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Original Research Article

Cardiovascular malformations in infants of diabetic mothers: a retrospective study

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ABSTRACT

Background: Despite improvements in medical care provided during pregnancy to diabetic mothers, the cardiac complications in their infants are still more frequent than in infants of general population.
Methods: A retrospective case-control study was performed between the years 2017-2018 on two groups of newborns, recording details of outcome of live born babies born to diabetic and non-diabetic mothers.
Results: Data were extracted from medical records, and the descriptive and analytical statistics of this information was duly applied. in a total of 50 studied infants, 40 cases (80%) of cardiovascular anomalies have been diagnosed. Most of the cardiac anomaly was hypertrophic cardiomyopathy. The incidence of cardiovascular anomalies in infants of diabetic mothers is significantly higher than the infants of non-diabetic mothers (P=0.002). The type of maternal diabetes (diabetes mellitus, overt or gestational diabetes) did not bring about any significant difference in the incidence of cardiac malformations in infants (P=0.406).
Conclusions: The incidence of cardiovascular anomalies in infants of diabetic mothers is significantly higher than the infants of non-diabetic mothers. Many of the infants were asymptomatic and therefore clinical examination and follow up in infants of diabetic mothers is important.

Keywords: Congenital cardiac anomalies, Gestational diabetes, Overt diabetes

INTRODUCTION

Congenital cardiac anomalies are the most common type of birth defect, and the incidence of these anomalies is estimated at 6 to 8 cases in 1000 live births.[1] The cause of this anomaly is usually unknown, with 1% of all cases relating to diabetes of pregnant mothers.[1] Prior studies indicate that maternal diabetes has teratogenic effects on the evolution of the fetal cardiovascular system, which increases the risk of anomalies by 1.7 - 4% in published studies.[2,3-8] With congenital heart disease occurring in up to 5% of fetuses of diabetic mothers, and with 90% of the cardiac lesions identifiable prenatally, it has been suggested that detailed fetal echocardiography is offered to all diabetic women during pregnancy.[9-13] However, when studied in relation to maternal initial HbA1c, the overall sensitivity for identifying congenital heart disease was 50% and specificity 54% and no critical level of HbA1c that provided optimal predictive power for congenital heart disease screening was identified.[14]

For this reason, we have performed this study with the purpose of determining the relationships between various types of maternal diabetes, glycemic control and the prevalence of various types of cardiovascular complications in neonates and comparing these findings to infants of non-diabetic mothers.

Experimental studies suggest that hyperglycemia during early embryogenesis may alter gene expression in key cellular components of the developing heart, in particular, the embryonic heart's outflow sections; however, the mechanism producing this altered gene expression is unclear.[15-19]

METHODS

A retrospective case-control study was performed between the years 2017-2018 on two groups of newborns at Kempegowda Institute of Medical Institute, Bangalore. The case group consisted of infants born to mothers with diabetes (including overt diabetes 52% and gestational diabetes 48%), and the control group was made up of infants born to non-diabetic mothers. Diagnostic criteria for diabetes has been made according to WHO criteria and diagnosis of GDM were based on the recommendations of the Second International Conference (1,2). Both groups were selected using an easy and simple sampling method.

Inclusion criteria for the case group were: infants born to mothers with diabetes (including overt diabetes and gestational diabetes), term infants, and mothers who received prenatal care. Inclusion criteria for the control group included: non-diabetes and healthy mother, term infants, and mothers who received prenatal care. Exclusion criteria were: preterm and IUGR infants, low Apgar score, mothers who did not receive prenatal care and mothers who did not have GDM diagnostic tests.

After the selection of the two infant groups-infants with diabetic mothers and infants with non-diabetic mothers-general information was recorded, including: age, gender, birth weight and gestational age at birth, Apgar score at birth, echocardiography records of newborns, clinical manifestations, maternal age, history of maternal disease, the type and duration of diabetes diagnosis and treatment, records of previous pregnancies and the presence of or lack of prenatal care. Information for mothers and infants was collected from the data records. Physical examinations were performed by a gynecologist and a pediatrician. The echocardiography was done by a cardiologist. Echocardiography was also performed on healthy infants. Data were analyzed by SPSS Version 18.0 software. The qualitative data of the absolute and relative frequency and quantitative data were analyzed using mean and standard deviation. Statistical analyses were also extracted from the chi-square test to compare qualitative information between the two groups; quantitative data were collected from an Independent-t-test. A P value <0.01 was considered to be significant.

