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## ORIGINAL ARTICLE

# CONGENITAL HEART DEFECTS AND ASSOCIATED FACTORS IN CHILDREN WITH CONGENITAL ANOMALIES

Feredegn Talargia, MSc[1], Girma Seyoum, PhD[2*], Tamirat Moges, MD[3]

## ABSTRACT

***Background****: Congenital heart defect is structural heat defect present at birth and accounts for nearly one-third of all major congenital anomalies. Worldwide, congenital heart defect constitute one of the major causes of infant mortality, particularly in developing countries.*
***Objective:*** *The objective of this study is to describe the occurrence and associated factors of congenital heart defects in Ethiopian children with congenital anomalies*
***Methods****: Hospital based cross-sectional study was carried out, involving children with congenital anomalies, in four referral public hospitals in Addis Ababa. The data were collected using a structured questionnaire, and the diagnosis of congenital heart defect in children was retrospectively retrieved from medical records.*
***Results****: The prevalence of congenital heart defect among children diagnosed with congenital anomalies was 35.8% among the 271 children with congenital anomalies. The most common congenital heart defect was Ventricular Septal Defect (30.9%), followed by Atrial Septal Defect (23.7%). Previous history of abortion Adjusted odd ratio (AOR) =1.96; CI= (0.277-0.935); p=0.03) and past history of drug intake during pregnancy (AOR= 2.149; CI= (0.252-0.861); p= 0.015) were significantly associated with congenital heart defect.*
***Conclusion****: The present study has shown that the burden of congenital heart defect among congenital anomalies was high. Mothers who had previous history of abortion and drug intake during pregnancy were significantly associated with the occurrence of congenital heart defect. Results of this study have given an insight into the magnitude of the problem and provided baseline data for future detailed studies, as there were very little data available in the past. In addition, results of this study would be used in developing strategies for improved management and*

## INTRODUCTION

Congenital heart defect (CHD) is a major cause of serious morbidity and mortality. It is defined as clinically significant structural heart disease present at birth (1). CHD is one of the most common congenital defects and accounts for nearly one-third of all major congenital anomalies; Population based studies on the prevalence of CHD worldwide was found to range between 8 to 12% live births and constant throughout the world (2).Another study done in urban America describes the prevalence of CHD occurring in approximately 3–9 of every 1,000 live births (3).

There are 8 common CHDs and these are VSD (Ventricular Septal Defect), ASD (Atrial Septal Defect), Patent Ductus Arteriosus (PDA), Coarctation of Aorta(CoA), Tetralogy of Fallot (TOF),Transposition of Great Vessel (TGA), Pulmonary Stenosis,(PS) and Aortic Stenosis( AS)., These CHDs account for 90% of all cases. The remaining 10% consists of more complex anomalies (4).

CHD occurs more predominantly in males than in females. Some anomalies such as VSD, TOF and Atria Ventricular Septal Defects (AVSD) are more common in males whereas ASD, PDA, COA and TGA are more common in females (5).The causes of most CHDs are unknown. Most cases of CHD are thought to be multifactorial and result from a combination of genetic predisposition and environmental factors (6).

Maternal exposure to environmental factors such as ambient air pollution, heavy metals, and micronutrients are related to CHD prevalence because chemicals in the soil, water, and air affect human beings directly or indirectly. The physical environment, such as solar radiation and magnetic fields, also has influence on prevalence of CHD. Furthermore, socio economic and lifestyle habits could affect prevalence of CHD (7).

1.Debreberhan University , School of Medicine, Department of Anatomy.
2.Addis Ababa University ,School of Medicine, Department of Anatomy.
3.Addis Ababa University, School of Medicine, Department of Pediatrics.
* Corresponding Author: girma91@yahoo.com

Worldwide, CHD is the principal heart diseases in children and constitute one of the major causes of infant mortality, particularly in developing countries (8,9). CHD, accounting for more than 20% of prenatal deaths, also is the most common of all congenital malformations (10). Reducing the prevalence of these diseases is urgent and requires a real inventory of the premises of the problem that would clarify the issue for more effective prevention strategies and improved management.

So far, very little information is available regarding the prevalence of CHD and identification of associated factors among children in Ethiopia . This study was designed to investigate the prevalence of CHD and determine associated factors among children diagnosed with congenital anomalies in Addis Ababa governmental hospitals. Results from this study would give an insight into the magnitude of the problem and provide baseline data for future detailed studies. In addition, the results would be useful in developing strategies for improved management and rehabilitation of patients with CHD.

