Placental Ferroportin Protein Abundance Is Associated With Neonatal Rather Than Maternal Iron Status in Women at High Risk for Gestational Iron Insufficiency

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Objectives: Murine data suggest that the placenta prioritizes iron (Fe) for its own needs when Fe is limited by upregulating transferrin receptor 1 (TFR1) and downregulating the Fe exporter ferroportin (FPN). Human data on the impact of maternal and neonatal Fe status on placental FPN are conflicting. The study aims were to identify determinants of placental FPN protein abundance in women at risk of Fe insufficiency and to assess the utility of the placental Fe deficiency index (PIDI), which is the FPN/TFR1 ratio, as a measure of maternal/fetal Fe insufficiency.

Methods: FPN and TFR1 protein abundance was measured by semi-quantitative western blots in placentae collected from 43 neonates born to teens (17.4 $\pm$ 1.1 y) carrying singletons (39.9 $\pm$ 1.3 weeks of gestation at birth) and from 57 neonates born to 26 women (31.3 $\pm$ 6.3 y) carrying multiples (35.5 $\pm$ 2.7 weeks of gestation at birth). Fe status biomarkers (Hb, SF, sTfR, TBI) and hormones (hepcidin, EPO, ERFE) were assessed in maternal and cord blood.

Results: FPN and TFR1 were detected in all samples analyzed between 30.4–41.7 weeks of gestation. In both cohorts, FPN protein abundance was associated with neonatal but not maternal factors. Higher FPN was associated with lower cord Hb ($p = 0.03$) in the multiples cohort and with higher cord EPO ($p = 0.002$) in the teens. In contrast, TFR1 was inversely associated with maternal Fe status; multiples cohort (SF, $p = 0.01$; sTfR, $p = 0.01$; TBI, $p = 0.003$; hepcidin $p = 0.01$), teens (SF, $p = 0.01$). The PIDI was predicted by maternal and neonatal Fe status but in opposite directions. In the multiples cohort, Fe deficient women (mid-gestation sTfR $>$ 8.5 mg/L, delivery SF $<$ 12 μg/L or TBI $<$ 0 mg/kg) had a lower PIDI ($p = 0.02$, $p = 0.003$, $p = 0.04$) but lower cord Hb was associated with a higher PIDI ($p = 0.004$). In the teens, lower mid-gestation hepcidin was associated with a lower PIDI ($p = 0.009$) but higher cord EPO was associated with a higher PIDI ($p = 0.006$).

Conclusions: Placental FPN protein was inversely associated with neonatal Fe status. The PIDI captures fetal and maternal regulation of placental Fe trafficking as it reflects Fe export to the fetus relative to Fe import from maternal circulation. More data are needed to assess the utility of the PIDI as an indicator of Fe insufficiency during pregnancy and how it relates to neonatal outcomes that are driven by placental health.

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