RESULTS

Data were extracted from medical records, and the descriptive and analytical statistics of this information was duly applied. Some of the relevant information is given in Table 1.

Thus, in a total of 50 studied infants, 40 cases (80%) of cardiovascular anomalies have been diagnosed. Most of the cardiac anomaly was hypertrophic cardiomyopathy. All 25 babies from the case group were diagnosed with congenital anomalies such as atrial septal defect, patent ductus arteriosus, patent foramen ovale and hypertrophic cardiomyopathy which merely require supportive care and follow-ups.

In the control group, of the 15 infants that had malformations like atrial septal defect, patent foramen ovale and patent ductu arteriosus. Prevalence of cardiovascular anomalies can be observed in Table 2.

Table 1: Comparison of age/BW/mother age according to diabetic status of patients studied.

Variables	Diabetic			Total	p value
	GDM	Overt Diabetic	Non-Diabetic		
Age in days	3.77±0.83	3.92±0.90	4.12±0.88	3.98±0.87	0.487
Birth Weight (kg)	3.28±0.26	3.35±0.30	2.73±0.23	3.02±0.39	<0.001**
Mother Age	27.69±1.55	30.75±2.01	23.84±2.39	26.50±3.56	<0.001**

Table 2: 2D Echo according to Diabetic status of patients studied.

2D Echo	Diabetic			Total (n=50)
	GDM (n=13)	Overt Diabetic (n=12)	Non-Diabetic (n=25)	
Normal	0(0%)	0(0%)	10(40%)	10(20%)
Abnormal	13(100%)	12(100%)	15(60%)	40(80%)
• PDA	5(38.5%)	3(25%)	8(32%)	16(32%)
• PFO	2(15.4%)	5(41.7%)	3(12%)	10(20%)
• HCMP	5(38.5%)	2(16.7%)	0(0%)	7(14%)
• VSD	1(7.7%)	1(8.3%)	2(8%)	4(8%)
• ASD	0(0%)	1(8.3%)	2(8%)	3(6%)

P=0.002**, Significant, Fisher Exact Test

Table 3: Comparison of 2D ECHO, duration of diabetes and apgar score according to GDM and Overt Diabetic of patients studied.

Variables	Diabetic		Total (n=25)	P value
	GDM (n=13)	Overt Diabetic (n=12)		
2D Echo				
• ASD	5(38.5%)	3(25%)	8(16%)	0.406
• HCMP	5(38.5%)	2(16.7%)	7(14%)	
• PFO	2(15.4%)	5(41.7%)	7(14%)	
• VSD	1(7.7%)	1(8.3%)	2(4%)	
• PDA	0(0%)	1(8.3%)	1(2%)	

All of the 50 infants (100%) that participated in the study underwent echocardiography after birth. The average time interval for the performance of echocardiography on these infants was overall 3.98±0.87 days after birth (3.84±0.86 days in the first group and 4.12±0.88 days in the second group).

In the group of 25 diabetic mothers, 12 (48%) suffered from overt diabetes, and the other 13 (52%)had gestational diabetes.

The mean duration of overt diabetes in diabetic mothers was 2 years. The mean duration of gestational diabetes in mothers diagnosed with GDM was 4.43 months.

The infants with cardiac anomalies had an average Apgar score of 8.33±1.15, and the newborns without malformations had an average of 9.24±0.69 (P=0.002). Among infants with cardiovascular malformations, there were 6 cases (28.6%) of cyanosis, 5 cases (23.8%) of bradycardia, 3 cases (14.3%) of respiratory distress and 3 patients with jaundice at the initial examination. Four of these infants (19%) had normal initial screenings.

