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## **Research Article**

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## OPTIMIZATION OF THERAPY OF MISCARRIAGE IN PATIENTS WITH ACQUIRED THROMBOPHILIA Kayumova D.T., Sadikova D.R., Yunusaliyeva D.A. TMA, department of Obstetrics and Gynecology in Family Medicine Uzbekistan

## ABSTRACT.

**Background:** Spontaneous miscarriage, defined as pregnancy loss before 22 weeks, occurs in 10-20% of clinically recognized pregnancies, most often occurring in the first trimester. Recurrent miscarriage, defined as three or more consecutive pregnancy losses, occurs in 1-2% of women. Although early miscarriage is relatively common, recurrent miscarriage presents unique challenges that require specific treatment strategies. Recurrent miscarriage is often associated with elevated levels of antiphospholipid antibodies (5-15%), sperm DNA damage (up to 85%), and hyperreactive endometrial stromal cells that can accept poor-quality embryos.

*Materials and Methods:* Our review analyzes the literature and guidelines published between 2019 and 2024, defining three main steps: observation, medical therapy, and surgery. The PRISMA method was used to systematically review and extract data from published studies.

**Results:** Hysteroscopic metroplasty has a success rate of 60-85% for women with uterine anomalies. Progesterone therapy may increase the chance of live birth by 20-30% in women with a history of multiple miscarriages. Combination therapy with an anticoagulant and aspirin is more effective than aspirin alone, improving outcomes by 50-60% in women with antiphospholipid syndrome.

**Conclusion:** Effective treatment of recurrent miscarriage involves individualized strategies including surgical correction, hormonal therapy, and immunological management. Evidence supports the use of targeted interventions to significantly improve live birth outcomes.

## ORTTIRILGAN TROMBOFILIYA BILAN KASALLANGAN BEMORLARDA HOMILA SAQLASH TERAPIYASINI OPTIMALLASHTIRISH. Kayumova D.T., Sadikova D.R., Yunusaliyeva D.A. TMA, Oilaviy tibbiyotda akusherlik va ginekologiya kafedrasi.

## ANNOTATSIYA.

**Kirish:** Homiladorlikning 22-haftasidan oldin yo'qolishi sifatida tavsiflangan spontan tushish, klinik jihatdan tan olingan homiladorlikning 10–20 foizida, ko'pincha birinchi trimestrda sodir bo'ladi. Homiladorlikning uch yoki undan ortiq ketma-ket yo'qolishi sifatida tavsiflangan takroriy abort ayollarning 1–2 foizida uchraydi. Erta abort nisbatan keng tarqalgan bo'lsa-da, takroriy abort muayyan davolash strategiyasini talab qiladigan noyob muammolarni keltirib chiqaradi. Takroriy abort ko'pincha antifosfolipid antikorlar darajasining oshishi (5–15%), sperma DNKsining shikastlanishi (85% gacha) va sifatsiz embrionlarni qabul qila oladigan giperreaktiv endometriyal stroma hujayralari bilan bogʻliq.

**Materiallar va usullar:** Bizning sharhimiz 2018 va 2024 yillar oraligʻida nashr etilgan adabiyotlar va klinik koʻrsatmalarni tahlil qiladi. Unda uchta asosiy bosqich ajratilgan: kuzatish, tibbiy terapiya va jarrohlik aralashuvi. PRISMA usuli tadqiqotlardan ma'lumotlarni tizimli tarzda koʻrib chiqish va ajratib olish uchun qoʻllanilgan.

**Natijalar:** Bachadon anomaliyalari boʻlgan ayollar uchun histeroskopik metroplastikaning muvaffaqiyat koʻrsatkichi 60–85% ni tashkil qiladi. Progesteron terapiyasi koʻplab homiladorlik yoʻqotgan ayollarda tirik tugʻilish imkoniyatini 20–30% ga oshirishi mumkin. Antikoagulyant va aspirin bilan birgalikda davolash faqat aspirindan koʻra samaraliroq boʻlib, antifosfolipid sindromi boʻlgan ayollarda natijalarni 50–60% ga yaxshilaydi.

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Xulosa: Takroriy abortni davolash uchun individual yondashuv zarur boʻlib, bu jarrohlik tuzatish, gormonal terapiya va immunologik muolajalarni oʻz ichiga oladi. Ilmiy ma'lumotlar shuni koʻrsatadiki, maqsadli aralashuvlar tirik tugʻilish ehtimolini sezilarli darajada oshiradi.

*Kalit so'zlar:* O'z-o'zidan homila tushishi, trombofiliya, AFS-sindrom, antikoagulyant davo, kutish taktikasi, medikamentoz terapiya, jarrohlik aralashuvi.

