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Noninvasive Tests for Prognosticating Outcomes in Patients With Chronic Liver Disease in Pregnancy: Ready for Prime Time?

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Abstract

Rates of cirrhosis and pregnancy in women of reproductive age are increasing, making pregnancy-specific prognostic markers of disease severity increasingly important. Gonsalkorala et al. describe albumin-bilirubin score and aspartate aminotransferase-to-platelet ratio index as superior prognostic tools to the Model for End-Stage Liver Disease (MELD) score in predicting live births and gestation beyond 37 weeks in pregnant women with cirrhosis, among 165 pregnancies in women with chronic liver disease. However, further efforts are needed to identify diagnostic and prognostic tools during pregnancy, as well as to refine and implement a multidisciplinary team-centered approach to the care of women with chronic liver disease during pregnancy.

Rates of cirrhosis in reproductive-aged women (1) and pregnancy in women with cirrhosis are on the rise, highlighting the need for prognostic measures of maternal and fetal outcomes in this high-risk population. In the current study, Gonsalkorala et al. (2) performed a retrospective chart review of 165 pregnancies in 100 women with chronic liver disease (CLD) at King's College Hospital from 1983 to 2017. The authors identified lower rates of full-term gestation through similar live birth rates among women with cirrhosis compared with noncirrhotic women (2). Comparing the MELD score with other disease severity scoring systems, they identified the albumin-bilirubin score (ALBI) and the AST-to-platelet ratio index (APRI) as the most accurate tools for predicting live births and pregnancy beyond 37 weeks of gestation. However, the area under the receiver operating characteristic (AUROC) for these 2 measures were 0.74 and 0.70, respectively, consistent with only “fair” discriminatory ability for pregnancy outcomes of interest in women with cirrhosis. Although this relatively low AUROC may partially be related to a low sample size in the cohort, it also calls for the need for improved prognostic models for CLD during pregnancy.

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CONFLICTS OF INTEREST

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Potential barriers to developing prognostic tools in pregnancy include an insufficient sample size of pregnant women with CLD and heterogeneity of study outcomes evaluated (Table 1). Shaheen and Myers (5) used the Nationwide Inpatient Sample to study 339 pregnancies with cirrhosis compared with controls matched on age, hospital, and year and found increased rates of pregnancy complications among patients with cirrhosis, including higher incidence of gestational hypertension, placental abruption, and uterovaginal hemorrhage, as well as higher rates of prematurity and growth restriction. In addition, women with hepatic decompensation during pregnancy had a high fetal mortality of 12%. However, a prognostic score for identifying women at highest risk was not evaluated, as laboratory data were unavailable.

Westbrook et al. (3) evaluated the MELD, MELD sodium, United Kingdom Model for End-Stage Liver Disease and Child-Turcotte-Pugh scores in 62 pregnancies in women with cirrhosis and found that both MELD and United Kingdom Model for End-Stage Liver Disease scores best predicted liver-related complications during pregnancy, with AUROCs of 0.8, although that study did not identify significant predictors of pregnancy-specific complications. A recent large Canadian study of 66,291 women found an increasing prevalence of cirrhosis among young women, again highlighting the need for prognostic markers of pregnancy in reproductive-aged women with cirrhosis (1). Further work should use such large data-bases to test existing scoring systems and potentially develop new ones that can ideally predict both maternal liver-related outcomes and pregnancy outcomes (with potentially distinct predictors for both outcomes).

When considering the use of noninvasive measures in pregnancy, it is important to consider normal pregnancy-associated changes in laboratory parameters that may affect interpretation of disease severity. Noninvasive markers currently available that can potentially be used in the context of pregnancy include the MELD, Child-Turcotte-Pugh, ALBI, APRI, Fibrosis-4, and serum FibroSure (BioPredictive, Paris, France)/FibroMeter (Echosens, Paris, France) tests. However, few have been validated for use in pregnancy. Low albumin levels due to hemodilution, particularly during late pregnancy, (6) and lower platelet counts during pregnancy (particularly in twin compared with singleton pregnancies) may impact scores such as ALBI and APRI to nonuniform degrees among pregnant women (7). Results of the ALBI, APRI, and Fibrosis-4 may be falsely elevated. The serum FibroTest or FibroSure, although a useful tool in clinical practice, especially in individuals with nonalcoholic fatty liver disease and viral hepatitis, has not been validated for use in pregnancy.

