Central Asian Journal of Medicine

FEATURES OF MICROBIOCENOSIS OF THE NASAL MUCOSA AND ITS ROLE IN ALLERGIC DISEASES (LITERATURE REVIEW)

Zukhra N. Orinbayeva [1], Zuhra A. Nuruzova [2], Dilnoza A. Shahobiddinova [3]

1 Assistant of the Department of Microbiology, Virology, and Immunology, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: zuxraorinbayeva91@gmail.com

2 Prof., DSc, Head of the Department of Microbiology, Virology, and Immunology, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: voyna_microbam@mail.com

3 Second-year student of the 1st Medical Faculty, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: dilnozashohobiddinova@gmail.com

ABSTRACT

In the modern world, allergic respiratory diseases have a huge place among all chronic diseases. The annual increase in the prevalence of allergic rhinitis and bronchial asthma among the global population makes relevant studies underlying their pathogenesis. Changes in the nasal mucosa alter its most important function — protection from aggressive environmental factors — allergens and pollutants. Inflammatory processes in the nasal cavity interfere with the normal mucosa functioning as a non-specific barrier and facilitate their further penetration into the microorganism.

This article provides an overview of the current scientific medical literature, summarizing the results of scientific research regarding microbiocenosis of the nasal mucosa and its effect on the development and formation of allergic rhinitis.

Key words: allergic rhinitis, allergic reaction, microbiocenosis of the nasal mucosa, pathophysiological mechanisms.

INTRODUCTION

Allergic diseases of the respiratory system are prevalent among chronic conditions, with allergic rhinitis and bronchial asthma being the most common forms [19, 23].

According to modern views, the development of allergic rhinitis is caused by an inflammatory reaction of the nasal mucosa mediated by IgE, which occurs upon contact with allergens. In our opinion, the role of microbiota in the pathogenesis of this disease is insufficiently studied and often underestimated, especially in the chronic form of the disease, the development of infectious complications, and hyperreactive states. When interacting with an allergen, a cascade of pro-inflammatory reactions is activated, aimed at removing the irritant agent. As a result, the secretion of mucus and transudate increases, which helps to eliminate both the allergen and the components of the normal microflora. This creates conditions for the colonization of the mucosa by new microbial communities, which probably leads to the formation of a pathological vicious circle and increases the risk of bacterial complications of allergic rhinitis.

Objective: based on the literature analysis, to demonstrate the possible role of nasal microbiota in the pathogenesis of complications of allergic rhinitis.

Allergic rhinitis (AR) is one of the most common diseases of the respiratory system, affecting up to 40% of adults and up to 25% of children [1]. It is often associated with bronchial asthma (BA), which is detected in 15-38% of patients with AR, and 55-85% of patients with AD report symptoms of AR [2].

Bronchial asthma is a chronic airway disease characterized by symptoms such as shortness of breath, wheezing, chest congestion, and coughing. An important link in bronchial asthma is mast cells, eosinophils, and lymphocytes. Bronchial asthma is one of the important diseases that progresses every year, as the number of patients diagnosed with the disease increases [3].

Your sentence is mostly clear, but I made a few adjustments for clarity and flow:

According to WHO forecasts, the 21st century has become the era of allergies, as the prevalence of allergic diseases increases by 2-3 times every 10 years. Statistics show that one in five people on our planet suffers from allergies. According to the WHO, allergic diseases currently rank third, but forecasts predict they will soon become the leading cause of illness, making the 21st century the “century of allergy'” [4].

Numerous epidemiological studies examining the spread of allergic diseases worldwide reflect a steady increase in the number of patients with allergic conditions, including among the pediatric population [14, 25, 26, 27].

According to a recent report by the World Health Organization (WHO), the number of asthma patients worldwide exceeds 339 million [5]. Experts predict that this number will rise to 400 million by 2025 [3, 4]. In the Russian Federation (RF), according to the Russian Ministry of Health, the total incidence of asthma in 2017

was more than 1,000 cases per 100,000 adults [5]. Additionally, epidemiological research estimates the prevalence of asthma at approximately 6.9% [6].

The disease is associated with a poor quality of life, a significant social burden, and an increased risk of adverse outcomes, including disability and death [7, 8]. Lack of control or only partial control of asthma symptoms, even in mild cases, is a serious risk factor for exacerbations, which can lead to a rapid decline in lung function and death [9]. Poor symptom control and unfavorable outcomes in asthma are often linked to treatment inconsistencies with evidence-based recommendations [10-12]. "The UK National Review has convincingly shown that 46% of asthma-related deaths could have been prevented if the recommended treatment principles had been followed in primary health care.

