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Frequency of common types of congenital heart diseases in infants of diabetic mothers

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ABSTRACT

BACKGROUND & OBJECTIVE: Infants born to diabetic mothers are at a heightened risk of having congenital malformations. Congenital heart defects are one of the major health problems in such patients. This study was conducted to assess the frequency of common types of congenital heart diseases (CHD) in infants of diabetic mothers (IDM).

METHODOLOGY: It was a cross-sectional, descriptive study conducted at Children's Hospital Lahore from 10th June 2022 to 9th December 2022. Through consecutive sampling, 160 IDM with CHD were included in the study. The CHD was diagnosed through echocardiography. Diagnostic tests, including pulse oximetry, chest X-rays, and electrocardiography (ECG), were carried out when necessary. Experienced consultant pediatric cardiologists conducted the echocardiography with the help of 2D color Doppler in M mode.

RESULTS: The frequency of common CHD in infants born to diabetic mothers was as follows: Patent ductus arteriosus (PDA) in 43 (26.87%), Ventricular septal defect (VSD) in 34 (21.25%), Hypertrophic cardiomyopathy in 28 (17.50%), Patent foramen ovale (PFO) in 20 (12.50%), Atrial septal defect (ASD) in 18 (11.25%), and Transposition of great arteries (TGA) in 17 (10.63%) cases. There is a significant difference in hypertrophic cardiomyopathy in different gestational ages, and a higher rate is seen in gestational age 40-42 weeks (p=0.018).

CONCLUSION: In our study, PDA and VSD were the most frequent CHDs in IDM, followed by hypertrophic cardiomyopathy. These findings emphasize the need for early detection and screening in this high-risk group.

KEYWORDS: Infants of Diabetic Mothers, Patent Ductus Arteriosus, Hypertrophic Cardiomyopathy, Ventricular Septal Defect, Congenital Heart Diseases.

INTRODUCTION

Diabetes mellitus (DM) is considered to be one of the major public health challenges worldwide. According to The News article, Pakistan stands 3rd in global DM prevalence, after China and India [1]. The prevalence of DM in Pakistan was recorded at 11.77% in 2016, 16.98% in 2018, and 17.1% in 2019 [2].

Gestational diabetes mellitus (GDM) is the paramount form of diabetes-related complications during pregnancy, with a rising global incidence. Despite worldwide progress in perinatal care, infants born to diabetic mothers (IDMs) remain susceptible to a range of issues during the neonatal period. These include various physiological, metabolic, and congenital problems, such as an elevated risk of congenital heart and neurological defects [3].

Maternal diabetes, whether pre-gestational or gestational, is known to have teratogenic effects during the first trimester, particularly during heart development. As a result, IDMs have a higher likelihood of cardiovascular malformations compared to those born to non-diabetic women. The prevalence of CHD in IDM infants is approximately 5% [4].

The common CHD associated with maternal diabetes include hypertrophic cardiomyopathy (HCM), patent ductus arteriosus (PDA), ventricular septal defect (VSD), atrial septal defect (ASD), transposition of the great arteries (TGA), left ventricular hypertrophy (LVH), patent foramen ovale (PFO), mitral regurgitation (MR), tricuspid regurgitation (TR), coarctation of the aorta (COA), aortic insufficiency (AI), Tetralogy of Fallot, and cardiomegaly [5].

Muhammad A and colleagues reported the following frequencies of congenital heart defects in neonates born to diabetic mothers: 16.8% for PDA, 12.9% for VSD, 8.9% for ASD, 7.9% for PFO, and 5.9% for TGA [6]. Similarly, Ferdousi S and team in Bangladesh found the frequencies of PFO to be 60.71%, PDA at 55.3%, hypertrophic

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cardiomyopathy (HCM) at 21.42%, and ASD at 10.71% [7]. Among these CHD, interventricular septal hypertrophy usually resolves by itself over a short period. Still, other conditions may necessitate intensive care, and, in some cases, medical or surgical interventions may also be required [5,8]. This underscores the importance of early diagnosis and the implementation of a screening protocol for CHD in IDM, who are at increased risk for these conditions.

Existing literature reports varying frequencies of CHD in infants of diabetic mothers across different regions, highlighting the need for region-specific data. This study, conducted in the neonatology unit and pediatric cardiology department of Children's Hospital Lahore (CHL), seeks to address the gap in regional data on the frequency of common CHD in IDMs. By identifying the most common CHDs in this high-risk population, the study aims to facilitate early diagnosis and appropriate interventions, ultimately improving outcomes for these infants. Additionally, these findings can guide screening protocols and support the development of strategies for managing congenital heart conditions in IDMs in comparable healthcare settings.

