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| **Placental growth factor as a marker of placental dysfunction in small for gestational age infants – A useful tool to predict pregnancies at highest risk of stillbirth?** |
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| **Introduction** Stillbirth is frequently associated with placental dysfunction. During pregnancy placental dysfunction may be suspected when the fetus is small for gestational age (SGA). However, discriminating between placental dysfunction causing SGA and constitutionally-small fetuses is a challenge in obstetric practice. Placental growth factor (PlGF), a biomarker of placental function, measurable in the maternal circulation, may have this discriminatory capacity. We aimed to determine whether PlGF identifies pregnancies at increased risk of stillbirth when an SGA infant is suspected antenatally.  **Material and Methods** Plasma PlGF was measured using an automated immunoassay (Triage®, Alere, San Diego, CA, USA). The detection range of the assay is 12‒3000 pg/mL. Low PlGF was defined as a concentration <5th percentile for gestation and very low PlGF was defined as a concentration <12pg/mL. PlGF was measured in normotensive women presenting who had an SGA infant (ultrasound fetal abdominal circumference <10th percentile for gestational age) at sites in Canada, New Zealand and the United Kingdom (n=411). The relationship between PlGF and the sampling-to-delivery interval was determined. The predictive accuracy of PlGF to identify SGA pregnancies that end in stillbirth was calculated.  **Results** Very low PlGF (<12 pg/mL) was associated with shorter sampling-to-delivery intervals than normal PlGF (13 vs. 29.5 days, P<0.0001). In total, there were 7 stillbirths and one neonatal death; 6 stillbirths and the neonatal death occurred in women with low PlGF and one stillbirth with normal PlGF. Therefore, low PlGF had 87.5% [47.4‒99.7] sensitivity and a specificity of 62.8% [57.9‒67.5] to predict pregnancies that end in stillbirth with negative and positive predictive values of 99.6% [97.8‒100.0] and 4.7% [1.8‒9.0], respectively. The positive likelihood ratio was 2.35 [1.8‒3.1] and the negative likelihood ratio was 0.2 [0.03‒1.2]. Thus, in this cohort, the post-test odds of perinatal death after a low PlGF result was 4.7% and the post-test odds after a normal PlGF was 0.4%.  **Conclusions** In SGA babies with low PlGF identifies cases with underlying placental dysfunction which either prompts early delivery or progresses to placental failure resulting in stillbirth. A positive PlGF should prompt increased frequency of antenatal surveillance and early delivery should be considered if signs of fetal compromise are detected. |
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