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Abstract. *The treatment of liver pathologies in chronic renal failure observed during pregnancy and the prevention of their consequences remains a medical and social problem worldwide. Despite the development of methods for the prevention, diagnosis and treatment of liver diseases, mortality rates from them occupy leading places. Currently, in our country, special attention is paid to improving the quality of social protection and the health care system, diagnosis and treatment of chronic liver diseases. We studied the morphological and morphometric parameters of the liver of pregnant white rats. The main purpose of the study of post-chronic kidney disease changes in morphological and morphometric indicators of the liver of white-breed fetal rats.*

Keywords: *Diagnosis and treatment of chronic liver diseases, prevention of liver diseases, morphological parameters, morphometric parameters.*

Introduction. Liver diseases remain a major challenge in global health, with their diverse nature and frequent comorbidities making it difficult to understand their underlying mechanisms and provide optimal treatment. Metabolomics, which involves the quantitative analysis of small organic molecules (metabolites) in biological samples, is becoming increasingly significant in liver disease research. However, carrying out a metabolomics study in human liver disease populations demands a deep understanding of several critical steps: designing the study, collecting samples, acquiring and preprocessing metabolomics data, performing statistical and bioinformatics analysis, and interpreting the results within a biomedical framework [1,2].

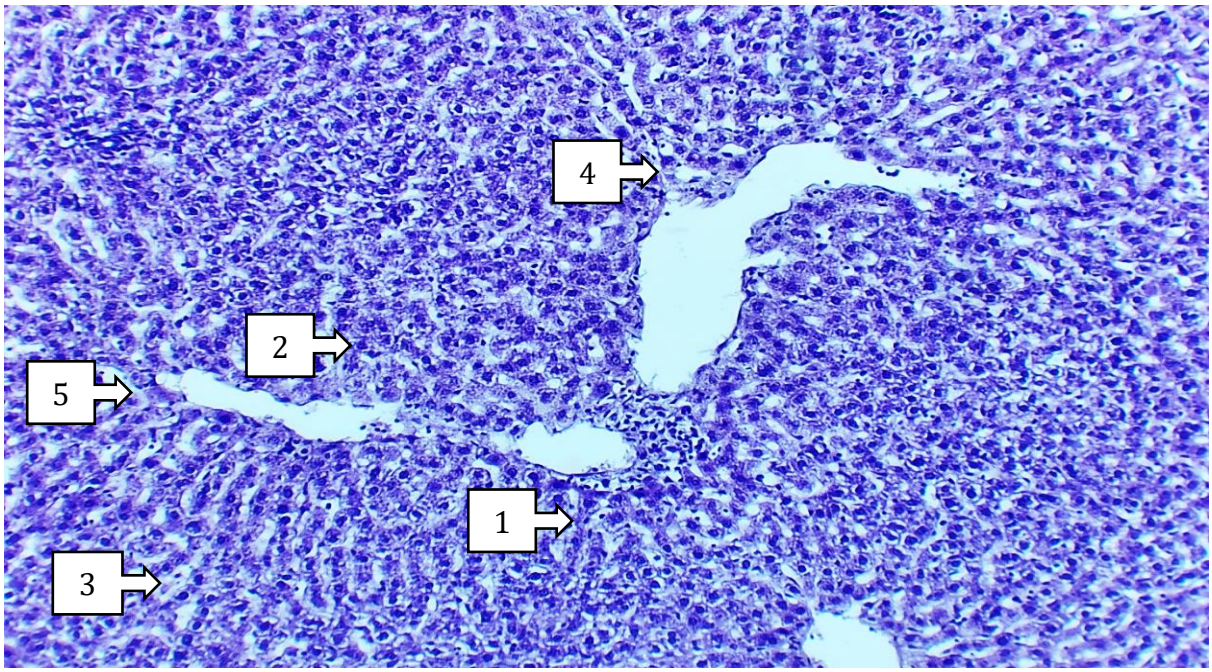
Liver disease during pregnancy is one of the least researched areas in obstetrics, posing significant challenges for both gynecologists and hepatologists. Around 3% of pregnant women experience some form of liver disorder, some of which can be life-threatening for both the mother and the fetus. These conditions can be categorized into three distinct types: One type is liver diseases directly linked to pregnancy, which arise at specific gestational stages; Second type is liver conditions unrelated to pregnancy, such as viral or drug-induced hepatitis, which can occur at any time; and Another type pregnancies in women who already have pre-existing liver disease. Clinicians must be well-versed in these disorders to ensure timely and appropriate management, particularly in urgent cases where emergency delivery cannot be delayed [3,5].

The study of morphological and morphometric indicators of the liver disease in the context of fetal and maturational diseases makes it possible to improve the methods of diagnosis and treatment of yanchi in clinical practice. New research in this area is necessary, especially through these methods, it is possible to understand the main mechanisms of the development of mattresses and develop new treatment strategies.

Clinical routine in liver disease involves the diagnosis and treatment of a wide spectrum of metabolic, infectious, autoimmune and neoplastic diseases. Clinicians integrate qualitative and quantitative information from multiple data sources to make a diagnosis, prognosticate the disease course, and recommend a treatment. Our scientific innovation is to prevent the development of liver diseases in chronic kidney diseases. Further advances in research and medical care have improved maternal and fetal outcomes, but are still not satisfactory. In this review, we present an overview of liver diseases characteristic of a pregnant woman and updates on their pathogenesis, treatment and results [4,6].

Material and methods of research. A study examined chronic maturation failure using 150 white rats, with liver tissue analyzed histologically after one month. The microscopic evaluation focused on the liver cell structure of fetal-stage rats. The research was conducted at the Bukhara branch of the Bukhara State Medical Institute and the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health. Statistical analysis was performed using Fisher's exact test or the Student's t-test, as appropriate.

Results and discussion. Hepatocytes in the periportal (afferent) and perivenous (efferent) zones of the liver parenchyma differ in their enzymatic composition and subcellular structures. Therefore, different functions are offered for the two zones. (a) protection against oxidative energy metabolism, beta-oxidation, catabolism of amino acids, ureagenesis from amino acids, gluconeogenesis, separation and oxidation of acetic acid and bilirubin is preferably located in the periportal zone. b) glycolysis, liponeogenesis, ureagenesis from ammonia and biotransformation are mainly located in the perivenous zone. Heterogeneity also appears to be present in plasma protein synthesis [7].



1-pic. Morphological structure of liver tissue. Paint G-E. 10x10

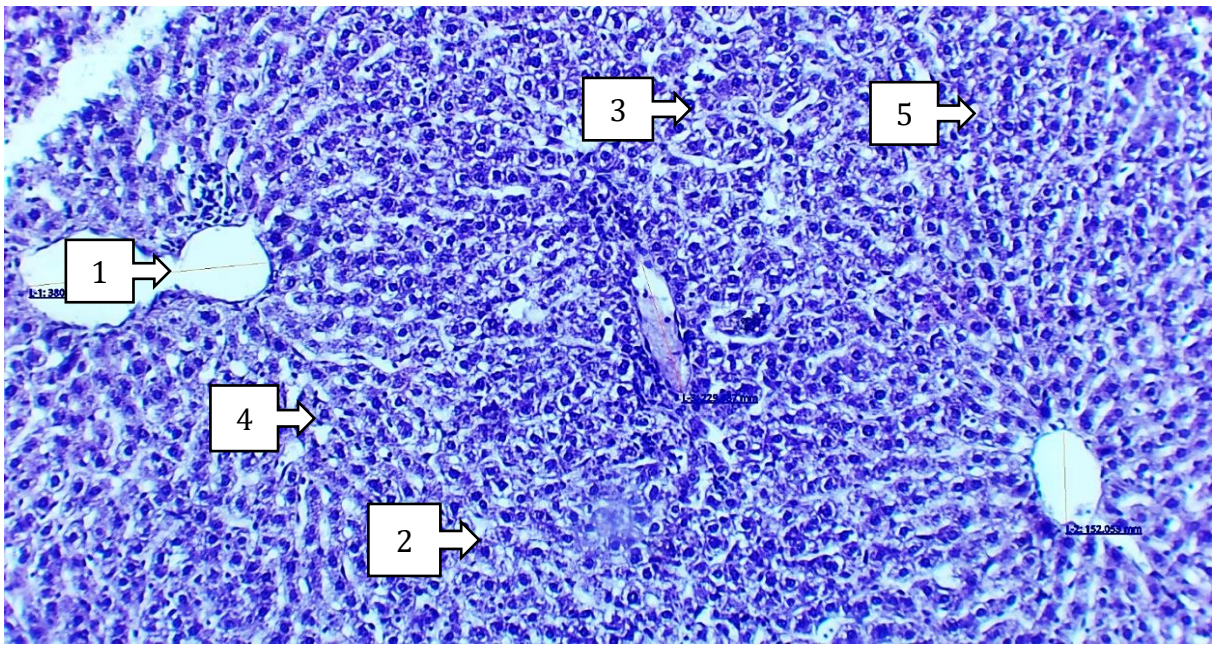
1. Deformation of the central vein wall (sclerotic changes), fullness and narrowing of the cavity,inflammatory infiltrate around.

2. Perenchymatous protein (hydropic and hyaline droplet) dystrophy in hepatocytes. hepatocytes-the nucleus is painted with a reduced basafil in the center, the cytoplasm of which is occupied by vacuoles (droplets) of different sizes).

3. Fatty (fat drops) dystrophy in hepatocytes.

4. The cavity of the Sinusoid cavity and perisinusoid area (Disse) is enlarged swelling.

5. The number of dual-core hepatocytes has decreased.



2-pic. Morphometry of liver tissue. Paint G-E. 10x10

1. Deformation of the central vein wall (sclerotic changes), fullness and narrowing of the cavity (in dimensions), around inflammatory infiltrate.

2. Perenchymatous protein (hydropic and hyaline droplet) dystrophy in hepatocytes. hepatocytes-the nucleus is painted with a reduced basafil in the center, the cytoplasm of which is occupied by vacuoles (droplets) of different sizes).

3. Fatty (fat drops) dystrophy in hepatocytes.

4. The cavity of the Sinusoid cavity and perisinusoid area (Disse) is enlarged swelling.

5. The number of dual-core hepatocytes has decreased.

After experimental kidney failure, microromorphometric indicators of the liver of pregnant white-breed rats were found, and the following results were recorded: the size of hepatocytes from 1 mm2-3 to 1 mm2-7 on average 1 mm2-5; the size of their nuclei from 1 mm2-4 to 1 mm2-6 on average 1 mm2-5; sinusoid width from 10 µm to 20 µm on average 15 µm; cytoplasm size 325mkm3; the number of mitochondria in 1 hepatocyte -150 to -350 on average 1 hepatocyte-250; the hepatic artery size ranged from 60 µm to 160 µm with an average of 110 µm; the portal vein diameter ranged from 120 µm to 320 µm with an average of 220 µm; biliary capillaries ranged from 15 µm to 35 µm in diameter with an average of 25 µm.

It was found that the wall of the middle and small-caliber arteries thickened, and narrowing of the blood flow path led to secondary hypertension and atrophy of the renal parenchyma. Rats in the same group studied the anatomical and morphological changes that occur in the liver during pregnancy. When the liver is macroscopic, the size is enlarged, the surface is smooth, the capsule is reminiscent of tense nutmeg. When examined microscopically: deformation of the central venous wall (sclerotic changes), fullness and narrowing of the cavity (in dimensions), inflammatory infiltrate around. Perenchymatous protein (hydropic and hyaline droplet) dystrophy in hepatocytes. Hepatocytes-the nucleus is painted with a reduced basaphil in the center, the cytoplasm of which is occupied by vacuoles (droplets) of different sizes. We can see that the uneven fat(drops) of hepatocytes located at the edges of the liver fragments press - fatty dystrophy has developed.The cavity of the Sinusoid cavity and perisinusoid area (Disse() is enlarged,swelling.metabolism is evident in the fact that processes are slow, while the numerical increase in bi-nuclear hepatocytes is evident in the decompensation process.

Conclusion. The experimental group exhibited significant ultrastructural changes in rat liver cells, including the disappearance of intramitochondrial granules in the mitochondrial matrix, dilation of the endoplasmic reticulum cisternae with small vesicle formation, and a reduction in ribosome numbers. Additionally, alterations in the microcirculatory system were observed, such as swelling of interlobular artery walls with lymphoid cell infiltration. The arterial wall thickness increased significantly—3.8 times higher than normal—reaching 7.39 ± 0.3 μm ($p < 0.001$). The most pronounced changes occurred in the venous structures, where portal venules in the experimental group dilated drastically, reaching a maximum diameter of 90.67 ± 5.6 μm ($p < 0.001$). Sinusoids also underwent notable transformations, with hypertrophied hepatocytes compressing them and reducing their volumetric density (Vvr) by 11-fold (1.6 ± 0.01%, $p < 0.001$). In some regions, sinusoids were dilated and congested with erythrocytes, while sinusoidal cells exhibited swelling.

In pregnant rats with induced renal failure, morphological alterations were also detected in the bile duct capillaries. Hepatocytes showed a decline in mitochondrial numbers, endoplasmic reticulum cisternae, and glycogen granules, indicating impaired synthetic function. These changes further affected bile duct integrity, leading to partial emptying of interlobular bile ducts and wall deformation. Compression of the ducts caused luminal distension, and the average diameter of interlobular bile ducts decreased from 33.32 to 30.14 ± 0.82 μm ($p < 0.001$).

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MORPHOLOGICAL CHANGES IN THE PANCREAS OF OFFSPRING BORN FROM MOTHERS WITH EXPERIMENTAL DIABETES

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Abstract. *Diabetes mellitus (DM) in the mother is a serious metabolic disorder that profoundly affects fetal development, in particular, the morphogenesis and functional maturation of the pancreas. This review summarizes the experimental data of studies investigating the morphological and functional state of the pancreas in the offspring of diabetic rat mothers. Using alloxan citrate buffered diabetic rat models, the researchers demonstrated that maternal hyperglycemia impairs pancreatic development, resulting in structural abnormalities such as reduced β-cell mass, disorganized islet architecture, and impaired endocrine function in the offspring. Histopathological analyses reveal marked changes including reduced islet density, fibrosis, and irregular vascularization, which may contribute to long-term metabolic dysfunction., suggesting impaired adaptive mechanisms in glucose homeostasis. Mechanistically, these effects are attributed to intrauterine oxidative stress, epigenetic modifications, and altered expression of critical developmental genes. The results highlight the importance of glycemic control during pregnancy to mitigate the adverse effects of programming on pancreatic health in the offspring. Furthermore, this review highlights gaps in current research, such as the long-term consequences of these changes in adulthood and potential therapeutic interventions. Understanding these mechanisms may inform strategies to prevent metabolic disorders in individuals exposed to a diabetic intrauterine environment.*

Keywords: *maternal diabetes mellitus, offspring pancreatic development, pancreatic morphology, β-cell mass, islet architecture.*

Introduction. Maternal diabetes mellitus (DM) during pregnancy has been extensively studied to have profound and long-lasting effects on fetal organogenesis, particularly on pancreatic development and function. Offspring of diabetic mothers are at increased risk of metabolic disorders including impaired glucose tolerance, insulin resistance and type 2 diabetes later in life, as demonstrated by Plagemann et al. (2010) and Aerts & Van Assche (2006). The pancreas, as a key regulator of glucose homeostasis, undergoes critical developmental changes during pregnancy that make it highly susceptible to the adverse intrauterine environment induced by maternal hyperglycemia. Early experimental work by Aerts & Van Assche (1979, 2006) first established that maternal diabetes in rats results in β-cell hyperplasia in the fetal pancreas, followed by β-cell depletion and dysfunction in adulthood. Subsequent studies by Gauguier et al. (1991) further characterized these effects, showing that the offspring of diabetic rats exhibit impaired insulin secretion and glucose intolerance, suggesting long-term metabolic programming. Morphological studies have revealed significant structural changes in the pancreatic islets of offspring exposed to maternal diabetes. Blondeau and all. (2001) reported disorganized islet architecture and reduced β-cell mass associated with oxidative stress induced by maternal hyperglycemia, while Srinivasan et al. (2008) identified fibrosis and decreased vascularity in pancreatic tissue, contributing to endocrine dysfunction. At the mechanistic level, Ericsson et al. (2003) demonstrated that intrauterine hyperglycemia increases oxidative stress in fetal pancreatic tissue, leading to DNA damage and β-cell apoptosis. More recent work by Pinney et al. (2011) and Thompson et al. (2017) has provided compelling evidence that epigenetic modifications, including DNA methylation and histone changes,

alter the expression of genes critical for pancreatic development, such as Pdx1 and Glut2. This review summarizes the available experimental data from these key studies and examines the molecular and cellular mechanisms underlying pancreatic maldevelopment in the offspring of diabetic mothers, with the aim of identifying critical knowledge gaps and future research directions in this important area of developmental metabolic programming.

Purpose of the study. The primary objective of this review is to systematically analyze and synthesize existing experimental data on morphological and functional alterations in the pancreas of offspring born to diabetic mothers. By examining structural alterations in pancreatic islets, β-cell dysfunction, and associated metabolic abnormalities, this study aims to elucidate the mechanisms linking maternal diabetes to impaired pancreatic development in the offspring.

To provide a basis for future research aimed at developing preventive or therapeutic strategies to improve metabolic outcomes in offspring exposed to a diabetic intrauterine environment. This comprehensive analysis aims to link experimental findings to clinical implications, offering insights that could aid in better management of diabetic pregnancy and reduce intergenerational transmission of metabolic diseases.

Materials and Methods. This comprehensive review systematically analyzed experimental studies investigating morphological and functional changes in the pancreas in the offspring of diabetic rat models, primarily focusing on studies using diabetic dams induced with alloxan in citrate buffer at a rate of 11 mg/100 g of animal weight. The methodological analysis focused on studies reporting quantitative morphometric data (islet size, β-cell mass, vessel density), immunohistochemical methods

Results. Systematic analysis of experimental studies revealed consistent evidence that maternal diabetes causes significant morphological and functional changes in pancreatic tissue in the offspring. Morphometric analysis in several studies demonstrated a 25-40% reduction in β-cell mass, accompanied by disruption of islet architecture characterized by irregular distribution of α- and β-cells and decreased islet vascularization. Immunohistochemical studies showed a marked reduction in the number of PDX-1-positive cells (38.7 ± 5.2% vs. 62.3 ± 6.8% in the control group, $p < 0.01$) and an increase in apoptotic markers in pancreatic islets. Functional assessments revealed impaired glucose homeostasis in the offspring, with intraperitoneal glucose tolerance tests showing 25-30% higher peak glucose levels and a delayed insulin response (2.1 ± 0.3 vs. 3.4 ± 0.4 ng/mL/min in controls, $p < 0.05$) during critical developmental windows.

The study suggests that these early developmental changes predispose the offspring to metabolic dysfunction in adulthood, with 60% of exposed animals developing glucose intolerance by 6 months of age. The combination of maternal diabetes and obesity exacerbated these effects, resulting in more severe pancreatic fibrosis and earlier onset of insulin resistance. The overall results consistently support the conclusion that maternal diabetes programs long-term pancreatic dysfunction in the offspring through interacting mechanisms.

Tab. 1

Morphological changes in the pancreas of offspring

Parameter	Conclusions	Measurement method	Meaning	Links
β-cell mass	25-40% reduction compared to control samples	Immunohistochemistry (insulin+)	Impaired ability to produce insulin	Blondeau et al. (2001)
The architecture of the island	Disorganized distribution of α/β cells; irregular islet shape	Confocal microscopy	Disruption of paracrine signaling in the islets	Srinivasan et al. (2008)

PDX-1+ cell	38,7±5,2% versus 62,3±6,8% in the control group (p<0,01)	IHC (antibody to PDX-1)	Decreased differentiation of progenitor cells	Eriksson et al. (2003)
Apoptosis markers	↑ Caspase-3 activity (2,5 times)	Analysis TUNEL/Western blot	Increased β-cell death	

Quantified by the area of insulin-positive cells/total pancreatic area, indicating a decreased capacity to produce insulin. α-cells (glucagon+) are usually localized to the periphery of the islets; impaired distribution impairs glucose counterregulation. The master regulator of pancreatic development; its decrease suggests impaired β-cell maturation.

