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Association between fetal fraction on cell-free DNA testing and first trimester markers for pre-eclampsia

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Objective

To evaluate the association of fetal fraction on cell-free DNA (cfDNA) testing with first trimester markers for pre-eclampsia and to investigate a possible association of low fetal fraction with increased risk for pre-eclampsia (PE) and fetal growth restriction (FGR).

Methods

This was a retrospective cohort study including all women with singleton pregnancies who had risk calculation for PE and FGR between 11+0 and 13+6 weeks' gestation and also decided to have cfDNA as a primary or secondary screening test for chromosomal abnormalities at any gestational age in two private Fetal Medicine clinics in Sydney and Melbourne, Australia, between March 2013 and May 2017. Logarithmically transformed fetal fraction results were adjusted for gestational age and maternal characteristics. Associations with mean arterial pressure (MAP), mean uterine artery pulsatility index (UtAPI), pregnancy-associated plasma protein A (PAPP-A), placental growth factor (PlGF) and risks for pre-eclampsia before 34 and 37 weeks' gestation and fetal growth restriction before 37 weeks' gestation were analyzed through univariate and multivariate linear regression.

Results

In total, 4317 singleton pregnancies subjected to NIPT with reported fetal fraction were included. Significant prediction of fetal fraction was provided by gestational age, in vitro fertilization, maternal age, BMI, chronic hypertension, diabetes mellitus and South Asian ethnicity and multiparity without previous history of PE or FGR. Fetal fraction was inversely associated with MAP and UtAPI and positively associated with PAPP-A and PlGF. The lower the fetal fraction, the higher was the risk for PE<34 weeks, PE<37 weeks and FGR<37 weeks (p<0. 001).

Conclusion

There is a significant association between fetal fraction results and first trimester markers for adverse pregnancy outcome. Low fetal fraction is associated with an increased risk for pregnancy complications, but its capacity to act an as independent first trimester marker in an algorithm screening for PE and FGR requires further research.