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Original Article

Clinical study of external dysmorphism in congenital heart disease

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ABSTRACT

Background: To study the clinical profile and dysmorphism associated in patients presenting to tertiary referral hospital with congenital heart disease (CHD). **Materials and Methods:** This prospective study was conducted in the Pediatric Cardiology Unit of Sri Jayadeva Institute of Cardiovascular Sciences, Bengaluru, between March 2013 and February 2015. Study subjects include children referred for investigation of suspected heart disease to the Pediatric Cardiology OPD during the study period. Children found to have some type of CHDs were included in the study. All recruited subjects were examined and worked up at outpatient follow-up clinics. **Results:** A total of 450 subjects were found to have CHDs; out of these, 183 (40.6%) were male and 267 (59.4%) were female. Mean age was 3.34 years (range - 4 days to 24 years) and mean weight was 11.15 kg (range - 2-60 kg). History of maternal diseases and intake of drugs during pregnancy was present in 99 (22%) cases (Odds ratio [OR]=7.4, p=0.0090) and maternal fever in 59 (15%) cases (OR=6.5, p<0.0001). Distribution of CHD cases includes cyanotic CHD in 162 (36%) cases, obstructive lesions in 111 (24.6%), and left to right shunt lesions in 288 (64%) cases. 79.4% cases have shown external dysmorphic features, and main dysmorphic features associated with CHDs were eye anomalies, ear anomalies, upturned nose, clinodactyly, and chest deformity. **Conclusion:** Eye and ear anomalies, clinodactyly, and chest deformity were the dysmorphic features significantly associated with CHDs. Consanguinity was found to be linked to CHD. Maternal drug intakes and maternal fever during pregnancy also have bearing on CHDs.

Key words: *Clinical profile of dysmorphism, Congenital heart disease, Dysmorphism*

Congenital heart diseases (CHDs) are the most prevalent and serious of all recognized structural birth defects[1]. Surviving infants often require surgery or interventions and lengthy hospitalizations and may have lifelong disabilities that impose a significant burden on families. Costs associated with the care of a child with a CHD are significant even in developed countries; particularly when lifetime costs of management are considered. The aim of this study was to present one center experience in evaluation of CHDs and to determine the role of identification of dysmorphism in relation to CHDs.

MATERIALS AND METHODS

This prospective study was conducted on children attending the Pediatric Cardiology Unit of Sri Jayadeva Institute of Cardiovascular Sciences, Bengaluru, between March 2013 and February 2015. Approval from the Institutional Ethics Committee was obtained before starting the study. Written consent from parents/legal guardians of the participants was obtained before recruitment. Children, who attend the Pediatric Cardiology OPD for investigation of suspected CHDs during the study period, were included in the study. On the other hand, cases having congenital cardiomyopathy, rheumatic heart disease, and secondary heart disease were excluded from the study.

Complete history was taken from all the recruited subjects including age, sex, parental consanguinity, family history, and pedigree pattern as well as perinatal history. History of maternal diseases such as hypertension, renal, and cardiac diseases and complications during pregnancy as hemorrhage, fever, pre-eclampsia and diabetes, congenital infections, and use of ovulation induction drugs were also recorded. All the subjects were also subjected to complete clinical examination including a survey of external dysmorphic features related to skull, face, neck, chest, abdomen, extremities, and complete cardiac and other systemic examinations.

2D echocardiography (HB 5500, Philips) was performed by experienced pediatric cardiologists in all the recruited subjects. Cytogenetic study using the conventional method of karyotyping with G-and C-banding technique, wherever feasible, was also done. On the basis of echocardiography, cases were classified into cases having cyanotic heart disease, left to right shunt, or obstructive lesions, as per the classification suggested by the American Heart Association.

RESULTS

During the study period, total 900 children were referred for evaluation of suspected heart disease to our pediatric cardiology unit. Out of these, 230 (25.56%) cases were referred for further

workup of known CHD. The most common cause of suspicion of heart disease by primary physician/pediatrician was recurrent respiratory infections in 255 (28.33%) cases, cyanosis in 83 (9.22%) cases, and incidental murmur (in otherwise asymptomatic child) in 66 (7.33%) cases. Other causes were feeding difficulty in 61 (6.78%) cases, presence of other congenital anomalies (e.g. cleft palate, lip, anorectal malformations) in 58 (6.44%), poor weight gain in 52 (5.78%), easy fatigability in 43 (4.78%), CHD on antenatal ultrasound in 36 (4.00%), presyncope in 8 (0.89%), and developmental delay in 8 (0.89%) cases.

Out of these, 450 excluded due to various reasons. 236 children had normal echocardiography, 94 had rheumatic heart disease, 34 cardiomyopathies, and 28 children found to have secondary heart disease. 20 children were receiving radiotherapy or chemotherapy and were excluded. Parents of 88 children did not give consent for inclusion in the study. Remaining 450 subjects were found to have some type of CHD and were included in the study. Out of these, 183 (40.6%) children were male and 267 (59.4%) were females. The mean age of recruited subjects was 3.34 years (range 4 days to 24 years) and mean weight was 11.15 kg (range - 2-60 kg).

