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Epidemiologic Study of Congenital Heart Diseases and Its Related Factors in Children Referred to the Pediatric Cardiac Clinic of Birjand University of Medical Sciences, Iran

Siavash Kafian Atary[1], Arvin Mirshahi[1], Ahmad Amouzeshi[2], Abas ali Ramazani[3], Zahra Soleimani Khomartash[4], Babak Bahman[1], Mahsa Hasanzadeh Tahery[1], *Forod Salehi[5]

[1]Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran. [2]Associate Professor, Cardiac Surgeon, Birjand University of Medical Sciences, Birjand, Iran. [3]Epidemiology Trainer, Research Center for Social Factors Affecting the Health, Department of Epidemiology and Biomedical Sciences, Faculty of Public Health, Birjand University of Medical Sciences, Birjand, Iran. [4]Birjand University of Medical Sciences, Birjand, Iran. [5]Department of Pediatrics, Vali-e-Asr Hospital, Birjand University of Medical Sciences, Birjand, Iran.

Abstract

Background: Congenital heart disease is the most common type of maternal abnormality and is the leading cause of mortality in the first year of life. The aim of this study was to determine the epidemiological and related factors of congenital heart disease (CHD) in children referred to the pediatric heart clinic of Vali-e-Asr Hospital of Birjand, Iran.

Materials and Methods: In this descriptive-analytical cross-sectional study, the study population included 300 patients with congenital heart disease who referred to the Vali-e-Asr Hospital, Birjand, Iran. A checklist form was used to complete the information contained in the patient records and contact their parents. The collected data were analyzed using SPSS software version 16.0 at a significance level of $p \leq 0.05$.

Results: The mean age of children with CHD at the time of diagnosis was 1.25 ± 2.92 years. 156 (52%) were male. The most common type of CHD included ventricular septal defect (28.7%), patent ductus arteriosus (18.2%), and atrial septal defect (14.6%). Down syndrome (3.8%) was the most common anomaly. In 57% of cases, there was a familial relationship between parents. There was a significant statistical difference between drug use in pregnancy, maternal age, age of patients, mother's education level, place of residency, and familial relationship of parents and CHD in the children $p \leq 0.05$.

Conclusion: Based on the results, the most common type of CHD included ventricular septal defect, patent ductus arteriosus, and atrial septal defect, respectively. There was a relationship between baseline and clinical characteristics (maternal age, patient age, familial relationship, and drug use in pregnancy), and CHD in the children.

Key Words: Children, Congenital heart disease, Epidemiology, Related factors.

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Corresponding Author:

Forod Salehi (M.D), Department of Pediatrics, Vali-e-Asr Hospital, Birjand University of Medical Sciences, Birjand, Iran.

Email: hamidsalehi500@yahoo.com

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1- INTRODUCTION

Congenital heart disease is the most common type of maternal abnormality and is the leading cause of death in the first year of life (1-8). The common process between all congenital heart abnormalities is the abnormal development of embryonic natural structures or a halt in the maturity of these structures in the early stages of the embryo, which include disorders in the walls of the heart, valves, and vessels (2, 5, 9, 10). Maternal malformations are two types: cyanotic and non-cyanotic, which are diagnosed in half of the cases until one month of age (6-8). Congenital anomalies of the heart vary in severity. Some are extremely loud and discovered at an early age; but beyond the range of people, there are mild defects that may not be marked until adulthood, and thus are discovered at an older age. Congenital heart malformations have an estimated 1% prevalence in the world (3, 5), and affect between 5 and 8 people in every 1,000 live births (4, 8, 11); of course, this is only an average It is all over the world and it is different in every region. Therefore, several genetic and environmental factors at this time can cause various malformations (3, 6, 10). Cardiovascular diseases are divided into two congenital and acquired general types.

