Congenital Cardiac Malformations in Pediatric Necropsies: Characteristics, Associations and Prevalence

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Abstract

Background: In Brazil, since 2001, the congenital abnormalities have represented the second cause of death in children younger than one year, with cardiovascular defects being responsible for 39.4% of these deaths.

Objectives: To establish the prevalence and the characteristics of the congenital cardiac malformations in pediatric necropsies performed in Hospital Regional da Asa Sul, Brasília, DF, Brazil, from January 1996 to December 2007.

Methods: This is a descriptive, cross-sectional study that reviewed 1,591 necropsies performed from January 1996 to December 2007 and found 189 (11.9%) with congenital cardiac malformations, included in this study.

Results: The cardiac abnormalities were observed mainly in the group of live births (117/61.9%), followed by the stillbirths (35/18.5%), the infant group (30/15.9%) and the preschoolers' group (7/3.7%), with no cases identified among school-aged children. The main alterations detected were: interatrial communication in 96 patients (27%), interventricular communication in 66 patients (18.5%) and patent ductus arteriosus in 51 (14.3%), with no predominance of either sex. In 133 patients (70.4%), the cardiopathies were multiple and in 96 (50.8%) they were associated with anomalies in other organs and systems; among these, 45 (23.8%) presented cardiopathies as syndrome components, especially trisomies, at all age ranges.

Conclusions: The results of the present study show a high prevalence of congenital cardiac anomalies in our country and distribution and association that were similar to the ones observed in developed countries. The high mortality associated to such anomalies highlights the need for more comprehensive research in order to identify the risk factors and seek the primary prevention of some of these defects. (Arq Bras Cardiol 2010; 94(3):275-280)

Key words: Heart defects, congenital / mortality; prevalence; autopsy.

Introduction

Congenital malformations are associated with high mortality and it has been estimated that approximately 3% of the newborns present an important malformation, with cosmetic or functional significance, being the main cause of death, disease or disability among children[1].

In Brazil, the congenital abnormalities constitute the second cause of child mortality, being responsible for 11.2% of these deaths[2]. Several studies have reported that the cardiovascular system is the one most often affected by congenital malformations, associated or not to other malformations[1,3-5]. In 1997, the cardiovascular defects were responsible for 39.4% of all child deaths due to malformations, followed by nervous system defects (18.8%)[2,6].

The impact of congenital abnormalities on child mortality depends on several factors, including their prevalence, the quality and availability of medical and surgical treatment and the effectiveness of primary prevention measures[7,8]. The awareness of the most prevalent anomalies and the possible associated risk factors can allow an early intervention directed at primary prevention, with a positive impact on the quality of life of the child and its family.

The aims of the present study are to estimate the prevalence and study the morphologic characteristics of congenital cardiac malformations identified in pediatric necropsies performed at Hospital Regional da Asa Sul, Brasília, DF, Brazil, from January 1996 to December 2007.

Methods

A descriptive, cross-sectional study was carried out, which consisted in the review of patients' files from the Cytopathologic and Pathologic Anatomy Center of Hospital Regional da Asa Sul (HRAS), of all deaths that occurred in this hospital between January 1996 and December 2007. The HRAS is a public hospital and a reference one for high-risk pregnancies in the Federal District (DF).

Among the necropsies performed at the HRAS, all that presented cardiac malformations were reviewed by the author and a pathologist. The following variables were analyzed: maternal and child's age, necropsy diagnosis, sex, cardiac malformations and associated ones. Cardiorespiratory

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Manuscript received July 25, 2009; revised manuscript received July 25, 2009; accepted September 21, 2009.

anatomical blocks and hearts that had been stored at the Service were reviewed and classified.

The ages were grouped according to the classification of Nelson Miyague as: stillbirths (children weighing more than 500 g that had intrauterine death), live births or neonates (children that were born alive and died up to the 28th day of life, either premature or not), infants (children that died between the 29th day and 11th month of life), preschoolers (children that died between 1 year and 6 years and 11 months of age) and school-aged children (children that died between 7-14 years and 11 months of age).

The project was approved by the Ethics Committee in Research of the State Secretary of Health of the Federal District (SES/DF) under protocol #211/08.

The data were analyzed using the BioEstat[9] statistical software, release 5.0. The statistical tests are described in the text.

