

Assessing the Frequency of Congenital Heart Diseases Among Children in Eastern Afghanistan

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Background: Congenital heart disease (CHD), characterized by anatomical and functional abnormalities of the heart, can impair an individual's quality of life and, if not treated with appropriate interventions, it can result in early death. Morbidity and mortality from CHD are greatly reduced by early diagnosis and timely therapy. Therefore, this study aimed to determine the frequency of various forms of CHD among affected children in Eastern Afghanistan considering age, gender, and region of distribution (countryside and city).

Patients and Methods: A retrospective hospital-based study was conducted on 1323 patients with a confirmed diagnosis of CHD who were referred for echocardiography to public and private hospitals in Jalalabad City, Afghanistan, from July 2018 to June 2022. Patients from day one of life till 18 years were included. The study participants were chosen using a non-probability convenience sampling technique, and the data were analyzed using the statistical package for social sciences (SPSS) version 27.0.

Results: In this study, males comprised 60.4% of the participants, while females made up 39.6%. More than three-quarters (86.4%) of the diagnoses were in children below 1 year of age. 86.5% of them were patients with acyanotic, and 13.5% had cyanotic CHD. The most common acyanotic heart disease was patent ductus arteriosus (PDA; 252.6%), followed by ventricular septal defect (VSD; 18.4%) and atrial septal defect (ASD; 8.5%). The most frequent cyanotic heart disease was Tetralogy of Fallot (TOF). 79.9% of the total cases were patients with simple CHD lesions, and 20.1% had complex CHD lesions. In addition, participants from rural areas had a higher (78.9%) frequency of CHD compared to those from urban areas (21.1%).

Conclusion: The study concluded that over 85% of CHD-diagnosed cases were under 1 year of age, with PDA, VSD, ASD, and TOF being the most commonly diagnosed acyanotic and cyanotic lesions. Participants from rural residence had a higher frequency of CHD compared to those from urban residence. Additionally, our study found that more males were affected by CHD compared to females. In order to avoid serious complications, reduce mortality, and improve quality of life, early identification and correction of disease is crucial.

Keywords: cyanotic heart disease, acyanotic heart disease, atrial septal defect, ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot

Introduction

Congenital heart disease (CHD), characterized by anatomical and functional abnormalities of the heart, which can impair an individual's quality of life and, if not treated with appropriate interventions, it can result in early death.^{1,2} Morbidity and mortality from CHD are greatly reduced by early diagnosis and timely therapy.¹ Early in pregnancy, at the mid-gestational stage, the heart and circulatory system are almost fully developed; therefore, this is a critical time for the development of CHDs.³ The exact cause of CHD is mostly unclear; however, there are many known risk factors including genetic defects, chromosomal abnormalities, intrauterine infections (rubella), certain drugs taken during the first trimester of pregnancy, and consanguineous marriages.³ There is a recognized etiology for approximately 15% of cases of CHD; 5–10% are associated with a chromosomal anomaly, 3–5% with single gene abnormalities, and 2% with recognized environmental factors. Nevertheless, a complex etiology accounts for a large number of cases.³

