Original Article

Evaluation of the prevalence, pre-natal risk factors, and clinical profiles of pediatric patients with congenital heart disease

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ABSTRACT

Introduction: Congenital heart diseases (CHD's) are among the major congenital malformations contributing to infant mortality. Most CHDs are diagnosed in infancy. Later, in childhood or adolescence, CHD patients may present differently. **Objectives:** The aim of the study was to evaluate the prevalence, maternal risk factors, and clinical profile of all children with CHD at a tertiary care center in Bhopal. **Materials and Methods:** This prospective and observational study was conducted at a tertiary care center in Bhopal from February 2018 to February 2020. Approval from the Ethical Committee was obtained before the commencement of the study. Children up to 13 years of age, admitted with the features of CHD for the 1 time in our institution, were included in this study. A detailed history and clinical examination were carried out and a diagnosis of CHD was confirmed with 2D echocardiography. **Results:** A total of 224 patients were admitted with the features of CHD for the 1 time during the study period. In our study, the most common lesion was ventricular septal defect (VSD) (29.01%) followed by atrial septal defect (14.73%), patent ductus arteriosus (12.5%), and tetralogy of fallot (TOF) (9.37%). Among the clinical presentation, fast breathing (90.17%) was the most common symptom. **Conclusion:** In our study, VSD was found to be the most common acyanotic CHD and TOF was the most common cyanotic CHD. The most common presenting feature was breathing difficulty. To improve prenatal detection of CHD's, it is imperative to have a deep understanding of maternal risk factors.

Key words: 2-D-Echocardiography, Combined congenital heart diseases, Complex congenital heart diseases, Congenital heart diseases

A congenital heart disease (CHD) is not a fixed set of anatomical anomalies that appear at birth, but rather a dynamic group of lesions that emerge during fetal life and undergo considerable changes after birth [1]. The reported birth prevalence of CHD is 8/1000 live births [2]. CHD's have traditionally been classified based on whether they cause cyanosis as cyanotic CHD's and acyanotic CHD's. Cyanotic lesions consist of tetralogy of fallot (TOF), transposition of the great arteries (TGA), and Ebstein's anomaly. Acyanotic lesions include ventricular septal defect (VSD), atrial septal defect (ASD), patent ductus arteriosus (PDA), pulmonary stenosis (PS), aortic stenosis (AS), and coarctation of the aorta (CoA) [3].

While the prevalence of acquired heart disease has decreased over the past decade, CHD prevalence has increased likely due to better detection and improved survival [4]. Many cyanotic CHDs are life threatening in the neonatal period. Acyanotic CHD (mostly VSD) is seen in about three-fourths of babies born with CHD [5]. The incidence of moderate-to-severe structural CHD in newborn infants is about 6–8/1000 live births [6].

Globally, there were more than 200,000 deaths associated with CHD, with the majority occurring in young people [7]. In spite of the relatively constant incidence of most CHDs at birth, advances in pre-operative diagnostic techniques, surgical techniques, intensive care, and anesthesia have led to better long-term outcomes [8]. Despite its prevalence, the exact etiology of CHD is still largely unexplained. It is considered to be multifactorial in nature with genetics and environmental factors playing a major role. Other factors such as teratogens may independently cause malformation, while maternal factors may also contribute to disease manifestations [9,10].

According to the American Heart Association, ASD, VSD, TOF, PDA, PS, AS, CoA, and atrioventricular septal defect together account for 85% of all CHD's [11]. CHD's have varying degree of presentation. The most of CHD's clinical presentation can be explained in physiological terms, such as outflow obstruction (pressure overload) and pulmonary over-circulation (volume overload). A child with CHD may manifest

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with congestive cardiac failure (CCF) or may have asymptomatic murmur. In India, the birth prevalence of children born with CHD is around 240,000/year [12] thus posing a heavy burden. Over a 1-year period (2016–2017), approximately 27,000 patients with CHD underwent cardiac surgery. Of this, about 9700 patients were infants (<1 year) and about 1700 were neonates (<1 month) [12]. This enormous burden of CHD among children highlights the importance of this study. Therefore, the aim of this study was to evaluate the prevalence, maternal prenatal risk factors, and clinical profile of all children with CHD at a tertiary care center in Bhopal.

MATERIALS AND METHODS

This prospective and observational study was conducted at a tertiary care center in Bhopal from February 2018 to February 2020. Approval by the Ethical Committee was obtained before commencement of the study. All the patients, up to 13 years of age, admitted with the features of CHD for the 1 time were included in this study. Furthermore, the patients admitted in neonatal intensive care unit (NICU), pediatric intensive care unit (PICU), and pediatric ward with signs and symptoms of CHD such as breathlessness, or features of CCF, bluish discoloration of lips, respiratory tract infection, refusal to feed, squatting position, clubbing, failure to thrive, and cardiac murmur were included in the study.

