Original Research Article

Study of extra-cardiac anomalies in children with congenital heart diseases

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Abstract

Background: Congenital heart diseases are frequently associated with other non-cardiac congenital malformations and may require intervention of a surgical or medical care independently from the cardiac problem. For these reasons, it would be worth to discuss the significance and the cost-effectiveness of screening all children with CHD. **Aim:** To study the pattern of various extra-cardiac malformations in congenital heart disease patient. **Material and Methods:** A total of 217 children with congenital heart diseases under 14 years were studied for the incidence and pattern of extra cardiac anomalies present in such cases with multiple investigations. **Results:** Out of the 217 subjects with cardiac anomalies, 87 subjects (40.09%) had VSD, 72 (33.18%) ASD, 48 (22.1%) had PDA and less than 2% had other cardiac anomalies. Out of 217 cases, 29 (13.4%) cases were found to be associated with extra cardiac anomalies. CNS (24.14%), craniofacial (24.14%) and skeletal (24.14%) anomalies were common extra cardiac anomalies. Renal anomalies were present in 6 (20.69%) of cases. **Conclusion:** Association of extra cardiac anomalies with CHD is important, as it would hence be beneficial to evaluate for these anomalies at an early age for timely management.

Key Word: Children, congenital heart disease, cardiac anomalies, extra cardiac anomalies

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INTRODUCTION

Congenital heart defects (CHDs) are a common variety of birth defects, in children with an overall prevalence of 8.1/1000 births. CHDs are the congenital malformations with greater effect on children morbidity and mortality as well as on costs of the health system.[1,2] They represent the main cause of death among the congenital malformations.[1] Extra-cardiac malformations such as intra-abdominal organ defects may associate with genetic syndromes are detected from 7 to 50% of the patients with CHD and impose a higher risk of morbidity and mortality to these patients, in addition to escalating the risks of surgical correction.[2,3] In which such patients may want surgical procedures or intensive care regardless of the heart condition.[2] The reported rates of CHD differ from one study to another because of disparities in diagnostic and registration criteria and the percentage of prenatally diagnosed cases included.[4] Chromosome aberrations significantly higher in fetuses than in live born infants which reduces viability, but also, the spectrum of CHD, as well as their association with extra-cardiac malformations.[5]CHDs are frequently associated with other non-cardiac congenital malformations and may require intervention of a surgical or medical care independently from the cardiac problem. For these reasons, some authors have been discussing the significance and the cost-effectiveness of screening all children with CHD to detect EM's by ancillary tests, such as abnormal ultrasound.[3,6] A number of studies have attempted to unravel association between specific cardiac defects and non-cardiac malformations. Among these associations, the only well-established ones are the association between Down syndrome and endocardial cushion defects (ECD) or ventricular septal defects (VSD) that between the agenesis of spleen and cono-truncal anomalies and between limb reductions and septal defects in patients with autosomal dominant Holt-Oram syndrome.[7] A very less work has been carried out in India on this aspect, So, keeping this in mind the present study was conducted to study the pattern of various extra-cardiac malformations in congenital heart disease patient.

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MATERIAL AND METHODS

This observational cross sectional study was carried out on patient age group of 0 to 14 years with congenital heart disease attending paediatric and cardiology outpatient department.

Sample size

Sample 'n' was calculated by using the formula - $n=z^2_{1-a}*p(1-p)/d^2$ Where, p= expected proportion (here 0.17 was taken as expected proportion of extra cardiac anomalies in congenital heart disease as incidence was up to 17%). d=absolute precision, 1-a/2 = desired confidence level.

Thus, the sample size was calculated as - 217 with 95% confidence

Inclusion criteria

- Children with congenital heart diseases under 14 years only.

Exclusion criteria

- Those who were not willing to give consent

Informed Consent

All eligible patient's parents or guardian were individually given an initial description of the proposed study by investigator. Interested participants were then presented with a written informed consent form. All details were kept under strict confidentiality. Analysis was also anonymous and personal identifiers were removed. Data Tools A detailed history interview and clinical examination of children with congenital heart diseases under 14 years was taken and those children with CHDs were further investigated. Investigations like Chest X-ray, Electrocardiogram and echocardiography were done. Other investigations like X-rays, USG, CT scan and MRIs were carried out wherever required to diagnose other extracardiac anomalies.