Congenital diseases are those that are present in the neonate at the moment of birth; however, acquired cases are overwhelming during neonate, infancy, childhood, adolescence, etc. (10). Congenital anomalies in the heart have been considered in many communities due to its complications and mortality and the high costs imposed on the health system. Congenital heart disease has different symptoms depending on the type and severity of the disease, and subsequently, they have various complications (8, 11). Several genetic and environmental risk factors have been proposed to increase the likelihood of CHD in several studies; some of them include familial marriages, family history of CHD, and some chromosomal disorders like Down syndrome, gender, taking teratogenic medications during pregnancy, exposure to X-rays during pregnancy, metabolic problems such as high and uncontrolled blood sugar, especially in the first trimester (3, 4, 6, 7, 12). The results of various studies suggest the cause of congenital heart disease is multi factorial (12), some of which are not known to cause specific abnormalities in them. The usual care of pregnancy and timely sonography can detect some cardiac anomalies, which leads to more research. It is recommended that fetal echocardiography is performed between the 17th and 20th weeks of gestation in certain groups (mothers with congenital anomalies in the heart or taking teratogenic agents during pregnancy, etc.) (6). Considering the lack of studies on the epidemiology of congenital heart disease in Birjand, South Khorasan, Iran, this study aimed to determine the epidemiologic characteristics of congenital heart disease in children referred to the pediatric heart clinic of Vali-e-Asr Hospital of Birjand University of Medical Sciences during the years 2015-2017. Since these diseases greatly reduce the quality of life of parents, especially mothers (13), and that of the whole family, epidemiological knowledge and planning for the management of these diseases will be of special significance.

2- MATERIALS AND METHODS

2-1. Study design and population

In this descriptive-analytical cross-sectional study, the study population included 300 patients with congenital heart disease, who were referred to the Pediatric Cardiac Clinic of Vali-e-Asr Hospital of Birjand University of Medical Sciences, Birjand, Iran, during 2015-2017.

2-2. Measuring tools

The data collection tool was a checklist form, which was used to complete the information contained in the patient records and contact with their parents. Information included age and gender, complaints of referral time, labor history, and congenital heart disease in first-degree relatives, taking medication during pregnancy by the mother, cigarette smoking and opium during maternal gestation, mother's exposure to x-rays during pregnancy, familial marriage, parental location and type of congenital heart disease. After suspicion of congenital heart disease, transthoracic echocardiography was performed and the diagnosis of congenital heart disease was given to the patient.

2-3. Ethical consideration

We collected the data, after approval of the thesis No.779, and the Ethics Committee of the University with the code of ethics, ir.bums.REC.1395.217 and patients were assured of the confidentiality of the information collected.

2-4. Inclusion and exclusion criteria

Inclusion criteria included heart murmur, cyanosis, failure to thrive, respiratory distress, syndromic diseases (Down syndrome, Williams syndrome, etc.), arrhythmogenic cardiac disorders and the exclusion criteria were the dissatisfaction of parents to enter the study and the unstable condition of the patient.

2-5. Data Analyses

Statistical analysis was performed using the SPSS software (version 16.0), and using the Chi-square statistical test for analyzed qualified variables. P-value less than 0.05 was statistically significant.

3- RESULTS

Of the 300 patients, 156 (52%) were male and 144 (48%) were female. The most common types of CHD include ventricular septal defect (VSD), (28.7%), patent ductus arteriosus (PDA) (18.2%), and ASD (14.6%). Of the 300 patients, 39 (13%) had the cyanotic disease and 261 (87%) had the non-cyanotic disease (**Table.1**). The most common complaint at the time of visit was a heart murmur (90%). The majority of patients had the term (60.3%). The mean age of mothers of children with congenital heart disease at the time of pregnancy was 29.14 ± 6.19 years, ranging from 16 to 48 years (p-value= 0.001). Mothers were 22 (7.2%) illiterate, 125 (41.7%) were under the diploma, 92 (30.7%) had an upper secondary school diploma and 61 (20.7%) had a bachelor's degree and higher (p-value = 0.001). In 57% of cases, there was a familial relationship between parents. 250 (83.3%) patients were from urban areas and 50 (16.7%) were from rural areas. The mean age of children with CHD at the time of diagnosis was 1.25 ± 2.92 years; in most cases, the diagnostic age was less than 1-year-old (221) (**Table.2**).

