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Nonalcoholic fatty liver disease in pregnancy

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# Nonalcoholic fatty liver disease-based risk prediction of adverse pregnancy outcomes: Ready for prime time?

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**Keywords:** Nonalcoholic fatty liver disease; Pregnancy complications; Pregnancy

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There is a growing body of evidence that nonalcoholic fatty liver disease (NAFLD) is associated with further development of cardiometabolic disease.<sup>1</sup> Pregnancy is deemed a window period to predict further metabolic or cardiovascular disease later in life. Physiological changes during pregnancy, such as circulatory volume increases, inflammatory changes, insulin resistance, and dyslipidemia, can present challenges to pregnant women.<sup>2</sup> Because of these changes, pregnancy complications can develop, and it has been reported that women who experience pregnancy complications are likely to develop further metabolic or cardiovascular disease after pregnancy.<sup>3-8</sup> Indeed, pregnancy is also a period of opportunity to identify women at high risk for long-term metabolic or cardiovascular disease.<sup>9</sup>

Recently, there have been several reports on pregnancy outcomes in women with NAFLD. NAFLD has been reported to be associated with diverse pregnancy complications, such as gesta-

tional diabetes mellitus (GDM), fetal overgrowth, or hypertensive disease during pregnancy.<sup>10-13</sup> In this issue of *Clinical and Molecular Hepatology*, El Jamaly et al.<sup>14</sup> conducted a systematic review of the literature to determine the current evidence regarding maternal and fetal outcomes in pregnant women with NAFLD. In the review of 22 studies that included 13,641 female patients with NAFLD, women with NAFLD were at increased risk of baseline diabetes mellitus (odds ratio [OR], 6.00; 95% confidence interval [CI], 2.21–16.31), baseline hypertension (OR, 3.75; 95% CI, 2.13–6.59), gestational hypertension (OR, 1.83; 95% CI, 1.03–3.26), and preeclampsia (OR, 2.43; 95% CI, 2.21–16.31). Moreover, NAFLD was associated with the risk of gestational diabetes (OR, 3.78; 95% CI, 2.21–6.44 for post history of gestational diabetes; OR, 2.81; 95% CI, 1.58–5.02 for current gestational diabetes), premature birth (OR, 2.02; 95% CI, 1.44–2.85), large for gestational age birth (OR, 2.01; 95% CI, 1.72–2.37), and history of prior miscarriage or abortion (OR, 1.15; 95% CI, 1.02–1.30). Overall, the authors showed that NAFLD was associated with increased risk of maternal diabetic or hypertensive complications and other

## Abbreviations:

CI, confidence interval; GDM, gestational diabetes mellitus; NAFLD, nonalcoholic fatty liver disease; OR, odds ratio

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adverse fetal outcomes, providing informative evidence in clinical management of women with NAFLD.

The current study is the first meta-analysis that reports a correlation between NAFLD and pregnancy outcomes. However, the authors could not exclude other liver-related competing conditions (hepatitis or liver transplantation), and some of the studies analyzed did not disclose the method of NAFLD diagnosis. Nevertheless, the large sample size and the quality of the included studies support that the estimated effect from the current meta-analysis is close to the true effect.

Based on the current and previous reports, a consensus can be drawn that NAFLD is a definite risk factor for several adverse pregnancy outcomes. While the traditional risk stratification system recommended by the practice guidelines can identify only a handful of pregnant women who eventually develop GDM or preeclampsia,<sup>13,15</sup> the incorporation of NAFLD into the preexisting risk stratification model improves the predictive performance for adverse pregnancy outcomes.<sup>16</sup> However, whether the early identification of NAFLD in pregnant women should be routinely implemented remains controversial. The cost-effectiveness analysis should be performed first, as the confirmative diagnosis of NAFLD requires either radiological or histological examination, which may be difficult to conduct in prenatal care.

The effect of NAFLD during pregnancy on the fetus is another important issue that needs to be addressed in future studies. As shown by the increased risk of GDM or fetal overgrowth in pregnant women with NAFLD, it is biologically plausible that the metabolic changes in women with NAFLD may also affect the fetus in utero. Consequently, fetal growth disturbance may be correlated with long-term cardiometabolic risk, such as obesity, diabetes mellitus, and cardiovascular disease, later in life.<sup>17</sup> Therefore, further studies are warranted to investigate the metabolic disturbance of the fetus in women with NAFLD and its impact in the neonatal, infant, and adult periods.

### Authors' contribution

All authors were responsible for the interpretation of data, drafting and critical revision of the manuscript.

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### Conflicts of Interest

The authors have no conflicts to disclose.

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