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Electrocardiography and echocardiography findings in infants of diabetic mothers: A case-control study

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ABSTRACT

Background: Gestational diabetes leads to various complications for the fetus, including heart abnormalities, and injuries during childbirth. This study aimed to investigate the changes of electrocardiogram (ECG), and echocardiography parameters in infants of diabetic mothers compared with those of healthy mothers.

Methods: In this case-control study, 75 infants of mothers with controlled diabetes (case group) as well as 75 infants of healthy mothers (control group), who were born in Birjand Vali-e-Asr Hospital in 2021 were enrolled. ECG and echocardiography were performed for all infants, and the desired parameters (P, QT interval, QTd, QTc, QTcd, T, Tpe, heart rate (HR) as well as ejection fraction (EF), fractional shortening (FS), and IVSd) were measured.

Results: The average QT interval and QTc parameters in the group of infants of diabetic mothers were higher than the healthy group ($P \leq 0.01$), while the average QTd in the infants of healthy mothers was higher than the infants of diabetic mothers ($P=0.01$). Furthermore, the average IVSd in the case group was higher than the control group ($P=0.01$). However, no differences in P, QTcd, T, TPe, HR, FS, EF, and heart axis parameters between the two groups were found ($P>0.05$).

Conclusion: In conclusion, significant differences between the infants of healthy mothers and those with gestational diabetes regarding the parameters of QT interval, QTd, QTc, and IVSd were found. However, no differences in P, QTcd, T, TPe, HR, FS, EF, and heart axis parameters between the two groups were found. Therefore, it is a clinical necessity to examine and screen the infants of diabetic mothers via ECG and echocardiography.

Keywords: Diabetes, Gestational; Heart Defects, Congenital, Pregnancy Complications, Echocardiography, Electrocardiography.

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Introduction

Diabetes is one of the most common diseases in the world, and is considered as the most common endocrine and metabolic disease (1). In 2010, 220 million people were suffering from this disease, and by 2030, this number will reach 336 million people (2). Diabetes has different types; the most common type is type 2 diabetes, in which a kind of insulin resistance is observed (3). Diabetes in pregnant mothers is defined in two ways: first, diabetes onset after the 20th week of pregnancy (gestational diabetes); second, diabetes diagnosed before the 20th week of pregnancy (overt diabetes) (4, 5). Uncontrolled or poorly controlled gestational diabetes is defined as a serum HbA1c level ≥7.5%, while controlled diabetes is defined as a serum HbA1c level <7.5% (6).

Diabetes causes various complications, including kidney, neurological, ocular, and vascular complications. Heart complications for infants of diabetic mothers are one of the most important complications of gestational diabetes. Other complications of gestational diabetes for the fetus include macrosomia, and injuries during childbirth, such as bone fractures, shoulder dislocations, nerve palsies, hypoglycemia, respiratory distress, and obesity. Fetal hyperinsulinemia leads to cardiac hypertrophy, which enhances the production of glycogen and fat in myocardial cells. This complication is more likely to occur in mothers with poor sugar control during pregnancy. It has been mentioned that diabetes can cause changes in heart function and electrocardiogram (ECG) in children. Noori et.al pointed out that parameters such as corrected QT interval (QTc), QT dispersion (QTd), QT interval, and corrected QT interval dispersion (QTcd) in infants of diabetic mothers were higher than the control group (7).

Considering that infants of diabetic mothers are at higher risk of hypertrophic cardiomyopathy (HCM), the most noticeable changes are the increase in the thickness of the interventricular septum along with the decrease in the size of the ventricular cavities, which could obstruct the left ventricular outflow. On the other hand, the diagnosis of disorders in infants of diabetic mothers through ECG parameters is cheaper and more accessible than echocardiography, and changes in ECG parameters, especially QT, QTcd, and QTc, make the patient prone to dangerous cardiac arrhythmias (8). Therefore, this study aimed to evaluate ECG and echocardiography parameters in infants of diabetic mothers compared to the infants of healthy mothers.

