Original Paper

Prevalence of Extra-Cardiac Malformations with Congenital Heart Disease among Hospital Admitted Children- A Study in a Tertiary Level Hospital of Bangladesh

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Abstract

Introduction: Congenital anomalies are a major cause of stillbirths and infant mortality. In this post genomic era, congenital heart diseases (CHDs) are still the most common and lethal of all birth defects in children. Although most of the CHD occur as a sporadic event many of them have a well-defined genetic basis. This genetic basis is expressed in the form of concomitant occurrence of extra-cardiac malformations (ECM) which may occur alone or as a part of a syndrome.

Objective: The present study was designed to find out the burden of CHDs in the hospital admitted children and to find out the prevalence of occurrence of clinically recognizable ECM associated with CHDs.

Methods: This is a cross-sectional hospital based study. Total patients admitted during the study period were 5264. Of these 335 patients were found suffering from different types of congenital heart diseases. This gives the hospital admission rate for CHD, as 63.6 per 1000 admission (6.36%). Out of total 335 cases of CHD, 273 (81.5%) were acyanotic and 62 (18.5%) were cyanotic. Among the CHD patients 68 (20.3%) had a significant ECM. Out of the 68 patients with a significant ECM 53 (77.9%) had a clinically recognizable genetic syndrome, whereas 15 cases (22.1%) had a major ECM which was not a part of a syndrome.

Conclusion: A high rate of hospital admission is found for CHDs in the pediatric setting, signifying the need for improvement of pediatric cardiology infrastructure in Bangladesh, which should help in providing better medical and surgical care for the patients with CHD. A significant proportion of patients with CHD have associated ECM, implicating a genetic background for the etiology of CHD. It also emphasizes the need for thorough evaluation of patient with CHD for ECM.

Key-words: Congenital heart disease; extra-cardiac malformations; consanguinity.

Introduction

Congenital heart disease (CHD) refers to structural or functional heart diseases, which are present at birth. These are primarily seen in neonates, infants and children; although it is not uncommon to see adults with uncorrected CHD. The reported incidence of CHD is 8-10/1000 live births according to various series from different parts of the world. The prevalence of CHD in the Indian subcontinent based on birth statistics and school based studies varies from as low as 0.8 to 5.2/1000 live births depending upon the age group considered[1,2,3,4].

The importance of genetic factors in the etiology of CHD is demonstrated by clinical, epidemiological and embryological studies. According to various studies it appears more likely that genetic variation can play a role in predisposition to the majority of heart defects[5]. Genetic syndromes, including chromosomal disorders, are commonly associated with CHD[6]. CHDs are frequently associated with other non-cardiac congenital malformations and may require intervention of a surgical or medical nature independently from the cardiac problem. Management of the congenital heart lesion may therefore be influenced by the medical and/or surgical treatment needed for all of the various extra cardiac malformations. For this reason, it is important to know how frequently one may expect to encounter

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congenital heart disease occurring in association with other anomalies. This study was designed to find out the prevalence of CHD among hospital admitted children and to find out the prevalence of ECM in CHD patient based on clinical features.

Material and methods

This is a cross-sectional hospital based study, done on 335 children, who were found to have suffering from CHD among 5264 children admitted to either the pediatric cardiology ward, pediatric general ward, pediatric intensive care unit (PICU) or to the neonatal intensive care unit (NICU) of Combined Military Hospital, Dhaka a tertiary level hospital from January 2011 to December 2012. All cases, old or new in the pediatric age group (0-12 years) irrespective of sex who were admitted either with a diagnosis of CHD, or who were found to have CHD has been included. Patients who do not have echocardiographic confirmation of the CHD, patent ductus arteriosus as a single defect in preterm infant before three months and patients with CHD those were not structural in nature were excluded from the study. Informed consent from all the patients was taken before undergoing the study. Detailed note was made regarding, the rationale behind admission, family history of CHD, consanguinity among parents and prior investigations if any as per the format designed for the study. Investigations that were done are echocardiography If not done previously, electrocardiogram and chest X-ray as a part of work up of CHD. Investigations which were attributable, to the reason for admission, such as complete hemogram and blood culture in cases of infective endocarditis were also done. Once the patients were diagnosed with a CHD, a detailed search was done by clinical examination for associated congenital anomalies. If warranted, investigations such as ophthalmological evaluation, hearing assessment, skeletal surveys, ultrasonogram of the abdomen and genetic studies e.g. Karyotyping were done based on the clinical features. Patients were then divided into 2 groups. Group-I (Non-syndromic group), includes patients with ECM but with no clinically identifiable syndrome. Group-II (Syndromic group), includes patients who fit into clinically recognizable syndrome. Syndrome delineation was done according to guidelines set forth by authorities in the field of dysmorphology. ECM, when found in Group-I were subdivided into minor and major malformations. A major malformations is one that has severe medical or cosmetic consequences such as gastrointestinal or skeletal malformations. A minor malformations represents a medically insignificant departure from normal development, such as wide-set eyes or a single palmar crease. Comparative analysis was done by test of proportions and chi-square test. 95% confidence interval was found for the prevalence of ECM among patients with CHD.

