Congenital Heart Disease in a Tertiary Care NICU; Pattern, Risk Factors and Outcome

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Abstract

Background: *Identification of congenital heart disease (CHD) is increasing, may be due to advancement of diagnostic technology and availability of trained man power. Several studies have been conducted in Bangladesh to identify the prevalence and pattern of CHD but paucity of data regarding etiology and outcome.*

Objective: *The aim of this study is to identify the frequency and risk factors of so that preventive measures can be taken.*

Methods*: This retrospective case control study was conducted in the neonatal intensive care unit (NICU), BSMMU, Dhaka from January 2021 to June 2022. All admitted neonates in NICU with the diagnosis of CHD were considered as cases. Twice number of newborn having gestational age and birth weight matched neonates diagnosed other than CHD in NICU were considered as control. Data were extracted from the Medical records of patient files and computer electronic data records of "Newborn Birth Defect (NBBD) surveillance in Bangladesh." The level of significance was set at 5% (P <0.05).*

Result: *Total 914 patient were admitted during the study period among them 119 patient were CHD (frequency rate 13%). Mean birth weight and gestational age of CHD group were 2376±783.85g & 35.80±3.26 weeks respectively. About 85.7% had acyanotic CHD, among them most prevalent were atrial septal defect (42%) then patent ductus arteriosus (11.8%). Cyanotic CHD were 17 (14.3%). Maternal DM significantly increase the risk of developing CHD, Odd's ratio 1.971 (CI: 1.182 - 3.285). Death were more in CHD group (34.5%) than control group (20.4%), p values = 0.005.*

Conclusion: *Frequency (13%) of congenital heart disease was high. Maternal diabetes mellitus increases the risk of developing CHD of their baby. Death were more among babies with CHD.*

Keywords: *Birth defect, Congenital heart disease, Diabetes mellitus, Newborn.*

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Introduction:

Congenital heart disease (CHD) is defined as a gross structural abnormality of the heart or intrathoracic great vessels that causes significant functional impairment.[1] The global estimated birth prevalence of CHD is 8/1000 live births ranges from 3.5-17.5 per 1000 live births with a significant geographical difference.[2]

In India, over 180,000 children are born with CHD every year with state wise variation and contribute to 10% of the present infant mortality.[3] In a regional government medical college hospital of Bangladesh the prevalence of CHD was 7.8/1000 live births.[4]

CHD prevalence in developing countries might be underestimated due to lack of proper healthcare systems and follow up, unavailable detection modalities and limited diagnostic techniques.

According to recent update report of the American Heart Association, atrial septal defect (ASD), ventricular septal defect (VSD), tetralogy of fallot

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(TOF), patent ductus arteriosus (PDA), pulmonary stenosis, aortic stenosis, coarctation of aorta, and atrioventricular septal defect accounts for 85% of all CHDs.[5]

Several studies have been conducted to investigate the etiology of CHDs, but the molecular etiology and mechanisms leading to CHD are still the subject of debate. One study was done in Brazil to identify the risk factors of CHD. In which maternal diabetes and maternal age above 35 years were associated with congenital heart disease, whereas the protection factors were maternal hypertension, congenital infection, and multiple gestation.[6]

A population-based case-control study (242 CHD cases, 966 controls) was conducted in northern Ireland by using an iPad questionnaire for mother with linkage to maternity and first trimester prescription records. Risk of CHD was associated with low maternal education, pregestational diabetes, self-reported maternal clotting disorders, prescriptions for the anticlotting medication enoxaparin and self-reported vaginal infections.[7]

In Bangladesh, birth defect is the 4th common cause of neonatal death.[8] In the previous studies defects of the central nervous system were found predominantly in most of the countries. Recently due to advancement in diagnostic tools specially for bedside Echo availability, cardiovascular defects are leading cause of birth defects. Isolated congenital heart disease incidence, types of defect, risk factors, their association and outcome are not well known in our center as well as in our country.

In developed countries, early detection and proper treatment have increased the survival rate and decreased mortality from 80 to 20% resulting in an increase in the number of adults surviving with CHD.[9]

It will be possible to prevent CHD by controlling identified risk factors during pregnancy. Thus measures can be taken to prevent CHD during pregnancy and also early detection and appropriate treatment of CHD will be possible thereafter. Therefore the aim of this study is to explore the burden, pattern, risk factors and outcome of congenital heart disease in a tertiary care hospital Bangladesh.