In 255 (85%) of mothers, there was no history of any background illness, while in 45 cases (15%) mothers had background disease, and gestational diabetes was the most common background disease in mothers (6%). 13.7 % of the children had CHD records in first-degree relatives. In the spring, the beginning of pregnancy was 66 (22%), and in summer, autumn and winter each were equal to 78 (26%). Only 3 (1%) of the mothers had consumed cigar-opium during pregnancy. There were 272 cases (90.7%) of mothers who had a history of drug use during pregnancy. 298 (99.3%) of the mothers had no history of X-ray during pregnancy, and 2 (0.7%) had a history of X-ray, one simple dental radiography, and another simple radiography of a leg. Congenital anomalies were present only in 50 (16.7%) patients, with Down syndrome with an incidence of 3.8%, the most common anomaly with CHD (**Table.3**).

Table-1: Distribution of congenital heart diseases of children based on the type of disease.

Type of congenital heart disease	Number (%)
Ventricular Septal Defect	86 (28.7)
Patent Ductus Arteriosus	56 (18.2)
Atrial Septal Defect	44 (14.6)
Aortic Valve	17 (5.7)
Pulmonary Stenosis	20 (6.7)
Mitral Valve Disease	18 (6)
Tetralogy of Fallot	16 (5.3)
Transposition of the Great Arteries	11 (3.7)
Atrioventricular Septal Defect	8 (2.7)
Pulmonary Atresia / Ventricular Septal Defect	5 (1.7)
Hypertrophic Cardiomyopathy	3 (1)
Hypoplastic Left Heart Syndrome	3 (1)
Total Anomalous Pulmonary Venous Connection	3 (1)
Double Outlet Right Ventricle	2 (0.7)
Ebstein Syndrome	1 (0.3)
Tricuspid Atresia	1 (0.3)
Single Ventricle Heart	1 (0.3)
Pulmonary Atresia	1 (0.3)
Coarctation of aorta	7 (2.3)
Total number of patients	300 (100)

Table-2: Comparison of the frequency distribution of congenital heart disease based on demographic data.

Variables		Number (%)	P-value Chi-square test
Age of patients	Under 1 year	221 (73)	0.001
	1 to 5 years	34 (11.3)	
	5 to 10 years	35 (11.7)	
	Over 10 years' old	10 (3.3)	
Age of mothers	Under 18 year	5 (1.7)	0.001
	18 to 38 years	243 (81)	
	Over 38 years old	52 (17.3)	
Mother's education level	Illiterate	22 (7.3)	0.001
	Under the diploma	125 (41.7)	
	Diploma and higher	92 (30.7)	
	Bachelor's degree and higher	61 (20.3)	
Place of residency	Rural	50 (16.7)	0.001
	Urban	250 (13.3)	
Family marriage	Positive	171 (57)	0.015
	Negative	129 (43)	

Table-3: Comparison of the frequency distribution of congenital heart disease based on clinical information.

Variables		Number (%)	P-value Chi-square test
Maternal Age	Preterm (Less than 37 weeks)	97 (32.3)	0.001
	Term (37 – 42 weeks)	181 (60.3)	
	Post-term (More than 42 weeks)	22 (7.3)	
Drug use in pregnancy	Positive	272 (90.7)	0.001
	Negative	28 (9.3)	

