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EDITORIAL

Cholestasis of pregnancy: in need of a more rapid diagnosis

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Cholestasis of pregnancy is a disease that remains a bit of a conundrum. The syndrome, commonly known as intrahepatic cholestasis of pregnancy (ICP), is comprised of pruritis and elevated bile acids. ICP has been associated with poor perinatal outcomes including higher rates of meconium-stained amniotic fluid,[1] preterm birth,[2] respiratory distress syndrome[3] and intrauterine fetal demise.[4] Additionally, although mothers do not experience any particular perinatal morbidity, they do have an increased future risk of cholelithiasis and other biliary and hepatic disease.[5,6] Despite the neonatal complications associated with ICP, there are no clear management recommendations regarding pregnant women with this complication from the American College of Obstetricians and Gynecologists.

Because of the neonatal concerns, management of ICP often includes antenatal testing to ensure fetal well-being and early delivery with confirmation of fetal lung maturity. However, even with reassuring antenatal testing, fetal death has been described.[7] More recently, the use of agents both to reduce the pruritis as well as reduce the bile acids themselves has been studied. It appears that among various agents utilized, ursodeoxycholic acid (UDCA) has the best efficacy to reduce both symptoms and bile acids.[8] Further, while bile acids appear to induce oxidative stress in the placenta, UDCA may reduce both oxidative stress and apoptosis.[9]

Despite these recent advancements in medical management, there are still some important clinical issues to refine. The first is the diagnosis of ICP. Women with cholestasis present with pruritis, particularly of the palms of the hands and soles of the feet. Unfortunately, pruritis in pregnancy is not particularly uncommon, reported in as many as 13% of women.[10] Thus, we might consider pruritis as a screening test for ICP with the diagnosis being made by confirmation of elevated bile acid levels. With regard to the confirmatory diagnosis of ICP, however, most hospital laboratories either send the test out or only run it occasionally. Thus, when faced with a woman with symptoms of cholestasis, but with laboratory confirmation and a formal diagnosis several days away, the management is unclear. To avoid the increased risk of fetal death, all women at 36 weeks or beyond could undergo amniocentesis for fetal lung maturity and be delivered.[11] However, such a management is likely to lead to more interventions and iatrogenic prematurity. Alternatively, expectant management or medical management can be employed along with antenatal testing until the diagnosis is made. Again, however, it appears that such management may not reduce the risk of fetal death.

In the current issue of the *Journal of Perinatology*, Lee *et al.*[12] report two interesting findings regarding ICP. First, they report a prevalence of 5.6% in a predominantly Latina population, in the setting of a prevalence of pruritis of 19.7%. Higher rates of ICP have been described previously among women from South America, particularly Chile,[10] as well as women from Sweden,[4] whereas the rates among non-Hispanic Caucasians in Australia and the Unites States have been reported at 1 to 3 per 1000.[13,14] However, prospective studies of the prevalence of ICP in Latinas in the United States have not previously been conducted. Thus, among our Latina gravidas, this problem appears to be as common as pre-eclampsia.

Additionally, these authors report the use of a pruritis scale and its screening test characteristics. Interestingly, with patient-reported pruritis scores of 4 on a 1 to 10 scale, the positive predictive value for ICP was 29%. When pruritis scores increased to 8 or more, however, the positive predictive value became 50%. These test characteristics may help to further refine the clinical management of women presenting with pruritis to labor and delivery at term. We might consider the scale in three ranges. For women with a score of 3 or less, it might be reasonable to utilize antepartum testing until a diagnosis is made. For those women with a score of 8 or higher, one-half of which will end up receiving a formal diagnosis of ICP, delivery to prevent the increased risk of fetal death seems reasonable, particularly at term. For women with scores in the intermediate range of 4 to 7, medical management with UDCA and antepartum testing until a diagnosis is confirmed might be a reasonable management scheme.

Although the use of the pruritis scale may help improve our ability to identify women who have cholestasis, more importantly, as clinicians we should insist on the ability to make the formal diagnosis sooner. From a health-care policy perspective, it is interesting that the women who are at the greatest risk of developing cholestasis are those with health care that is generally the most marginalized. In turn, the care for those at risk of developing ICP has lagged behind many other conditions of pregnancy because we are commonly unable to make a rapid diagnosis.

Thus, from a clinical vantage point, we should each encourage our clinical laboratories to facilitate a more rapid determination of

bile acid levels. Placing the medical–legal aspects aside, optimizing patient care for women at risk of cholestasis of pregnancy depends on making a more rapid diagnosis.

AB Caughey
Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, San Francisco, CA, USA
E-mail: abcmd@berkeley.edu

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