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COMPARISON OF CONGENITAL HEART DISEASE IN INFANTS OF DIABETIC AND NON-DIABETIC MOTHERS

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ABSTRACT

Objectives: To compare frequency of congenital heart defects in infants of diabetic versus non-diabetic mothers.
Study design: Case-control study.
Place and Duration of the study: Children Hospital, Pakistan Institute of Medical Sciences, Islamabad from October-2024 to March-2025.
Methodology: A total of 390 term neonates born to diabetic (cases) and non-diabetic (controls) mothers were included. All the neonates born to cases and controls were assessed for presence of congenital heart defects by performing echocardiography. Chi-square test was used to compare frequency of congenital heart defects between groups. Data was analyzed using SPSS version 22.
Results: Median maternal age was 29.00 (8.00) years. Median gestational age was 39.00 (3.00) weeks. There were 139 (35.60%) male and 251 (64.40%) female babies. Median birth weight was 3.50 (0.70) kg. Frequency of congenital heart defect in infants whose mothers were diabetic was 43 (22.05%) while in infants whose mothers were non-diabetic was 20 (10.26%), (p = 0.002); [Odds ratio (OR) = 0.404]. Most common type of congenital heart defect in infants with congenital heart defect whose mothers were diabetic (n = 43) was transposition of great arteries found in 17 (39.53%) infants while in infants with congenital heart defect whose mothers were not diabetic (n = 20), most common congenital heart defect type was ventricular septal defect found in 6 (30.00%) infants, (p = 0.003).
Conclusion: Diabetes can contribute to higher chances of developing congenital heart defects in term neonates.

INTRODUCTION

Elevated blood sugar levels caused by insulin resistance and decreased insulin production characterize type 2 diabetes which is chronic metabolic condition. [1] It affects millions of people worldwide with an approximate of 463 million people across the globe and a prevalence of 26.7% in Pakistan. [2] Similarly, another unique form of diabetes in women is the pregnancy-related diabetes known as gestational diabetes mellitus (GDM) which is characterized by glucose intolerance developing throughout the second and third trimesters with or without remission following the end of pregnancy. [3] Though the pathophysiological mechanism of this condition is not completely known, gestational diabetes is thought to be caused by alterations in hormones that occur during pregnancy influencing the responsiveness to insulin. [4]

Globally, the prevalence of GDM has been quite high and it has been found that this pregnancy related condition affects approximately 14.7% of the pregnant population. [5] Pakistan is currently ranked among the nations that carry the highest burden of diabetes and similar to this trend the burden of GDM is also very high in Pakistan with an approximated prevalence of GDM being reported at 16.7%. [6] Similarly, at provincial level highest prevalence was observed in the province of Baluchistan followed by Khyber Pakhtunkhwa, Sindh and then Punjab. [6] There are several factors that increase the propensity of developing GDM including geriatric pregnancy, body mass index (BMI) in overweight and obese range, positive diabetic and GDM history in the family and history of thyroid disease in the family. [7]

There are several fetal complications associated with GDM including hyperinsulinemia, shoulder dystocia, infant hypoglycemia, macrosomia, hyperbilirubinemia and still birth. [8] Congenital heart defect (CHD) is another significant complication thought to be related to GDM, however, research on the causative link between CHD and diabetes as well as frequency comparison of CHD between diabetic and non-diabetic women have shown quite variable findings with some studies showing a significant relationship between maternal diabetes and presence of CHD in infants while others demonstrating no such relationship. [9, 10] Present study thus focuses on determining the causal relationship between maternal diabetes and occurrence of CHD in infants by comparing the frequency of CHD in infants of diabetic versus non-diabetic mothers.

METHODOLOGY

This case control study was conducted at Children Hospital, Pakistan Institute of Medical Sciences, Islamabad from October-2024 to March-2025 after getting approval from institutional ethical committee (Ref No: F.1-1/2015/ERB/SZABMU/1338 dated 23-10-2024). Sample size calculation was performed using WHO sample size calculator using following formula:

$$n = \frac{\left\{ z_{1-\alpha/2}\sqrt{2\bar{P}(1-\bar{P})} + z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)} \right\}^2}{(P_1-P_2)^2}$$

Sample size calculation was performed by using level of significance 5%, power of 80% and anticipated frequency of CHD in diabetic and non-diabetic mothers of 7.5% and 1.6%, respectively. [9] This gave a sample size of 390 (195 in each group). Study sample was selected by using non-probability consecutive sampling technique.

