Frequency and Pattern of Congenital Heart Defects in Infant of Diabetic Mother at Tertiary Care Hospital

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Abstract

Background and Objective: This study was conducted to evaluate the frequency and pattern of congenital heart defects (CHD) in the infant of pregestational and gestational diabetic mothers presenting at NICU and the causality department of NICH Karachi Pakistan.

Methods: It was a cross-sectional study conducted at NICH Karachi, from July to October, 2022. Infants born to diabetic mothers were enrolled in the study and the frequency and pattern of congenital heart diseases were determined by echocardiography which was performed by a pediatric cardiologist who has had expertise in his field for more than 10 years.

Results: A total of 147 infants were enrolled in the study with the majority of them being 0 to 15 days of age (n=138, 93.9%) and were male gender (n=88, 59.9%). Nearly a quarter of mothers had pre-gestational diabetes (n=35, 23.8%) while 112 (76.2%) mothers had gestational diabetes. Out of 147, 67 (45.57%) infants had congenital heart defects. The most common heart defect was PFO (n=35, 23%) followed by PDA (n=22, 14.9%), VSD (n=8, 5.4%), ASD (n=4, 2.7%), HCM (n=4, 2.7%), TOF (n=4, 2.7%) and TGA (n=2, 1.36%). A significant difference was seen for ASD (p<0.001), VSD (p<0.001), TGA (p=0.011), HCM (p<0.001), and TOF (p<0.001) in congenital heart defect among infants born to mother having pre-gestational diabetes and gestational diabetes.

Conclusion: This study analyzed that nearly half of the infants born to diabetic mothers had congenital heart defects. Thus, it highlights a need for the development of postnatal screening programs for CHD in our population for managing this problem timely. To reduce morbidity and mortality, early CHD diagnosis with screening echocardiography is advised.

Keywords: *Diabetes mellitus, gestational diabetes, pre-gestational diabetes, congenital defects, heart diseases.*

INTRODUCTION

Raised blood sugar brought on by reduced insulin secretion and/or efficacy characterizes the syndrome known as diabetes mellitus (DM), which can have a variety of genetic, environmental, and pathogenic causes [1]. 1 to 14% of all pregnancies are affected by DM, and 90% of all pregnancies that are complicated by DM are gestational diabetes mellitus (GDM) [2]. Diabetic women are more likely to give birth to neonates who have congenital anomalies and malformations.

There are primarily four groups in the etiological classification created by the American Diabetes Association (ADA) in January 2021. These include gestational diabetes, type 1 diabetes, type 2 diabetes, and diabetes caused by particular processes (such as MODY & monogenic diabetes, *etc.*) [3]. Pregnancy-related short and long-term adverse outcomes for the mother, the fetus, and the newborn were observed with all types of DM [4-7]. Hypoglycemia, hypocalcemia, hypomagnesemia, hyperbilirubinemia, and polycythemia are some of the short-term postnatal complications that affect neonates of diabetic mothers and are primarily brought on by fetal hyperinsulinemia, hypoxemia, and preterm delivery [8-10]. Heart defects, kidney defects, gastrointestinal tract defects, neurological anomalies, skeletal defects, unusual facies, and microphthalmos are examples of structural anomalies [11]. The severity of the mother's diabetes and the age and length of glucose intolerance during pregnancy are most likely to have an impact on the fetal outcome [12]. Pregnancy complications are still very common in DM especially pregestational diabetes mellitus(PGDM), although great progress has been made in managing glycemic control in pregnant women [4, 13].

A congenital heart defect (CHD) is a disorder in the heart or its major vascular structures that exists at birth. Atrial septal defect (ASD), ventricular septal defect (VSD), transposition of the great vessels (TGA), truncus arteriosus(TA), coarctation of the aorta(COA), and hypertrophic cardiomyopathy(HCM) are the most common prenatal cardiac anomalies identified in children of diabetic mothers [1]. Congenital cardiac abnormalities can appear at different ages, ranging from those that are initially asymptomatically and worsen with age to those that have severe symptoms at presentation and high mortality rates [14]. One of the more common types of birth defects, congenital cardiovascular disorders impact approximately 6-8 infants per 1000 live births [15]. One in 100 of these cases is brought on in part by some maternal illness. Congenital cardiac problems are much more likely to develop in mothers who have diabetes [15, 16].

