

NON OBESE YOUNG INDIAN WOMEN MENSTRUAL IRREGULARITIES HAVE NORMAL QT AND CORRECTED QT PARAMETERS – A CASE CONTROL STUDYDr. Malathi Balamurugan^{1*} and Dr. Balamurugan Maruthamuthu²¹Associate Professor, Department of Physiology, Karuna Medical College, Velayodi, India.²Chief Consultant and Medical Director, Vadavalli Medical Centre, Coimbatore, India.***Corresponding Author: Dr. Malathi Balamurugan**

Dr. Malathi Balagurugan, Associate Professor, Department of Physiology, Karuna Medical College, Velayodi, India.

Article Received on 22/07/2018

Article Revised on 12/08/2018

Article Accepted on 02/09/2018

ABSTRACT

Background: Menstrual irregularities (MI) is a wide spectrum of clinical disorders with prevalence of 2%- 17% in India. The QTc interval duration, which is related to cardiac arrhythmia, sudden death and a sign of cardiac autonomic neuropathy, has not been investigated thoroughly in these patients. **Aim:** To investigate the potential alterations in electrocardiographic – QT parameters in lean and ideal weight young Indian patients with MI. **Methodology:** 19 patients with MI who were lean or ideal weight as per WHO criteria and 25 BMI matched normally menstruating women served as study participants. All of them underwent assessments clinically and by appropriate laboratory tests. Using Bazetts formula QT interval, minimum and maximum QT interval (QT Max and QT Min), QT dispersion (QTd), QT interval corrected for heart rate (QTc), minimum and maximum QT interval (QTcmin and QTcmax, respectively) rate, corrected QT dispersion (QTcd). Unpaired Student t test was used, Pearsons correlation and Binary logistic regression analysis was done to bring out the association between the variables. **Results:** QT ($0.378 \pm .027$ vs $0.429 \pm .053$, P value < 0.001) ; QTmax max ($0.419 \pm .035$ vs 0.464 ± 0.064 , P value < 0.01) ; QTmin ($0.355 \pm .033$ vs $0.399 \pm .047$, P value = < 0.01) ; QTc interval (0.406 ± 0.092 vs $0.472 \pm .052$, P value= < 0.01) , QTc max (0.471 ± 0.032 vs 0.512 ± 0.068 , P value= < 0.05), QTc min (0.399 ± 0.030 vs 0.439 ± 0.050 , P value= < 0.01) were significantly altered. QTd ($0.064 \pm .027$ vs 0.065 ± 0.038 , P value= 0.951) and QTcd (0.072 ± 0.044 vs 0.071 ± 0.043 , P value = 0.958) were not significantly. QT parameters correlated significantly with other parameters. Neck circumference and RR interval came out to be significantly greater individual impact predictors of MI. **Conclusion:** In this study the non- obese young women with menstrual irregularities had normal QT interval compared to controls .Therefore they do not have an increased risk of cardiac arrhythmias compared to the controls.

KEYWORDS: Non-obese, Menstrual irregularities, QT interval, Corrected QT interval.**INTRODUCTION**

Menstrual irregularities is a wide spectrum of clinical disorders with wide range of prevalence rate all over the world and in India it is 2%- 17%.^[1,2] There are several types menstrual irregularities, like Polymenorrhoea-increased frequency of cycles (with intervals of 21 days or less), Oligomenorrhoea – decreased frequency (interval between menstruation exceeds 35 days), Amenorrhoea (absence of menstruation > 60 days in reproductive age group), Dysmenorrhoea (cramps or painful menstruation), Hypomenorrhoea (a decrease in menstrual flow or a decreased duration of menstruation) and Menorrhagia (an abnormally heavy and/- or prolonged menstrual period).^[3]

Many females also complain of pain, anxiety, depression, fatigue, and vomiting during the menstrual cycle throughout their reproductive life.^[3] Psychological factors, stress and deprivation were found to be

associated with menstrual irregularities.^[4] Cardiovascular risk in women with menstrual dysfunction is very limited.

