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ANTIPHOSPHOLIPID SYNDROME IN OBSTETRICS

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Abstract. This article aims to provide an in-depth overview of APS in obstetrics, including its pathogenesis, clinical manifestations, diagnosis, and management strategies. Antiphospholipid syndrome (APS) is an acquired autoimmune disorder characterized by the presence of antiphospholipid antibodies (aPL) and a predisposition to both arterial and venous thrombosis. While APS affects various organ systems, its impact on obstetrics is particularly significant. This article aims to provide a comprehensive review of APS in obstetrics, focusing on its pathogenesis, clinical manifestations, diagnosis, management, and the implications for both the mother and the fetus. Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by the presence of antiphospholipid antibodies (aPL) that can lead to an increased risk of recurrent thrombosis and adverse pregnancy outcomes.

Key words: antiphospholipid syndrome (APS), accurate diagnosis, cerebrovascular diseases, clinical criteria.

Introduction. APS has significant implications for obstetric care and requires comprehensive management to optimize outcomes for both the mother and the fetus. Antiphospholipid syndrome in obstetrics is a complex condition that requires a comprehensive understanding for successful management. Early recognition, accurate diagnosis, and effective management strategies are crucial to improve outcomes for both the mother and the fetus [1]. A multidisciplinary approach involving obstetricians, hematologists, and other specialists is necessary for optimal care. Continued research into APS and advancements in its management will further enhance our ability to provide quality care to pregnant individuals affected by this syndrome. Recurrent miscarriage, early delivery, oligohydramnios, prematurity, intrauterine growth restriction, fetal distress, fetal or neonatal thrombosis, pre-eclampsia/eclampsia, HELLP syndrome, arterial or venous thrombosis and placental insufficiency are the most severe APS-related complication for pregnant women.

Materials and methods. The aim of the present literature review was to discuss available literature data concerning antiphospholipid syndrome in children and its role in cerebrovascular diseases, including pediatric arterial ischemic stroke (AIS), migraine and cerebral venous thrombosis. Additionally, we analyzed the possible role of polymorphisms of genes encoding proteins involved in the prothrombotic state in the occurrence of cerebrovascular diseases in children.

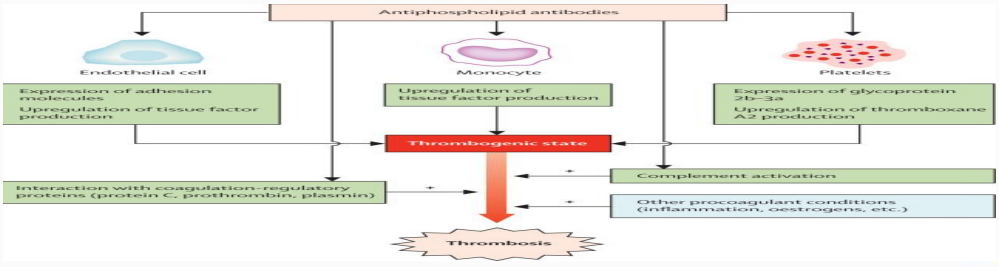


Figure 1. Antiphospholipid syndrome

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Antiphospholipid syndrome remains a significant concern in obstetrics due to its association with adverse maternal and fetal outcomes. Early recognition, accurate diagnosis, and effective management are crucial in improving pregnancy outcomes for APS patients [2, 3]. Through a multidisciplinary approach involving obstetricians, hematologists, and other specialists, a comprehensive care plan can be developed to reduce the risks and provide optimal care for women with APS during pregnancy. Further research and advancements in APS management are needed to enhance our understanding and develop better therapeutic strategies for these high-risk pregnancies.