Methods

In this case-control study, the study population included infants of diabetic mothers and infants of healthy mothers, who were born in the gynecology and obstetrics ward of Birjand Vali-e-Asr Hospital in 2021. The infants of mothers with gestational diabetes (diabetes onset after the 20th week of pregnancy), whose diabetes was controlled (serum HbA1c level <7.5%), were included in this study. Another inclusion criterion was signing the informed consent. The exclusion criteria were the existence of congenital heart defects in infants, as well as the history of pre-eclampsia, eclampsia, hypertension, hyperlipidemia, hypothyroidism, hyperthyroidism, and smoking in the mothers. Also, mothers with uncontrolled or poorly controlled gestational diabetes (serum HbA1c level ≥7.5%) were excluded from the study. These inclusion and exclusion criteria were evaluated in all mothers based on a precise history, laboratory, and clinical examination performed by an obstetrician-gynecologist.

In this study, the sampling method was convenience sampling. The sample size was estimated 69 participants in each group, considering the frequency of the disorder in the group of diabetic and healthy mothers equal to 38% and 14%, respectively (9), and with the 95% confidence interval and 90% power. Moreover, the final sample size was considered 75 people in each group. Therefore, 75 infants of diabetic mothers and 75 infants of healthy mothers were included in this study. Then, P, QT interval, QTd, QTc, QTcd, T, Tpeak-to-Tend interval (Tpe), and heart rate (HR) parameters in ECG and ejection fraction (EF), fractional shortening (FS), and thickness of the interventricular septum using the interventricular septal end diastole (IVSd) parameter in M-mode echocardiography were measured in

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both groups. The ECG and echocardiography were performed and analyzed by an expert pediatric cardiologist. The data were entered into SPSS v.18. Qualitative and quantitative data were reported as frequency percentage and mean ± standard deviation (SD), respectively. The normality was checked using Kolmogorov-Smirnov test. The Chi-squared test, and independent t-test were also performed. The significance level was considered P ≤0.05.

Results

According to Table 1, 150 infants participated in two groups. The first group included 75 infants of healthy pregnant women (control group), and the second group included 75 infants of mothers with controlled gestational diabetes (case group). Eighty-six infants (57.3%) were boys, and 64 (42.7%) were girls. The average age of birth was 37.6 ± 2.2 weeks. Also, the average age of birth in diabetic mothers and healthy mothers were 37.6 ± 1.3 weeks, and 37.8 ± 2.7 weeks, respectively, between which there was no significant statistical difference (P =0.06).

Table 1. Demographic information of the two study groups

Group	Infants of healthy mothers	Infants of mothers with gestational diabetes	P-value
Sex of infants			
Female (%)	36 (48.0%)	28 (37.3%)	0.07*
Male (%)	39 (52.0%)	47 (62.7%)	
Gestational age (weeks, Mean ± SD)	37.8 ± 2.7	37.6 ± 1.3	0.06**
Total	75 (50.0%)	75 (50.0%)	

* Chi-squared test

** Independent t-test

According to Table 2, there were no significant differences between the two groups regarding P, QTcd, T, TPe, and HR parameters (P >0.05). However, there were significant differences between the two groups regarding the mean of QT interval, QTd, and QTc parameters (P ≤0.05). The QT interval and QTc parameters were higher in the infants of mothers with gestational diabetes (P =0.003, and P <0.001, respectively), while QTd parameter was lower in this group (P <0.001). According to Table 3, there were no significant differences between the heart axes of the two groups (P >0.05).

According to Table 4, there was a significant difference between the two groups regarding the interventricular septal end diastole (IVSd) parameter; the mean of IVSd was higher in the group of infants of mothers with gestational diabetes (P <0.001). However, there were no significant differences between the two groups regarding the mean of FS and EF parameters (P >0.05).