QT interval prolongation, corrected for heart rate (QTc), either spontaneous or drug-induced, is associated with an increased risk of torsades de pointes and sudden death.^[5] A prolonged QT interval is a risk in long QT syndrome,^[6] after myocardial infarction,^[7] and even in healthy individuals.^[8,9]

In our previous study in a group of lean Polycystic ovarian syndrome (PCOS) patients significant differences in QT interval parameters were observed though corrected QT parameters were not altered. With corrected QT parameters, all were increased more than normal values in both patients and controls. This shows hormonal changes per se may not be the cause for the prolonged corrected QT parameters seen in PCOS.^[10]

Also HRV parameters,^[11] and Poincare parameters showed cardiac autonomicity is affected in PCOS.^[12] Therefore we inclined to evaluate if QT parameters were affected in non-obese patients with menstrual problems.

It has been shown that there are gender differences in heart rate, QT interval duration, and in the relation between ventricular repolarization and cardiac cycle length.^[13] Women have slower cardiac repolarization than men, which manifests as longer heart rate corrected QT intervals (QTc) on the electrocardiogram (ECG),^[14] and have a higher heart rate.^[15] This sex difference is apparent only after puberty.^[16]

Furthermore, women are more prone than men to develop torsades de pointes ventricular arrhythmias after administration of drugs that prolong cardiac repolarization (eg, antiarrhythmic drugs, terfenadine, erythromycin, etc).^[17,18] A further QT interval prolongation at long cycle lengths,^[15] and a more significant effect of QTc-prolonging drugs in women, compared with men, have been demonstrated.^[19] There is a role for sex hormones in the response to drugs that alter cardiac repolarization, potassium channel expression, ion currents, and QT response to drugs.^[20]

During the menstrual cycle there is a dynamic change in circulating levels of estrogen and progesterone. In the absence of a drug that alters cardiac repolarization, QTc does not change during the menstrual cycle.^[21] The role of the main sex steroid hormones has been extensively studied with inconsistent findings. Overall, estradiol is considered to promote QTc lengthening while progesterone and testosterone shorten QTc.^[5] The observed shorter QT interval during the luteal than the follicular phase may be attributable to the increase in serum progesterone and sympathetic tone.^[22] There is also complex regulation of QTc by sex steroid hormones involving gonadotropins, the relative concentrations of sex steroid hormones (which depends on gender, i.e., progesterone/estradiol ratio in women).^[5]

The aim of the present study was to investigate the effects of potential alterations in QT interval in non-obese patients with menstrual irregularities. We hypothesized that patients with menstrual irregularity are associated with altered QT parameters.

MATERIAL AND METHODS

This case control study was conducted in the Department of Physiology, Karuna medical college. Both study and control groups gave written informed consent. Also clearance from the Institute's Human Ethics Committee was obtained. The patient study group included women who presented to the gynaecologists with complaints of dysfunctional uterine bleeding, or infertility and any abnormal uterine bleeding like Amenorrhoea, oligomenorrhoea, dysmenorrhoea, menorrhagia, metrorrhagia etc.

Sample size calculation According to the disease prevalence in India (1,2) the sample size was calculated. Calculated sample size was 19, with the prevalence (p value) set at 0.5 and precision (d value) at 0.05, within the confidence interval of 95%.

Subjects

a. Patient group: 19 non-pregnant ideal and lean weight (measured by BMI – body mass index as per the WHO criteria,^[23] **women with menstrual irregularity.**

b. Control group: 25 regularly menstruating (every 27–32 days) volunteer medical students, doctors, nurses, and staff of the hospital and who were matched BMI were included.