4- DISCUSSION

This study aimed to determine the epidemiologic characteristics of congenital heart disease in children referred to the pediatric heart clinic of Vali-e-Asr Hospital of Birjand University of Medical Sciences, Iran. The findings of this study showed that the most common congenital heart disease among children was the VSD, which was seen in 28.7% of patients. The ventricular septal defect was found in studies in Pakistan (29.2%), India (38%), Nigeria (27.1 to 46.6%) (14, 15), Brazil (37.5%) (16), Oman (24.9%), China (62.7%), Japan (94%) (17), Iceland (45.7%), Saudi Arabia (33.9%), and the United States (41.8%) (15). In addition, in domestic studies such as Yazd (27%), Khorramabad (44%) (6), Rasht (29.4%) (8), and Kashan (47.8%) (10), the ventricular septal defect has been reported as the most common congenital heart disease. The second most common congenital heart disease in our study was PDA, which was observed in 18.2% of the patients. Similar to this finding with a frequency of 14.5% and 12.1% in two studies in Nigeria (14, 15), with a frequency of 22.6% in a study in Pakistan (12). However, PDA was found to be the fourth most commonly diagnosed heart disease (9.5%) in the study of Abqari et al. (18), in India with 400 children with CHD, which in terms of both rank and rate and in terms of frequency was less than our findings. The third most common congenital heart disease in our study was atrial septal defect that was observed in 14.6% of patients. It is known as a common CHD in children (5, 6, 10, 12, 14-16, 18). Pei et al. (19) in China, and in the study of Nikyar et al. (4) in Gorgan (Iran) reported the most common CHD. Tetralogy of Fallot, with a prevalence of 19.9% in Kashan, Iran (10), 18% in India (18), 13.2% in Pakistan (12), 12.7% in Rasht, Iran (8), 8.9% in Yazd, Iran (5), 7.8% in Nigeria (15), and 9.9% in Brazil are reported (16). However, the prevalence of tetralogy of Fallot in our study was different and less than that (5.5%). The most common CHDs in this study are VSD, PDA, and ASD, accounting for more than 60% of CHD in this study; this finding is similar to the results of most studies in this field (20). Concerning the gender distribution of patients with CHD, the findings of the various studies are inconsistent. In our study, there was no significant difference between the sexes of patients and their association with CHD. In some studies, the prevalence of CHD has been reported more frequently among males (4, 6, 18, 21). However, in a series of other studies, the prevalence of CHD among females was more reported (5, 15). In studies in Iceland and Saudi Arabia, the prevalence of CHD in males and females is also the same (6, 22), which is consistent with the results of our study. In this study, the parents of 171 children with congenital heart disease had a relativistic relationship; in other words, the frequency of family

marriage among children with CHD was 57% in our study. The frequency of the parental relationship in a study in Pakistan is 48.8% (12), in Khorramabad-Iran, 28% (6), and 11.4% in Kashan, Iran (10). It is observed that the frequency of family marriage in our study is more than all of the above studies. In addition, findings from the study by Haq et al. (12) in Pakistan showed that parental kinship is a risk factor for congenital heart disease. Unlike this study, in the study of Roodpeyma et al. (23) in Tehran, parental kinship relationship was not a significant risk factor for congenital heart disease in children. In this study, 17.3% of mothers were older than 35 years old at the time of pregnancy. In Ou et al.'s study, in China (24) with a higher maternal age of 30, the risk of congenital heart disease increased significantly. In Fung et al.'s study (2), the risk of CHD was 1.18 times higher for the maternal age for every 10 years.

In this study, 32.3% of infants with CHD had preterm birth, and 7.3% of them had post-term births. In two similar studies conducted within the country, the frequency of term birth in neonates with CHD has been reported more (6, 8). The frequency of term neonates was approximately 7 times higher than the preterm infants (25). In the study of Tanner et al. in England, the prevalence of CHD in preterm infants was higher than that of termed infants (26). Our study findings are not consistent with reference books and studies; one of the possible reasons for this is due to the high mortality rate among preterm infants born with congenital anomalies, which before access to medical facilities and echocardiography have died due to the severity of congenital complications. In current study, the most common clinical finding among children with CHD was cardiac murmur, which was heard in 90% of patients. A group of infanticide murmurs and most childhood murmurs are benign or harmless; nevertheless, cardiac murmurs, especially during the neonatal period, can be a prime indication of the presence of heart disease (27). A study by Du et al. (28) on infants with cardiac murmurs showed that 84% of them had CHD, and only 16% had functional murmurs. In another study, 86% of infants with cardiac murmurs had congenital heart defects (29). In a study in Thailand, 59% of infants with cardiac murmurs had CHD (30). Gregory et al. (31) also found that about half of the children referred with cardiac murmurs had congenital heart disease. In the present study, only 1% of mothers had a history of smoking, and 99% did not consume cigarettes. The presence of many toxic compounds and carcinogens and mutations mutants in cigarette smoke has been proven (32).

A study by Fung et al. (2) in Canada has shown that maternal smoking during pregnancy is associated with an 8.2-fold increase in the risk of CHD. Although the incidence of smoking was low in our study, we should note that we questioned smoking directly by the mother herself, while the mother's indirect exposure to smoke (smoke inhaled from cigarette in the environment) is also a threat to the health of the mother and the fetus and is more prevalent and should be studied in further studies. In this regard, a study by Ou et al. (24) in China has shown that the exposure of the mother to cigarette smoke (inactive cigarette smoking) is associated with a 1.11 increase in the risk of newborn birth to congenital heart disease. A study by Taksande et al. (21) in India has also shown that exposure to cigarette smoke is associated with an increase of 10.45 times the risk of congenital heart disease.