Table 2. ECG-related parameters in the two groups

Group	Mean (mm)	SD	t	P-value*
P				
Infants of healthy mothers	0.05	0.01	1.91	0.07
Infants of mothers with gestational diabetes	0.04	0.01		
QT interval				
Infants of healthy mothers	0.26	0.02	-2.82	0.003
Infants of mothers with gestational diabetes	0.27	0.03		

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Group	Mean (mm)	SD	t	P-value*
QTd				
Infants of healthy mothers	0.14	0.16	4.17	<0.001
Infants of mothers with gestational diabetes	0.06	0.06		
QTc				
Infants of healthy mothers	0.36	0.05	-3.38	<0.001
Infants of mothers with gestational diabetes	0.40	0.05		
QTcd				
Infants of healthy mothers	0.05	0.01	1.21	0.18
Infants of mothers with gestational diabetes	0.05	0.02		
T				
Infants of healthy mothers	0.08	0.14	0.74	0.55
Infants of mothers with gestational diabetes	0.08	0.02		
Tpe				
Infants of healthy mothers	0.02	0.01	-0.24	0.15
Infants of mothers with gestational diabetes	0.02	0.01		
HR				
Infants of healthy mothers	132.14	15.13	0.13	0.74
Infants of mothers with gestational diabetes	132.08	19.07		

* Independent t-test

Table 3. Frequency of left and right heart axes in the two groups

Group	Frequency (%)		P-value*
	Left axis	Right axis	
Infants of healthy mothers	65 (86.7%)	60 (80.0%)	0.56
Infants of mothers with gestational diabetes	10 (13.3%)	15 (20.0%)	

* Chi-squared test

Table 4. Echocardiography-related parameters in the two groups

Group	Mean	SD	t	P-value*
Interventricular septal end diastole (IVSd, mm)				
Infants of healthy mothers	4.7	1.13	-8.39	<0.001
Infants of mothers with gestational diabetes	6.6	1.60		
EF (%)				
Infants of healthy mothers	74.0%	9.0	0.24	0.64
Infants of mothers with gestational diabetes	73.3%	9.2		
FS (%)				
Infants of healthy mothers	42.0%	9.9	0.85	0.13
Infants of mothers with gestational diabetes	40.5%	8.6		

* Independent t-test

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Discussion

The present study was conducted to investigate the changes of ECG and echocardiography parameters in infants of diabetic mothers (case group) compared with the infants of healthy mothers (control group). For this purpose, infants of diabetic and healthy mothers who were born in Birjand Vali-e-Asr Hospital in 2021 were examined.

This study showed that the average QT interval in infants of diabetic mothers was higher than the infants of healthy mothers. Moreover, the average QTd in infants of healthy mothers was higher than the diabetic mothers, and the average QTc in infants of diabetic mothers was higher compared with the control group. Also, the average IVSd in infants of diabetic mothers was higher than the control group. The results of this study are consistent with the results of a study conducted in India, which was performed on 229 diabetic mothers and 229 non-diabetic mothers. This study found that mothers with gestational diabetes significantly demonstrated more heart complications than healthy mothers (10). Furthermore, the results of our study are consistent with another study conducted in Iran. A study conducted in Arak University of Medical Sciences on 60 diabetic mothers showed that diabetic mothers, even with good control of gestational diabetes, are still at higher risk of cardiac hypertrophy, subclinical diastolic dysfunction, and left ventricular resting defects. The results of this study revealed that sugar control is not enough to prevent heart failure (11).

Also, Arslan et al. investigated the effect of left ventricular hypertrophy on QT variables of infants of diabetic mothers; 47 infants of diabetic mothers and 30 infants of healthy mothers were examined. ECG and echocardiography were performed for all infants, and infants of diabetic mothers were divided into two groups based on septal thickness. The results showed that the thickness of the interventricular septum was significantly higher in the diabetic group than in the healthy group. The QT and QTc intervals were also more critical in the diabetic group than in the healthy group. Also, in this study, a positive correlation between IVSd and QT was identified, which can be a risk factor for the development of arrhythmia in infants of diabetic mothers (12).