METHODOLOGY

This descriptive, cross-sectional research was conducted in the neonatology and pediatric cardiology units of the CHL from 10 June 2022 to 9 December 2022. A sample size of 160 full-term infants was calculated based on the expected prevalence of TGA in IDM (5.9%) [6], with a margin of error of 3.7% and a confidence level of 95%. Non-probability, consecutive sampling was employed to recruit participants.

Participants included infants under one year of age, born full-term to diabetic mothers, and diagnosed as having congenital heart diseases on the basis of echocardiography. The exclusion criteria involved preterm neonates (before 37 weeks), those with severe birth asphyxia, neonatal sepsis, and significant central nervous or pulmonary anomalies. Additionally, infants born to mothers with clinical conditions like hypertension, heart failure, tuberculosis, chronic kidney disease, and pre-eclampsia, or those using medications other than insulin, were excluded, as well as infants with syndromic features or born to mothers over 35 years old.

After obtaining ethical approval from the research evaluation unit of CPSP (CPSP/REU/PED-2018-075-4868), all the infants (age newborn year of age) meeting the inclusion and exclusion criteria were enrolled in the study. Demographic data, including age, current weight, gestational age at time of birth, and gender, were collected using a predesigned questionnaire. A thorough examination was performed to detect both cardiac and non-cardiac abnormalities. The diagnostic tests, including pulse oximetry, chest X-rays, echocardiography, and electrocardiography (ECG), were carried out according to indications. Experienced consultant pediatric cardiologists conducted the echocardiography with the help of 2D color Doppler in M mode.

The focus of the study was on infants with confirmed congenital heart defects as detected by echocardiography, as it is considered the gold standard in this regard, excluding those with normal echocardiography results to ensure that the analysis concentrated on the prevalence and characterization of CHDs in this high-risk population. All findings and types of congenital heart diseases identified were documented for further analysis.

The data analysis was performed using SPSS version 20. Qualitative variables, including gender and the presence of CHD, for e.g., PDA, VSD, HCM, etc., were assessed to calculate their frequencies and corresponding percentages. For quantitative variables such as age, weight, and gestational age at birth, the mean and standard deviation (SD) were determined. Additionally, potential effect modifiers—such as age, gender, weight, and gestational age at birth—were stratified to examine their influence on the various types of (CAD's) and they were analyzed using the chi-square test, with statistical significance established at $p < 0.05$.

RESULTS

Mean of current age was 6.86 ± 2.58 months while that of gestational age was 38.26 ± 1.26 weeks. The mean weight of participants was 5.53 ± 1.26 kg. Out of the 160 patients, 103 were boys (64.37%) and 57 were girls (35.63%) with male to female ratio of 1.7:1 (Table-I).

Table-I:Distribution of patients by age, gestational age, weight and gender (n=160).

Variables	Categories	No. of Patients n(%)	Mean ± SD
Age (in months)	≤6	82(51.25)	6.86 ± 2.58
	7-12	78(48.75)	
Gestational age at birth	37-39 weeks	133(83.12)	38.26 ± 1.26
	40-42 weeks	27(16.88)	
Weight (killogram)	≤5	77(48.13)	5.53 ± 1.26
	>5	83(51.87)	
Gender	Female	57(35.63)	-
	Male	103(64.37)	

Table-II: Frequency of common types of CHD in IDM.

Congenital heart defects	Frequency n(%)
Patent ductus arteriosus (PDA)	43(26.87)
Ventricular septal defect (VSD)	34(21.25)
Hypertrophic Cardiomyopathy (HCM)	28(17.50)
Patent foramen Ovale (PFO)	20(12.50)
Atrial septal defect (ASD)	18(11.25)
Transposition of great arteries (TGA)	17(10.63)
Total	160(100)

In this study, the most common CHD in IDM was patent ductus arteriosus (PDA) (n=43, 26.87%), followed by ventricular septal defect (VSD) (n=34, 21.25%), while the least common was transposition of great arteries (TGA) (n=17, 10.63%) Table-II.

Stratification of different CAD's with respect to age is given in Table-III. Table IV shows the stratification of different CHD's with respect to the gender of the infant. Stratification of different CHD's with respect to gestational age and weight are shown in Table-V & VI, respectively. There is a significant difference in hypertrophic cardiomyopathy in different gestational ages, and more percentage is seen in gestational age 40-42 weeks (P=0.018).