Inclusion criteria for both groups included young women aged 16–30, they were lean or ideal weight according to BMI and W/H ratio, waist circumference less than < 80 cm, they were not on any medications affecting lipid or carbohydrate metabolism at least for past 2 months. Exclusion criteria included, women below 16 and above 30, pregnant women, lactating women, had attained menopause, those who had undergone hysterectomy and women taking lipid lowering drugs for the past 2 months. Women on oral hypoglycemic drugs or insulin sensitizing agents, oral contraceptives, and sex steroids for last 2 months and those patients on current infertility treatment were excluded. Control group were in their follicular phase (6–8 days the start of menstruation) and cases were amenorrhoeic during data recording.

The anthropometric parameters, Baseline cardiovascular parameters and QT parameters were registered. They are

The anthropometric parameters

a. Body mass index (BMI): Height and weight (wt) were measured for the study group. Height was measured in centimeters using the height measuring scale .Using Electronic weighing machine weight was measured. From this BMI was obtained by dividing weight in kg by square of the height (in meters). They were selected according to World Health Organization obesity is graded as underweight (BMI < 18.5 kg/m²), normal (18.5–24.9 kg/m²), pre-obese (25.0–29.9 kg/m²), and class I obese (30.0–34.9 kg/m²).^[23]

b. Waist circumference: Subject in standing position , points were marked on them.^[24] It was measured half way between the lower border of the ribs and the iliac crest in the horizontal plane. Two measurements to the nearest 0.5 cm were measured. A third measurement was taken if the variation between the measurements were >2 cm. The mean of the 2 closest measurements was calculated. For females waist circumference 80–87.9 cm was graded as overweight and ≥ 102 cm as obese.^[24]

c. Waist hip ratio (WHR): Calculated to find if they have increased risk with abdominal obesity. WHR > 0.85

in women which denotes risk and lower cut-offs (0.80 in women).^[25]

d. Neck circumference (NC): Measured vertically against the major axis of the neck at the height just below the Adam's Apple,^[26] in the midway of the neck, between mid-cervical spine and mid anterior neck, to within 1 mm, using non-stretchable plastic tape with the subjects standing upright with accordance by the by National Institute of Tech and Evaluation guidelines.^[27] Neck circumference is a good clinical predictor of menstrual irregularity, hirsutism, infertility, insulin resistance and the PCOS.^[26] Also NC >37 cm in men and NC >34 cm in women are best cutoff points to determine subjects with central obesity.^[28]

Baseline cardiovascular parameters

a. Resting heart rate (RHR): In sitting posture, after 5 min of complete rest, the pulse rate was counted for complete 1min by palpating the left radial artery at wrist.

b. Resting blood pressure (RBP): After 20 min of quiet supine rest, systolic and diastolic blood pressure was recorded, from right arm to the nearest 2 mmHg. Blood pressure was defined as the points of the appearance and disappearance of Korotokoff sounds, respectively. Instrument used was manual sphygmomanometer (a Novaphone make).

c. Rate-Pressure Product (RPP): a determinant of myocardial oxygen consumption and workload was calculated using the formula.^[29] $RPP = (BHR \times SBP) \times 10^{-2}$

QT parameters

The participants in supine position, eyes open, after lying in 20 minutes of complete rest, a continuous lead II ECG was recorded for a minute. All ECGs were evaluated blindly The RR and QT intervals are to be measured from seven cardiac cycles from a recording of lead II of the resting ECG. The QT interval was measured from the earliest onset of the QRS complex to the terminal portion of the T wave, at the baseline.^[30] The RR interval from the preceding cardiac cycle is to be measured from the peaks of the R waves to correct the QT interval for heart rate (QTc). This was calculated using Bazett formula.^[31]

QT and QTc Parameters obtained were

1. QTmax = Longest calculated QT interval.
2. QTcmax = Longest calculated corrected QT interval.
3. QTmin = Shortest calculated QT interval.
4. QTcmin = Shortest calculated corrected QT interval.
5. QTd = The difference between maximum QT interval and minimum QT interval.
6. QTcd = The difference between QTcmax and QTcmin.

