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Prolonged QT interval in the infants of diabetic mothers

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Abstract

Background: The prevalence of gestational diabetes mellitus is rising. Myocardial hypertrophy is the most common cardiac disorder in the infants of diabetic mothers, which hypothetically can cause fatal arrhythmias. This study investigated prolonged QT in the newborns of diabetic mothers in Afzalipour Hospital in Kerman City, in 2015.

Methods: This case-control study was conducted on 49 neonates of diabetic mothers and 30 babies of healthy mothers. Routine echocardiograms and Tissue Doppler Imaging (TDI) were performed for all the newborns. QTc values were computed from randomly selected beats on ECG.

Results: Twenty-nine (59%) newborns in case group had septal hypertrophy which was higher than control group ($P < 0.05$). There was no difference between case and control groups in QTc values ($P > 0.05$), and there was no relationship between septal hypertrophy and QT prolongation. Twenty-one percent of the infants in control group, had septal hypertrophy. Although parameters of M-Mode Echocardiography were similar, TDI showed differences between the two groups. (TDI) is applicable for the measurement of both systolic and diastolic functions.

Conclusion: Findings revealed that the screening and treatment of diabetes during pregnancy need a revision in our context. In addition, there is a paucity of studies concerning the evaluation of TDI in the newborns of diabetic mothers. We recommend conducting studies to compare the routine echocardiograms with TDI in these high risk infants.

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Introduction

Despite the progression in screening and treatment of diabetes during pregnancy, maternal and fetal complications have remained high during these years (1,2). The main mechanism of these complications is mother's hyperglycemia, which causes increased endogenous insulin levels in the fetuses (2). Gestational Diabetes Mellitus (GDM) is defined as high fasting blood sugar or abnormal results for Glucose Tolerance

Test (GTT), as first seen during pregnancy (2,3). Studies performed urban areas in Iran show a prevalence of 5% to 14% for GDM (34-5).

Different studies have shown that high blood glucose in pregnant women increases morbidity and mortality in fetuses and neonates (6-7-8). Cardiac complications in these infants are two to four folds more than normal and the most common cardiac problem is myocardial hypertrophy. Studies indicate that hypertrophic cardiomyopathy has a prevalence of about 30% among infants of diabetic mothers (29101112).

Arrhythmia is one of the important complications in hypertrophic cardiomyopathy which can lead to ventricular and supraventricular tachycardia as well as sudden death in all ages (2,12). Long QT is one of the most prevalent forms of these arrhythmias induced by hypertrophied ventricular myocardium. Long QT prevalence is about 1 in 2000 newborns, in the general population (1,2).

Most of the studies about this type of arrhythmia were done on adults and adolescent cases of hypertrophic cardiomyopathies, and all of them showed a higher prevalence of long QT than normal population (2,12).

A few studies have been performed on infants in this field, but there is almost no study focusing on newborns, especially infants of diabetic mothers. Only in one study Arslan D et al., evaluated the newborns of diabetic mothers for prolongation of QT intervals (12). Their results showed that QT dispersion in these newborns, with septal hypertrophy, was longer than the newborns of healthy (non-diabetic) mothers. Results of this unique study, in addition to the increasing prevalence of diabetic women, and abnormal Glucose Tolerance Tests in Iran and specifically Kerman and lack of similar sufficient studies, indicate that hypertrophic cardiomyopathy and probable arrhythmias and other complications of this condition could have dangerous consequences on the infants of diabetic mothers in our country. Therefore, our goal in this study was investigating the presence of hypertrophic cardiomyopathy and unveiling probable long QT as its result in newborns of diabetic mothers (all types of diabetes) in Kerman. Besides, we compared the results with the newborns of non-diabetic mothers to determine the relationship of this type of arrhythmia with left ventricle function on echocardiography and Tissue Doppler Imaging in order to diagnose and prevent fatal complications.

Materials and Methods

This case-control study was performed on 79 infants in Afzalipour Hospital in Kerman. All infants were born between May and August 2015, and were clinically healthy. Case group included 49 newborns up to 28 days old with Gestational (GA) more than 34 weeks, born to diabetic mothers, (either type 1, type 2 or gestational diabetes). Control group included 30 newborns up to 28 days old of non-diabetic mothers and a GA more than 34 weeks. Exclusion criteria for case and control groups were newborns with major congenital cardiac anomalies, hypoglycemia or hyperbilirubinemia, also newborns of mothers with Lupus Erythematous disease who may show arrhythmia. GA less than 34 weeks was also considered as an exclusion criterion as it is an indication for hospitalizing the neonates in NICU. This condition can affect echocardiography and ECG results.

