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Maternal iron absorption and iron transfer to the fetus during pregnancy in normal- weight and overweight/obese women and effects on infant iron status: a prospective multicenter case control study

Background: Overweight/obesity causes low-grade systemic inflammation and up-regulates the iron regulator hepcidin and reduces fractional iron absorption (FIA) even when iron stores are low. Pregnancy increases the dietary iron requirement to support expansion of maternal blood volume and fetal needs. It is unclear whether and/or to what extent overweight/obese pregnancy influences FIA, iron transfer to the fetus and risk of iron deficiency in the mother and newborn. Iron deficiency early in life has multiple negative effects on child development. With obesity increasing in prevalence in most countries, if obesity before and during pregnancy has detrimental effects on infant iron status this may impair child development, and have important public health consequences.

In this study, we (1) determined the impact of maternal overweight/obesity on: a) FIA in pregnancy; b) transfer of iron to the fetus and c) newborn iron status; (2) investigated the relationship between BMI, hepcidin, plasma ferritin (PF) and inflammatory markers; and (3) compared differences in maternal iron needs during the 2nd and 3rd trimester; and (4) estimated the infant's iron requirement during the first two years of life.

Methods: In this ongoing multicenter (Switzerland, Thailand, Mexico) prospective case-control study (normalweight n=36; overweight/obese n=36) we administered labeled [57Fe]- or [58Fe]-FeSO4 to women during the 2nd and 3rd trimester of pregnancy. We measured FIA determining erythrocyte incorporation of iron stable isotopes 14 days after administration, and monitored, from pregnancy week (PW) 12 to PW 36, iron-, inflammation and hepcidin. Iron transfer to the fetus was determined as iron stable isotope concentration in cord blood. Iron status and iron stable isotope concentrations were then monitored in children at 3, 6, 12, 18 and 24 months.

Results: Subject characteristics (mean±SD) in PW 12 for the normal-weight/obese were: age: $32\pm6/33\pm5$ years, BMI: $20.8\pm2.5/41.0\pm7.4$ kg/m2, hemoglobin: $12.1\pm0.9/13.5\pm0.8$ g/dL and PF: $61\pm23/47\pm24$ µg/L. Preliminary data indicate 83% and 24% lower FIA in the 2nd trimester compared to the 3rd in normal-weight and overweight/obese pregnant women, respectively. Iron isotopes were readily detectable in cord blood. The [58Fe]/[57Fe]-ratio measured in cord blood correlated positively with the [58Fe]/[57Fe]-ratio determined in the mother in the 3rd trimester.

Conclusions: In normal pregnancy, FIA increases over time to support increased iron needs of mother and fetus. This is consistent with decreasing hepcidin concentrations during pregnancy. Our preliminary data indicate there is a sharply reduced increase in FIA in overweight/obese pregnant women compared to normal weight women, suggesting increased hepcidin may continue to play an important regulatory role in the former group even in the 3rd trimester. Thus, although iron demands are strongly increased, overweight/obesity may impair adequate iron supply to the expecting mother and the fetus due to persistent subclinical inflammation.

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