Results

The total number of deaths in Hospital Regional da Asa Sul, from January 1996 to December 2007, was 4,319 and 1,591 necropsies were performed during this period, of which 189 (11.9%) presented congenital cardiac malformations. There was a slight predominance of the male sex (52.4%) when compared to the female sex (47.1%), albeit without statistical significance, as well as one case (0.5%) of undetermined sex ($\chi^2 = 0.282$; $p = 0.59$). A total of 117 (61.9%) malformations were observed in the group of live births or neonates, 35 (18.5%) in the group of stillbirths, 30 (15.9%) in the group of infants and 7 (3.7%) in the group of preschoolers, with no malformation cases being observed in the group of school-aged children.

From 1996 to 1999, the rate of necropsies was 52%, progressively decreasing to 35% from 2000 to 2002, 24.6% from 2003 to 2006 and 14% in 2007. Table 1 shows the temporal variations that occurred in this period, with no statistical significance between the different proportions of congenital cardiac malformations observed at the necropsies performed throughout the study period (meta-analysis for several proportions, p=0.33).

The most common cardiac abnormalities in the 189 patients were the interatrial communication (IAC) in 96 (27%) of them, the interventricular communication (IVC) in 66 (18.5%) and patent ductus arteriosus (PDA) in 51 (14.3%) (Table 2). In total, 357 congenital cardiac defects were identified and in 133 of them (70.4%), the cardiopathies were multiple, with the predominance of the following associations: IAC + PDA, IAC + IVC, IAC + IVC + PDA, IAC + aorta coarctation and PDA + IVC. These associations were predominantly present in children with chromosomal/gene alterations.

When the distribution of these abnormalities was analyzed in relation to the age ranges, it was observed that the interatrial and interventricular communications and the patent ductus arteriosus represented 59.8% of all observed malformations, being the most prevalent ones among neonates, stillbirths and infants. Among the preschoolers, the IAC and IVC were the only abnormalities observed.

Of the 35 stillbirths, 30 (85.7%) presented cardiac malformations associated with other organs and systems, with a predominance of musculoskeletal system malformations in 8 (26.7%) (clubfoot, dolichocephaly and short thorax), central nervous system malformations in 6 (20%) (holoprosencephaly, anencephaly and rachischisis), sensory system malformations in 5 (16.7%) (microphthalmia, nose agenesis, macroglossia), urinary system malformations in 4 (13.3%) (horseshoe kidney), circulatory system malformations in 3 (10%) (single umbilical artery) and respiratory system malformations in 1 (3.3%) (pulmonary dysplasia). Of the group of 35 stillbirths, 7 patients (20%) presented a syndromic diagnosis, with three having unclassified trisomies, two with Patau syndrome, one with Down syndrome and the last one with Dandy-Walker syndrome.

Among the live births, 58 (49.5%) presented cardiac malformations associated with other organs and systems, with a predominance of musculoskeletal system malformations in 14 cases (24.1%) (clubfoot, diaphragmatic hernia, short neck, conically shaped skull, malformations in the upper and lower limbs), genitourinary system malformations in 13 cases (22.4%) (horseshoe kidney, polycystic kidney, kidney agenesis and external genitalia agenesis), digestive system malformations in 13 (22.4%) (esophageal, biliary tract and duodenal-jejunal atresia, intestinal malformations, Imperforate anus, Merkel's diverticulum), sensory system malformations in 8 cases (13.8%) (exophthalmia, microphthalmia, auricular malformations), central nervous system in 7 cases (12%) (holoprosencephaly, corpus callosum agenesis, anencephaly) and immunological system malformations in 3 cases (5.2%) (splenic agenesis and polysplenia).

A higher prevalence of syndromic diagnoses was observed among the live births, with 31 (26.5%) cases, with trisomies being the most frequent defects (Down, Edwards and Patau syndrome).

Among the infants, 2 (6.7%) presented cardiac malformations associated to sensory system malformations (ear agenesis and malformations), one case (3.3%) presented a central nervous system malformation (corpus callosum agenesis) and one (3.3%) presented a musculoskeletal malformation (inguinal hernia). In three of these patients, the abnormalities were part of an associated syndrome, with two cases being associated to Down syndrome and one to Edwards syndrome.

In the group of preschoolers, two presented cardiac abnormalities associated with central nervous system malformations (microcephaly) and one to a digestive system malformation (Merkel's diverticulum). In this group, there was only one patient with Down syndrome, associated with IVC and atrioventricular septal defect.

Forty-five children presented cardiac malformations associated with syndromes with multiple anomalies (Table 3). In this group, trisomies predominated, mainly Down syndrome at all age ranges, except in the still birth group, affecting mainly girls (7/2). The IVC was present in 25 (55%) of these children.

