



International Journal of Pediatrics and Neonatology

ISSN Print: 2664-8350
ISSN Online: 2664-8369
Impact Factor: RJIF 5.26
IJPN 2023; 5(1): 10-14
www.pediatricsjournal.net
Received: 06-09-2022
Accepted: 08-11-2022

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Prevalence of congenital heart defects in infants of diabetic mothers in Aseer region, Southwestern, Saudi Arabia

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DOI: <https://doi.org/10.33545/26648350.2023.v5.i1a.30>

Abstract

Background: Maternal diabetes mellitus is a risk factor for adverse maternal and fetal outcomes, including anatomical malformations such as congenital heart defects (CHD).

Objectives: To determine the prevalence of CHD in babies born to mothers with pre-existing or gestational diabetes.

Patients and Methods: A retrospective study of all births of type 1, type 2 diabetic mothers, gestational diabetic mothers, and non-diabetic mothers admitted to the newborn nursery and the neonatal intensive care unit between July 2011 and June 2022 was performed.

Results: A total of 2079 mothers and their offspring were enrolled in the study. Of 2079 mothers 1397 (67.2%) were non-diabetic and 682 (32.8%) were diabetic. In terms of diabetic status, the incidence of cardiovascular anomalies in infants of diabetic mothers is significantly higher than the infants of non-diabetic mothers ($p < 0.0001$). The most frequent echocardiographic findings were patent ductus arteriosus (38.3%), hypertrophic cardiomyopathy (37.1%), and ventricular septal defect (32.7%).

Conclusions: The incidence of CHD in infants of diabetic mothers is significantly higher than in infants of non-diabetic mothers. Screening diabetic mothers for fetal cardiac malformations seems highly advisable in such cases.

Keywords: Babies born to mothers, diabetic status, the incidence

Introduction

Diabetes Mellitus is a common entity which is a syndrome of multiple factors like genetic, environmental, and pathogenic origin which is characterized by increased blood glucose level resulting from impaired insulin secretion and/or effectiveness^[1]. Women with diabetes in pregnancy (type 1, type 2 and gestational) are at increased risk for adverse pregnancy outcomes. Adequate glycemic control before and during pregnancy is crucial to improving outcome^[2].

Diabetes mellitus complicates 1–2% of all pregnancies, Maternal diabetes mellitus increases perinatal mortality and morbidity five-fold compared with normal pregnancies. Despite improvements in medical care provided during pregnancy to diabetic mothers, congenital malformations in their infants are still more frequent than in infants of the general population.

Due to the teratogenic effect of maternal diabetes^[3], the reported incidence of congenital malformations among the newborns of diabetic mothers is five times greater than that of the general population^[4, 5].

Cardiac malformations are one of the most common types of these malformations which occur in about 8.5% of cases that is about 10 times more than its incidence in normal population (0.8%)^[6, 7]. The exact cause of cardiovascular defects is usually not known but some are genetic while few have an environmental etiology, with 1% of all cases relating to diabetes of pregnant mothers^[8]. The most common heart malformations in fetuses of diabetic mothers include: ventricular septal defect, transposition of great arteries, aortic stenosis, pulmonary atresia, dextrocardia, and conotruncal defects (Tetralogy of Fallot,

truncus arteriosus and double outlet right ventricle) [9-11]. Most of the cases are usually asymptomatic, however some may present immediately following delivery with decreased cardiac output, respiratory distress and other symptoms of cardiac failure requiring aggressive medical therapy. Many reported literatures claim spontaneous resolution in survivors within 4-6 months nonetheless there are reports of patients continuing to have abnormal dimensions into the second year of life [12]. In this study we aimed to determine the prevalence of congenital heart defects in babies born to mothers with pre-existing or gestational diabetes and to compare the findings in babies of non-diabetic mothers.

Patients and Methods

A retrospective study was conducted at the newborn nursery (NBN) and the neonatal intensive care unit (NICU) of Abha Private Hospital, Abha, Southwestern, Saudi Arabia between July 2017 and June 2022. The inclusion criteria include all births of type 1, type 2 diabetic mothers (T1DM and T2DM), gestational diabetic mothers (GDM), and non-diabetic mothers. The exclusion criteria were mothers below 20 and over 40 years of age, and other risk factors such as drug-induced congenital malformation.