Results

During the period January 2011 to December 2012, total 5264 patients were admitted to the pediatric department of combined military hospital Dhaka. Among them, 335 patients had CHD. This gives a hospital admission rate for CHD, as 63.6 per 1000 admissions (Table-I).

Table-I: Hospital admission rate.

Total no. of patients admitted during the study period	5264
No. of patients with CHD	335
Hospital admission rate	63.6/1000 admissions

Out of 335 cases of CHD, 273(81.5%) of the cases were acyanotic, whereas 62(18.5%) were cyanotic. The predominant acyanotic CHD was found to be VSD and the predominant cyanotic CHD was found to be TOF (Table-II).

Table-II: Profile of CHD.

Acyanotic CHD	Cases	Cyanotic CHD	Cases
Ventricular septal defect (VSD)	97	Tetralogy of Fallot (TOF)	26
Atrial septal defect (ASD)	72	Transposition of great arteries(TGA)	17
Patent ductus arteriosus (PDA)	47	Total anomalous pulmonary venous drainage(TAPVC)	7
Pulmonary valve stenosis (PS)	15	Tricuspid atresia (TA)	5
Atrio- ventricular septal defect	9	Pulmonary atresia (PA)	4
Coarctation of Aorta(CoA)	7	Hypoplastic left heart syndrome (HLHS)	2
Mitral valve prolapsed (MVP)	6	Ebstein anomaly (EA)	1
Dilated cardio myopathy (DCM)	5		
Dextrocardia	4		
Aortic regurgitation(AR)	4		
Mitral regurgitation (MR)	3		
Aortic stenosis (AS)	2		
Mitral stenosis (MS)	2		
Acyanotic Total	273 (81.50%)	**Cyanotic Total**	62 (18.50%)

Out of the total 335 cases of CHD, 53 were admitted in the neonatal period, 85 in their infancy, 110 in the preschool period and 87 in later childhood (Fig-I).

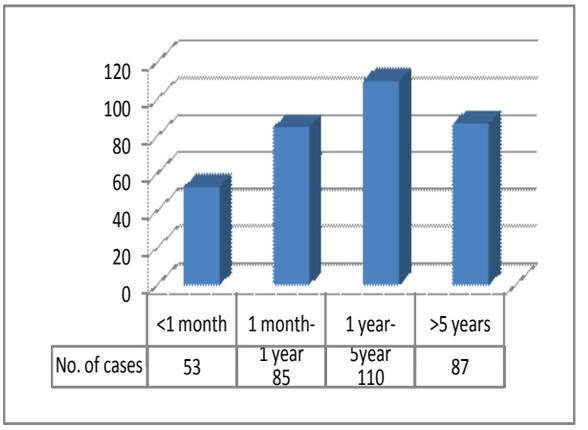

Fig-1: Age wise distribution of CHD cases.

Males formed the major share of the patients, accounting for 53.4% of the total study group. This finding was consistent in both acyanotic and cyanotic type of CHD and no statistical difference was found (Table-III).

Table-III: Sex distribution of patients admitted with CHD.

Type of CHD	Acyanotic CHD (n=273)	Cyanotic CHD (n=62)	All CHDs (n=335)
Male	145 (53.1%)	34 (54.8%)	179 (53.4%)
Female	128 (46.9%)	28 (45.2%)	156 (46.6%)

Out of the total study group, 68 patients had a significant ECM. Significant ECM referred to either a major ECM (those malformations with a significant medical or cosmetic consequence) or a clinically recognizable genetic syndrome (Table-IV).

Table-IV: Prevalence of significant ECM (Major ECM and clinically recognizable syndromes) in patients with CHD.

Presence of significant ECM	Patients with CHD (n=335)
Yes	68(20.3%)
No	267(79.7%)

Out of the 68 patients with a significant ECM, 77.9% of the patients had a clinically recognizable genetic syndrome, whereas 22.1% of the patients had a major ECM which was not a part of a syndrome (Table-V).