A written valid consent from parents or legal guardian/ caretaker was obtained. Preterm neonates (<37 weeks of gestation), patients above 13 years of age, and patients came for follow-up were excluded from the study. A detailed history and clinical examination were carried out and CHD was suspected in the presence of the symptoms mentioned above. Diagnosis was confirmed with 2D echocardiography. The following details were obtained through questionnaires: Family history of CHD, parental consanguinity, maternal age at conception, maternal medical, gestational and obstetric history, smoking, alcohol, and medications.

Data were entered into MS Excel sheet. Categorical variables were described in the form of percentage. Continuous variables such as age were summarized as mean and standard deviation. P<0.05 was considered to be statistically significant.

RESULTS

Over the study period of 2 years, 224 children were admitted with the features of CHD. Out of which, 117 were males (52.23%) and 107 were females (47.76%), with a male: Female (M: F) ratio of 1.09:1. Our study included 68 neonates from NICU, 86 children from PICU, and 70 children from pediatric ward. Table 1 shows the demographic profile of patients. According to the distribution of age groups, the patients between 1 and 12 months accounted for 37.94% of the population. Hinduism was the predominant religion of study participants followed by Islamism, Catholicism, and Sikhism. In the study, the most of the participants were rural dwellers and were of lower class. The study population was largely made up of third-born children based on birth order.

Table 1: Demographic profile of patients with CHD

	Total number	%
Gender		
Male	117	52.23
Female	107	47.76
Total	224	100
Age		
0–1 months	49	21.87
1–12 months	85	37.94
1–5 years	63	28.12
>5 years	27	12.05
Religion		
Hinduism	112	50
Islam	78	34.82
Catholic	19	8.48
Sikhism	15	6.69
Birth place		
Urban	109	48.66
Rural	115	51.33
Socioeconomic status		
Lower	121	54.01
Middle	103	45.98
Birth order		
First order	33	14.73
Second order	82	36.6
Third order	109	48.66

CHD: Congenital heart diseases

Table 2 shows the admission weight of patients with CHD in males and females between 0 and 1 month, 1 and 12 months, 1 and 5 years, and >5 years.

Among the clinical presentation, fast breathing (90.17%) was the most common symptom followed by fever (73.21%), failure to thrive (43.3%), cyanosis (38.39%), refusal to feed (31.69%), clubbing (21.87%), squatting position (12.05%), and cardiac murmur (8.03%) as shown in Table 3.

Table 4 highlights the spectrum of CHDs in all patients. In our study, the most common lesion found to be present was VSD (29.01%) followed by ASD (14.73%), PDA (12.5%), TOF (9.37%), and TGA (8.48%). Least common lesions found to be present were TAPVC (3.57%), PS (3.12%), ASD+VSD (3.12%), COA (2.67%), VSD+PDA (2.67%), tricuspid atresia (1.78%), ASD+VSD+PDA (1.78%), truncus arteriosus (1.33%), hypoplastic left heart syndrome (1.33%), PAPVC (0.89%), DORV (0.89%), and Ebstein's anomaly (0.89%). Among complex CHDs, DORV+PDA+pulmonary artery hypoplasia (0.89%) and TGA+COA+PDA (0.89%) were present.

Table 5 shows various maternal risk factors associated with CHD's. History of consanguineous marriage was present in parents of 23.9% males and 17.7% female patients. Maternal exposure to various environmental factors was also determined as shown in Table 5. The most common pregnancy complication was preeclampsia among in the mothers of 10.25% male and 7.47%

Table 2: Admission weight of patients with CHD

Gender	Age	Admission weight (g) (Mean±SD*)
Male	0–1 month	2508±578
	1–12 months	5283±853
	1–5 years	8100±645
	>5 years	12878±591
Female	0–1 month	2450±534
	1–12 months	5212±677
	1–5 years	6994±564
	>5 years	11734±767

*SD=Standard deviation, CHD: Congenital heart diseases

Table 3: Presenting complaints among patients with CHD

Signs and symptoms	n (%)
Fast breathing	202 (90.17)
Fever	164 (73.21)
Failure to thrive	97 (43.3)
Cyanosis	86 (38.39)
Refusal to feed	71 (31.69)
Clubbing	49 (21.87)
Squatting position	27 (12.05)
Cardiac murmur	18 (8.03)