A checklist was used to gather data on: Postnatal age (in days), gender (male, female), Gestational Age (in weeks), mother's diabetes type and history of insulin therapy (before and during pregnancy).

M-Mode echocardiography, Color Doppler echocardiography and Tissue Doppler Imaging were performed to evaluate ventricular septal thickness, posterior wall thickness, left atrium and aorta size and left ventricle

ejection fraction. Septal thickness was measured in millimeters and values less than 6 mm were considered as normal.

ECG (12 leads) was performed on every newborn in both groups and damaged strips were repeated to assure credibility. The QT interval, (from the beginning of Q wave to the end of T wave), was measured for all the newborns and then QTc was calculated using Bazett's formula (corrected QT= $QT/\sqrt{RR}$), where (RR) is the interval between two adjacent R waves on ECG). Five random QT intervals on electrocardiograms were chosen, then QTcmin, QTcmax and QTcmean were calculated. Measurements were done blindly by two different physicians, these two and the attending physician had no information about the diabetic history of mothers. This study was approved by the ethics committee of Kerman University of Medical Sciences (N:IR.KMU.REC.1395.11). All the parents gave written consent prior to the study on their newborns.

Independent sample t- Test was used to compare quantitative variables and Chi-square test was used to compare qualitative values in the two groups. To investigate relations between two quantitative variables, Pearson's correlation coefficient was applied. All the analyses were performed using SPSS software, version 20.

Results

In this study 49 newborns were in case group (30 females and 19 males, with an average postnatal age of 3.5 days and an average GA of 36 weeks and 3 days), and 30 newborns were in control group (17 males, 13 females, average postnatal age= 3.5 days and average GA of 36 weeks and 9 days). There were no significant differences in newborns' postnatal age, GA, infant gender and mothers' age between the two groups, which show adequate conformation (all P-values were > 0.05). The average birth weight in case and control groups was 2.94 kg and 2.66 kg, respectively. This difference was not statistically significant.

Septal thickness, posterior LV wall thickness and Tissue Doppler criteria (Aa, Sa, Ea) in case and control groups were statistically different (all P-values were < 0.5). Other echocardiographic criteria were not different between the two groups (Table 1 and Table 2).

This study showed that 59.18% of the infants in case group and 21.43% of the babies in control group had hypertrophic cardiomyopathy, which was statistically different (p = 0.001).

Table 1. Comparison of Echocardiographic parameters in case and control groups

Echocardiography Criteria	Case Group (49)	Control Group (30)	p-value
LA/AO	1.181±0.31	1.04±0.31	0.06
LVPWT	4.77±1.02	4.01±0.86	0.0007
LVEF	63.01±9.95	59.23±7.24	0.07
LVFS	31.91±3.92	29.41±6.39	0.03
LVEDd	10.75±2.92	11.88±3.83	0.14
LVESd	8.57±2.17	9.75±2.41	0.03
Sa	8.97±3.03	6.76±3.03	0.0006
Ea	10.35±4.53	7.68±3.16	0.006
Aa	10.37±3.42	7.72±2.98	0.008
Septal Thickness	6.26±1.38	5.29±1.31	0.002

Table 2. Septal hypertrophy detection in case and control groups

Control Population N (%)	Case Population N (%)		Condition
22 (78.75)	20 (40.82)	Has not *	Hypertrophic Cardiomyopathy
6 (21.43)	29 (59.18)	Has **	
p-value 0.001			

* Intraventricular septal thickness < 6 mm

** Intraventricular septal thickness ≥ 6 mm

ECG strips evaluation showed that average QTc mean (in cm/s) and QTc max were higher in case group, but there was no significant difference between case and control groups. (P-value = 0.63 and 0.8, respectively).

QTc min values were higher in control group than case group, with no statistically significant differences (P-value = 0.87). (Table 3)

There was a direct relationship between ventricular septal thickness and QTc prolongation, but it was not statistically significant (Table 4).