Nonserologic tests can also potentially be used in pregnancy to more accurately predict liver disease stage and potential implications on pregnancy outcome. Liver biopsy, recently evaluated by Ludvigsson, may be associated with preterm birth, (8) but it can be performed if indicated for diagnostic purposes during pregnancy (6). However, even if cirrhosis was identified on liver biopsy, the percutaneous approach does not provide portal pressure measurements. Therefore, biopsy would not preclude the need for screening upper endoscopy in the pregnant patient with cirrhosis. Upper endoscopy is critical for the safe management of cirrhosis and noncirrhotic portal hypertension in pregnancy, although it is important to counsel women regarding potential procedure-related risks such as preterm birth and small size for gestational age (6,9). Thus, these tests are potentially too invasive as

initial diagnostic tests in those women who are not already known to have cirrhosis when they present for pregnancy care.

Transient elastography is used during pregnancy in Europe as an important additional diagnostic/prognostic tool. However, its use during pregnancy is not Food and Drug Administration approved in the United States. Transient elastography would potentially be a useful tool for assessing risk of fibrosis and predicting the degree of portal hypertension, especially in the setting of pregnancy when platelet count may not be an accurate predictor of cirrhosis. Transient elastography has been studied during pregnancy in the context of preeclampsia (10), and higher scores have been associated with pregnancy complications. It has even been used for obstetric-specific indications such as to assess cervical stiffness (11). Thus, it offers the opportunity to predict both liver-related and pregnancy-related outcomes. As the number of women with cirrhosis and CLD seen during pregnancy increases, the potential use of transient elastography would provide useful information in the diagnosis and prognostication of liver disease, as well as pregnancy outcomes.

A notable strength of this study is the introduction of a combined hepatology and obstetric clinic. This multidisciplinary approach can help optimize the care of high-risk women with liver disease in pregnancy and ensure that respective subspecialty management is carefully coordinated. Moreover, this team approach may enhance linkage of care in the postpartum period, when women will need ongoing management of advanced liver disease.

As we continue to care for more pregnant women with cirrhosis, the role of accurate, noninvasive prognostic markers will carry even greater importance. Based on this study by Gonsalkorala et al., noninvasive tests may be a viable but not fully optimized option in this complex patient population. The importance of a multidisciplinary strategy will also play a key role in achieving the best maternal and fetal outcomes. Prospective databases with comprehensive clinical and laboratory information on patients with CLD will be critical to further delineate care protocols.

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Table 1

Noninvasive studies evaluating for use in cirrhosis patients during pregnancy

	AUROC	Score cutoff	Study outcome
APRI (2)	0.70 (sensitivity 83%; specificity 55%) 0.641	APRI = 0.84	Full-term gestation Live birth
ALBI (2)	0.741 (sensitivity 81%; specificity 59%)	ALBI = -2.7	Live birth
MELD	0.631 (2) 0.8 (3) (sensitivity 83%; specificity 83%)	MELD 10	Live birth Liver-related complications
MELD sodium	0.673 (2)		Live birth
UKELD	0.8 (3) (sensitivity 83%; specificity 79%)	UKELD 47	Liver-related complications
CTP	No association (3) Increased risk (4)	CTP = B	Liver-related complications Hepatic decompensation
Platelet count	0.856 (78% sensitivity; 89% specificity) (3)	Platelet count $<110 \times 10^9$	Presence of varices on endoscopy in second trimester

ALBI, albumin-bilirubin score; APRI, aspartate aminotransferase-to-platelet ratio index; AUROC, area under the receiver operating characteristic; CTP, Child-Turcotte-Pugh; MELD, Model for End-Stage Liver Disease; UKELD, United Kingdom Model for End-Stage Liver Disease.