Risk of preeclampsia, small for gestational age and placental abnormalities in pregnancies with major congenital heart disease

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Objective
Abnormal placental development was associated with congenital heart defects (CHD) due to concomitant lower neonatal and placental weights, reduced first trimester placental growth factor and abnormal vascularization or cord insertion. The aim of our study is to explore the prevalence of preeclampsia (PE), hypertensive disorders of pregnancy (HDP), small for gestational age (SGA) and placental abnormalities (PA) in pregnancies with fetal CHD.

Methods
Retrospective cohort study of singleton pregnancies with prenatal diagnosis of major CHD seen at a tertiary Fetal Echocardiography Center (Policlinico San Donato, Milan, Italy) from 2003 to 2018. Intrauterine deaths, aneuploidies, non-structural cardiac anomalies, minor CHD and venous system anomalies were excluded. The outcomes assessed were: PE, HDP, SGA and PA (praevia, abruption, accreta, abnormal cord insertion). Chi-square, Fisher’s, Wilcoxon tests and Dwass-Steel-Critchlow-Fligner multiple comparison procedure were used, as appropriate. Logistic regression analysis with adjustment for maternal age, parity, comorbidities and type of conception was also applied.

Results
480 pregnancies with major CHD were compared with 456 normal controls. The CHD group showed significantly increased prevalence of both PE (14/480; 2.9%; adjusted OR=6.50 [CI 95%=1.39-30.41], p=0.02) and HDP (21/480; 4.5%; adjusted OR=2.62 [CI 95%=1.03-6.67], p=0.04) as compared to the control group (HDP: 15/456; 3.3%; PE: 4/456 0.9%). PA showed a non-significant trend (CHD: 22/480, 4.5%, control group: 15/456, 3.3%, adjusted OR 2.56 [CI 95%=0.99-1.02, p=0.05]). HDP and PE were particularly increased in Tetralogy of Fallot (HDP 5/50, 10%, p=0.04; PE 4/50, 8%, p=0.004) and Hypoplastic Left Heart Syndrome (HDP 3/18; 16.7%, p=0.03; PE 2/18; 11.1%, p=0.02) when compared with control group. Atrioventricular septal defect presented a significant association with PA (3/22; 13.6%, p=0.04). Median birth weight centile was significantly lower in CHDs than in controls (median [IQR] 39.3 [24.8-56.5] vs 46.3 [30.4-63.5], p<0.0001) with a significantly higher rate of SGA in CHDs than in controls (CHD: 35/401; 8.7%, control group: 17/430; 3.9%; adjusted OR: 3.37 [CI 95%: 1.51-7.51], p=0.003). SGA was more frequent in tetralogy of Fallot (6/50; 12%, P=0.01), atrial or ventricular septal defects (8/65; 12.3%, p=0.005) and cardiomyopathy (3/12; 25%, p=0.01) than in control group (17/430; 3.9%).

Conclusion
This study defines a significant association between PE, HDP, SGA and major fetal CHD. The absolute risks remain rather low; however, common mesodermal origin of heart and placenta supports our results indicating the need for screening or monitoring for these complications when CHD is prenatally diagnosed. Further large prospective studies are needed.