An estimated 3.12 million babies worldwide were predicted to have CHD in 2019, which represents 2.3% of the population. Furthermore, 13.3 million individuals worldwide were reported to have CHD, resulting in 217,000 deaths, 150,000 of which included infants under the age of 1 year.⁴ In addition, approximately 30% of all major congenital malformations and a large number of cardiac surgery procedures performed worldwide are related to CHD.⁵ However, due to exorbitant costs and poor facilities, many babies with CHD are unable to undergo life-saving surgery, which contributes to the high mortality rate from CHD. This problem is also present in Afghanistan and other South Asian countries. Despite significant advancements in medicine, CHD is still one of the main causes of death, which can affect people of all ages, from infancy to adolescence.⁶ Poorer nations in Asia and Africa with the highest CHD age-standardized mortality rates (ASMRs) in 2017 were Afghanistan (17/100,000) and Sudan (18.3/100,000).⁷ According to an epidemiological study report, the prevalence of CHD varies from 4/1000 to 50/1000 live births. The causes of this variation are differences in the environment, genetics, and socioeconomic status.⁸ The Asian population is more significantly impacted than non-Asian populations because of a higher prevalence of consanguineous marriages, diabetes, and obesity.^{9,10} In India, the prevalence of CHD ranges from 0.8 to 26.4/1000 children.¹⁰ A study conducted by Molaei et al reported a prevalence rate of CHD up to 4/1000 live births in Iran.¹¹ Several studies conducted in China have indicated that the prevalence of CHD ranges from 1.5 to over 20 cases per 1000 live births.¹² A study conducted at Aga Khan University Hospital by Hassan found that the prevalence rate of CHD was up to 4/1000 live births in Karachi Pakistan.¹³ Globally, there are differences in the patterns of isolated CHD; in India, Libya, Sudan, Saudi Arabia, and other western nations, ASD, AVSD, and VSD were the most prevalent.^{14–18} ASD, VSD, PDA, and AVSD were reported to be the most prevalent in Iran and Korea.^{19,20} However, VSD and PDA were the most commonly reported isolated CHDs in Pakistan and Mexico.^{21,22} Regarding the variation of frequency between gender and CHD, several studies reported that there is a predominance of male sex among patients with CHD compared to females.^{6,9,21,23–26} However, other studies have reported that the number of CHD cases was greater among females,^{26–29} or there was no gender difference.^{30–32} This difference may be due to geographical, racial, socioeconomic, ecological, and genetic factors, or it could be due to more male reporting due to cultural eccentricity.^{25,33} A study conducted by Rizvi et al found that the rate of CHD in rural Pakistan is much greater than what is observed in urban healthcare settings.^{34,35} Additionally, contrary to common belief, rural regions in China exhibit a lower prevalence of CHD compared to urban areas. This unexpected difference may be due to unrecognized cases of CHD, which continue to pose a significant public health challenge in many developing nations.³⁶ Children with CHD can present in a variety of ways. They can be asymptomatic and CHD is only discovered by chance when a murmur is detected during a routine neonatal check-up or upon examination for an unrelated illness. Alternatively, symptoms like cyanosis, clubbing of the fingers and nails, or full-blown congestive heart failure might be presented by them.⁶ CHD abnormalities can arise as a single lesion or in conjunction with another cardiac condition.¹ Examples of solitary or single congenital heart disease lesions that are frequently detected are Pulmonary Stenosis (PS), Ventricular Septal Defect (VSD), and Atrial Septal Defect (ASD). Examples of complex CHD lesions are Atrioventricular Septal Defect (AVSD), Tetralogy of Fallot (TOF), and Transposition of the Great Arteries (TGA).¹ TOF and TGA are the two most prevalent cyanotic congenital heart diseases, causing oxygen saturation levels to drop below 90%. In contrast, the majority of septal defects, including ventricular septal defect, atrial septal defect, and atrioventricular septal defect, are grouped as acyanotic congenital heart disease with oxygen saturation levels exceeding 95%. Acyanotic and cyanotic heart disease are the two broad categories of congenital cardiac defects, with the former being more prevalent. The most prevalent cyanotic and acyanotic congenital heart diseases are Tetralogy of Fallot and Ventricular Septal Defect.²¹

In Afghanistan, as most births still occur at home and routine neonatal screening is uncommon, it is exceedingly challenging to determine the actual birth prevalence of CHD. Thus, Afghanistan lacks the level of comprehensive research on pediatric heart disorders of similar western and neighboring countries. Most critically ill patients with CHD in Afghanistan do not receive treatment on time or die before receiving it. Therefore, the present study aimed to investigate the age, gender, and rural and urban area distribution of CHD, as well as the frequency of different kinds of CHD among affected children in Eastern Afghanistan.

Materials and Methods

Study Design and Setting

A retrospective hospital-based study was conducted on 1323 participants with a confirmed diagnosis of CHD who were referred for echocardiography to public and private hospitals in Jalalabad City, Afghanistan, from July 2018 to June 2022. This study received ethical approval from the institutional review board (IRB) of Nangarhar University Faculty of Medicine (No. 144, dated November 15, 2022). The inclusion criteria were: 1) Patients from day one of life till 18 years of age with clinical suspicion of cardiac problem raised by history of recurrent chest infections, presentation with cyanosis, feeding difficulty and failure to thrive, or detection of murmur in asymptomatic patients were enrolled by nonprobability convenience sampling technique for echocardiography to confirm their diagnosis. 2) residents of Eastern Afghanistan. Patients with acquired heart disease (rheumatic heart disease, infective endocarditis and myocarditis), resident of other provinces, and those who were from eastern region but had repeated echocardiography and incomplete available records were excluded from the study. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Sample Size and Sampling Procedure