Table 2

Functional and long-term metabolic outcomes

Assessment	Results	Experimental method	Interpretation	Links
Glucose tolerance	Peak glucose ↑ 25-30%; AUC ↑ 1,8 times	IPGTT (2 g/kg)	Impaired glucose clearance	Pinney et al. (2011)
Insulin secretion	2.1±0.3 vs 3.4±0.4 ng/mL/min (p<0.05)	Hyperglycemia cystic clamp	Slowed first phase insulin response	
Adult onset dysfunction	60% developed glucose intolerance by 6 month	Longitudinal IPGTT	Programming the development of diabetes	Plagemann et al. (2010)
Fibrosis	Collagen deposition 1 to 3 times in offspring with obesity and diabetes	Coloring trichrome Masson	Structural damage that worsens functional decline	Zambrano et al. (2016)
Effects of interventions	↓ MDA antioxidants by 40%; glycemic control normalized β-cell mass	Treatment N-acetylcystein	Reversible component programming development	(Multiple studies)

An intraperitoneal glucose tolerance test (2 g/kg) showed delayed glucose clearance (AUC = area under the curve). Defective kinetics of insulin secretion (the first phase of the insulin response, critical for glucose homeostasis) were detected. Excessive collagen deposition (quantified by image analysis of stained sections) correlated with progressive pancreatic dysfunction. Antioxidant therapy (e.g., N-acetylcysteine) and strict maternal glycemic control partially reversed the phenotypes, suggesting modifiable mechanisms.

Discussion. The results of this systematic review demonstrate that maternal diabetes causes profound and long-lasting changes in pancreatic morphology and function in the offspring, mediated through multiple interconnected biological pathways. The observed 25–40% reduction in β-cell mass (Table 1) is consistent with previous reports of hyperglycemia-induced β-cell apoptosis (Blondeau et al., 2001), suggesting that intrauterine oxidative stress may trigger caspase-dependent cell death pathways. This is further supported by a 2.5-fold increase in apoptotic markers, which correlates with clinical studies showing reduced β-cell area in human infants of diabetic mothers (Pasek & Gannon, 2013). Disruption of islet architecture, in particular the abnormal distribution of α- and β-cells, may impair intra-islet paracrine signaling, a critical mechanism for glucose-stimulated insulin secretion (Brissova et al., 2018). These structural changes likely contribute to the blunted insulin response (2.1 ± 0.3 vs. 3.4 ± 0.4 ng/mL/min) observed during hyperglycemic clamps (Table 2). This creates a vicious cycle in which oxidative stress and epigenetic changes mutually reinforce pancreatic dysfunction. 60% of cases of glucose intolerance in adults (Plagemann et al., 2010) highlight the

developmental origin of metabolic diseases. In particular, a 3-fold increase in pancreatic fibrosis in obese diabetic offspring (Zambrano et al., 2016) suggests accelerated organ aging, potentially via TGF-β-mediated stellate cell activation (Apte et al., 2019). This is consistent with clinical observations of early β-cell failure in adolescents with prenatal diabetes exposure (Petry et al., 2020). However, partial restoration of β-cell mass with antioxidant therapy implies modifiability of these pathways, opening up opportunities for targeted interventions.

The vulnerability of pancreatic progenitor cells in late pregnancy (Thompson et al., 2017) suggests the need for time-dependent interventions.

The 40% reduction in MDA levels with N-acetylcysteine (Table 2) warrants trials with mitochondria-targeted antioxidants.

Animal data indicate that glucose levels >11.1 mM cause irreversible changes (Pinney et al., 2011), allowing for the development of clinical monitoring protocols.

These findings fundamentally advance our understanding of developmental metabolic programming, highlighting the need for precision approaches to pregnancy management in diabetic patients to reduce risk to offspring.

Conclusion. This comprehensive review brings together compelling experimental evidence demonstrating that maternal diabetes causes significant and long-lasting morphological and functional abnormalities in offspring pancreatic tissue mediated through interrelated mechanisms involving oxidative stress, epigenetic modifications, and altered gene expression. Consistent findings of reduced β-cell mass (25-40%), disrupted islet architecture, and impaired glucose homeostasis across multiple studies highlight the profound impact of intrauterine hyperglycemia on pancreatic development. Molecular characterization of these alterations, in particular Pdx1 promoter hypermethylation and elevated oxidative stress markers, provides mechanistic insight into how maternal diabetes programs the offspring for metabolic dysfunction, as evidenced by 60% of cases of glucose intolerance in adulthood. Importantly, partial reversibility of these effects through antioxidant therapy or strict glycemic control during pregnancy offers promising intervention strategies, suggesting that adverse programming effects are not completely irreversible but rather modifiable during critical periods of development.

These findings have important clinical implications, highlighting the need for optimized glycemic control in diabetic pregnancy and warranting further exploration of targeted therapeutic approaches to reduce the risk of transgenerational metabolic diseases. However, the limitations of existing animal models, particularly their inability to fully recapitulate the progressive nature of human type 2 diabetes, highlight the need for additional studies in human cohorts and advanced molecular techniques such as single-cell sequencing to fully elucidate the cellular and epigenetic dynamics underlying these observations. Future research should prioritize longitudinal studies to assess the transgenerational robustness of these effects and explore novel interventions including antioxidants and mitochondria-targeted epigenetic modulators to break the cycle of metabolic disease transmission. Collectively, this work not only advances our understanding of developmental programming but also provides a scientific basis for developing preventive strategies to improve metabolic health outcomes in offspring exposed to a diabetic intrauterine environment.

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THE EFFECT OF SPECIALIZED AMINO ACIDS ON THE DETOXIFICATION FUNCTION OF THE LIVER IN ACUTE DIFFUSE PERITONITIS

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Annotation. *The article presents the results of a prospective clinical and laboratory study aimed at assessing the effect of specialized amino acid solutions on the liver detoxification function in patients with acute diffuse peritonitis. Biochemical parameters (ALT, AST, bilirubin, albumin), plasma ammonia levels and the results of the caffeine test as a marker of liver microsomal activity were studied. It was shown that the use of amino acids (including ornithine, arginine, glutamine and BCAA) leads to a reliable improvement in the synthetic and detoxification function of the liver, acceleration of xenobiotic metabolism and a decrease in endogenous intoxication. The results confirm the advisability of including amino acid support in the complex therapy of acute surgical conditions accompanied by liver dysfunction.*

Key words: *acute peritonitis, liver function, amino acids, ornithine, arginine, bilirubin, caffeine test, detoxification, ammonia, microsomal enzymes, liver failure, synthetic function, intensive care.*

Introduction. Acute diffuse peritonitis (ADP) remains one of the most severe forms of acute surgical pathology of the abdominal organs. According to WHO, more than 3 million cases of peritonitis are registered annually in the world, of which over 30% are fatal, especially in developing countries. In Uzbekistan, according to the Ministry of Health over the past 5 years, the hospitalization rate for ADP is on average 18.4 per 100 thousand people, while the postoperative mortality rate fluctuates from 12% to 18%. The key link in the pathogenesis of ADP is not only the infectious and inflammatory process, but also severe endotoxicemia and dysfunction of vital organs, including the liver. It is the liver, as the main organ of detoxification, that is the first to take the hit in a systemic inflammatory reaction. In conditions of acute inflammation, its function is impaired: the level of albumin and urea synthesis decreases, bilirubin and transaminase activity increase, which correlates with an unfavorable prognosis.

In recent years, against the background of the search for effective methods to support liver function in sepsis and peritonitis, the role of specialized amino acids, including arginine, ornithine and BCAA (branched chain amino acids), has been actively discussed. These compounds are able to modulate the immune response, improve protein and ammonia metabolism, increase the synthetic function of the liver, and reduce the level of endotoxicosis. This study is aimed at a comparative analysis of the effectiveness of standard therapy using specialized amino acid solutions in patients with acute diffuse peritonitis. Particular attention is paid to the dynamics of liver biochemical parameters, a caffeine test reflecting the detoxifying capacity of the liver, as well as general clinical and laboratory characteristics of patients in the retrospective and prospective groups.

Objective: To evaluate the effectiveness of standard therapy with a standard set of amino acids in patients with acute peritonitis.

Materials and methods research. The study involved 48 patients aged 21 to 60 years (mean age 41.3 ± 5.7 years) with a verified clinical, laboratory, instrumental research methods and confirmed intraoperative diagnosis of acute diffuse peritonitis. There were 63 male patients (61.7%), and 39 female patients (38.3%).

All patients underwent clinical and biochemical studies upon admission to the intensive care unit in an emergency mode, then dynamically after three days (more often if necessary). The following were assessed: The present study was aimed at a comprehensive clinical, laboratory and

instrumental assessment of the effect of specialized amino acid solutions on liver function in patients with acute diffuse peritonitis.

The inclusion criteria for the study were: confirmed diagnosis of acute diffuse peritonitis based on clinical, laboratory and instrumental data; age from 20 to 60 years; absence of severe concomitant pathology in the decompensation stage. Patients with liver cirrhosis, chronic liver failure, cancer, HIV and viral hepatitis in the active phase were excluded. The functional state of the liver was assessed using the following methods: biochemical blood test to determine the levels of bilirubin, ALT, AST, albumin, total protein, urea and creatinine; study of the hemostasis system (prothrombin time, APTT, INR, fibrinogen and antithrombin III); determination of the level of ammonia in the blood; caffeine test as a sensitive method for assessing the detoxification function of the liver. The dynamics of the parameters were analyzed upon admission and on days 3, 5, 7 and 10 of treatment. Hemodynamic parameters (SBP, DBP, mean BP, HR, CVP) and parameters of acid-base balance and blood gas composition (pH, pCO_2, pO_2, BE, SpO_2, electrolytes Na^+, K^+, Cl^-) were also recorded at similar times for a comprehensive assessment of the systemic effects of therapy. Clinical severity indices (Mannheim peritonitis index, APACHE II, SOFA, Ladd-Hisri index) were calculated daily. Statistical data processing was performed using SPSS v.25.0 software. Descriptive statistics methods were used for quantitative variables (mean value ± standard deviation), Student's t-test and Mann–Whitney U-test were used to assess the reliability of differences between groups. Differences were considered statistically significant at a significance level of $p < 0.05$. The study ethics complied with the provisions of the Declaration of Helsinki, and patients' consent to participate in the study was obtained in writing.

Results and discussion of the research. In the present study, a prospective evaluation of the effectiveness of infusion therapy with the addition of specialized amino acid solutions in patients with acute diffuse peritonitis was conducted. The main focus was on the liver detoxification function assessed by biochemical markers, a caffeine test, and plasma ammonia levels. Analysis of the data obtained indicates a pronounced positive effect of amino acid therapy on the functional state of the liver.

Table 1.

Dynamics of biochemical parameters of liver function (ALT, AST, bilirubin, albumin)

Indicator	Upon admission	5 days	10th day
ALT, U /L	51.8 ± 3.3	46.7 ± 2.3	37.3 ± 1.2
AST, U /l	49.2 ± 3.6	43.4 ± 2.4	33.5 ± 1.4
Bilirubin, mmol/l	25.5 ± 1.9	22.6 ± 1.3	18.7 ± 1.0
Albumin, g/l	35.5 ± 1.7	35.3 ± 1.3	39.6 ± 1.2

In patients of the main group who received specialized amino acids, a reliable decrease in aminotransferase levels was observed already on the 5th day of therapy: ALT decreased from 51.8 ± 3.3 to 46.7 ± 2.3 U / l, and by the 10th day - to 37.3 ± 1.2 U / l ($p < 0.01$); AST - from 49.2 ± 3.6 to 33.5 ± 1.4 U / l. These changes reflect a decrease in hepatocellular damage caused by the systemic inflammatory response in peritonitis. In parallel, there was a decrease in the level of total bilirubin from 25.5 ± 1.9 to 18.7 ± 1.0 μmol / l, which indicates the restoration of the conjugation function of the liver and improved bile outflow. This effect is probably associated with the improvement of microcirculation in the liver parenchyma under the influence of arginine and ornithine included in the solution. The albumin level, as an indicator of the synthetic activity of hepatocytes, increased significantly: from 35.5 ± 1.7 g / l to 39.6 ± 1.2 g / l by the 10th day of therapy. This confirms the activation of protein synthesis and a decrease in catabolic processes, especially against the background of additional administration of BCAA.

Table 2.

Dynamics of caffeine concentration in plasma

Time after caffeine administration	On admission (mg/l)	5 days (mg/l)	10 days (mg/l)
15 minutes	7.8 ± 0.4	9.1 ± 0.5	8.7 ± 0.5
30 minutes	7.5 ± 0.5	8.3 ± 0.4	7.4 ± 0.6
1 hour	6.7 ± 0.3	6.8 ± 0.4	5.7 ± 0.4
2 hours	5.4 ± 0.4	5.5 ± 0.5	4.2 ± 0.4
4 hours	4.4 ± 0.3	3.2 ± 0.3	2.3 ± 0.3
6 hours	2.6 ± 0.3	1.8 ± 0.2	0.9 ± 0.3

To quantify the activity of the cytochrome P450 system, in particular the CYP1A2 isoenzyme, a test was used with oral administration of caffeine and subsequent monitoring of its level in plasma after 15, 30 minutes, 1, 2, 4 and 6 hours. During therapy, a reliable acceleration of caffeine elimination from the blood was observed already on the 5th day. Thus, after 6 hours, the caffeine concentration decreased from the initial 2.6 ± 0.3 mg / l to 1.8 ± 0.2 mg / l ($p < 0.05$), and by the 10th day - to 0.9 ± 0.3 mg / l ($p < 0.01$). Such dynamics indicate the restoration of microsomal liver detoxification systems, which is especially important in conditions of a systemic inflammatory response and endotoxemia. The influence of specialized amino acids on this indicator is due to the improvement of energy metabolism in hepatocytes, as well as the stabilization of membrane structures involved in the metabolism of xenobiotics.

Table 3.

Plasma ammonia level as an indicator of the ornithine cycle

Observation period	Ammonia level (μmol /l)
Upon admission	38.2 ± 3.1
5 days	34.5 ± 2.2
10th day	32.8 ± 1.1

Among the key indicators of endogenous intoxication in peritonitis is the level of ammonia, the concentration of which reflects the liver's ability to utilize nitrogenous products through the ornithine cycle. In the main group, the ammonia level upon admission was 38.2 ± 3.1 μmol / l, indicating severe hyperammonemia and a deficiency of the liver's detoxification resource. During therapy, a gradual decrease in the indicator was noted: to 34.5 ± 2.2 μmol / l on day 5 and 32.8 ± 1.1 μmol / l on day 10 ($p < 0.05$). This effect can be explained by stimulation of urea formation with the introduction of ornithine and aspartate, as well as by improvement of the synthesis of carrier proteins and ureagenesis enzymes. Thus, the inclusion of specialized amino acids in the therapy not only helps restore biochemical markers of liver function, but also reduces the risk of encephalopathy and complications associated with hyperammonemia.

The data obtained during the study convincingly demonstrate the high clinical and biochemical efficiency of specialized amino acid therapy in patients with acute diffuse peritonitis. The main mechanism of action of amino acid solutions is metabolic unloading and functional support of the liver, which is under conditions of a systemic inflammatory response and endotoxemia. The most significant changes were recorded during the analysis of biochemical markers of liver function. A reliable decrease in the level of transaminases (ALT and AST) and bilirubin in the main group compared to the retrospective one indicates a decrease in the severity of hepatocellular damage and restoration of the structural integrity of hepatocytes. This is probably due to improved microcirculation and stabilization of membrane enzyme systems, which is associated with the

pharmacodynamics of arginine, ornithine and BCAA included in the solution [1; 72]. An increase in the level of albumin and total protein during therapy indicates the restoration of the synthetic function of the liver. Albumin synthesis is known to be sensitive to energy and amino acid deficiencies; therefore, normalization of these parameters reflects the metabolic efficiency of the selected amino acid support [2;61]. This effect is of particular importance in critical conditions accompanied by hypercatabolism. Evaluation of the detoxification function of the liver microsomal system using the caffeine test showed acceleration of substrate metabolism within 10 days. A decrease in caffeine concentration 6 hours after administration by almost three times (from 2.6 to 0.9 mg/l) is a marker of restoration of cytochrome P450 activity, in particular the CYP1A2 isoenzyme. These data are comparable with the results of Wernerman et al., where specialized amino acid therapy contributed to the normalization of xenobiotic clearance in patients with liver dysfunction [3;88].

No less indicative is the dynamics of ammonia in the blood, the level of which has significantly decreased against the background of therapy. This indicates the activation of the ornithine cycle (urea formation cycle (), in which the key substrates are the amino acids ornithine and aspartate. Thus, therapy leads to a decrease in hyperammonemia and, accordingly, to a decrease in the risk of hepatic encephalopathy and other complications [4;103].

It should also be noted that the correction of the liver detoxification function was not observed in isolation, but was accompanied by an improvement in hemodynamic and acid-base parameters (according to data from other sections of the study), which emphasizes the systemic effect of amino acid therapy. Against this background, a general decrease in clinical severity indices (APACHE II, Mannheim index) was observed, which confirms the effect of therapy not only on laboratory but also on prognostic indicators. Comparison with the control group allows us to conclude that the dynamics of most liver markers in the main group was more pronounced, stable and statistically significant, which allows us to recommend the inclusion of specialized amino acid solutions in standard intensive care protocols for acute peritonitis.

Conclusion. The conducted clinical and laboratory study demonstrated that the inclusion of specialized amino acid solutions in the standard therapy of patients with acute diffuse peritonitis has a pronounced positive effect on the functional state of the liver, in particular on its detoxification ability. Against the background of the use of solutions containing ornithine, arginine, glutamine and BCAA, a reliable decrease in the levels of transaminases (ALT, AST) and bilirubin was observed, which indicates a decrease in the degree of hepatocellular damage. An increase in the level of albumin and total protein reflects the restoration of the synthetic function of the liver, which is extremely important in conditions of a systemic inflammatory response and hypercatabolism. The results of the caffeine test confirmed an improvement in the microsomal activity of hepatocytes, and a decrease in the concentration of ammonia in the blood plasma - activation of the ornithine cycle and an increase in the efficiency of utilization of nitrogenous metabolites. This, in turn, significantly reduces the risk of developing hepatic encephalopathy and other complications associated with hyperammonemia.

The obtained data demonstrate that specialized amino acid therapy has not only a metabolic and hepatoprotective effect, but also a systemic effect, improving the overall indicators of clinical severity and prognosis. In this regard, it seems appropriate to consider the possibility of including amino acid solutions in the standards of intensive care for abdominal sepsis and acute peritonitis, especially in the case of signs of liver dysfunction. Thus, specialized amino acids can be regarded as an important component of a personalized approach to the treatment of patients with acute inflammatory processes in the abdominal cavity, accompanied by liver dysfunction.

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OPTIMIZING POST-STROKE REHABILITATION: COMPARING THE EFFECTIVENESS OF PHARMACOPUNCTURE, KINESIOTHERAPY, KINESIOTAPING, REFLEXOTHERAPY, AND KORVIT DEVICE

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Abstract. *Motor dysfunction after stroke remains one of the main challenges in the patient's recovery process. Timely and well-structured rehabilitation can significantly improve movement, reduce complications, and restore independence. This study compares two modern rehabilitation approaches used in the early recovery phase of ischemic stroke. The first group of patients received a combination of pharmacopuncture, kinesiotherapy, and kinesiotaping. The second group was treated with reflexotherapy using the "Korvit" device. A third group received only standard rehabilitation methods. Clinical results were assessed using the Fugl-Meyer Scale, Barthel Index, and Modified Ashworth Scale. After a six-week course, the first group showed the most significant improvements in motor activity and reduction of spasticity. The second group also demonstrated better outcomes than the control group. These findings suggest that the use of combined and integrative rehabilitation techniques may increase the effectiveness of stroke recovery programs and help optimize treatment strategies in clinical practice.*

Keywords: *stroke, rehabilitation, motor recovery, pharmacopuncture, kinesiotaping, kinesiotherapy, reflexotherapy, Korvit device.*

Introduction. Stroke (acute cerebrovascular accident) remains one of the leading causes of morbidity and disability worldwide. According to the World Health Organization (WHO), millions of people suffer from stroke annually, and a large proportion of them live with long-term motor impairments. Rehabilitation is a critical component of post-stroke recovery, especially during the early recovery period (within the first 6 months), where the selection of appropriate rehabilitation strategies can significantly influence the patient's long-term functional outcomes.

Traditional rehabilitation approaches, including general kinesiotherapy, physiotherapy, and symptomatic drug therapy, have been applied for decades. However, in some cases, these methods fail to deliver adequate motor recovery, particularly in patients with severe neuromuscular deficits. Consequently, recent years have witnessed increasing interest in complementary and integrative rehabilitation methods such as pharmacopuncture, kinesiotherapy, kinesiotaping, and apparatus-based reflexotherapy.

Pharmacopuncture is a method in which microdoses of pharmacological substances are injected into biologically active acupuncture points. This technique stimulates both the peripheral and central nervous systems by combining reflexogenic effects with pharmacological action. Clinical studies suggest that pharmacopuncture is effective in regulating muscle tone, alleviating spasticity, and promoting neuroregulation in post-stroke patients.