## PATIENTS AND METHODS

Prospective cross sectional study was conducted at public hospitals in Addis Ababa. The study sites were Saint Paul's Hospital, Tikur Anbesa Specialized Hospital, Yekatit 12 Hospital and Zewditu Memorial Hospital.

***Method of data collection:*** The study was a hospital-based cross sectional study among children diagnosed with congenital anomalies in Addis Ababa governmental hospitals. The Source population were all children with congenital anomaly in the selected governmental hospitals. Study population were all children with congenital anomaly during the study period in the selected hospitals. All children diagnosed with congenital anomalies and those who were less than 18 years old, during the study period, were included in the study. All children who were severely ill during the study period and cases older than 17 years and referred to Tikur Anbesa Specialized Hospital from the other three selected hospitals were excluded. In addition, cases with unclear diagnosis or not confirmed by a pediatrician also were excluded from the study.

The sample size was calculated using a statistical formula: n = Z2 p (1-p)/w2, where n= sample size, Z= critical value given confidence interval, P= proportion, W=margin of error (Z= 1.96, p= 0.5, w= 0.05).

This calculation of the sample size was based on a similar study conducted in Sudan [22]where a p-value of 20 %, 95% confidence interval and 5% margin of error was used. Using the above formula and substitute the given value the sample size was calculated as: n = Z2 p (1-p)/w2 = (1.96) 2(.2) (.8) / (.05)2 =245.8≈246, with a 10% non-respondent rate added. Therefore, the final sample size was calculated to be 271.

A total of four hospitals were selected from 11 governmental hospitals. The selection was based on patient load and being referral centers. Selection of study subjects was done using simple random sampling. The congenital anomaly cases in those hospitals were counted, and the respective proportions were calculated for each hospital. Congenital anomaly cases, among all children, were screened based on their respective diagnosis profile from their respective medical cards/medical records. Confirmation of the diagnosis by the physician with echocardiography. The echocardigraphy was done after identification of congenital anomaly. Children who fulfilled the inclusion criteria were included until the desired sample was achieved.

Data collectors were recruited in each of the selected governmental hospitals and they were trained for two days, regarding the objectives of the study, inclusion and exclusion criteria and on sampling procedures. Data on socio-demographic and clinical information were gathered from the respective patients' cards. In addition, parents or care givers of the children who gave consent were interviewed and provided data variables such as maternal age, parity, history of Diabetes Mellitus, drug intake, exposure to X-ray, history of CHD in the family, residential area, history of chronic disease and number of antenatal clinic visits.

The data were collected at pediatrics clinics, pediatrics emergency and pediatrics outpatient department which provided medical care services for all cases of congenital defects. During data collection, pediatricians and neonatologists were consulted, for presence of congenital anomaly, when there was an unclear diagnosis. The proportion of children with CHDs was calculated by dividing the number of birth CHD cases (numerator) by the total number of children diagnosed with congenital anomalies (denominator).

***Data analysis and interpretation:*** Data were entered, and analyzed by Epidata version 3.1and SPSS (statically package of social science) version 23 software respectively. Data were summarized in tables and bar graph. Categorical variables were reported as proportions and compared using Chi square tests. Continuous data will be described by mean and standard deviation. Bivariate followed by multivariate logistic regression analyses was done to determine factors associated with congenital heart defects. The 95% confidence interval was determined and an associated factor with p-value of less than 0.05 was considered to be significant.

***Ethical consideration:*** Ethical clearance was obtained from Departmental Research Ethics Review Committee (DRERC) of TASH, Institutional Review Board (IRB) of St. Paul's Millennium Medical College and Addis Ababa Public Health Research and Emergency Management Core Process. The permission to look into the medical records of children at the Yekatit and Zewditu was secured based on the letter from DRERC of TASH. Informed consent was obtained from parents/care takers of the children.

## RESULTS

***Socio demographic characteristics:*** The study population consisted of children in the age group of less than 18 years old from heterogeneous groups in terms of residential area, ethnicity and religion.

A total of 271 mothers/primary care takers of children, with a response rate of 100%, were included in the study. The highest proportion of children in the study population were in the age group of 2-6 years 109 (40.3%) while children in the age group of 13-17 years were the smallest, 28 (10.3%). The mean age of the children was 5.09±4.64. Out of the total study participants 134 (49.4%) were males and 137 (50.6%) were females.

