Original Article

QT interval changes in term pregnant women living at moderately high altitude

G Batmaz, AN Aksoy[1], S Aydın, NK Ay[2], B Dane

Departments of Obstetric and Gynecology and [2]Cardiology, Faculty of Medicine, Bezmialem Vakıf University, İstanbul, [1]Department of Obstetrics and Gynecology, Nenehatun Hospital, Erzurum, Turkey

Abstract

Objective: This study aimed to compare the QT interval changes in women with term pregnancy living at moderately high altitude (1890 m in Erzurum, Turkey) with those of women living at sea level (31 m in İstanbul, Turkey).
Materials and Methods: One-hundred ten women (n = 55, for each group) with full-term and single child pregnancies. Two different locations in that state were selected: İstanbul, Turkey, which is at 31 m above sea level (Group 1) and Erzurum, Turkey, at 1890 m above sea level (Group 2). Physicians from the two locations participated in the study. We estimated QTc, QTc Max, QTc Min, QT, and QTcd intervals.
Results: Moderately high altitude group had significantly longer QT parameters (QTc, QTc Max, QTc Min, QT, and QTcd intervals) compared with sea level group ($P < 0.01$, for all).
Conclusions: According to our results, QT interval changes occur in term pregnant women living moderately high altitude. These changes may be associated with pregnancy-related cardiovascular complications in moderately high altitude.

Key words: Moderately high altitude, pregnancy, QT interval

Date of Acceptance: 20-Dec-2015

Introduction

The altitude of a location is calculated as the distance from the mean sea level in the territory. Altitude is measured in feet in the United States and England but is measured in meters in the rest of the world. In the Eastern anatolian territory of Turkey, Erzurum, at 1890 m, has the highest altitude in Turkey. In contrast, İstanbul, Turkey at 31m, has a much lower altitude. Exposure to high altitude leads to a decrease in arterial blood oxygen saturation.[1] People living at high altitude for a long period experience changes in their respiratory, cardiovascular and hematological systems in response to an increase in hypoxemia blood viscosity, decrease in blood volume, and fall in cardiac output.[2,3]

Address for correspondence:
Dr. G Batmaz,
Department of Obstetric and Gynecology, Faculty of Medicine,
Bezmialem Vakıf University, Adnan Menderes Bulvari,
Fatih, Istanbul, Turkey.
E-mail: drgoncabatmaz@yahoo.com

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/1119-3077.188707

Pregnancy leads to changes in the respiratory, cardiovascular and hematological systems. These include a decrease in mean arterial pressure and peripheral vascular resistance, as well as an increase in circulating volume, heart rate, and cardiac output. Heart rate variability, which refers to variability in the QRS interval of body surface electrocardiography (ECG), has been shown to alter during pregnancy.[4,5] Early atrial and ventricular beats can be seen during pregnancy.[6] In addition to these changes, pregnant women living at high altitude also experience an increase in erythropoietin and hematocrit levels, cerebral vasodilation, and pulmonary vasoconstriction, and right ventricular hypertrophy has also been reported.[7,8]

How to cite this article: Batmaz G, Aksoy AN, Aydın S, Ay NK, Dane B. QT interval changes in term pregnant women living at moderately high altitude. Niger J Clin Pract 2016;19:611-5.

In ECG, the QT interval shows the duration of ventricular depolarization–repolarization and the distance between the longest QT interval (QT max) and the shortest QT interval (QT min) is called QT dispersion. If the corrected QT interval (according to heart rate) is used, it is called corrected QT dispersion (QTcd). It has been accepted that QTcd shows localized heterogeneity in myocardial repolarization. Regardless of the effects of high altitude, different electrical impulse speeds in different ventricular areas aggravate a previously existing silent arrhythmia or lead to de novo arrhythmias due to neurohormonal and hemodynamic changes during pregnancy.[9]

We hypothesized that maternal cardiovascular circulation might be affected by moderately high altitude. For this purpose, we compared the differences in QT interval changes in women with term pregnancy living at moderately high altitude (1890 m in Erzurum/Turkey) with those of women living at sea level (31 m in İstanbul/Turkey).