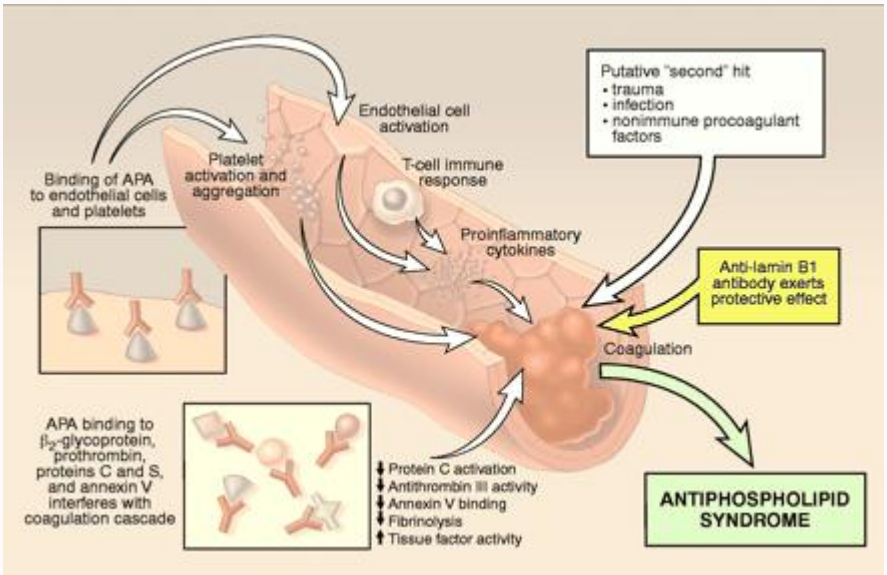


Figure 2. Pathogenic mechanisms in antiphospholipid syndrome.

Clinical criteria of APS diagnosis are large- and small-vessel thrombosis as well as obstetric problems; laboratory criteria are the presence of antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies and anti-β2-glycoprotein-1). The presence of at least 1 clinical and 1 laboratory criterion allows definitive diagnosis of APS. Primary APS is diagnosed in patients without features of connective tissue disease; secondary APS is diagnosed in patients with clinical signs of autoimmune disease [4]. A high frequency of catastrophic APS as well as a high tendency to evolve from primary APS to secondary syndrome during the course of lupus and lupus-like disease is a feature of pediatric APS. The most characteristic clinical presentation of APS in the pediatric population is venous thrombosis, mainly in the lower limbs, and arterial thrombosis causing ischemic brain stroke. Currently, no diagnostic criteria for pediatric APS exist, which probably results in an underestimation of the problem. Antiphospholipid syndrome in children is a rare disorder. The most characteristic clinical presentation of antiphospholipid syndrome (APS) in the pediatric population is venous thrombosis and arterial thrombosis causing ischemic stroke. However, no diagnostic criteria for pediatric APS exist at present, which probably results in an underestimation of the problem. We discussed data concerning APS in children and its role in cerebrovascular diseases, including pediatric arterial ischemic stroke, migraine and cerebral venous thrombosis. Standard treatment for obstetrics APS includes preconception low dose aspirin (LDA, 100 mg/day, orally) combined with low molecular weight heparin (LMWH) at prophylactic doses (0.4–0.6 mg/kg/day; 4000–6000 IU/day, subcutaneously) from the moment of the positive pregnancy test.