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Different percentages of heart abnormalities were reported in studies. According to a study by Ferdousi *et al.* out of 56 newborns, 60.71% had patent foramen ovale (PFO), 55.3% had patent ductus arteriosus (PDA), 21.42% had hypertrophic cardiomyopathy (HCM), and 10.71% had an atrial septal defect (ASD) [1]. Another study by Abu-Sulaeiman *et al.* listed the prevalence of congenital heart diseases as follows: patent ductus arteriosus (PDA) 70%, patent foramen ovale (PFO) 68%, atrial septal defect (ASD) 5%, small muscular ventricular septal defect (VSD) 4%, mitral valve prolapse (MVP) 2%, and pulmonary stenosis (PS) 1%, hypertrophic cardiomyopathy (HoCM) was also noted in 38% of cases, D-transposition of the major arteries (D-TGA), tetralogy of Fallot (TOF), and hypoplastic left heart syndrome were the three most severe types of CHD seen (1% each) [17].

Data on children born to diabetic mothers in Pakistan is sparse. So, to determine the frequency and pattern of congenital cardiac defects in children born to diabetic mothers, this study was carried out at the National Institute of Child Health, a tertiary care hospital.

MATERIALS AND METHODS

This cross-sectional study included patients from the emergency and NICU department of the National Institute of Child Health, Karachi from July to October, 2022 through a non-probability consecutive sampling technique. All neonates from 0 to 28 days of life of both genders born to diabetic mothers according to operational definition were included in the study. An infant of a diabetic mother (IDM) was defined as an infant born to a mother having diabetes previously or developed during pregnancy known as GDM. Mothers known to have DM before conception were labeled as PGDM and those mothers who developed glucose - intolerance during pregnancy were regarded as GDM. GDM was diagnosed as per the diagnostic criteria of the ADA Guideline [18].

Congenital Heart diseases were defined according to operational definitions and confirmed on echocardiography including PDA, VSD, ASD, PFO, TGA, HCM, and TOF. A sample size of 76 was calculated using the WHO sample size calculator, with a confidence level of 95%, absolute precision of 5%, and p = 5.2% for normal findings among infants of IDM [1]. The calculated sample size was 76. However, for a larger sample size total of 147 patients were enrolled in the study.

Neonates with a history of hypoxic-ischemic encephalopathy or sepsis along with those born to mothers with a history of chronic kidney disease, chronic liver disease, heart failure, tuberculosis, or drug intake(other than insulin for diabetes) were excluded. Age, gestational age at birth, gender, and other pertinent information from the pre-designed questionnaire were recorded as demographic information. The mother's prenatal record was examined for the kind of diabetes she had, and her OGTT/HbA1c results (OGTT was performed btw 26-32 weeks of gestation, and HbA1c was performed in the first trimester. HbA1c was considered deranged if >6.5 while OGTT if 2-hour plasma glucose >200mg/dl according to ADA criteria) [18] and the treatments she took during pregnancy. A thorough examination was conducted to detect any cardiac and extracardiac problems. Electrocardiography (ECG), echocardiography, and a chest X-ray were performed. A skilled paediatric cardiologist at the National Institute of Cardiovascular Diseases performed echocardiography utilizing 2D colour Doppler in M mode. All of the investigation findings were recorded.

Data were analyzed using SPSS version 23.0. Descriptive statistics including frequencies and percentages were calculated for summarizing categorical variables. Chi-square or Fisher-exact test was applied to compare frequency of CHD defects among mother who had gestattional diabetes and pregestational diabetes. P-value less than or equal to 0.05 was taken as statistically significant.

RESULTS

A total of 147 infants were enrolled in the study with the majority of them being 0 to 15 days of age and were male. Table **1** displays their socio-demographic profile and clinical history of them. 60 (40.8%) mothers were primiparous whereas the remaining were multi-parous (n=87, 59.2%). Nearly a quarter of mothers had pre-gestational diabetes (n=35, 23.8%) while 112 (76.2%) mothers had gestational diabetes.

Table 1: Descriptive statistics for socio-demographic profile.