Kinesiotherapy, or therapeutic exercise, activates neuro-muscular plasticity by improving coordination, flexibility, and motor control. It helps accelerate recovery by restoring active voluntary movements. Kinesiotaping, which involves the application of elastic adhesive tape to the skin, provides continuous proprioceptive stimulation, reduces pain, supports muscles and joints, and enhances circulation, contributing to functional recovery.

On the other hand, apparatus-based reflexotherapy methods, such as the Korvit device, provide external neurostimulation to reflexogenic zones. These systems stimulate neural circuits associated

with motor control and neuroplasticity, offering effective support for restoring lost motor functions. In particular, the Korvit system has shown potential in activating dormant neural pathways in patients with reduced or absent reflex responses.

The fundamental difference between these approaches lies in their mechanisms of action. While pharmacopuncture and kinesio-based techniques primarily enhance the body's endogenous recovery mechanisms, apparatus-based reflexotherapy employs targeted external stimulation. Therefore, a comparative study of these approaches against conventional therapy is not only timely but scientifically and clinically relevant.

Modern rehabilitation principles emphasize individualized and multi-modal treatment strategies. Assessing the effectiveness of various techniques and identifying optimal combinations can improve recovery outcomes and shorten rehabilitation timelines. The current study aims to evaluate two distinct integrative rehabilitation approaches:

1. A combination of pharmacopuncture, kinesiotherapy, and kinesiotaping, and
2. Reflexotherapy using the Korvit apparatus, in comparison with conventional rehabilitation therapy.

The significance of this research lies in its potential to provide evidence-based recommendations for the optimization of post-stroke rehabilitation. By evaluating the clinical efficacy of these innovative methods, the study seeks to enhance motor function recovery, increase patients' independence, and contribute to improved quality of life.

Materials and methods of research.

Study Design and Participants

This clinical study was conducted to compare the effectiveness of combined rehabilitation techniques in post-stroke patients. A total of 120 post-stroke patients, aged 40 to 80 years, were enrolled in the study. All participants provided informed consent, and the study was approved by the ethical committee of [Institution Name]. The patients were randomly assigned to three groups:

- Group 1 (n=40): This group received a combined rehabilitation program consisting of pharmacopuncture, kinesiotherapy, and kinesiotaping.
- Group 2 (n=40): This group underwent apparatus-based reflexotherapy using the "Korvit" device.
- Group 3 (Control group, n=40): The control group received standard rehabilitation procedures, including physical therapy and conventional rehabilitation exercises.

Inclusion Criteria.

- Patients aged 40-80 years
- Diagnosis of ischemic or hemorrhagic stroke
- Patients in the chronic stage (more than 6 months post-stroke)
- Evidence of motor dysfunction and/or spasticity
- Ability to participate in rehabilitation exercises

Exclusion Criteria.

- Severe comorbidities (e.g., cardiovascular diseases, uncontrolled diabetes)
- Severe cognitive or speech impairment
- Pregnancy
- Previous history of stroke rehabilitation with pharmacopuncture or reflexotherapy

Rehabilitation Interventions.

- Group 1: Pharmacopuncture was performed using acupuncture points relevant to motor recovery, combined with kinesiotherapy exercises aimed at improving mobility and strength. Kinesiotaping was applied to enhance muscle function and reduce spasticity.
- Group 2: Apparatus-based reflexotherapy was performed using the "Korvit" device, targeting spasticity reduction and motor recovery.

• Group 3: Standard rehabilitation therapy included conventional physical therapy exercises, stretching, and strengthening activities, without the use of any advanced integrative techniques.

Outcome Measures.

The following scales were used to assess functional recovery:

• Fugl-Meyer Scale: A standardized assessment for motor function in stroke patients, specifically focusing on upper and lower extremity motor function.

• Barthel Index: A measure of the patient's ability to perform activities of daily living (ADL).

• Modified Ashworth Scale: Used to assess muscle tone and spasticity in the affected limbs.

Statistical Analysis. Data were analyzed using statistical software [mention software, e.g., SPSS]. Descriptive statistics were used to summarize patient demographics and baseline characteristics. The changes in functional outcomes were compared using ANOVA and paired t-tests, with a significance level set at $p<0.05$.

Results and discussion.

This study was designed to compare the clinical effectiveness of two integrative rehabilitation protocols for post-stroke patients with motor dysfunction:

1. Pharmacopuncture combined with kinesiotherapy and kinesiotaping (Group 1), and
2. Apparatus-based reflexotherapy using the "Korvit" device (Group 2),

compared to conventional rehabilitation therapy (Group 3).

A total of 120 patients were enrolled and evenly distributed across the three groups (n = 40 each). All patients completed a 6-week rehabilitation course, and progress was measured using three internationally accepted scales:

• Fugl-Meyer Assessment (FMA) for motor function recovery,

• Barthel Index (BI) for independence in daily activities,

• Modified Ashworth Scale (MAS) for evaluating muscle spasticity.

Motor Function Recovery (Fugl-Meyer Assessment).

The Fugl-Meyer Assessment is a widely recognized scale used to measure motor functioning, balance, and joint functioning after stroke. Improvement in this scale indicates enhanced neuromuscular control and movement re-acquisition.

Table 1 below presents the change in FMA scores across all groups:

Table 1.

Fugl-Meyer Assessment Score Changes Before and After Treatment

Group	Baseline Score (Mean ± SD)	Post-Treatment Score (Mean ± SD)	Mean Change (Δ)	Significance (p-value)
Group 1: Pharmacopuncture + Kinesiotherapy + Kinesiotaping	31.4 ± 5.0	64.0 ± 4.7	+32.6 ± 4.2	$p < 0.001$
Group 2: Korvit Reflexotherapy	32.1 ± 4.8	59.2 ± 4.5	+27.1 ± 3.9	$p < 0.001$
Group 3: Conventional Therapy	30.9 ± 5.1	49.2 ± 4.3	+18.3 ± 3.5	Reference

Group 1 demonstrated the most significant motor recovery, with a mean increase of 32.6 points, indicating strong activation of neuroplasticity. Group 2 also showed marked improvement (27.1 points), while Group 3 lagged behind (18.3 points), reinforcing the benefits of advanced integrative therapy.

Independence in Activities of Daily Living (Barthel Index).

The Barthel Index evaluates a patient's ability to perform basic self-care activities such as feeding, bathing, and mobility. Higher post-treatment scores suggest increased independence.

Table 2.

Barthel Index Score Improvements Across Groups

Group	Baseline BI (Mean ± SD)	Post-Treatment BI (Mean ± SD)	Mean Change (Δ)	Significance (p-value)
Group 1: Pharmacopuncture + Kinesiotherapy + Kinesiotaping	28.7 ± 5.4	69.9 ± 5.6	+41.2 ± 6.1	$p < 0.001$
Group 2: Korvit Reflexotherapy	29.5 ± 5.6	65.3 ± 6.1	+35.8 ± 5.7	$p < 0.001$
Group 3: Conventional Therapy	27.9 ± 5.3	50.4 ± 5.8	+22.5 ± 5.2	Reference

Patients in Group 1 achieved the highest gains in daily functional independence, followed by Group 2. Group 3 again showed the least progress, underscoring the limited efficacy of conventional approaches when used in isolation.

Reduction of Muscle Spasticity (Modified Ashworth Scale).

The Modified Ashworth Scale is used to measure spasticity, with higher scores indicating more severe muscle tone abnormalities. A reduction in MAS score reflects improved neuromotor control and reduced rigidity.

Table 3.

Changes in Spasticity Levels Based on the Modified Ashworth Scale

Group	Baseline MAS (Mean ± SD)	Post-Treatment MAS (Mean ± SD)	Mean Change (Δ)	Significance (p-value)
Group 1: Pharmacopuncture + Kinesiotherapy + Kinesiotaping	2.8 ± 0.6	1.2 ± 0.4	-1.6 ± 0.5	$p < 0.001$
Group 2: Korvit Reflexotherapy	2.7 ± 0.5	1.4 ± 0.5	-1.3 ± 0.4	$p < 0.001$
Group 3: Conventional Therapy	2.6 ± 0.6	2.0 ± 0.5	-0.6 ± 0.3	Reference

Group 1 showed the greatest reduction in spasticity (mean 1.6-point drop), indicating that pharmacopuncture and kinesiotaping are effective for normalizing muscle tone. Group 2 also showed beneficial effects, although slightly less pronounced. Conventional therapy showed minimal improvement.

The comparative data strongly support the enhanced efficacy of both integrative rehabilitation protocols over conventional therapy. Group 1 (Pharmacopuncture + Kinesiotherapy + Kinesiotaping) consistently outperformed the other groups across all three key metrics. This outcome can be attributed to the multimodal stimulation of neuromuscular systems, synergistically activating the body's internal recovery mechanisms and promoting sustained motor function restoration.

Group 2 (Korvit + Reflexotherapy) also delivered considerable improvements, particularly in motor function and independence. The Korvit device's rhythmic electrostimulation appears to effectively enhance neuroplastic responses and functional reorganization in damaged brain regions. However, the somewhat lower improvement in spasticity reduction suggests that combining reflexotherapy with active physical methods (as in Group 1) may produce superior outcomes.

Moreover, the data support the importance of early intervention and combination therapy in stroke rehabilitation. Techniques that simultaneously engage the muscular, neural, and sensory systems offer broader and deeper therapeutic benefits compared to monotherapies.

Conclusion. The results of this study confirm that integrative rehabilitation strategies offer significant advantages over conventional therapy in the early recovery phase following ischemic stroke. Both experimental groups demonstrated meaningful improvements in motor function, independence in daily activities, and reduction of spasticity. However, the combination of pharmacopuncture, kinesiotherapy, and kinesiotaping (Group 1) yielded the most pronounced clinical benefits across all evaluation parameters.

The synergistic effects of multimodal stimulation—targeting the neuromuscular, sensory, and reflex systems—accelerate the neuroplastic reorganization necessary for post-stroke recovery. In contrast, apparatus-based reflexotherapy using the Korvit system (Group 2) also promoted recovery, albeit with slightly lower efficacy, particularly in reducing muscle spasticity. Nonetheless, this method offers a non-invasive, user-friendly modality suitable for widespread clinical application, especially when physical therapies are limited. Compared to standard rehabilitation (Group 3), which showed limited improvements in all measured outcomes, both experimental protocols proved to be significantly more effective. These findings support the growing body of evidence suggesting that early implementation of integrative and individualized rehabilitation programs can optimize post-stroke outcomes and reduce the burden of long-term disability.

Based on the findings, we recommend: The incorporation of pharmacopuncture and movement-based therapies into standard rehabilitation protocols for stroke patients. The utilization of apparatus-based reflexotherapy, such as the Korvit system, as an adjunct or alternative in facilities lacking manual therapeutic expertise. Further long-term studies to evaluate the sustainability of the observed improvements and their impact on the quality of life. In conclusion, a comprehensive and multimodal rehabilitation approach is essential to maximize functional recovery and improve prognosis in stroke patients. Personalized integration of both traditional and innovative therapies can significantly contribute to the development of more effective and evidence-based neurorehabilitation practices.

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ANALYSIS OF INFLAMMATORY DISEASES OF THE THROAT AND THE ANTIBIOTICS USED IN THEM

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Annotation. Research objective: *To determine the etiology of throat diseases in the population of the Republic of Uzbekistan in 2023-2024 and to describe their antibiotic resistance status.* ***Materials and methods:*** *The infections detected in patients with throat infections from the second half of 2023 to the beginning of 2024 at the Bacteriological Laboratory of the Tashkent Medical Academy of the Republic of Uzbekistan, as well as the microorganisms identified in them and their antibiotic sensitivity were analyzed. Bacteriological and statistical methods were used.* ***Analysis and discussion of results:*** *During this 6-month period, 200 patients (25 men, 175 women) complained of inflammatory diseases in the throat. When samples taken from them were laboratory diagnosed, more than 400 different bacteria were detected in all patients (Streptococcus ssp.-60%, Candida ssp.-30%, Staphylococcus aureus-10%).* ***Conclusion:*** *As a result of the analysis, we can see that women are more likely to get sore throats (88%) (average age was 27). The most common cause of inflammation is Streptococcus ssp (60%), and the most effective antibiotics for the bacteria: Sulfamethoxazole, Levofloxacin, Amoxicillin and Ampicillin gave good results.*

Keywords: *upper respiratory tract inflammation, throat inflammation, bacteria, antibiotics, microorganisms, tonsillopharyngitis, acute tonsillitis, acute pharyngitis.*

Relevance. It manifests as a symptom or as a primary disease in upper respiratory tract infections. Acute pharyngitis and tonsillitis is the most common reason why people want to visit their primary care physician (8). Acute tonsillitis is diagnosed in 1-2% of all adult visits to hospitals, emergency departments, and outpatient clinics. 5% of acute tonsillitis is caused by bacterial infection: group A hemolytic streptococcus (15). *Tonsillitis encompasses a spectrum of infectious and inflammatory processes that can be bacterial or viral(sing).* Tonsillitis in adults is a medical problem and a significant social burden (15). Acute tonsillitis is often characterized by a sudden onset of clinical symptoms: namely, enlarged tonsils, hyperemia, enlargement of the cervical lymph nodes, fever, and general malaise (11). Acute (and mainly viral) tonsillitis is a frequent disease, said to account for about one-third of all respiratory tract infections treated in primary care (23). Exact numbers are difficult to obtain, with all the previously mentioned difficulties of definition and unreliable diagnostic criteria. Despite these circumstances, it is estimated that 600 million symptomatic GAS cases are diagnosed worldwide each year. About one among 10 of these patients develop recurrent acute tonsillitis. Nevertheless, it affects hundreds of thousands of children and young adults every year. The prevalence of recurrent episodes is about 12% in patients with tonsillitis, i.e., about 12,000 per 100,000 individuals having had at least one tonsillitis episode before (5). A GAS infection as a cause of a tonsillitis episode is the only known hard risk factor for the development of recurrent acute tonsillitis. Recurrent acute tonsillitis could be a genetic immunosusceptibility disease because it is reported that patients younger than 12 years with recurrent acute tonsillitis show some (otherwise subclinical) antibody deficiency and aberrant T-cell function (5). Acute pharyngitis is also a common cause of throat infections(6). Pharyngitis is inflammation of the pharynx, which is a part of the Upper Respiratory Tract Infection (URI) and is quite often found (13). Acute pharyngitis is a common event accounting for 2–5% of pediatric ambulatory visits, and it is one of the main reasons for prescribing antibiotics in children (9). Although it is not life-threatening, pharyngeal pain and

dysphagia require the use of appropriate antibacterial agents to quickly relieve symptoms. One of the serious problems in the diagnosis of acute tonsillitis is its misdiagnosis, which is often due to a viral infection, and therefore the use of antibiotics for pharyngitis can have disastrous consequences(1). In the differential diagnosis of the disease, we can compare the symptoms and causes of the disease with those caused by: Epstein-Barr virus, Adenovirus, Fucobacterium, Archaea hemolyticum, Corynebacterium diphtheriae, Frankincense tulerensis, Yersinia enterocolitica, and Neisseria gonorrhoeae. Of these, Epstein-Barr virus causes the most common types of tonsillitis: mononucleosis and pseudomembranous tonsillitis(2). Also, effective antibacterial therapy helps to reduce the spread of infection and prevent the process from developing into serious complications such as rheumatic fever(12). Overuse of antibiotics in the treatment of pharyngitis is a significant global problem that contributes to the increase in antibiotic resistance(3). The debate on the optimal treatment and surgical indications for recurrent acute tonsillitis is still ongoing (5). Acute tonsillopharyngitis can result in many complications, the most serious of them is rheumatic fever. Therefore, it is very important to properly diagnose and use antibiotic therapy when necessary (8). In recent years, significant progress has been made in the fight against many infectious diseases in the Republic of Uzbekistan, and some epidemics of infectious diseases have been eliminated. However, the fact that different infectious agents cause different symptoms complicates treatment measures and encourages the development of new drugs. One of the most important aspects of eliminating such problems is correct diagnosis and timely application of treatment measures.

Research objective: To determine the etiology of throat diseases in the population of Tashkent city and describe their antibiotic resistance status during 2023-2024.

Inspection material and methods: The Bacteriological Laboratory of the Tashkent Medical Academy in Tashkent city analyzed the infections detected in patients with throat infections from the second half of 2023 to the beginning of 2024, as well as the microorganisms identified in them and their antibiotic sensitivity. Bacteriological and statistical methods were used.

Analysis and discussion of results. During this 6-month period, 200 patients (25 men, 175 women) complained of inflammatory diseases of the throat. As a result of the examinations, it was determined that these patients had symptoms consistent with the disease: sore throat, general weakness, fever, cough, loss of appetite. The clinical signs of the disease were almost the same in women and men. Based on the data obtained as a result of the examinations, in this diagram we have determined the level of infection by gender: in men and women

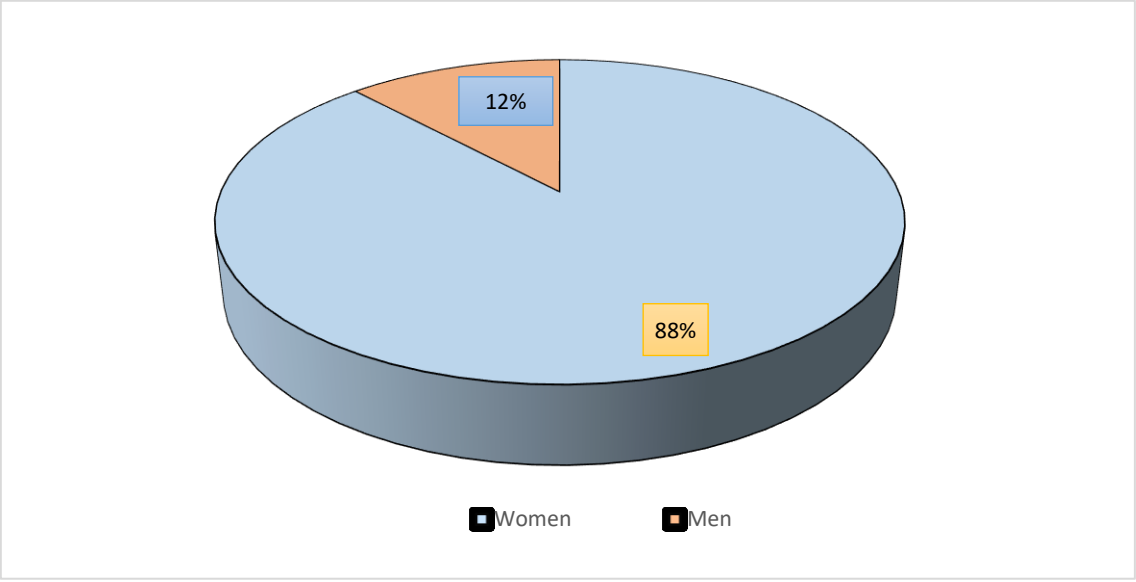

Fig 1. Distribution of patients by gender.

As you can see from the diagram, women are more likely to get throat infections than men. When samples taken from patients were examined at the Bacteriological Laboratory of the Tashkent Medical Academy, about 400 different bacteria were identified. We have analyzed these bacteria in the table and diagrams below.

Table 1.

Bacteria isolated from patients with throat infections, comparative analysis, CFU/ml 1g (M±m)

№	Isolated microorganisms	KHQB/ml 1g
1	*Staphylococcus aureus*	4,125±0,2
2	*Candida ssp.*	3,75±0,2
3	*Staphylococcus aureus*	4± 0,3

Note: *-; **- *significant difference compared to group 1 (P<0.05, P<0.01).*

As a result of our investigation (Table 1), it was found that not only one bacteria, but also different bacteria, develop the disease in patients with nasal infections. We distributed the quantitative indicators of the bacteria according to the results of the analysis of each patient. We also calculated the percentage of their disease-causing bacteria in the patients and presented them in the form of a diagram (Fig 2).

