Antiphospholipid syndrome and pregnancy

Professor Anisur Rahman explains why it is important for patients with antiphospholipid syndrome to be managed during pregnancy by multi-disciplinary teams, including obstetricians and midwives

Antiphospholipid syndrome (APS) is an autoimmune disease which means that the immune system creates abnormal antibodies that attack components of the body itself thus causing the disease. In APS, these antibodies target proteins that are linked to phospholipids in cell membranes. The most important of these proteins is called beta-2-glycoprotein I.

Although patients with APS may experience a range of different symptoms, the most characteristic features that are used to define the disease are vascular thrombosis and pregnancy morbidity. Therefore, midwives may encounter patients with APS in their everyday practice.

By definition, APS is diagnosed in patients who test positive for antiphospholipid antibodies and who have suffered either vascular thrombosis or pregnancy morbidity, or both. The definition of pregnancy problems that qualify for diagnosis of APS is complex but can be summarised as either one late fetal loss (after 10th week of gestation) or three early fetal losses (before week 10), or one or more premature births before week 34 due to eclampsia, severe pre-eclampsia or placental insufficiency.

There are four major scenarios relating to APS and pregnancy, namely:

1. Patients who are known to have APS due to having had thrombosis but with no history of pregnancy problems (first pregnancy or previous uncomplicated pregnancy). These patients will probably be taking an anti-coagulant, such as warfarin. Since warfarin is contra-indicated in pregnancy, this should have been changed to subcutaneous heparin, which will be continued throughout pregnancy
2. Patients with APS who have had APS-related pregnancy problems (with or without a history of thrombosis). Currently, the standard management of these cases is with subcutaneous heparin plus oral low-dose aspirin throughout pregnancy. If the patient has had no previous history of thrombosis and does not normally take anticoagulants outside pregnancy, it is still common practice to continue heparin for six weeks postpartum because this is a high-risk period for thrombosis
3. Patients who have incidentally tested positive for antiphospholipid antibodies but have never had either thrombosis or pregnancy problems. For example, many people with other autoimmune diseases, such as lupus, may have had antiphospholipid tests as part of their routine screening. There is no evidence supporting use of heparin in these patients but they are often given low-dose aspirin throughout pregnancy
4. Patients who are concerned about having APS but who have never been tested. Patients may be concerned, for example, because of a history of previous miscarriage and symptoms such as migraine, which can occur in APS but which are also common in the general population. The tests for APS are simple to carry out but complex to interpret. There are three blood tests: the anti-cardiolipin test, the lupus anticoagulant test and the anti-beta-2-glycoprotein I test. An individual patient can be positive in one, two or all three tests. Those who are triple positive are at the highest risk of developing APS. Ideally, these tests should be repeated at least 12 weeks later to make sure that they remain positive—though this would not necessarily be feasible in the scenario of a pregnant woman where a decision about treatment needs to be made.

It is important to remember that about 5% of the healthy population test positive for antiphospholipid antibodies in at least one of these tests even though they do not have APS (false-positive tests). This means that it would not be helpful to test every pregnant woman for these antibodies because it would create a large number of worried well people.

So who should be tested? Any woman with an unexplained late pregnancy loss should be tested for APS. The issue of early miscarriages is more difficult because the majority of women with a single early miscarriage do not have APS. On the other hand, a patient who is only tested and found to be positive after suffering a third miscarriage may understandably feel that they should have been diagnosed earlier. It is important to discuss with a patient who wants to be tested the pros and cons of having the test, and whether a positive test would lead to treatment with aspirin or aspirin plus heparin. These

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treatments, particularly heparin, can themselves have adverse effects such as an increased risk of bleeding. It is very important that pregnant women with APS should be managed by a multi-disciplinary team including obstetricians, haematologists and sometimes rheumatologists. Monitoring of these pregnancies is important as there is an increased risk of intra-uterine growth retardation and pre-eclampsia.

APS Support UK

APS is a life-threatening autoimmune disease that causes the blood to clot too quickly. The condition can cause potentially fatal events such as strokes, heart attacks, blood clots in the lung and DVTs. In pregnancy, APS is the most significant treatable cause of recurrent miscarriage and can increase the chance of stillbirth up to five times; it is also associated with other complications such as pre-eclampsia and premature births.