Regarding the maternal age in this study population, 156 mothers were younger than 35 years, including 32 younger than 19 years; 16 were 35 or older and 17 cases lacked this information. Even when adding these 17 mothers to the 16 that were 35 or older, the younger group predominates, representing the population treated at our hospital. The

present study did not show a statistically significant association between the maternal age ≥ 35 years and the presence of congenital abnormalities (meta-analysis for several proportions p = 0.056), not even when the latter were components of Down syndrome (Fisher exact test: p = 0.16).

Discussion

Congenital cardiopathies are the most frequent fetal malformations. Results from different studies have shown incidences varying from 4:1.000 - 50:1.000 live births[10]. These abnormalities appear as the main cause of death in childhood in the first-world countries. With improvements in the diagnosis and treatment, the mortality due to congenital cardiopathies has decreased considerably in the last years, thus increasing the prevalence of congenital cardiac malformations, which has a devastating socioeconomic and emotional impact, requiring more efforts regarding prevention measures.

In Brazil, the prevalence of these defects varies between 5.5:1000-13.2:1000 live births[6,8,11-15]. Since 2001, the congenital abnormalities are the second cause of mortality in children younger than one year in our country, according to the Mortality Information System of the Ministry of Health, being responsible for 11.2% of these deaths, with 39.4% of all children's deaths due to malformation being ascribed to cardiovascular defects in 1997[16]. However, there have been few studies on congenital cardiac malformations in our country[7,8,11-14,17].

The total number of deaths in Hospital Regional da Asa Sul, Brasília, Federal District, Brazil, was 4,319, from January 1996 to December 2007, of which 1,591 (36.84%) were submitted to necroscopic examination.

Of these, 189 (11.9%) presented isolated congenital cardiac malformations, single or multiple, or associated to abnormalities in other organs or systems, with temporal variation in the study period presenting no epidemiological effect on the population.

The statistical analysis showed that the number of necropsies performed and the ones that presented congenital malformations during the study period remained uniform, in spite of the progressive decrease in the number of necropsies. The high prevalences observed in the present study can be attributed to the characteristics of the HRAS, which is a reference hospital for the treatment and diagnosis of maternal and children's diseases and high-risk pregnancies.

None of the Brazilian reports allow a direct comparison with our study. The congenital cardiac defects have a wide-ranging presentation, from those that progress without associated symptoms to those related to significant symptomatology and high mortality, demonstrating the variety of abnormalities and degrees of cardiovascular structural involvement that can be observed morphologically.

The presence of any structural alteration at birth, diagnosed through the macroscopic assessment in all necropsies performed between 1996 and 2007 was considered congenital malformation.

Approximately 40 types of cardiovascular anatomic defects have been described[18]. Twenty-three different cardiac malformations were identified among the 189 studied necropsies. The large variety of possible alterations, together

Table 1 - Association between the number of deaths, performed necropsies and congenital cardiopathies diagnosed at the necropsy, per year, at HRAS, between 1996 and 2007

Year	Total deaths	Total necropsies n (%)	Congenital Cardiopathies n (%)
1996	428	204 (47.6)	19 (9.3)
1997	451	217 (48.1)	23 (8.7)
1998	470	247 (52.5)	36 (14.6)
1999	340	201 (59.1)	20 (10)
2000	316	105 (33.2)	18 (17.1)
2001	397	152 (38.3)	21 (13.2)
2002	333	111 (33.3)	9 (8.1)
2003	305	87 (28.5)	15 (17.2)
2004	352	84 (23.9)	9 (10.7)
2005	320	67 (20.9)	6 (9)
2006	278	70 (25.2)	9 (12.9)
2007	329	46 (14)	4 (8.7)
Total	4319	1591 (36.8)	189 (11.9)

with the different study methods, population selection and regional differences reflect the difficulty to obtain comparable data and explains the discrepancies reported in the literature[13]. However, the results observed in the present study do not differ much from the ones found in the national and international literature.

In a retrospective study carried out in a university hospital in Belo Horizonte, state of Minas Gerais[11], Brazil, the prevalence of cardiac malformations was 11.82% births (live births and stillbirths) and 87.52% among the stillbirths, diagnosed at the necropsy. In another study in necropsies carried out in a university hospital in Niteroi, state of Rio de Janeiro, Brazil, between 1967 and 1992, the frequency of congenital malformations was 9%, of which 50% of them were cardiac malformations[12]. However, in this report, there is no information about the most frequent types of cardiac malformations and their distribution per age range.