Table-III: Stratification of CHD according to age.

Congenital Heart Defects		≤6 months (n=82) n(%)	7-12 months (n=78) n(%	P-value
ASD	Yes	09 (10.98)	09 (11.54)	0.910
	No	73 (89.02)	69 (88.46)	
VSD	Yes	17 (20.73)	17 (21.79)	0.869
	No	65 (79.27)	61 (78.21)	
PDA	Yes	25 (30.49)	18 (23.08)	0.291
	No	57 (69.51)	60 (76.92)	
PFO	Yes	10 (12.20)	10 (12.82)	0.905
	No	72 (87.80)	68 (87.18)	
TGA	Yes	10 (12.20)	07 (8.97)	0.509
	No	72 (87.80)	71 (91.03)	
HC	Yes	11 (13.41)	17 (21.79)	0.163
	No	71 (86.59)	61 (78.21)	

Table-IV: Stratification of CHD according to gemder.

Congenital Heart Defects		Male (n=103) n(%)	Female (n=57) n(%	P-value
ASD	Yes	12 (11.65)	06 (10.53)	0.829
	No	91 (88.37)	51 (89.47)	
VSD	Yes	23 (22.33)	11 (19.30)	0.654
	No	80 (77.67)	46 (80.70)	
PDA	Yes	25 (24.27)	18 (31.58)	0.318
	No	78 (75.73)	39 (68.42)	
PFO	Yes	13 (12.62)	07 (12.28)	0.950
	No	90 (87.38)	50 (87.72)	
TGA	Yes	09 (8.74)	08 (14.04)	0.298
	No	94 (91.26)	49 (85.96)	
HC	Yes	21 (20.39)	07 (12.28)	0.196
	No	82 (79.61)	50 (87.72)	

Table-V: Stratification of CHD according to gestational age.

Congenital Heart Defects		37-39 weeks (n=133) n(%)	40-42 weeks (n=27) n(%)	P-value
ASD	Yes	13 (9.77)	05 (18.52)	0.189
	No	120 (90.23)	22 (81.48)	
VSD	Yes	32 (24.06)	02 (7.41)	0.054
	No	101 (75.94)	25 (92.59)	
PDA	Yes	36 (27.07)	07 (25.93)	0.903
	No	97 (72.93)	20 (74.07)	
PFO	Yes	18 (13.53)	02 (7.41)	0.380
	No	115 (86.47)	25 (92.59)	
TGA	Yes	15 (11.28)	02 (7.41)	0.552
	No	118 (88.72)	25 (92.59)	
HC	Yes	19 (14.29)	09 (33.33)	0.018
	No	114 (85.71)	18 (66.67)	

Table-VI: Stratification of CHD according to birth weight.

Congenital heart defects		≤5 kg (n=77) n(%)	>5 kg (n=83) n(%)	P-value
ASD	Yes	10 (12.99)	08 (9.64)	0.503
	No	67 (87.01)	75 (90.36)	
VSD	Yes	15 (19.48)	19 (22.89)	0.598
	No	62 (80.52)	64 (77.11)	
PDA	Yes	20 (25.97)	23 (27.71)	0.804
	No	57 (74.03)	60 (72.29)	
PFO	Yes	12 (15.58)	08 (9.64)	0.256
	No	65 (84.42)	75 (90.36)	
TGA	Yes	08 (10.39)	09 (10.84)	0.926
	No	69 (89.61)	74 (89.16)	
HC	Yes	12 (15.58)	16 (19.28)	0.539
	No	65 (84.42)	67 (80.72)	

DISCUSSION

CHD is one of the most prevalent malformations, affecting 0.8 to 1 percent of live-born infants, and is on the rise globally [9]. Infants born to mothers, whether having gestational or pre-gestational, are at risk of having congenital malformations. The most common defects include congenital heart disease and poly-malformation syndromes [10]. This study at Children's Hospital Lahore identified common CHDs in infants of diabetic mothers to aid in early diagnosis and guide screening and management strategies in similar settings.

Among our 160 participants, 103 (64.37%) were boys, and 57 (35.63%) were girls, which is comparable to the study by Muhammad A et al. [6], where 67 (66.3%) of 101 neonates with CHD born to diabetic mothers were male, and 34 (33.7%) were female. However, it is important to note that Muhammad A et al.'s study focused on neonates aged 0-29 days, with the majority (97, 96.0%) between 0 and 10 days, whereas the mean age in our study was 6.86 ± 2.58 months, indicating a difference in study populations.