CHD: Congenital heart diseases

Table 4: Prevalence of lesions among patients with CHD

Spectrum of CHD's	n (%)
VSD	65 (29.01)
ASD	33 (14.73)
PDA	28 (12.5)
TOF	21 (9.37)
TGA	19 (8.48)
Total anomalous pulmonary venous connection (TAPVC)	8 (3.57)
PVS	7 (3.12)
ASD+VSD	7 (3.12)
CoA	6 (2.67)
VSD+PDA	6 (2.67))
Tricuspid atresia	4 (1.78)
ASD+VSD+PDA	4 (1.78)
Truncus arteriosus	3 (1.33)
Hypoplastic left heart syndrome	3 (1.33)
Partial anomalous pulmonary venous connection (PAPVC)	2 (0.89)
DORV	2 (0.89)
Ebstein's anomaly	2 (0.89)
Complex CHD	
DORV+PDA+pulmonary artery hypoplasia	2 (0.89)
TGA+COA+PDA	2 (0.89)

CHD: Congenital heart diseases, VSD: Ventricular septal defect, ASD: Atrial septal defect, PDA: Patent ductus arteriosus, TOF: Tetralogy of fallot, TGA: Transposition of the great arteries, CoA: Coarctation of the aorta, DORV: Double outlet right ventricle

female patients followed by gestational diabetes in mothers of 5.9% male and 4.6% female patients.

Table 5: Maternal prenatal risk factors among patients with CHD's

Prenatal risk factors	Male patients n (%)	Female patients n (%)
Parental consanguinity	28 (23.9)	19 (17.7)
Family history of CHD	17 (14.52))	14 (13.08)
Maternal obesity	5 (4.27)	7 (6.54)
Maternal age at conception		
<20	21 (17.9)	18 (16.82)
20–25	8 (6.8)	9 (8.4)
26–30	12 (10.25)	17 (15.88)
30–35	31 (26.49)	26 (24.2)
>35	35 (29.9)	37 (34.57)
Maternal environmental exposure		
Smoking	17 (14.5)	19 (17.75)
Alcohol consumption	6 (5.1)	3 (2.8)
Teratogenic medications	5 (4.27)	2 (1.86)
Pregnancy complications		
Preeclampsia	12 (10.25)	8 (7.47)
Gestational diabetes	7 (5.9)	5 (4.6)
Fever	5 (4.27)	7 (6.5)
Rubella	1 (0.85)	2 (1.86)
Other infections	3 (2.5)	6 (5.6)

CHD: Congenital heart diseases

DISCUSSION

The present study was conducted among 224 children in whom CHD was suspected and later on confirmed by 2D echocardiography. A relevant case history with special emphasis on prenatal, antenatal, and family history was taken. A detailed clinical examination of each patient was performed. In our study population, we noted a male preponderance. This was similar to other studies in which a higher prevalence of CHD among males was observed [13,14]. This male predominance can be explained by the frequent occurrence of CHD's of conotruncal origin in males [15]. This may also be due to the fact that the most of the population brings male offsprings for the treatment more frequently.

In the present study, 37.94% of patients presented between 1 and 12 months of age. These findings are similar to those found by Meshram and Gajimwar; perhaps, due to the improved awareness and the availability of better facilities as compared to decades ago [16]. The majority of the participants (50%) in our study were Hindus. In recent years, many studies have examined the association between religious involvement and health outcomes [17]. A strong inverse relationship was found between religious/spirituality (R/S) practices and CHD in one case–control study [18]. Despite the controversy, research on R/S and CHD is still lacking, with some studies reporting a lack of correlation [19].

In the present study, a majority of patients were from rural areas and were of lower class. These findings were similar to other studies, in which, an inverse association between socio-economic

status (SES) and CHD was found [11]. In another study also, the burden of CHD was higher in rural areas as compared to urban areas [20]. The probable explanation could be that the patients with low SES are likely to experience delayed medical diagnosis and minimal access to health care.

Childbirth order has been linked to several adverse life outcomes, including morbidity and mortality. About 48.66% of infants examined in our study were third born. The findings of our study are similar to those of Meshram and Gajimwar who reached the similar conclusion that the higher the birth order, the more likely it was to develop disease [16]. The increase in the incidence of CHD with a higher birth order is indirect evidence of environmental influences that cause the disease [21].

In our study, the mean admission weight of male patients between 0 and 1 month was 2508±578 g, between 1 and 12 months was 5283±853 g, between 1 and 5 years was 8100±645, and >5 years was 12878±591 g. Similarly, the mean admission weight of female patients between 0 and 1 month was 2450±534 g, between 1 and 12 months was 5212±677 g, between 1 and 5 years was 6994±564, and >5 years was 11734±767 g. In another study, it was found that CHD occurs more frequently in very low birth weight infants weighing <1500 g [22].