Table 1: Bazett-Corrected QTc Values for Diagnosing QT Prolongation.^[32]

Rating (msec)	Adult Male (msec)	Adult Female (msec)
Normal	<430	<450
Borderline	430–450	450–470
Prolonged	>450	>470

Statistical Analysis The statistical test used was unpaired Students 't'-test. Pearsons correlation analysis was done between the QT parameters and the baseline parameters. A linear logistic regression was done to find the predictors of baseline parameters and QT parameters to the likelihood of participants having a menstrual problem. Statistical significance of P-value is set at at p < 0.05.

RESULTS

Baseline characteristics of lean and ideal weight menstrual irregularity patient (MI) and control group showed Mean \pm SD of age of the patient was 20.90

± 3.053 and the control was 24.08 ± 4.64 , p value < 0.01. According to BMI (case 19.43 ± 1.80 vs control 20.71 ± 2.78 , p value 0.072) and Waist Circumference (case 68.75 ± 11.00 vs control 76.00 ± 8.51 , p value <0.05), they belonged to lean and ideal weight group. With W / H ratio (case 0.796 ± 0.044 vs control 0.810 ± 0.037) which didnot show significant difference, they were of no high risk. Neck circumference (32.47 ± 3.13 vs 30.50 ± 1.94 , p value = <0.05) though it was significantly altered, even according to Neck circumference both the group did not have insulin resistance & Central obesity. (Refer table 2).

Table 2: Baseline characteristics of the MI and Control group.

Parameter	Case	Control	P value
Age (in yrs)	20.90 ± 3.053	24.08 ± 4.64	< 0.01**
BMI (Kg / m²)	19.43 ± 1.80	20.71 ± 2.78	0.072 (NS)
Weight (Kg)	47.06 ± 5.94	50.49 ± 9.60	0.153 (NS)
Waist Circumference (cms)	68.75 ± 11.00	76.00 ± 8.51	< 0.05*
W / H ratio	0.796 ± 0.044	0.810 ± 0.037	0.288 (NS)
Neck circumference (cms)	32.47 ± 3.13	30.50 ± 1.94	< 0.05*

**- Moderately Significant. *- Significant

Baseline cardiovascular parameters showed Resting heart rate, (case 74.53 ± 5.07 vs control 73.40 ± 7.12 , with a p value= 0.561). RSBP (case 104.53 ± 5.53 vs control 106.56 ± 13.55 , p value=0.542). DBP (67.16 ± 6.74 vs 72.56 ± 10.54 , p = 0.058.) were not significantly altered. (Refer Table 3).

insignificant. QT interval ($0.378 \pm .027$ vs $0.429 \pm .053$, P value < 0.001), QT max ($0.419 \pm .035$ vs 0.464 ± 0.064 , P value <0.01) and QTmin ($0.355 \pm .033$ vs $0.399 \pm .047$, P value = <0.01) were significantly increased in controls than patient group. QTd ($0.064 \pm .027$ vs 0.065 ± 0.038 , P value= 0.951) was insignificantly. (Refer Table 4; Fig: 1)

Comparison of QT parameters gave a Mean RR interval ($0.794 \pm .087$ vs $0.829 \pm .096$, p = 0.212), was

Table 3: Baseline cardiovascular parameters of the MI and Control group.

Parameter	Case	Control	P value
RHR	74.53 ± 5.07	73.40 ± 7.12	0.561 (NS)
RSBP (mm Hg)	104.53 ± 5.53	106.56 ± 13.55	0.542 (NS)
RDBP (mm Hg)	67.16 ± 6.74	72.56 ± 10.54	0.058 (NS)
RPP	77.98 ± 7.59	78.00 ± 14.84	0.996 (NS)

NS- not significant

Table 4: Comparison of RR interval and QT parameters of the lean and ideal weight MI patient and Control group.

