ORIGINAL RESEARCH

QT Interval in Pregnant and Non-pregnant Women

Majid Zamani[1], Mehrdad Esmailian[1], Zahra Yoosefian[2*]

1. Department of Emergency Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Emergency Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Introduction: Prolongation of QT interval might result in dangerous cardiac arrhythmias, including Torsades de Pointes (TdP), consequently leading to syncope or death. A limited number of studies carried out in this respect to date have shown that QT interval might increase during pregnancy. On the other hand, it has been shown that each pregnancy might result in an increase in the risk of cardiac accidents in patients with long QT interval. Therefore, the present study was undertaken to compare QT intervals in pregnant and non-pregnant women. **Methods:** Pregnant women group consisted of 40 women in the second and third trimesters of pregnancy and the non-pregnant control group consisted of healthy women 18-35 years of age. All the patients underwent standard 12-lead electrocardiogram (ECG). The QT interval was measured for each patient at lead II. The mean corrected QT interval (QTc) and QT dispersions (QTd) were compared between the two groups. **Results:** Mean heart rates in the pregnant and non-pregnant groups were 98.55±14.09 and 72.53±13.17 beats/minutes (P<0.001). QTd and QTc means were in the normal range in both groups; however, these variables were 49.50±12.80 and 43.03±18.47 milliseconds in the pregnant group and 39.5±9.59 and 40.38±17.20 milliseconds in the control group, respectively (P<0.001). **Conclusion:** The QT interval was longer in pregnant women compared to non-pregnant women; however, it was in the normal range in both groups. Therefore, it is important to monitor and manage risk factors involved in prolongation of QT interval and prevent concurrence of these factors with pregnancy.

Key words: Pregnancy; electrocardiography; arrhythmias; ventricular tachycardia

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Introduction:

Long QT syndrome, which is characterized by an increase in QT interval on electrocardiogram (ECG), makes patients susceptible to cardiac arrhythmias, including Torsades de Pointes (TdP), followed by repeated syncope episodes and even sudden death (1). The syndrome has two forms: hereditary and acquired. The hereditary form is a familial genetic canalopathy (2) and the acquired form is a reversible condition induced by an environmental factor, usually a drug from various groups, including some antihistamines, antibiotics, antipsychotic drugs or gastrointestinal prokinetics (3). In addition, several risk factors have been identified involved in prolongation of QT interval and the related arrhythmias, which include hypokalemia, hypomagnesemia, hypothyroidism, and hemodialysis. Concurrence of these factors can increase the risk of ventricular arrhythmia and the subsequent accidents. Therefore, in patients with these risk factors care should be exercised in concomitant prescription of the drugs mentioned above (1). Corrected QT (QTc) and QT dispersion (QTd) indexes are used to evaluate the QT index; QTc is used to correspond the QT interval with the heart rate and both in fact show various dimensions of ventricular repolarization (4). Various physiologic changes occur during pregnancy, including changes in the cardiovascular system. Cardiac arrhythmias are not uncommon during pregnancy and might create different problems for the mother and the fetus (5). On the other hand, female gender is considered as an independent risk factor for long QT syndrome; in this context, QT interval is almost 10% longer in adult females. Various studies have introduced sex hormones (both male and female) as a factor effective on the QT interval (6-9). Considering hormonal changes occurring during the pregnancy, it is possible for the QT interval to be affected. Insufficient data is available in relation to the effect of pregnancy on QT interval. Although the interval is expected to be decreased in pregnancy due to tachycardia, some studies have shown that the interval increases in pregnant women (10). Lechmanova et al. explained the reasons for an increase in QT and QTd intervals in pregnancy as follows: enlarged abdominal organs, hormonal and sympathetic changes, and finally an increase in the impedance of tissues located between the heart and the body surface due to the gradual ac-

***Corresponding Author:** Zahra Yoosefian, Department of Emergency Medicine, Beheshti Hospital, Vali-Asr avenue, Shiraz, Iran; Tel: 00989131059813
Email address: yoosefian@sums.ac.ir
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cumulation of water and sodium during pregnancy (10). On the other hand, studies have shown that patients with long QT syndrome (LQTs) run a higher risk of developing TdP immediately after pregnancy (11-13). Based on above-mentioned, the present study was designed to evaluate and compare the QT interval in pregnant and non-pregnant women to assess the effect of pregnancy on QT interval.

