

## Research Article

# Antiphospholipid Syndrome – A silent killer

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### Abstract

Antiphospholipid Syndrome (APS) is a multisystem autoimmune disorder characterized by venous thrombosis, recurrent pregnancy loss, fetal death and presence of antiphospholipid antibodies (aPL). The entity remains hidden unless suspected and investigated by the clinician. The target antigens of the antibodies are phospholipid binding proteins. By binding the phospholipids expressed by the trophoblasts, aPLA inhibit successful embryonic implantation into the endometrium. APS can be treated by combination of aspirin and heparin. The combination promotes successful embryonic implantation in the early stages of pregnancy and prevents thrombosis of the uteroplacental vasculature after placentation. Low molecular weight heparin has found to be more convenient, safe and effective in treatment of antiphospholipid antibody syndrome and inherited and acquired thrombophilias.

**Keywords:** Antiphospholipid Syndrome, Recurrent pregnancy loss, Low molecular weight heparin, Low dose aspirin

## 1. Introduction

Antiphospholipid Syndrome (APS) is an autoimmune disorder characterized by recurrent venous or arterial thrombosis of the placental blood vessels leading to recurrent fetal loss. The condition is associated with persistently high levels of antibodies against the membrane anionic phospholipids (Anti cardiolipin antibody, antiphosphatidylserine) or their associated plasma proteins (apo-lipoprotein H) or there is evidence of circulating anticoagulant. Antiphospholipid Syndrome is accompanied by systemic lupus erythematosus (SLE) or other rheumatic or autoimmune disorder, in which case it is referred as secondary APS. In the absence of this, it is referred as primary APS. The condition is more common in women than men. It is most frequently seen in obstetric patients suffering from spontaneous abortions, pre eclampsia and intra uterine growth restriction. Research has proved that the antibodies are not only the markers of the entity, but are directly responsible for the clinical picture.<sup>2</sup>

## 2. Pathophysiology

The antiphospholipid antibodies, namely, anticardiolipin antibodies and lupus anticoagulant react against proteins that bind to anionic phospholipids on plasma membranes. The exact cause is unknown but there is evidence of alteration of the homeostatic regulation of blood coagulation. The antibodies that arise out of autoimmune reaction are responsible for thrombosis and vasculopathy seen in this syndrome.<sup>3</sup> Following are some of the hypotheses which explain the pathophysiology of APS.

- A defect in the cellular apoptosis which exposes membrane phospholipids to the binding of various plasma proteins such as beta -2 glycoprotein I. The resultant phospholipid-protein complex becomes the target of autoantibodies.
- Oxidized beta -2 glycoprotein I bind to and activate dendritic cells in a manner similar to activation triggered by Toll like receptor 4 (TLR 4) which increase the production of antibodies.<sup>4</sup>

Other possible mechanisms of aPL antibodies causing increased coagulability are as follows.

- Production of antibodies against coagulation factors including prothrombin, protein C, protein S and annexins.
- Activation of platelets to enhance endothelial adherence.
- Activation of vascular endothelium which in turn facilitates the binding of platelets and monocytes.

Complement activation may play an important role in the pathogenesis of APS leading to pregnancy loss.<sup>5</sup>

## 3. Diagnosis

According to the revised criteria developed following consensus statement, at least one clinical and one laboratory criterion as mentioned below must be present to classify the condition as APS.<sup>6</sup>

### 3.1 Clinical criteria

- One or more episodes of arterial, venous or small vessel thrombosis in any tissue or organ (cerebral, coronary, renal, hepatic, pulmonary, ocular, extremities, adrenal) confirmed by findings of imaging studies, Doppler studies or histopathology.
- History of repeated DVT, CVA, pulmonary embolism, myocardial infarction in a young individual in the absence of other risk factors.
- One or more spontaneous abortions after ten weeks of gestation.
- One or more preterm births due to placental insufficiency resulting from pre eclampsia or eclampsia.
- Three or more unexplained consecutive unexplained spontaneous abortions before ten weeks of gestation.

### 3.2 Laboratory Criteria

- Presence of medium to high levels of IgG or IgM anticardiolipin antibodies.
- Presence of anti beta 2 glycoprotein I.

- iii. Presence of lupus anticoagulant on two occasions at least two weeks apart.

### 3.3 Clinical markers of APS

- i. History of thrombo-embolic episodes at an early age without evidence of any other aetiology.
- ii. History of late first trimester abortions, recurrent abortions or premature births.
- iii. History of cardiac murmur or cardiac valvular vegetations.
- iv. Evidence of haematological abnormalities like thrombocytopenia or haemolytic anemia.
- v. History of nephropathy.
- vi. Unexplained adrenal insufficiency.
- vii. Avascular necrosis of bones in the absence of other risk factors.
- viii. Pulmonary hypertension.

## 4. Treatment

Heparin (unfractionated or Low molecular weight) and low dose aspirin are the mainstay of treatment for prevention of pregnancy loss due to APS. The use of these two drugs for the treatment has been approved by the advisory board members of the 12<sup>th</sup> Congress of aPL and the fifth conference of sex hormones ,pregnancy and Rheumatic diseases(Florence ,Italy 2007).<sup>7</sup>

Following dose schedule is suggested by the experts.<sup>8</sup>

- Unfractionated heparin (UF)-15,000-20,000 units/day subcutaneously in two divided doses along with low dose aspirin. Or
  - Low molecular weight heparin (LMWH)-40mgs /day subcutaneously along with low dose aspirin. (1-2mgper kg body weight/day)
- The effectiveness of low molecular weight heparin over unfractionated heparin has been demonstrated by various studies.<sup>9</sup>

LMWH has following advantages over UF heparin.

- 1- Less risk o bleeding
- 2- less platelet activation
- 3- No progression or regression of thrombus size.
- 4- Convenient dose schedule. Less follow up laboratory tests.

## 5. Conclusion

Antiphospholipid Syndrome (APS )is an autoimmune condition that may manifest with fetal loss, thrombosis or autoimmune thrombocytopenia. It is characterized by the presence of anti phospholipid antibodies, which react against proteins that bind to anionic phospholipids on plasma membranes, disturbing the homeostatic regulation of blood coagulation, resulting in venous thrombosis and vasculopathy. The syndrome is best treated by combination of low molecular heparin and low dose aspirin.

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