Congenital Heart Diseases in a Reference Service: Clinical Evolution and Associated Illnesses

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Abstract

Background: **Several factors, which include prenatal diagnosis and availability of new therapeutic procedures, have contributed to change the profile of patients with congenital heart disease (CHD). Knowing these changes is important to a better health care.**

Objectives: **Description of profile of patients with CHD in a reference service in the State of Rio Grande do Sul, Brazil.**

Methods: **It is a cross-sectional study including 684 patients with CHD in a service of pediatric cardiology from January 2007 to May 2008. We interviewed the patients (and/or their parents) and examined these patients (congenital malformations, anthropometric measures). Moreover, their charts were reviewed in order to detail heart diseases, procedures and echocardiography.**

Results: **Patients were from 16 days to 66 years old, 51.8% were female, and 93.7% were Caucasian. The mean age at diagnosis was 15.8 ± 46.8 months. Ventricular septal defect, patent ductus arteriosus and tetralogy of Fallot were the most prevalent CHD. 59.1% of examined patients, whose average age was 44.3 ± 71.2 months, have been undergoing therapeutic procedures; 30.4% had congenital extracardiac malformations; and 12 patients had genetic syndrome. Regarding development, 46.6% had low weight and height gain, and 13.7% had neuropsychomotor delay. Furthermore, 18.4% had family history of congenital heart disease.**

Conclusions: **Neuropsychomotor delay and low weight and height gain may be related to CHD. Establishing a profile of patients with CHD, who were treated at an institution of reference, may function as a basis in which health care of this population can be planed appropriately. (Arq Bras Cardiol 2010; 94(3):313-318)**

Key words: **Heart defects, congenital; referral and consultation; clinical evolution**

Introduction

Congenital heart diseases (CHD) are common in alive newborns, and are even more frequent in fetuses and have high mortality rate in child's first year of life[1]. According to studied population, prevalence of CHD undergoes transformations and may reach up to 1% in postnatal population[2].

Two Brazilian studies analyzed prevalence of congenital heart diseases in alive newborns and identified 5.5:1,000 newborns between 1989 and 1998[3] and 9.58:1,000 newborns between 1990 and 2003[4]. These malformations can be isolated cases, part of syndromes or results of genetic diseases, such as deletion of chromosomal regions, or it can be caused by environmental factors (use of teratogenic drugs by mothers, infections during pregnancy)[5].

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There are few published studies in Latin America that have analyzed the profile of patients with CHD, most of which is related to the Latin-American Collaborative Study of Congenital Malformations (ECLAMC)[6]. A Colombian study found prevalence of 1.2 birth cases per 1,000 alive newborns with congenital heart disease between 2001 and 2005. However, 65.5% had severe heart diseases, and 32.7% had associated extracardiac malformations[7]. Such studies are important to improve the plan of population's health care and, consequently, to reduce morbimortality rate.

The objectives of this study were: (i) obtaining the profile of patients with congenital heart diseases, who were treated at a reference service in the State of Rio Grande do Sul, Brazil; (ii) establishing the main types of congenital heart defects and (iii) analyzing the presence of associated malformations and other demographic characteristics of patients.

Methods

This was a transversal study from January 2007 to May 2008 in which 684 patients with congenital heart diseases were

included randomly by raffle. These patients were treated in pediatric cardiology department of our institution, in the State of Rio Grande do Sul, Brazil. Patients with Down Syndrome, Edwards Syndrome and Patau Syndrome were excluded. Patent ductus arteriosus in children under three months old and patent foramen ovale were not considered as congenital heart diseases.

Interviews with patients and/or their parents aim getting information about prenatal and perinatal periods, symptoms, neuropsychomotor development, presence of other congenital malformations and family history of congenital heart diseases and genetic syndromes. Physical examination emphasized congenital malformations and anthropometric measures (percentiles of weight, height and head circumference by age, according to parameters of National Center for Health Statistics/ National Center for Chronic Disease Prevention and Health Promotion-2000)[8]. Charts of patients were also reviewed in order to obtain more detailed information about heart diseases and performed procedures. Echocardiography of all patients were performed by a trained examiner, according to protocol of sequential analysis and functional assessment in equipment such as Toshiba Power Vision 6000, model SSA-370. We also obtained results from other imaging examinations, including angiography and magnetic resonance.

This study was approved by the Institutional Ethics Committee, and all patients signed a Free and Informed Consent (FICT).