According to L.V.Kovalchuk, L.V.Gankovskaya, and R.Ya.Meshkova (2017), as well as the results of epidemiological studies conducted in various countries, the prevalence of allergic rhinitis (based on treatment data) ranges from 4% to 32%. At the beginning of the 21st century, this figure was 24% in England, 13–19.6% in Germany, 20.6% in Norway, and 10–30% in the USA. In Russia, the prevalence of allergic rhinitis ranges from 12.7% to 24% on average. Among children, the prevalence is 0.7–14.95% in those aged 6–7 years and 1.4–39.7% in those aged 13–14 years.

The incidence of allergic rhinitis is higher in boys than in girls; however, during adolescence, this difference disappears, with similar rates observed in both sexes. Allergic rhinitis accounts for approximately 50% of all chronic rhinitis cases [13].

A particularly sharp increase in the incidence of asthma in the Republic of Uzbekistan was observed in the second half of the 20th century. According to statistical data from the Republican Scientific Specialized Allergological Center (RNSAC) in Uzbekistan, approximately 140,000 people suffer from bronchial asthma [14].

The microbiocenosis of the nasal cavity is a dynamic system composed of a multitude of microorganisms, including those that persist on the mucous membranes of the respiratory tract and those that enter the nose accidentally with inhaled air [15, 16]. The composition of nasal microbiota varies significantly depending on factors such as age (children, adults, elderly), season (temperature, insolation), habitat (urban, rural, or country setting), existing ENT pathologies (allergic rhinitis, sinusitis, infectious rhinitis), antibiotic resistance, immune system status (primary or secondary immunodeficiency syndrome, autoimmune pathology), and the presence of acute and/or chronic infectious diseases [17, 18]. It is also essential to study the population-specific characteristics of nasal

microbiocenosis, which are unique to individuals living in particular geographical regions.

Dysbiosis and secondary immune disorders are closely interconnected conditions. The key role of normal microbiocenosis in adaptation (or maladaptation in dysbiosis) supports I.I.Mechnikov's thesis on the fundamental role of dysbiosis in the development of pathological processes [19]. A comparison of microbiocenosis indicators with the characteristics of inflammatory disease progression has shown that the severity of the pathological process depends on the extent of negative changes in microbiological parameters. In our opinion, this underscores the necessity of studying microbiocenoses in various diseases. Dysbiosis can be considered either as an etiological factor or as a predisposing factor for the development of pathological processes [1, 4, 9, 13].

The microbial community of the nasal mucosa plays a key role in maintaining the health of the upper respiratory tract. Over the past five years, studies have shown that the nasal microbiota of healthy individuals is predominantly composed of Actinobacteria, particularly *Corynebacterium* and *Propionibacterium*, with relatively lower levels of Firmicutes (e.g., *Staphylococcus*) and Proteobacteria (e.g., *Enterobacter*).

Age-related changes also influence the nasal microbiota. In healthy individuals under the age of 50, Actinobacteria predominate, whereas in the elderly, there is an increased proportion of Firmicutes, particularly *Staphylococcus* species.

In addition, the nasal microbiota can change in response to various diseases. For example, patients with allergic rhinosinusitis exhibit an imbalance in their microbiota, which may contribute to inflammation and obstruction [13].

Thus, maintaining a healthy nasal microbiota is essential for preventing upper respiratory tract diseases and supporting overall immune function.

Staphylococcus aureus is detected in 20–70% of children with allergic rhinitis (AR) and bronchial asthma (BA), with microbial contamination in these children being 1.5–2 times higher than in healthy individuals. In cases where AR and BA coexist, the predominant microflora includes *Staphylococcus aureus*, while *Staphylococcus haemolyticus***,** *Staphylococcus epidermidis*, and *Corynebacterium* spp. may also be present. Other bacteria, such as *Streptococcus viridans***,** *Streptococcus haemolyticus***,** *Neisseria*, and *Klebsiella* spp., are considered incidental findings. Carriage of *Staphylococcus aureus* in allergic rhinitis (AR) is associated with more severe nasal congestion and prolonged rhinosinusitis. Patients with postnasal drip syndrome often develop bronchitis, as well as persistent otitis media lasting 2–4 weeks and resistant to antibacterial therapy.

