

## Original Research Article

# Epidemiological investigation of congenital heart diseases among children during the years 2016 to 2021

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## ABSTRACT

**Background:** Congenital heart disease is a type of birth defect that affects about 1% of babies born each year and is the leading cause of death in infancy that is diagnosed at birth or later in life. Due to the high importance of this issue and high mortality and morbidity, the aim of this study was epidemiological investigation of congenital heart diseases in children during 2016 to 2021.

**Methods:** In this cross-sectional analytical study, all children admitted to Bo Ali Hospital in Ardabil with primary diagnosis of congenital heart disease or secondary diagnosis during hospitalization along with all children referred to the clinic of this hospital with diagnosis of congenital heart disease were included in the study.

**Results:** A total of 449 children with congenital heart disease were included in the study. 235 cases (52.33%) were boys, 35 cases (7.79%) had diabetic mothers and 12 cases (2.6%) had obese mothers. 20 cases (4.4%) were the result of multiple pregnancy and 31 cases (6.9%) were preterm. Significantly, preterm birth was more in children with cyanotic disease ( $p=0.036$ ) and multiple births and maternal diabetes and aneuploidy were more in children with cyanotic disease compared to Asianotic children ( $p$  value equal to 0.008 respectively and 0.001 and 0.001).

**Conclusions:** The frequency of congenital heart diseases, gender composition and related risk factors such as preterm birth and maternal diabetes were aligned and similar to domestic and foreign studies. Maternal diabetes and preterm birth can be considered as risk factors for congenital heart diseases.

**Keywords:** Congenital heart disease, Diabetes, Newborns, Preterm, Prevalence

## INTRODUCTION

Congenital heart disease (CHD) is a type of congenital defect that affects about 1% of newborns every year.<sup>1</sup> Among all birth defects, this abnormality is the main cause of death in infancy that is diagnosed at birth or later in life.<sup>2</sup> About 8-10% of congenital heart diseases are related to chromosomal aneuploidy such as down syndrome, trisomy 13, trisomy 18, Turner and D-George syndrome, so that the prevalence of congenital heart disease in patients with down syndrome is reported to be about 45%.<sup>3</sup> Fetal echocardiography is an important tool

in the diagnosis of CHD, which provides accurate diagnosis of fetal arrhythmia and its management.<sup>4</sup> CHD includes several types of heart defects that are usually grouped based on the nature of the heart structural defect, resulting blood flow patterns, observed familial recurrence risks, and shared susceptibility genes.<sup>5</sup> Phenotypes are often classified into major categories such as right-sided lesions, left-sided lesions, conotruncal defects, lateral defects, and isolated septal defects.<sup>6</sup> A meta-analysis of the global birth prevalence of CHD found that "mild lesions" of ASD, VSD, and patent ductus arteriosus (PDA) accounted for 57.9% of the CHD burden. The prevalence of these mild lesions as well as

severe complicated CHD has increased by 10% every 5 years since 1970.<sup>7</sup> Late complications of CHD include heart failure, arrhythmia, pulmonary arterial hypertension, and endocarditis. Older patients with CHD may have acquired cardiovascular complications such as hypertension, diabetes, and hyperlipidemia. Drug treatment of CHD is mainly based on pathophysiological conditions or acquired heart disease. For example, the treatment of systemic right ventricular failure with digoxin has been recommended.<sup>8</sup> Major advances have been made in the treatment of cardiac disorders in children. Cardiovascular interventional therapies through catheterization have evolved as a major technological achievement over the past 10 years. Cardiac imaging methods such as intracardiac echocardiography, transesophageal echocardiography (TEE), 3D imaging systems, MRI, and advanced angiography have made it possible to treat many types of CHD through a cardiac catheter without open and complicated surgeries.<sup>9</sup>

Due to the high importance of the issue of congenital heart diseases due to their high prevalence and high mortality and morbidity, and on the other hand, the dependence of the incidence of these diseases on genetic patterns and environmental factors, a correct understanding of their prevalence in different societies can be used in drawing up screening and management plans. It is very important to reduce the mortality and morbidity of these diseases. Based on the mentioned cases and on the other hand, the lack of previous studies in the province, we decided to design and implement a cross-sectional study with the aim of epidemiological investigation of congenital heart diseases in children.