Šamánek[19,20] and Brent[21] reported a prevalence of 6.2% of congenital cardiopathies in necropsies, responsible for 7.4% of the total mortality among live births and 41.4% of the congenital malformations diagnosed in Bohemia, currently the Czech Republic for 25 years, before the introduction of advanced methods of neonatal cardiac surgery. The most frequent abnormalities were the interventricular communication and the patent ductus arteriosus[19].

In all studies that have been published, not only in Brazil[7,12,15-17] but also in other countries[20,21], one can observe the high prevalence of congenital cardiac malformations in live births and stillbirths, with the most frequent congenital defects being the interventricular and interatrial communications[13] and the patent ductus arteriosus[21]. These congenital cardiac defects,

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Table 2 – Distribution of the number of cases of children with cardiac malformations submitted to necropsies at HRAS, between 1996 and 2007, by sex and age range

	Stillbirths		Neonates		Lac Infants		Preschoolers		
	Masc.	Fem.	Masc.	Fem.	Masc.	Fem.	Masc.	Fem.	n (%)
IAC	6	5	39	28	8	7	2	1	96 (27)
IVC	11	7	15	18	6	8	0	1	66 (18,5)
PDA	2	2	16	22	5	4	0	0	51 (14,3)
pulmonary hypoplasia	1	0	7	5	3	0	0	0	16 (4,5)
Aortic Coarctation	0	2	5	2	3	1	0	0	13 (3,7)
Aortic arch hypoplasia	1	1	6	5	0	0	0	0	12 (3,4)
LSVCP	0	1	5	3	1	0	0	0	10 (2,8)
Single Ventricle	2	1	4	3	0	0	0	0	10 (2,8)
Aortic dextroposition	0	1	2	5	1	0	0	0	9 (2,5)
TGV	0	0	1	2	3	2	0	0	8 (2,3)
Single atrium	2	1	1	2	1	1	0	0	8 (2,3)
Aortic valve atresia	0	1	3	4	0	0	0	0	8 (2,3)
Double RV outflow tract	0	2	3	0	1	2	0	0	8 (2,3)
Dextrocardia	0	1	3	1	2	0	0	0	7 (2)
LV hypoplasia	1	0	3	3	0	0	0	0	7 (2)
Pulmonary valve atresia	1	1	1	2	0	1	0	0	6 (2)
RV hypoplasia	0	0	2	2	0	0	0	0	4 (1)
Single arterial trunk	1	1	2	0	0	0	0	0	4 (1)
Atresia mitral	1	0	2	1	0	0	0	0	4 (1)
TAPVD	0	0	2	2	0	0	0	0	4 (1)
Tricuspid atresia	0	0	2	1	0	0	0	0	3 (0,8)
Tetralogy of Fallot	0	0	0	1	1	0	0	0	2 (0,6)
Total (%)	29(8,1)	27(7,6)	124(34,8)	112(31,4)	35(9,8)	26(7,3)	2(0,5)	2(0,5)	357(100)

IAC - interatrial communication; IVC - interventricular communication; PDA - patent ductus arteriosus; LSVCP - Persistence of the left superior vena cava; TGV - Transposition of the great vessels; RV - right ventricle; LV - left ventricle; TAPVD - total anomalous pulmonary venous drainage.

which affect mostly children from the neonatal age[22] or even infants, are the most prevalent ones regardless of the population and the methodology used[14], in agreement with the results of the present study. Some trends observed in the present study are also in agreement with the literature: higher frequency of multiple or associated cardiac malformations, in comparison to isolated ones and the number of patients with genetic syndromes.

Several measures for the prevention of congenital abnormalities have been taken in developing countries. It is difficult to safely determine the cause-effect relation between the environmental factors and the malformations. It is believed that approximately 25% of the congenital anomalies have a genetic etiology, whereas 15% are ascribed to environmental factors (ionizing radiation, prenatal infections, chronic maternal disease, environmental agents and drugs) and 60% are of unknown causes[23].

In the present study, 45 (23.8%) children presented cardiopathies as syndrome components and it is the noteworthy the high prevalence of chromosomal diseases, especially trisomies, in all age ranges: 15.6% of the stillbirths; 68.9% of the live births, 13.3% of the infants and 2.2% of the preschoolers. The high prevalence of chromosomal diseases in children with cardiopathies and multiple abnormalities is in agreement with what has been described in the literature, although the percentages found in the literature vary, depending on the methods used and the places where the studies were carried out and this reinforces the recommendation of performing a chromosomal analysis of all newborns or stillbirths with multiple abnormalities[11].