A total of 4409 hospital visits at public and private children's health clinics were subjected to an echocardiography examination for the diagnosis of CHD, with 2333 children diagnosed by a pediatric echocardiologist. From the 2333 diagnosed cases, complete data on CHD type with relevant information was available for 1323 children and was thus included in this study for subsequent analysis (Figure 1). Using a non-probability convenience sampling technique, children who presented to the doctor with at least one of the clinical suspicions of a cardiac problem, such as a history of recurrent chest infections, cyanosis, feeding difficulties, inability to develop properly, or the detection of a murmur in symptomless children, and were residents of Eastern Afghanistan, were enrolled to undergo echocardiography to confirm their diagnosis. Children who lived in other provinces, had repeated echocardiograms but were from the eastern regions,

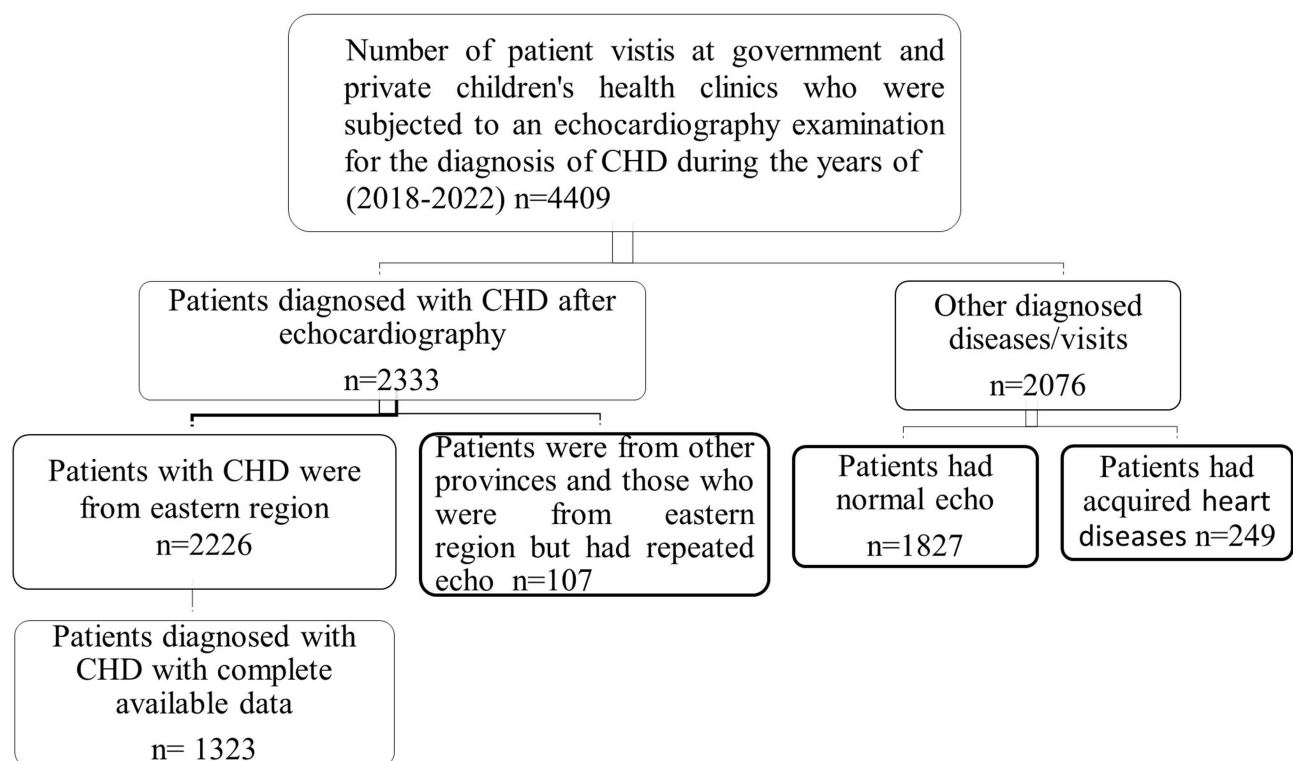


Figure 1 Flow chart of cases recorded, diagnosed with CHD, and numbers included in analysis.

or exhibited clinical symptoms of acquired heart illness (rheumatic heart disease, infective endocarditis, and myocarditis) were excluded from the study.