When the signs and symptoms were taken into consideration, we found that fast breathing was the most common symptom presents in 90.17% of patients followed by fever (73.21%). These findings were comparable to another study [16]. Other signs and symptoms noted in our study were failure to thrive (43.3%), cyanosis (38.39%), refusal to feed (31.69%), clubbing (21.87%), squatting position (12.05%), and cardiac murmur (8.03%). A study done by Molaei *et al.* observed that respiratory distress (70%) was the most common complaint and cyanosis (24.4%) was the second most common complaint [23].

In our study, the most common lesion found to be present was VSD (29.01%) followed by ASD (14.73%) which is in congruence with another study [16]. Similarly, in a study by Mehak *et al.*, VSD was found to be the most common lesion followed by ASD [24]. While few other studies differ from our findings among which a higher incidence of VSD, PDA, and TOF was observed [25]. The most common combined lesion observed in our study was ASD+VSD (3.12%). Complex lesions present in patients were: DORV+PDA+pulmonary artery hypoplasia (0.89%) and TGA+COA+PDA (0.89%). These findings are comparable to another study, in which, it was found that ASD+VSD was present among 1.6% of patients [24].

A positive family history was found to be present among 14.52% of males and 13.08% of females. In another study, 17.9% had a positive family history of CHD [26]. Marriages between couples related as second cousins or closer are regarded as consanguineous. It has been estimated that at least 10.4% of the present world population are consanguineous, with first cousin marriages especially popular [27]. Parental consanguineous marriage was present among 23.9% males and 17.7% female patients in the present study. Many studies have shown a positive correlation between consanguinity and CHD's [28].

Pre-pregnancy obesity was present among mothers of 4.27% males and 6.54% females. These results are in line with the findings of other study which has also found a positive association between maternal obesity and CHD [29]. Women with body mass index above the normal range are more likely to have gestational diabetes mellitus, which is an established teratogen [30]. The increased risk of CHD's observed in obese mothers has thus been attributed to diabetes mellitus.

Advanced maternal age is thought to be a considerable risk factor for CHD's. In our study, age at conception was >35 years among mothers 29.9% males and 34.57% females. This finding coincides with the previous study, in which, an increased risk of CHD associated with maternal age ≥35 was reported [31]. In contrast, another study reported little evidence between CHD and advanced maternal age, ≥35 at delivery [32]. CHD, however, is believed to have genetic etiology, with gene mutations likely to increase more frequently with maternal age [33].

Maternal prenatal environmental factors such as smoking, alcohol consumption, and teratogenic medications have a major influence on the growth of fetus. In spite of the decrease in smoking and alcohol consumption rates in women over time, maternal smoking is still highly related to all types of CHD's. In our study, a positive maternal history for smoking was present among 14.5% of males and 17.75% of females followed by alcohol consumption in mothers of 5.1% of males and 2.8% of females. Similar findings were found in another study, in which, smoking was significantly more prevalent than alcohol consumption in mothers [26]. According to a meta-analysis by Zhang *et al.,* maternal smoking during pregnancy has a cardiovascular teratogenic effect and their offspring may suffer from approximately 10% relative increase in the risk of CHDs on an average [34]. In our study, a history of teratogenic medication intake was found among mothers of 4.27% males and 1.86% females. However, according to the Fung *et al.* [26], it is not clear whether the association with CHD is related to the use of medication or to the underlying medical condition for which medications were used.

The most common pregnancy complications found in our study were Preeclamsia and Gestational Diabetes Mellitus . 10.25% male and 7.4% female babies were born to mothers with Preeclamsia followed by 5.9% male and 4.6% female babies were born to mothers with Gestational Diabetes Mellitus. A positive association between preeclampsia and congenital malformations has been reported in a previous study [35]. An increased risk of CHD's among offsprings born to diabetic mothers has been reported in a study [36]. The prevailing hypothesis explaining this association is glucose affecting gene expression in embryonic development through epigenetic changes (histone acetylation and microRNA expression) [37]. There has been an improvement in pre-natal care and more awareness of glucose regulation before pregnancy in recent years. Nevertheless, our study results indicate that this improved care has not decreased the risk of offsprings born to diabetic mothers.

Our study had limitation as well. It was not a multicentric study and hence it cannot show an exact prevalence of CHD's. Therefore, large multicentric trials should be undertaken in future.

CONCLUSION

CHDs are among the major congenital malformations contributing to infant mortality. Our study reveals a growing burden of CHD among infants. In a developing country like India, a lack of awareness and resources explains why most CHDs are diagnosed very late. The diagnosis of CHDs at an early stage is vital for timely treatment, close monitoring, and prevention of further complications. To increase and improve pre-natal detection of CHD's, it is imperative to have a deep understanding of maternal risk factors.

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