Distribution of important risk factors for CHDs is presented in Table 1. History of maternal drug intake during pregnancy, apart from routine iron folic acid and calcium supplementations, (odds ratio [OR]=7.4, p=0.0090), and maternal fever (OR=6.5, p<0.0001) were significantly associated with CHDs in infants. About 324 (72%) patients were born out of non-consanguineous marriage, and 126 (28%) were born of consanguineous marriage (p=0.015, OR=2.4). Frequency of 1st cousin consanguinity was the most prominent pattern (17.6% vs. 4%, respectively, p=0.013, OR=3.1). Maternal smoking and alcohol consumption could not be related since maternal alcohol, and smoking was not found in our study. 12 (2.6%) children had a sibling with history of CHD.

On the basis of echocardiography, CHDs were classified into left to right shunt lesions (254 cases, 56.44%), cyanotic heart disease (122 cases, 27.11%), and obstructive lesions (74 cases, 16.45%) as per the classification suggested by the American Heart Association (Table 2). The heart malformations were classified into 23 categories. Patients with more than one defect were included only in the category of the most serious defect. The most common CHD was ventricular septal defect (VSD) found in 138 (30.2%) cases followed by atrial septal defect (ASD) in 62 (13.8%), pulmonic stenosis (PS) in 49 (10.9%), and patent ductus arteriosus (PDA) in 48 (9.6%) cases as shown in Table 2.

Significantly high number of cases (357, 79.4%) with CHDs were found to have external dysmorphic features (OR=2.6, p=0.0009). Among the dysmorphic features, a significant anomalies observed were eye anomalies (long eyelashes, wide set eyes, and hypertelorism) (OR=176.6, p<0.0001), ear anomalies (OR=217.6, p<0.0001), upturned nose (OR=68.7, p=0.0002), clinodactyly (OR=58.7, p=0.0015), and chest deformity (OR=37.07, p=0.0145). On the other hand, no significant difference was shown related to sex, consanguinity, or positive family history of CHD. Analysis of subgroups related to various types of CHDs showed no significance related to age, sex, family history, and consanguinity (Table 3).

Table 1: Distribution of various risk factors (n=450)

Risk factors	Number (%)		Odds ratio	p value
	Present	Absent		
Dysmorphic features	357 (79.4)	93 (20.6)	2.6	0.0009
Maternal drug intake	99 (22)	351 (78)	7.4	0.0090
Maternal fever	69 (15.3)	381 (84.7)	6.5	<0.0001
History of consanguinity	324 (72)	126 (28)	2.4	0.015

Table 2: Distribution of congenital heart diseases (n=450)

Type of Heart Disease	Number (%)
Ventricular septal defect	136 (30.2)
Atrial septal defect	62 (13.8)
Pulmonic stenosis	49 (10.9)
Patent ductus arteriosus	43 (9.6)
Pulmonary hypertension	31 (6.8)
Tetralogy of fallot	25 (5.6)
Pulmonary regurgitation	19 (8)
Double outlet right ventricle	17 (4.2)
Patent foramen ovale	13 (2.9)
Bicuspid aortic valve	10 (2.2)
Transposition of great artery	8 (1.8)
Coarctation of aorta	6 (1.3)
Dextrocardia	5 (1.1)
Total anomalous pulmonary venous connection	4 (0.9)
Tricuspid atresia	3 (0.7)
Atrioventricular canal defect	3 (0.7)
Pulmonary atresia	3 (0.7)
Partial anomalous pulmonary venous connection	3 (0.7)
Subaortic membrane	2 (0.4)
Cor triatriatum	2 (0.4)
Double inlet left ventricle	2 (0.4)
Double chambered right ventricle	2 (0.4)
Holmes heart	1 (0.2)

DISCUSSION

In this study, subjects with facial dysmorphic features particularly with long eyelashes, upturned nose, ear anomalies, wide-set eyes, and clinodactyly were constituted more than two-third of the studied cases. Other important features included chest deformity, V-shaped lip, low hairline, dermatoglyphic lines, polydactyly and clefting of lips, and forehead abnormalities. Schellberg et al. [2], in a study in Germany, have reported that more than (90%) of the patients have extracardiac malformations. In a study from Egypt done by Tennstedt et al., 85 (66%) cases were associated with extracardiac malformations [3].

