https://doi.org/10.3329/cbmj.v12i1.64272

Incidence and Risk Factors of Congenital Heart Diseases in Syndromic Neonates

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Abstract

Congenital heart defects (CHD) are the most common types of major birth defects, leading cause of infant morbidity and mortality. Syndromic babies are more affected by CHD. This observational study was conducted in a tertiary care hospital of military facility in Bangladesh. Eighty syndromic neonates were studied through history, physical examination and investigated for incidence and risk factors for CHD. Out of 80 syndromic neonates 61(76.3%) were found having CHD. Male female ratio was 1.18:1. Average age at diagnosis was 25±1.6 days of age. Down Syndrome (DS) and Congenital Rubella Syndrome (CRS) were the most common syndromes. Ventricular Septal defect (VSD) and Atrial septal defect (ASD) II were the most common CHD. Consanguinity, extracardiac malformations, maternal illness (HTN, DM, Hypothyroidism etc.), both fertility and non-fertility medication are also found to be associated with CHD in Syndromic neonates. CHDs have serious implications and it is important to understand them and how they may affect the child so that appropriate medical and surgical treatment may be provided. So, early detection of CHD in neonate will be able to decrease morbidity as well as mortality.

CBMJ 2023 January: vol. 12 no. 01 P: 17-21

Keywords: Congenital heart defects, syndromic neonates, incidence, risk factors

Introduction

Congenital heart defects (CHD) are the most common types of major birth defects, leading cause of infant morbidity and mortality. The prevalence of CHD reported in different studies ranges from 4-50/1000 live births.[1] Significant progress has been made in recent decades in relation to the earlier detection of CHD, both prenatally and neonatally while advances in surgical and other treatments have improved survival and quality of life.

Rubella, also known as German Measles, is a mild illness that presents with fever and rash. However, the public health importance of rubella relates to the teratogenic effects when rubella infection is acquired in the early months of pregnancy. Rubella infection of the fetus can result in fetal death or in the birth of an infant with serious congenital birth defect.[2] It is estimated that between 100,000 and 238,000 children are born yearly with Congenital Rubella Syndrome (CRS) worldwide – most in the developing countries.[3]

Down syndrome (DS) is the most common chromosome abnormality among live born

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infants.[4] The phenotype of DS is characterized by more than 80 clinical features, including cognitive impairments, muscle hypotonia, short stature, facial dysmorphisms, congenital heart disease, and several other anomalies. Indeed CHDs are considered to be the most important clinical phenomenon of DS as they contribute to significant morbidity and mortality.[5] The prevalence of CHD in patients with Down syndrome ranges from 40 to 50%.[6,7,8] Parents of a child with DS need to work closely with their child's doctors to determine what route (surgical or medical) will best serve their child. Some congenital syndromes with associated CHD is given in the following table-I.

Table I: Syndromes with chromosomal anomalies[9]

Syndrome	Chromosomal Anomaly	Most Common CHD
Down syndrome	Trisomy 21	CAVC, VSD, ASD, PDA
Edward's syndrome	Trisomy 18	VSD, ASD, PDA
Patau's syndrome	Trisomy 13	VSD, ASD, PDA
Cat-eye syndrome	Tetrasomy 22p	TAPVR
Turner's syndrome	45, XO	CA, BAV, AS

CAVC = common atrioventricular canal; VSD = ventricular septal defect; ASD = atrial septal defect; PDA = patent ductus arteriosus; TAPVR = total anomalous pulmonary venous return; CA = coarctation of the aorta; BAV = bicuspid aortic valve; AS = aortic stenosis.

In Bangladesh, a study was carried out in Dhaka in 1994-95 on 120 disabled children. Amongst them 25 (20.83%) were seropositive for rubella specific antibody. It was found that 40% mother of the seropositive children had clinical history suggestive of rubella in the 1st trimester and 12% in the 2nd trimester of the pregnancy.[10]

A substantial proportion of CHD is detected at delayed age. Delayed age at diagnosis of CHD poses a significant delay in treatment specially in cases of acyanotic CHD.[11,12]

Considering economic and social burden of the birth prevalence of syndromic baby-associated CHDs well established by multiple studies using modern diagnostic methods, attention can now be directed toward understanding the etiology of these defects. The objective of the present study was to find out the incidence and risk factors of congenital heart defects in syndromic neonates.

Methods

This observational study was conducted in a tertiary care hospital of military facility in Bangladesh. All neonate (0-1 month of age) who were visiting to the department of Neonatology and Cardiac OPDs and in-patient department of the Combined Military Hospital (CMH), Dhaka, were screened for presence of syndrome with CHD. After taking informed consent from the patients' parents or guardian detailed evaluation in respect of history, general examination, systemic and thorough cardio-respiratory examination were done in those patients. Neonates who were critically ill or undergoing any surgical procedure were excluded from this study. Finally, a total of eighty neonates participated in this study. Diagnosis of syndromic was clinical; based on physical characteristics initially. These cases were confirmed by karyotyping afterwards. Then 2D and color Doppler echocardiography (Simens® acuson CV70) was done at Paediatric Cardiology Department, CMH Dhaka to evaluate

the cardiac status and all the findings were noted in the data collection form.

All data were analyzed through standard statistical methods by using Statistical Package for Social Science (SPSS) software version 20.0 (SPSS Inc., Chicago, USA). Statistical tests like unpaired Student's "t" test and Chi-square test were done. P value ≤0.05 was considered as statistically significant.