Socio-demographic Profile	Frequency (%)
Age	
0-15 days	138 (93.9)
>15 days	9 (6.1)
Gender	
Male	88 (59.9)
Female	59 (40.1)
Birth Weight	
<2.5 kg	1 (0.7)
2.5-3.5 kg	34 (23.1)
>3.5 kg	112 (76.2)
Gestational Age	
Pre-term	16 (10.9)
Term	131 (89.1)
Mode of Delivery	
Spontaneous vaginal delivery	40 (27.2)
Lower segment Cesarean section	107 (72.8)

Out of 147, 67 (45.57%) of infants had congenital heart defects while 80 (54.4%) were normal. Out of 67 (45.57%), the most common heart defect was PFO (n=35, 23%) followed by PDA (n=22, 14.9%), VSD (n=8, 5.4%), ASD (n=4, 2.7%), HCM (n=4, 2.7%), TOF (n=4, 2.7%) and TGA (n=2, 1.36%). Fig. **(1)** depicts the pattern of congenital heart defects among infants of

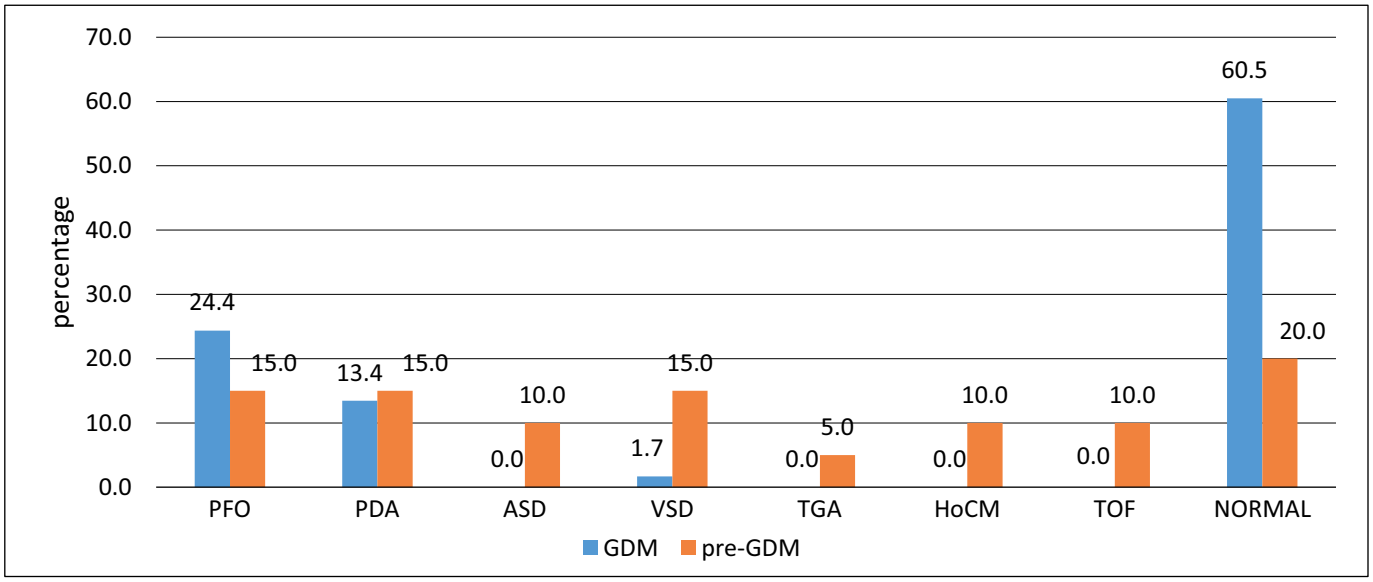

Fig (1): Frequency of congenital heart defects among infants of mothers having pre-gestational and gestational diabetes.

mothers with gestational and pre-gestational diabetes. A significant difference was seen for ASD ($p<0.001$), VSD ($p<0.001$), TGA ($p=0.011$), HoCM ($p<0.001$), and TOF ($p<0.001$) in congenital heart defect among infants born to mother having pre-gestational diabetes and gestational diabetes.

DISCUSSION

Although there has been a great deal of progress in the treatment of diabetic women during pregnancy, there is still a risk of birth abnormalities due to maternal diabetes. Additionally, children of diabetic moms are more likely to develop chronic, non-communicable diseases than adults [19]. In diabetes-affected pregnancies, the fetus frequently develops abnormally, with altered growth and nutrient distribution as well as congenital abnormalities [20]. Because of the development of the industrialized lifestyle, not only in high-income nations but also in middle- and low-income countries, the prevalence of obesity and type 2 diabetes (T2D) and consequently the prevalence of gestational diabetes mellitus (GDM), has rapidly grown [21]. This study was done to find out how common congenital heart disease is among babies whose mothers had diabetes because of the rising trend of the disease and sedentary lifestyle.