## ОПТИМИЗАЦИЯ ТЕРАПИИ НЕВЫНАШИВАНИЯ У БОЛЬНЫХ С ПРИОБРЕТЕННОЙ ТРОМБОФИЛИЕЙ. Каюмова Д.Т., Садыкова Д.Р., Юнусалиева Д.А. ТМА, Акушерство и гинекология в семейной медицине

## Узбекистан

#### АННОТАЦИЯ.

Введение: Самопроизвольный выкидыш, определяемый как потеря беременности до 22-й недели, встречается у 10–20% клинически признанных беременностей, чаще всего происходя в первом триместре. Невынашивание беременности, которое определяется как три или более последовательных потери беременности, встречается у 1– 2% женщин. Хотя ранний выкидыш является довольно распространённым явлением, рецидивирующий выкидыш представляет собой уникальные проблемы, требующие особых стратегий лечения. Невынашивание беременности часто связано с повышенными уровнями антифосфолипидных антител (5–15%), повреждением ДНК сперматозоидов (до 85%) и гиперреактивными эндометриальными стромальными клетками, которые могут принимать эмбрионы низкого качества.

Материалы и методы: Этот обзор анализирует литературу и рекомендации, опубликованные в период с 2018 по 2024 год, и выделяет три основные метода лечения: наблюдение, медицинскую терапию и хирургическое вмешательство. Для систематического обзора и извлечения данных из опубликованных исследований использовался метод PRISMA.

**Результаты:** Гистероскопическая метропластика имеет показатель успеха 60–85% для женщин с аномалиями матки. Прогестероновая терапия может повысить вероятность живорождения на 20–30% у женщин с историей многократных выкидышей. Комбинированная терапия с антикоагулянтом и аспирином более эффективна, чем только аспирин, улучшая результаты на 50–60% у женщин с антифосфолипидным синдромом.

Заключение: Эффективное лечение невынашивания беременности требует индивидуального подхода, включающего хирургическую коррекцию, гормональную терапию и иммунологическую поддержку. Научные данные подтверждают, что целенаправленные вмешательства значительно повышают вероятность живорождения.

*Key words:* Spontaneous miscarriage, thrombophilia, APS syndrome, anticoagulants, expectant management, drug therapy, surgical intervention.

**Ключевые слова:** Самопроизвольный выкидыш, тромбофилия, АФС-синдром, антикоагулянты, ожидающая тактика, медикаментозная терапия, хирургическое вмешательство.

Introduction. Spontaneous miscarriage, also called spontaneous abortion, is a common problem in pregnancy, affecting approximately 10-20% of clinically recognised pregnancies. It can be caused by chromosomal abnormalities, uterine problems, hormonal disorders, infections, or immunological dysfunctions, among others, and refers to the loss of the fetus before the 22<sup>nd</sup> week of pregnancy [1]. Women who have suffered a miscarriage experience severe emotional and psychological stress, and the physical recovery process from miscarriage can also be problematic [2]. Recurrent miscarriage is defined as the loss of three or more consecutive pregnancies. It is a condition that indicates the presence of underlying causes that require identification and more specialized care [3]. Supportive measures such as expectant management or surgical procedures such as dilation and curettage have been the mainstays of miscarriage treatment in the past. As the scientific understanding of the causes of miscarriage has evolved, treatment strategies have also evolved, with personalized, evidencebased therapies increasingly being used and becoming the standard of care [4]. Medical treatments, including manual vacuum aspiration and misoprostol, are often used in cases of early miscarriage [5]. Modern ultrasound equipment allows for earlier detection of fetal abnormalities, and genetic screening for couples who have experienced recurrent miscarriages has been developed due to advances in genetic research [6]. New standards of care, such as the use of low-dose aspirin and anticoagulant therapy in women with antiphospholipid syndrome (APS), have been developed as a result of recent studies that have examined the role of thrombophilia, autoimmune diseases, and immunological factors in miscarriage [7]. In addition, the use of probiotics and anti-inflammatory agents have been suggested as potential therapeutic interventions to improve pregnancy outcomes, given the increasing focus on the microbiota and uterine environment [8]. Despite these advances, miscarriage continues to be a challenging area of medical practice. The most significant problem is the inability to accurately determine the cause of miscarriage, particularly in early losses; chromosomal abnormalities are the most common cause, but other factors such as hormonal imbalances, immune dysfunctions, and uterine abnormalities may remain undetected

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[9]. In selecting articles based on their relevance, peer-reviewed status, and publication date, priority was given to clinical trials, meta-analyses, and established guidelines. References from leading journals were also reviewed to ensure a thorough collection of relevant material.

The aim of the work: to conduct an analysis of modern sources of domestic and foreign literature devoted to the issues of miscarriage in APS.

**Materials and methods.** A comprehensive literature review was conducted using publications from the last five years (2019–2024). The databases used included Cyberleninka, Cochrane Library, and PubMed. Priority was given to peer -reviewed clinical trials, systematic reviews, meta-analyses, and established clinical guidelines. A total of 38 relevant articles were selected based on their relevance to miscarriage in antiphospholipid syndrome (APS), with a focus on evaluating the effectiveness of various therapeutic approaches, particularly anticoagulant and antiplatelet therapies. Inclusion criteria emphasized studies examining pregnancy outcomes in women with APS, especially those with elevated levels of antiphospholipid antibodies (aPL). Both randomized controlled trials and large observational studies were included to ensure a broad evidence base.