Statistical analysis: All the data of the study was analysed using parametric and non parametric test for drawing valid conclusions in the study and its significance in the view of medical use by using SPSS EpiInfo 6, MS Excel.

RESULTS

A total of 217 patients with CHD were enrolled, out of which 106 (48.85%) were between age one month to one year, 70 (32.26%) were between one to 5 years, 25 (11.52%) were <1 month of age and 16 (7.37%) were more than 5 years of age. 129 (59.4%) were males and 88 (40.6%) were females. Consanguinity was present in 13 (5.9%) cases of cardiac anomalies and syndromic features were seen in 6 (2.76%) cases.

Table 1: Distribution of cases according to cardiac anomalies

Cardiac anomaly	No. of cases	Percentage
Ventricular septal defect (VSD)	87	40.09%
Atrial septal defect (ASD)	72	33.18%
Patent ductus arteriosus (PDA)	48	22.12%
Patent foramen ovale (PFO)	19	8.76%
Tricuspid regurgitation	5	2.30%
Bicuspid aortic valve	3	1.38%
Double outlet right ventricle (DORV)	3	1.38%
Total anomalous pulmonary venous drainage (TAPVC)	3	1.38%
Tetralogy of Fallot (TOF)	5	2.30%
Pulmonary atresia (PA)	4	1.84%
Pulmonary valve stenosis (PS)	2	0.92%
Mitral regurgitation (MR)	1	0.46%
Aortic regurgitation (AR)	1	0.46%
Coronary fistula	1	0.46%
Coarctation of aorta	1	0.46%
Truncus arteriosus type I	1	0.46%
Aortic stenosis (AS)	1	0.46%

Out of the 217 subjects with cardiac anomalies, 87 subjects (40.09%) had VSD, 72 (33.18%) ASD, 48 (22.1%) had PDA and less than 2% had other cardiac anomalies.

Table 2: Distribution of extra cardiac anomalies

Parameters	Extracardiac anomaly		Total (n=217)
	Present (n=29)	Absent (188)	
Age (years)			
< 1 month	11	14	25
1 month- 1 year	11	95	106
1 year - 5 years	5	65	70
> 5 years	2	14	16

Gender			
Male	15	114	129
Female	14	74	88

Out of 217 cases, 29 (13.4%) cases were found to be associated with extra cardiac anomalies. The incidence of extra cardiac anomalies up to one year of age is statistically significant (Chi square =23.43, p<0.0001). The association of sex of the subjects and extra cardiac anomalies is statistically not significant (p=0.42). Out of the total 13 consanguinity cases, extracardiac anomalies were present in 5 (17.34%) cases (Z value=1.81, p value>0.05). Out of the 6 Syndromic feature cases, extra cardiac anomalies were present in 3 (10.34%) cases (Z value=1.81, p value>0.05). The association of consanguinity and syndrome features with extra cardiac camels is statistically not significant.

Table 3: Distribution of cases according to extracardiac anomalies

Extracardiac anomalies	No. of cases (n=29)	Percentage
GIT anomalies	1	3.45%
Genital anomalies	1	3.45%
Renal anomalies	6	20.69%
Eye anomalies	3	10.34%
Craniofacial anomalies	7	24.14%
Skeletal anomalies	7	24.14%
Ear anomalies	2	6.49%
CNS anomalies	7	24.14%
Respiratory anomalies	1	3.45%
Other anomalies	1	3.45%

In this study, CNS (24.14%), craniofacial (24.14%) and skeletal (24.14%) anomalies were common extra cardiac anomalies. Renal anomalies were present in 6 (20.69%) of cases. Lesser common anomalies were respiratory, GIT, genital and single umbilical artery.