Table-V: Profile of significant ECM.

Type of significant ECM	Patients with significant ECM (n=68)
Syndromes	53(77.9%)
Major ECM	15(22.1%)

35.3% of the patients with significant ECM (major ECM + syndromes), were born to consanguineously married couples. Two third of the patients with a major ECM (not as a part of a syndrome) had a history of parental consanguinity. This association of major ECM with consanguinity was found to be statistically significant (Table-VI).

Table-VI: Consanguinity among patients with significant ECM (major ECM and clinically recognizable syndromes).

	No. of patients	Non-Consanguineous Parents (% of the type of ECM)	Consanguineous Parents (% of the type of ECM)
Syndromes	53	38(71.7%)	15(28.3%)
Major ECM	15	6(40.0%)	9(60.0%)
Significant ECM (Total)	68	44(64.7%)	24(35.3%)

X2 = 7.30; P < 0.05 - significant

Group-I consists of patients with CHD but no identifiable syndrome; this was found to be 84.18%. Group-II consists of patients, in whom CHD occurred as a part of a recognizable syndrome; this was found to be 15.82% (Table-VII).

Table-VII: Association with syndromes.

Association with syndromes	No. (%) of cases
Group - I (Non-Syndromic)	282(84.18%)
Group - II (Syndromic)	53(15.82%)

ASD and VSD were the most common acyanotic CHD, whereas TGA was the common cyanotic CHD associated with ECM. Gastrointestinal system was affected in 60.0%, musculoskeletal in 33.3% and genitourinary in 6.7% of the patients with major ECM in Group-I. Gastrointestinal system was seen most commonly affected (Fig-2).

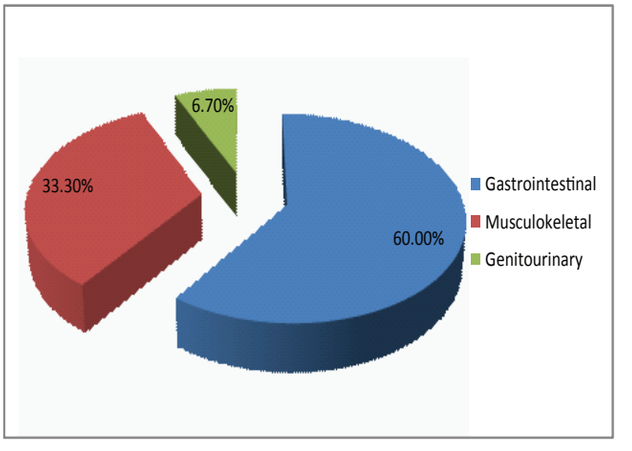

Fig-2: System wise distribution of major ECM.

Out of the 53 cases belonging to the syndromic group, Congenital Rubella Syndrome (CRS) was the most common accounting for 39.6% of the patients in this group (Fig-3).

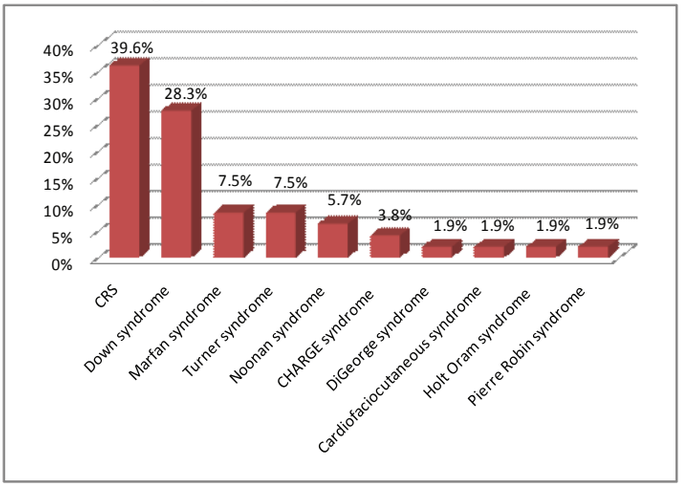

Fig-3: Prevalence of specific syndrome.