Methods:

This was a retrospective case control study conducted in the Neonatal intensive care unit (NICU), Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2021 to June 2022. All admitted neonates in NICU with the diagnosis of congenital heart disease were considered as cases. According to departmental protocol those having abnormal fetal echo findings, abnormal physical examination suspicion of CHD or abnormal bed side echo finding done by neonatologist were referred to Pediatric cardiology department for confirmation of CHD. If CHD was diagnosed then follow up echo was done before discharge. Twice number of gestational age and birth weight matched neonates diagnosed other than congenital heart disease admitted in NICU were considered as control.

Data were extracted from the Medical records of patient files and computer electronic data records of "Newborn Birth Defect (NBBD) surveillance in Bangladesh". This program is going on in 20 medical colleges and institutes in Bangladesh and supported by WHO-SEARO and Directorate General of Health Services (DGHS), Ministry of health and family welfare, Bangladesh for better understanding of epidemiology and to develop strategic framework for the care and prevention of birth defect in this region. Bangabandhu Sheikh Mujib Medical University (BSMMU) plays role as a nodal center since its mission towards improvement of newborn health.

Information included full demographic and clinical data were extracted from patients files and electronic database. Maternal variables like maternal age at conception, full obstetric history, maternal illness (diabetes, hypertension and SLE), teratogens exposure (smoking and alcohol), maternal infection (Fever with rash and TORCH infection), medications (hypoglycemic, antihypertensive, antiepileptic and antibiotics), type of delivery and place of delivery were determined and recorded.

Family history included the presence of CHDs, other congenital or chromosomal abnormalities, and sibling deaths were also recorded.

Perinatal variables like gestational age, birth weight, sex, perinatal depression, early neonatal illness (like RDS, MAS, Sepsis, Premature birth and it's complications) were also collected. Post natal history like presenting features of heart disease, any dismorphism, any complications (heart failure, shock etc), types and duration of respiratory support, treatment option, duration of hospital stay and outcome of CHD were collected from records. Radiological imaging and USG were used to identify

the association of neurological, urogenital, gastrointistinal anomalies and orthopedic deformities. Outcome was measured by in hospital death or discharge of the newborn from NICU.

This study was approved by the institutional review board (IRB) of Bangabandhu Sheikh Mujib Medical University (Reg. no 755).

Quantitative variables were expressed as mean and standard deviation or median and interquartile range. Qualitative variables were expressed as absolute and relative frequencies. Categorical variables were compared by Pearson's chi-square test with adjusted residual analysis or Fisher's exact test as appropriate. Numerical variables were compared by student t test. Odds ratio (OR) for risk factor was calculated. All the risk factors found to be significant on univariate analysis are subjected to multivariate logistic regression analysis. The level of significance was set at 5% ($P < 0.05$), and all analyses were performed using SPSS, version 20.0

Result:

Total 914 patient were admitted during the study period. Among them 119 patient were diagnosed as a case of congenital heart disease (frequency rate 13%). Twice number (240) of control were also included to compare with cases.

Mean birth weight and gestational age of CHD group and control group were almost similar 2376±783.85g & 35.80±3.26weeks and 2321.67 ± 740.17g & 35.28 ± 3.24weeks respectively. Most of the CHD babies were inborn (62.2%) and delivered by caesarean section (73.9%). There was slight male predominance 52.1%. Similar finding were seen in control group. In delivery room bag & mask ventilation was need more in congenital heart disease group (14.3%) than control group (5.7%) which is significant (p value = 0.021), (Table I).

Table I

Baseline characteristics of the study population (N=359)

Variable	Cases, n=119	Control, n=240	p value
Mean birth weight (gram) ±SD	2376 ± 783.847	2321.67 ± 740.171	0.515
Mean gestational age (weeks) ±SD	35.80 ± 3.261	35.28 ± 3.244	0.158
Place of delivery			0.713
Inborn	74 (62.2%)	154 (64.2%)	
Outborn	45 (37.8%)	86 (35.8%)	
Sex		0.218	
Male	62 (52.1%)	138 (57.5%)	
Female	56 (47.1%)	102 (42.5%)	
Ambiguous	0 (00%)	1 (0.8%)	
Mode of delivery			0.285
Caesarean (%)	88 (73.9%)	190 (79.2%)	
Vaginal (%)	31 (26.1%)	50 (20.8%)	
Fetal growth velocity			0.455
Small for gestational age	19 (16%)	46 (19.2%)	
Appropriate for gestational age	96 (80.7%)	190 (79.2%)	
Large for gestational age	4 (1.7%)	4 (3.4%)	
Bag & mask ventilation needed at birth	17 (14.3%)	16 (5.7%)	0.021

Values are expressed as mean ± SD or n (%).