Term neonates, aged 1-28 days, male and female, who were born to diabetic and non-diabetic mothers were included. Patients with history of fetal anomalies detected on anomaly scan at 20 weeks, congenital

neurological anomalies and chromosomal abnormality syndromes were excluded.

All patients meeting the requirements for enrollment were enrolled in the study following acceptance of the study proposal from ethics committee and informed agreement of the parents of participants. Baseline characteristics including gestational age at birth, gender of baby, birth weight, maternal age and maternal education status were documented. Mothers were assessed for presence of diabetes based on this patients were defined as cases (who were pregnant women with diabetes) and controls (who were pregnant women without diabetes). Diabetic mothers included both pre-existing diabetics (defined by HbA1C% of 6.5% or greater or history if anti-diabetic medications use) as well as those who were diagnosed as case of gestational diabetes (defined by presence of ≥ 1 values of fasting blood sugar levels of ≥ 92 mg/dl and blood sugar levels of ≥ 153 mg/dl after two hours of consumption of 75-gram oral glucose conducted at 24 to 28 weeks of gestation). After this division, all the neonates born to cases and controls were assessed for presence and type of CHD by performing echocardiography which was performed by consultant pediatric cardiologist.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 22. Quantitative variables normality was checked by Shapiro-Wilk test which showed that gestational age at birth, birth weight and maternal age were not distributed normally and were thus presented as median interquartile range (IQR). Gestational age at birth, birth weight and maternal age were compared between groups by using Mann Whitney U-test. Qualitative variables (gender of baby, type of maternal diabetes, maternal education status, presence of CHD and type of CHD) was presented as frequency and percentages and were compared between groups using Chi-square test or likelihood ratio, as per applicability. A p-value of ≤ 0.05 was considered as statistically significant.

RESULTS

In this study, 390 term neonates were included. Median maternal age was 29.00 (8.00) years. Among all mothers, 195 (50.00%) were illiterate and 195 (50.00%) were literate. Median gestational age was 39.00 (3.00) weeks. There were 139 (35.60%) male and 251 (64.40%) female babies. Median birth weight was 3.50 (0.70) kg. Patient demographics are compared between groups in Table-I:

Table-I: Comparison of patient demographics between groups (n = 390)

Parameter	Cases (n = 195)	Controls (n = 195)	p-value
Median maternal age	30.00 (8.00) years	29.00 (8.00) years	0.391[a]
Maternal education status Illiterate Literate	97 (49.74%) 98 (50.26%)	98 (50.26%) 97 (49.74%)	0.919 [b]
Median gestational age	39.00 (3.00) weeks	40.00 (3.00) weeks	0.833 [a]
Gender of baby Male Female	72 (36.92%) 123 (63.08%)	67 (34.36%) 128 (65.64%)	0.597 [b]
Median birth weight	3.80 (0.60) kg	3.30 (0.50) kg	< 0.001[a]

a = Mann Whitney U-test, b = Chi-square test

Overall frequency of CHD among neonates of present study was 63 (16.15%). Frequency of CHD in infants whose mothers were diabetic (n = 195) was 43 (22.05%) while in infants whose mothers were non-diabetic (n = 195) was 20 (10.26%), (p = 0.002); [Odds ratio (OR) = 0.404]. This comparison of frequency of CHD between groups is given in Table-II:

Table-II: Comparison of frequency of CHD between groups (n = 390)

CHD	Cases (n = 195)	Controls (n = 195)	p-value
Yes	43 (22.05%)	20 (10.26%)	0.002 [b]
No	152 (77.96%)	175 (89.74%)	

Abbreviation: CHD = Congenital heart disease. b = Chi-square test

Most common type of CHD in infants with CHD whose mothers were diabetic (n = 43) was transposition of great arteries (TGA) found in 17 (39.53%) infants followed by ventricular septal defect (VSD) found in 14 (32.56%) infants, tetralogy of fallot (TOF) found in 5 (11.63%) infants, atrial septal defect (ASD) found in 4 (9.30%) and patent ductus arteriosus (PDA) found in 3 (6.98%) infants while in infants with CHD whose mothers were not diabetic (n = 20), most common CHD type was VSD found in 6 (30.00%) infants followed by ASD in 5 (25.00%), PDA in 5 (25.00%), TGA in 3 (15.00%) and TOF in 1 (5.00%) infants, (p = 0.003). Comparison of frequency of type of CHD between groups is given in Table-III:

