Placental Weight and Small for Gestational Age: Within-siblings Fixed-effect Variance Regression Component Analysis

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Methods:

Background:

Higher placental weight has been described as an adaptive mechanism to fetal hypoxia in small for gestational age (SGA) infants. However, placental weight alone may not be a good marker reflecting intrauterine growth restriction. Thus, we examined the extent to which fetoplacental ratio (FPR), defined as the ratio between birth-weight and placental weight, was associated with the risk of delivering SGA infants after adjustment for maternal smoking, iron deficiency anemia and choriodecidual necrosis as surrogates of fetal hypoxia.

Methods:

We completed a within-sibling analysis using data from the US National Collaborative Perinatal Project resulting in 3,494 term infants from 1,803 primiparous women who delivered ≥2 singleton, between 1959 and 1966. We used linear fixed-effects regression models to explore the effect of time-varying measured factors on placental weight and conditional logistic regression to estimate the effects of the tertiles of FPRs (1st small, 2nd normal and 3rd large) on the probability of delivering SGA infants. We implemented a mean deviation algorithm in order to treat mothers’ specific intercepts as fixed unknown parameters. Therefore, the estimated model coefficients represent the within-siblings effects of the covariates. The advantage of these estimates is that they are not susceptible to bias due to unmeasured mother-specific time-invariant covariates as each mother serves as her own control.

Results:

We found that the mean birthweight and mean placental weight increase by infant order, while the mean FPR decreases (Figure 1 and 2). Maternal iron deficiency anemia increased placental weight by 15.4 grams (95% confidence interval (CI)= 8.1, 22.7) and choriodecidual necrosis conversely reduced it by -7.2 grams (95%CI = -12.5, -1.8) (Table 1). After multivariate adjustment, newborns with a small FPR (1st-tertile:≤7) had 2 times higher chance of being SGA than their siblings with a large FPR (3rd-tertile:≥9) (odds ratio = 2.0, 95%CI: 1.2-3.5) (Table 1).

Discussion:

A small FPR was associated with higher odds of delivering a SGA infant. In contrast to a SGA infant with a large FPR, a small FPR should be interpreted as a sign of adverse intrauterine environment. This information can have important implications toward understanding IUGR and should help to differentiate SGA who are constitutionally small from those who had not met their optimal growth and thus, were intrauterine growth restricted.