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EDITORIAL COMMENT

Spontaneous preterm birth and congenital heart defects: What is known?

Prematuridade e cardiopatia congénita: o que sabemos?

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Congenital heart defects (CHD) are the most prevalent congenital malformation and the leading cause of childhood mortality and morbidity.[1] Preterm birth, which occurs in 5–18% of newborns worldwide, is also a leading cause of childhood mortality and morbidity and is associated with an increased risk of neurodevelopmental disorders.[2] The combination of CHD and preterm birth results in even higher mortality and morbidity, with preterm children born with CHD having a 2–4-fold higher mortality[3] and an increased risk of neurodevelopmental disorders. Additionally, some CHD types are associated with delayed brain maturation, potentially exacerbating the negative effects of preterm birth on the brain.

The study by Palma et al.[4] aims to clarify the crosstalk between CHD and preterm birth further. Using data from a single center, the authors found that 23% of newborns with CHD were preterm infants, and the presence of CHD increased the likelihood of being preterm by two-fold. The preterm group did not have a statistically different neonatal mortality compared to the term group with CHD.

It is worth mentioning that the authors' estimate of the relationship between CHD and preterm birth may be biased due to the use of only live births in the analysis. The study assumes that preterm births only happen from live births when the true risk set is all pregnancies (including fetuses still in-utero). By only looking at live births, the study ignores pregnancies that end in miscarriage, elective termination, or fetal death, which can be related to exposure and lead to biased results. Additionally, it is also important to note that a significant number of CHD cases may have been missed in this study, as only 40–50% of CHD cases are diagnosed within the first week and 50–60% within the first month of life. The study only included cases diagnosed during prenatal and neonatal periods, which could have resulted in missing cases, particularly in term neonates who typically have a shorter hospital stay. To reduce ascertainment bias,

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the authors excluded mild cardiac defects, but this may have also introduced selection bias.

We should point out, however, that even though these possible selection biases, the estimates presented by Palma et al. are in line with previous reports that found an association between any CHD and an approximately two-fold increased risk of preterm birth. For example, Laas et al.[5] conducted a population-based study on CHD, including 2189 live births with CHD (excluding isolated atrial septal defects) born between 2005 and 2008 and found that 13.5% of newborns with CHD were preterm. The likelihood of preterm birth was two times higher in the CHD group compared to the general population (odds ratio 2.0, 95% confidence interval 1.6–2.5), mainly due to a higher rate of spontaneous preterm birth. The increased risk of preterm birth in the CHD group remained even after excluding newborns with chromosomal or other anomalies.

Matthiesen et al.[6] also reported similar results, with a sample size of 1 040 474 births from Denmark. CHD was associated with an increased risk of spontaneous preterm birth, with an adjusted hazard ratio of 2.1 (95% CI, 1.9–2.4) compared to the general population. Specific subtypes of CHD were associated with even higher risks, including pulmonary stenosis combined with a septal defect, pulmonary stenosis or atresia, tetralogy of Fallot, coarctation or interrupted aortic arch, and hypoplastic left heart syndrome. The majority of the association was attributed to preterm pre-labour rupture of membranes. The study found no other explanation for this association, particularly from maternal genetics, polyhydramnios, or indicators of fetal or placental growth.

No definitive cause for this increased risk for preterm birth in CHD could be found, and several mechanisms have been speculated. It likely results from a combination of genetic predispositions and environmental exposures. Preterm birth in infants with CHD could also occur due to abnormal blood flow patterns in the fetus. Regarding other possible confounders, including multiple births, congenital syndromes or extracardiac malformations, in the present study, only the last one had a statistical significance between term and PTB congenital heart disease patients. Further research is needed to examine the connection between changes in fetal circulation and the risk of spontaneous preterm birth in fetuses with CHD.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Lanzoni M, Morris J, Garne E, et al. European monitoring of congenital anomalies – JRC-EUROCAT report on statistical monitoring of congenital anomalies (2006–2015). Publications Office of the European Union; 2017.
2. Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379:2162–72.
3. Laas E, Lelong N, Ancel PY, et al. Impact of preterm birth on infant mortality for newborns with congenital heart defects: the EPICARD population based cohort study. BMC Pediatr. 2017;17:124.
4. Palma A, Morais S, Silva P, et al. Congenital heart defects and preterm birth: outcomes from a referral centre. Rev Port Cardiol. 2023;42, http://dx.doi.org/10.1016/j.repc.2022.05.009.
5. Laas E, Lelong N, Thieulin AC, et al. Preterm birth and congenital heart defects: a population-based study. Pediatrics. 2012;130:e829–37.
6. Matthiesen NB, Østergaard JR, Hjortdal VE, et al. Congenital heart defects and the risk of spontaneous preterm birth. J Pediatr. 2021;229, 168–174.e5.