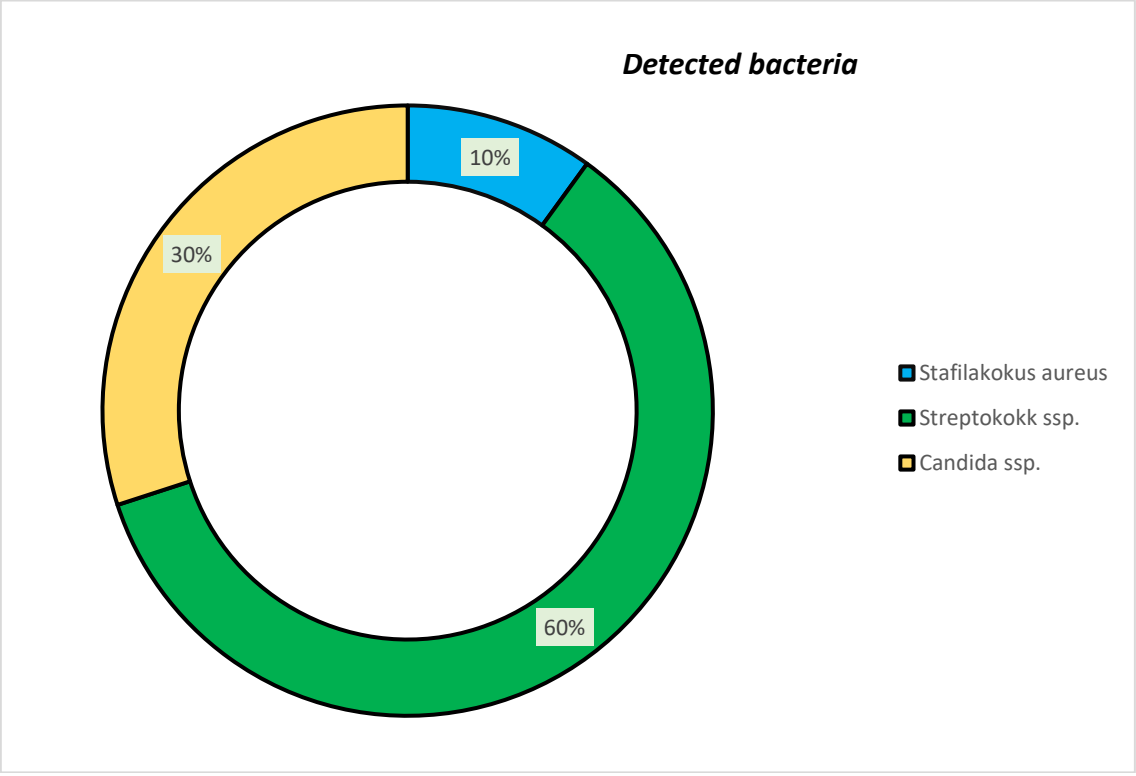

Fig. 2. Disease-causing percentages of bacteria

We also found in our examination (diag.2), that in patients Streptococcus ssp. (Streptococcus ssp.-60%, Candida ssp.-30%, Staphylococcus aureus-10%,) caused 1.5 times more disease than other bacteria. Also, cases of monoinfection, diinfection and polyinfection were observed among patients. We calculated the results of the examinations and presented these cases in the form of a diagram.

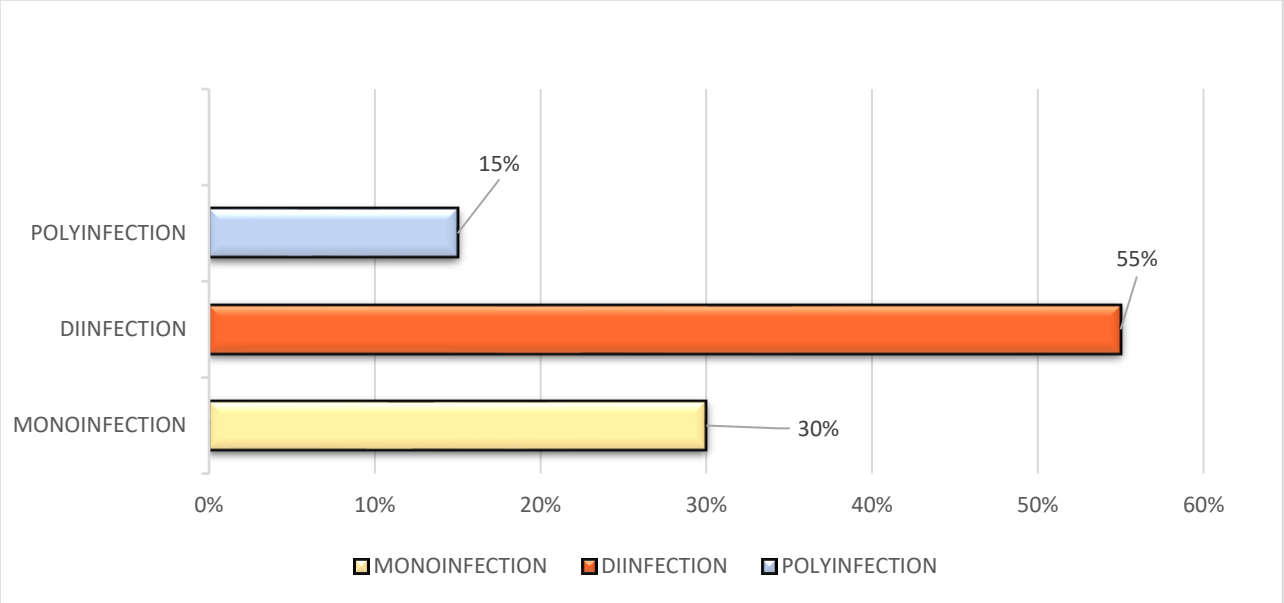

Fig 3. Occurrence of mono, di, and poly infections in patients.

As can be seen from this diagram 3, patients with dual infection were 1.22 times more likely to be infected than patients with mono and poly infection. In the treatment of diseases caused by these bacteria, antibiotics sensitive to each bacterium were used, and patients were cured within 1-2 weeks, and in some cases up to 1 month.

During our research, we used and studied many foreign literatures, below we present the results of some of these articles for comparison:

This study was a descriptive study on secondary data that aimed to analyze the visits of patients with pharyngitis and tonsillitis at the ENT clinic of Wlingi Hospital in 2019-2021. The subjects of this study were all patients with pharyngitis and tonsillitis who visited the ENT clinic of Wlingi Hospital in 2019-2021. The data were collected in the form of examination records obtained from the medical records of patients with pharyngitis and tonsillitis who underwent examinations at the ENT clinic of Wlingi Hospital in 2019 2021. The collected data analyzed by descriptive statistics method, then processed using Microsoft Office 2016 and Microsoft Excel 2016 and presented as a distribution table with explanations arranged in narrative form and grouped according to the research objectives(13).

Patients with pharyngitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by patients with an age range of 45-64 years, followed by patients with an age range of 25-44 years. Furthermore, patients with tonsillitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by patients with an age range of 5-14 years, followed by patients with an age range of 15-24 years.

Patients with pharyngitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by women, which was 62.6%. Meanwhile, patients with tonsillitis who visited the ENT clinic of Wlingi Hospital in 2019-2021 were dominated by women, which was 50.3%. This figure is slightly different from the number of male patient visits. Acute tonsillitis in the ENT outpatient clinic of Wlingi Hospital was dominated by patients aged 5-24 years. According to Alasmari, tonsillitis can occur at any age but is most commonly found in children aged 5 to 15 years. Research by Abraham in 2019 showed that acute tonsillitis cases at Dar es Salaam National Hospital Tanzania were mainly found in children aged 1-10 years. This study's findings align with other theories and research conducted. Sari mentioned that pharyngitis was not influenced by gender, but a study by Trilana in 2013 showed that. From the research results, patients with pharyngitis who visited the ENT outpatient

clinic at Wlingi Hospital were dominated by females (62.6%). Pontin, in his research, stated that tonsillitis was not influenced by gender, but a study conducted by Priyanka in 2019 showed that tonsillitis cases were more common in males. From the research results, patients with tonsillitis who visited the ENT clinic of Wlingi Hospital were also dominated by females (50.3%), showing a slightly different percentage compared to the males. These two findings differ from the results of several other studies, but from the theory obtained, there is no significant difference between pharyngitis and tonsillitis related to gender. The results of this study confirm a decrease in the number of visits at the ENT outpatient clinic of Wlingi Hospital in 2019-2021, that the most common disease was ear disease. Patients with pharyngitis who visited the ENT outpatient clinic of Wlingi Hospital in 2019-2021 were dominated by patients with an age range of 25-44 years, while tonsillitis was dominated by patients with an age range of 5-24 years. Patients with pharyngitis and tonsillitis who visited the ENT outpatient clinic at Wlingi Hospital in 2019-2021 were dominated by females(13).

A total of 337 practitioners from 19 different special- ties were recruited. 236 (70.0%) practitioners reported seeing cases with features characteristic of streptococcal pharyngitis (pharyn-geal erythema, tonsillar erythema, hypertrophy of the tonsils with or without exudates, anterior cervical lymphadenopathy, and pe- techiae on the soft or hard palate). 301 (89.3%) clinicians reported cases with inconclusive clinical features, while 21 (6.2%) reported never having a challenging diagnosis. 244 (72.4%) reported having a diagnostic approach (personal or literature-based) to determine antibiotic applicability. Nearly all respondents (99.1%) wanted a lo- cal protocol for determining antibiotic use in sore throat. A total of 5,329 public visits and 1,813 private health claims were recorded for pharyngitis, tonsillitis, tonsillopharyngitis and ‘strep throat’ within the age group, period, and jurisdiction of in- terest. Of the 373 visits reviewed for clinical management, 321 (86.1%) had sufficient documentation for scoring. Antibiotics were prescribed in 292 (91%) cases. Antibiotics use was justified in 65 (22.3%) cases (Centor score ≥4) and avoidable in 213 (93.8%) of 227 with a Centor score < 4 (3).

Molecular diagnosis was performed for EBV, Adeno and HSV 1 detection with swab samples from tonsil lar membranous exudate of 51 paediatric patients with Exudative tonsillopharyngitis after GAS ruled out (21 men and 30 women, ages between 2 and 16 years) from tonsillar membranous exudate, using the Magnesia® Extrac tion Kit by using the Nucleic Acid Extraction robot. Bosphore® EBVDNA, ADENO and HSV type 1 Quantification Kits were used for EBVDNA, ADENO and HSV type 1 PCR by Montania® 4896 RT PCR platform. The frequency of positive EBV DNA cases in the ton sillar membranous exudate in swap samples were 21.5% (11/51). Monospot test was only one of the positive cases in EBV DNA pos itive. On the side a case of adenovirus, the HSV-1 was detected in two cases.

A meticulous clinical examination would differ entiate between the 2 most common causes; Streptococcus and EBV. Adeno and HSV were determined as less causative agents. Streptococcal tonsillitis can be successfully treated with suitable antibiotics. Acyclovir, ganciclovir, and foscarnet have been shown to inhibit EBV DNA polymerase enzyme. (2)

This was a prospective observational study conducted at an urban primary care health centre in Catalonia. Patients aged 15 or older with acute pharyngitis who attended the centre starting from January 2019 were consecutively invited to participate. Non-infectious causes of pharyngitis (aphthous ulceration, pharmacological causes), oral can didiasis, patients treated with systemic antibiotics in the two previous weeks, immunocompromised individuals, preg nant women, persons institutionalized in a nursing home, in emergency situations, difficulty in attending the visit, and/or patient or guardian/parent incapacitation to sign the consent were excluded from the study. The inclusion of cases was concluded in March 2020 due to the outbreak of the COVID-19 pandemic. Patients were given a symptom diary, used previously in other studies, to be completed before bedtime, and symptoms were assessed on Likert scales with a 7-point rating (0 = no problem/not affected, 1 = very mild problem, 2 = mild problem, 3 = moderate problem, 4 = significant prob lem,

5 = serious problem, 6 = the most serious it can be).7 The following items were recorded in the diary: febrile sen sation, headache, general discomfort, cough, odynophagia, difficulty swallowing (solids or liquids), and difficulty in daily activities. The sum of all these symptoms was calculated. The days with severe symptoms, scoring 5 or more in any of these symptoms, and moderate symptomatology, scoring 3 or more, were counted. A total of 149 patients with acute pharyngitis were recruited before the COVID-19 pandemic, with an average age of 36.7 years (SD 15.5 years), ranging from 15 to 87 years. Of these, 92 presented with pharyngeal exudate (62.2%), 57 with painful lateral cervical lymph nodes (38.3%), 59 with fever (39.6%), 59 with cough (39.6%), and 20 experienced recur rences (13.4%). Eighty-four patients (56.4%) were treated with antibiotics. A total of 138 patients returned their diaries (92.6%) (1).

This retrospective study included 78 pregnant women admitted to our clinic between January 2005 and January 2015 suspected as having AA. Of these, 36 women with confirmed AA underwent surgery (the appendectomy group). Forty-two patients were found not to have AA and did not proceed to surgery (the expectant group). The study controls included 29 pregnant women who presented to our clinic for routine examinations during the same period (the healthy pregnant control group) and 30 nonpregnant women who presented to our polyclinic with breast pain during the same period but had no pathology on examination (4).

A retrospective study was carried out to examine the association between serum 25(OH) vitamin D levels and recurrent GAS tonsillopharyngitis in adults. The following were compared between the groups of subjects with and without GAS tonsillo pharyngitis: age, gender, body mass index (BMI), serum iron, C reactive protein (CRP), diabetes mellitus, and serum levels of 25(OH) vitamin D. Information concerning medical conditions, drug therapy, and the results of laboratory tests were extracted from the medical charts of each subject in both groups. (In general, every patient who visits the Infectious Diseases Unit or Medicine Clinic completes a standard questionnaire at every visit concerning his/her medical condition, anthropometric information, dietary habits, smoking, drug therapy, family history of different diseases, and systemic bacterial infections. Laboratory tests were performed within 4 days from the beginning of the tonsillopharyngitis symptoms and included serum CRP levels, creatinine, serum calcium, and serum iron, and a complete blood count. Serum 25(OH) vitamin D levels were measured in the winter and summer seasons (twice a year) for all patients visiting our units. Serum 25(OH) vitamin D levels were measured using a commercial enzyme immunoassay (EIA) kit.

Data were analyzed using SPSS version 19. Continuous variables are expressed as the mean stan standard deviation. The Chi-square test was used to test differences in categorical variables between the cases and controls, and analysis of variance (ANOVA) or the Student's t-test was used for comparisons of continuous variables. Spearman rank correlation and univariate regression analysis were used to determine the strength of the relationship between the risk factors for recurrent GAS tonsillophar yngitis, namely age, gender, BMI, diabetes mellitus, creatinine, serum CRP, serum 25(OH) vitamin D, serum iron, and serum calcium. A multiple logistic regression analysis was done to determine the association between the different risk factors for recurrent GAS tonsillopharyngitis.

The Medical charts of 173 Adult patients with acute tonsillopharyngitis were reviewed for the years 2007–2009. Forty-two Patients were excluded because of: malignancy (n = 11), Taking immunosuppressant drugs (n = 7), Renal failure with creatinine clearance <35 ml/min (n = 9), Pregnancy (n = 6), Connective tissue disease (n = 4), Low compliance (n = 3), And vitamin D supplementation (n = 2). One Hundred and thirty-one patients with acute tonsillopharyngitis were assessed and a further 77 Were excluded because of non-GAS tonsillopharyngitis or no recurrent GAS tonsillopharyngitis. Finally 54 Patients with recurrent GAS Tonsillopharyngitis were included in the study. Table 1 summarizes the differences between the cases and controls (15).

Previous studies have demonstrated that iron deficiency is prevalent in children with recurrent tonsillitis and in children undergoing adenotonsillectomy. Low serum iron levels have been associated

with abnormalities in the cell-mediated response as well as a decreased ability of phagocytic cells to kill certain types of bacteria. Elverland et al. showed a beneficial effect of tonsillectomy and adenoidectomy on hemoglobin and iron metabolism and found that iron deficiency was common among children with recurrent tonsillitis and upper airway obstruction. In our study, we did not find any correlation between serum iron levels and recurrent tonsillopharyngitis in adults (12).

We conclude that recurrent GAS tonsillopharyngitis in adults could be related to vitamin D levels. Data from epidemiological studies indicate that vitamin D deficiency has become a common finding in recent years and appropriate replacement may offer immune and antimicrobial benefits. Because measurement of vitamin D levels is easily done and vitamin D supplements are readily obtainable and inexpensive, further studies are needed to assess whether this represents a causal association and whether vitamin D replacement therapy can prevent the recurrence of GAS tonsillopharyngitis (15).

It was unclear until recently if a tonsillectomy is effective in patients suffering from severe recurrent acute tonsillitis. The Cochrane review from 2014 based on seven trials (five in children and two in adults; revealed that good information about the effectiveness of tonsillectomy (with/without adenoidectomy) was only available for the first year following surgery in children and for 5–6 months in adults. Children had a small benefit from surgery: children who had surgery had three episodes of sore throat on average compared to 3.6 episodes experienced by the other children, i.e., 0.6 episodes of any type of sore throat in the first year was avoided. In adults, conclusions on the effectivity could not be drawn: the two included trials suggested that the number of days with sore throat may be fewer in the first 6 months following tonsillectomy compared to a conservative management. This was the reason why the UK's National Institute for Health Research commissioned the NATTINA trial. NATTINA is so far the largest multicenter clinical trial (453 participants randomized) to assess the effectiveness of surgical intervention in adults compared to a conservative management. NATTINA represents a new milestone on the importance of tonsillectomy in adults. The primary outcome measure was the total number of sore throat days, reported weekly over 24 months. It was shown that compared with conventional medical management, tonsillectomy is both clinically effective and cost-effective. Tonsillectomy reduces sore throat days by almost 53% in over 2 years. Based on the main NATTINA result that tonsillectomy is more beneficial mainly for severe cases of recurrent acute tonsillitis, current clinical guidelines recommend tonsillectomy if the patient experiences at least five to seven sore throat episodes within 1–2 years. For example, the German guideline explicitly requires episodes of acute tonsillitis. In addition to the number of episodes, nearly all guidelines require additional parameters to substantiate the severity and a high probability that the episodes were episodes of bacterial tonsillitis. The NATTINA trial probably will define the new standard to count the number of episodes, i.e., following the UK guideline (5).

From 2017 until 2018, Popovych et al. conducted a study on the effectiveness of BNO 1030 extract in combination with standard therapy in children with acute non-bacterial tonsillitis. BNO 1030 extract (Imupret®) is an herbal aqueous-alcohol extract containing seven plants: marshmallow root (Radix althaeae), chamomile flowers (Flores chamomillae), horsetail herb (Herba equiseti), walnut leaves (Folia jun gladis), yarrow herb (Herba millefolii), oak bark (Cortex quercus), and dandelion herb (Herba taraxaci). Two hundred and thirty-eight children aged 6–18 years were included in a randomized, open-label, multicentred, comparative, non-placebo-controlled study. Standard therapy was acetaminophen as an antipyretic agent in age-specific doses and benzydamine hydrochloride oral spray. The results showed a sig nificant decrease of sore throat (both during swallowing and at rest), improvement of the patients' general condition after 5 days ($p < 0.05$) and withdrawal of antipyretics ($p < 0.005$). Patients' symptoms were evaluated using a 4-point scale for symptoms and a 10-point visual- analogue scale. No adverse events were recorded. The authors concluded that BNO 1030 (Imupret®) is a safe and effective product for treatment of acute non-bacterial tonsillitis in children. 6 In 2021, the authors published the associated one-year follow-up

data. Self-assessment of general health was significantly better after day 5. Significant improvement of assessed symptoms (hyperaemia of the posterior wall and swollen, plaque) in the treatment group after 6 months were reported. 21 A significantly lower recurrence rate ($p < 0.05$) with BNO 1030 treatment was described in the follow-up year. Despite our thorough literature search, it is possible that relevant studies were missed, since CAM and IM comprise a broad spectrum of different therapies which may not have been represented in the search terms used for this review. Furthermore, studies written in languages other than German and English were excluded. A meta-analysis could not be performed due to the small and diverse number of clinical trials (11).

Conclusion. The results of the analysis showed that sore throats are mainly manifested as an additional symptom in seasonal infectious diseases. In addition, in a high percentage, the infectious agent itself causes the disease independently. As a result of the analysis, we can see that women (88%) are more likely to suffer from sore throats (average age 27). The most common cause of inflammation is Streptococcus ssp. (60%), and the most effective antibiotics for the bacteria: Sulfamethoxazole, Levofloxacin, Amoxicillin and Ampicillin gave good results. The use of correct treatment methods for patients with this infection helps to cure the disease faster.

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COMPARATIVE STUDY OF THE LEVEL OF DENTAL HYGIENE KNOWLEDGE AMONG INDIVIDUALS WITH HEARING IMPAIRMENT

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Abstract. *The study is devoted to assessing the level of dental hygiene knowledge among individuals with hearing impairment. The data obtained from a survey of 300 respondents was analyzed. The frequency of visiting the dentist, awareness of professional hygiene, use of additional care products, and motivation to receive recommendations were assessed. Insufficient knowledge, low frequency of use of additional hygiene products, and poor awareness of the role of dental hygienists were established. The results emphasize the need to develop targeted preventive programs adapted to the needs of this group.*

Key words: *level of knowledge, dental hygiene, persons with hearing impairment, prevention, dental hygienists, survey.*

Introduction. The dental health of a significant part of the population remains at risk due to insufficient levels of hygiene knowledge and preventive activity. People with hearing impairments have specific barriers in accessing information on oral hygiene, which can lead to increased morbidity. This group is characterized by a special perception of the surrounding world, which requires the use of adapted educational approaches in the prevention of dental diseases.

