

## OBSTETRICS AND GINECOLOGY

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**Titer of antiphospholipid autoantibodies.  
Is it connected with clinical manifestation?***K. N. Chudotvorov<sup>1</sup>, S. V. Chepanov<sup>2</sup>,  
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Antiphospholipid syndrome is a systemic autoimmune disease characterized by persistent antiphospholipid autoantibodies, the development of thrombophilic conditions and recurrent pregnancy loss. In this study the incidence of antiphospholipid antibodies of different titers among the women with one or more episodes of fetal loss in the anamnesis was determined. According the data obtained, autoantibodies in medium and high titers for cardiolipin and beta-2-glycoprotein-1 were more common among the women with two or more episodes of recurrent pregnancy loss compared with the women who have only one episode of pregnancy loss. In a group of women with one episode of pregnancy loss, antibodies in high titers were not detected. Based on this, it can be assumed that autoantibodies in medium and high titers have the most significant pathogenetic effect on the outcome of pregnancy. In contrast, autoantibodies in low titers are considered to be dubious and clinically insignificant.

*Keywords:* antiphospholipid syndrome, antiphospholipid autoantibodies, recurrent pregnancy loss, miscarriage.

**Introduction**

Recurrent pregnancy loss, along with a wide range of vascular manifestations (venous and/or arterial thrombosis), is a manifestation of antiphospholipid syndrome (APS) [1]. Antiphospholipid syndrome is a systemic autoimmune disease characterized by persis-

tent autoantibodies of several typical specificities and the development of thrombophilic conditions [2]. Persistent antiphospholipid antibodies have a multifaceted effect on the hemostatic system and damage its protective units: the endothelial barrier, the function of natural anticoagulants, endogenous fibrinolysis; they activate the platelet link of hemostasis and they are associated with many obstetric complications and infertility. Antiphospholipid antibodies are a heterogeneous group of autoantibodies that interact with phospholipids, phospholipid protein complexes and phospholipid binding proteins [3]. The independent randomized studies showed that the prevalence of antiphospholipid antibodies in the general population ranged from 1 % to 5 %, but the antibody titers in most of these studies were low [4]. Nowadays, the question of the significance of a high or low titer of antiphospholipid autoantibodies on the outcome of pregnancy is quite controversial.

## Research objective

We studied the incidence of antiphospholipid antibodies of different titers among the women with one or more episodes of fetal loss in the anamnesis.

## Materials and methods

The retrospective study of 37 women with recurrent pregnancy loss and identified autoantibodies to cardiolipin and beta-2-glycoprotein-1 was conducted. Two groups of women were formed: the first group (19 people) had one episode of recurrent pregnancy loss, the second group (18 people) had two or more episodes. The levels of autoantibodies to beta-2-glycoprotein-1 and cardiolipin were determined in the serum of women's peripheral blood by enzyme-linked immunosorbent assay using commercial test systems [Orgentec Diagnostika GmbH (Germany)].

## Results

The analysis revealed that among the women with a recurrent pregnancy loss, antibodies to cardiolipin were detected in 40.5 % (n=15) of cases, antibodies to beta-2-glycoprotein-1 in 86.5 % (n = 32) of cases. The combined detection of antibodies to cardiolipin and beta-2-glycoprotein-1 was detected in 27 % (n = 10) of cases. According to the range of antibody levels, the women were divided into groups with a low (10–20 IU/ml), medium (20–40 IU/ml) and high (more than 40 IU/ml) antibody levels. The percentage of patients was as follows: a low level of antibodies was noted in 51.4 % (n = 19) of cases, average in 37.8 % (n = 14) of cases, high in 10.8 % (n = 4) of cases. We also analyzed the correlative dependence of antibody titer and the number of recurrent pregnancy loss. It was found that the women with only one episode of pregnancy loss have autoantibodies to cardiolipin and beta-2-glycoprotein-1. In this subgroup low titers of anti-cardiolipin autoantibodies were detected in 63.2 % (n = 12) cases; but medium titers of these autoantibodies were detected in 36.8 % (n = 7) cases. High titers of anti-cardiolipin autoantibodies in this subgroup of women did not occur. In women with two or more episodes of recurrent pregnancy loss, autoantibodies against cardiolipin in low titers were detected in 38.9 % (n = 7) of cases, in medium titers they were detected also in 38.9 % of cases (n = 7). This subgroup of women was distinct for having cases of high titer seropositivity for autoantibodies towards cardiolipin, which were found in 22.2 % (n = 4) of cases.

## Conclusion

According to the data of this research, the identification of autoantibodies in low titers is considered to be dubious and clinically insignificant. It is considered only as a risk factor for the development of thrombophilic conditions. Women who have identified autoantibodies in the medium titers need the antithrombotic preventive therapy during pregnancy. Women with recurrent pregnancy loss and high titers of autoantibodies are under high risk of pregnancy loss. The next pregnancy in them ended with fetal death in 80 % of cases.

According to the data obtained, autoantibodies against cardiolipin and beta-2-glycoprotein-1 in medium and high titers were more common among the women with two or more episodes of recurrent pregnancy loss compared to the women who have had only one episode of pregnancy loss. In a group of women with one episode of pregnancy loss, high titers of autoantibodies were not detected. Based on this, it can be assumed that autoantibodies in medium and high titers have the most significant pathogenetic effect on the outcome of pregnancy. Also, it has been described in literature that because of the involvement of immune mechanisms in the pathogenesis of pregnancy loss, the chances for a successful outcome of a pregnancy without treatment are constantly reduced with every next failure: thus, after 3 failures, the chance to bear a child is 30 %, and after 5 failures — only 5 %. The more the number of pregnancy losses, the less they likely to be successful [5].

Hence, it is necessary to identify autoantibodies to cardiolipin and beta-2-glycoprotein-1 in women with recurrent pregnancy loss in order to prevent new episodes of miscarriage.

## References

1. Chepanov S.V., Krivonos M.I., Arzhanova O.N., Shlyakhtenko T.N., Saidov N.Kh., Korniyushina E.A., Chudotvorov K.N., Sedikhin V.Yu., Selkov S.A. Characteristics of autoantibodies associated with recurrent Pregnancy loss. *Akusherstvo i ginekologiya*, 2019, no. 3, pp. 72–77. (In Russian)
2. Meroni P.L., Borghi M.O., Grossi C., Chighizola C.B., Durigutto P., Tedesco F. Obstetric and Vascular Antiphospholipid Syndrome: Same Antibodies but Different Diseases? *Nat. Rev. Rheumatol.*, 2018, vol. 14, no. 7, pp. 433–440.
3. Tkachenko O.Yu., Lapin S.V., Shmonin A.A., Solovyova L.N., Bondareva E.A., Sel'kov S.A., Chepanov S.V., Totolian A.A., Roggenbuck D. Ranging of antiphospholipid antibodies in the patients with thrombophilia and recurrent miscarriage. *Meditainskaia immunologiya*, 2018, vol. 20, no. 5, pp. 753–762. (In Russian)
4. Yu Song, Hai-Yan Wang, Jie Qiao, Ping Liux, Hong-Bin Chi. Antiphospholipid Antibody Titers and Clinical Outcomes in Patients With Recurrent Miscarriage and Antiphospholipid Antibody Syndrome: A Prospective Study. *Chin. Med. J.*, 2017, vol. 5, no. 130 (3), pp. 267–272.
5. Howard J.A. *Recurrent Pregnancy Loss: Causes, Controversies, and Treatment*. New York, CRC Press Publishers, 2015.

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