Does the maternal serum sFlt-1/PlGF ratio test distinguish between growth restricted and non-growth restricted small-for-gestational-age fetuses?

Rajiv P [1,2], Cade T[1], Jones G[1,], Brennecke S[1,3]

[1]Department of Maternal-Fetal Medicine, The Royal Women's Hospital, Melbourne, Australia
[2]Monash University, School of Medicine, Melbourne, Australia
[3]The University of Melbourne, Department of Obstetrics and Gynaecology, Melbourne, Australia

BACKGROUND

Fetal growth restriction (FGR) secondary to chronic placental insufficiency is a major cause of perinatal morbidity and mortality.

- Small for gestational age (SGA) fetuses can be classified as constitutionally small (non-FGR SGA) or pathologically small (FGR SGA).
- Poor antenatal detection of FGR has been associated with a significant increase in stillbirths, adverse perinatal outcomes and adult-onset complications.[1]
- The maternal serum ratio of soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF) is an indicator of placental insufficiency in the latter half of pregnancy.[2]
- As placental insufficiency is a major cause of FGR[3], the sFlt-1/PlGF ratio test may be a clinically useful tool to distinguish between FGR and non-FGR SGA fetuses.

AIM

To determine if the sFlt-1/PlGF ratio can distinguish between FGR and non-FGR SGA fetuses in singleton pregnancies of birthweight less than or equal to the 10th percentile.

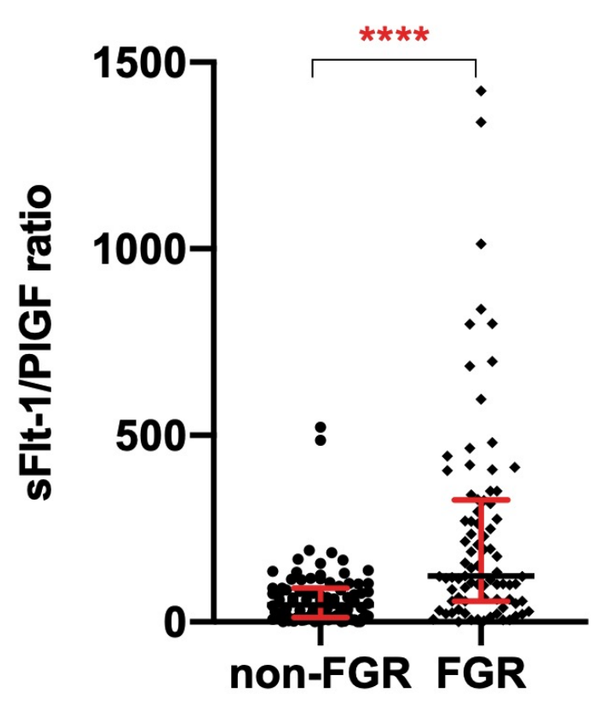
METHODS

- Retrospective audit of singleton pregnancies with fetal birthweight ≤ 10th percentile
- Women delivered between September 2016 - July 2019
- 172 pregnancies included 82 'FGR SGA' and 90 'non-FGR SGA' pregnancies. 5 were excluded due to congenital malformation, 1 due to chromosomal abnormality and 13 due to multiple pregnancy.
- FGR cases had indicators of placental insufficiency such as reduced amniotic fluid index, abnormal fetal vessel Dopplers, abnormal CTG findings and relevant placental histopathology findings
- Non-FGR cases did not have the above indicators of placental insufficiency
- Data sourced from patient medical records and online pathology and imaging database
- sFlt-1, PlGF and sFlt-1/PlGF ratio compared between FGR SGA and non-FGR SGA pregnancies.
- Statistical analysis performed using STATA and GraphPad.

RESULTS

- Total of 808 women included in audit with 82 'FGR SGA' and 90 'non-FGR SGA' pregnancies.
- The **sFlt-1/PlGF ratio was significantly higher in FGR SGA cases compared to non-FGR SGA cases** as determined by the Mann-Whitney U test (46.0 [12–90] vs 122.5 [56–326], median [IQR], p<0.0001). See Figure 1.
- It is known that preeclampsia is also associated with an increase in the sFlt-1/PlGF ratio throughout pregnancy.[4]
- Using a multivariate linear regression model with logistic transformation, when adjusting for preeclampsia (PE), the presence of **FGR is associated with a 72% increase in the sFlt-1/PlGF ratio** (ß=0.5430, $100\times\left(e^{ß}-1\right)\%$ = 72.11%, p=0.013).

Figure 1: sFlt-1/PlGF ratio in cases of FGR SGA and non-FGR SGA pregnancies



CONCLUSION

The sFlt-1/PlGF ratio test successfully discriminates FGR SGA from non-FGR SGA pregnancies. When adjusting for preeclampsia, FGR SGA pregnancies still show a statistically significantly increase in the sFlt-1/PlGF ratio.

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