Table 4: Association between cardiac and extra cardiac anomalies

Cardiac anomaly	Extra cardiac anomaly		Z value	P value
	Present	Absent		
Ventricular septal defect (VSD)	7	85	1.12	>0.05
Atrial septal defect (ASD)	13	59	1.37	>0.05
Patent ductus arteriosus (PDA)	9	39	1.13	>0.05
Patent foramen ovale (PFO)	2	17	0.42	>0.05
Tricuspid regurgitation	1	4	0.37	>0.05
Bicuspid aortic valve	0	3	1.75	>0.05
Double outlet right ventricle (DORV)	2	1	1.34	>0.05
Total anomalous pulmonary venous drainage (TAPVC)	1	2	0.69	>0.05
Tetralogy of Fallot (TOF)	1	4	0.37	>0.05
Pulmonary atresia (PA)	1	3	0.53	>0.05
Pulmonary valve stenosis (PS)	1	1	0.85	>0.05
Mitral regurgitation (MR)	0	1	1.003	>0.05
Aortic regurgitation (AR)	0	1	1.003	>0.05
Coronary fistula	0	1	1.003	>0.05
Coarctation of aorta	0	1	1.003	>0.05
Truncus arteriosus type I	0	1	1.003	>0.05
Aortic stenosis (AS)	0	1	1.003	>0.05

Although the incidence of extra cardiac anomalies was higher in case of VSD (7), ASD (13) and PDA (9), it is not statistically significant. Anomalies like MR, AR, CoA, coronary fistula, trunks arteriosus type I and AS were not associated with extra cardiac anomalies.

Table 5: Distribution of type of extra cardiac anomalies according to specific system

Type of extra cardiac anomaly	No. of cases
CNS anomaly	7
Hydrocephalus	5
Defects of neural tube closure	1 (meningomyelocele)
Microcephaly	1
Craniofacial anomalies	12
Cleft lip	5
Cleft palate	7
Eye anomalies	3
Microopthalmia	2
Squint	1
Ear anomalies	2
Microtia	1
Ear tag	1
Musculoskeletal anomalies	7
Vertebral anomaly	1
Polydactyly	3
Syndactyly	3
Respiratory anomalies	1
Tracheo-oesophageal fistula	1
Genital anoamlies	1
Ambigous genitalia	1
Renal anomalies	6
Ectopic kidney	1
Cystic/dysplastic kidney	4
Vesicourethal reflex	1
GIT anomalies	2
Anorectal malformations	2
Other anomalies	1
Single umbilical artery	1
Total	**42 (19 types)**

In the present study nineteen different types of extra cardiac anomalies were observed in 29 cases the most common type being cleft palate a craniofacial anomaly. It was observed that the most common CNS anomaly was hydrocephalus (11.6%). A common renal anomaly was dysplastic kidney (9.3%) and syndactyly (6.9%) and polydactyl (6.9%) were common musculoskeletal anomalies. Out of the 29 cases, 4 (13.7%) cases were associated with multiple extra cardiac anomalies. Out of 217 CHD cases, 6(2.76%) cases were associated with syndromes. Of these 2(0.9%) cases were associated with Down syndrome and each of the remaining 4 cases was associated with VACTERL, amniotic band syndrome, Digeorge syndrome and Hunter's syndrome.