In statistical analysis, we used average, standard deviation, median and Mann-Whitney test, for continuous variables, and frequency and chi-square, for categorical variables. For that matter, we used the program Statistical Package for Social Sciences (SPSS). A critical alpha of 0.05 was considered as a level of statistical significance.

Results

In this study, 48.2% of 684 patients were male. Most patients were Caucasian (93.7%), 3.1% were *Pardo* (mixture of Caucasians, Blacks and Amerindians) and 3.2% were Black. 60.3% were European descendant; 10.6% African, 15.6% indigenous, and 1.9% Latin American. The average age at interviews was 12.7 ± 9.8 years old (from six days to 66 years old). The average age at diagnosis of heart disease was 15.8 ± 46.8 months old, with a median of one month, ranging from the first day of life up to 40 years old. Almost half patients were diagnosed with heart disease before completing one month old. Furthermore, 3.1% were also diagnosed in fetal period (Figure 1).

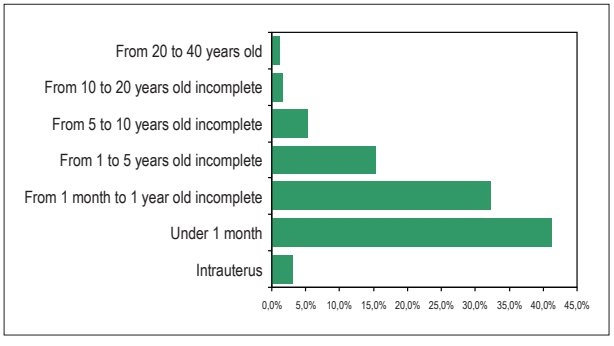

Figure 1 - Distribution of patients according to age at diagnosis of congenital heart disease

Regarding the type of congenital heart disease, 32.5% were cyanotic. The most common heart disease was ventricular septal defect – isolated cases or associated with other injuries (Table 1). The heart diseases, which were diagnosed after 20 years old, are: atrial septal defect in four patients; aortic coarctation in one patient; Ebstein's anomaly in two patients, complex heart disease (double outlet left ventricle, with discordant atrioventricular connection and severe pulmonary stenosis) in one patient. The heart diseases, which were diagnosed in patients between 12 and 20 years old, are: ventricular septal defect in two patients; atrial septal defect in one patient, *truncus arteriosus* – type I in one patient; Ebstein's anomaly in two patients; patent ductus arteriosus in one patient and partial anomalous pulmonary venous drainage in one patient. Aortic arch was located in the left in 93.7% of cases and in the right in 3.4% of cases. We could not determine its position in other patients.

The heart diseases associated with right aortic arch are tetralogy of Fallot; double outflow of right ventricle; pulmonary atresia with ventricular septal defect; atrioventricular septal defect with double outlet left ventricle (aorta arising anterior to pulmonary artery, severe pulmonary stenosis and dextrocardia); corrected transposition of great arteries; tricuspid atresia with pulmonary atresia and pulmonary atresia with dextrocardia and left isomerism. There were six cases of dextrocardia with *situs solitus*, one case of *situs inversus* with levocardia, four cases of left isomerism with levocardia, one case of left isomerism with dextrocardia, two cases of *situs inversus* with dextrocardia and one case of right isomerism with dextrocardia. All cases were associated to intracardiac malformations.

In this study, 59.1% of patients were treated with therapeutic procedures, with average age of 44.3 ± 71.2 months old, median of 19.2 months, ranging from first day of life up to 59 years old. Surgery of a 59 years old patient was closure of atrial septal defect. Average time from diagnosis to first performed procedure was 12.1 months. Distribution of patients according to the first performed therapeutic procedure is shown in Table 2. Total correction of tetralogy of Fallot was the most frequent first performed procedure.

Other congenital malformations were found in 30.4% of patients – isolated cases or associated with syndromes. Syndromes of twelve patients were confirmed by geneticist, and syndromes of six patients were under suspect (they were been examined). The most common was Noonan syndrome. These data are shown in Table 3.