Parameter	Case	Control	P value
RR	$0.794 \pm .087$	0.829 ± 0.096	0.212 (NS)
QT	$0.378 \pm .027$	0.429 ± 0.053	<0.001***
QTmax	$0.419 \pm .035$	0.464 ± 0.064	<0.01**
QTmin	$0.355 \pm .033$	0.399 ± 0.047	<0.01**
QTd	$0.064 \pm .027$	0.065 ± 0.038	0.951 (NS)

***- Highly Significant. **- Moderately Significant. NS- not significant

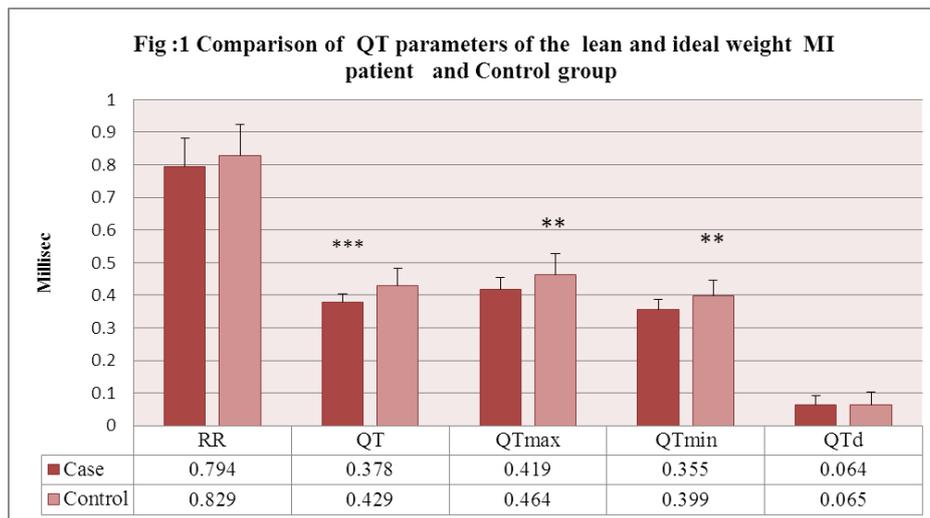


Fig. 1: Comparison of QT parameters of the lean and ideal weight MI patient and Control group.

Comparison of corrected QT parameters showed QTc interval (0.406 ± 0.092 vs $0.472 \pm .052$, P value= <0.01), QTc max (0.471 ± 0.032 vs 0.512 ± 0.068 , P value= <0.05) and QTc min (0.399 ± 0.030 vs 0.439 ± 0.050 , P

value= <0.01, were significantly shorter in cases than in control group. QTcd (0.072 ± 0.044 vs 0.071 ± 0.043 , P value = 0.958) was not significantly different (Refer Table 5; Fig: 2)

Table 5: Comparison of corrected QT parameters of the lean and ideal weight MI patient and Control group.

Parameter	Case	Control	P value
QTc	0.406 ± 0.092	0.472 ± 0.052	<0.01**
QTc max	0.471 ± 0.032	0.512 ± 0.068	< 0.05*
QTc min	0.399 ± 0.030	0.439 ± 0.050	<0.01**
QTcd	0.072 ± 0.030	0.071 ± 0.043	0.958 (NS)

