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RESEARCH LETTER
Congenital Heart Disease

Prevalence of congenital heart defects in assigned children for intercountry adoption

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Worldwide, congenital anomalies are a leading cause of foetal death, infant mortality, and morbidity in childhood. According to the European Surveillance of Congenital Anomalies (EUROCAT), of the 5.1 million births in the European Union each year ~2.5% have a congenital anomaly. EUROCAT is a European network of population-based registries for the epidemiologic surveillance of congenital anomalies, which was established in 1979. Since 2015, the EUROCAT Central Registry is operated by the European Commission's Joint Research Centre (Ispra, Italy), as part of the European Platform on Rare Diseases Registration.[1]

Congenital heart defects (CHDs) are the most frequent group of congenital anomalies accounting for nearly one-third of babies with major congenital anomalies diagnosed prenatally or in infancy in Europe. The spectrum ranges from complex cardiac anomalies with high mortality to small innocent septal defects. According to EUROCAT data, the prevalence of CHDs in live birth without genetic anomalies in Europe during the period 2000–18 was 0.58%.[2]

This study aims to determine the prevalence of CHDs in a series of assigned children for intercountry adoption by analysing their preadoption medical reports.

We analysed the preadoption medical reports of 1233 children who were assigned for intercountry adoption to Spanish families during the period 2000–18, and that reported on the existence (or not) of present CHDs or that had already been spontaneously or surgically corrected. Data on the origin countries, types of diagnosed CHDs and, when described, data on the social, health, and obstetric history of the biological mother were collected. Of the 1233 preadoption medical reports, 926 were performed from Russia, 74 from China, 57 from the Indian subcontinent (India, 52; Nepal, 5), 48 from Eastern European countries (Ukraine, 34; Bulgaria, 5; Romania, 4; Poland, 2; Moldova, 2; Lithuania, 1), 48 from Kazakhstan, 31 from Ethiopia, 25 from Southeast Asia (Vietnam, 18; Philippines, 7), and 24 from Latin American countries (Colombia, 11; Bolivia, 4; Brazil, 2; Uruguay, 2; Panama, 2; Nicaragua, 1; Haiti, 1; Ecuador, 1).

Table 1 shows the prevalence of CHDs reported in the preadoption medical reports of assigned children for intercountry adoption, and the prevalence of these CHDs observed in EUROCAT study in live births without genetic anomalies during the period 2000–18.

The prevalence of CHDs in assigned children for intercountry adoption was 8.6%, being 14.8 times higher than that observed of the EUROCAT study. Congenital heart defects whose prevalence were significantly higher were aortic valve atresia/stenosis (AVA/S) (26.7 times higher), pulmonary valve stenosis (PVS) (23.5 times higher), paten ductus arteriosus (PDA) (19.5 times higher), atrial septal defect (ASD) (16.9 times higher), tetralogy of fallot (TF) (13.9 times higher), and ventricular septal defect (VSD) (11.4 times higher). Regarding the origin country of these children, the highest prevalence of CHDs was observed in Kazakhstan (12.5%), Russia (9.7%), and China (5.4%). Of the total CHDs, most frequently reported were VSD (42.5%) and ASD (34%).

The underlying causes of CHDs can include cytogenetic abnormalities, single-gene disorders, environmental aetiologies, or most commonly, multifactorial aetiologies.[3] Increased environmental risk factors for CHDs in pregnant women, such as drinking alcohol, drugs intake (cocaine and other), smoking in 1st trimester, teratogenic drugs (some antiepileptic, lithium, isotretinoin, angiotensin-converting enzyme inhibitors, statins), viral infections in 1st trimester (rubella, cytomegalovirus, herpes, coxsackie, influenza), exposure to some organic solvents, air pollution,[3–6] and inadequate management of maternal chronic health conditions (e.g. diabetes mellitus types 1 and 2, obesity, hypertension, folic acid deficiency, phenylketonuria, lupus, some connective tissue disorders, thyroid conditions)[3,7–9] must be considered for explaining the very high prevalence of CHDs among children who are assigned for intercountry adoption. In addition, social determinants of health in some countries, such as economic, cultural, and religious factors and, in particular, a poor health care system or lack of affordable medical, may influence CHD diagnosis at early stage and breaking pregnancy when possible.[3]

In children with history of CHDs, data of the social, health, and obstetric history of the biological mother reported in the preadoption medical records were analysed. Unfortunately, these data are rarely described in preadoption medical reports performed from China and

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Table 1 **Prevalence of congenital heart defects reported in the preadoption medical reports of assigned children for intercountry adoption, and in EUROCAT study 2000–18**

