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Comparison of QT Interval between Neonates with Maternal Gestational Diabetes and Healthy Mothers

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ABSTRACT

Background: The risk of developing metabolic syndrome and diseases, such as diabetes mellitus, has been increased as a worldwide rise in obesity. Gestational diabetes mellitus (GDM) or maternal hyperglycemia is a risk factor for cardiac dysfunction in neonates. The present study compared the QT interval in neonates with maternal GDM and healthy mothers.

Methods: This case-control study was carried out on term neonates with maternal GDM (case group; n=42) and healthy non-diabetic mothers (control group; n=42) in Sayyad-e-Shirazi hospital in Gorgan, Northeast of Iran, within March 2016 and February 2017. A pediatric cardiologist evaluated septal hypertrophy by Doppler echocardiography (Zonare ZS3) during the first 2 weeks after birth. A standard 12-lead electrocardiogram was recorded for 10 sec, and a corrected QT (QTc) value was calculated. The data were analyzed by the latest version of SPSS software (version 16) using the Chi-square and t-test for the assessment of the differences in the QT values and other indices between the two groups. P-values less than 0.05 were considered statistically significant.

Results: The results of the present study showed congenital heart diseases (CHDs) in six neonates. Significantly higher QT (249±36 and 245± 28 ms), septal thickness (6.09±1.07 and 5±1 mm), and lower QTc value (382±44.06 and 392± 34 ms) were observed in the case group, compared to those reported for the control group (P<0.001). The QTc dispersion was significantly different between the subjects under insulin therapy and participants receiving an antihyperglycemic oral regimen.

Conclusion: In this study, significant thicker cardiac septum and higher QT interval were observed in the neonates born from mothers with GDM in comparison to those from healthy mothers. This could suggest close cardiac monitoring of these neonates due to the higher probability of CHDs.

Keywords: Congenital heart disease, Diabetes, Gestational, Newborn, QT interval

Introduction

The risk of developing metabolic syndrome and diseases, such as diabetes mellitus, has been increased as a worldwide rise in obesity and variously reported in different regions. The incidence of pre-gestational and gestational diabetes mellitus (GDM) is growing (1-3). It has been declared that pre-gestational diabetes and GDM have major health effects on both mothers and neonates. In pre-gestational diabetes, there is a higher rate of stillbirth, perinatal mortality, macrosomia, and prematurity (4, 5). Maternal hyperglycemia during pregnancy or so-called GDM defined as impaired glucose tolerance initiating or firstly diagnosed during pregnancy and usually resolving after delivery has been reported in 2-5% of the normal pregnancies (3, 6).

The last recommendation for the screening of GDM suggested by the International Association of Diabetes and Pregnancy Study Groups is a one-stage screening procedure, including a 2-hour 75 g oral glucose tolerance test (OGTT). A single abnormal fasting glucose concentration at 1 or 2 h is sufficient for the diagnosis of GDM (6, 7). The GDM can cause macrosomia, neonatal

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hypoglycemia, cardiac congenital anomalies, and increased fetal mortality. It is thought that oxidative stress due to GDM affects fetal development (2, 6, 8).

Congenital heart disease (CHD) is one of the birth defects with an incidence of approximately 1% and a common cause of mortality in neonates. The important teratogen in diabetes mellitus is hyperglycemia that can affect the newborn before conception and during the first trimester; however, in GDM, it is associated with hypertrophic cardiomyopathy. Several studies have demonstrated the association of maternal diabetes with 4-5 times the risk of CHDs. In diabetic mothers, the left ventricular involvement is more common, and cardiac output decreases due to septal enlargement. The mechanism of hypertrophic cardiomyopathy in these neonates seems to be a result of hyperinsulinemia and increased expression of insulin receptors causing proliferation and hypertrophy of cardiac cells (9).

Other cardiac defects in GDM include transposition of the great arteries, double outlet right ventricle, truncus arteriosus, hypoplastic left heart syndrome, and ventricular septal defects (3). Some studies have claimed that wall hypertrophy and septal enlargement can affect QT and corrected QT (QTc) dispersion (10). Considering the critical role of maternal glycemic control in the fetal cardiac structure and function, the present study aimed to compare the QT interval between the newborns of mothers with GDM and healthy mothers.

Methods

This case-control study was carried out on term neonates with a gestational age of ≥ 39 weeks and age of ≤ 28 days divided into cases born from mothers with GDM (n=42) and controls with healthy non-diabetic mothers (n=42) in Sayyad-e-Shirazi hospital in Gorgan, Northeast of Iran, within March 2016 and February 2017. The diagnosis of GDM was made based on the diagnostic criteria through a single-stage 75 g OGTT and single abnormal fasting glucose concentration at 1 or 2 h (6).

The demographic data, including post-natal age and gender of the neonates, were collected. The treatment of maternal GDM was also included. The exclusion criteria were a) neonates of mothers with insulin-dependent diabetes mellitus and other disorders affecting the fetal cardiac structure or function, b) family history of hyperlipidemia, c) preeclampsia and/or eclampsia, (d) maternal hypertension, hypothyroidism, and hyperthyroidism, e) maternal heart disease and liver or kidney failure, f) history of smoking, drug abuse, or alcohol consumption during pregnancy, (g) neonatal hypoglycemia or electrolyte imbalance, h) neonatal hyperbilirubinemia, i) preterm birth, and j) hospitalization for any reason during pregnancy.