Materials and Methods

Study design and participants

This descriptive study was approved by the Ethics Committee of Bezmialem Vakıf University, İstanbul, Turkey and written informed consent was obtained from all participants. Two different locations in that state were selected: İstanbul, Turkey which is at 31m above sea level (Group 1) and Erzurum, Turkey, at 1890 m above sea level (Group 2). A group of 110 women aged between 20 and 40 years with full-term pregnancies (≥37 gestational weeks) admitted to the obstetric departments of two institutes for the control were enrolled in this study. All women were of Turkish ethnicity and permanently resident at that altitude. Patients with multiple pregnancies, complicated pregnancies (e.g., preeclampsia, fetal malformation, gestational diabetes mellitus and placenta previa), smoking, chronic illnesses (e.g., hypertension, diabetes mellitus), and no certain menstrual history were excluded from the study.

The age, height, weight, and body mass index (BMI) of patients were recorded. The systolic and diastolic blood pressures of all subjects were measured from the right brachial artery using a mercury sphygmomanometer after at least 5 min of resting and patients were weighed wearing light clothing and barefoot by a weighing scale with a sensitivity of 0.1 kg. Height measurements were carried out while patients were standing barefoot with a sensitivity of 0.01 m. BMI was measured by dividing body weight in kilograms by the square of the height in meters (kg/m^2).

Electrocardiography

ECG (12-lead) was used for QT interval measurements. ECGs were recorded by a Cadioline delta 1 plus machine at a rate of 25 mm/s and 10 mm/mV. The QT interval was measured in milliseconds from the beginning of the Q wave to the end of the T wave on the isoelectric line. The derivations in which the end of the T wave was not clear were ignored. According to the Bazzet formula (QT/√R-R), the corrected QT interval was measured using heart rate. The mean of three subsequent corrected QT intervals in a lead was accepted as the QTc of that lead. The patients with QTc intervals from at least nine leads were enrolled in the study. QTc dispersion was measured by finding the difference between the longest QTc interval (QTcmax) and the shortest QTc interval (QTc min). All the measurements were taken manually.

Statistical analysis

Data were analyzed using SPSS software 12.0 (SPSS Inc., Chicago, IL, USA) and expressed as mean ± standard deviation; $P < 0.05$ was considered statistically significant. The Kolmogorov–Smirnov test was used to test for normality of variables. If data were not normally distributed, comparisons were determined using the Mann–Whitney U-test. Comparisons were determined using the independent samples *t*-test when the data were normally distributed, and Fisher's exact test was used to compare the percentage values.

Results

The demographic characteristics including mean age (years), gravid, and parity are presented in Table 1. There were no

Table 1: Clinical characteristic of patients living at sea level and moderately high altitude

	Sea level group (*n*=55)	Moderately high altitude group (*n*=55)
Age (years)	28.9±4.6	29.7±4.2
Body mass index (kg/m^2)	29.5±1.1	29.10±1.1
Parity	2.62±1.1	2.70±1.13
Mean gestational age (weeks)	38.96±1.17	39.01±1.1

Data were expressed as mean±SD. SD=Standard deviation

Table 2: The comparison of electrocardiographic parameters, systolic and diastolic arterial blood pressure in groups

	Group 1 (*n*=55)	Group 2 (*n*=55)	*P*
QT interval (ms)	330±28.8	360±30	<0.01†
QTc interval (ms)	409±29.7	415±32	<0.05*
QTc maximum (ms)	425±29	448±30	<0.01†
OTc minimum (ms)	389±28	412±28.5	<0.01†
QTcd (ms)	28±15.6	48.8±8	<0.01†
SAP (mm Hg)	110±11	127±9.3	<0.01†
DAP (mm Hg)	70±8.3	72±8.4	0.564

Values are median±SD. *$P<0.05$; †$P<0.01$; compared with moderately high altitude group. HR=Heart rate; SAP=Systolic arterial pressure; DAP=Diastolic arterial pressure; SD=Standard deviation, QTcd=Corrected QT dispersion, QTc=Corrected QT differences in clinical characteristics between the groups. ECG parameters in groups are presented in Table 2. The QT, corrected QT, QTc Max, QTc Min, and QTcd intervals were within normal limits in the two groups, but it was significantly longer at moderately high altitude when compared with sea level altitude. Systolic blood pressure was found statistically to be significantly higher in subjects at moderately high altitude when compared with sea level altitude. On the other hand, for diastolic arterial pressure, even with high readings, the difference was not statistically significant.