	Russia (*n* = 926)	China (*n* = 74)	India Nepal (*n* = 57)	Europe Eastern (*n* = 48)	Kazakhstan (*n* = 48)	Ethiopia (*n* = 31)	Vietnam Philippines (*n* = 25)	Latin America (*n* = 24)	Total (*n* = 1,233)	EUROCAT[a] (2000–18)
Total CHDs: *n*, (%)	90 (9.7)	4 (5.4)	2 (3.5)	2 (4.2)	6 (12.5)	1 (3.2)	0 (0)	1 (4.2)	106 (8.60)	(0.582)
Transposition of great vessels (TGV)			1 (1.7)						1 (0.08)	(0.025)
Ventricular septal defect (VSD)	39 (4.2)[b]	2 (2.7)		1 (2.1)	3 (6.2)				45 (3.65)	(0.321)
Atrial septal defect (ASD)	31 (3.3)[c]	2 (2.7)			3 (6.2)				36 (2.92)	(0.172)
Tetralogy of Fallot (TF)	4 (0.4)[d]								4 (0.32)	(0.023)
Pulmonary valve stenosis (PVS)	6 (0.6)		1 (1.7)			1 (3.2)		1 (4.2)	9 (0.73)	(0.031)
Aortic valve atresia/stenosis (AVA/S)	3 (0.3)			1 (2.1)					4 (0.32)	(0.012)
Coarctation of aorta (CA)	2 (0.2)								2 (0.16)	(0.029)
Paten ductus arteriosus (PDA)[e]	5 (0.5)[f]								5 (0.41)	(0.021)

[a]Prevalence (%) of CHDs in live births—EUROCAT data—Period 2000–18—All registries—Excluded genetic anomalies. Updated data including birth year 2018 (29 September 2020). Source: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en.
[b]VSD: four cases were surgically corrected and four closed spontaneously.
[c]ASD: three cases were surgically corrected and six closed spontaneously.
[d]TF: all cases were surgically corrected.
[e]PDA as only CHD in term infants (≥37 weeks) and still present 6 months after birth or if surgery/catheter closure is required.
[f]PDA: two cases were surgically corrected and three closed spontaneously.

Table 2 Data collected on maternal history during pregnancy in preadoption medical reports of the 926 children from Russia

	Children with CHDs ($n = 90$)	Children without CHDs ($n = 836$)	Odds ratio
Maternal history during pregnancy	*n* (%)	*n* (%)	
Drinking alcohol	31 (34.4)	239 (28.6)	1.31
Illegal drugs intake	5 (5.6)	53 (6.3)	0.87
Smoking	9 (10)	141 (16.9)	0.55
Uncontrolled pregnancy	19 (21.1)	168 (20.1)	1.06

CHDs, congenital heart defects.

Nepal. It is important to remember that the absence of information on medical pathologies and social problems of the mother in preadoption medical reports does not exclude their existence.

Medical reports of the two children with CHDs from India and the child from Ethiopia did not describe data from the mother. Medical report of the child with CHD from Latin America only described that the mother was a prostitute. Of the six children with CHDs from Kazakhstan, only two medical reports described data from the mother indicating that the pregnancy had not been controlled. Medical reports of the two children with CHDs from Eastern Europe only indicated that the mother was an alcoholic. Data collected on maternal history during pregnancy in preadoption medical reports of the 926 children from Russia are described in *Table 2*. It highlights that 31 (34.4%) of the children with CHDs had a history of alcohol prenatal exposure (odds ratio = 1.31). These children showed the following CHDs: present VSD (8), ASD (6) and PVS (3); surgically corrected TF (2), VSD (4) and ASD (2); closed spontaneously VSD (3), ASD (2), and PDA (1).

Burd *et al.*[10] reviewed the prevalence of CHDs associated with foetal alcohol spectrum disorder (FASD). In the 12 case series studies of subjects with FASD, the proportion of cases with ASD, VSD, other defects, or unspecified CHDs ranged from 33% to 100%. From the 14 retrospective studies, the rate of ASD and VSD was 21%, other structural defects 6%, and unspecified defects were 12%. For the two case–control studies, the odds ratio of CHDs ranged from 1.0 (subjects with foetal alcohol effect) to 18.0 (subjects with foetal alcohol syndrome). In the one prospective study of CHDs, the odds ratio for a child to have CHDs and FASD was 1.0.

This study shows that the prevalence of CHDs among assigned children for intercountry adoption is very high. Regarding the underlying causes, it is possible that multifactorial aetiologies or environmental aetiologies, especially prenatal alcohol exposure, have an important influence as a potential pathogenesis of CHDs in these children.

Conflict of interest: none declared.

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