About 80% of congenital heart disease baby were diagnosed after birth and a small fraction about 19.3% by fetal Echocardiogram. Most of the babies were asymptomatic (46.3%). Among congenital heart disease only 15.1% developed heart failure where as 50.4% babies had feature of shock. About 37% of CHD had associated anomalies, among them GIT and CNS anomalies were predominant both were 18.2%. About 42% patient needed mechanical ventilator care. Mean duration of oxygen therapy and hospital stay of studied population were 10.96 ± 11.36 days and 13.18 ± 11.59 days respectively, (Table II).

Table II

Characteristics of congenital heart disease (N=119)

Variable	Value, n (%)
Mode of diagnosis of CHD	
Antenatally diagnosed	23 (19.3%)
Upon clinical Presentation	52 (43.7%)
Incidental findings	44 (37%)
Presentation of CHD	
Asymptomatic	55 (46.3%)
Cyanosis	06 (5.0%)
Respiratory distress	53 (44.5%)
Tachypnea	02 (1.7%)
Sepsis like features	03 (2.5%)
Heart failure	
Yes	18 (15.1%)
No	101 (84.9%)
Shock	
Yes	60 (50.4%)
No	59 (49.6%)
PPHN	
None	87 (73.1%)
Severe	13 (10.9%)
Moderate	11 (9.2%)
Mild	8 (6.7%)
Associated anomaly	
Yes	44 (37.0%)
No	75 (63.0%)
Types of Associated anomaly, n=44	
Gastrointestinal	8 (18.2%)
Syndromic	2 (4.5%)
Pulmonary	2 (4.5%)
Central nervous system	8 (18.2%)
Musculoskeletal	2 (4.5%)
Chromosomal	7 (15.9%)
Other	15(34.1%)

Table II (Cont'd)

Variable	Value, n (%)
Needed mechanical ventilator	
Yes	50 (42%)
No	69 (58%)
Need for non invasive respiratory support	
Yes	48 (40.3%)
No	71 (59.7%)
Duration of O_2 support, days mean±SD	10.96±11.36
Duration of hospital stay, days mean±SD	13.18±11.59

Values are expressed as mean ± SD or n (%). CHD = congenital heart disease

More than three fourth (85.7%) had acyanotic congenital heart disease, among them most prevalent were atrial septal defect (42%) then patent ductus arteriosus (11.8%). Combined ASD plus PDA were 24.4%. Cyanotic congenital heart disease were 17 out of 119cases (14.3%), among them predominant were complex congenital heart disease 13 (76.5%) out of 17 number. About one fourth of congenital heart patient had persistent pulmonary hypertension (PPHN), (Table III).

Table III

Echocardiographic finding of congenital heart disease (N=119)

Variable	Frequency	Percentages
Type of CHD		
Acyanotic	102	85.7%
Cyanotic	17	14.3%
Cyanotic CHD, n=17		
Complex CHD	13	10.9%
Ebstein anomaly	2	1.7%
HLHS	1	0.8%
TOF	1	0.8%
Acyanotic CHD, n=102		
ASD	50	42.0%
ASD+PDA	29	24.4%
PDA	14	11.8%
ASD+VSD+PDA	5	4.2%
ASD+VSD	4	3.4%
VSD+PDA	2	1.7%
Others	2	1.7%

Values are expressed as n (%). CHD = congenital heart disease; HLHS = hypoplastic left heart syndrome; TOF = tetralogy of fallot; ASD = atrial septal defect; PDA = patent ductus arteriosus; VSD = ventricular septal defect and PPHN = persistent pulmonary hypertension of newborn.

