The highest risk group is women with total bile acids ≥100 μmol/L.[359,367,375,376] Levels of bile acids in mother and fetus are correlated, supporting a causal relationship between bile acid levels and fetal complications.[359,375,377] IUFD appears to develop suddenly, and this contributes to the lack of specific recommendations on antenatal monitoring.

Pregnancy Management

No method of fetal monitoring has been shown either to predict those at risk of adverse perinatal outcomes or to reduce the risk of IUFD. Thus, monitoring should be guided by best obstetrical practice. The American College of Obstetricians and Gynecologists recommends delivery at 36-37 weeks or at diagnosis if diagnosed after 37 weeks.[378] Concerns regarding preterm deliveries have led some to recommend a more individualized approach, considering the known risks of iatrogenic preterm delivery (e.g., respiratory distress)[359] versus the small but less well-characterized risk of IUFD.[379]

UDCA reduces maternal and fetal bile acid levels.[380] A meta-analysis of nine randomized controlled studies, including 173 women with ICP and 303 non-ICP controls, showed UDCA (doses 450-1,000 mg per day) was associated with improved pruritus, serum ALT levels, and bile acid levels.[381] Although meta-analyses suggest that UDCA may reduce risk of fetal complications, differential use of early delivery based on bile acid levels and maternal symptoms confounds interpretation.[381] In the largest randomized, placebo-controlled study of UDCA in women with ICP (24% with baseline total serum bile acids ≥40 μmol/L) (n = 306 UDCA and 300 placebo), there was no difference between groups in the primary composite outcome of perinatal death, preterm delivery, and neonatal intensive care unit stay for greater than or equal to 4 hours: 23% in the UDCA group versus 27% in the placebo group (adjusted risk ratio, 0.85; P = 0.28).[382] Subgroup analyses limited to women with baseline total bile acids ≥40 showed no difference (18% in both groups),[382] but whether women with bile acids ≥100 μmol/L may benefit remains an open question, even though a *post hoc* analysis of this subgroup also found no difference. Thus, UDCA is regarded as a safe first-line therapy for management of pruritus and liver test abnormalities but has not been shown to reduce fetal complications. For refractory pruritus, rifampicin, cholestyramine, and SAMe have been suggested, but there is no evidence of benefit.[383-385] Cholestyramine, especially at high doses, can exacerbate vitamin K deficiency and the risk of fetal intracranial hemorrhage. Additionally, increased risk of postpartum hemorrhage related to vitamin K deficiency in women with ICP has led to the recommendation to monitor PT and treat mothers with vitamin K if the PT is elevated, although data are limited.[386,387]

GUIDANCE STATEMENTS

- Pruritus presenting in the second or third trimester plus total bile acids >10 μmol/L without other causes of pruritus is diagnostic for ICP. Elevation of AST and ALT are frequent but not required for the diagnosis.
- Women with ICP should be tested for HCV, if not previously performed.
- Pruritus management is multifaceted and includes UDCA (10-15 mg/kg) as first-line therapy. For refractory symptoms, antihistamines, cholestyramine, rifampin, and SAMe may be considered, although the evidence is scant.
- UDCA is safe in pregnancy and reduces serum bile acid levels, although data supporting a benefit in reducing fetal risks, including IUFD, are lacking.
- Vitamin K should be supplemented when PT is prolonged. More frequent monitoring of PT may be considered for women on cholestyramine.
- Women with persistent symptoms or elevated liver tests or total bile acids postpartum should be evaluated for other causes of chronic liver diseases, including genetic variants associated with cholestasis.

HYPERTENSIVE DISEASES OF PREGNANCY

Preeclampsia/Eclampsia

Preeclampsia-related liver disease is unique to pregnancy and is usually seen in the third trimester or immediately postpartum, but may occur earlier. It is a multisystem disorder defined as *de novo* hypertension after the 20th week of gestation with additional maternal organ dysfunction, including renal, hepatic, neurologic, or hematologic complications. Although proteinuria is often present, it is not required for