The present study analyzed that the frequency of CHD in our sample was 45.57%. Another Pakistani study reported that abnormal findings on echocardiography were seen in 47.3% of infants of the diabetic mother [15]. A burden of 47.5% CHD was reported by Muhammad and his coworkers in a similar study from Peshawar, Pakistan [22]. Frequency of CHD among infants of the diabetic mother was found to be 49% in Iran [23], 10.2% in Nepal [24], 28% in India [25], and 12.1% in the USA [26]. The disparity in frequency from country to country could be possible because of different ways of managing diabetes, the difference in the studied sample, and the approach for identifying cardiac anomalies.

The pattern of findings in the present study was PFO being the commonest followed by PDA, VSD, ASD, HCM, TGA, and TOF. Muhammad and coworkers reported top three CHD were PDA (16.8%), VSD (12.9%), and ASD (8.9%) followed by PFO (7.9%) and TGA (5.9%) [22]. In a study by Shamoon *et al.* the pattern of top most anomalies was similar to our study but the frequency of PDA (32.6%), VSD (25.3%), ASD (14.5%), TGA (7.9%), HoCM (5.7%) was higher than our study [15]. In contrast to our study, higher PFO (69.5%) and PDA (41%) rates were reported by Arjamandnia [23]. A higher frequency of PDA (38.4%) and VSD (23.1%) was demonstrated in a Nepali study. In addition to this, PFO was not found in this study. However, the author found tetralogy of Fallot and D-transposition of great arteries in 7.7% of cases [24].

Women with pregestational diabetes and women with gestational diabetes may have different mechanisms behind the connection between maternal diabetes and CHD abnormalities [27]. During the crucial time of heart development, women with pregestational diabetes would have a diabetic intrauterine environment. However, gestational diabetes does not appear until the 24th to 28th weeks of pregnancy [28], which is after the crucial time for heart development.

In the present study, the majority of the study participants had gestational diabetes (76.2%). The present study found that the frequency of PFO and PDA is higher in the gestational diabetes group whereas frequencies of ASD, VSD, TGA, TOF, and HoCM are higher in pre-gestational diabetes. In contrast to our findings, another similar study from Pakistan demonstrated an almost equal likelihood of CHD among mothers having pre-gestational and gestational diabetes with 44.5% frequency of CHD in infants of mothers with gestational diabetes *versus* 50.8% CHD frequency among infants born to mothers having pre-gestational diabetes [15]. An Indian study

reported a huge difference in CHD frequency between pre-gestational and gestational diabetes. According to a study, compared to 14% of kids born to mothers with gestational diabetes, 94% of babies born to pregestational diabetic mothers had cardiac abnormalities [25]. A study was conducted in Iran to determine the prevalence of heart abnormalities which reported that newborns of mothers having pre-gestational diabetes had a greater frequency of malformations than those with gestational diabetes (7.8% *versus* 10.3%) [27]. Maternal pre-gestational DM (both types 1 and 2) was associated with a four-fold increase in the offspring risk of CHDs in a cohort of two million births during 34 years, according to Zhang *et al.* [29]. One of the factors responsible for the difference in study findings is glycemic control management among the patients which could vary from population to population.

The current study has certain significant flaws, such as the fact that it studied a limited sample size while sharing the experience of a single-center institute. Further, it is a cross-sectional study in nature. Thus, taking the follow-up of newborns after three months could change the frequency of CHD. Additionally, the study did not focus on how glycemic management during pregnancy could affect the incidence of congenital abnormalities in newborns. It would therefore be unwise to generalize these findings to the entire Pakistani population due to these constraints. The inadequacies in the current study might be filled by a bigger multi-center study.

CONCLUSION

This study analyzed that nearly half of the infants born to diabetic mothers had congenital heart defects. Thus, it highlights a need for the development of postnatal screening programs for CHD in our population for managing this problem timely. To reduce morbidity and mortality, early CHD diagnosis with screening echocardiography is advised.

ETHICS APPROVAL

The study was commenced after taking approval from the hospital ethics committee (IERB-29/2021)) and was conducted according to the guidelines of the Declaration of Helsinki.

CONSENT FOR PUBLICATION

Written informed consent was taken from parents/ guardians before the enrolment of their children into the study.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

AUTHORS' CONTRIBUTIONS

SBA and MK: study conceptualization, SBA and MS: methodology and proposal writing, SBA, MS, and ASS: data collection, data analysis, and interpretation, SBA and MS: Original draft preparation, SBA: writing review and editing. All authors read and approved the final draft of the manuscript for publication.

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