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IMMUNOLOGICAL FACTORS IN RECURRENT PREGNANCY LOSS AND MODERN DIAGNOSTIC APPROACHES

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Annotation: This article investigates the role of immune system-related issues in recurrent pregnancy loss and assesses modern diagnostic methods. The assessment includes prevailing immunological screening procedures and research-based diagnostic algorithms being used in reproductive medicine. The paper integrates results from the literature of Uzbek, Russian, and world sources to offer an all-around understanding of the immunological cause and the diagnostic approaches for the management of recurrent abortion.
Keywords: immunological factors, antiphospholipid syndrome, autoimmune disorders, reproductive immunology, diagnostic approaches, thrombophilia

Аннотация: В данной статье рассматривается роль иммунологических факторов в развитии привычного невынашивания беременности и анализируются современные диагностические методы. Анализ охватывает современные протоколы иммунологического скрининга и научно обоснованные диагностические алгоритмы, применяемые в репродуктивной медицине. В исследовании обобщены данные из узбекских, российских и международных источников для комплексного понимания иммунологической этиологии и диагностических стратегий лечения привычного невынашивания беременности.
Ключевые слова: иммунологические факторы, антифосфолипидный синдром, аутоиммунные заболевания, репродуктивная иммунология, диагностические подходы, тромбофилия

Annotatsiya: Ushbu maqola homiladorlikning takroriy yo'qolishida immunologik omillarning rolini o'rganadi va zamonaviy diagnostika usullarini tahlil qiladi. Tahlil reproduktiv tibbiyotda joriy qilingan immunologik skrining protokollari va dalillarga asoslangan diagnostika algoritmlarini o'z ichiga oladi. Tadqiqot immunologik etiologiya va takroriy abortni boshqarishning diagnostika strategiyalarini to‘liq tushunish uchun o‘zbek, rus va xalqaro manbalardan olingan ma’lumotlarni sintez qiladi.
Kalit so'zlar: immunologik omillar, antifosfolipid sindrom, otoimmün kasalliklar, reproduktiv immunologiya, diagnostika yondashuvlari, trombofiliya

INTRODUCTION

Recurrent pregnancy loss is defined as two or more consecutive pregnancy losses prior to the 20th week, and it has an occurrence rate of roughly 1-2% in couples trying to conceive, thus making it one of the reproductive medicine's major obstacles [1]. The majority of the sporadic miscarriages are attributed to chromosomal abnormalities, and the immunological factors becoming the leading cause in the recurrent cases, with unexplained pregnancy losses being 20-50% caused by immunological factors [2]. The immunological causes of recurrent pregnancy loss are very complicated and involve a range of mechanisms such as autoimmune disorders, alloimmune incompatibility, and thrombophilia, which all impact maternal-fetal tolerance [3]. Scientific understanding of the immune system's role in pregnancy loss has changed

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tremendously in the last few decades, with considerable progress in reproductive immunology illuminating the intricate relationships between mother's immune system and fetus in development. Today's studies reveal that the successful outcome of pregnancy necessitates a very careful immune balance, the maternal immune system having to accept and tolerate semi-allogeneic fetus while at the same time keeping the protective immunity against the possible pathogens [4]. Any of the above-mentioned immune equilibrium disruptions such as autoantibody production, natural killer cell activations, or cytokine imbalance might lead to the loss of pregnancy.

METHODOLOGY AND LITERATURE ANALYSIS

The present research utilizes systematic literature review method to explore the publications that are related to or discuss the immunological factors of recurrent pregnancy loss and the diagnostic procedures. The study is based on the analysis of articles that appeared in Uzbek medical journals, literature of Russian reproductive medicine and international peer-reviewed journals thus leading to offering a wider perspective on what is known and what is done in the clinics [5]. The analytical framework divides the immunological factors into three major areas: autoimmune diseases and the production of antibodies against the patient’s own antigens, alloimmune disorders with the abnormal maternal immune response to the paternal antigens being the major case, and thrombophilic disorders that impair placental perfusion by causing thrombus formation through the release of prothrombotic agents [6]. Autoimmune factors are mainly represented by antiphospholipid syndrome, which is regarded as the most established immunological reason behind recurrent pregnancy loss; besides, the presence of antiphospholipid antibodies has been detected in 15-20% of women suffering from recurrent miscarriage [7].