Children with AR who exhibit bacterial colonization on the mucosa show greater sensitization to allergens compared to those without bacterial colonization [20].

In her scientific article published in 2022, A. M. Lazareva stated the following: opportunistic pathogenic microorganisms predominate in respiratory atopy (AR, ABA) compared to respiratory pseudoatopy (PRS, AT). An increase in the number of bacteria from the *Enterobacteriaceae* and *Enterococcus* families on the nasal mucosa indicates dysbiosis, highlighting the significance of these microbial groups in the development of allergic pathology in the upper and lower respiratory tract in individuals with atopy. A key distinguishing feature between these groups is the higher concentration of *Enterobacteriaceae* in AR compared to PRS, as well as the predominance of *Enterococcus* species in ABA compared to AT. Thus, in allergic rhinosinusitis and bronchial asthma, regardless of the underlying cause of inflammation, pronounced dysbiosis is observed, characterized by an increased presence of opportunistic microflora on the nasal mucosa compared to the control group [21].

According to a scientific study conducted by M. I. Efimova in 2020, the persistence of *Staphylococcus aureus* on the mucous membranes of children with asthma is associated with higher levels of total IgE in blood serum compared to patients who do not harbor this microorganism in their mucosal microbiota. Growing evidence suggests that staphylococcal toxins act as superantigens and play a role in modulating chronic inflammatory respiratory diseases. A more comprehensive understanding of the role of *Staphylococcus aureus* and its superantigens in the etiology and pathogenesis of asthma could lead to the development of new therapeutic strategies for treating these conditions [22].

Conclusion The microbiota of the nasal mucosa plays a key role in maintaining respiratory health and influencing the development of allergic diseases such as allergic rhinitis and bronchial asthma. Alterations in microbiota composition, particularly the predominance of opportunistic microorganisms, may contribute to inflammatory processes and allergic reactions. Notably, the persistence of *Staphylococcus aureus* on the mucous membranes of the upper respiratory tract is associated with more severe allergy symptoms and elevated serum IgE levels in children with bronchial asthma. These findings highlight the significance of studying microbiocenosis as a contributing factor in the pathogenesis of allergic diseases and underscore the need for further research to develop novel therapeutic strategies. A deeper understanding of the microbiota and its interactions with the immune system could serve as a foundation for improving the diagnosis and treatment of allergic rhinitis and asthma, as well as for preventing complications associated with these conditions.

REFERENCES

1. Canonica GW, Baena-Cagnani CE, Blaiss MS, Dahl R, Kaliner MA, Valovirta EJ. GAPP Survey Working Group. Unmet needs in asthma: Global Asthma Physician and Patient (GAPP) Survey: global adult findings. Allergy. 2007;62(6):668-674. https://doi.org/10.1111/j.1398-9995.2007.01352.x

2. Chuchalin AG, Khaltaev N, Antonov NS, Galkin DV, Manakov LG, Paola Antonini P, Murphy M, Solodovnikov AG, Bousquet J, Pereira MH and Demko IV. Chronic respiratory diseases and risk factors in 12 regions of the Russian Federation. International Journal of Chronic Obstructive Pulmonary Disease. 2014;9:963-974. https://doi.org/10.2147/COPD.S67283

3. Diagnosing asthma: a 21st century challenge. Accessed June 03, 2020. https: // www.asthma.org.uk/a54e6a69/globalassets/get-involved/external-affairs-campaigns/diagnostics/diagnosing-asthma-21st-century-challenge.pdf

4. Diagnosing asthma: a 21st century challenge. Accessed June 03, 2020. https://www.asthma.org.uk/a54e6a69/globalassets/get-involved/external-affairs campaigns/ diagnostics/diagnosing-asthma-21st-century-challenge.pdf

5. Dusser D, Montani D, Chanez P, Blic JD, Delacourt C, Deschildre A, Devillier P, Didier A, Leroyer C, Marguet C, Martinat Y, Piquet J, Raherison C, Serrier P, Tillie-Leblond I, Tonnel A-B, de Lara MT and Humbert M. Mild asthma: an expert review on epidemiology, clinical characteristics and treatment recommendations. Allergy. 2007;62(6):591-604.

6. Foreman A., Wormald P. Different biofilms, different disease? A clinical outcomes study. Laryngoscope. 2010, 120:1701

7. Gordts F., Halewyck S., Pierard D. et al. Microbiology of the middle meatus: a comparison between normal adults and children. J. Laryngol. Otol. 2000, 114:184-188.