Discussion

The worldwide prevalence of CHD at birth ranges from 3.7-17.5 per 1000 live births; in Bangladesh based on a single study this has been found to be 25 per 1000 live births[1,4]. Hospital based studies incorporating the entire pediatric age group, may represent the true burden of CHD, dealt by the medical community. The hospital admission rate from birth to 14 years for CHD between 2003- 2004, in the NHS hospitals of England was found to be 1.8 per 1000 hospital admissions[7].This is in stark contrast to the figure of 26.4 per 1000 hospital visits and admissions quoted by Kapoor et al. from India and to the figure of 5.8 per 1000 hospital admissions quoted by Shah et al. from Kathmandu[8]. Though the huge admission rate of CHD quoted by Kapoor et al. maybe because of the inclusion of hospital OPD visits, it still reveals the magnitude of the problem. In the present study, the hospital admission rate for CHD from birth to 12 years, covering the entire pediatric age group, was found to be 63.6 per 1000 hospital admissions (Table-I). Compared to the study done in India and Kathmandu, the present study reveals a huge case load. The reasons for this contrast may be, present study was done in a tertiary level hospital, whereas the study done in India and Nepal included all levels of hospitals. And delay in diagnosis, which may deem the patient unfit for surgical management, and hence repeated admissions for medical line of management.

The etiology of CHD remains enigmatic and both genetic and environmental factors play a role; a multifactorial mode of inheritance has been suggested[9]. CHDs may be diagnosed at virtually any age. Some conditions always are discovered in neonates; others rarely are identified during infancy. With early intervention, neonatal mortality from the heart diseases can fall from 2-3/1000 to 0.6-0.8/1000 live births[10]. In the present study the predominant acyanotic CHD was found to be VSD and the predominant cyanotic CHD was found to be TOF (Table-II), The age profile of CHD in our study (Fig-1) is similar to other studies reported from India which were based on hospital admissions[4,11]. Gender difference in the incidence of childhood diseases has long been recognized, usually being unfavorable to the male sex[12]. Consanguinity often has genetic implications for the offspring. Backer et al., in a study of 891 cases of CHD found that 40.4% of the parents of the CHD were consanguineously married compared to 28.4% of the control population[13]. In the present study, males constituted 53.4% and females constituted 46.6% of the study group. This gives a male to female ratio of 1.15:1(Table-III). This finding is similar to other hospital admission based studies done in India and Nepal[8,14]. Congenital cardiac malformations are frequently associated with other non- cardiac congenital malformations and chromosomal anomalies. Such patients may require intervention of a surgical or medical nature independently from the cardiac problem. CHD sometimes associated with clinically recognigible syndromes. Syndrome delineation was done according to guidelines set forth by authorities in the field of dysmorphology[15,16]. In the Baltimore Washington infant Study (BWIS) of 2102 neonates with CHD, significant ECM was found in 26.8%; 18.5% of the neonates had a clinically recognizable syndrome whereas the rest 8.3% of the neonates had an isolated ECM[17]. Similarly Greenwood et al. found ECM in 25.2% of the neonates with CHD, two thirds of who belonged to recognizable syndrome[18]. In the present study 20.3% of the patients with CHD, had an associated significant ECM (Table-IV). 95% confidence interval was found to be 22 – 40 %. Of this 20.3% of patients with significant ECM, 77.9% were found to have a clinically recognizable syndrome and in the remaining 22.1% ECM was found to occur in isolation (Table-V). The Findings suggest that there is a high association of CHD with clinically recogniz-

able syndrome. This will help in further counseling of the parents and for proper medical and surgical care. The most commonly affected system with ECM, are the gastrointestinal and musculoskeletal[19]. In the present study more than half of the isolated major ECM, were in the gastrointestinal system and the remainder were in the musculoskeletal and genitourinary system (Fig-2). Due to the small size of the study group, association of a particular major ECM with a particular CHD could not be made. In the present study, more than three fourths of the isolated major ECM, occurred in offspring's of consanguineously married couples. This was also found to be statistically significant with a P value of <0.05 (Table-VI). Genetic syndromes, including chromosomal disorders, are commonly associated with CHD[20]. In our study, out of the 53 cases belonging to the syndromic group, congenital rubella syndrome (CRS) was the most common accounting for 39.6% of the patients in this group (Fig-3). In recent times Grech & Gatt, found that 65% of the individuals with CHD and associated ECM had a recognizable genetic syndrome[21].

Conclusion

The hospital admission rate for CHD is higher in Bangladesh when compared to developed countries such as the UK. This point to the need for better pediatric cardiology infrastructure in the present Bangladesh scenario. A multi centre large scale study may be done to find out the prevalence of CHD in Bangladesh. More than half of the patient with ECM and CHD had an associated recognizable syndrome and hence pediatricians should be able to identify at least those commonly occurring syndrome for the proper evaluation, management and counseling.

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