Table IV

Comparison of maternal and neonatal characteristics between case and control

Factors	Cases, n=119	Control, n=240	p value
Maternal age, years mean±SD	28.93 ± 4.586	28.73±4.480	0.682
Maternal Hypertension			0.894
Yes	21 (17.6%)	41 (17.1%)	
No	98 (82.4%)	199 (82.9%)	
Maternal DM			0.004
Yes	42 (35.3%)	51 (21.2%)	
No	77 (64.7%)	189 (78.8%)	
Maternal hypothyroidism			0.381
Yes	15 (12.6%)	23 (9.6%)	
No	104 (87.4%)	217 (90.4%)	
Fever with rash in 1st trimester Yes			0.557
No	3 (2.5%)	10 (4.2%)	
116 (97.5%)	230 (95.8%)		
Parity			0.929
Multi	70 (58.8%)	140 (58.3%)	
Primi	49 (41.2%)	100 (41.7%)	
Parenteral consanguinity			1.00
Yes	4 (3.4%)	8 (3.3%)	
No	115 (96.6%)	232 (96.7%)	
CHD in family			0.668
Yes	2 (1.7%)	3 (1.2%)	
No	117 (98.3%)	237 (98.8%)	
Death	41 (34.5%)	49 (20.4%)	0.005

Values are expressed as mean ± SD or n (%). CHD = congenital heart disease; DM = diabetes mellitus.

Mean maternal age of patient with congenital heart disease were 28.93 ± 4.586 years and almost equal in control group (p = 0.682). There was no significant difference of parity, parenteral consanguinity, family history, maternal hypertension, maternal hypothyroidism and fever with rash in 1st trimester between two groups. Maternal DM was significantly higher in congenital heart disease group (35.3%) than control group (21.2%), p value 0.004. Death were more in CHD group (34.5%) than control group (20.4%), p values = 0.005. (Table IV).

Regression analysis showed parity, maternal hypertension, maternal hypothyroidism maternal infection, consanguinity, family history of CHD and fetal growth had no significant impact on congenital heart disease. Maternal DM significantly increase the risk of developing congenital heart disease, Odd's ratio 1.971 (CI: 1.182 - 3.285), (Table V).

Spontaneous resolution occurs in 2 patient (1.7%) and medical treatment needed in 76 (63.9%) patient. Successfully 51 patient (42.9%) has been discharged and 10.1% took discharge on request. Discharge on risk bond were 11.8% and referred were only 1 patient. Unfortunately total 41 patient (34.5%) died due to complications of congenital heart disease, (Table VI). Among them death in cyanotic heart disease were 8 (47.1%) and in acyanotic heart disease were 33 (32.7%).

Table V

Multivariate regression analysis of CHD according to maternal and newborns characteristics

Characteristics	Odd's ratio	95% C.I.		p value
		Upper	Lower	
Parity	0.994	0.624	1.584	0.979
Maternal DM	1.971	1.182	3.285	0.009
Maternal HTN	1.323	0.708	2.471	0.381
Maternal Hypothyroidism	1.419	0.693	2.909	0.339
Maternal infection	0.188	0.188	2.963	0.747
Consanguinity	0.965	0.274	3.398	0.955
CHD in family	0.800	0.120	5.324	0.818
Fetal growth	0.419	0.080	2.185	0.302

CHD = congenital heart disease; DM = diabetes mellitus; HTN = hypertension.

Table VI

Outcome of patients with congenital heart disease (N=119)

Variable	Frequency	Percentages
Outcome		
Spontaneous resolution	2	1.7%
Medical treatment only	76	63.9%
Death	41	34.5%

Values are expressed as n (%)

Discussion:

Congenital heart diseases represent a significant global health burden and a major cause of mortality & morbidity in neonates and infants.[10] In this retrospective study, we reviewed the frequency and patterns of CHD among newborn at our tertiary academic hospital in Bangladesh.

The frequency of all CHD among our studied population is 13/1000. There seems to be a big variation in the incidence of CHD between different nations. The prevalence of CHD in a regional government medical college in Mymensingh, Bangladesh was 7.8/1000 live births.[4] Almost similar prevalence of CHD was10.13/1000 live births in Government Medical College, Nagpur, Maharashtra, India.[11] The reported rates have been <1% in Europe and USA.[10,12] In India, several papers were published reporting a CHD incidence of 4-26 per 1,000 live births.[13] Although the difference in the prevalence between different populations is not well-studied and not well-explained by strong evidence, this variation might be related to multiple genetic and environmental factors including ethnicity and consanguineous marriage.[14,15] In our study antenatally detected rate of CHD was low 23 (19.3%) may be due to lack practice of doing fetal Echo, whereas 60% of cases with CHD detected by antenatal screening, only 40% were confirmed by postnatal echo in Jordan.[16]