Methods:

Study design and setting

This prospective cohort study was carried out from April 2011 to December 2012 in Shahid Behesthi Hospital, Shiraz, Iran. The protocol of the study was approved by Shiraz University of Medical Sciences and the Ethics Committee of the same university. Informed consent forms were taken from all the subjects.

Participants

The subjects were randomly selected from women referring to the clinic for routine pregnancy examinations. In addition, the control group subjects were randomly selected from the individuals accompanying patients referring to the clinic. 40 women in the second and third trimesters of pregnancy (over 13 weeks of gestational age according to a sonographic examination of the first trimester) were included in the pregnant women group and 40 non-pregnant women who were in their fertile years were included in the control group. Inclusion criteria of the study were an age range of 18-35 years, interest in and ability to take part in the study, an interval of at least one year between the present pregnancy and the previous one. In addition, exclusion criteria were the presence of any arrhythmia in ECG, use of any medication influencing QT interval, affliction with any cardiac and renal disease.

Data collection

Serial evaluation of ECGs was carried out and the cardiac enzymes, including troponin I and cardiac isoenzymes creatine kinase, were checked. Cardiac enzymes were evaluated every six hours up to three times. In addition, ECGs were evaluated whenever chest pain recurred. The age, gender, marital status, occupation, living place and phone number of patients were questioned and registered. They were asked to refer to the exercise test unit of Imam Hossein Hospital during one week after discharging. When the patients returned to the exercise test unit, they were asked about the incidence of cardiac symptoms and signs, recurrence of chest pain or referring to the treatment center again. After the exercise test, the results were collected and patients with positive test underwent angiography. Then, the patients were followed for a month. At the time of discharge, the patients or their relatives received instructions in relation to the symptoms and signs of cardiac diseases.

Endpoints

History of medications used and cardiac diseases, the patients' demographic data, and the gestational ages were recorded. All the subjects were questioned in relation to the occurrence of any of the symptoms and signs of syncope, palpitation, vertigo, angina, and asthma (a collection of symptoms and signs, which might have a cardiac origin) in the six-month period before taking part in the study for the control group and at the beginning of pregnancy for the pregnant group. A standard 12-lead ECG (paper speed of 25 mm/s and a current of 0.5 mv/cm) was recorded from each subject. The QT interval, from the beginning of Q to the end of T, was measured and recorded. Then Bazett's formula, $QTc=QT/\sqrt{RR}$, was used to match the interval with the heart rate. QT dispersion (QTd) was also calculated as the difference between the maximum and minimum QT intervals in a 12-lead ECG (4). The ECGs were also used to determine the presence or absence of any arrhythmia and the axes of QRS and P waves.

Statistical analysis

Data were collected, sorted and analyzed with SPSS 18. Independent t-test was used to compare continuous data between the two groups. Chi-squared test was used to compare qualitative data and frequencies of symptoms and signs between the two groups. Descriptive data were presented as means ± SD. Statistical significance was defined at $P<0.05$.

Results:

Eighty subjects participated in the present study: 40 in the pregnant women group and 40 in the control group, with mean ages of 29±2.8 and 28±3.2 years, respectively. The mean gestational age of pregnant women was 29.21±7.40 weeks (19-42). Sixteen patients (41%) had their first pregnancy, 134 (33.3%) second pregnancy, eight (20.5%) third pregnancy, one (2.6%) fourth pregnancy and one (2.6%) fifth pregnancy. QRS and P waves of all the subjects were in the normal range, with no significant differences between the two groups ($P>0.05$). QTc and QTd were higher in the pregnant group versus the control (0.001). It should be pointed out that the means of these two variables were in the normal range. Table 1 presents the details of comparisons of QTc, QTd, and heart rates between the two groups. In general, there were no significant differences between the means of QTc and QTd between pregnant women in their second trimesters and those in their third trimesters ($P>0.05$) (Table 2).