Study Variables and Data Collection Procedure

The researcher screened all the children who were examined by an independent pediatric echocardiologist, who confirmed the diagnosis of CHD and determined their eligibility for the study. Type and lesion of CHD, regional distribution, gender, age at the time of presentation, and the total number of cases of CHD were considered during the data collection. A child diagnosed with CHD was the dependent variable. The demographic profile of the child, including age, sex, and place of residence, was recorded from the medical record of each case, which served as independent variables. CHD was classified as simple or complex based on the echocardiographic diagnosis. Cardiac anomalies with three or more associations with components required to sustain life and complicated changes in hemodynamics were classified as complex defects.³⁷

Statistical Analysis

Initial data were entered into an excel spreadsheet and then exported to SPSS version 27.0 for analysis. Descriptive statistical analysis was performed to identify the age, gender, and regional (urban and rural) distribution of CHD, as well as the categorical data, which were summarized as frequency and percentage and compared using the chi-square test. The level of significance was set at $p < 0.05$.

Results

Patient Characteristics

In this study, a total of 1323 participants were enrolled, with ages ranging from 1 day to 15 years old (Figure 2) of whom 60.4% were male and 39.6% were female, resulting in a male-to-female ratio of 1.5:1. The majority (86.4%) of patients were diagnosed with CHD under 1 year of age. Table 1 shows the demographic characteristics of the patients, while Table 2 presents the age distribution of CHD among the study participants.

CHD Profile

Of the included patients with CHD, 86.5% had acyanotic and 13.5% had cyanotic CHD (Table 3). PDA, followed by VSD, ASD, PFO, and PS, were the most commonly diagnosed isolated acyanotic heart lesion, at 22.6%, 18.4%, 8.5%,

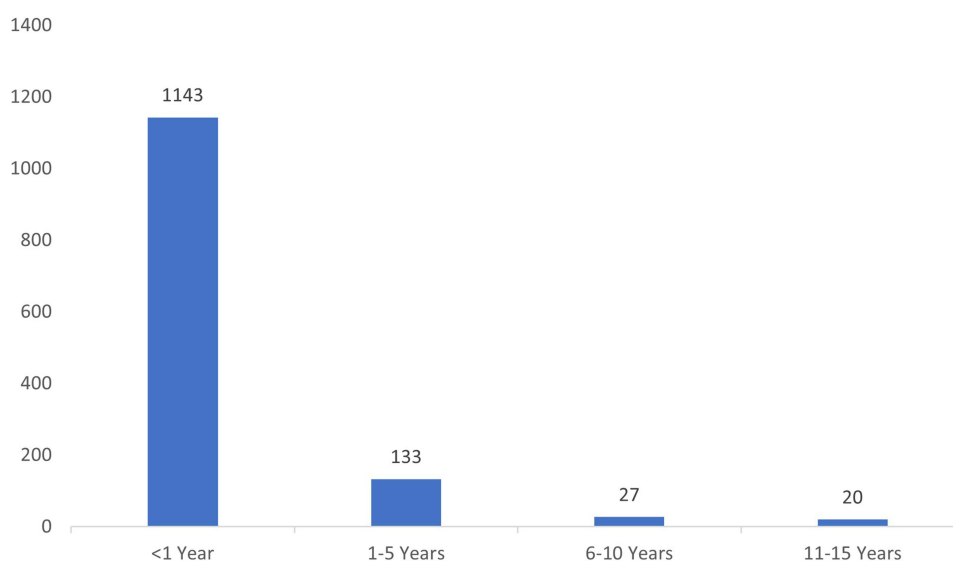


Figure 2 Distribution of age groups among study participants.

Table 1 Demographic Characteristics of Diagnosed CHD Participants

Variables	Number	Percentage	P value [†]
Demographic characteristics			
Age range (years)*			
- <1	1143	86.4%	P=0.000
- 1–5	133	10.1%	
- 6–10	27	2.0%	
- 11–15	20	1.5%	
Sex*			
- Male	799	60.4%	P=0.000
- Female	524	39.6%	
Region*			
- Urban	279	21.1%	P=0.000
- Rural	1044	78.9%	

Notes: *Data presented as number, percentage. [†]P-values were obtained from a chi-square test and one-sample Binomial test.