## METHODS

In this cross-sectional study, all referred children (hospitalized or clinic) to Bu-Ali Hospital in Ardabil diagnosed with congenital heart disease during the years 2016 to 2021 were included in the study. Required information including the type of congenital heart disease (based on echocardiography findings performed by a pediatric cardiologist), demographic characteristics (age, age of birth, gender), information related to pregnancy (multiples, viral diseases in the first trimester of pregnancy) and the mother's information (body mass index, history of diabetes) were recorded and collected from the patients' files in the prepared checklist. Children with incomplete information included in the file and lack of complete proof of diagnosis of congenital heart disease (for example, contradictory results in echocardiography) were excluded from the study. Finally, 449 children with congenital heart disease were included in the study.

### Statistical analysis

Data were analyzed and evaluated by SPSS version 21 software. Descriptive indices of mean (standard deviation) and frequency tables and graphs were used to better display the data. Normal distribution of data was

checked by Kolmogorov Smirnov test. Chi-square test was used to check the relationship between existing parameters. A significance level of  $P < 0.05$  was considered.

## RESULTS

Of all the studied samples, 235 cases (52.33%) were boys and 214 cases (47.66%) were girls. In general, 7.8% of patients had diabetic mothers, 2.7% had obese mothers, and 4.45% had multiple pregnancies. Chromosomal aneuploidy was present in 12.9% of patients and 6.9% of all studied children were preterm. The highest number of congenital heart diseases was related to asianotic cases (353 cases, 78.6%) and cyanotic cases were seen in only 96 cases (21.4%) of children. TGA was the most common cyanotic congenital heart disease with frequency in 34 cases (35.41%). Also, TOF, HLHS, DORV, and TAPVC were found in 30 cases (31.25 percent), 8 cases (8.33 percent), 6 cases (6.25 percent), and 6 cases (6.25 percent), respectively included. The most common congenital asianotic heart disease was related to VSD with 114 cases (26.57%). Also, PDA with 106 cases (24.70%), ASD with 95 cases (22.14%), PS with 66 cases (15.38%) were other common cases (Table 1).

**Table 1: Frequency of congenital heart clinical symptoms at the time of presentation.**

Sign type	Abundance	
	Number	Percent
Heart murmur	293	65.25
Cyanosis	87	19.37
Respiratory distress	36	8.01
Tachycardia	10	2.22
Growth disorder	8	1.78
Inappropriate feeding	7	1.55
Without sign	7	1.55
Edema	1	0.22

Among the studied Asianotic patients, only one heart disease was reported for 291 cases. And 62 cases had at least two types of asianotic heart disease, of which 11 cases of ASD and VSD, 7 cases of VSD and PDA, and 7 cases of ASD and PDA were reported. Heart murmur was the most common clinical finding with 293 cases (65.25%). Also, cyanosis and respiratory distress were common in 87 cases (19.37%) and 36 cases (8.01%) respectively (Table 1).

Most of the samples were in the age group of 1 to 6 months (146 cases, 32.5%). 1 to 28 days old and also at birth with 112 cases (24.9 percent) and 98 cases (21.8 percent) respectively, other age groups were common in patients. In general, among the 449 patients studied, 109 cases (24.3%) received surgical treatment, 259 cases (57.7%) received drug treatment, and 81 cases (18%) did not receive any treatment. In cyanotic patients, 62 cases (64.6%) received surgical treatment and in asianotic

patients, 47 cases (13.3%) received surgical treatment (Table 2).

Total 109 cases (24.3) of all the studied patients underwent surgical treatment, and in 10 cases (2.2 percent) the final result was the patient's death (Table 3).