Discussion:

The results of present study showed a longer QT interval in pregnant women versus non-pregnant. However, QTd and QTc means were in the normal range in both groups. A research in available library and electronic sources showed only a limited number of studies with similar themes. There are some studies on the effect of pregnancy on patients with LQTS (12-16). Lechmanova et al. (2002) evaluated QT interval and T-loop morphology in pregnant and non-pregnant women. They com-

pared 37 healthy pregnant women with gestational ages of 36-40 weeks with 18 healthy non-pregnant women. All the subjects underwent electrocardiography and vectorcardiography evaluations. Finally, it was concluded that QTc and QTd were significantly higher in pregnant women compared to the control group (10), consistent with the results of the present study. Isezuo et al. (2004) evaluated and compared QT intervals between pregnant women with and without eclampsia. They did not make comparisons with the control non-pregnant women. In general, the mean QTc in the group with eclampsia (47.0 milliseconds) and the group without it (43.6 milliseconds) was higher than that in the present study (41.75 milliseconds) (17). Seth et al. concluded that pregnant women with a previous definitive diagnosis of LQTS run a lower risk of cardiac accidents during pregnancy, including syncope and sudden death due to cardiac arrest. However, during the first nine months after delivery, the risk of cardiac accidents, especially life-threatening accidents, increases. After this period, the risk level returns to the baseline before pregnancy (13). Rashba et al. (1998) reported similar results (12). None of the two studies above evaluated the question whether the QT interval changes during pregnancy or after it. Seth et al. described the reason for a decrease in cardiac accidents due to LQTS during pregnancy and an increase in such accidents after pregnancy as follows: Pregnancy results in an increase in the referral of women to health and treatment centers, which might lead to prevention of cardiac accidents. On the other hand, although the QT intervals were not different between nulliparous women and those with previous pregnancies, women with no history of delivery before the age of 15 had experienced more cardiac accidents and received more treatments with β-blockers, all of which might have prompted them to refrain from becoming pregnant (13).

During the period after delivery, hemodynamic changes occur, which might be related to an increase in arrhythmias. For example, cardiac output, which increases significantly during pregnancy, decreases suddenly. Rashba et al. proposed the hypothesis that an increase in cardiac accidents in patients with LQTS after delivery might be attributed to a change in adrenergic activity. They also reported that an increase in heart rate during pregnancy could have a protective effect in patients with LQTS, who might have a longer QT interval at lower heart rates; after delivery, this rate returns to the baseline. Therefore, this protective role is negated, increasing the odds of QT interval Prolongation, and incidence of arrhythmias (12). Some other studies have shown that other factors such as an increase in stress, fatigue, insomnia, and other environmental factors are effective in increasing the risk of cardiac accidents due to LQTS during pregnancy. Another opinion about the possible cause of the relationship between pregnancy and a change in QT interval is the relation between sex hormones and ventricular repolarization. Several studies have evaluated this relationship but no definitive results have been achieved. One of the risk is that both exogenous and endogenous sex hormones can influence QT interval (6, 7, 18, 19). In general, during sexual maturation the QT interval is shortened about 20 milliseconds in males; however, it does not undergo any changes in females. In fact, the QT interval is not significantly different between the two sexes and the shortening during sexual maturation is responsible for the difference (20). Some studies have suggested that testosterone is related to shorter repolarization in men (21). Based on a report by Naagawa et al. the QT interval in the luteal phase is shorter than that in the follicular phase, which might be attributed to the effect of progesterone (18). Therefore, it is possible that the QT interval is influenced by hormonal changes due to pregnancy. However, some studies have shown that hormonal changes in pregnancy decrease the risk of TdP in pa-

Table 1: Comparisons of QTc, QTd, and heart rates between the pregnant and non-pregnant groups

Variables	Groups	Minimum	Maximum	Mean±SD	P
Heart rate	Pregnant	68	130	98.55±14.09	<0.001
	Control	51	118	72.53±13.17	
QTd	Pregnant	30	80	49.50±12.80	<0.001
	Control	20	60	39.50±9.59	
QTc	Pregnant	380	460	430.30±18.47	<0.001
	Control	370	440	403.80±17.20	

Table 2: Comparison of QTc and QTd between the second and third trimesters

Variable	Trimester	Number of patients	Mean ± SD	P
QTc	Second	17	431.3±15.98	0.726
	Third	23	429.1±20.43	
QTd	Second	17	48.67±11.80	0.915
	Third	23	49.13±13.78	

tients with LTQS (13). One of the limitations of the present study was the unavailability of the patients' previous ECGs for making comparisons. On the other hand, there were limitations in the selection of controls; selection of controls from first-degree relatives was more logical and not possible. Further studies are necessary to confirm or refute the results of the present study.

Conclusion:

The QT interval in pregnant women was in the normal range but longer compared to non-pregnant women. Therefore, other factors that might be involved in prolongation of the QT interval should be taken into account and care should be exercised to prevent their concurrence with pregnancy as far as possible.

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