Data collection

Information for mothers and infants were collected from the medical records including maternal age, history of maternal chronic diseases, diabetic status, the type, duration of diabetes, diagnosis, treatment and glycemic control, records of previous pregnancies, and the presence of or lack of prenatal care.

Diagnosis of gestational diabetes mellitus made as per diagnostic criteria of American Diabetic Association Guidelines [13]. Maternal diabetes had been divided into 3 types. T1DM was defined as insulin dependent diabetes that is diabetes beginning from childhood. T2DM was defined as insulin resistance or adult type diabetes. Type 3 or GDM for the first time appeared during pregnancy period. Both type 1 and type 2 were considered pre-gestational diabetes.

The following data were collected for each newborn included in the study:

Demographic characteristics: gender, birth weight, gestational age at birth, and mode of delivery. Clinical characteristics: Apgar score at 1 and 5 minutes after birth, obstetric trauma, respiratory and cardiac assessment for respiratory distress, tachycardia, cardiac murmurs, cyanosis, abdominal and neurological examination, or presence of neonatal jaundice and neonatal blood glucose level in the first day of life were recorded.

Echocardiography examination was performed by a pediatric cardiologist for all the newborn infants participating in the study within 7 days of delivery. Cardiovascular malformations were carefully searched by all standard views of M-mode, 2-D, and color Doppler echocardiography. Echocardiographic assessment was to document presence of pulmonary hypertension as well as presence of patent foramen oval (PFO) and/or patent ductus arteriosus (PDA), to detect other congenital heart diseases, to evaluate chamber enlargement and pulmonary artery dilation and to evaluate ventricular function as well. Hypertrophic cardiomyopathy is considered in this study when echocardiographic observation of the interventricular septum to the posterior left ventricular wall exceeds 1:3. [2]. Atrial septal defects were significant when they measured

>3 mm in size. The study was approved by the local ethical committee of the hospital.

Statistical analysis

Quantitative data were presented as mean+ standard deviation (SD), while qualitative data were demonstrated as frequency and percent (%). The significance of comparison between mean values of two groups was evaluated by Student's t-test for continuous normally distributed variables. Categorical data were assessed by chi-square test and Independent-Samples Mann-Whitney U Test. The significance of comparison between more than two groups was performed by analysis of variance for parametric continuous variables. Significant differences were denoted by $p < 0.05$. Statistical analysis was performed using the Statistical Software Package SPSS 23 (SPSS, Inc., Chicago, IL).

Results

During the study period, a total of 2079 mothers and their offspring were enrolled in the study. Of 2079 mothers 1397 (67.2%) were non-diabetic and 682 (32.8%) were diabetic. Of 682 diabetic mothers, 426 (62.4%) had GDM, 216 (31.7%) had T2DM and 40 (5.9%) had T1DM as shown in figure 1.

Characteristics of mothers (diabetic or non-diabetic) and their infants are shown in table 1. In terms of gestational age, most of pregnancies 1762 (84.8%) were term, 312 (15%) were preterm and only 5 (0.2%) were post-term. Table 2 shows the incidence of CHD among different groups of patients. Of 2079 infants, 321 (15.4%) had CHD and the remaining 1758 (84.6%) had not. In terms of diabetic status, the incidence of cardiovascular anomalies in infants of diabetic mothers is significantly higher than the infants of non-diabetic mothers ($p < 0.0001$). Based on the diabetic status, echocardiographic findings among different groups are shown in table 3. Patent ductus arteriosus (PDA) had the highest incidence of 38.3% followed by hypertrophic cardiomyopathy (HCM) (37.1%), then ventricular septal defect (VSD) (32.7%).

Regarding the clinical manifestations of IDM, macrosomia was reported in 302 (44.3%) of infants. Most infants (503 [73.8%]) developed respiratory distress. Among 682 IDM, 249 (36.5%) had CHD, most of them (165 [66.3%]) were asymptomatic. Extracardiac malformations were detected in 54 (7.9%) infants. The majority of IDM (486; 71.2%) developed hypoglycemia in the first 3 hours after birth (table 4). Our results demonstrated that uncontrolled diabetes was significantly associated with a higher incidence of CHD in the offspring ($p < 0.001$).