In our study, 357 (79.4%) patients had dysmorphism, which was comparable to previous studies. However, Bassili et al. [4] and Stephensen et al. [5] have reported that extracardiac malformations in their cases were often genitourinary and gastrointestinal malformations while skull and face malformations were less common. Previous studies have also reported the high

Table 3: Dysmorphic features seen in study population (n=450)

Dysmorphism	Number (%)
Long eyelash	240 (53.3)
Upturned nose	132 (29.4)
Wide-set eyes	105 (23.3)
Clinodactyly	90 (20)
Chest deformity (Pectus carinatum)	40 (9)
Low set ear	30 (6.6)
V-shaped lip	18 (4.0)
Ear anomaly (large ear)	18 (4.0)
Low hairline	15 (3.3)
Fused eyebrow	12 (2.6)
Malformed ears	12 (2.6)
Hypertelorism	9 (2.0)
Mongoloid slant	9 (2.0)
Polydactyly	9 (2.0)
Small forehead	9 (2.0)
Single crease	9 (1.9)
Cleft lip	6 (1.3)
Small ear	6 (1.3)
Oblique set ear	3 (0.6)
Abnormal neck	3 (0.6)
Stubby hand	3 (0.6)
Web neck	3 (0.6)
Eye anomaly (cataract, isomorphism)	3 (0.6)
Epicanthal fold	3 (0.6)
Antimongoloid slant	3 (0.6)
Undescended testes	3 (0.6)
Thumb anomaly	3 (0.6)
High arched palate	3 (0.6)
Long philtrum	3 (0.6)
Thick upper lip	3 (0.6)
Small chin	3 (0.6)
Sparse eyebrow	2 (0.4)
Long posterior heel	2 (0.4)
Bird like face	2 (0.4)
Multiple nipple	2 (0.4)

prevalence of chromosomal defects and syndromes such as Down's syndrome [6]. However, in our study, we could not study the presence of chromosomal anomalies due to non-availability of genetic testing in our setup.

Our study shows the genetic relation of CHD as a positive association with consanguinity was seen, particularly for first cousin parental consanguinity and positive family history of sibling with CHD. This data have to be interpreted keeping the fact that study group comprised of referral cases from all over the state and country representing various ethnicities. Bassili et al. [4] have reported a higher rate of parental consanguinity and positive family history in their studied sample in Alexandria, Egypt. Similarly, Becker et al. [7], in a study from Saudi Arabia, have reported that first cousin consanguinity was significantly higher than in the general population that was also associated with certain types of CHD. The relatively elevated risk of CHDs associated with consanguineous marriage may warrant more health education sessions to transfer this information to the public.

The common CHDs in a study by Tennstedt et al. [3] include VSD (28%), atrioventricular septal defect (16%), hypoplastic left heart (16%), double outlet right ventricle (12%), and coarctation of the aorta (6%) while pulmonary valve stenosis/atresia (3%), and ASD (0.5%) were less common. In the study by Hoffman et al. [8], the most common CHD was VSD (40%) while Stephensen et al. [5] found VSD (45.7%), ASD (12.2%), and PDA (11.5%) as common CHDs in their study.

The recurrence risks for future siblings are 2-6% and for offspring are 1-10%, but in a few families, the recurrence and transmission risks may be much higher. In our study, 12 (2.6%) had siblings with CHD, which is comparable with previous data.

CONCLUSION

CHD and importance of external dysmorphic features for early diagnosis and management of these disorders are well recognized. Eye anomalies, Ear anomalies, Clinodactyly, and chest deformity were significantly associated with CHD. Consanguinity was found to be linked to CHD. Maternal drug intake during pregnancy, maternal fever during pregnancy has bearing on CHD. Identification of dysmorphic features can be beneficial for early referral to rule out associated CHD.

REFERENCES

1. Driscoll D, Allen HD, Atkins DL, Brenner J, Dunnigan A, Franklin W, et al. Guidelines for evaluation and management of common congenital cardiac problems in infants, children, and adolescents. A statement for healthcare professionals from the Committee on Congenital Cardiac Defects of the Council on Cardiovascular Disease in the Young, American Heart Association. Circulation. 1994;90(4):2180-8.
2. Schellberg R, Schwanitz G, Grävinghoff L, Kallenberg R, Trost D, Raff R, et al. New trends in chromosomal investigation in children with cardiovascular malformations. Cardiol Young. 2004;14(6):622-9.
3. Tennstedt C, Chaoui R, Körner H, Dietel M. Spectrum of congenital heart defects and extracardiac malformations associated with chromosomal abnormalities: Results of a seven year necropsy study. Heart. 1999;82(1):34-9.
4. Bassili A, Mokhtar SA, Dabous NI, Zaher SR, Mokhtar MM, Zaki A. Risk factors for congenital heart diseases in Alexandria, Egypt. Eur J Epidemiol. 2000;16(9):805-14.
5. Stephensen SS, Sigfusson G, Eiriksson H, Sverrisson JT, Torfason B, Haraldsson A, et al. Congenital cardiac malformations in Iceland from 1990 through 1999. Cardiol Young. 2004;14(4):396-401.
6. Settin A, Al Marsafawy H, Al Husseiny A, Dowidar M. Dysmorphic features, consanguinity and cytogenetic pattern of congenital heart diseases: A pilot study from Mansoura locality, Egypt. Int J Health Sci. 2008;2(2):101-11.
7. Becker SM, Al-Halees Z, Molina C, Paterson RM. Consanguinity and congenital heart disease in Saudi Arabia. Am J Med Genet. 2001;99(2):8-13.
8. Hoffman JI. Congenital heart disease: Incidence and inheritance. Pediatr Clin North Am. 1990;37(1):25-43.

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