Discussion

In this study, we compared the QT interval changes in term pregnant women living at sea level with those living at moderately high altitudes. We found significantly longer QT parameters (QTc, QTc Max, QTc Min, QT, and QTcd intervals) in the moderately high altitudes group compared with the sea level group.

It is known that high altitude adaptations (such as an increase in blood viscosity, a reduction in blood volume, and a decline in cardiac output) are associated with the changes in oxygen uptake and transport that occur in response to hypoxemia.[10-12] The QT interval varies according to biological characteristics such as age, gender, race, nutritional state, and perhaps many others.[13] Ventricular repolarization can also be affected by hormonal and electrolyte changes during pregnancy[14] and increased sympathetic neural out-flow.[15] High altitude exposure over a long period causes pulmonary hypertension, right ventricular hypertrophy, and insufficiency.[16,17] Right ventricular hypertrophy due to high altitude can cause ECG changes. The longer the QTcd, the lower the ventricular repolarization homogeneity and the higher the ventricular instability.[18] It has been shown that an increase in QTcd increases the risk of ventricular arrhythmias, syncope, and sudden cardiac death.[19]

According to our findings, pregnant women living at a moderately high altitude had longer QT, QTc, QTcd, and QTc max and QTc min durations compared with those of women living at sea level. These differences were statistically significant even though within normal limits. In contrast to our results, Guntekin *et al.* reported no significant difference between high altitude and sea level habitants in respect to heart rate and QT variables.[20] Altitude difference in our study was similar to their study. However, our study population consisted of term pregnant women while theirs consisted of healthy men and women. It was shown that cardiovascular influences may occur due to hormonal and hemodynamic changes and an expanding uterus during pregnancy.[4-6] It is unclear, however, as to which physiological mechanisms explain these difference results.

Our data obtained from pregnant women living at different altitudes show that depolarization is slower in pregnant women at moderately high altitude, and it is thought that this slow rate is compensated for by rapid repolarization. It is unclear why a slower depolarization occurs in pregnant women at high altitude. There may be a neuroendocrine response caused by chronic hypoxia. In fact, Panjwani *et al.* reported elevated plasma epinephrine, norepinephrine, dopamine, and cortisol levels following high altitude exposure.[21] Also, decreases in plasma volume, increases in hemoglobin concentration and erythropoietin production caused by high altitude[2,12] may have an influence on impulse conduction in women living moderately high altitude. On the other hand, this slower depolarization may be a result of environmental effects of ischemia caused by high altitude. We suggested that pregnant women living at moderately high altitudes might have a higher risk for cardiovascular complications because of longer QTcd intervals.

Many drugs can prolong the QT interval and a combination of these drugs when used together can increase the possibility of arrhythmia.[22] Kim *et al.* showed that spinal anesthesia prolongs the QTc interval in healthy individuals.[23] Saarnivaara *et al.* showed that changes in ventricular repolarization due to anesthetic agents can lead to a prolonged QTc interval.[24] Studies show that postoperative intravenous (IV) bolus oxytocin infusion, which is the most commonly used medical agent in abortion, normal birth, and cesarean section, significantly increases the QTc interval.[25,26] Sen *et al.* showed that after IV oxytocin infusion, the QTc interval does not change, but they stated that this is due to the slow infusion rate.[27] Another study shows that after IV oxytocin infusion in patients undergoing curettage in the first trimester of pregnancy under general anesthesia, there is a transient increase in the QTc interval.[26] Because of these findings, caution should be taken with pregnant women at high altitudes before giving anesthesia and oxytocin.

According to our investigation, we found higher systolic blood pressure values in pregnant women living at moderately high altitude compared with the women living at sea level. According to the literature, researchers show that preeclampsia and gestational hypertension are more common in pregnant women living at high altitudes than pregnant women living at lower altitudes.[28,29] Also, Kumtepe *et al.* showed that the incidence of eclampsia is higher among women living at high altitudes.[30] These studies confirm our study which shows a significant difference in systolic blood pressure in normotensive women living at different altitudes. In contrast to our results, Kametas *et al.* reported lower mean arterial pressure values in the high altitude compared with the sea level group. While altitude difference was 4350 m in their study, it was 1860 m in our study. Also, they examined pregnant women at 5–41 weeks of gestation while our study population was selected from term pregnant women.[31] Our findings are compatible with the data of Moore *et al*.,[32] who found higher mean arterial pressure values in the high altitude compared with the sea level. Also, they reported that the prevalence of preeclampsia at 3100 m was 4 times higher than at 1600 m.