Regarding signs and symptoms, current or past, 27% of patients were asymptomatic, 55.4% had clinical manifestation of heart failure, and 32.5% had cyanosis. Patients with cyanotic heart disease presented more significantly history of dyspnea compared to non-cyanotic patients (76.1% and 45.5% respectively, $p < 0.001$). History of recurrent infections of upper airways was found in 38.9%, of lower airways in 13.6%,

Table 1 - Distribution of patients according to the kind of congenital heart disease and male/female proportion (M:F)

Congenital heart disease	Number (%) of patients	M:F
VSD with or without bicuspid aortic valve or PDA	95 (13,9)	1:1,3
Tetralogy of Fallot	88 (12,9)	1:0,7
Obstructive lesions of RVOT	67 (9,8)	1:1,5
Isolated ASD	66 (9,6)	1:1,9
CoA with or without associated mild injury	53 (7,7)	1:1
transposition of great arteries	36 (5,3)	1:0,7
Isolated bicuspid aortic valve	29 (4,2)	1:0,6
Obstructive lesions of LVOT	28 (4,1)	1:0,5
Ebstein's anomaly	22 (3,2)	1:1,7
VSD associated with obstruction RVOT	21 (3,1)	1:0,7
AVSD	19 (2,8)	1:1,4
ASD associated with obstruction of RVOT	19 (2,8)	1:1,1
VSD associated with obstruction of RVOT	18 (2,6)	1:0,8
Double RVOT	18 (2,6)	1:1
Mitral valvopathy	12 (1,8)	1:1
ASD associated with VSD	12 (1,8)	1:1,4
PDA	11 (1,6)	1:1,7
Corrected transposition of great arteries	10 (1,5)	1:0,7
Pulmonary atresia with VSD	10 (1,5)	1:1,5
Absent atrioventricular connection	10 (1,5)	1:1,5
double inlet ventricle	8 (1,2)	1:0,3
Truncus arteriosus	6 (0,9)	0:6
pulmonary atresia	5 (0,7)	1:0,2
Anomalous pulmonary venous return	5 (0,7)	1:4
AVSD associated with double RVOT	5 (0,7)	1:1,5
Interrupted aortic arch	3 (0,4)	0:3
Cor triatriatum	2 (0,3)	0:2
Obstruction of RVOT and LVOT	1 (0,1)	1:0
Hemitruncus	1 (0,1)	0:1
Pulmonary valve insufficiency	1 (0,1)	0:1
Aortic valve insufficiency	1 (0,1)	1:0
AVSD associated with double aortic arch	1 (0,1)	1:0
Double aortic arch with pulmonary valve agenesis	1 (0,1)	0:1

VSD – ventricular septal defect; PDA – patent ductus arteriosus; ASD – atrial septal defect; AVSD – atrioventricular septal defect; RVOT – right ventricle outflow tract; LVOT – left ventricle outflow tract; CoA – coarctation of the aorta.

Table 2 - Distribution of patients according to the first performed therapeutic procedure

Procedure	Number (%) of patients
Total correction of tetralogy of Fallot	65 (9,5)
Systemic-Pulmonary Shunts	36 (5,6)
Balloon Pulmonary valvuloplasty	33 (4,8)
Isolated closure of atrial septal defect	31 (4,5)
Corretion of coarctation of isolated aorta	31 (4,5)
Isolated closure of ventricular septal defect	21 (3,1)
Isolated Ligation of arterial ductus	18 (2,6)
Atrial septostomy	16 (2,3)
Pulmonary artery banding	15 (2,2)
Balloon aortic valvuloplasty	13 (1,9)
Resection of aortic subvalvar ring	11 (1,6)
Jatene Surgery	9 (1,3)
Others	105 (15,2)

of gastrointestinal tract in 1.9%, of urinary tract in 4.7%, and of meninges in 0.7%. There was no difference regarding the occurrence of these infections among patients with cyanotic or non-cyanotic heart disease. 0.3% of patients had defined diagnosis of immunodeficiency. 10.4% had seizures. 10.1% of patients prematurely born. Table 4 shows the most frequent abnormalities of theses patients in prenatal period and their heart diseases.

Regarding neuropsychomotor development, 13.7% of patients had some degree of delay. Patients with cyanotic heart disease had, more frequently, a history of neuropsychomotor delay when compared to non-cyanotic patients (20.3% and 10.6% respectively, $p = 0.001$). Patients with low weight and/or height gain had higher prevalence of neuropsychomotor delay when compared to patients with no low gain (22.3% and 6.3% respectively, $p < 0.001$). 22.7% of 459 patients in school or after-school age had some degree of learning difficulty at school, which was more frequent among cyanotic patients when compared to non-cyanotic patients (29.3% and 19.4% respectively, $p = 0.024$).