Table 3. The comparison of QTc Values in case and control groups

Electrocardiographic Parameters	Case (49) Mean±SD	Control (30) Mean±SD	p-value
QTc min (cm/s)	381.51±38.09	383.1±51.33	0.87
QTc max (cm/s)	468.06±46.9	465.06±60.68	0.80
QTc mean	424.44±37.22	419.71±50.53	0.63

Table 4. The relationship between septal thickness and QTc values

Variable	Interventricular Septal Thickness			
	All the newborns		Case group	
	Coefficient of Correlation	p-value	Coefficient of Correlation	p-value
QTc min	0.07	0.8	–	–
QTc Max	0.11	0.3	–	–
QTc Mean	0.02	0.2	0.1	0.3

In case group, 44 mothers had gestational diabetes, 20 individuals received insulin during pregnancy, 5 mothers had overt diabetes, and 3 of them received insulin.

QTc mean had no significant difference in the newborns of overt diabetic mothers in comparison with infants of gestational diabetic mothers. However, QTc mean was higher in infants of

overt diabetic mothers with a longer history of insulin therapy (data not shown).

Discussion

In this study septal hypertrophy index in case group, was 59%; which was twofold higher then former similar studies. Evidence shows that septal hypertrophy is addressed in about 30% of newborns of diabetic mothers (1). Tabib's study in Tehran and Arslan's study in Turkey showed a prevalence of 40% and 34%, respectively (12,13). Cardiomyopathy increases the risk of heart failure and hospitalization in infants. In order to find the causes of increasing septal hypertrophy in the newborns of diabetic mothers in Kerman, further epidemiological studies are needed. In the control group, 6 newborns (20%) had septal hypertrophy; this was unexpected because there was no documented history of diabetes or other significant diseases in mothers in the control group. Probable causes might be improper diabetic screening and/or having no appropriate prenatal care. Since hyperglycemia during pregnancy, even for a limited period, can lead to hypertrophic cardiomyopathy [6, 7], and as some participating mothers were migrant foreign subjects (Afghans) who were not well informed about diabetes and had almost no prenatal care, the results seem to be justifiable. Thus, there should be concerns regarding more precise diabetes screening in pregnant women in Kerman city to prevent maternal and/or neonatal complications. Electrocardiographic investigations showed no significant difference between case and control groups regarding QTc max, QTc min and Qtc mean (p-value >0.5). This result contradicts with the findings of the study conducted by Arslan et.al. in 2014 (in this study the structure and sample size were similar to ours). Arslan et al. found that QT was prolonged in newborns with septal hypertrophy as they expected(12), but in our study, despite the higher frequency of septal hypertrophy in case group, there was no significant relationship between septal hypertrophy and QT prolongation (p-value = 0.2). For further investigations, It is recommended that studies with larger sample sizes be conducted. QT values in newborns of overt diabetic mothers who received insulin were higher, but there was no statistically significant difference between overt and GDM groups (p-value > 0.05). Insulin therapy during pregnancy had no relationship with QT prolongation in newborns (p-value >0.05).

Since sufficient studies are not performed on the relationship between septal hypertrophy and QT prolongation and the sample size is rather small, it is not possible to reject the probability of QT prolongation in these newborns decisively. But it seems that numbers of long QT cases are not that much to necessitate screening ECGs for all the newborns of diabetic mothers. However, this issue needs further investigations.

Systolic and diastolic function evaluation can be performed using various echocardiographic methods. The most important and precise methods are measuring FS (fraction shortening) using M-Mode and 2D measuring mitral inflow velocity to determine diastolic function and Tissue Doppler Imaging (TDI). The latter method (TDI) is newer, more precise and its design is based on myocardial velocity, thus both systolic and diastolic functions can be studied (14).

In our study we used Tissue Doppler Imaging (TDI) along with conventional echocardiography on the newborns. In the current study all three criteria of Tissue Doppler Imaging, Aa (p-value = 0.008), Ea (p-value = 0.006) and Sa (p-value = 0.0006), had statistically significant differences between case (newborns of diabetic mothers) and control (newborns of non-

diabetic mothers) groups. As this method has not been used exclusively for the infants of diabetic mothers who are high risk for developing unrecognized cardiac problems and because our study showed significant differences between TDI and conventional echocardiography results, it seems that a study can be designed to compare the conventional echocardiograms and Doppler Tissue Imaging to determine systolic and diastolic functions in newborns of diabetic mothers. In addition, the helpfulness of either method can be investigated.

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