8. Goncharov A.G., Prodeus A.P., Shevchenko M.A., Markhaichuk A.Z., Razina A.S., Goncharova E.A., Malyarov A.M., Rusina E.V., The role of microbiota in the pathophysiological mechanisms of allergic rhinitis formation 2020 Bulletin of the I. Kant Baltic Federal University. Ser.: Natural and Medical Sciences. 2020. No. 3. pp. 100-121.

9. Global Initiative for asthma (GINA). Global strategy for asthma management and prevention, updated 2020. https://ginasthma.org/wp-content/uploads/2020/04/GINA-2020-full report final wms.pdf

10. Giavina-Bianchi P., Aun M.V., Takejima P., Kalil J., Agondi R.C. United airway disease: current perspectives. J. Asthma Allergy, 2016, vol. 9, pp. 93–100. doi: 10.2147/JAA.S81541

11. Genuneit, J. Overview of systematic reviews in allergy epidemiology / J. Genuneit, A. M. Seibold, C. J. Apfelbacher, G. N. Konstantinou, et al. Task Force 'Overview of Systematic Reviews in Allergy Epidemiology (OSRAE)' of the EAACI Interest Group on Epidemiology // Allergy. - 2017. - Vol. 72. - P. 849-856

12. Kozulina, I. E. Allergy today. Analysis of new epidemiological data / I. E. Kozulina, O. M. Kurbacheva, N. I. Ilyina // Russian Journal of Allergy, 2014, vol. 11, No. 3, pp. 3-10.

13. Kovalchuk, L. V., Gankovskaya, L. V., & Meshkova, R. Ya. (2017). Klinicheskaya immunologogiya i allergologiya s osnovami obshchei immunologii. Moscow. (in Russian).

14. Lambrecht B.N., Hammad H. The immunology of the allergy epidemic and the hygiene hypothesis. Nat. Immunol., 2017, vol. 18, no. 10, pp. 1076–1083. doi: 10.1038/ni.3829

15. Levy ML. National Review of Asthma Deaths (NRAD). British Journal of General Practice [Internet]. Royal College of General Practitioners. 2014; 64(628):564.2-564. https://doi.org/10.3399/bjgp14x682237

16. M.I. Efimova, S.V. Krasilnikova, D.Y. Ovsyannikov, T.I. Eliseeva, E.V. Bolshova, T.V. Nosova, L.V. Malysheva, V.A. Bulgakova, I.I. Balabolkin. The effect of the microbiota of the nasal mucosa on the level of total immunoglobulin E in blood serum in children with bronchial asthma. Pediatrics named after G.N. Speransky. 2020; 99 (2): 56–63.

17. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy. 2004;59(5):469-478. https://doi.org/10.1111/j.1398-9995.2004.00526.x

18. Mukherjee M, Stoddart A, Gupta RP et al. The epidemiology, healthcare and societal burden and costs of asthma in the UK and its member nations: analyses of standalone and linked national databases. BMC Med. 2016;14:113. https://doi.org/10.1186/s12916-016-0657-8

19. Nazarov, A. A. (1990). Atopicheskaya bronkhial’naya astma: (regional’nye osobennosti klinicheskogo techeniya, immuno-allergologicheskaya kharakteristika i novye sposoby terapii): autoref. Dr. diss. Moscow, 40. (in Russian).

20. Price D, Fletcher M, van der Molen T. Asthma control and management in 8,000 European patients: the Recognise Asthma and Link to Symptoms and Experience (REALISE) survey. NPJ Prim Care Respir Med. 2014;24:14009

21. Paller, A. Major comorbidities of atopic dermatitis: beyond allergic disorders / A. Paller, J. C. Jaworski, E. L. Simpson, M. Boguniewicz, J. J. Russell, et al. // Am J Clin Dermatol. - 2018. - Vol. 19. - № 6. - P. 821-838.

22. The Ministry of Health of Russia. Statistical collection 2017. Moscow: Ministry of Health of the Russian Federation; 2018. The link is active on 10/20/20. Minzdrav Rossiii. Statisticheskij sbornik 2017

23. World Health Organization. Asthma [Internet]. Geneva: WHO; 2020. Accessed October 20, 2020. https://www.who.int/ru/news-room/fact-sheets/detail/asthma) Jesse, Russell Аспириновая бронхиальная астма: моногр. / JesseRussell. - M.: VSD, 2017. – 195 с.