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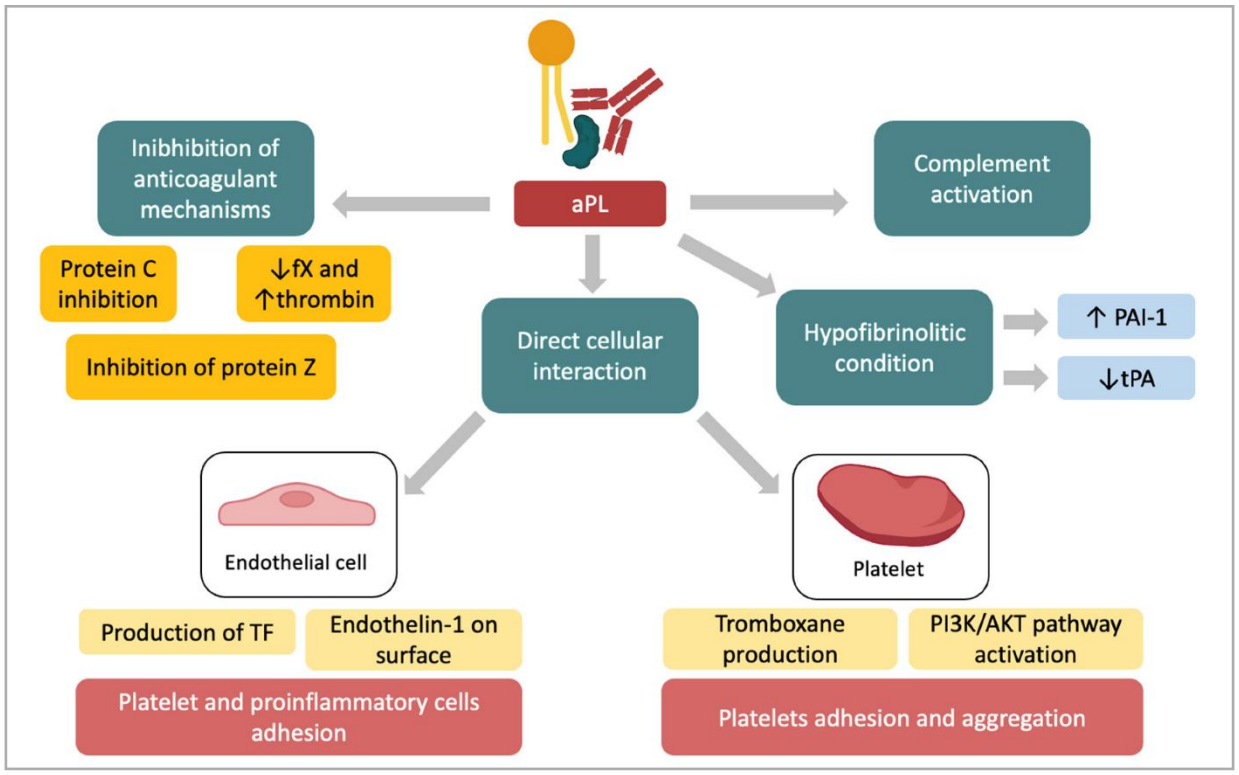


Figure 3. Antiphospholipid antibodies (aPL) prothrombotic activity.

Usually, LDA combined with LMWH treatment is continued throughout pregnancy and 6 weeks postpartum. In patients with previous thrombotic events, secondary thromboprophylaxis with full unfractionated or LMWH doses or anti-vitamin K therapy should be administered [5]. The latter must be avoided between weeks 5 and 12 of gestation. A recent metanalysis evaluated the efficacy of heparin alone or in combination with LDA for the treatment of women with RPL and aPL positivity. It was found that heparin (alone or in association with LDA) improves the live birth rate, as compared to LDA or a placebo. Such an observation was not found for LDA alone. A likelihood of a good pregnancy outcome in women with APS of around 75–80% under correct management has been estimated. The initial assumption of extraplacental thrombotic phenomena leading to pregnancy morbidity led to consider heparin as a useful treatment for OAPS. On the other hand, the demonstration of additional pathogenic mechanisms of aPL-mediated placental damage and the efficacy of the drug in OAPS has now suggested additional mechanisms of action. Actually, LMWH is able to block the binding of aPL to trophoblast cells and to endometrial EC. As a consequence, the LMWH is able to prevent the negative activity of aPL on trophoblast invasiveness, proliferation and differentiation, as well as on EC angiogenic processes at the endometrial level. Pregnant women with antiphospholipid syndrome present a greater risk of miscarriage and intrauterine growth restriction, since clots may form in the placenta and as a consequence of this the foetus may not receive the necessary blood supply for its development [6]. It is estimated that positive antiphospholipid antibodies may be detected in approximately 15 % of women who have had three or more miscarriages.

Conclusion. An important difference between the two conditions is that a thrombophilia state is a common feature in vascular APS, whereas clot occlusions of the decidual spiral arteries are seldom observed in obstetric APS, and infarctions are found in only one-third of APS placentae. Conversely, inflammation, which is undetectable in vascular APS, is frequently observed in the placentae of patients with obstetric APS and has been documented in the

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placentae of pregnant mice with fetal loss mediated by antiphospholipid antibodies. Attempts to identify different antibodies or epitopes responsible for the two clinical manifestations of APS have so far been unsuccessful. Possible mechanisms exist that might explain the development of the two clinical presentations, including the tissue distribution and expression level of the main target antigen of antiphospholipid antibodies

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