**- Moderately Significant. *- Significant NS- not significant

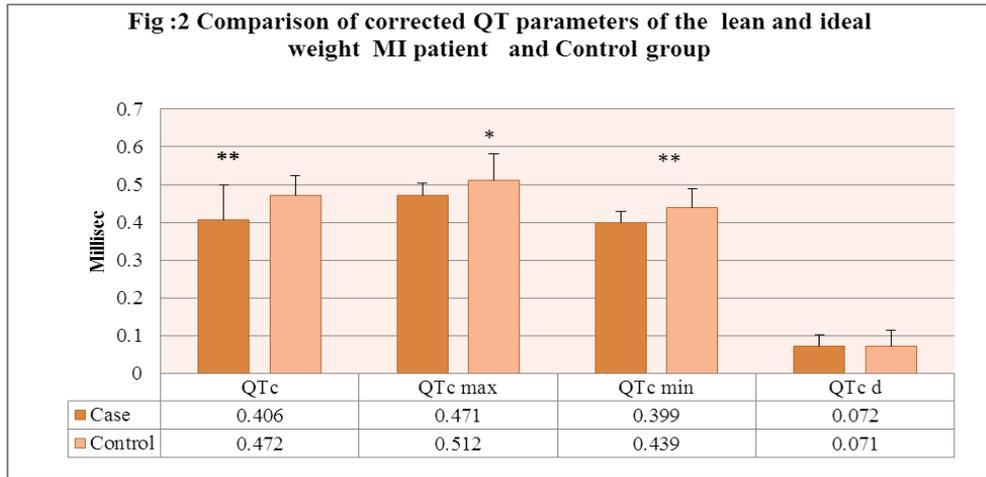


Fig. 2: Comparison of corrected QT parameters of the lean and ideal weight MI patient and Control group.

Correlation between QT parameters with MI and Baseline parameters showed QT, QTmax, QT min, QTc, QTcMax and QTc Min were positively correlated with the disease. Apart from this, age had a significant correlation with QT, QTmax, QT min, QTcMax , QTcmin and waist circumference with QT, QT min, QTc, QTcMax and QTc Min . WHR showed significant

correlation with QT min, QTc, and QTc Min . (Refer Table 6).Correlation between QT parameters with and Baseline cardiovascular parameters showed resting diastolic BP was correlated with QTmax, QTd, QTc, QTcMax and QTc Min. Systolic BP was correlated with QT ad QTc min. others were not significantly related. (Refer Table 7).

Table 6: Correlation between QT parameters with MI and Baseline parameters.

		QT	QTmax	QTmin	QTd	QTc	QTcmax	QTcmin	QTcd
MI	r value	.506**	.389**	.469**	.010	.426**	.343*	.439**	-.008
	p value	.000	.009	.001	.951	.004	.023	.003	.958
AGE	r value	.341*	.348*	.353*	.107	.199	.416**	.428**	.119
	p value	.024	.021	.019	.489	.196	.005	.004	.443
WT	r value	.218	.161	.252	-.076	.040	.116	.216	-.080
	p value	.154	.298	.099	.623	.797	.452	.159	.605
BMI	r value	.187	.056	.248	-.251	.061	.030	.245	-.248
	p value	.225	.719	.104	.101	.693	.844	.109	.105
WC	r value	.301*	.276	.330*	.013	.363*	.323*	.381*	.031
	p value	.047	.070	.028	.936	.015	.033	.011	.842
WHR	r value	.281	.106	.334*	-.283	.433**	.084	.351*	-.293
	p value	.065	.493	.027	.062	.003	.590	.020	.053
NC	r value	.034	.094	.121	-.004	.079	.100	.130	.001
	p value	.826	.544	.433	.979	.608	.520	.401	.992

**-. Moderately Significant. *- Significant

Table 7: Correlation between QT parameters and baseline cardiovascular parameters.

		RR	QT	QTmax	QTmin	QTd	QTc	QTcmax	QTcmin	QTcd
RHR	r value	-.445**	-.215	-.195	-.245	.006	-.080	.002	-.047	.063
	p value	.002	.162	.204	.109	.967	.604	.988	.760	.683
RSBP	r value	.001	.304*	.225	.266	.014	.174	.249	.306*	.012
	p value	.993	.045	.143	.081	.930	.259	.104	.044	.937
RDBP	r value	.014	.280	.404**	.272	.312*	.319*	.450**	.307*	.323*
	p value	.929	.065	.007	.074	.039	.035	.002	.043	.033
RPP	r value	-.266	.043	.000	.008	-.012	.050	.134	.153	.022
	p value	.081	.783	.999	.958	.938	.747	.385	.321	.886

**-. Moderately Significant. *- Significant

A logistic regression analysis was done to find the effect of Age ,BMI, Waist circumference, W / H ratio, Neck circumference, RHR, RSBP, RDBP, RPP and QT

parameters on the likelihood of participants having MI. The model explained with adjusted R Square 44.5 % of dependable variables were explained by independent

variables . Neck circumference and RR interval came out to be significantly greater individual impact predictors of MI. (Table:8).