In this study, the overall rate of A-D drug use during pregnancy was 15.7% among mothers. In our study, there was a significant relationship between maternal drug consumption during pregnancy and its concomitant association with CHD.

Drugs used during pregnancy can affect the fetus. In Fung et al.'s study (2), the use of medication during pregnancy was associated with a 2.5-fold increase in the risk of congenital heart disease. In the present study, only 2 (0.7%) of the mothers were exposed to X-ray during pregnancy. In the study of Yang et al. (33) in China, only 0.5% of mothers with maternal anomalies were exposed to X-rays during pregnancy.

In this study, a total of 15% of mothers had underlying illnesses; gestational diabetes was the most common underlying illness with a frequency of 6%. After gestational diabetes, hypothyroidism was found to be in the second and third grade with a prevalence of 3.7% and pre-pregnancy diabetes with a frequency of 2.3%. Uncontrolled maternal diabetes increases the risk of cardiac structural diseases in infants by up to 30%, especially hypertrophic cardiomyopathy, ventricular septal defect or transposition of great artery (19). Given that it has been reported that severe glycemic control before fertilization and during pregnancy reduces the risk of infants with congenital heart disease (34), therefore, mothers' training can be effective in reducing the rate of neonates with congenital heart disease.

In the present study, 13.7% of children with congenital heart disease had a positive CHD history in their first-degree family. In the study of Mohsenzadeh et al. (6) in Khorramabad, 10.3% of patients with congenital heart disease had a family history of CHD, which was almost the same as our study. Generally, a family history of congenital heart disease is one of the genetic risk factors that increased the risk of CHD. In the study of Moss et al. it has been reported that 1 to 4 % of infants born from parents of congenital heart disease are affected (35). Considering that in our study, most patients with CHD did not have a definite history of CHD in first-degree family members; more extensive studies are needed to investigate the effect of family history on congenital heart disease. The prevalence of associated diseases among children with CHD was 16.7% in the present study. Down syndrome, with a frequency of 3.8% (25), was the most commonly reported disease. Club-Foot with 1.3% and Pirobbin syndrome with 1% were next. In a study in Gorgan, associated abnormalities were observed in 2.2% of cases (including central nervous system and Down syndrome abnormalities), which was still lower than our study (4). Generally, chromosomal abnormalities account for approximately 8 to 10% of cases of congenital heart disease (35), and Down syndrome was the most common chromosomal abnormality observed in patients with CHD, as approximately 40 to 50% of patients with Down syndrome have heart defects (25). Therefore, with routine pregnancy care, children with Down syndrome can be prevented from entering the community and its subsequent complications, and in the case of having a child with Down's syndrome, cardiac follow up is recommended.

4-1. Limitations of the study

Lack of sufficient information of the cities near Birjand about the existence of pediatric cardiologists, long-distance access to children's heart clinic and delay in diagnosis of congenital heart disease by colleagues were the most important limitations of our study.

5- CONCLUSION

Due to the mild nature of a large proportion of congenital heart disease, most patients did not require immediate intervention for treatment. However, the necessity of accurate examination of children at the beginning of life can be an effective step in the diagnosis and early intervention of congenital heart disease and thus improve the quality of life of patients, especially mothers. Considering

the meaningful relationship between mother's low education, high maternal age during pregnancy, parental marriage and maternal use of medication during pregnancy and concomitant congenital heart disease, considering a proper screening program and holding training classes especially for the above groups seem logical. Advice on proper age-appropriate pregnancy, the avoidance of the arbitrary use of drugs during pregnancy and the avoidance of family marriages or carrying out necessary follow-up in case of family marriages and underlying illnesses should be part of maternal education and mothers' training can be effective in reducing the number of infants with congenital heart disease. Due to excessive concomitance of Down syndrome with congenital heart diseases, by recommending routine pregnancy care, children with Down syndrome and their subsequent complications can be prevented and in the case of having a child with Down syndrome, exact cardiac follow-up is recommended.

6- CONFLICT OF INTEREST: None.

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