Longitudinal evaluation of fetal growth and placental perfusion in euploid fetuses with isolated CHD

Inversetti A, Fesslova V, Giorgione V, Candiani M, Cavoretto P
Università Vita-Salute San Raffaele, Milan, Italy

Objective
The aim of this study is to evaluate longitudinal patterns of fetal growth from the first to the third trimester and fetal-placental perfusion from the second to the third trimester in a cohort of fetuses with CHD.

Methods
70 fetuses with isolated CHD and 150 controls were prospectively and retrospectively selected from two fetal medicine units from 2011 to 2017. Twin pregnancies, aneuploidies and genetic syndromes were excluded. CHD were also clustered in cyanotic (hypoplastic left heart syndrome, tetralogy of Fallot, transposition of great arteries, double outlet right ventricle, pulmonary atresia, truncus arteriosus communis, total abnormal pulmonary venous connection, Ebstein anomaly, critical pulmonary stenosis) versus non cyanotic (aortic arch anomalies, non-critical pulmonary stenosis, atrioventricular and ventricular septal defects, situs inversus, aberrant right subclavian artery). Prenatal diagnosis was confirmed in the second trimester and first trimester fetal biometry was retrospectively retrieved. Standard fetal biometry, umbilical, uterine and middle cerebral arteries Dopplers were serially measured with at least 2 measurements per fetus in at least 2 different trimesters. Z-scores of biometry were constructed using growth charts of a normal population. A multivariate mixed regression was performed to examine patterns of growth in the overall study group and in the two subgroups with different CHD.

Results
Abnormal cranial growth and neurodevelopmental disorders were reported in infants after surgical correction of congenital heart defects (CHD). Recent studies have demonstrated abnormal cranial and brain development with associated mild placental insufficiency in the second and third trimester of pregnancy in a heterogeneous group of CHD. During the second and third trimester, CHD groups showed smaller head circumference (HC) (second trimester HC z-score: CHD -0.79 (+/-1); controls +0.18(+/-0.91); p=0.01; third trimester HC z-score: CHD -0.54(+/-0.8); controls +0.05(+/-0.55); p<0.01). Cyanotic CHD showed a smaller BPD and HC z-scores as compared to non-cyanotic CHD both in the second and third trimester (second trimester BPD z-score: cyanotic -0.45(+/-1.3); non cyanotic +0.19(+/-1.1), p< 0.01; third trimester BPD z-score: cyanotic -0.56 (+/-0.7); non cyanotic +0.09 (+/-0.6), p< 0.01; second trimester HC z-score: cyanotic -1.14(+/-0.83); non cyanotic -0.03(+/-0.07), p< 0.01; third trimester HC z-score: cyanotic -0.71 (+/-0.56); non cyanotic: +0.09 (+/-0.54), p< 0.01). During the second and third trimester, CHD groups showed higher umbilical artery PI (UA PI) compared to controls (UA PI z-score: CHD +0.61(+/-0.9); controls -0.1(+/-0.8); p=0.02) and significantly higher UA PI was detected in the cyanotic group in the third trimester (third trimester UA PI z-score: cyanotic +0.59 (+/- 0.74); non cyanotic -0.12 (+/-0.81), p<0.01). Fetuses with cyanotic CHD demonstrated statistically significant HC restriction with a slope of -0.02/week of gestational age (p<0.001) and BPD restriction with a slope of -0.04/week (p<0.001). Significant UA PI increase showed a slope of +0.00057/week (p=0.004). No significant differences were found within the groups for head biometry during the first trimester and for cisterna magna, transverse cerebellar diameter, posterior cerebral ventricle diameter size, femur length, abdominal circumference, middle cerebral artery (MCA PI) and uterine artery (UtA) Doppler measurements at any stage. Mean birth weight was significantly restricted in the CHD group compared to controls (median 2900 g (+/-514) versus 3335 g (+/-612), p<0.01).

Conclusion
CHD fetuses presented reduced cephalic growth from the second trimester, particularly in the cyanotic group, with lower birth weight and mild placental dysfunction. Normal cerebellar measure may indicate an asymmetric cerebral development possibly due to greater growth delay on the forebrain/midbrain rather than on the hindbrain. Further prospective research is needed to investigate detailed segmental brain growth and to clarify the extent to which altered haemodynamic,
placentation and genetics-epigenetics are related to abnormal neurodevelopment in fetuses with CHD.