Table-III: Comparison of frequency of type of CHD between groups (n = 390)

Type of CHD	Cases (n = 43)	Controls (n = 20)	p-value
ASD	4 (9.30%)	5 (25.00%)	
VSD	14 (32.56%)	6 (30.00%)	
PDA	3 (6.98%)	5 (25.00%)	0.002 [c]
TOF	5 (11.63%)	1 (5.00%)	
TGA	17 (39.53%)	3 (15.00%)	

Abbreviations: CHD = Congenital heart disease, ASD = Atrial septal defect, VSD = Ventricular septal defect, PDA = Patent ductus arteriosus, TOF = Tetralogy of Fallot, TGA = Transposition of great arteries. c = Likelihood ratio

DISCUSSION

Diabetes in pregnancy is linked with a wide variety of adverse outcomes in mother and the newborns. [11, 12] Some of these complications that lead to the adverse outcomes in the mothers and their newborn babies include abnormally excessive liquor due to polyhydramnios, higher chances of delivering the baby through cesarean section, both excessive and low weight of the newborn at the time of birth, low blood sugar levels in the baby, preterm birth and requirement for the newborns to be admitted at the neonatal intensive care unit. [13, 14] Present study focused on an important complication of this pregnancy related morbidity in the neonates.

In present study, average age of the pregnant women who were diagnose for having diabetes was thirty years. This finding is attributable to the association of maternal age of thirty years or more with the higher risk of developing diabetes during pregnancy which has been reported in multiple previous studies. [15, 16] Overall frequency of CHD among neonates of present study was 16.15%. Compared to this, a study was conducted by Sial et al. which included neonates who were born at a tertiary care center in Taxilla, Pakistan in which they reported that the frequency of CHD was 33.3% which was quite high compared to present study. [17] In another study conducted by Imran et al. among newborns, it was found that the frequency of this structural malformations was 18% which was comparable to present study. [18] The exact reason behind this variation is unknown but differences in the sample sizes and patients demographics may have played some role for resulting in such variations.

Among diabetic mothers, the frequency of CHD in their neonates was 22.05%. Compared to this, a study was conducted by Alyousif et al. in which they reported frequency of this maternal diabetes related neonatal complication to be at 25.76% which was comparable to present study. [19] Upon comparative analysis of the frequency of CHD among newborns, it was found that the babies of women who suffered from diabetes

during their pregnancy had significantly higher frequency of CHD as compared to those who were not diabetics, (p = 0.002), [Odds ratio (OR) = 0.404]. Compared to this, Lasheen et al. also reported that the frequency of CHD was significantly higher among newborns whose mothers were affected by diabetes during their pregnancy as compared to those whose mothers were non-diabetic (p < 0.001). [9] Contrarily, Afrin et al. found that presence of diabetes during pregnancy had no significant impact on the CHD frequency among the neonates (p = 0.535). [10]

Most common type of CHD that were found in the neonates of the diabetic mothers was TGA and VSD. This trend can be explained by the fact that these are the most common types of CHD that are observed among the neonates whose mothers have positive history of diabetes during their pregnancy. [20, 21] Among non-diabetics, the most common type of CHD was VSD which can be explained by the fact that this CHD is the most prevalent type of CHD that occurs in the general population. In this instance, a study was conducted by Jamil et al. focusing on the spectrum of CHD types existing in the general population and they reported that the highest frequency, among various type of CHD, was observed for VSD. [22] In another study conducted by Singh et al. similar trend of VSD being the most frequent type of CHD was observed. [23] Finally, upon comparative analysis of the distribution of various types of CHD between groups, a significant difference was observed among neonates born to diabetic versus non-diabetic mothers (p = 0.003).

Based on the results of present study it is evident that having diabetes during pregnancy is associated with significantly higher frequency of CHD for which it is strongly recommended that all the neonates whose mother suffer from diabetes should be screened for having CHD as soon as possible after birth. There were no limitations of present study.

CONCLUSION

In conclusion, diabetes can contribute to higher chances of developing congenital heart defects in term neonates.

CONFLICT OF INTEREST

None.

INFORMED CONSENT

Obtained from the parent in written form.

ETHICAL APPROVAL

Obtained from the institution (Ref No: F.1-1/2015/ERB/SZABMU/1338 dated 23-10-2024).

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