Another study investigating QT prolongation in infants of diabetic mothers was conducted by Bagheri et al. in Kerman. In this study, 49 infants of diabetic mothers and 30 infants of healthy mothers were examined. The findings of this study showed that 59% of infants of diabetic mothers showed septal hypertrophy, which was significantly more than the control group. However, unlike this study, there was no significant differences in QTc values (13). The findings of this study showed the importance of screening in the management of cardiac complications in infants of diabetic mothers. Although a significant leftward shift of electrical axis is suggested in the infants of diabetic mothers (14), this study revealed no significant difference between the heart axes of the two groups

Diabetes is especially harmful to cardiovascular health in women. Indeed, the increased relative risk of vascular diseases associated with the diagnosis of type 2 diabetes is more significant in women and is considered independent of other well-known cardiovascular risk factors. This higher risk for cardiovascular diseases in women may result from placental hormones or enhanced secretion of inflammatory cytokines in pregnancy, which increase insulin resistance and develop atherogenesis. It may be first detected during routine screening for gestational diabetes (15-17).

In the survey conducted in 2021, it has also been shown that gestational diabetes significantly affects the structure and function of heart and blood circulation of the fetus. Heart defects such as myocardial hypertrophy are increased in infants of diabetic mothers. Improving the effects of gestational diabetes on children mainly depends on preventing diabetes before pregnancy (18). The fetal heart is more susceptible to congenital abnormalities in gestational diabetes. Heart dysfunctions and myocardial hypertrophy are more frequent in infants of women with diabetes (19).

Maternal diabetes significantly affects the structure and function of the fetal heart as well as the fetoplacental circulation, thus altering placental vasculature with a wide range of cardiac abnormalities from minor septal defects to complex heart disease. Gestational diabetes primarily affects placental

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circulation. Alterations in placental development and subsequent vascular dysfunction occur in six out of seven women with various degrees of diabetes. Common placental alterations in these patients contain fibrinoid necrosis, villous immaturity, and increased syncytial knots. These changes promote maternal vascular perfusion/uteroplacental circulation. The types and effects of this disorder depend on how early hyperglycemia occurs in pregnancy (20). In addition to the coagulopathy caused by pregnancy, maternal hyperglycemia enhances thrombogenic conditions. This phenomenon in combination with excessive umbilical cord tortuosity leads to ischemia and vascular stasis, which is accompanied with thrombosis in the fetal vascular tree, and increased perinatal mortality (21). Furthermore, umbilical vessels have been demonstrated pathological alterations consistent with early atherosclerosis. A thin umbilical cord with a single umbilical artery is correlated with increased negative fetal outcomes in gestational diabetes (22). Fetal hypoxia is accompanied with increased erythropoiesis and the subsequent polycythemia. Increased production of catecholamines causes cardiac hypertrophy and hypertension. Moreover, it can be the cause of 20-30% of stillbirths observed in non-controlled diabetic pregnancies (23).

Given the 50-60% lifetime risk of type 2 diabetes due to gestational diabetes, regular diabetes screening is emphasized in current women's health guidelines for women with gestational diabetes. Appropriate strategies are crucial in women with previous gestational diabetes in order to prevent and manage cardiovascular risks. Furthermore, proceedings that diminish the risk of gestational diabetes might be necessary if future correlated cardiovascular risks are not reduced by achieving normoglycemia. Preconceptional counseling may reduce these long-time risks, especially among women with higher risk of cardiovascular disease (24). This study has some strengths. First, the mothers were critically evaluated by an obstetrician-gynecologist before the study in order to precisely consider the inclusion and exclusion criteria. Second, echocardiography and ECG were performed and analyzed by an expert pediatric cardiologist, which lowers the percentage of errors. However, this study is limited due to the relatively small number of participants.

Conclusion

This study revealed that the QT interval, QTc, and IVSd parameters of ECG and echocardiogram were significantly higher in infants of diabetic mothers compared with those of healthy mothers, while QTd parameter was lower in the case group. However, this study found no differences between P, QTcd, T, TPe, HR, FS, EF, and heart axis parameters between the two groups. Therefore, according to the cardiac complications observed in this study, it is a clinical necessity to examine and screen the infants of diabetic mothers via ECG and echocardiography.

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Ethics approval: This study was approved by Birjand University of Medical Science's Research Ethics Committee (Approval ID: IR.BUMS.REC.1400.293). Moreover, informed consent was obtained from all mothers involved in the study.

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Consent to participate: Informed consent was obtained from all mothers involved in the study.

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