According to our knowledge, no study has so far studied the depolarization–repolarization process in pregnant women living in areas with an altitude difference. Our study has two limitations. The most important limitation is manual calculation of P-wave and QT measurements using a magnifying lens instead of computer-assisted P-wave calculations, but several studies have suggested that manual P-wave dispersion measurement on paper-printed ECGs obtained at a standard signal size and paper speed may have a questionable accuracy and reproducibility.[33] Second limitation is the fact that we have no information about cardiovascular complications of pregnancies that may occur during pregnancy, childbirth, or postpartum period. Hence, further studies are needed to evaluate the association between numerical QT interval differences and the clinical outcome of pregnancies.

Conclusion

We found increased QT, QTc, and QTcd intervals in pregnant women living at high altitudes compared with those living at sea level. According to our results, pregnant women living at high altitudes have exaggerated physiological changes due to hypobaric hypoxia, and one of the results is changes in the ECG parameters. It suggested that changes in ECG parameters at high altitude might increase pregnancy-related cardiac complications.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Hannon KR, Pendergast DR, Strauss HC. Electrocardiogram at an altitude of 3600 m with reference to T wave depression. Aviat Space Environ Med 2014;85:653-7.
2. Steinacker JM, Liu Y, Böning D, Halder A, Maassen N, Thomas A, *et al.* Lung diffusion capacity, oxygen uptake, cardiac output and oxygen transport during exercise before and after an himalayan expedition. Eur J Appl Physiol Occup Physiol 1996;74:187-93.
3. Humphreys S, Deyermond R, Bali I, Stevenson M, Fee JP. The effect of high altitude commercial air travel on oxygen saturation. Anaesthesia 2005;60:458-60.
4. Faber R, Baumert M, Stepan H, Wessel N, Voss A, Walther T. Baroreflex sensitivity, heart rate, and blood pressure variability in hypertensive pregnancy disorders. J Hum Hypertens 2004;18:707-12.
5. Voss A, Malberg H, Schumann A, Wessel N, Walther T, Stepan H, *et al.* Baroreflex sensitivity, heart rate, and blood pressure variability in normal pregnancy. Am J Hypertens 2000;13:1218-25.
6. Gowda RM, Khan IA, Mehta NJ, Vasavada BC, Sacchi TJ. Cardiac arrhythmias in pregnancy: Clinical and therapeutic considerations. Int J Cardiol 2003;88:129-33.
7. Antezana AM, Richalet JP, Noriega I, Galarza M, Antezana G. Hormonal changes in normal and polycythemic high-altitude natives. J Appl Physiol (1985) 1995;79:795-800.
8. Kamitomo M, Longo LD, Gilbert RD. Right and left ventricular function in fetal sheep exposed to long-term high-altitude hypoxemia. Am J Physiol 1992;262 (2 Pt 2):H399-405.
9. Nakagawa M, Katou S, Ichinose M, Nobe S, Yonemochi H, Miyakawa I, *et al.* Characteristics of new-onset ventricular arrhythmias in pregnancy. J Electrocardiol 2004;37:47-53.
10. Penaloza D, Arias-Stella J. The heart and pulmonary circulation at high altitudes: Healthy highlanders and chronic mountain sickness. Circulation 2007;115:1132-46.
11. Paralikar SJ, Paralikar JH. High-altitude medicine. Indian J Occup Environ Med 2010;14:6-12.
12. Tarazona-Santos E, Lavine M, Pastor S, Fiori G, Pettener D. Hematological and pulmonary responses to high altitude in Quechuas: A multivariate approach. Am J Phys Anthropol 2000;111:165-76.
13. Okin PM, Devereux RB, Howard BV, Fabsitz RR, Lee ET, Welty TK. Assessment of QT interval and QT dispersion for prediction of all-cause and cardiovascular mortality in American Indians: The strong heart study. Circulation 2000;101:61-6.
14. Varon ME, Sherer DM, Abramowicz JS, Akiyama T. Maternal ventricular tachycardia associated with hypomagnesemia. Am J Obstet Gynecol 1992;167:1352-5.
15. Greenwood JP, Scott EM, Stoker JB, Walker JJ, Mary DA. Sympathetic neural mechanisms in normal and hypertensive pregnancy in humans. Circulation 2001;104:2200-4.
16. Mirrakhimov M, Winslow R. The cardiovascular system at high altitude. In: Blatties CM, Fregly MJ, editors. Handbook of Physiology: Environmental Physiology. 4th ed. Oxford University Press; 1996. p. 1241-58.
17. Tuncer M, Gunes Y, Guntekin U, Aslan S, Gumrukcuoglu HA, Eryonucu B, *et al.* Association of increased QTc dispersion and right ventricular hypertrophy. Med Sci Monit 2008;14:CR102-5.
18. Day CP, McComb JM, Campbell RW. QT dispersion: An indication of arrhythmia risk in patients with long QT intervals. Br Heart J 1990;63:342-4.
19. Galinier M, Vialette JC, Fourcade J, Cabrol P, Dongay B, Massabuau P, *et al.* QT interval dispersion as a predictor of arrhythmic events in congestive heart failure. Importance of aetiology. Eur Heart J 1998;19:1054-62.
20. Guntekin U, Gunes Y, Tuncer M, Gumrukcuoglu HA, Kaya Y. The effect of altitude on P-wave and QT duration and dispersion. Pacing Clin Electrophysiol 2008;31:889-92.
21. Panjwani U, Thakur L, Anand JP, Malhotra AS, Banerjee PK. Effect of simulated ascent to 3500 meter on neuro-endocrine functions. Indian J Physiol Pharmacol 2006;50:250-6.
22. Elming H, Sonne J, Lublin HK. The importance of the QT interval: A review of the literature. Acta Psychiatr Scand 2003;107:96-101.
23. Kim Y, Kim SY, Lee JS, Kong HJ, Han DW. Effect of dexmedetomidine on the corrected QT and Tp-e intervals during spinal anesthesia. Yonsei Med J 2014;55:517-22.
24. Saarnivaara L, Klemola UM, Lindgren L, Rautiainen P, Suvanto A. QT interval of the ECG, heart rate and arterial pressure using propofol, methohexital or midazolam for induction of anaesthesia. Acta Anaesthesiol Scand 1990;34:276-81.
25. Guillon A, Leyre S, Remérand F, Taihlan B, Perrotin F, Fusciardi J, *et al.* Modification of Tp-e and QTc intervals during caesarean section under spinal anaesthesia. Anaesthesia 2010;65:337-42.
26. Charbit B, Funck-Brentano C, Samain E, Jannier-Guillou V, Albaladejo P, Marty J. QT interval prolongation after oxytocin bolus during surgical induced abortion. Clin Pharmacol Ther 2004;76:359-64.
27. Sen S, Ozmert G, Turan H, Caliskan E, Onbasili A, Kaya D. The effects of spinal anesthesia on QT interval in preeclamptic patients. Anesth Analg 2006;103:1250-5.