Table 8: Regression analysis between QT parameters and baseline parameters with MI.

Model	Standardized Coefficients Beta	t	Sig.	95.0% Confidence Interval for B	
				Lower Bound	Upper Bound
(Constant)		-1.031	.313	-25.412	8.483
AGE	.023	.123	.903	-.043	.048
WEIGHT	-.333	-1.030	.313	-.060	.020
BMI	.331	1.006	.324	-.071	.206
WAISTCIR	.078	.407	.687	-.016	.023
WHR	-.179	-.961	.346	-7.003	2.554
NECKCIR	-.521	-3.756	.001**	-.151	-.044
RHR	-.375	-.716	.481	-.116	.056
RSBP	-1.048	-1.333	.195	-.124	.027
RDBP	.252	1.298	.207	-.008	.035
RPP	1.169	1.124	.272	-.040	.137
AvgRR	3.176	2.129	.044*	.521	33.808
QT	.526	1.340	.193	-2.838	13.347
QTmax	-1.222	-.142	.888	-164.843	143.612
QTmin	-5.253	-.689	.497	-224.354	111.996
QTd	-.656	-.150	.882	-144.162	124.605
QTcB	.276	1.232	.230	-1.189	4.711
QTcmaxB	.427	.053	.958	-138.329	145.674
QTcminB	5.193	.739	.467	-101.691	215.102
QTcdB	.925	.156	.878	-149.874	174.326

**** - Moderately Significant. * - Significant**

DISCUSSION

Menstrual irregularities, a gynecologic morbidity, is discriminately prevalent in our country.^[33] because of its varied clinical presentations. Women all over the world are concerned by menstrual disorders, but like other aspects of sexual and reproductive health, it is not included in the Global Burden of Disease estimates.^[34] Evaluating and treating menstrual problems is a big burden and should be generally considered.

Abnormally long and short QT intervals have been shown to be associated with an increased risk for life-threatening ventricular arrhythmias and sudden cardiac death.^[32] In our previous studies in the spectrum of Polycystic ovarian disease in non – obese women, we found QT interval was normal and QTc prolongation was found in both group though not significantly altered suggesting the disease itself perse does not lead to QT alterations.^[10] Cardiac autonomic function can be affected in PCOS, overall decrease in geometric and total variability of HRV,^[12] as well as increased sympathetic and decreased parasympathetic components of HRV.^[11]

As critical percentage of body fat is essential to trigger normal menstruation,^[35] in this study we delineated young women with visceral obesity as per, waist circumference, waist hip ratio, neck circumference and by BMI they were not obese . We found QT interval, QT max and QT min were significantly altered but were within normal limits. Corrected QT parameters showed

shorter QTc interval, QTc max and QTc min compared to controls significantly. There was a positive correlation between diastolic and systolic resting blood pressure and neck circumference and RR interval came out to be individual predictors of the disease with regression analysis.

This could be due to altered progesterone - estrogen ratio in menstrual dysfunction,^[5] being progesterone playing a luteal phase shortening of QT interval and increased sympathetic tone in normally menstruating women.^[22] The increased QT in controls is because they were in their follicular phase. Also could be increased androgen levels compared to the controls, though both the groups were in their follicular phase some patients were amenorrhic.