Lupus anticoagulant, anticardiolipin antibodies, and anti-beta-2-glycoprotein-I antibodies, among others, are types of antibodies that interfere with placental blood supply and inhibit trophoblasts hence causing abortion. Systemic lupus erythematosus and other autoimmune diseases also lead to pregnancy loss through a variety of mechanisms such as inflammation, complement activation, and blood vessel dysfunction. Alloimmune theories, though contentious, propose that the mother's immunological response to paternal antigens being inadequate may not activate the protective mechanisms required for the pregnancy to continue. Increased peripheral natural killer cells plus altered cytokine profiles have been noticed in some women with recurrent miscarriages, but the clinical relevance is still under discussion [8]. The latest diagnostic methods give priority to the systematic assessment that includes comprehensive medical history, physical examination, and specific laboratory tests [9]. The advanced diagnostic protocols may include tests for natural killer cells, cytokine profiling, and HLA typing; however, the clinical importance of these investigations is still a matter of active research and discussion in the reproductive medicine community [10].

RESULTS AND DISCUSSION

The antiphospholipid syndrome is pointed out to be the most important clinical immunological fa ctor in the recurrent pregnancy losses through the analysis of the presentday literature, also, the r obust evidence supporting the diagnostic testing and treatment efficacy is given as the reason. Th e international consensus guidelines advise that all women with recurrent pregnancy loss should be systematically screened for antiphospholipid antibodies, and if positive, the women are to be given anticoagulant therapy in the next pregnancy which has been shown to increase the live birt h rate substantially. The diagnostic criterion consists of the coexistence of lupus anticoagulant or anticardiolipin antibodies or anti-beta-2-glycoprotein-I antibodies on two occasions at least 12 weeks apart, together with clinical signs of early pregna

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ncy loss or thrombosis. Treatment protocols that pair low-dose aspirin with prophylactic heparin have also led to improved pregnancy outcomes in antipho spholipid syndrome women, thus making evidence-based intervention backed by numerous randomized controlled trials.

Thyroid autoimmunity is a condition that affects the immune system and it is claimed to be the cause of recurrent pregnancy loss in women at least partially. Detection of thyroid peroxidase and thyroglobulin antibodies in higher amounts among women with recurrent pregnancy loss compared to the general population has sparked discussions around the causal relationship and treatment of the condition which are still under examination. The significance of natural killer cells in the development of recurrent pregnancy loss has not yet been properly established; the clinical proof is not strong enough to accept the therapeutic interventions based on the activity of natural killer cells or to reject them based on the inconsistent evidence regarding their predictive value. While some studies have reported higher numbers of natural killer cells in women suffering from recurrent healing, the dependence between the natural killer cells found in blood and those in the uterus is still not clarified, and there are no common reference ranges across laboratories. Theories regarding the balance of cytokines suggest that the change from a Th2-dominant to a Th1-dominant immune response may lead to the loss of pregnancy, however, the clinical use of cytokine profiling remains at the stage of research with no approved treatment interventions.

The Thrombophilia screening is not an easy decision for doctors as it consists of a lot of things to be considered, since the inherited thrombophilias have different associations with the case of pregnancy loss and still the routine screening is being debated with the selective testing being recommended based on personal or family history of thromboembolism. Current Evidence suggests that the mutation of factor V Leiden and the mutation of prothrombin gene show little association with pregnancy loss and that the deficiency of protein C, protein S, and antithrombin show stronger associations but are less common in the population. The combination of immunological diagnostics with clinical practice is going to require the careful application of evidence-based testing protocols in which excessive investigation that might lead to overdiagnosis and inappropriate treatment is going to be avoided. The state-of-the-art diagnostic algorithms give priority to the systematic evaluation of the established immunological factors whose therapeutic implications have been very clearly proven, particularly the antiphospholipid syndrome, while at the same time being critically appraised and even distanced from the investigational markers which are not backed up with clinical validation.

CONCLUSION

Immunological factors account for a great part of the etiology of recurrent pregnancy loss, with the antiphospholipid syndrome being the most established and therapeutically addressable condition that necessitates systematic diagnostic evaluation. Present-day diagnostic methods should concentrate on the evidence-based testing of antiphospholipid antibodies, thyroid autoimmunity, and selective thrombophilia based on clinical indications, while keeping a watchful eye on investigational markers such as natural killer cell assays and cytokine profiling that have no standardized protocols and no proven therapeutic interventions. The difficulty of maternal-fetal immunological relations asks for constant scientific inquiry to clarify the factors that take place during pregnancy loss and to invent diagnostic and therapeutic methods that are targeted. The clinical practice should mix a thorough evaluation of immunological factors with an evidence-based approach that does not include extensive testing and unproven interventions, thus utilizing the resources on those diagnostic modalities that have already shown clinical utility

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and treatment implications and may thus contribute to improving the pregnancy outcomes for couples suffering from recurrent pregnancy loss.

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