28. Keyes LE, Armaza JF, Niermeyer S, Vargas E, Young DA, Moore LG. Intrauterine growth restriction, preeclampsia, and intrauterine mortality at high altitude in Bolivia. Pediatr Res 2003;54:20-5.
29. Moore LG, Shriver M, Bemis L, Hickler B, Wilson M, Brutsaert T, *et al.* Maternal adaptation to high-altitude pregnancy: An experiment of nature – A review. Placenta 2004;25 Suppl A: S60-71.
30. Kumtepe Y, Dündar O, Cetinkaya K, Ingeç M. Preeclampsia and eclampsia incidence in the eastern anatolia region of Turkey: The effects of high altitude. J Turk Ger Gynecol Assoc 2011;12:26-30.
31. Kametas NA, McAuliffe F, Krampl E, Chambers J, Nicolaides KH. Maternal cardiac function during pregnancy at high altitude. BJOG 2004;111:1051-8.
32. Moore LG, Hershey DW, Jahnigen D, Bowes W Jr. The incidence of pregnancy-induced hypertension is increased among Colorado residents at high altitude. Am J Obstet Gynecol 1982;144:423-9.
33. Dilaveris PE, Gialafos JE. P-wave duration and dispersion analysis: Methodological considerations. Circulation 2001;103:E111-1.