The pattern of distribution of CHD in our study was somehow different from other reports worldwide. ASD was the most common CHD among our studied population followed by PDA and VSD. Isolated ASD was found in 50 (42%) cases and isolated PDA in 14 (11.8%) cases. Total VSD cases were 11 (9.3%). Similar observation was reviewed by Rahim et al. that CHD patterns in a local province in Iran and concluded a total incidence of 12.3 per 1,000 with ASD and TOF to be the most commonly diagnosed lesions.[17] Siddique et al in Rajshahi Medical College Hospital, Bangladesh and Fatema et al. in Combined Military Hospital, Dhaka also found ASD was the commonest lesion.[18,19] Most worldwide CHD studies have reported VSD to be the most common CHD.[14,20] In contrast to our study, order of frequency of CHD were found VSD (29%), ASD (24%), PDA (10%), complex congenital heart disease (8%), TGA (8%) and TOF (6%) in a government medical college of Bangladesh.[4]

The rate of cyanotic lesions among CHD cases in our study was 14.3% (17/119). In Bangladesh higher rate of cyanotic CHD was reported by Islam MN et a. (29%) of cyanotic congenital heart disease in Mymensingh Medical College Hospital and Roy K et al. 30%

cyanotic CHD in Rajshahi Medical College Hospital.[4,21] In contrast to our study higher incidence of cyanotic CHD was also reported by Fatema et al. from CMH, Dhaka 28.8% and Mohammad Abdullah Al Mamun et al. from Bangladesh Shishu Hospital and Institute 28.7%.[22,23] One study in Maharashtra, India found cyanotic CHD were 33.26%.[11] Similar to our study from Jordan university, Al Ammouri reported that 11% of their cohort to have cyanotic CHD.[24] The rate of cyanotic lesions among CHD cases was quite low (6%) in other study.[16]

CHD is seen as an isolated birth defect or in association with other systemic anomalies. The prevalence of coexisting anomalies in our study was 37% with similar findings 40% in KSA and around 25% in Europe and India.[12,25] But prevalence of coexisting anomalies in Jordan was only 13%, which is much less than our findings. Khasawneh et al., Islam MN et al. Trevisan from Brazil reported that Trisomy 2 chromosomal abnormalities was predominant associated anomalies in patients with CHD.[26] Where as in our study, Musculoskeletal and CNS anomalies are more associated with CHD and next one is chromosomal anomalies.

In our study we found only maternal DM is the causal risk factor for developing CHD. Daniela Anderson also reported that risk factors associated with congenital heart disease were maternal diabetes (relative risk, 1.55; 95% CI, 1.11-2.20) and maternal age above 35 years (relative risk, 2.09; 95% CI, 1.73-2.51).[7] A study done by Suluba et al. showed maternal rubella infection, teratogens, maternal age and diabetes mellitus are responsible for CHDs.[27] In contrast to our study, S. Begum and S.K. Dey did not find DM as a risk factor of CHD in Special Care Baby Unit (SCABU), BIRDEM.[28]

The rate of mortality among CHD cases was very low 8.7% in Jordan.[16] Meshram and Gajimwar showed 19.23% patients expired among CHD.[11] In our study mortality rate was high around 34.5% which is nearly to other study (30.1%) conducted by Mohammad Abdullah Al Mamun, in Bangladesh.[24] The pooled standardized mortality ratio in patients with congenital heart disease was 2.48, which was significantly higher than in patients without congenital heart disease in Brazil.[7]

There were some limitations in this study. It is a retrospective and single center study. Echocardiogram is not routinely done in all patient, rather only suspected patient was selected in NICU for Echocardiogram. So in that case may be some missing cases.

Conclusion:

Rate of congenital heart disease is high in our center. Diabetes mellitus is independently associated with congenital heart disease. A significant percentage of CHD patient died due to complications. Early detection and appropriate glucose control can reduce complication of DM in pregnancy.

Limitation:

It is a retrospective and single center study. Echocardiogram is not routinely done in all patient, rather only suspected patient was selected in NICU for Echocardiogram. So in that case may be some missing cases.

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Author Contributions:

Conception and design: SKD; Literature search and manuscript writing: MAH; Data collection and Compilation: FY; Statistical analysis and interpretation of data: IJ; Manuscript revising: MKHS; Approval of the final version of manuscript: SKD, MAH, FY, IJ, MKHS; Guarantor accuracy and integrity of the work: SKD.

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