**Table 2: Frequency of receiving treatment and its types in congenital heart patients.**

Type of disease	Number	Surgeries (%)	Medical (%)	Without receiving treatment (%)
<b>Acyanotic</b>	353	47 (13.3)	230 (65.2)	76 (21.5)
<b>Cyanotic</b>	96	62 (64.6)	29 (30.2)	5 (5.2)
<b>Total</b>	449	109 (24.3)	259 (57.7)	81 (18)

**Table 3: Frequency of types of treatment and final outcome in children with congenital heart disease.**

Type of treatment result	Surgeries		Medical		Without treatment		Total	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
<b>Death</b>	10	2.22	39	8.68	10	2.22	59	13.14
<b>Certain cure</b>	36	8.01	106	23.6	0	0	142	31.62
<b>Under follow up</b>	63	14.03	114	25.38	71	15.81	248	55.23
<b>Total</b>	109	24.27	259	57.68	81	18.04	449	100

**Table 4: Frequency of cyanotic congenital heart diseases by gender.**

Group variables		Cyanotic		Acyanotic		P-value
		Number	Percent	Number	Percent	
<b>Gender of infant</b>	Female	46	47.9	168	47.6	0.99
	Male	50	52.1	185	52.4	
<b>Maternal diabetes</b>	+	16	16.7	19	5.4	0.001
	-	80	83.3	334	94.6	
<b>Parite</b>	+	9	9.4	11	3.1	0.008
	-	87	90.6	342	96.9	
<b>Aneuploidy</b>	+	24	25	34	9.6	0.001
	-	72	75	319	90.4	
<b>Pre-term birthday</b>	+	2	2.1	29	8.2	0.036
	-	94	97.9	324	91.8	
<b>Mother overweight</b>	+	2	2.1	10	2.8	0.69
	-	94	97.9	343	97.2	
<b>Family history</b>	+	7	7.3	28	92.7	0.84
	-	89	7.9	325	92.1	

Total 50 cases (52.08%) of the patients with cyanotic congenital heart disease were boys and 46 cases (47.91%) were girls. In terms of sex, there was no difference between the two cyanotic and asianotic groups. In children with cyanotic disease, the frequency of diabetic mothers, the frequency of multiple pregnancy, and the frequency of aneuploidy were higher compared to the cyanotic group.

Also, according to the chi-square analysis test, preterm births were significantly higher in the asianotic patients group than in the cyanotic patients group. Also, the difference in frequency of obese mother and family history of disease in two cyanotic and asianotic groups was not significant (Table 4).

## DISCUSSION

In this study, among 449 patients, 78.6% had congenital asianotic heart disease and 21.4% had cyanotic heart disease, respectively, VSD with a frequency of 26.57%, PDA with a frequency of 24.7%, and ASD with a frequency of 14%. 22.0% (generally 18.18%), the most common types of asianotic disease and TGA with a frequency of 35.4% in cyanotic diseases (generally 7.9%) and TOF with a frequency of 31.31% in cyanotic diseases (generally 6.8 percent) included the most common types of diagnosed diseases. In the study of Derakhshan et al, which was conducted in Iran in 2022, ASD with a frequency of 20% and PDA with a frequency of 50% were diagnosed as the most common diseases, which was similar to our study.<sup>10</sup>

In the study of Mohsenzadeh et al in 2013 in Iran, in line with the present study, 93.5% of children with congenital disease had Asianotic disease, and VSD and ASD are known as the most common congenital heart diseases with a frequency of 44% and 21%, respectively. Also, in this study, maternal diabetes was present in 9.3% of patients, which in our study was also 7.79%.<sup>11</sup> In the study by Zhao et al in 2018 in China, the frequency of VSD, ASD and PDA was stated to be 36, 18.8 and 8.6%, respectively, which compared to the present study and other studies in Iran, the frequency PDA has been less. These differences can be in the amount of performed screenings and genetic-environmental differences.<sup>10-12</sup>

In the present study, 52.33% of children with congenital heart disease were boys and 47.66% were girls, and there was no significant difference between the two asianotic and cyanotic groups in terms of gender, and in the studies of Zhao et al; and Matbah and Colleagues also generally found no significant difference between the frequency of boys and girls among patients with congenital heart disease. However, in the study by Mohsenzadeh et al in Khorramabad, 63% of children with congenital heart disease were boys.<sup>11-13</sup>

In the present study, 7.7% and 2.6% of children with congenital heart disease had diabetic and obese mothers, respectively. In the study of Mohsenzadeh et al, in line with the present study, 9.3% of children with congenital heart disease had diabetic mothers. This is while Matbah et al stated the frequency of diabetic mothers in children with congenital heart disease to be 14%. Such differences can occur in the context of genetic, nutritional, and cultural issues, as well as accurate screenings.