***Prevalence of Congenital Heart defects:*** In the present study, among 271 children diagnosed with congenital anomalies, 97(35.8%) had CHD. The types of CHDs identified were VSD, ASD, PDA, CoA, TOF, TGA, PS and AVSD. The prevalence of ASD, AVSD, CoA and VSD were 23.7%, 9.3%, 4.1% and 30.9%, respectively, while the prevalence of PDA,PS,TGA, and TOF were 15.5%, 3.1%, 2.1**%** and 11.3%, respectively (Figure 1).The most common type of CHD was VSD 30(30.9%), followed by ASD 23(23.7%). The prevalence of ASD and VSD in male children was 17.6% and 33.3%, respectively, while the prevalence in female children was 30.4% and 28.3%, respectively, (Figure 1).

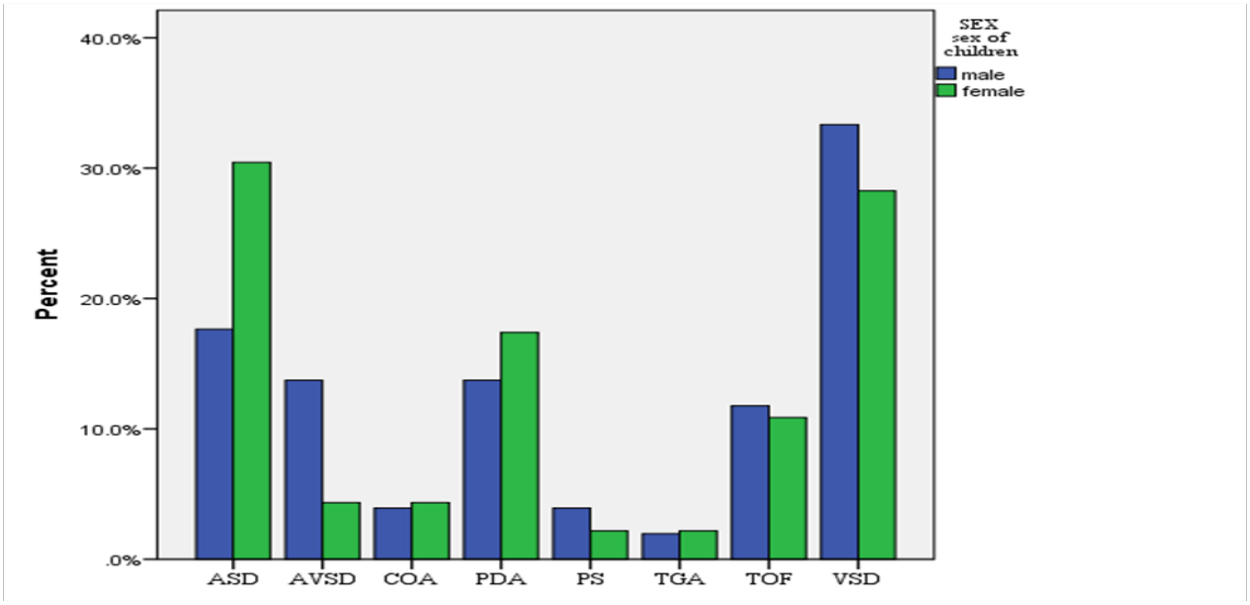


Figure 1: Distribution of types of CHD by sex among children diagnosed with congenital anomalies.

***Factors associated with congenital heart defects:*** In the current investigation, previous history of abortion and drug intake during pregnancy (any reported/ recorded drug intake during any stage of pregnancy ) demonstrated significant association (P<0.05) with the presence of CHD among children diagnosed with congenital anomalies (Table 1). However, the type of drug used during pregnancy was not specified.

The present study also revealed that children whose mothers had previous history of abortion were twice more likely to have CHD (AOR=1.964 95%CI (0.277-0.935), P=0.03). Children whose mothers had previous drug intake were also twice more likely to develop CHD (AOR=2.149, 95%CI (0.252-0.861), P=0.015) (Table 1).