DISCUSSION

Congenital heart disease is the most common birth defect in children with an incidence of 8.1 per 1000 live births. The study was conducted to find out the pattern of extra cardiac anomalies in children with CHD. In this study, 217 subjects with cardiac anomalies were enrolledin the span of two years to find out the association and pattern of extra cardiac anomalies in congenital heart diseases. In the present study, out of 217 cases 29 (13.4%) patients had extra cardiac anomalies. A similar study conducted by Karande *et al* showed that out of 560 cases, 98 (17.5%) cases were associated with extra cardiac anomalies.[8] Another similar study conducted by Bhushan Deo *et al* in Rural Medical College, Loni, Maharashtra, India showed that out of 120 CHD cases, 22 (18.3%) cases were associated with extra cardiac anomalies.[9]Yet another study conducted by Sarkar M *et al* on prevalence of extra cardiac anomalies in CHD cases found that out of 335 CHD patients, 68 (20.3%) had extra cardiac anomalies.[10] In the present study, extra cardiac anomalies were found most commonly upto the age of 1 year which is statistically significant ($p<0.0001$). The next common age group was 1 year to 5 years. No specific study found to compare with the present study. In present study of the 29 cases of extra cardiac anomalies, 15 were boys and 14 were girls. Similar study conducted by Karande *et al* shows that out of 98 cases of extra cardiac anomalies 52 were boys and 46 were girls. No particular gender predominance was noted in either of the above mentioned studies.[8] In present study, out of 29 cases of extra cardiac anomalies with CHD, 5 cases (17.4%) had a history of consanguinity. Out of the remaining 188 cases of CHD (not associated with extra cardiac anomalies), only 8

cases (4.5%) had a history of consanguinity. Although, the association of extra cardiac anomalies with consanguinity is stronger, it is statistically not significant (p>0.05). The present study shows no statistically significant association between syndromes and extracardiac anomalies (p>0.05). Of the 29 cases of CHD with extra cardiac anomalies, only 3 cases (10.34%) were syndromic. A similar study conducted by Sarkar MF *et al* shows that 24 (35.3%) cases out of 68 cases of extra cardiac anomalies had history of consanguinity. On the contrary, 53 (77.9%) cases out of 68 cases of extra cardiac anomalies had syndromic association.[10] In the present study, craniofacial, skeletal and CNS anomalies 7 (24.14%) each, were most common followed by renal anomalies 6 (20.69%). A similar study done by Karande *et al* shows majority of the defects were craniofacial anomalies.30 Sarkar MFR *et al* found GIT system was affected in 60% cases, musculoskeletal in 33.3% and GUT in 6.7% of the patients.[8] Grech and Gatt conducted a similar study on syndromes and malformations associated with CHD in a population based study in Malta in which, out of 14 extra cardiac anomalies only 4 were musculoskeletal defects.[11] Association between cardiac anomalies and extra cardiac anomalies was not statistically significant. Out of 29 cases of CHD with extra cardiac anomalies, 13 had ASD (5.9%), 9 had PDA (4.1%) and 7 had VSD (3.2%). Even though association of extra cardiac anomalies with ASD, VSD and PDA were higher, it is not statistically significant. A similar study conducted by Bhushan Deo *et al* found that out of 120 CHD cases, 7 VSD, 6 PDA and 4 ASD cases were associated with extra cardiac anomalies.[9]So, this study is comparable to the present study. The present study shows that 19 types of extra cardiac anomalies where found in 29 cases of CHD, in which cleft palate was the commonest type of anomaly. Hydrocephalus was the most common CNS anomaly (11.6%). Other frequently seen anomalies were dysplastic kidney (9.3%)(most common renal anomaly), cleft palate (11.6%)(most common craniofacial anomaly), syndactyly (6.9%) and polydactyl (6.9%) (common musculoskeletal anomalies). No specific study was found to compare these findings. In the present study, it was observed that out of 29 cases of CHD with extra cardiac anomalies 4 (13.7%) cases were associated with multiple extra cardiac anomalies. On the contrary, a study conducted by Karande *et al* shows that out of 98 patients with extra cardiac anomalies 56 (58%) cases had multiple congenital defects.[8] Out of 217 CHD cases, 6 cases (2.76%) were associated with syndromes. Of the 6 cases, 2 of them(9%) had Down syndrome and each of the remaining four cases had VACTERL, amniotic band syndrome, Digeorge syndrome and Hunter's syndrome. A similar study done by Deo *et al* showed that out of 81 cases of CHD 3 cases had down syndrome which was the most common syndrome in their study.[9] Thus, the present study is compatible with above study.

CONCLUSION

Extra cardiac anomalies are common in CHD cases. Association of extra cardiac anomalies with CHD is thus important. It would hence be beneficial to evaluate for these anomalies at an early age for timely management.

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