Distribution of patients under 12 years old, according to percentiles of anthropometric measures (weight and height) at the physical examination, showed that 23.7% and 29.1% of patients, respectively, had height and weight below 10th percentile. 5.9% and 4.5% of patients had weight and height above 90th percentile, respectively. Distribution of patients under three years old, according to percentile of head circumference by age, showed that 21.2% of patients were below 10th percentile.

46.6% of patients (or their relatives) reported history of low weight and/or height gain. These patients had more recurrent

Table 3 – Patients with genetic syndromes associated with congenital heart disease

Syndrome	Heart disease (number of patients)
Noonan	Severe PS (2)
Noonan	Mild PI (1)
Noonan	Moderate PS and mild apical muscular VSD (1)
Noonan	Tricuspid atresia with pulmonary atresia (1)
Noonan	AVSD, DLVOT, A arising anterior to PA (1)
Noonan	Partial AVSD
Suspicion of Noonan	Moderate PS (1)
Suspicion of Noonan	Mild VSD, ASD and moderate PS (1)
Di George	IAA, VSD, bicuspid aortic valve (1)
Trisomy 8	Large VSD and double aortic valve lesion (1)
Treacher-Collins	DRVOT with anterior A to PA and severe PS (1)
Treacher-Collins	Mild stenosis of left pulmonary branche (1)
18q22 deletion	ASD ostium secundum (1)
Ellis-Van Creveld	AVSD with double aortic arch (1)
Suspicion of Williams	VSD (1)
Suspicion of Marfan	Mitral valve prolapse and aortic ectasia (1)
Suspicion of Holt-Oram	ASD ostium secundum (1)

PS – pulmonary stenosis; PI – pulmonary insufficiency; VSD – ventricular septal defect; AVSD – atrioventricular septal defect; DLVOT – double left ventricle outflow tract; A – aorta; PA – pulmonary artery; ASD – atrial septal defect; IAA – interrupted aortic arch; DRVOT – double right ventricle outflow tract.

Table 4 – Abnormality on prenatal period and congenital heart disease

Abnormality	congenital heart disease
Diabetes mellitus type I	CoA, double ventricle outflow tract
Gestational diabetes mellitus	Tetralogy of Fallot, VSD, TGA, ASD with obstruction of RVOT
	Tetralogy of Fallot, double RVOT – Fallot type, AVSD with double RVOT
Alcohol	Tetralogy of Fallot
	PDA, VSD
Toxoplasmosis and tetracycline	Taussig-Bing, tetralogy of Fallot
Fluoxetine	Hemitruncus
Phenobarbital	VSD, PDA
Propylthiouracil	ASD
X-ray	ASD, bicuspid aortic valve
Valproic acid and ritalin	Pulmonary branche stenosis
Anti-retroviral to HIV	Tetralogy of Fallot
Amitriptyline and carbamazepine	VSD
Captopril and hydrochlorothiazide	
Phenobarbital, phenytoin and carbamazepine	

VSD – ventricular septal defect; PDA – patent ductus arteriosus; ASD – atrial septal defect; IAC – atrial septal defect; RVOT – right ventricle outflow tract; CoA – coarctation of the aorta.; TGA – transposition of great arteries.

infections of the upper airways (46.4% and 32.3% respectively, $p < 0.001$) and more recurrent pneumonia (18.8% and 9% respectively, $p < 0.001$) when compared to patients with no low weight gain. Patients with cyanotic heart disease had a history of low weight gain more frequently when compared to non-cyanotic patients (58.6% and 40.9% respectively, $p < 0.001$).

Regarding family history, 2% had parents related by blood, 18.4% had family members with congenital heart disease, and 9.2% had relatives with genetic syndromes (mainly Down syndrome). Eight patients had a twin (brother or sister) with congenital heart disease. Two twin sisters with Noonan syndrome were included in this study. One of them has severe pulmonary stenosis, and the other one has mild pulmonary valve insufficiency. Two twin brothers with outflow perimembranous ventricular septal defect were also included. One female patient with atrial septal defect reported that her twin sister has the same heart disease.

Discussion

In this transversal study, which was performed in a reference center for congenital heart diseases in southern Brazil, we observed that the heart disease most common were ventricular septal defect, associated or non-associated to other cardiac malformations. Furthermore, in almost one third of our sample, we found, at least, one associated extracardiac malformation.