Table: 1. Bivariate analysis between maternal characteristics and presence of congenital heart disease

| **Variable** | **CHD** | | **COR (95%CI)** | **P value** |
|---|---|---|---|---|
| | **No N (%)** | **Yes N (%)** | | |
| Maternal age | | | | |
| <20 | 7(53.8 ) | 6(46.2) | 1.26(0.35-4.49) | 0.563 |
| 20-35 | 145(65.6) | 76(34.4) | 0.8(0.77-3.77) | |
| >35 | 22(59.5 ) | 15(40.5) | | |
| Previous history of abortion | | | | |
| No | 146(67.6 ) | 70(32.4 | 2.1(0.91-4.780) | *0.023 |
| Yes | 28(50.9) | 27(40.1) | | |
| Previous history of drug intake | | | | |
| No | 148(67.9) | 70(32.3) | 2.2(1.194-4.037) | *0.011 |
| Yes | 26(50.9) | 27(49.1) | | |
| Folic acid intake | | | | |
| No | 8(66.7) | 4(33.3) | 0.9(0.26-3.04) | 0.856 |
| Yes | 166(64.1) | 93(35.9) | | |
| History of chronic disease of the mothers | | | | |
| NO | 162(65.9) | 84(34.10) | 2.1(0.913-4.780) | 0.081 |
| Yes | 12(48.0) | 13(52.0) | | |
| History of Alcohol intake during pregnancy | | | | |
| No | 156(66.1) | 80(33.9) | 1.8(0.9-3.8) | 0.09 |
| Yes | 18(51.4 ) | 17(48.6) | | |
| History of cigarette smoking during pregnancy | | | | |
| No | 172(63.9) | 97(36.1) | | 0.999 |
| Yes | 2(100.0) | 0(0.0) | | |

* values have significant association with CHD (P<0.05); N=number; COR=crude odd ratio
Values in brackets indicate percentages of maternal characteristics.

Table 2: Bivariate analysis between children's characteristics and presence of congenital heart disease.

| Variable | CHD | | COR (95% CI) | P value |
|---|---|---|---|---|
| | No N (%) | Yes N (%) | | |
| **Sex** | | | | |
| Male | 83(43.7) | 51(52.6) | 1.2(0.7-1.9) | 0.442 |
| Female | 91(52.3) | 46(47.4) | | |
| Gestational age | | | | |
| **Pre-term** | 161(53.6) | 91( 46.6) | 0.6(0.28-1.34) | 0.218 |
| Term | 13(65.4) | 6(34.6) | | |
| Family history of CHD | | | | |
| No | 167(64.7) | 91(35.3) | 0.6(0.21-1.95) | 0.428 |
| Yes | 7(53.8) | 6(46.2) | | |
| Pregnancy types | | | | |
| Single | 161(63.9) | 91(36.1) | 0.6(0.28-1.34) | 0.218 |
| Twin | 13( 68.4) | 6( 31.6) | | |
| **Birth order** | | | | |
| 1st | 74(71.2) | 30(28.8) | 0.6(0.28-1.132) | |
| 2nd | 45(62.5) | 27(37.5) | 0.8(0.4-1.7) | |
| 3rd | 26(57.8) | 19(42.2) | 1.01(0.45-2.28) | 0.274 |
| >3rd | 29(58.0) | 21(42.0) | | |

*N= number; COR=crude odd ratio

- Values in brackets indicate percentages of maternal characteristics.

## DISCUSSION

The present study has shown a relatively high prevalence of CHD among children diagnosed with congenital anomalies and identified the risk factors associated with CHD. The present study has recorded a prevalence of 35.8% which is slightly higher than the average worldwide prevalence of CHDs (33.3%) among all major congenital anomalies (2).

The current prevalence of CHDs is similar with the findings of studies done in Ecuador with children attending echocardiography, which reported a prevalence of 35.95% (11).However, the prevalence observed in the present study is not in line with that reported (46%) by way of a cross sectional survey carried out in Nigeria (12). This significantly higher prevalence of CHDs in the study conducted in Nigeria may be due to difference in study settings.

In the current study, history of Abortion was found to be significantly associated with the presence of CHD. Results of other investigations also showed that the prevalence of CHD was higher in stillbirth, spontaneous abortion and prematurity (13,14). These findings were also consistent with findings from a systematic review and meta-analysis done in China where the risk of CHD increased by 18% in spontaneous abortion and by 58% in induced abortion in mothers with previous history of abortion (15). A case control study conducted by Li et. Al (16), on the other hand, reported that there was no any significant positive association between number of maternal abortion (spontaneous, induced abortion) and prevalence of CHD.

The history of drug intake during pregnancy has been found to have a significant positive relationship with prevalence of CHD. This observation is in line with the findings of a published article which reported that the risk of CHD increased after the mother was treated with several drugs (17).