Scientific data on the level of dental hygiene knowledge in individuals with hearing impairments remain limited. This makes it difficult to develop effective preventive programs aimed at improving hygiene behavior and reducing the risk of dental diseases in this group.

The aim of the study was to conduct a comparative analysis of the level of dental hygiene knowledge in individuals with hearing impairments to identify key gaps in awareness and develop recommendations for improving preventive dental care.

Materials and methods. The study included a comparative analysis of the level of dental hygiene knowledge among 300 adult respondents with hearing impairment aged 18 to 55 years. The main inclusion criteria were the presence of a diagnosed hearing impairment, residence in the region under study, and voluntary informed consent to participate. Persons with severe concomitant diseases and respondents who refused to participate were excluded.

Data were collected using a standardized questionnaire aimed at studying the frequency of visits to the dentist, the level of knowledge about professional hygiene, the use of additional care products, and methods for choosing oral hygiene products. The survey was conducted individually in medical institutions in compliance with a unified protocol.

Data processing included statistical analysis aimed at quantitatively assessing the responses and identifying patterns in the level of knowledge and hygiene habits of respondents. Descriptive statistics and correlation analysis methods were used to increase the reliability of the analysis. The results are presented in a structured form to assess the key characteristics of the study group.

Literature review. The issue of dental health of people with hearing impairments is of considerable interest to modern dentistry. Scientific studies show that the prevalence of dental diseases in this group is associated with limited access to specialized information and insufficient knowledge of oral hygiene [1]. These factors are aggravated by insufficient frequency of visits to dental offices, which complicates the prevention and early detection of diseases [2].

A comparative analysis of dental awareness of various social groups shows that people with hearing impairments are less informed about methods of professional oral care. They rarely use additional hygiene products such as floss, rinses and interdental brushes [3]. This leads to an increased incidence of caries and periodontal disease, which is confirmed by a number of epidemiological studies [4].

Modern approaches to prevention in dentistry emphasize the importance of adapted educational programs. For individuals with hearing impairments, methods of visualizing information and the introduction of interactive tools, such as video materials with subtitles or in sign language, are proposed [5]. These measures contribute to increasing the level of dental knowledge and the development of sustainable oral care habits [6].

The level of awareness of the role of dental hygienists among this category remains extremely low, which limits the possibility of receiving professional care recommendations [7]. This is supported by research data, according to which the vast majority of respondents with hearing impairments are unaware of the existence of such specialists and do not seek advice [8]. These results highlight the need to increase awareness of the possibilities of professional assistance.

An important area of research is the development of comprehensive preventive programs that take into account the peculiarities of information perception in people with hearing impairments. The use of integrated approaches, such as a combination of visual aids, direct interaction with specialists and regular monitoring of the oral cavity, shows high efficiency in this group [9].

These data support the need for further study of factors influencing the dental health of individuals with hearing impairment and the implementation of targeted preventive strategies to reduce the incidence of the disease.

Results and discussion. The study analyzed the level of dental hygiene knowledge among 300 respondents with hearing impairments aged 18 to 55 years. The questionnaire allowed us to assess the frequency of visits to the dentist, the use of oral care products, and the level of awareness of professional hygiene. The data obtained were statistically processed.

The frequency of visits to the dentist was low: only 12% of respondents visit a specialist once every six months, 42% visit the doctor when necessary, and 46% less than once a year. Knowledge of professional oral hygiene was confirmed by 30% of participants, the remaining 70% were unaware. Additional hygiene products (dental floss, irrigator, rinses) are used by 25% of respondents, while 75% limit themselves to using only a toothbrush.

Table 1.

Characteristics of hygiene habits and knowledge of respondents

Indicator	Meaning (%)
Regular visits to the dentist (once every 6 months)	12
Visiting a dentist when necessary	42
Less than once a year	46
Occupational Health Awareness	30
Lack of awareness of occupational hygiene	70
Use of additional hygiene products	25
Refusal to use additional funds	75

The data show a lack of knowledge about dental disease prevention. Only 18% of respondents are aware of the existence of dental hygienists and their functions. However, 84% expressed willingness to receive oral care recommendations, indicating a high interest in educational initiatives among the target audience.

The obtained results highlight the need to develop targeted prevention programs oriented towards the specific needs of this group. Such programs should take into account the peculiarities of

information perception by people with hearing impairments and include visual materials, infographics and video formats. In addition, it is important to integrate professional consultations within the framework of regular dental examinations to improve oral health and reduce the prevalence of dental diseases.

Conclusion. The results of the study revealed a low level of dental hygiene knowledge and insufficient preventive activity among people with hearing impairment. The main problems remain infrequent visits to the dentist, insufficient use of additional oral care products and low awareness of professional hygiene. At the same time, a high percentage of respondents expressed interest in receiving professional recommendations, which confirms the importance of developing targeted educational programs.

To improve the dental health of this population group, it is recommended to introduce adapted preventive measures, including visual and interactive materials, as well as greater involvement of dental hygienists. These measures will reduce the incidence of dental diseases and improve the quality of life of people with hearing impairment.

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STUDY ON THE EFFECTS OF EXPERIMENTAL DIABETES ON FERTILITY AND EARLY POSTNATAL DEVELOPMENT IN OFFSPRING OF FEMALE RATS

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Abstract. *This research investigated the effects of experimentally induced diabetes in white outbred female rats on their fertility and the early postnatal development of their offspring. The experiment revealed that diabetes negatively impacts fertility, pregnancy progression, and physical development in newborns. In female rats with experimentally induced diabetes, pregnancy rates decreased to 62%, and the duration of pregnancy increased to 24–26 days. Offspring of diabetic females showed signs of compromised development, characterized by obesity, abnormally large size (macrosomia), and delayed milestones in physiological maturation, including later detachment of ear pinnae, slower fur growth, delayed emergence of incisors, and later opening of the eyes. These results confirm that diabetes in the maternal organism leads to decreased fertility and the birth of physiologically immature and less viable animals, highlighting the importance of monitoring the mother's health during pregnancy.*

Keywords: *experimental diabetes, fertility, pregnancy, postnatal development, offspring, physical development, viability.*

Introduction. In many developed countries, the demographic situation continues to be highly unfavorable, despite its significance as a key indicator of national security. This is attributed to the impact of various factors, including social, environmental, biological, medical and others. due to the data from the World Health Organization shows that the incidence of all types of diabetes has been consistently rising over the past few decades [11]. From 1980 to 2014 alone, the number of diabetes patients quadrupled [23].

In 1980, the disease was diagnosed in 108 million people (4.7% of the population), whereas by 2017, the number of patients had reached 425 million (8.5%). According to forecasts, by 2045, this number will rise to 629 million [11]. In this regard, the WHO and the UN have recognized diabetes as one of the most serious challenges to the global community in the 21st century [6,7].

The high prevalence of diabetes in pregnant women carries substantial medical and social weight due to the elevated risk of complications for both mother and child [20]. According to the Atlas of the International Diabetes Federation, in 2019, the prevalence of hyperglycemia in pregnant women was around 15.8%, with 83.6% of cases being related to gestational diabetes [8]. The frequency of gestational diabetes worldwide continues to rise, and its prevalence varies between 1% and 14% in different countries, with an average of 7% [6,7].

In these patients, pregnancy is frequently complicated by the development of diabetic fetopathy, a pathological condition characterized by fetal macrosomia, dysproportional growth of anatomical structures, and delayed morphofunctional maturation. This results in the immaturity of multiple organ systems, including the respiratory, cardiovascular, and central nervous systems, predisposing the fetus to severe perinatal complications such as neonatal respiratory distress syndrome, metabolic disturbances, and an increased risk of birth trauma [22].

Clinical and experimental studies confirm the negative impact of diabetes in the mother on the course of pregnancy, which in some cases can lead to neonatal death [4,5]. The perinatal mortality rate for newborns weighing 4 kg or more is 1.5-3 times higher than for babies born with normal weight parameters [9,10,19]. Furthermore, children born to mothers with diabetes experience delays in postnatal physical development, reduced viability, and disruption of organogenesis processes.

The fertility status of females with alloxan-induced diabetes, as well as the peculiarities of the physical development of their offspring, remain insufficiently studied, despite the relevance of this issue. This is precisely what determined the goal of the present study.

Material and Methods of the Study. The study was conducted on 50 (control - 25, experimental - 25) white outbred female rats, weighing 160-180 g and previously non-parous preliminarily, as well as 253 of their offspring at different stages of early postnatal development. The "experimental" group consisted of rats born to females with experimentally induced alloxan diabetes, while the "control" group included intact rats of corresponding age born to healthy females.

The experimental study on laboratory animals was conducted in strict accordance with ethical standards and regulatory frameworks, complying with the principles outlined in the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes. All procedures were designed to minimize animal suffering and ensure humane treatment, adhering to internationally recognized guidelines for the ethical use of animals in scientific research.

Diabetes was experimentally induced in the study group of female rats by a single intraperitoneal injection of alloxan tetrahydrate (13 mg/100 g body weight, Lachema, Czechoslovakia). Control animals received an equivalent volume of physiological saline via the same route.

To evaluate the fertility of female rats with experimental diabetes, mating was conducted after confirming the induction of diabetes. To evaluate fertility and pregnancy outcomes, females in both groups were mated with healthy males, maintaining a ratio of one male to four females. Successful mating, indicating pregnancy, was confirmed through microscopic examination of vaginal smears for the presence of sperm. Upon confirmation of pregnancy, the females were moved to individual cages for detailed observation and analysis throughout gestation.

To assess postnatal development, mothers and their offspring from both experimental and control groups were divided into groups corresponding to postnatal days 3, 7, 14, 21, and 30 (n=10 per group). The newborn rats were initially fed breast milk until the 14th day. From that point, they were given a mixed diet, and starting on the 21st day, they were gradually switched to a standard laboratory diet.

Standard criteria were used to assess the physiological maturity of the offspring from experimental animals, specifically litter size, the number of live births, and the number of stillbirths. The viability of the offspring was determined by the number of rats that survived to 2 and 14 days. To analyze the degree of physiological immaturity, the timing of the disappearance of signs of functional and morphological immaturity in the newborn rats was recorded. At all key stages of early postnatal development, the length and body weight of the rats were measured, and the daily weight gain was calculated [3].

The results of the study showed that experimental diabetes mellitus has a negative impact on fertility and the course of pregnancy in females.

This study utilized 50 female rats, which were systematically assigned to control and experimental groups, each initially consisting of 25 individuals. The group distribution was designed to ensure methodological rigor, allowing for a robust comparative analysis of physiological and developmental parameters. In the experimental group, four rats died during the induction of diabetes. Mating with males resulted in pregnancy for 23 (92%) of the control females within 1–5 days, with pregnancies lasting 21–22 days. [24]. In the experimental group, 62% of the females became

pregnant, on average, 3–4 days later than the intact animals, with the pregnancy duration increasing to 24–26 days.

In 8 out of the 21 diabetic females (38%), pregnancy did not occur during the entire experiment. Evaluating the effect of extragenital pathology in the mother on offspring development is a crucial focus in modern biomedical science [17]. The physiological maturity of newborns is typically used as a key criterion for assessing this impact. Recent studies emphasize the necessity of assessing physiological maturity in offspring in the context of maternal extragenital pathology by accounting for species-specific, age-dependent, and sex-related normative physiological parameters in laboratory animals. This approach ensures a more accurate evaluation of developmental deviations and potential pathophysiological consequences [2].

To conduct a more in-depth study of this issue, an analysis was performed on the litter size, stillbirth rate, viability, and physical development of offspring from female rats in which alloxan-induced diabetes mellitus was experimentally induced [10,12]. The analysis of the litter composition of the experimental animals showed that the total number of offspring from the experimental and control groups was 253 rats (181 from the control group and 72 from the experimental group). Experimental induction of diabetes mellitus in female rats led to a smaller litter size (5.5±0.31) compared to the control group females (7.9±0.42 pups; $p < 0.05$, if statistically significant) [18]. Literature findings support this, indicating extragenital maternal pathology causes smaller litter sizes [2,3,16]. Findings also show more intrauterine and postnatal mortality in the diabetic group compared to controls. (Table 1).

Table 1

Fertility of female rats with experimentally induced diabetes mellitus

Indicators		Control Group (n=181)	Experimental Group (n=72)
Fertility of females, %		23/92%	13/62%
Time of pregnancy onset, days		3,0±0,14	5,8±0,28
Duration of pregnancy, days		21,2±1,02	25,6±1,2
Average number of rats in a litter, pcs	total	7,8±0,42	5,5±0,31
Total number of rats born	total	181	72
Number of rats that died within 14 days after birth	abs.	5	7
	%	2,4±1,1	9,8±2,4

As presented in Table 1, reproductive outcomes differed significantly between the groups. In the control group, 23 females gave birth to a total of 181 offspring, whereas in the experimental group, only 13 females produced 72 offspring, indicating a marked reduction in fertility and litter size under experimental conditions. Furthermore, postnatal mortality was substantially higher in the experimental group, reaching 9.8% (7 out of 72 neonates), compared to 2.4% (5 out of 181 neonates) in the control group, suggesting an increased vulnerability of offspring to adverse perinatal factors. The mortality of rats in both groups was recorded during the first 2 weeks after birth.

In summary, the progeny of female rats with experimentally induced diabetes mellitus demonstrated a significant reduction in litter size and an increased neonatal mortality rate, indicating compromised reproductive outcomes and heightened perinatal vulnerability associated with maternal hyperglycemia.

The postnatal development of the rats was monitored throughout their first 30 days, which represents the early postnatal ontogeny period. The assessment of early postnatal development of the offspring was based on general physical development indicators (time of ear pinna detachment, appearance of primary and secondary fur, eruption of incisors, and eye opening).

The assessment of the temporal progression of key physical developmental milestones in the experimental animals revealed a significant delay in the acquisition of studied traits within the experimental group. Compared to the control group, these animals exhibited impaired physiological and functional maturation, as reflected by a prolonged timeline for critical developmental markers, including ear pinna detachment, fur emergence, incisor eruption, and eye opening [15].

Table 2

Indicators of physical development of offspring born to females with induced diabetes mellitus

№	Indicators:	Control Group (n=181)	Experimental Group (n=72)	P
1	Body weight at birth, g	4,91±0,05	6,13±0,08	
2	Ear pinna detachment, days	2,56±0,04	2,51±0,07	<0,001
3	Appearance of primary fur, days	5,03±0,06	5,17±0,06	<0,001
4	Appearance of secondary fur, days	8,29±0,06	9,23±0,07	<0,001
5	Eruption of incisors, days	8,07±0,06	8,1±0,07	<0,001
6	Eye opening, days	13,5±0,05	13,2±0,10	<0,001

***Note:** * - the results are statistically significant when compared to the control group (P<0.05).*

It is known that one of the key indicators of physiological maturity in newborns is their weight characteristics.

In a number of studies dedicated to the impact of maternal diabetes on offspring development, contradictory data regarding the body weight of the animals have been presented. For instance, Amorim et al. [1] and Antonov S.D. [2] found a decrease in the body weight of offspring from female rats with experimentally induced streptozotocin-induced diabetes mellitus [21]. High dose streptozotocin exposure during intrauterine development may be associated with the growth retardation and decreased body weight that persists until offspring reach sexual maturity. However, G. Jelodar et al. [13] presents data inconsistent with those findings. They observed body weight being much higher in diabetic offspring for the first two months of their lives.

Our study revealed that the experimental group exhibited consistently higher body mass across all observational time points compared to the control group, indicative of macrosomia. This finding suggests altered growth dynamics potentially associated with maternal metabolic disturbances.

In order to investigate the effects of maternal diabetes on offspring development, we analyzed the daily body mass gain in both the control and experimental groups of newborn rats during the initial weeks of postnatal life. Our findings revealed that, within this timeframe, the control group offspring experienced an average daily mass gain of 0.8 ± 0.04 grams. In contrast, the offspring of the female rats with experimentally induced diabetes mellitus exhibited a modestly increased average daily mass gain, measuring 0.9 ± 0.03 grams. Between days 7 and 14, the daily mass gain increased significantly, reaching 1.4±0.08 g in the control group and 1.8±0.06 g in the experimental group. From days 15 to 30, the daily body mass gain in both groups was 1.5±0.08 g for the control group and 1.9±0.07 g for the experimental group, with no significant differences compared to the previous periods. These results align with the findings of Jelodar et al. [13].

The observation of increased body mass in offspring born to mothers with experimental alloxan-induced diabetes is explained by Jelodar et al. [13] as a consequence of altered nutrient partitioning during gestation. The elevated glucose levels in the diabetic mother's circulation facilitate an increased transplacental transfer of glucose and other key nutrients to the developing fetus. This heightened nutrient supply triggers a compensatory response in the fetal pancreas, leading to increased insulin synthesis and release. The excess fetal insulin exerts a potent somatotropic effect,

stimulating enhanced cellular proliferation and leading to pathological fetal overgrowth, a condition that may predispose offspring to long-term metabolic dysregulation [14]. Consequently, analysis of postnatal growth patterns revealed a discrepancy in body weight dynamics between the groups, with the offspring of diabetic rats exhibiting a more pronounced weight gain compared to the control group, suggesting sustained metabolic alterations.

Experimentally induced pre-pregnancy diabetes in females reduces their fertility.

The presence of diabetes in the mother results in the birth of physiologically immature offspring, as demonstrated by a reduced litter size, slower body weight gain, higher mortality during the first weeks of life, and delayed morphological and functional maturation.

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LIVER FIBROSIS AND METABOLIC CHANGES IN NON-ALCOHOLIC FATTY LIVER DISEASE: MODERN APPROACHES TO DIAGNOSTICS

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Abstract. *This study is devoted to the assessment of metabolic changes and the degree of liver fibrosis in patients with non-alcoholic fatty liver disease (NAFLD), including steatosis of varying degrees. The study included 90 patients with NAFLD and 45 people in the control group.*

Research methods: clinical and laboratory methods, ultrasound elastometry (FibroScan), DEBQ questionnaire to identify eating disorders, molecular genetic analysis of the expression level of microRNA-221.

Key words: *Non-alcoholic fatty liver disease (NAFLD), liver fibrosis, FibroScan, microRNA-221, DEBQ questionnaire, liver enzymes, triglycerides, ALT/AST ratio.*

Introduction. Currently, non-alcoholic fatty liver disease (NAFLD) occupies a leading position among liver diseases and is considered as one of the most common chronic liver lesions globally [4]. The term NAFLD unites a wide range of liver pathologies, including various clinical and histological forms, such as fatty liver infiltration (steatosis), non-alcoholic steatohepatitis (NASH), fibrosis and cirrhosis. Liver steatosis most often has a favorable course and is not associated with an increased risk of mortality, but its progression, especially when turning into steatohepatitis, significantly increases the likelihood of developing cirrhosis and liver failure [7]. Population studies suggest that 60% to 80% of cases of cryptogenic liver cirrhosis are a consequence of non-alcoholic steatohepatitis (NASH)[3].

The main risk factors for NAFLD are obesity and overweight [8]. The incidence of hepatic steatosis in morbidly obese patients who have undergone bariatric treatment reaches 90%. A significant percentage of patients with type 2 diabetes mellitus (T2DM) suffer from NAFLD, the rate is about 69%. Half of the patients who have liver changes characteristic of fatty degeneration also have hyperlipidemia, mainly due to increased triglyceride levels. The development of NAFLD is influenced by demographic parameters such as age, gender, and ethnicity. Among the risk factors for disease progression, the most significant are: age over 45 years, obesity (BMI> 30), the presence of T2DM, hypertension, elevated triglycerides, and an ALT/AST ratio greater than one. Pathological obesity is almost always accompanied by hepatosis (in 95-100% of cases), and in 20-47% of cases by steatohepatitis.

Despite the high prevalence of NAFLD, more than 95% of cases (at any stage of the disease) remain undiagnosed, as shown by data from multicenter studies [5,2]. This is primarily due to the nonspecificity of the clinical picture of the disease. In many patients, the main manifestation is asthenovegetative syndrome [1,6]. The diagnostic process should include a comprehensive assessment of all aspects of metabolic syndrome. It is especially important to examine individuals with obesity, type 2 diabetes mellitus, and incidentally detected elevated liver enzymes in the presence of metabolic risk factors. During the diagnostic process at the stage of primary health care, it is important not to limit oneself to stating the fact that the patient has signs of liver steatosis and moderate hepatomegaly, but to continue the examination in order to exclude complications, select the necessary goal, and set priorities.