APS Support UK is an organisation that aims to save and improve the lives of patients with APS by achieving earlier diagnosis and the best possible treatment through awareness, education and research.

We may be a small charity but punch well above our weight. Our activities include:

- Offering information and understanding to anyone affected by APS through our website: aps-support.org.uk; our telephone and email enquiry services; charity newsletters, updates and e-shots; plus social media channels
- Raising awareness of APS in the medical community: we work with NHS Choices and Patient UK to provide current information for healthcare professionals. We have produced an online GP training course in partnership with the Royal College of GPs, and have a similar course planned that may be hosted on the i-learn platform of the Royal College of Midwives
- Supporting research: one of our key aims is to support research into APS and we have committed over £540 000 to-date into research that we believe will have a real impact on the APS community. We are also a non-commercial partner of the National Institute of Health Research and collaborate with, and support, APS researchers in the UK wherever possible.

Lucy Thomas: APS patient story

I'd always been led to believe that I wouldn't be able to conceive as I have Polycystic Ovary Syndrome. My husband and I had been together 10 years, and we'd always assumed we wouldn't be able to start a family of our own. However, after returning from Australia to visit our newborn nephew, we decided we'd like to try for a family, and planned to see a fertility specialist; so, it came as a great and welcome surprise that I suddenly fell pregnant in January 2014 without any intervention.

I had a bleed at about eight weeks but, otherwise, the pregnancy was going according to plan. Then, in July 2014, at 29 weeks pregnant, everything changed. During a routine midwife appointment, she was concerned about the size of our baby. I was sent to the hospital for a Doppler scan—and we weren't prepared for everything that was about to unfold.

A few days later, I suffered a placental abruption and it was decided that I needed an emergency caesarean. My husband was called and rushed to be by my side for the birth of our daughter but, after further complications, was told he couldn't stay in the room.

I was put under a general anaesthetic, my husband kissed my forehead, and the next thing I remember is waking up with my sister and husband looking over me. I asked where Isabelle was. My husband broke it to me that Isabelle had died during delivery. She was born weighing 880 g—which we later learnt was classified as a low birth weight baby or the technical term: intra-uterine growth restriction.

The recovery from the surgery was slow. My legs and abdomen had swollen and I couldn't walk for five days. I stayed in hospital during this time and over the coming days and weeks, I found it increasingly difficult to breathe and stand up straight. I had chest pains that were quickly attributed to referred pain from the operation. As I had never had surgery before, I didn't know what to expect. I trusted that the medics knew what they were talking about and that I would be okay in a few days. Gradually, my condition deteriorated. I felt faint and anxious, I had sharp chest pains, and I couldn't walk at more than a snail's pace, nor straighten my back from a hunched over position.

One morning, three weeks after the surgery, I woke up with a swelling feeling at the back of my right leg. There was no visible swelling but something was not right. I went to my GP who sent me to hospital as a precaution but the hospital consultant was keen to send me home; there was nothing visibly wrong with me. I persisted, however. I knew they'd missed something. In the end, he humoured me and said he'd get me a lung scan. I waited in hospital for a further three days for that scan. When it eventually came, it confirmed multiple bilateral pulmonary embolism—blood clots in both lungs.

Fast forward seven months, I have now been diagnosed with APS and am on lifelong anticoagulation, which is not without its risks but it outweighs the risks of the alternative. The sad thing is that under current guidelines, so many people have to endure the pain of losing three babies before they will even be considered for testing, despite a simple blood test being all that's needed to confirm diagnosis in the majority of cases.

With increased awareness of APS amongst the medical profession and the wider community, I hope that people can recognise the signs and symptoms, and end the needless suffering that so many families have to endure. A woman with APS has an 80% chance of a successful pregnancy if it is correctly diagnosed and treated.

We are lucky to have the support of wonderful family and friends – on Isabelle's first birthday, we were surprised with a wonderful video; they'd all come together and made birthday cakes – with friends and family from Australia, New York, Madrid, France and the UK all involved. **BJM**