Results of another study conducted by Kuciene *et.al*. (13) also were consistent with the current study which showed that the prevalence of CHD was higher in Children whose mothers use medication during pregnancy. Potentially, almost any drug used by pregnant mothers could be teratogenic. However, some of the mothers in the present study area have been taking contraceptive pills, unaware of their pregnancy. In other studies, maternal drug intake during pregnancy had no significant association with the presence of CHDs (18).

Maternal age is a risk factor for CHD even in the absence of any chromosomal abnormality in the newborn. Whether the basis of the risk resides with the mother's oocyte is unknown (19). The prevalence of CHD in this study is high in mother's whose ages were below twenty (42.6%) and above 35 (40.5%), however, the prevalence of CHD was relatively lower in mothers whose ages were between 20 and 35years (34.4%). This finding is consistent with that reported in a study done in China (20). Similar studies conducted in India and America indicated that CHD was more prevalent when maternal age increased, even in the absence of any chromosomal abnormalities (7,19).With maternal age above 35 years, there is a high frequency of chromosomal abnormalities in the embryo e.g. Down syndrome and other trisomies. The possibility of new gene mutation also increases with age (6,19,21).

The prevalence of CHD was slightly higher in male children (52.6%) than in females (47.4%), with a ratio of 1.1:1. Similar sex distribution of CHD also was reported by other studies (5,22,23). However, some other investigations reported that CHDs were more common in female children (24), while other studies showed no difference in sex distribution of CHD (25). The frequency of the types of CHDs varied with the sex of the child (5,23,26). In the current study, VSD, AVSD, TOF and PS were more common in male children while ASD and PDA were common in female children. This observation is similar with that reported by Sharmanet al. (23).Other similar studies also showed that VSD and TOF were more common in male children where as ASD and PDA more common in female children (27). However, other studies reported that ASD and VSD were more prevalent in males and females, respectively (26).

Family history of CHD did not show any significant positive relationship with the frequency of occurrence of CHD in this study.

However, a study conducted in Egypt showed a significant association between history of CHD in the family and prevalence of congenital anomalies (28).The association was even much stronger in siblings from consanguineous marriages. Consanguineous marriages were not practiced among the study participants of the present study, but these are common in Egypt and in Middle East countries (18,26,28).

In this study, maternal history of chronic disease and multi parity were not associated with the presence of CHDs. Study carried out in Pakistan showed that there were no significant association between maternal chronic disease and occurrence of CHDs (18) which was consistent with the findings of the current study. It is known from the literature that maternal history of chronic disease and multi parity have been associated with CHDs. Several maternal chronic diseases especially Diabetes Mellitus, Hypertension, CHD and Epilepsy were associated with higher prevalence of any form of CHD (29,13,30).
In the current study maternal alcohol consumption during pregnancy has no association with the occurrence of CHDs. This finding goes in line with a systematic review and Meta-analysis done in Italy, where alcohol consumption during pregnancy was not associated with a risk of CHD (31). However, a study carried out in China reported that the probability of having CHD in mothers who drank alcohol during pregnancy was higher compared to mothers who did not consume alcohol (21). Although the proportion of mothers who consumed alcohol during pregnancy and who had a history of chronic disease was not large, these variables also showed association with CHD although the association was not significant.

Cigarette smoking during pregnancy did not have a significant association with the presence of CHDs, which was inconsistent with the findings of the study conducted in China where the habit of smoking was common (21).

The frequency of different types of CHDs observed in this study is consistent with other studies conducted in Africa as well as in other countries. The most common type of CHD was VSD followed by ASD which was similar with that reported by a study in the Sudan which was 33.4 % (22) and in China 29.9% (11). The prevalence of VSD in the current study, in studies in the Sudan and in China were 30.9%, 33.4% and 29.9%, respectively. However, this level of prevalence of VSD was not consistent with that reported by a Nigerian investigation which was considerably higher (49%) (32).

Other studies conducted in also have identified ASD as the commonest CHD followed by VSD (1,20,33).

***Conclusion:*** The present study showed that the burden of CHDs among congenital anomalies was high (35.8%). Mothers who had previous history of abortion and drug intake during pregnancy were significantly associated with the occurrence of CHD. Results of this study can give an insight into the magnitude of the problem and provide baseline data for future detailed studies, as there was very little data available in the past. In addition, the results would be used in developing strategies for improved management and rehabilitation of patients with CHD. Further detailed national studies that would influence decision making should be conducted.

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