Results

Out of 80 syndromic neonates, 61(76.3%) were found having CHD and 19 were having no CHD. Male female ratio of the syndromic neonates was 1.18:1. Average age at diagnosis was 25±1.6 days of age. Down Syndrome (DS) and CRS were the most common syndrome respectively followed by DiGeorge/velocardiofacial syndrome. CHD were found in 46.5%, 75% and 100% cases of DS, CRS and DiGeorge syndrome respectively (Table-II).

Table II: Incidence and distribution of CHD

Name of the Syndrome	**No (%) (n=80)**	**Frequency of CHD in individual syndrome (%)**
Down syndrome	43 (70.5)	20 (46.5)
CRS	8 (13.1)	6(75)
DiGeorge/velocardio-facial syndrome	3 (4.9)	3(100)
Edward's syndrome	2 (3.3)	1 (50)
Turner's syndrome	3 (4.9)	1(33)
Noonan syndrome	1 (1.6)	1(100)
William Syndrome	1 (1.6)	1(100)

In all CHD cases under this study, 37.7% and 13.8% of cases with VSD and ASD II respectively. It also found 10.1% case with complex CHD (Table-III). Risk factors associated with CHD is found in 50 (81.9%) cases and no risk factor was found in 11(18.03%) cases of CHD. Consanguinity, extracardiac malformations and maternal illness (HTN, DM, Hypothyroidism, etc.) are found associated with cardiac anomalies in 15 neonates (24.6%), 12 neonates (19.6%) and 5 neonates (8.2%). Both fertility medication (6.6%) and non-fertility medication (6.6%) are also found to be associated with CHD in Syndromic neonates (Table-IV)

Table III: Distribution and incidence of CHD (n=61)

Distribution and incidence of CHD	**No (%)**
Ventricular septal defect (VSD)	23(37.7)
Atrial septal defect (ASD II)	8(13.8)
Patent ductus arteriosus (PDA)	6(9.8)
Coarctation of aorta (CoA)	3(4.9)
Pulmonary stenosis (PS)	4(6.9)
Aortic stenosis (AS)	2 (3.3)
Transposition of great arteries (TGA)	3(4.9)
Tetralogy of Fallot (TOF)	1(1.6)
Atrial-ventricular canal defect (AVCD)	1(1.6)
Tricuspid atresia (TA)	1(1.6)
Left heart hypoplasia (LHH)	2(3.3)
Dextrocardia	1(1.6)
Complex CHD	6 (10.1)

Table IV: Risk factors for CHD (n=61)

Risk factors	n (%)
Consanguinity	15 (24.6)
Extracardiac malformations	12 (19.6)
Fertility medication	4(6.6)
Maternal drug use (Non Fertility medication)	4 (6.6)
Maternal smoking	1 (1.6)
Maternal illness (HTN, DM, Hypothyroidism etc.)	5(8.2)
Maternal previous abortion	3(4.9)
CHD in sibling	4 (6.6)
History of CHD in parents	1 (1.6)
Dysmorphic syndromes	1 (1.6)

Discussion

Many clinical cardiac findings were not recognized as such by the treating physicians and should have led to earlier referral of most of the patients. Massin *et al.*[12] found that 8.9% patient with a CHD had a delayed age of diagnosis. In this study the average age at diagnosis was 25± 1.6 days of age, which significantly differs from the study conducted by Massin & Dessy.[12] Sex ratio in this study was 1.18:1. Stoll & Alembik[13] found the ratio as 1.13:1, which is almost similar to this study.

In this study, we found 46.5% of the patient of Down syndrome associated with CHD. A similar finding (43%) was found by Weijerman *et al.*[8]; they also found a high incidence of PPHN at 5.2% in DS cases. Nazme *et al*.[14] found that 78% of the child with CRS having CHD in in two tertiary level hospitals of Bangladesh. In this study we found 75% of the CRS neonate having CHD, which is almost similar to above mentioned studies.

Formigari *et al.*[15] described 75% of DiGeorge Syndrome presented with peculiar cardiac anomaly, whereas our study found only three such cases with CHD. Small sample size may be the cause of finding increased percentage in this study. Twenty to 40% of the Turner Syndrome was associated with CHD, as found by Formigari *et al.*[15], which is similar to our study. Stoll *et al.*[13] found that 38.7% and 13.5% patient with VSD and ASD II in all syndromes with CHD. this study found 37.7% and 13.8% of cases with VSD and ASD II respectively. It also found 10.1% case with complex CHD.

Consanguinity, extracardiac malformations and maternal illness (HTN, DM, Hypothyroidism etc) are found associated with cardiac anomalies in 15 neonates (24.6%), 12 neonates (19.6%) and 5 neonates (8.2%). Similar findings were reported by Roodpeyma *et al.* and Hassan *et al.*[16,17]

In recent years, heart defects are becoming amenable to accurate investigation at anatomic and molecular levels;[18] therefore, in near future, we wish to see an exponential increase in knowledge about the specific cause of each single CHD.

Conclusion

CHDs have serious implications, and it is important to understand them and how they may affect the child so that appropriate medical and surgical treatment may be provided. So, early detection of CHD in neonate will be able to decrease morbidity as well as mortality. Early detection may help prevent complications that may adversely affect the outcome of cardiac intervention or cardiac surgery.

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