DISCUSSION

The results of echocardiography performed on infants in each group of this study are predominantly compatible with the results of previous studies. In this study, the incidence of cardiovascular anomalies in infants of diabetic mothers is significantly higher than the infants of non-diabetic mothers (P=0.002); accordingly, the frequency of anomalies is 2.5 times higher among these infants. The comparable results were also obtained in a similar study performed on 64 infants hospitalized at Vali-e-Asr Hospital in 2004 by Najafian study.[20] These results were also seen in other similar studies conducted by Wren, Birrell and Hawthorne, 2003 and Schaefer, 2000.[1,2]

Regarding the current study, the most common cardiac anomalies in infants of diabetic mothers were PDA, PFO, and hypertrophic cardiomyopathy.

The prevalence of cardiovascular anomalies for all types of malformations in infants born to diabetic mothers is 42.8% and the incidence of other diseases, such as ventricular septal defect, atrial septal defect, displacement of mediastinal great vessels and valve atresia, is estimated at 11.4%. In the study by Najafian, the prevalence of cardiovascular malformations in infants of diabetic mothers was estimated at 46.9%, and the incidence of VSD was about 3%.[20] Also, in a study performed by Dimitriu et al, the prevalence of cardiac anomalies was reported at 23% regardless of pulmonary hypertension and hypertrophic cardiomyopathy.[21]

In the present study, associated anomalies in infants of diabetic mothers were cleft palate and spina bifida. This could be due to a higher prevalence of cardiovascular anomalies in infants of diabetic mothers compared to the anomalies in other organ systems which is also mentioned in other studies.[2] In that study, 37.6% of the total anomalies consisted of cardiovascular anomalies and, thereafter, skeletal anomalies with an estimation of 14.7%.

According to the present results, the type of maternal diabetes (diabetes mellitus, overt or gestational diabetes) did not bring about any significant difference in the incidence of cardiac malformations in infants (P=0.406).

However in a study conducted, a greater connection was noted between the prevalence of cardiac anomalies of infants and overt diabetes of the mother.[22] According to our study, the duration of diabetes mellitus both in terms of years of overt diabetes and in months of gestational diabetes during pregnancy did not cause any significant difference in the incidence of cardiovascular anomalies in infants. In a study conducted by Weber, Botti, and Baylen, it was concluded that appropriate glycemic control of the expectant mother could reduce cardiovascular anomalies in her infant.[23] It determined that the effect of glycemic control preventing cardiac anomalies in infants during pregnancy had been underestimated.[24]

In this study, the frequencies of the prenatal visit were obtained 100% in both diabetic and non-diabetic mothers. All pregnant women performed screening tests for gestational diabetes after 24 weeks of pregnancy.

In the present study, 4 infants of diabetic mothers (11.4%) had respiratory distress, 5 cases (14.3%) developed bradycardia and 3 cases (8.3%) were diagnosed with sepsis. Respiratory distress has been also reported as an important cause of hospitalization of infants born to diabetic mothers in other studies.[21]

In this study, 4 cases of infants diagnosed with cardiac anomaly (19%), didn't show any initial clinical symptom. These findings indicate the importance of clinical examination and follow-up for infants born to diabetic mothers. In accordance with the present research in comparison with the results of similar studies, the importance of medical care for maternal diabetes and its effect on the prevalence of cardiac disease in infants is clearly apparent.

Among 50 patients participating in this survey, none performed fetal echo cardiography. Postnatal diagnostic procedures for diabetic mothers were performed 3.6 days after birth (delivery). However, in the Najafian study, the average time for diagnostic procedures was estimated at 8.6 days.[20] Early diagnostic procedures can lead to better supportive care for infants of diabetic mothers. However, special care to infants of diabetic mothers is essential to prevent complications such as respiratory distress, sepsis, and hypoglycemia. Further prospective studies should be proposed for diabetic pregnant women with diabetes control and serum glucose level monitoring in order to reveal the impact of therapeutic interventions on reducing infant morbidity among diabetic mothers.

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