**Results.** Out of 38 selected studies published between 2019 and 2024, 26 were clinical trials or observational cohort studies, 8 were systematic reviews or meta-analyses, and 4 were clinical guidelines. The reviewed literature consistently reported a link between antiphospholipid syndrome (APS) and increased risk of early and recurrent miscarriage, as well as other obstetric complications. In studies examining treatment approaches, the use of low-dose aspirin (LDA) in combination with anticoagulant therapy (primarily low molecular weight heparin) was the most frequently studied intervention. This combination was associated with higher live birth rates compared to either therapy alone or no pharmacologic intervention. The majority of sources (over 70%) reported a statistically significant improvement in pregnancy outcomes with this dual therapy.

Several studies included in the review assessed timing and mode of administration, with a trend toward improved outcomes when therapy was initiated before or early in pregnancy. Minor complications, such as bleeding or injection site reactions, were reported in a small proportion of cases. Treatment adherence and patient monitoring practices were variably reported across studies.

A smaller subset of studies (n=6) investigated alternative or adjunctive treatments, such as hydroxychloroquine, corticosteroids, and immunoglobulins, though evidence for these interventions was less consistent and often based on smaller patient populations or retrospective data. No significant findings were reported regarding the effectiveness of treatment in asymptomatic aPL carriers without a history of pregnancy loss, highlighting the need for further research in this subgroup.

Discussion. APS is an autoimmune disease in which laboratory tests reveal aPL, predisposing pregnancy to complications such as intrauterine growth restriction, preeclampsia, and miscarriage. Pregnancy complications in APS significantly depend on the level of antiphospholipid antibodies (aPL), which are detected in 5–15% of the population. Recurrent pregnancy losses and first trimester miscarriages are among the adverse outcomes closely associated with elevated aPL levels [11]. The risk of pregnancy complications increases significantly in women with elevated aPL titers, even if they have no history of thrombosis. However, the risk of miscarriage remains high, especially in asymptomatic patients. Higher aPL titers increase the likelihood of miscarriage, especially in the presence of lupus anticoagulant (LA) or "triple positive" status (LA, aPL, and antibodies to  $\beta 2$  glycoprotein I) [12]. Thromboprophylaxis with low-dose aspirin (LDA) and an anticoagulant improves pregnancy outcomes in women with elevated aPL levels. An anticoagulant is particularly effective in reducing the risk of thromboembolic complications during pregnancy and the postpartum period, and LDA reduces the risk of first-trimester miscarriage. According to studies [13], thromboprophylaxis is recommended for high-risk women, including those with a history of pregnancy complications or persistently positive tests for aPL, LA. For these patients, the combined use of an anticoagulant and LDA is a strategy that reduces the risk of thrombosis and miscarriage. An anticoagulant in combination with aspirin is a standard treatment for recurrent miscarriages, especially in women diagnosed with APS. APS causes an unexplained coagulopathy that disrupts the uteroplacental blood flow. An anticoagulant by inhibiting thrombin synthesis, and aspirin, being an anti-inflammatory drug, reduces blood viscosity and improves placental blood supply. The synergy of these drugs confirms the effectiveness of combination therapy to improve the prognosis of pregnancy in women with APS. Studies show that when taking an anticoagulant and aspirin, the probability of live birth increases by 40-50%, and the risks of miscarriage, preeclampsia and the negative impact of intrauterine growth retardation are reduced. The treatment plan includes subcutaneous administration of an anticoagulant or oral administration of aspirin - both methods are easy to implement in an outpatient setting. A dual anticoagulant + aspirin regimen is indicated for women with a history of recurrent miscarriages or a positive aPL test. Anticoagulant therapy is considered first-line therapy for pregnant women with APS who wish to continue the pregnancy. This approach is gradually being introduced into clinical practice, especially in patients with habitual miscarriages. As with any therapy, complications including bleeding and thrombocytosis are possible, so careful monitoring of the patient is important to minimize side effects during treatment. Currently, active research is aimed at optimizing the dosage, timing of therapy, and selection of patients with the best prognosis in order to reduce the risk of adverse reactions and improve

the effectiveness of treatment. Future work will help to develop optimal management regimens for women with APS, which will lead to improved pregnancy rates and reproductive health [14].

**Conclusion**. Miscarriage, especially in the presence of acquired thrombophilia and APS, remains a complex clinical problem requiring an individualized approach to therapy. Analysis of modern and foreign sources confirms the effectiveness of the combined use of anticoagulants and NDA in women with APS at the pregravid stage and throughout pregnancy, which can significantly reduce the risk of not only miscarriage, but also improve pregnancy outcomes. The introduction of personalized treatment strategies based on evidence-based medicine, early diagnosis and comprehensive monitoring of patients opens up new opportunities to improve the reproductive prognosis. However, further research is needed to optimize therapy regimens, clarify indications and identify biomarkers that can more accurately determine risk groups and improve treatment effectiveness.

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