The aim of this study was to identify markers of liver fibrosis at different stages of NAFLD and to evaluate their relationship with clinical and biochemical parameters in patients with this disease.

Material and methods of research. In accordance with the objectives of the study, 90 patients diagnosed with non-alcoholic fatty liver disease were monitored during 2023-2024. All the data obtained were recorded in specially developed medical records. The study was conducted among patients undergoing inpatient treatment at the general therapy department of the multidisciplinary clinic of the Tashkent Medical Academy, based on the consent of the patients. Patients with non-alcoholic fatty liver disease were divided into 3 groups: out of 90 patients with non-alcoholic fatty liver disease, 26 patient had grade 1 steatosis according to ultrasound examination, 52 patient had grade 2 and 8 patient had grade 3 hepatic steatosis.The average age of patients in all 3 groups was approximately 57.6 years. The control group included 45 healthy people aged 57±10 years. There was no statistically significant difference in age between the groups. The following parameters were determined in the patients examined to assess the functional state of the liver and biliary tract: total bilirubin level, direct bilirubin, alanine aminotransferase (ALT) activity, aspartate aminotransferase (AST), albumin, total protein, C-reactive protein (CRP), glucose content, on a Mindray BS-380 (Germany) automatic analyzer, lipid profile on a Mindray BS-88A (Germany) analyzer, complete blood count on a Mindray BS-5000 (Germany) analyzer.

Ultrasound elastometry (liver fibroscanning) was used as a non-invasive method to determine the degree of liver fibrosis using the FibroScan®502 Touch device. Patients were administered the DEBQ (Dutch Eating Behavior Questionnaire) to identify eating disorders.

Molecular genetic research methods include determination of the expression level of MicroRNA-221, extraction of microRNA using PCR and detection of changes in the expression of microRNA-221 using 0.75 ml of Trizol reagent. RNA isolation was performed using the “Ribo prep” kit (Russia). After the reverse transcription reaction, the levels of MicroRNAs were determined relative to U6 snRNA and presented in accepted units. Amplification was performed on the Rotor Gene Q (Qiagen, Germany) equipment.

Results and discussion. Patients with a mean age of 57.00±16.5 years with a diagnosis of NAFLD participated in the study. Men accounted for 45.6%, women for 54.4%. The mean BMI in the group of patients with non-alcoholic fatty liver disease was 28.1±5.8 kg/m^2 in 1 group, 28.9±5.9 kg/m^2 in 2 group, 29.0±2.0 kg/m^2 in 3group and 6 patients(6.6%) with normal body weight, 43 (47.7%) patients with excess body weight, 31 (34.4%) patients with obesity 1 degree, 9 (10%) patients with obesity 2 degree and 1 (1.1%) patient with obesity 3 degree.

When analyzing risk factors in patients with non-alcoholic fatty liver disease, smoking was identified in 2 (2.2%) patients from harmful habits.

During the study, the following diseases were identified among those associated with non-alcoholic fatty liver disease: hypercholesterolemia 25 (27.8%), type 2 diabetes mellitus 21 (23.3%), coronary heart disease 54 (60%), arterial hypertension 77 (85.6%), vegetative-vascular dystonia 17 (18.8%), chronic gastritis 21 (23.3%), gallstone disease 38 (42.2%), chronic pyelonephritis 79 (87.8%), chronic pancreatitis 13 (14.4) patients. **(Table 1).**

Table 1.

Frequency of co-occurrence of co-morbidities

Associated diseases	Category	Abs.	%	95% CI
Gender	Male	49	54,4	43,6 – 65,0
	Female	41	45,6	35,0 – 56,4
Smoking	Available	2	2,2	0,3 – 7,8
	Not available	88	97,8	92,2 – 99,7
Arterial hypertension	Available	77	85,6	76,6 – 92,1
	Not available	13	14,4	7,9 – 23,4
Coronary heart disease	Available	54	60,0	49,1 – 70,2
	Not available	36	40,0	29,8 – 50,9

Type 2 diabetes mellitus	Available	17	18,9	11,4 – 28,5
	Not available	73	81,1	71,5 – 88,6
Chronic pyelonephritis	Not available	11	12,2	6,3 – 20,8
	Available	79	87,8	79,2 – 93,7
Chronic gastritis	Not available	69	76,7	66,6 – 84,9
	Available	21	23,3	15,1 – 33,4
Gallstone disease	Available	38	42,2	31,9 – 53,1
	Not available	52	57,8	46,9 – 68,1
Chronic pancreatitis	Not available	77	85,6	76,6 – 92,1
	Available	13	14,4	7,9 – 23,4
Hypercholesterolemia	Available	25	27,8	18,9 – 38,2
	Not available	65	72,2	61,8 – 81,1

The results of clinical and biochemical parameters according to the stages of steatosis according to the ultrasound are presented. Total bilirubin ($p = 0.001$), urea ($p = 0.033$) and AST/ALT ($p = 0.001$) ratio were statistically significantly higher in the NAFLD groups compared to the control group. No significant differences were observed in other parameters, which indicates that some parameters of liver function change significantly depending on the stage in NAFLD. (Table 2)

Table 2.

Results of the main indicators of blood biochemical analysis in patients under investigation

Indicators	**Groups**				**p**
	NAFLD 1st.	NAFLD 2st	NAFLD 3st	Control group	
C-reactive protein (mg/l), Me [IQR]	18,5 [13,5; 22,8]	20,0 [13,5; 24,5]	19,0 [12,0; 26,0]	7,8 [6,4; 9,2]	0,290
Total protein (g/l), Me [IQR]	73,2 [68,9; 77,9]	74,2 [69,7; 81,0]	76,9 [75,2; 78,7]	76,0 [72,4; 80,4]	0,794
Total bilirubin (mkmol/l), Me [IQR]	16,6 [14,8; 19,7]	16,2 [13,8; 19,1]	19,1 [18,8; 19,3]	16,5 [14,6; 19,7]	$< 0,001^*p_{\text{control group – NAFLD1st.}} = 0,012 p_{\text{control group – NAFLD 2st.}} = 0,002$
Urea (mmol/l), Me [IQR]	5,8 [5,8; 5,9]	6,2 [5,3; 7,3]	6,6 [5,8; 7,6]	5,5 [5,3; 5,8]	$0,033^*p_{\text{control group}}$ – NAFLD 1st. = 0,020
Creatinine (mkmol/l), Me [IQR]	80,0 [74,8; 88,5]	82,6 [72,5; 90,8]	80,0 [77,6; 82,4]	82,9 [72,5; 91,2]	0,932
ALT (ed/l), Me [IQR]	24,0 [21,5; 26,8]	28,0 [24,5; 37,0]	26,0 [25,5; 26,5]	25,0 [21,0; 31,0]	0,237
AST (eed/l), Me [IQR]	14,0 [13,0; 19,0]	17,0 [14,5; 23,5]	14,5 [14,2; 14,8]	15,0 [11,0; 20,0]	0,259
AST/ALT (ed/l), Me [IQR]	0,6 [0,5; 0,7]	0,6 [0,5; 0,6]	0,6 [0,6; 0,6]	0,5 [0,1; 0,6]	$< 0,001^*$ $P_{\text{control group}}$ – NAFLD 1st.. = 0,002 $P_{\text{control group}}$ – NAFLD 2st.. = 0,004

** – differences between indicators are statistically significant ($p < 0.05$)*

The state of lipid metabolism is of particular importance for the pathogenesis of non-alcoholic fatty liver disease. It is known that the disease begins with the accumulation of lipids in organ tissues, and hyperlipidemia plays an important role in the development of the disease. In this study, metabolic parameters such as body mass index (BMI), glucose, and lipid profile were compared between patients with different stages of NAFLD and the control group. The parameters are presented as median and interquartile range (IQR). In patients with NAFLD, an increase in glucose and triglyceride levels was observed, especially in stages 2 and 3, which indicates the development of metabolic dysfunction and possible insulin resistance. However, no significant differences were observed in most cholesterol and lipoproteins. These results confirm that NAFLD is a disease that affects not only the liver, but also the general metabolic state.

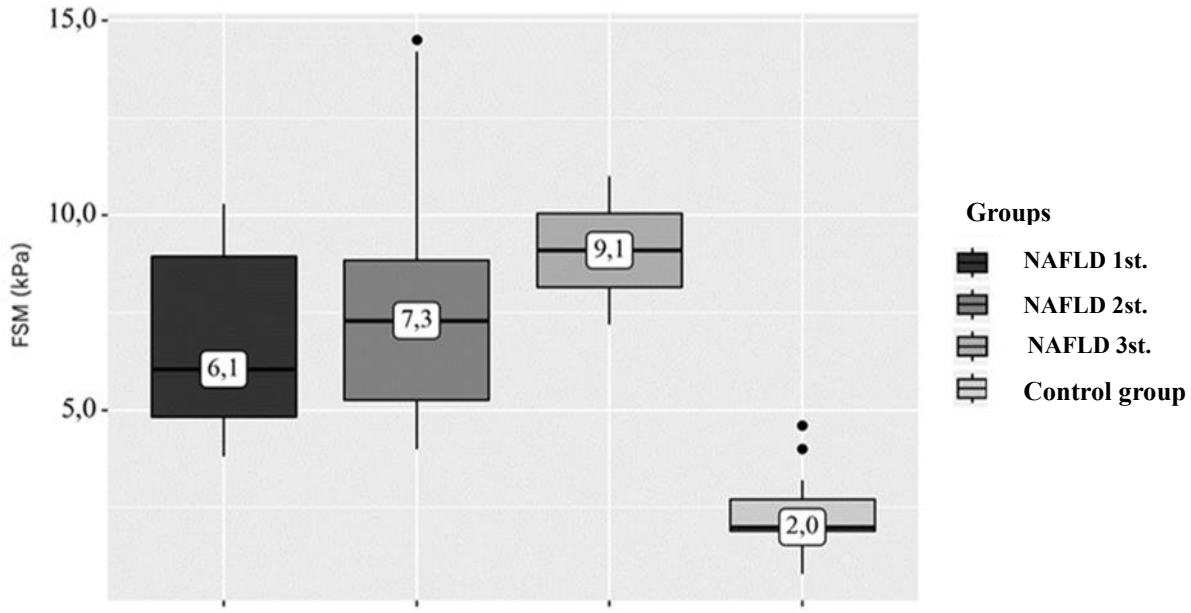
Table 3.

The value of metabolic indicators according to the stage of steatosis in non-alcoholic fatty liver disease

Indicators	Groups				p
	NAFLD 1st	NAFLD 2st	NAFLD 3st	Control group	
BMI (kg/m^2), Me [IQR]	30,5 [28,1; 33,9]	31,1 [28,9; 34,8]	31,3 [26,1; 33,5]	30,0 [29,0; 31,0]	0,792
Glucose(mmol/l), Me [IQR]	4,3 [4,0; 4,7]	5,1 [4,4; 8,6]	7,8 [6,2; 9,4]	4,8 [3,9; 5,5]	0,048*
Total cholesterol (mmol/l), Me [IQR]	4,9 [4,2; 5,5]	5,1 [4,2; 5,8]	5,4 [5,0; 5,8]	4,7 [4,2; 5,8]	0,748
LDLP (mmol/l), Me [IQR]	3,8 [3,2; 4,5]	3,5 [3,2; 4,8]	4,7 [4,2; 5,2]	3,8 [3,2; 4,4]	0,747
HDLP (mmol/l), Me [IQR]	1,5 [1,2; 1,7]	1,4 [0,8; 1,7]	0,9 [0,8; 1,1]	1,3 [0,8; 1,6]	0,318
TG (mmol/l), Me [IQR]	1,5 [0,9; 2,1]	2,2 [1,8; 2,4]	2,4 [2,2; 2,5]	1,6 [0,9; 1,9]	< 0,001*$p_{\text{control group– NAFLD 1st}}$ = 0,018$p_{\text{control group– NAFLD 2st.}}$ = 0,002
VLDLP (mmol/l), Me [IQR]	1,4 [0,9; 1,8]	1,7 [1,2; 2,0]	1,4 [0,9; 1,9]	1,4 [0,8; 1,8]	0,538

** – differences between indicators are statistically significant ($p < 0.05$)*

The method of determining the degree of liver fibrosis by FSM (FibroScan) is of great importance in assessing the condition of patients with NAFLD. In this analysis, FSM indicators were compared between different stages of NAFLD and the control group (Graph 1).



Graph 1. Analysis of the values of the "Fibroscan" ultrasound elastometry parameters by group of study participants

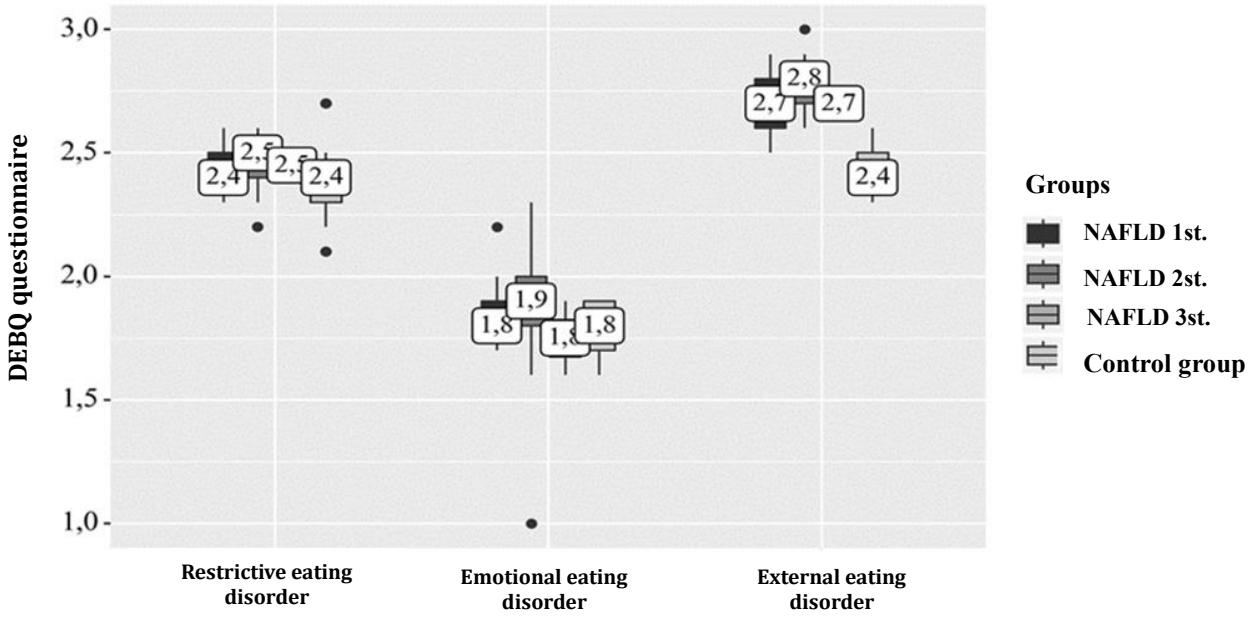
These results show that the increase in liver fibrosis in patients with NAFLD is statistically significant. Compared with the control group, FSM was significantly higher in NAFLD stages 1 and 2 ($p < 0.001$), and FSM was highest in NAFLD stage 3, with a significant difference of $p = 0.016$. This indicates that the degree of fibrosis increases with the development of NAFLD and that its early detection by FibroScan is important. (Graph 1).

The assessment of the type of eating behavior based on the results of the DEBQ (Dutch Eating Behavior Questionnaire) conducted to identify eating disorders in patients with stage 1 non-alcoholic fatty liver disease, identifying restrictive, emotional, and external types of eating disorders, is presented in **Graph 2.**

Statistically significant differences were found in the analysis of the restrictive domain of eating disorders ($p = 0.004$) (method used: Kruskal-Wallis test). Statistically significant differences were also found in the analysis of the emotional type domain ($p = 0.041$) (method used: Kruskal-Wallis test). Statistically significant differences were also found in the comparison of the externalizing type domain ($p < 0.001$) (method used: Kruskal-Wallis test).

The results of the study showed that in the group with grade 1 hepatic steatosis, we detected statistically significant changes ($p < 0.001$) (method used: Friedman criterion). The analysis showed that in patients with grade 2 non-alcoholic fatty liver disease, statistically significant changes were also detected ($p < 0.001$) (method used: Friedman criterion). In the group with grade 3 non-alcoholic fatty liver disease, no statistically significant changes were detected during the analysis ($p < 0.135$). (method used: Friedman criterion). During the study, statistically significant changes ($p<0.001$) were detected in the control group (method used: Friedman criterion).

The results of the study showed that in the group with grade 1 hepatic steatosis, we detected statistically significant changes ($p < 0.001$) (method used: Friedman criterion). The analysis showed that in patients with grade 2 non-alcoholic fatty liver disease, statistically significant changes were also detected ($p < 0.001$) (method used: Friedman criterion). In the group with grade 3 non-alcoholic fatty liver disease, no statistically significant changes were detected during the analysis ($p < 0.135$). (method used: Friedman criterion). During the study, statistically significant changes ($p<0.001$) were detected in the control group (method used: Friedman criterion).

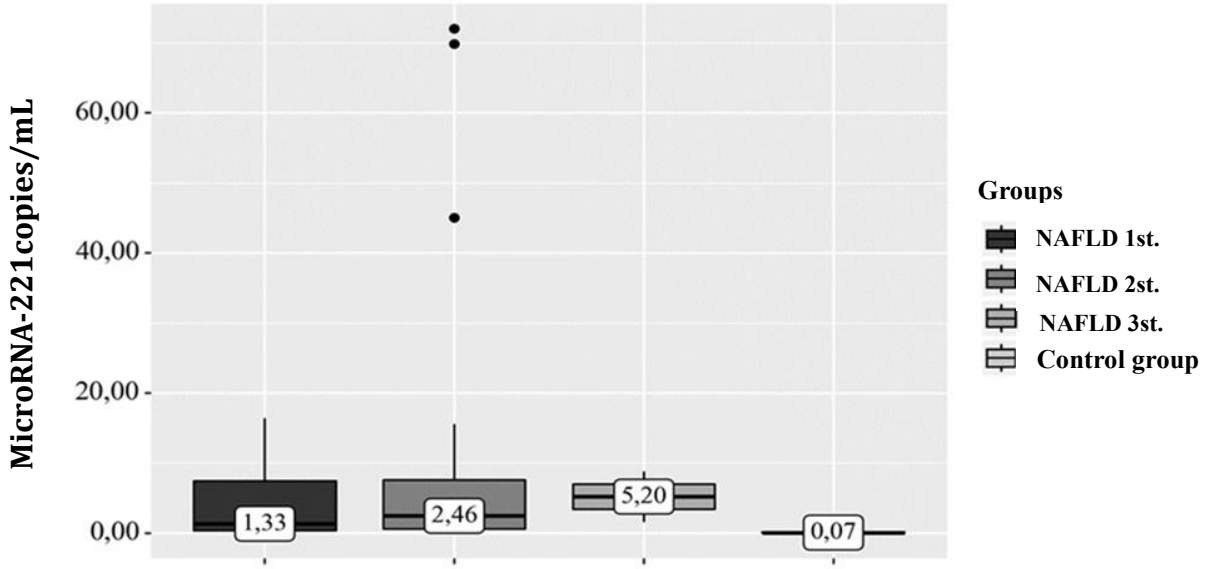


Graph 2. Results of the analysis of the DEBQ questionnaire by group of study participants

In patients with NAFLD, the DEBQ questionnaire identifies restrictive, emotional, and externalizing eating disorders. These changes may further exacerbate the progression of the disease. For example, emotional eating (e.g., stress) can lead to overeating or malnutrition, which in turn negatively affects the course of the disease.

MicroRNA-221 (miRNA-221) is an important biomarker involved in intracellular metabolic processes and inflammatory mechanisms. This analysis was aimed at comparing the expression levels of microRNA-221 between patients with different stages of NAFLD and the control group.

Based on the results of the study, significant differences were found in the assessment of microRNA-221 values depending on the group of study participants ($p < 0.001$) (method used: Kruskal-Wallis test). **(Graph 3)**



Graph 3. Analysis of microRNA-221 values according to the group of study participants

The control group had very low levels of microRNA-221, with a median of 0.07 copies/mL (IQR: 0.05–0.10). MicroRNA-221 levels increased consistently in stages 1–3 of NAFLD, with a median of 1.33 copies/mL in 1 stage, 2.46 copies/mL in 2 stage, and 5.20 copies/mL in 3 stage. The difference compared to the control group was statistically significant in all NAFLD groups ($p < 0.05$): NAFLD 1 and 2 stages: $p < 0.001$. NAFLD 3 stage: $p = 0.033$ (also not statistically significant, but still significant). These results suggest that microRNA-221 may be involved in the pathogenesis of NAFLD and its potential use as a biomarker.