In our study, the most common CHD was PDA (26.87%), followed by VSD (21.25%) and HCM (17.50%). In contrast, the study by Abu-Sulaeiman RM et al. [11] reported much higher frequencies of PDA (70%) and PFO (68%), while HCM (38%) was more common, and ASD was less frequent (5%). Abu-Sulaeiman study highlights potential variations in the presentation of congenital heart defects across different populations [11]. In contrast to our findings, the research by Muhammad A. et al.[6] reported lower frequencies of these defects, with PDA at 16.8%, VSD at 12.9%, ASD at 8.9%, PFO at 7.9%, and TGA at 5.9%. Our findings show higher rates of all defects except HCM, which was not reported in the Muhammad A study. These differences again suggest variability in the occurrence of CHD among IDM neonates across different populations [6].

A study conducted in Southwestern Saudi Arabia found that the prevalence of CHD was notably lower in infants of non-diabetic mothers compared to diabetic ones($p<0.0001$). In comparison, the study from Saudi Arabia reported higher frequencies, with PDA at 38.3%, hypertrophic cardiomyopathy at 37.1%, and VSD at 32.7% [12].

In our study, we did not review maternal antenatal records for gestational or pre-gestational diabetes, as it focused on infants up to one year old at Children's Hospital. However, a meta-analysis shows that both gestational diabetes (GDM) and pre-gestational diabetes (PGDM) considerably raise the risk of CHD compared to the non-diabetic population, with PGDM linked to a 3.5-fold increase in malformation risk. Proper prenatal care, both before and during pregnancy, is essential to reduce the effects of hyperglycemia on the development of the fetal heart [13].

In relation to our study, prior research indicates that infants born to women having gestational diabetes mellitus requiring insulin during the 3rd trimester are 20.6 times more likely to develop cardiovascular abnormalities compared to infants of non-diabetic women [14]. Given its ability to detect both structural and functional heart changes, fetal Doppler echocardiography is considered a valuable non-invasive diagnostic tool for cardiac issues. Ideally, every newborn of a diabetic mother should have an echocardiogram within the initial 12 to 48 hours after birth to detect potential malformations and evaluate heart functions [14,15]. Common functional problems of the heart, like hypertrophy of the myocardium, can lead to complications such as cardiomegaly and heart failure, leading to low cardiac output in newborns and increased neonatal morbidity and mortality [14].

Our findings further prove that maternal DM can produce a large spectrum of CHD. Even if not screened during the newborn period, a high level of suspicion of CHD is essential in children having a history of maternal DM and offered screening echo in case clinical signs and symptoms are suggestive of either cardiac defect, poor growth, or recurrent illness like chest infections [16]. Moreover, effective management of diabetic pregnancy, including preconception counseling, glycemic control, and proper fetal surveillance, is crucial for reducing the risk of CHD in infants of diabetic mothers [17].

In our study, another notable finding that needs to be highlighted here is the significant difference in the occurrence of hypertrophic cardiomyopathy (HCM) based on gestational age, with a higher percentage in infants born at 40 to 42 weeks. In contrast, Abou Shady NM reported that HCM is more frequent in infants of women having pre-gestational compared to gestational DM, with poor maternal glycemic control and large for gestational age linked to a higher frequency of HCM [18]. Conversely, Roodpeyma S et al. found no significant association between the types of diabetes among mothers and the frequency of HCM or CHD, with P-values of 0.9 for both conditions and also reported no significant relationship between being large for gestational age and the rates of HCM (p=0.4) of CHD (p = 0.6) [19].

Several limitations were noted in this study. First, the study being cross-sectional cannot establish causal relationships between maternal diabetes and CHD. Second, the exclusion criteria might have led to some selection bias, potentially affecting the frequency and types of CHD observed. Finally, the being single center study, might limit the applicability of it's finding to other healthcare settings or the region.

CONCLUSION

In our study, PDA and VSD were the most frequent CHDs in IDM, followed by hypertrophic cardiomyopathy. These findings emphasize the need for early detection and screening in this high-risk group.

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Authors' Contribution:

Muhammad Tayyab : Substantial contributions to the conception and design of the work.

Zeeshan Afzal : The acquisition and analysis of data for the work.

Wajiha Rizwan : Drafting the work and reviewing it critically for important intellectual content.