Discussion

Congenital heart disease is one of the most common malformations occurring in 0.8- 1% of live-born infants and is increasing in prevalence worldwide [14]. Infants of diabetic mothers are more prone to develop congenital malformations. The risk of congenital defects increases by 2-12% compared to normal neonates, the most frequent being CHD and poly-malformation syndrome [15]. Our study aimed to estimate the prevalence of cardiac malformations in babies born to mothers with pre-existing and gestational diabetes, to find the pattern of cardiac malformations and to compare the findings in babies of non-diabetic mothers.

Our results showed that a total of 2079 infants were enrolled in the study, out of them 682 (32.8%) were infants of diabetic mothers. The overall incidence of CHD among infants of diabetic and non-diabetic mothers was 15.4%, however the incidence of CHD among infants of diabetic mothers was 36.5%. The incidence of CHD among our study population was higher than been reported by other studies inside and outside Saudi Arabia [16-19]. The differences in incidence of CHD in other studies are due to different sample size and duration of study period. The higher incidence in our study may be attributed to the high altitude of our area compared with local studies within Saudi Arabia.

In our study the incidence of CHD was slightly higher in infants born to pre-gestational (T1DM and T2DM) than gestational diabetes. These results are comparable to the results reported from other studies [19, 20]. In the present study the most common echocardiographic findings in IDM were patent ductus arteriosus (PDA) (38.3%), hypertrophic cardiomyopathy (HCM) (37.1%) then ventricular septal defect (VSD) (32.7%). These results are supported by the studies of Abu-suliman and Sobaih [2] and Shankar [21] and as they reported that the most common cardiac anomalies in IDM were PDA, patent foramen ovale (PFO) and HCM. The association of maternal diabetes and HCM specifically septal wall hypertrophy is a well-known phenomenon, and it has been previously reported [22, 23]. Other researchers

suggested that either increased fetal endogenous catecholamine production or hormonal interactions of growth hormones and insulin produced this effect. A high level of fetal insulin may also explain the development of HCM [24, 25]

Regarding the clinical manifestations in IDM, most of cases who had CHD were asymptomatic (66.3%), however the others presented shortly after birth with decreased cardiac output and other symptoms of heart failure. Impaired maternal glucose tolerance has been associated with several morbidities [26]. Our data demonstrated that macrosomia was reported in 44.3% of infants, extracardiac malformations were detected in 7.9% of infants. The majority of IDM developed jaundice (84.5%), hypoglycemia (71.2%) and plethora (52.1%).

Our results reported that uncontrolled diabetes was significantly associated with a higher incidence of CHD in the offspring ($p < 0.001$). These results are like those reported in the literature [27, 28]. The fact that poor diabetic control and hyperglycemia are associated with an increased risk of congenital malformations in offspring is well documented [29, 30]. Several epidemiological studies have demonstrated the strong association between maternal glycemic level control at the time of conception and during early gestation and the incidence of congenital anomalies [31, 32]. More than 50% of these anomalies affect the central nervous system or cardiovascular system [33-34].

Table 1: Characteristics of mothers (diabetic and non-diabetic) and their infants

Variables	IDM (n=682)	Non-IDM (n= 1397)	P value
Maternal age (y) ^a	28.1±2	27.9±5.1	0.32
Consanguinity ^b	236 (34.6)	473 (33.9)	0.7
Maternal hypertension ^b	76 (11.1)	152 (10.9)	0.9
GA (wk) ^a	36.9±1.9	37.0±0.5	0.06
BW (g) ^a	3412±410	2892±401	< 0.001
Male gender ^b	349 (51.1)	703 (50.3)	0.73
Apgar score at 1 min ^a	8.7±1.2	8.8±1.1	0.06

^a Values are mean ±SD

^b Number (percent)

$p < 0.05$; significant

IDM; infants of diabetic mothers, GA; gestational age, BW; birth weight

Table 2: CHD incidence among different groups of patients

Diabetic status	Total number,% 2079 (100)	Normal 1758 (84.6)	CHD 321 (15.4)	P value
Non-diabetic	1397	1325 (94.8)	72 (5.2)	< 0.0001
T1DM	40	26 (65.0)	14 (35.0)	0.07
T2DM	216	109 (50.5)	107 (49.5)	0.83
GDM	426	298 (70.0)	128 (30.0)	<0.0001