Abbreviation: CHD, Congenital heart disease.

Table 2 Distribution of CHD with Age Among Study Participants

Type of CHD	Age Range (Years)			
	<1	1–5	6–10	11–15
Sample lesions n (%)				
PDA*	261 (22.8%)	31 (23.3%)	6 (22.2%)	1 (5%)
VSD*	206 (18.0%)	33 (24.8%)	3 (11.1%)	4 (20%)
ASD*	99 (8.7%)	11 (8.3%)	1 (3.7%)	1 (5%)
PFO*	188 (16.4)	8 (6%)	3 (11.1%)	1 (5%)
PS*	20 (1.7%)	3 (2.3%)	3 (11.1%)	1 (5%)
AS*	3 (0.3%)	1 (0.8%)	–	1 (5%)
Dextrocardia*	15 (1.3%)	1 (0.8%)	–	–
Complex lesions n (%)				
Complex lesions*	182 (15.9%)	14 (10.5%)	4 (14.8%)	3 (15.0%)
TOF*	37 (3.2%)	9 (6.8%)	3 (11.1%)	2 (10%)
CAVSD*	1.1%	2.3%	3.7%	–
DTGA+VSD*	0.8%	1.6%	–	–
VSD+PA+PDA*	1.1%	2.3%	–	–
Ebstein's anomaly*	–	–	–	5.9%
Significance [†]	$\chi^2(66) = 362.580, p = < 0.001$			

Notes: *Data presented as number, percentage, [†]P-values were obtained from a chi-square test.

Abbreviations: CHD, Congenital heart disease; PDA, Patent ductus arteriosus; VSD, Ventricular septal defect; ASD, Atrial septal defect; PS, Pulmonary valve stenosis; AS, Aortic Stenosis; BCA, Bicuspid aortic valve; MVP, Mitral valve prolapse; CAVSD, Complete atrioventricular septal defect; TOF, Tetralogy of Fallot; DTGA, Dextro-transposition of the great arteries; PA, Pulmonary atresia.

Table 3 Distribution of CHD According to Type and Lesion Among Study Participants

Variables	Number	Percentage	P value [†]
Type and lesion of CHD			
CHD Type*			
- Acyanotic	1145	86.5%	P=0.000
- Cyanotic	178	13.5%	
CHD Lesions*			
- Simple	1057	79.9%	P=0.000
- Complex	266	20.1%	

Notes: *Data presented as number, percentage. [†]P-values were obtained from a chi-square test and one-sample Binomial test.

Abbreviation: CHD, Congenital heart disease.

15.1%, and 2%, respectively. TOF was the most common cyanotic heart lesion found in CHD patients (3.9%). Regarding CHD lesions, 79% of the total cases had simple CHD, and 20.1% had complex CHD lesions. Both cyanotic and acyanotic heart disease were more prevalent in males compared to females (Figure 3). The majority, 196 (24.5%) males, had PDA, while it was 103 (19.7%) in females. On the other hand, the majority, 132 (16.5%) males, had VSD, while it was 114 (21.8%) in females (Table 4). In addition, participants from rural areas had a higher frequency of CHD compared to those from urban areas (Figure 4).

Discussion

A major group of non-communicable diseases that cause a high rate of morbidity and mortality in children are CHD.⁶ The reported prevalence of CHD has increased as a result of early referral to a pediatric cardiologist and improved knowledge among general physicians due to advancements in the healthcare system.^{6,38} The findings of this study are limited to the Eastern Afghanistan; therefore, they cannot accurately reflect the incidence and prevalence of CHD throughout the country. To the best of our knowledge, there are currently no local studies or reports on cases of CHD from either the public or private level in Eastern Afghanistan. Therefore, the present study was conducted to determine the age, gender, and regional (urban and rural) distribution of CHD, as well as the frequency of different kinds of CHD among affected children in Eastern Afghanistan. In this study, a total of 1323 participants were enrolled; the age range of the patients was 1 day to 15 years old of whom 60.4% were male and 39.6% were