It is important to emphasize that early diagnosis, especially for mild injuries, is growing and also contributes to increasing incidence of congenital heart diseases. Prenatal diagnosis has been a major contributor to incidence increasing of findings. As well as other Brazilian articles[9], most patients in this study were diagnosed on the first year of life, when first symptoms usually appeared, representing 73.5% of cases. 3.1% of patients were diagnosed during prenatal period. In international literature, 43.6% of patients with heart disease are diagnosed during the first week of life, 70% are diagnosed up to six months old, and 86% are diagnosed up to two years old[10,11].

As a result of advances in diagnostic methods, especially in early therapeutic procedures, number of susceptible individuals to height delay – the most common clinical problem – increased, due to a growth in life expectancy of these patients[1]. This association is more significant if it is an isolated case in patients with cyanotic heart disease[12]. In this

study, patients with cyanotic heart disease had more often a history of low weight gain when compared to non-cyanotic patients.

According to literature, among cyanotic patients, those patients with pulmonary arterial hypertension were the most severely affected with weight delay[13]. Evidences show, without classifying patients in cyanotic or non-cyanotic congenital heart disease, that height and weight at birth and during this study and height and weight growth of patients with congenital heart disease were lower when compared to healthy children[2]. Furthermore, low weight gain is more common than height delay[12].

There are also cases in which probability of children with cardiovascular malformations being small for gestational age has increased, especially those children with tetralogy of Fallot, complete atrioventricular septal defect, left ventricle hipoplasia or great ventricular septal defect[14]. In national literature, there are cases of correlation between low weight at birth (≤ 2,500 g) and higher incidence of congenital heart desease[4].

Regarding congenital heart disease types, this study showed that ventricular septal defect, associated or non-associated with other cardiac malformations, is the most common heart disease, followed by tetralogy of Fallot and obstruction of right ventricle outflow. When compared to studies in Londrina (State of Paraná, Brazil)[3], although our institution apparently is characterized as a center of reference of similar complexity – receiving many patients from the state or other states -, there is a higher prevalence of severe heart diseases.

This rate of severe heart diseases is higher because our sample was constituted by patients who were in attendance in an ambulatory service. For that reason, these patients have been examined frequently, increasing estimated values. A prospective study in Iceland[10] showed a trend of increasing prevalence of mild heart diseases, probably due to great efficiency in diagnosis and abortion procedures in cases of more severe injuries. Incidence of severe heart diseases, in that study, had no changes over time. Besides, severe heart diseases appear with a lower prevalence.

Patients with congenital heart diseases may have other malformations, chromosomal defects or well-established syndromes. In this study, extracardiac malformations were found in almost one third of patients. Malformation of ears and ocular hypertelorism were the most prevalent injuries. This rate is higher than another studies[15], which, even in 1971, have described similar extracardiac malformations in approximately 25% of patients. We must be cautious in comparing our data with other data in literature.

While most studies treat of prevalence in a certain region during a specified period of time, this study provides a random sample of ambulatory, transversal in time, in which patients with less severe heart disease, survivors of previous surgeries and complications of neonatal period, were allocated. An example is the absence of patients with hypoplastic left heart syndrome in the sample. This is a heart disease with high mortality rate in neonatal period, according to literature[16,17].

Moreover, it is important to emphasize that this study is a description of patients who were treated in a specialized service and necessarily is influenced by referral and anti-referral patterns. For example, this study has lower frequency of patients with mild heart diseases, because many of these patients have been examined infrequently when compared to patients with severe heart diseases. There is a possibility that many patients with mild injuries could have had spontaneous resolution of the defect, small atrial or ventricular septal defect and mild pulmonary valve stenosis.

Conclusion

Information such as that reported in this study is important to establish a general framework of the profile of patients with congenital heart diseases, who were in attendance daily in an institution of reference. Moreover, it is important as basis for new studies, because the profile of these patients has undergone significant transformations in recent years, due to an increasing of life expectancy of patients with complex diseases and, consequently, due to an increasing of impact of comorbidity, sequelae and residual injuries. It is needful to stress importance of neuropsychomotor delay and/or weight delay, because they are the main sequelae when associated with kinds of therapeutic procedure of each patient. It is worth discussing etiology of increasing incidence of cardiac malformations, as well as diseases associated with extracardiac malformations.

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