Objective: To assess the association of angiogenic factors and placental underperfusion (PUP) in late-onset small for gestational age (SGA) births.

Methods: A cohort of SGA singleton fetuses delivered after 34 weeks was created. In all cases, uterine arteries (UtA), umbilical artery (UA), and middle cerebral artery (MCA) were evaluated at diagnosis. Maternal serum concentrations of placental growth factor (PlGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) were also measured at diagnosis by ELISA. From each case, the placenta was histologically evaluated for signs of PUP using a hierarchical and standardized classification system. Logistic regression analysis was used to evaluate the independent association of angiogenic factors and Doppler parameters, both measured at diagnosis.

Results: A total of 122 pregnancies suspected of SGA were included, 70 (57.4%) subsequently fulfilling criteria of PUP. In this group there were 85 placental findings qualifying for PUP. Both mean UtA pulsatility index z-values (1.26 vs. 0.84 [p=0.038]) and PlGF MoMs (0.21 vs. 0.55 [p=0.002]) significantly differed between cases with and without PUP. Logistic regression showed that only PlGF independently predicted PUP (OR 0.11; 95% CI 0.025-0.57; p=0.008).

Discussion: Term SGA neonates with histological abnormalities reflect latent insufficiency in uteroplacental blood supply. Due to a higher risk of adverse perinatal outcome, it underlines a need for new prenatal, Doppler or biochemical, markers of placental disease. Angiogenic factors can play a pivotal role in the identification of SGA neonates.

Conclusions: Placental growth factor plasma levels at diagnosis of SGA are associated with the presence of histological signs of PUP.