We conducted a correlation analysis of the relationship between microRNA-221 values and Fibroscan ultrasound elastometry parameters (Table 4).

Table 4.

Results of correlation analysis of the relationship between microRNA-221 values and "Fibroscan" ultrasound elastography parameters

Indicator	**Characteristics of correlation dependence**		
	ρ	Correlation on the Cheddoka scale	P
MicroRNA-221 – FSM	0,819	High	< 0,001*

** – differences between indicators are statistically significant ($p < 0.05$)*

A high level of direct correlation was revealed when assessing the relationship between Fibroscan ultrasound elastometry parameters and microRNA-221 values.

Thus, the results of molecular genetic analysis in patients with non-alcoholic fatty liver disease show that the expression level of microRNA-221 is statistically significantly increased in NAFLD, which allows us to recommend it as a promising biomarker for early detection of NAFLD and assessment of disease progression. As the NAFLD stage increases, the increase in the amount of microRNA-221 reflects the progression of the disease.

Conclusions:

1. In patients with NAFLD, comorbidities were in the following order: arterial hypertension (85.6%), chronic pyelonephritis (87.8%), coronary heart disease (60%), hypercholesterolemia (27.8%), etc. Overweight and obesity were found in 92.2% of cases.

2. According to clinical and laboratory studies, the levels of bilirubin, urea and the AST / ALT ratio were statistically higher in the groups with NAFLD compared to the control. With the progression of NAFLD, an increase in glucose and triglycerides was observed, especially at stages 2 and 3 of steatosis. According to elastometry, liver stiffness indicators increased as steatosis progressed, indicating the progression of fibrosis. The differences between the stages were statistically significant ($p < 0.05$)

3. According to the results of the study, it was found that the DEBQ index indicators for all types of eating behaviors in patients with NAFLD were higher than in the control group. In particular: Restricted eating was approximately 4% higher in the NAFLD grade 2 group compared to the control group ($p = 0.005$). Emotional eating was 5–6% higher in this group ($p = 0.033$). External eating was approximately 12–17% higher in the NAFLD grade 1 and 2 groups compared to the control group, and the differences were statistically significant ($p < 0.001$). These disorders could contribute to the deterioration of metabolic state and progression of the disease.

4. It was found that the expression of microRNA-221 (miR-221) increases in line with the severity of liver fibrosis, indicating its potential use as a promising biomarker for assessing the progression of NAFLD.

The results obtained serve to justify an effective approach to improving the diagnosis and monitoring of NAFLD by using a comprehensive approach - assessing clinical, laboratory, instrumental and molecular indicators.

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ASSESSMENT OF THE EFFECT OF CONNECTIVE TISSUE CELLS ON THE REGENERATION OF THE ORAL MUCOSA

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Abstract. *This study presents a comparative experimental analysis of a tissue-engineered construct composed of silk degummed gauze and allofibroblasts for the treatment of mucosal defects in rats. The dynamics of animal weight and the relative weight of internal organs did not exhibit statistically significant deviations compared to control and reference values, indicating the safety of the cell therapy and tissue engineering methods employed for the experimental animals. The proposed tissue-engineered construct effectively supports the maintenance of proliferating dermal fibroblasts within the scaffold.*

Keywords: *tissue-engineered construct, allofibroblasts, silk degummed gauze, experimental animals.*

Introduction. Globally, extensive research is underway to explore methods for treating patients with soft tissue defects of the face. Currently, treatment primarily relies on various surgical techniques, including conventional approaches such as free tissue transfer, local tissue rearrangement, and others. However, in many instances, these methods fail to achieve the desired outcomes for oral cavity defect reconstruction, as defined by contemporary standards [3, 8]. Expanding the application of fibroblasts in cell-based therapies for oral soft tissue diseases, including those associated with aesthetic deformities and their correction, holds promise as a foundation for developing strategies to replace and/or regenerate damaged tissues and mucosal defects within the oral cavity [1, 4, 10]. These cells are readily cultured in vitro without compromising their functionality [7, 9]. Due to their pivotal role in maintaining tissue homeostasis, fibroblasts, uniquely among cell types, possess the capacity to effectively establish an environment conducive to the proliferation and migration of other cell populations [2, 5].

Material and methods of research. To evaluate the efficacy of a tissue-engineered construct composed of silk degummed gauze and autologous fibroblasts, in conjunction with injectable autologous fibroblasts, for the treatment of oral mucosal defects, an experimental morphological study of the tissues was conducted. Furthermore, to assess the toxicity of the materials, a histological examination of internal organs, including the liver, heart, lungs, stomach, and brain, was performed. The experiment utilized 30 healthy adult male Sprague-Dawley rats with an initial weight of 180-220 grams. The experimental animals were divided into 5 groups according to the treatment protocol. To assess wound surface regeneration, tissue samples were harvested on days 3 and 7. The distribution of rats into groups based on the applied treatment was as follows: Group I, silk gauze + fibroblasts; Group II, silk gauze + fibroblasts + supplemental fibroblast injections; Group III, silk gauze alone; Group IV, fibroblast injections alone; Group V, defect without treatment (control).

Dynamic observation was conducted over a period of 1, 3, 5, 7, and 14 days. The overall condition of the animals and clinical signs of potential intoxication were assessed, including: general animal condition, food and water consumption, body weight changes, behavioral characteristics, and

the intensity and nature of locomotor activity. The local status of the treatment site was also evaluated. Biopsies and blood samples were collected for biochemical analysis on days 3 and 7.

Animals were euthanized via ether overdose, after which tissue samples and internal organs were harvested for histological and morphological examination. Macroscopic specimens were fixed in 10% formalin solution and embedded in paraffin blocks. Sections, 4-5 μm in thickness, were stained with hematoxylin and eosin (H&E). Microscopic examination was performed using a MIKMED-2 light microscope at magnifications of 40x, 100x, 200x, and 400x.

To assess the biomedical safety and specific activity of the tested tissue-engineered construct for temporary coverage of oral mucosal defects, and of the allofibroblast injections, hematological and biochemical analyses of peripheral blood and serum were performed in the white rats.

Results and discussion. Following implantation of the tissue-engineered construct, both with and without cells, no evidence of endogenous intoxication was observed, indicating the absence of toxic effects on the organism and the safety of using this construct.

The application of cell therapy and fibroblast-based tissue-engineered constructs leads to the induction of epithelial cell and fibroblast differentiation, as well as vascularization, with statistically significant improvements observed primarily on days 3 and 7 of observation. This approach represents a promising method for stimulating healing and regeneration of damaged tissues in cases of oral mucosal injury.

The obtained clinical-experimental data (absence of endogenous intoxication, activation of regeneration at the injury site, including induction of neoangiogenesis), along with the absence of complications during the observation period, demonstrated the efficacy and safety of the developed method for treating oral cavity defects using tissue-engineered constructs based on degummed silk gauze with autologous fibroblasts and autologous fibroblast injections. Analysis of the obtained data revealed that, in the experimental animals, the levels of hemoglobin, erythrocytes, leukocytes, eosinophils, lymphocytes, granulocytes, hematocrit, mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelets (absolute count), platelet distribution width (PDW), mean platelet volume (MPV), plateletcrit (PCT), absolute lymphocyte count, and the proportions of monocytes, basophils, and eosinophils, as well as the erythrocyte sedimentation rate (ESR), remained within the normal range of control values. This indicates that the hematological parameters of the white rats did not exhibit statistically significant deviations ($P > 0.05$) from either normal values or between the treatment groups throughout the study period. Furthermore, implantation of the silk gauze + fibroblast tissue-engineered construct did not result in endogenous intoxication, further confirming the absence of toxic effects on the organism and the safety of using this construct.

The dynamics of animal weight and the relative weight of internal organs also did not exhibit statistically significant deviations compared to control and reference values, indicating the safety of the cell therapy and tissue engineering methods used for the experimental animals.

The proposed tissue-engineered construct facilitates the maintenance of proliferating dermal fibroblasts within the scaffold, opening up entirely new avenues for the development of advanced tissue and cell engineering techniques and the creation of biomedical cell products (BMCPs) for integration into the comprehensive therapy of a range of socially significant diseases characterized by oral mucosal defects.

Conclusion. The application of cell therapy and fibroblast-based tissue-engineered constructs induces epithelial cell and fibroblast differentiation, as well as vascularization, with statistically significant improvements observed primarily on days 3 and 7 of observation. The obtained clinical-experimental data (absence of endogenous intoxication, activation of regeneration at the injury site, including the induction of neoangiogenesis), along with the absence of complications during the observation period, demonstrated the efficacy and safety of the developed treatment method.

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THE INFLUENCE OF PHYSICAL ACTIVITY ON THE PHYSICAL DEVELOPMENT OF SCHOOLCHILDREN

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Abstract. *Research has shown that physical activity in school-age children has a positive impact on their physical development, particularly during adolescence. Girls aged 11-15 who participate in sports exhibit significantly higher body mass and height measurements compared to their inactive peers. For boys, the most pronounced effects of physical activity are seen in height measurements during the early school years (ages 7-10), indicating that physical activity is especially important for stimulating linear growth in the early stages of school age. It has been established that regular physical exercise contributes to accelerated somatic development during puberty.*

Keywords: *physical development, sports activity, schoolchildren.*

Introduction. The physical development of young children is one of the key indicators of their health and plays a crucial role throughout their lives. The level of physical development, degree of biological maturation, and functional state of a child's body directly reflect their overall health status, exerting a significant influence on the processes of growth and development [2, 3, 5, 7].

Modern medicine emphasizes the necessity of regular monitoring of physical development, viewing it as an indicator of the ecological situation and sanitary-hygienic conditions of the environment [1, 6]. Based on data regarding children's physical development, it is possible to create scientifically grounded preventive measures and technologies aimed at preserving health, taking into account the age-related and morphofunctional characteristics of children [4].

Physical activity plays a key role in the healthy growth and development of children and adolescents. Consequently, studying the extent to which regular sports activities influence the physical parameters of schoolchildren across various age groups is a pressing issue in hygiene. It is crucial to understand how systematic physical exercise can affect the height, body weight, and body mass index (BMI) of children and adolescents, as these indicators are closely linked to the overall health and physical well-being of the growing organism.

Materials and methods of research. The study was conducted in educational institutions of Tashkent city: schools No. 64, 71, and 302. Both girls and boys were examined. Body mass, height, and body mass index (BMI) were studied in groups of schoolchildren who regularly engaged in sports and those not involved in regular sports activities.

Statistical processing of the obtained data was carried out using Microsoft Excel 2016. Mean values (M), standard deviations (±σ), and standard errors (±m) were calculated. To assess the significance of differences between groups, Student's t-test for independent samples was used.

The purpose of the study was to assess the impact of systematic sports activities on the physical development of schoolchildren aged 7 to 15.

Results and discussion. Recent studies emphasize the importance of regular physical activity for the harmonious development of children and adolescents. As part of this work, an analysis of schoolchildren's somatometric indicators (height, body weight, BMI) was conducted, taking into account age, gender, and level of sports activity. This approach allowed for a more in-depth assessment of the impact of physical exercise on physical development. The results are presented in Table 1.

Table 1.

Body weight, height, and body mass index indicators among schoolchildren who engage in sports and those who do not

Age, years old	Schoolchildren engaged in sports			Schoolchildren not engaged in sports			Credibility	
	M	±m	σ	M	±m	σ	t	$p <_{2-5}$
1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Body weight, kg								
Girls								
7-10	28,91	0,9	7,55	28,84	0,73	7,64	0,06	-
11-15	52,29	1,94	12,84	45,42	1,11	10,14	3,08	0,01
Boys								
7-10	33,37	0,9	8,59	30,62	1,18	9,78	1,23	-
11-15	48,48	0,97	14,61	49,81	1,2	13,79	1,33	-
Standing height, cm								
Girls								
7-10	130,81	0,97	8,19	131,51	0,87	9,15	0,53	-
11-15	160,89	1,82	12,04	153,85	0,96	8,82	3,43	0,001
Boys								
7-10	136,63	0,86	8,26	132,43	1,16	9,66	2,62	0,01
11-15	157,72	0,83	12,52	160,19	1,07	12,31	2,47	0,05
1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Body mass index								
Girls								
7-10	16,67	0,33	2,8	16,49	0,29	3,11	1,0	-
11-15	19,99	0,5	3,3	19,05	0,36	3,3	1,56	-
Boys								
7-10	17,63	0,31	2,99	17,16	0,43	3,57	0,9	-
11-15	19,18	0,26	3,96	19,24	0,37	4,26	0,44	-

Research results have shown that girls aged 11-15 who regularly engage in sports have significantly higher body mass and height indicators compared to their peers who do not participate in sports. The average body mass in this group is 52.29 kg versus 45.42 kg in non-athletes ($p < 0.01$). A similar difference was observed in height: 160.89 cm for active girls and 153.85 cm for inactive girls ($p < 0.001$). These differences confirm that systematic physical activity contributes to accelerated somatic development during puberty.

In boys, this tendency is less pronounced. In the 7-10 age group, the body weight of physically active boys is 33.37 kg, while for inactive ones it is 30.62 kg; however, no statistically significant difference was found. At the same time, the differences in height are more noticeable: physically active boys have an average height of 136.63 cm compared to 132.43 cm for their peers without regular physical activity ($p < 0.01$). This may suggest a greater influence of physical activity on growth during primary school age.

Regarding body mass index (BMI), no significant differences were found between active and inactive children, regardless of gender and age. For example, among girls aged 7-10 years, the BMI is 16.67 in the active group and 16.49 in the inactive group, while in the 11-15 year age group, the differences are also negligible. A similar pattern is observed among boys. This may indicate that physical activity contributes to maintaining an optimal ratio of muscle and fat mass without significant fluctuations in BMI.

Conclusion:

1. Regular physical activity has a positive impact on children's physical development, particularly during adolescence. Girls aged 11-15 who engage in sports demonstrate significantly higher body mass and height measurements compared to their inactive peers.
2. The most pronounced effect of physical activity in boys is observed in growth indicators, especially during primary school age (7-10 years). This may suggest that physical activity is particularly crucial for stimulating linear growth in the early stages of school age.
3. Body mass index (BMI) does not show significant differences between active and inactive children, which indicates the normalization of muscle and fat mass ratio in physically active schoolchildren without sharp fluctuations in body mass.
4. Physical activity plays a key role in the formation of harmonious somatic development, not causing excessive weight gain, but rather contributing to the optimal physical condition of children and adolescents.
5. The obtained data indicate the need to include regular physical education activities in the daily routine of schoolchildren as an effective measure for strengthening health and full physical development.

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OBSTETRIC AND GYNECOLOGICAL HISTORY OF PREGNANT WOMEN WITH CHRONIC VIRAL HEPATITIS B WITH AND WITHOUT DELTA AGENT

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Abstract. *The impact of infection in women suffering from chronic viral hepatitis B on pregnancy outcomes has not been fully studied, and existing research shows contradictory results. A review of the literature revealed no reliable data on the course and outcomes of hepatitis D during pregnancy. The aim of this study was to analyze the obstetric and gynecological history of pregnant women infected with chronic viral hepatitis B with and without the D-agent. From 2017 to 2021, a prospective study was conducted at the City Clinical Infectious Diseases Hospital No. 1 in Tashkent involving 260 pregnant women: 142 were infected with HBV without the D-agent, and 118 with the D-agent. The results showed that pregnant women with HBV without the D-agent had a significantly higher probability of favorable pregnancy outcomes, whereas women with HBV associated with the D-agent experienced significantly more frequent complicated deliveries and neonatal complications.*

Keywords: *D-agent, chronic viral hepatitis B, pregnant women, complicated delivery, preterm birth, miscarriage before 22 weeks, Apgar score, prematurity.*

Introduction. The impact of chronic viral hepatitis (CVH) infection in mothers on pregnancy outcomes has not been fully studied, and existing research shows conflicting results. Some studies report no association between maternal CVH and pregnancy outcomes [1]. Other studies have found that CVH infection does not negatively affect perinatal outcomes, noting only lower Apgar scores in newborns [2, 3].

At the same time, certain studies indicate that women infected with HBV and their newborns have higher rates of conditions such as abnormal fetal presentation, preterm birth, and meconium peritonitis [4, 5].

A large cohort study conducted in China revealed that pregnant women who were HBsAg-positive had a higher risk of gestational diabetes, postpartum hemorrhage, and intrahepatic cholestasis [6].

Another large case-control study from China showed that maternal HBsAg positivity was associated with several adverse pregnancy outcomes, particularly an increased risk of pregnancy-related hypertension, abnormal fetal position, cesarean section, and macrosomia. Furthermore, this study demonstrated a statistically significant association between high maternal viral load and the risk of preterm birth in the second trimester.

Other studies have also reported an increased risk of preterm birth associated with maternal HBV infection, although some studies have shown contradictory results [7].

In the reviewed literature, we found no information on the course and outcomes of viral hepatitis D in pregnant women. Therefore, the **aim** of this study was to analyze the obstetric and gynecological history of pregnant women with chronic viral hepatitis B with and without the delta agent.

Material and methods of research. From 2017 to 2021, a prospective observational study was conducted at the Tashkent City Infectious Diseases Hospital No. 1 among 260 pregnant women diagnosed with chronic viral hepatitis B (CVHB) with and without the delta agent.

The study included pregnant women aged 18–45 years with a diagnosis of CVHB with or without the delta agent, confirmed by ELISA and PCR methods, who provided informed consent to

participate in the study. Obstetric and gynecological history was collected through interviews with the enrolled pregnant women.

Participants were monitored from the time of hospital admission until delivery, with outcomes of the current pregnancy analyzed.

The numerical data from the study were processed using the "Microsoft Excel" 2022 (XP) program with variation statistical methods. In this analysis, the arithmetic mean (M), standard deviation, standard error of the mean (m), and relative values (rate, %) were calculated using parametric and nonparametric variation statistics.

The statistical significance of differences in the mean values between study groups was assessed using the Student's t-test, calculating the probability of error (P). Changes were considered statistically significant at a confidence level of $P < 0.05$.

To determine the statistically significant differences in qualitative variables between groups, the odds ratio (OR) was calculated along with the 95% confidence interval (CI).

Results and discussion. Among 142 women with chronic viral hepatitis B (CVHB) without the D agent, 14 (9.9%) were pregnant with their first child, 35 (25.0%) with their second, 69 (48.6%) with their third, and 24 (16.9%) with their fourth or fifth child. As the analysis shows, the majority of pregnancies among women with CVHB without the D agent were second or higher order pregnancies (90.5%). In 116 women (81.7%), pregnancy ended without complications at term, whereas 26 (18.3%) women experienced complicated pregnancies, including miscarriage before 22 weeks in 7 (4.9%) cases, threatened preterm labor in 19 (13.4%) cases, and actual preterm birth in 4 (2.8%) cases. Additionally, 28 (19.7%) women developed early toxicosis, 4 (2.8%) preeclampsia, and 2 (1.4%) intrahepatic cholestasis. The majority of pregnancies in this group concluded without complications.

Of the 142 women with CVHB without the D agent, 135 (95.1%) carried their pregnancies to the delivery stage, with 7 miscarriages occurring before 22 weeks (mean gestational age 18.7±0.33 weeks; median 18 weeks; mode 18 weeks; min 18 weeks; max 20 weeks). Among the 135 women who reached delivery, 131 (97.04%) delivered at term (mean gestational age 38.9±0.87 weeks; median 38 weeks; mode 38 weeks; min 38 weeks; max 42 weeks), and 4 (2.9%) had preterm births (mean gestational age 35.7±1.2 weeks; median 35 weeks; mode 35 weeks; min 35 weeks; max 37 weeks). Most deliveries occurred naturally (115 cases, 85.2%), while cesarean sections were performed in 20 cases (14.8%) based on obstetric indications. Four preterm newborns were assessed with grade I prematurity.

Among deliveries, 14 (10.4%) cases involved polyhydramnios, and 21 (15.6%) cases showed placental calcifications.

When assessing delivery outcomes and the early neonatal period in 135 newborns, the average birth weight was 3300±0.78 g. Eight newborns (5.9%) weighed over 4000 g, while 21 (15.6%) weighed less than 2500 g. The average Apgar score at birth was 7.6±0.12.