In the present study, 31 cases (6.9%) of all the children studied were preterm and also significantly, preterm birth was more common in patients with asianotic congenital heart disease than cyanotic. In Zhao et al.'s study, as well as Mohsenzadeh et al, 11.4% and 20% of the studied children with congenital heart disease were born preterm, respectively, which indicates the existence of a relationship between preterm birth and the presence of congenital heart disorders. In the study of Leirgul et al, congenital heart diseases were significantly more in girls.<sup>14</sup> In the study by Mohammad et al, 81.25% of congenital heart disease patients were asianotic and 18.75% were cyanotic, which was similar to the present study.<sup>15</sup> The most common Asianotic CHDs in the study by Mohammad et al were VSD, PS and PDA, respectively. The most common type of cyanotic congenital heart disease was ToF, which was not consistent with the present study. Mills et al in the study "Congenital heart defects and maternal obesity: a population-based study" in 2010, showed that with increasing obesity (BMI>40) in pregnant mothers, the rate of congenital heart defects increases, but overweight does not increase any which of the types of heart diseases is not in line with the present study. In the present study, there was no significant relationship between maternal

overweight and types of congenital heart diseases.<sup>16</sup> In the study "Risk of congenital heart defects in children who were exposed to maternal diabetes: a systematic review and meta-analysis" in 2019, Chen et al showed that congenital heart defects are related to maternal diabetes and this relationship is more in the context of the disease. Congenital heart has been cyanotic. Along with the aforementioned study, in the present study there was a significant relationship between maternal diabetes and cyanotic congenital heart diseases.<sup>17</sup> In 2010, Richard et al in the study of "Hidden Chromosomal Abnormalities Known in Children with Congenital Heart Defects" showed that the prevalence of CHDs in patients is closely related to chromosomal abnormalities. In line with this study, in our study there is a significant relationship between chromosomal anomalies and cyanotic congenital heart diseases.<sup>18</sup> In Hoffman et al.'s study, which was a cohort study in the field of congenital heart disease, 46% of patients were diagnosed at the age of less than one week, 42.3% at the age of 1 week to one year, and 10.5% at the age of 1 to 4 years. In our study, this number was 51.32 in one to six months, which was the highest age of diagnosis of congenital heart disease.<sup>19</sup> In the study of RongRong Sun and his colleagues, which was an epidemiological study in relation to congenital heart diseases and their cause, diagnosis and symptoms, it is mentioned that respiratory distress, heart murmur is the most common clinical symptom at the time of diagnosis. In the current study, heart murmur, cyanosis and respiratory distress were the most common.<sup>20</sup>

This study has some limitations. This study was designed and implemented cross-sectionally without a control group, and for this reason, it was not possible to calculate the odds ratio of congenital heart disease based on the investigated risk factors such as maternal diabetes, preterm birth, gender, etc. Because this study was retrospective and dependent on the information included in the file, some samples were excluded from the study due to the deficiencies in the files.

## **CONCLUSION**

According to the results of the present study, in most cases, the frequency of congenital heart diseases, gender composition, and related risk factors such as preterm birth and maternal diabetes were consistent and similar to domestic and foreign studies. Maternal diabetes and preterm birth can be considered as risk factors for congenital heart diseases, which reinforces the need for screenings during pregnancy and even before pregnancy. On the other hand, controlling the course of pregnancy and managing factors that cause preterm births, including infections, can also have a significant impact on reducing the incidence of congenital heart diseases. It is suggested that by designing and conducting studies with a control group or long-term cohort studies, the risk of congenital heart diseases can be measured better and more accurately based on the desired parameters such as maternal diabetes and preterm birth. It is also suggested

to conduct similar studies in all the hospitals of Ardabil so that the information can be expressed more accurately and comprehensively.

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