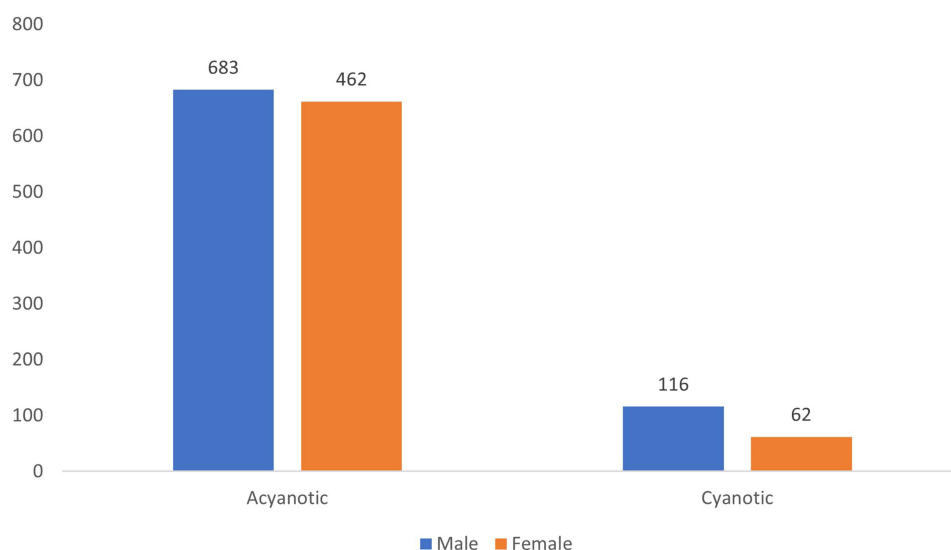
**Figure 3** Distribution of acyanotic and cyanotic heart disease according to gender.

Table 4 Distribution of Common Diagnosed Types of CHD According to Gender

Type of Defect	Male	Female
PDA*	196 (24.5%)	103 (19.7%)
VSD*	132 (16.5%)	114 (21.8%)
ASD*	61 (7.6%)	51 (9.7%)
PS*	14 (1.8%)	13 (2.5%)
COA*	5 (0.6%)	2 (0.4%)
AS*	3 (0.4%)	2 (0.4%)
PFO*	134 (16.8%)	66 (12.6%)
Dextrocardia*	10 (1.3%)	6 (1.1%)
Complex lesions*	171 (21.4%)	95 (18.1%)
TOF*	36 (4.5%)	15 (2.9%)
CAVSD*	8 (1.0%)	9 (1.7%)
VSD+ASD+PDA*	7 (0.9%)	3 (0.6%)
DTGA+ VSD*	5 (0.6%)	4 (0.8%)
VSD+PA+PDA*	4 (0.5%)	2 (0.4%)
Significance [†]	$\chi^2(22) = 36.3, p=0.028$	

Notes: *Data presented as number, percentage, [†]P-values were obtained from a chi-square test.

Abbreviations: CHD, congenital heart disease; PDA, patent ductus arteriosus; VSD, ventricular septal defect; ASD, atrial septal defect; PS, pulmonary stenosis; AS, aortic stenosis; BCA, bicuspid aortic valve; CAVSD, complete atrioventricular septal defect; TOT, tetralogy of Fallot; DTGA, dextro-transposition of the great arteries; PA, pulmonary atresia.

female. The findings of this study consistent with the results of several studies published previously;^{6,9,21,23–26} however, other studies have reported that the number of CHD cases was greater among females,^{26–29} or there was no gender difference.^{30–32} This difference may be due to geographical, racial, and social factors, or it could be due to more male reporting due to cultural eccentricity.²⁵ Regarding the age groups, our study found that more than three-fourths of patients were diagnosed with CHD under 1 year of age. An explanation for this is the early presentation of CHD manifestations and progressive deterioration. The findings presented here contradict to the findings of a study reported by Ibadin et al,³⁹ whereas they are comparable to the findings of studies reported by Khan et al,²¹ Akhter et al,²⁵ Asghar et al,¹³ Subramanyan et al,⁴⁰ George and Frank-Briggs.⁴¹ This study reported that the most common times of presentation or echo diagnosis of CHD among children were below 1 year of age. The results of this study are in line with the findings of other reported studies.^{3,13} The study revealed that the participants from rural areas had a higher frequency of CHD compared to those from urban areas. The findings of this study are consistent with the findings of studies conducted by other authors.^{34,35} This study found that the number of acyanotic cases of CHD was 1145 (86.5%), which was higher than that of cyanotic cases (178, 13.5%). The findings of this study are in line with those of studies reported by other authors.^{6,21,26} Among the cyanotic types, TOF was the commonest cyanotic congenital heart disease, being 3.9%, respectively. This is incomparable to worldwide, where the incidences of CHD in TOF (10%).⁴² This is lower than what is reported in other studies.^{21,26,43} There was male predominance in both cyanotic and acyanotic heart disease. Our finding is consistent with previous conducted studies,^{6,33} but contrasts with the findings of a study conducted by Burki MK and Babar GS,³² who found that both genders were equally affected. This difference may be due to a number of factors, such as socio-economic, cultural, ecological, and genetic factors. Furthermore, as revealed in the current study, isolated CHD accounted for 79.9% of all