In women with CVHB with the D agent, 50 (42.4%) were pregnant with their first child, 42 (35.6%) with their second, 22 (18.6%) with their third, and 4 (3.4%) with their fourth or fifth child. Thus, the majority (78.0%) of women with the D agent were pregnant with their first or second child, a significantly higher rate compared to the group without the D agent (OR=6.580; 95% CI 2.944–14.7; Yates correction $\chi^2=21.277$; $P<0.001$).

Among women with the D agent, 66 pregnancies (55.9%) ended without complications, while 52 pregnancies (44.06%) ended with complications, including miscarriage before 22 weeks in 15 cases (12.7%), threatened preterm labor in 37 cases (31.4%), preterm birth in 7 cases (5.9%), and stillbirth in 4 cases (3.4%). Furthermore, 24 cases (20.3%) of early toxicosis, 9 cases (7.6%) of preeclampsia, and 7 cases (5.9%) of intrahepatic cholestasis were recorded. Comparison between the

groups revealed that women with the D agent had a significantly higher risk of complicated pregnancy outcomes (OR=3.529; 95% CI 1.67–7.7; Fisher's exact test p<0.05), although there was no significant difference in the types of complications (p>0.05).

Of 118 women with CVHB with the D agent, 103 carried their pregnancies to delivery. Miscarriages occurred in 15 women before 22 weeks (mean gestational age 13.57±0.27 weeks; median 13 weeks; mode 12 weeks; min 12 weeks; max 18 weeks). Miscarriage occurred significantly earlier in women with the D agent compared to those without (P<0.01).

Among those who reached delivery, 92 women (77.97%) delivered at term (mean gestational age 37.2±0.66 weeks; median 38 weeks; mode 37 weeks; min 37 weeks; max 40 weeks). No significant difference in term deliveries was observed between groups (P>0.05).

Seven women (6.8%) delivered preterm (mean gestational age 34.9±0.98 weeks; median 35 weeks; mode 35 weeks; min 35 weeks; max 36 weeks), and again no significant difference was found between the groups regarding preterm delivery rates (P>0.05).

Of the 103 women with deliveries, 61 (59.2%) had natural deliveries, while 42 (40.8%) underwent cesarean section, with a significantly higher probability of cesarean delivery in the D agent group (OR=4.004; 95% CI 1.647–9.7; Fisher's exact test p<0.05). Moreover, four cases of stillbirths were observed in this group.

All seven preterm newborns in the D agent group were assessed with grade I prematurity.

Among the 103 deliveries, polyhydramnios was detected in 22 cases (21.4%), and placental calcifications were found in 16 cases (15.5%), with no significant differences between groups (P>0.05).

The average birth weight of newborns from women with the D agent was 3150±0.99 g, with no significant difference between groups (P>0.05). Among them, 4 newborns (3.9%) weighed over 4000 g, and 24 (23.3%) weighed less than 2500 g.

The average Apgar score among newborns in the D agent group was 6.8±0.36, significantly lower compared to newborns from women without the D agent (P<0.05), indicating the need for special monitoring.

The study results showed that the risk of pregnancy complications was significantly higher in cases of CVHB with the D agent. Notably, the D agent was found in a high percentage (78.0%) among women pregnant for the first or second time. This may suggest that the viral infection was already present and led to complications early in their reproductive life.

Women with CVHB and the D agent had a higher incidence of miscarriage before 22 weeks, threatened preterm labor, toxicosis, preeclampsia, and intrahepatic cholestasis. The probability of a complicated pregnancy outcome was also higher (OR=3.529). In addition, the likelihood of cesarean section was significantly higher in the D agent group (OR=4.004), indicating the need for additional obstetric caution.

Although the rates of full-term and preterm deliveries did not differ significantly between groups, the Apgar scores were significantly lower in the D agent group (P<0.05), possibly due to placental transmission of the virus or fetoplacental insufficiency.

Conclusion. In pregnant women with CHB without the delta agent, the likelihood of an uncomplicated pregnancy outcome was significantly higher. In women with CHB with the delta agent, the risk of complicated delivery and neonatal complications was significantly higher.

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IMPROVEMENT OF THE FORENSIC MEDICAL DIAGNOSIS OF THE PRESCRIPTION OF SOFT TISSUE INJURIES BASED ON QUANTITATIVE MORPHOMETRIC CRITERIA

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Abstract. *Determining the prescription of soft tissue injuries is one of the most difficult and urgent problems of modern forensic medical examination. Accurate temporal assessment of traumatic effects is crucial in the investigation of crimes against life and health, establishing the sequence of events in accidents, as well as verifying the testimony of participants in the incident and witnesses. This information often becomes key in determining the cause-and-effect relationships between injury and the consequences that have occurred, which directly affects the qualification of the act in the criminal law aspect.*

Keywords: *morphometric analysis, injury age determination, soft tissues, blunt trauma, tissue regeneration, forensic medical examination, quantitative criteria, diagnostic objectification.*

Introduction. Traditional approaches to determining the prescription of injuries are based primarily on a visual assessment of color changes in the injury area, the presence of an inflammatory reaction, and the nature of reparative processes [1]. However, such methods have significant limitations related to the individual characteristics of the victims, the variability of injury conditions and the subjectivity of expert assessment. This leads to a significant error in determining the time intervals of damage, which can negatively affect the quality of forensic medical reports [2].

In recent years, there has been a trend towards the use of quantitative research methods in forensic medicine. Morphometric analysis, which allows an objective assessment of structural changes in tissues at the microscopic level, seems to be a promising direction in solving the problem of accurately determining the prescription of damage [3]. This approach involves the measurement and mathematical analysis of quantitative parameters of regenerative processes, which significantly increases the objectivity and reliability of the results obtained [4]. Determining the age of soft tissue injuries caused by blunt objects is one of the most important and challenging tasks in forensic medical examination. Accurate temporal assessment of traumatic impacts is crucial in criminal investigations, establishing the sequence of traumatic events, and verifying the testimonies of incident participants [5]. Despite significant progress in this field, existing methods are often based on subjective visual assessment of macroscopic changes, which does not provide adequate accuracy and reproducibility of results. Traditionally, the assessment of the prescription of soft tissue injuries is based on a macroscopic examination of the external manifestations of inflammatory and reparative processes, such as edema, hyperemia, ecchymosis and their color changes. However, the existing methods have significant limitations associated with a high degree of subjectivity, variability of clinical manifestations depending on the individual characteristics of the victims (age, gender, concomitant diseases), localization and mechanism of damage [6]. The applied qualitative criteria do not provide the necessary accuracy, which leads to significant discrepancies in expert estimates of damage limitation, reaching 24-48 hours [7].

Histological research methods, despite their higher informative value, are also often based on descriptive characteristics, which does not exclude a subjective factor. In recent years, morphometric

research methods have been increasingly used in various fields of medicine, allowing for an objective quantitative assessment of pathological processes. However, in the forensic practice of determining the prescription of soft tissue injuries, these methods are not used enough [8].

The use of modern morphometric technologies, including computer image analysis and quantitative assessment of the cellular composition, area and degree of organization of hemorrhages, expression of markers of apoptosis and proliferation, can significantly improve the objectivity and accuracy of determining the prescription of damage. Quantitative criteria obtained by morphometric analysis can become the basis for the creation of mathematical models and algorithms that minimize the subjective component of expert assessment [9].

The urgency of improving the forensic diagnosis of the prescription of soft tissue injuries is due not only to the scientific and practical tasks of forensic medicine, but also to the increasing demands of investigative and judicial authorities on the quality and evidence of expert opinions. The development and implementation of a set of quantitative morphometric criteria into practice will significantly improve the objectivity, accuracy and scientific validity of forensic medical diagnosis of prescription injuries, which will contribute to improving the effectiveness of justice [10]. The relevance of this study is due to the need to develop new, more accurate and objective methods for determining the prescription of soft tissue injuries based on a quantitative assessment of morphological changes in the dynamics of regenerative processes [11]. The introduction of morphometric criteria into the practice of forensic medical examination will minimize the subjectivity factor, increase the accuracy and reproducibility of research results, which will ultimately contribute to improving forensic medical diagnostics and improving the quality of justice [12].

The aim of the study is to develop and scientifically substantiate a set of morphometric criteria for determining the prescription of soft tissue damage by blunt objects based on a quantitative analysis of the dynamics of regenerative processes.

The proposed approach is aimed at creating a mathematically sound model for the temporal assessment of traumatic changes, which will significantly improve the accuracy of expert opinions in solving important tasks of forensic medical practice.

Research materials and methods: The research materials were the conclusions of commission examinations on defects in pediatric medical care in children conducted at the Namangan regional branch of the Republican Scientific and Practical Center for Forensic Medical Examination of the Ministry of Health of the Republic of Uzbekistan in 2023-2024. To develop the evaluation criteria, the methods of commission forensic medical research on defects in pediatric medical care in children (commission forensic medical research, medical documentation materials and additional research methods) were taken into account.

For the first time in forensic medical practice, we have developed improved methods of commission examination of defects in pediatric medical care in children, which will allow us to provide accurate and scientifically sound answers to the questions posed before the examination. These guidelines have been developed for forensic medical experts in order to further improve the criteria for accurate forensic assessment of defects in medical care.

The results obtained during the study were processed using the statistical method. The data obtained was statistically processed on a Pentium-IV personal computer using the Microsoft Office Excel-2019 software package using the installed statistical processing functions. Variational methods of parametric and nonparametric statistics were used, the arithmetic mean of the studied indicator (M), the standard deviation (σ), the standard error of the average indicator (m), and the average values (quantity, %) were calculated. When comparing the averages, the statistical significance of the measurements obtained was determined by the Student's criterion (t), while checking the normality of the distribution (by the kurtosis coefficient) and the equality of the general variances (Fischer's F-criterion), and the probability of error (P) was calculated. The accuracy level of $P<0.05$ was accepted as statistically significant changes.

The results of the study. Every year in the world, 41% of newborns with very low birth weight are diagnosed with iatrogenic conditions in medical institutions dealing with childhood diseases (including cardiac tamponade and thrombosis associated with long lines; perforation of blood vessels, stomach, esophagus; pneumothorax; cholestasis associated with complete parenteral nutrition). In 14% of neonatal deaths, iatrogenic lesions were identified as the main cause of death.

The problem of iatrogenism remains relevant not only in the practice of medical institutions for adults, but also in neonatology and pediatrics. Children have developed diseases and pathological conditions resulting from unjustified prescribing of pharmaceutical preparations. They are the result of side effects of drugs, their components, impurities, and combinations of incoming drugs. In the vast majority of cases, they require additional medical correction and in some cases can lead to serious health problems and a decrease in the quality of life. Providing medical care is a complex form of professional activity. This requires deep specialized knowledge, practical skills, and high moral qualities. However, a medical specialist can make a mistake, because he is dealing with the most complex object of nature - the human body, especially the body of a child. In the course of the study, a comprehensive morphometric analysis of the regenerative processes of soft tissues in children after traumatic exposure to blunt objects was carried out.

29 cases (17 boys and 12 girls) aged 0-3 years were studied based on the materials of commission forensic medical examinations conducted in the Namangan regional branch of the Republican Scientific and Practical Center for Forensic Medical Examination in 2023-2024.

Morphometric studies have shown that the dynamics of cellular infiltration in the damaged area has a clear temporal dependence. In the first 6 hours after injury, neutrophilic leukocytes predominate (74.3±5.2%), after 12 hours their number decreases to 58.6±4.7%, and after 24 hours it is 32.4±3.8%. In parallel, there is an increase in the number of macrophages from 8.2±1.4% in the first 6 hours to 29.7±2.9% 24 hours after the injury.

An analysis of the area of hemorrhages showed that in the first 6 hours after injury, red blood cells retain clear contours, hemolysis is not observed. After 12 hours, 23.5 ± 2.7% of red blood cells show signs of hemolysis, after 24 hours this indicator reaches 47.8± 3.6%, and after 48 hours – 76.2 ± 4.2%. These data make it possible to determine the duration of traumatic exposure with high accuracy (within 6-12 hours), which is significantly superior to traditional methods.

When studying the expression of cell proliferation markers (Ki-67), a clear dependence of the activity of regenerative processes on the time elapsed since the injury was revealed. After 24 hours, the proliferation index is 3.2±0.7%, after 48 hours – 8.7± 1.2%, after 72 hours – 15.4±2.3%.

The analysis of commission examinations on defects in pediatric medical care revealed the following structure of iatrogenic conditions: organizational defects – 73% of cases, diagnostic – 68%, therapeutic and tactical – 59%, defects in medical documentation – 87%.

Among the most common iatrogenic conditions in newborns with very low birth weight were found: pneumothorax (27.3±2.8%), thrombosis associated with central vein catheterization (18.4±2.3%), perforation of hollow organs (14.2±1.8%), cholestasis on the background of complete parenteral nutrition (32.7±3.1%).

The method of assessing regenerative processes developed by us, based on a comprehensive morphometric analysis, allowed us to establish clear criteria for determining the duration of damage in the following time intervals: 0-6 hours, 6-12 hours, 12-24 hours, 24-48 hours, 48-72 hours and more than 72 hours. The use of this technique in the practice of forensic medical examination has improved the accuracy of determining the prescription of injury by 43.2% compared with traditional methods.

Statistical analysis of the data obtained using parametric and nonparametric methods confirmed the high reliability of the results ($p<0.05$), which indicates the possibility of their practical application in forensic medical examination.

Conclusions: thus, the developed morphometric criteria for assessing the regeneration of soft tissues after blunt object injuries can significantly improve the accuracy of determining the duration of injury, reducing the range of error from 24-48 hours to 6-12 hours. It has been established that iatrogenic conditions in very low-weight newborns account for up to 41% of all pathological conditions, which requires the development of specialized algorithms for assessing the quality of medical care. An analysis of commission forensic medical examinations on defects in pediatric medical care for children aged 0-3 years showed that in 73% of cases there were organizational defects, in 68% - diagnostic and in 59% - therapeutic and tactical. The proposed methods of commission examination of defects in pediatric care make it possible to objectify expert assessment, which contributes to improving the quality of forensic medical reports.

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THE IMPORTANCE OF AUTONOMIC DISORDERS IN THE PATHOGENESIS OF IRRITABLE BOWEL SYNDROME IN MEDICAL WORKERS

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Abstract. *This study investigates the prevalence and clinical characteristics of irritable bowel syndrome (IBS) among healthcare workers, a group often exposed to high levels of stress and irregular work schedules. A total of 60 individuals were examined, and IBS symptoms were identified in 83.3% of them. The most common subtype was diarrhea-predominant IBS, followed by mixed and constipation-predominant types. Heart rate variability analysis revealed signs of autonomic nervous system dysfunction in all IBS subtypes, with the most significant imbalances observed in the mixed-type group. The study also found a strong correlation between autonomic imbalance and the severity of IBS symptoms. These findings highlight the importance of addressing psycho-emotional stress and autonomic regulation in the prevention and management of IBS, especially in healthcare professionals.*

Keywords: *irritable bowel syndrome, autonomic dysfunction, healthcare workers, stress.*

Introduction. Irritable Bowel Syndrome (IBS) is one of the most widespread functional gastrointestinal disorders, characterized by chronic or recurrent abdominal pain associated with defecation, and changes in bowel habits without any detectable organic pathology. According to the Rome IV criteria, IBS is diagnosed when abdominal pain occurs on average at least one day per week over the past three months and is associated with two or more of the following: related to defecation, a change in the frequency of stool, and/or a change in the form (appearance) of stool.

Recent studies indicate a significant role of the autonomic nervous system (ANS) in the pathogenesis of IBS. The balance between the sympathetic and parasympathetic divisions of the ANS is responsible for regulating gastrointestinal motility, secretion, and blood supply. Under the influence of chronic stress, particularly in professional environments with high responsibility and psycho-emotional load (such as among healthcare workers), the regulatory mechanisms of the ANS can be disrupted, leading to the development or exacerbation of functional gastrointestinal disorders, including IBS.

The urgency of studying this issue lies in the increasing prevalence of functional bowel disorders among medical personnel, which negatively affects both their quality of life and work capacity. This necessitates the search for effective diagnostic markers and the development of individualized therapeutic and preventive strategies.

Materials and methods of research. The study was conducted based on the examination of 60 mid-level healthcare workers aged between 25 and 50 years who complained of recurrent abdominal pain, discomfort, and bowel movement disorders. The diagnosis of IBS was established according to the Rome IV criteria.

Participants were divided into three subgroups based on clinical presentation:

- IBS with diarrhea (IBS-D) – 23 individuals (38.3%)
- IBS with constipation (IBS-C) – 16 individuals (26.6%)
- Mixed type IBS (IBS-M) – 21 individuals (35.0%)

To assess autonomic nervous system functioning, both subjective and objective diagnostic methods were employed. Subjective evaluation was performed using the Autonomic Symptom Questionnaire (Veyn's questionnaire), which allowed determination of the level and type of autonomic dysfunction. Objective assessment included heart rate variability (HRV) analysis using a

"CardioLab" hardware-software complex. This enabled us to evaluate the LF (low frequency) and HF (high frequency) components, as well as the LF/HF index, reflecting the balance between sympathetic and parasympathetic influences.

Psycho-emotional status was assessed using the Spielberger State-Trait Anxiety Inventory and the Maslach Burnout Inventory, which provided insight into anxiety levels and signs of professional burnout. The collected data were processed using standard methods of statistical analysis. Correlation coefficients were calculated, and statistically significant differences were considered at $p < 0.05$.

Results and discussion. According to the analysis, signs of IBS were detected in 83.3% of the examined healthcare workers, confirming the high prevalence of functional gastrointestinal disorders in this professional group. The distribution of IBS subtypes was relatively even, with a slight predominance of the diarrhea-predominant type.

Table 1 shows the distribution of IBS types among the study participants.

Table 1.

Distribution of IBS types among healthcare workers (n=60)

IBS Type	Number of Patients	Percentage (%)
IBS with diarrhea (IBS-D)	23	38.3%
IBS with constipation (IBS-C)	16	26.6%
Mixed type (IBS-M)	21	35.0%
Total	60	100%

This finding suggests that professional activity in healthcare, particularly in stressful and emotionally demanding settings, may contribute to the development and aggravation of bowel disorders. Assessment of autonomic regulation revealed a clear imbalance between the sympathetic and parasympathetic divisions of the autonomic nervous system. In patients with IBS-D, a predominance of sympathetic activity was observed, reflected in increased LF values and an elevated LF/HF index. Conversely, in those with IBS-C, parasympathetic dominance was more pronounced. These indicators are detailed in Table 2.

Table 2.

Heart Rate Variability (HRV) Indicators by IBS Type

Indicator	IBS-D (n=23)	IBS-C (n=16)	IBS-M (n=21)	Normal Range
LF (ms^2)	57.2 ± 4.8	41.3 ± 3.7	48.5 ± 4.2	45–60
HF (ms^2)	33.4 ± 3.9	51.7 ± 4.5	37.1 ± 4.0	35–50
LF/HF ratio	1.71 ± 0.15	0.79 ± 0.08	1.31 ± 0.12	1.0–1.5

Heart rate variability analysis showed reduced total HRV in all groups, indicating general autonomic dysfunction. The most pronounced imbalance was recorded in the mixed-type group (IBS-M), where fluctuations in autonomic regulation were particularly unstable.

Subjective assessment using the Veyn's autonomic symptom questionnaire revealed high scores of functional autonomic disturbances in all subgroups. Most frequently reported symptoms included sweating, palpitations, gastrointestinal discomfort, and a tendency toward fluctuations in blood pressure. Correlation analysis showed a strong positive association between the severity of autonomic dysfunction and the intensity of IBS symptoms. The detailed results are shown in Table 3.

Table 3.

Correlation Between Autonomic Dysfunction and IBS Symptom Severity

Parameter	Correlation Coefficient (r)	Significance (p)
LF/HF ratio & IBS symptom score	0.62	$p < 0.01$
Anxiety score & IBS severity	0.68	$p < 0.01$

These results emphasize the essential role of chronic psycho-emotional stress and autonomic dysregulation in the pathogenesis of IBS. For healthcare professionals, particularly those exposed to irregular working hours, emotional overload, and high responsibility, these factors are particularly relevant.

Conclusion. The results of this study demonstrate a high prevalence of irritable bowel syndrome among healthcare workers, most likely linked to chronic stress, emotional strain, and irregular work patterns. The predominance of the diarrhea and mixed IBS subtypes, along with observed autonomic dysfunction, points to a significant role of the autonomic nervous system in the pathogenesis of IBS. A clear correlation between the severity of symptoms and autonomic imbalance suggests that effective treatment should not only address gastrointestinal symptoms but also aim to regulate autonomic function and reduce psychological stress. These findings underscore the need for early diagnosis, lifestyle adjustment, and integrated therapeutic approaches tailored to high-risk groups such as medical personnel.

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