$p < 0.05$; significant. T1DM; type 1 diabetes mellitus. T2DM; type 2 diabetes mellitus. GDM; gestational diabetes mellitus

Table 3: Echocardiographic findings among the study population based on the diabetic status

CHD Type	Type 1 diabetic (n= 14)	Type 2 diabetic (n= 107)	Gestational diabetes (n= 128)	Non-diabetic (n= 72)
PDA*	5 (35.7)	49 (45.8)	41 (32.0)	28 (38.9)
HCM	6 (42.9)	54 (50.1)	59 (46.1)	0 (0)
VSD	4 (28.6)	48 (44.9)	44 (34.4)	9 (12.5)
PFO	5 (35.7)	38 (36.5)	40 (31.3)	16 (22.2)
ASD	7 (50.0)	28 (26.2)	33 (25.8)	21 (29.2)
TR	3 (21.4)	22 (20.6)	21 (16.8)	11 (15.3)
TGA	2 (14.3)	4 (3.7)	2 (1.6)	0 (0)

*Number (percent)

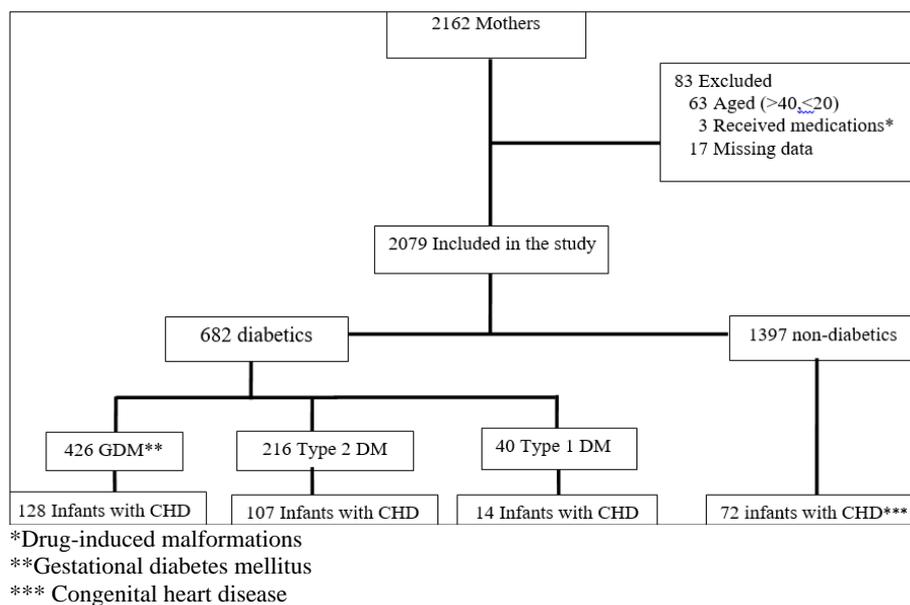
PDA; patent ductus arteriosus, HCM; hypertrophic cardiomyopathy, VSD; ventricular septal defect, PFO; patent foramen ovale, ASD; atrial septal defect, TR; tricuspid regurgitation, TGA; transposition of great arteries

Table 4: Clinical manifestations in 682 infants of diabetic mothers

Findings	N (%)
Macrosomia	302 (44.3)
Perinatal asphyxia	119 (17.4)
Central cyanosis	15 (2.2)
Respiratory distress	503 (73.8)
Cardiac malformations	249 (36.5)
Extracardiac malformations	54 (7.9)
Jaundice	576 (84.5)
Plethora	355 (52.1)
Hypoglycemia	486 (71.2)

Table 5: The incidence of CHD among offspring of controlled and uncontrolled diabetic mothers

	Controlled (N = 455)	Uncontrolled (N = 227)	P value
Congenital heart disease			
Yes	129	192	<0.001
No	326	35	

**Fig 1:** Flow chart of the study population

Conclusions

The incidence of CHD in infants of diabetic mothers is significantly higher than in infants of non-diabetic mothers. These findings demonstrate that screening diabetic mothers for fetal cardiac malformations seems highly advisable in such cases.

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