Chronic cholestatic liver disease and pregnancy - rare conditions but not to be confused with intrahepatic cholestasis of pregnancy. (Mini-commentary on BJOG-19-1615.R1)

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Mini-commentary on BJOG-19-1615.R1: Pregnancy outcomes in women with primary biliary cholangitis and primary sclerosing cholangitis

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Chronic cholestatic liver disease and pregnancy is rare as time for diagnosis peaks after reproductive years or late reproductive years. As a consequence, studies are few in this topic. M.Cauldwell and colleagues report maternal and fetal outcome in a retrospective case series of 61 pregnant women with primary biliary cholangitis or primary sclerosing cholangitis (BJOG 2020 xxxx). The collected time span is 20 years including ten different centres, reflecting the relatively rare conditions during pregnancy. As a consequence, the built-in variations of monitoring, treatment and care are considerable. So far, there is no published consensus guideline on how to monitor and care for pregnant women with these progressive autoimmune liver disorders, from mild disease or to affected liver function with cirrhosis. The current study concludes continuous use of ursodeoxycholic acid (UDCA) during pregnancy and awareness of the risk for preterm birth, that was associated with peak serum alaninaminotransferase at booking and peak maternal serum bile acid during pregnancy. Pregnancy was well tolerated in this case series of selected population with a probable overweight of mild to moderate cases.

During the last decade, an increasing number of studies have been published regarding intrahepatic cholestasis of pregnancy (ICP), maternal peak bile acid and pregnancy outcome. A recent meta-analysis (Ovadia et al, Lancet 2019;393:899-909)) demonstrates a risk for stillbirth in ICP with maternal peak bile acid concentrations at or above 100 μmol/L and risk for preterm birth at or above 40 μmol/L. With current knowledge, there is no obvious reason to believe that maternal bile acids in pregnant women with PBC or PSC will affect fetal pregnancy outcome differently. The UK PITCHES trial (Chapel et al, Lancet 2019;394:840-860) could not show an amelioration in maternal bile acid levels with UDCA treatment in ICP. A probable explanation may be a total bile acid enrichment with the treatment. If this is true also for patient with chronic cholestatic liver disease with long-term treatment with UDCA and pregnancy has to be explored. Attention is also recommended towards the variations in measurements of bile acid concentration in different studies and comparisons. There is an obvious mixture of fasting and post-prandial samples, with or without treatment with UDCA.

PBC, PSC and associated inflammatory bowel disease may need additional treatment with immunosuppressive drugs, such as azatioprin, with known but less common side effects such as cholestatis. An increased demand on the metabolism of estrogens and progesterone during pregnancy might hypothetically induce such side effects. Additional treatments have to be reported in more detail for future studies. Further, there is an ongoing discussion regarding severe early cases of ICP and benefit of treatment. Criteria for ICP is exclusion of other liver diseases presenting with same symptoms and biomarkers (such as PBC, PSC and chronic hepatitis C) and disappearance of pruritus and elevated liver tests postpartum. One might speculate that early severe ICP may mimic early signs of chronic liver diseases with pregnancy acting as a stress test for the liver. A situation that may be rare, but obstetricians have to pay attention to. Delayed diagnosis and inadequate follow-up or treatment dose not benefit the patient, but increased knowledge does. Finally, only 34 per cent had evidence of preconception counselling in the study by M.Caudwell et al. Let us hope that we with time realise the importance of preconception counselling for all women with a significant chronic disease.

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