Doppler echocardiography (Zonare ZS3) was performed by a pediatric cardiologist in the Cardiology Clinic of Golestan University of Medical Sciences, Gorgan, Iran in the first 2 weeks after birth. Assessments and measurements were made in M-mode from the parasternal axis near the papillary muscle. Septal hypertrophy was also evaluated. The subjects in the case group were divided into two groups based on the interventricular septal thickness. Moreover, a standard 12-lead electrocardiogram (ECG) was recorded for 10 sec using the Cardiofax C Nihon Kohden's ECG by the pediatric cardiologist of the team. Regarding the 12-lead ECG (with a speed of 25 mm/sec), a QTc between 350 and 440 ms is considered normal, and the values of > 440 ms are reported as borderline QT prolongation. In addition, the QT interval of lower than 400 ms is regarded as normal (11). The QTc value was calculated based on Bazett's formula (QTc = QT / √ RR interval). All arrhythmias were also reported.

Data analysis

The collected data were analyzed in the latest version of SPSS software (version 16) using descriptive statistics (i.e., mean and standard deviation). The Chi-square and t-test were used for the evaluation of the differences in the QT values and other qualitative indices between the groups. A p-value of less than 0.05 was considered statistically significant.

Results

There was no significant difference in terms of age (3-8 days), gender (male to female: 0.9), and birth weight (3.075 and 3.062 kg) between the two groups (P=0.81). The CHDs were observed in six neonates, including ventricular septal defect, atrial septal defect, and patent foramen ovale. There was a significant difference between the two groups in the QT interval, septal thickness, and QTc value (Table 1).

Based on the therapy received for diabetes, the neonates with maternal GDM were also divided into two groups of antihyperglycemic oral medicine (n=28) and insulin therapy (n=14). There was a statistically significant difference

Table 1. Comparison of mean values of QT, corrected QT, and septal thickness in neonates with gestational diabetes mellitus mothers and healthy non-diabetic mothers

	Case (n=42) Mean±standard deviation	Control (n=42) Mean±standard deviation	P-value*
Septal thickness (mm)	6.09±1.07	5±1	<0.001
Corrected QT (ms)	382±44.06	392±34	<0.001
QT (ms)	249±36	245±28	<0.001

*Chi-square test

between the two groups in terms of the QTc value (P=0.046) which was higher in the insulin-treated group (401.64±34.96 and 373±45.5 ms). Although the mean values of the QT and septal thickness were higher in the case group, they were not statistically significant.

Discussion

In this study, the QT interval and septal thickness were compared between 42 neonates with maternal GDM and 42 neonates with healthy non-diabetic mothers. There was no significant difference in age, gender, and birth weight between the two groups, which could be considered a strength in the interpretation of the results; however, other studies demonstrated an increase in birth weight in maternal GDM, compared to that reported for control groups (4).

In the present study, the two studied groups had a significant difference in the QT interval, septal thickness, or QTc value, similar to the results of studies performed by Ren Y et al., Hăşmăşanu et al., and Garg et al., indicating an increase in left ventricular walls and septal thickness in fetuses with maternal GDM, compared to those of normal pregnancies (12-14). These similar results could be suggestive of the hazardous effect of GDM on CHD in neonates born from GDM mothers.

Elevated QT and QTc dispersions may be risk factors for arrhythmias in newborns with diabetic mothers, and it is necessary to further investigate this subject in future studies (10). As a result, even in the absence of arrhythmias in the studied neonates, close monitoring should be considered. In one study, fetal heart rate was considered an early predictor of GDM, and this considerable result may be considered in future studies (15). It is suggested that neonates with diabetic mothers have abnormality in cardiac function even in the absence of septal hypertrophy (16); therefore, other features of cardiac function should be considered for these patients. Although in the present study, there was a higher rate of septal hypertrophy in newborns with GDM mothers, there were no remarkable signs of heart failure in the studied cases.

The cases with maternal GDM and insulin treatment had a statically significant higher QTc value, compared to the subjects treated with diet; nevertheless, they did not differ in septal hypertrophy as claimed in a previous study carried out by Bhorat et al. In the aforementioned study, an increase in QTc value was reported in the insulin-treated group (17); however, it was similar to the results of a study conducted by Dervisoglu et al. in which no significant relation was observed between the two groups (18). In the current study, there was not a significant difference in neonatal birth weight between the two groups in GDM; nevertheless, other studies claimed a lower birth weight in metformin-treated pregnancy (19).

Conclusion

According to the results of the present study, there was a significantly higher mean QT interval and septal thickness and lower QTc value in the neonates of mothers with GDM. The QTc dispersion was significantly higher in the subjects under insulin therapy and those treated with restricted diets. This might indicate a higher risk of developing arrhythmia in the newborns of diabetic mothers receiving insulin therapy as claimed in previous studies. Therefore, close monitoring and screening all pregnant women for GDM and assessing fetal and neonatal cardiac function seem to be necessary. It could be beneficial to carry out further studies on cardiac complications in the neonates of mothers with GDM.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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