In all age ranges, except in the stillbirth group, Down syndrome was the most common chromosomal syndrome, affecting

Table 3 - Syndromes and associated congenital cardiac malformations in children submitted to necropsy at the HRAS between 1996 and 2007.

Associated Syndromes	Congenital cardiac malformations
Trisomy 21 (Down)	IAC, IVC, PDA, double RV outflow tract, pulmonary stenosis, truncus arteriosus communis, anomalous drainage of pulmonary veins, polycystic kidneys, horseshoe kidney, Merkel diverticulum, short neck, low ear implantation, ear agenesis, nipple agenesis and single umbilical artery.
Trisomy 18 (Edwards)	IVC, single ventricle, tricuspid and mitral valve fusion, double RV outflow tract, PLSVC, pulmonary artery hypoplasia, LV hypoplasia
Trisomy 13 (Patau)	IAC, IVC, PDA, TGV, pulmonary artery hypoplasia, holoprosencephaly, cyclopia, microphthalmia, overriding aorta, pulmonary atresia, cleft lip, dolichocephaly, inguinal hernia, outer ear agenesis
Trisomy 9	PLSVC
Unclassified trisomy	IAC, IVC, PDA, TGV, mitral atresia, conically shaped skull, short neck, pseudo-truncus arteriosus, pulmonary artery hypoplasia, agenesis of basal vessels, single umbilical artery, PLSVC, TAVB, horseshoe kidney, double RV outflow tract, low implantation of tricuspid valve, aortic arch hypoplasia, aorta dextroposition
Dandy Walker	Single ventricle, horseshoe kidney, single umbilical artery, PDA, pulmonary valve atresia
Pentalogy of Cantrell	Ectopia cordis
Polysplenia	Bilateral ventricular hypertrophy, IAC, annular pancreas, Merkel diverticulum, cervical-auricular vertebral complex.
Malformative	IAC, IVC, aorta coarctation, PLSVC, pulmonary valve atresia, holoprosencephaly, cleft lip, cleft palate, polysplenia, ventricular hypertrophy
Prune Belly	IAC, PDA, pulmonary artery hypoplasia, aortic arch hypoplasia
Potter	IAC, cystic kidneys, pulmonary atresia, lower-limb agenesis, kidney agenesis, rectal agenesis, PLSVC, dolichocephaly
Hypoplasic left heart	Aortic valve atresia, mitral atresia, LV absence, aorta atresia, ascending aorta hypoplasia
Marfan	Bivalve aorta, left subclavian originating from ascending aorta and ductus arteriosus junction

IAC - interatrial communication; IVC - interventricular communication; PDA - patent ductus arteriosus; PLSVC - persistent left superior vena cava; TGV - Transposition of the great vessels; RV - right ventricle; LV - left ventricle; ADPV - anomalous drainage of the pulmonary veins ; TAVB - total atrioventricular block.

mainly girls (7/2) and the interventricular communication was present in 55% of these children. Other genetic syndromes might have been underestimated, as their diagnoses depend on procedures that are not available yet at our hospital. Maternal age ≥ 35 years has been associated with the presence of congenital abnormalities, with risk increasing with age[2,10]. However, this association was not observed in the present study, or in cases where the congenital cardiopathy is the component of a syndrome, especially Down syndrome, which is not in agreement with what has been observed by other authors[11,24]. Such divergence might be due to the size of the present sample and the predominance of young mothers. The maternal age of the present study population is noteworthy – 156 mothers were 35 years or younger, including 32 mothers younger than 19 years, which reflects the population treated at our hospital.

Vidal et al[25] also reported a proportional increase in the number of women younger than 20 years treated at the Instituto Materno Infantil de Pernambuco, a tertiary and reference hospital for high-risk pregnancies and newborns.

Conclusions

The results of the present study show a high prevalence of congenital cardiac abnormalities in our country, with distribution and associations that are similar to the ones observed in developed countries. The high mortality associated with these abnormalities, which constitute the second cause of child death in Brazil, raises the awareness of the need to perform more comprehensive researches, in order to know the risk factors and institute prevention programs for some of these defects.

Acknowledgements

To Professor Manuel Ayres, for his assistance with the statistical analysis. To Dr. Alberto Henrique Barbosa and Dr. Regina Maria de Araújo Froz, for their support of this study.

This study is part of the monograph presented as a requirement for the Bachelor of Science (BSc) degree in Biological Sciences at Universidade Católica de Brasília (UCB).

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any post-graduation program.

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