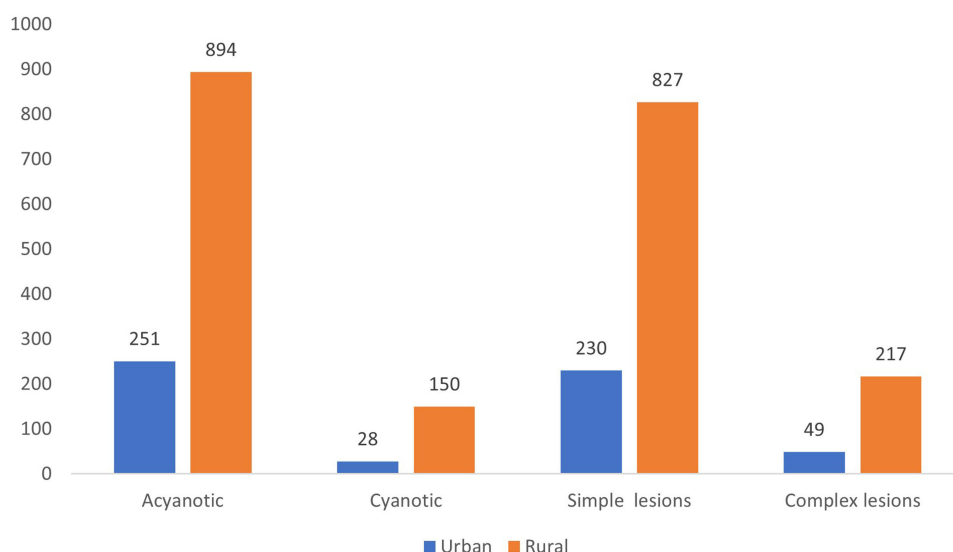


Figure 4 Distribution of acyanotic, cyanotic, simple, and complex lesions according to residence.

cases of CHD, which is similar to the findings of those studies conducted in Egypt and Saudi Arabia.^{44–46} Conversely, Mexico, India, Libya, and Nigeria reported lower proportions of isolated CHD,^{14,15,22,47} whereas a much higher proportion of isolated CHD cases was reported in Pakistan.²¹ This discrepancy could be attributed to differences in the age at diagnosis. Specifically, those with more complex CHD may die earlier, potentially before they are diagnosed.²¹ In terms of identifying an isolated acyanotic CHD, the present study revealed that patent ductus arteriosus, ventricular septal defect, and atrial septal defect were the most commonly observed. Our study was only consistent with those of studies performed in Guatemala and Saudi Arabia, where patent ductus arteriosus was the most commonly reported isolated acyanotic CHD.^{47–49} Furthermore, the tetralogy of Fallot was the most frequently observed cyanotic anomaly, which is comparable to the findings of other national and international studies.^{44,50}

VSD, PDA, and AVSD were the most commonly isolated abnormalities reported by the Egyptian study; in contrast, AVSD and ASD were the most common in another investigation.⁵¹ Globally, there are differences in the patterns of isolated CHD; in Libya, Sudan, Saudi Arabia, India, and other western nations, ASD, AVSD, and VSD were the most prevalent.^{14–18} ASD, VSD, PDA, and AVSD were reported to be the most prevalent in Iran and Korea.^{19,20} However, VSD and PDA were the most commonly reported isolated CHDs in Mexico and Pakistan.^{21,22} The current study confirmed the differences in the kind and character of CHD in various national and international geographic locations. The present study reported that VSD+PDA and VSD+ASD were the most common anomalies in the pattern of multiple CHDs. This finding is consistent with previous research conducted in Egypt.^{46,51} The primary explanations for the variation in the pattern of the various multiple CHD types between studies include the study design, demographic factors (such as age and ethnicity), time period, accessibility to prenatal healthcare, and pregnancy termination.⁵² The current study shows a higher frequency of complex CHD among male participants; this finding also agrees with the findings documented by previous authors.^{3,26,37} Our study reported 20.1% of complex CHD cases, which was similar to other national,^{9,23} and international studies.^{6,37} The rising trend seen in this study may also be due to the fact that our center is a major referral center for the diagnosis of CHD; thus, most complex cases of CHD are referred to our center. Different screening procedures, distinct diagnostic facilities, and the genetic, socioeconomic, and environmental diversity of various study groups can all be used to explain this variation in the frequency of CHD. Certain biochemical processes during embryogenesis may be impacted by interactions between genes and the environment or between genes. It has been proposed that the pattern of CHD may be determined by genetic factors, particular processes of embryogenesis, and cell characteristics.⁴⁸

The present study had several limitations. First and most importantly, the lack of complete medical records for data collection in our hospitals is due to the absence of a standard electronic database. Therefore, they cannot accurately reflect the incidence and prevalence of CHD throughout the country. I suggest putting the records of the patients in an

electronic database system to facilitate their retrieval as needed. Such steps can help us investigate the possible risk factors contributing to CHD, as we still have no idea about it in our country. Second, the study was limited by its small sample size; a larger sample size could have resulted in more accurate reporting of the prevalence. Furthermore, our study is confined to Eastern Afghanistan; hence, it does not provide the true prevalence of CHD in the total population. Additional research is needed nationwide to accurately determine the true prevalence of CHD among children in Afghanistan.

Conclusion

The study concluded that more than three-fourths of CHD-diagnosed cases were less than one year of age, with PDA, VSD, ASD, and TOF being the most frequently diagnosed acyanotic and cyanotic congenital heart disease. Participants from rural residence had a higher frequency of CHD compared to those from urban residence. Additionally, our study found that more males were affected by CHD compared to females. In order to avoid serious complications, reduce mortality, and improve quality of life, early identification and correction of disease is crucial. Many lesions can be surgically corrected; thus, the availability of local expertise and raising awareness among parents and professionals is vital for timely interventions.

Recommendations

First, it is recommended to raise awareness about the potential risks of consanguineous marriages and advocate people for marrying outside of close relatives to enhance genetic diversity and mitigate the risk of congenital anomalies. Second, health education programs should emphasize the importance of optimal maternal age for pregnancy, particularly discouraging pregnancies in very young or older women to reduce health risks for both mother and child. Third, healthcare providers should ensure that women of childbearing age are educated on the harmful effects of teratogenic drugs during pregnancy and promote the use of safer alternatives. Fourth, prevention and timely treatment of maternal infections should be prioritized through regular antenatal check-ups and vaccination programs to minimize adverse effects on fetal development. Fifth, promote the importance of prenatal care, particularly the provision of essential micronutrients such as folic acid and iron to reduce the risk of birth defects and improve maternal and infant health. Furthermore, encourage skilled birth attendance and discourage home deliveries without trained professionals, ensuring access to emergency obstetric care to improve maternal and neonatal outcomes. Finally, I suggest conducting a series of researches, both prospective and retrospective, to add the missing information in this field.

Abbreviations

ASD, Atrial Septal Defect; ASMR, Age Standardized Mortality Rates; CHD, Congenital Heart Disease; PDA, Patent Ductus Arteriosus; PS, Pulmonary Stenosis; SPSS, Statistical Package for Social Science; TGA, Transposition of the Great Arteries; TOF, Tetralogy of Fallot; VSD, Ventricular Septal Defect.

Data Sharing Statement

In order to respect ethical standards and protect study participants' privacy, data cannot be made public. As a result, data can be obtained upon request by sending an Email to ghafarsherzad15@gmail.com, Assistant Professor, Department of Biochemistry, Faculty of Medicine, Nangarhar University, Nangarhar, Afghanistan.

Ethical Approval and Informed Consent

This paper is the outcome of a series of retrospective studies carried out in Afghanistan after obtaining ethical approval from the institutional review board (IRB) of Nangarhar University Faculty of Medicine (No. 144, dated November 15, 2022). Consent was not required to access the medical records of deceased patients. However, for the remaining participants, informed consent was provided by a parent of all patients via phone prior to the study. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declared no conflicts of interest.

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