But studies have reported conflicting results of the hormonal fluctuations observed during a single menstrual cycle on the QT interval.^[36] Progesterone shortens the action potential duration and QT interval in women.^[37,38]

Studies of EPT (Estrogen+ Progesterone therapy) have found no change in the QT, thus supporting a counteractive role for progesterone against estrogen. Progesterone causes upregulation of IKs, and suppression of ICa, L channel currents. However, women taking oral contraceptives reportedly have a higher incidence of ventricular ectopy than untreated

controls,^[39] suggesting that estrogen or progesterone may be arrhythmogenic.

Observational human studies also report overall QT shortening with endogenous testosterone. Proposed mechanism is upregulation of IKr, IKs, and IK1 and suppression of ICa, L channel currents.^[36] The shortening of the QT interval during puberty in males implies that androgen (specifically testosterone) rather than estrogen may contribute to gender differences in QTc.^[40] This same study reported that women with virilization have shorter JT intervals than castrated men and normal women This suggest these group of young women may have increase in testosterone levels and/or increase in progesterone and/or altered estrogen progesterone ratio. In a guinea pig model, administration of 100nM of testosterone caused dose-dependent shortening of the action potential duration through suppression of ICa, L channels and enhancement of IKs channels in ventricular myocytes.^[41]

Several reports have defined the upper limit of normal heart rate-corrected QT interval. However, little is known about the clinical implication of a shortened QT interval and the lower limit of normality of the QT interval. With the detection of the arrhythmogenic risk of a short QT interval, a new primary electrical abnormality is identified. In the evaluation of patients with syncope, aborted sudden cardiac death, atrial fibrillation, and/or a positive family history for syncope and sudden death, this evaluation should play a considerable role. ECG pattern we see in affected patients are constantly short QT intervals (QTc₃₂₀ ms), a short or even absent ST segment, and often tall, narrow, and symmetrical T waves in the precordial leads.^[43]

CONCLUSION

In this study the non- obese young women with menstrual irregularities had normal QT interval compared to controls .Therefore they do not have an increased risk of cardiac arrhythmias compared to the controls. The limit for a pathological rate corrected QT interval is to date below 320 ms. However, it is vaguely understood and unclear whether borderline shortened QT intervals, bradycardia-associated shortened QT intervals, or, finally, fluctuating QT intervals are of clinical significance. More studies with larger sample size and with estimation of hormones per se in different clinical menstrual dysfunction may give good clarity in this spectrum of disease.

REFERENCES

1. Singh MM, Devi R, Gupta SS. Awareness and health seeking behaviour of rural adolescent school girls on menstrual and reproductive health problems. *Indian Journal Medical Science*, 1999; 53: 439–443.
2. Vaidya RA, Shringi MS, Bhatt MA, et al. Menstrual pattern and growth of school girls in Mumbai. *Journal Family Welfare*, 1998; 44: 66–72.
3. Khushbu Rani, SC Tiwari, 1 Uma Singh,2 GG Agrawal,3 Archana Ghildiyal, and Neena Srivastava.Impact of Yoga Nidra on psychological general wellbeing in patients with menstrual irregularities: A randomized controlled trial.*Int J Yoga*, 2011 Jan-Jun; 4(1): 20–25.
4. Allsworth JE, Clarke J, Peipert JF, Hebert MR, Cooper A, Boardman LA. The influence of stress on the menstrual cycle among newly incarcerated women. *Womens Health Issues*, 2007; 17: 202–9.
5. JoeElie Salem, Joachim Alexandre, Anne Bacheloth, Christian Funck-Brentano Influence of Steroid Hormones on Ventricular Repolarization *Pharmacology & Therapeutics* November, 2016; 167: 38-47.
6. Schwartz PJ. The congenital long QT syndromes from genotype to phenotype: clinical implications, *J Intern Med*, 2006; 259: 39-47
7. Algra A, Tijssen JGP, Roelandt JR, Pool J, Lubsen J. QTc prolongation measured by standard 12-lead electrocardiography is an independent risk factor for sudden death due to cardiac arrest. *Circulation*, 1991; 83: 1888-94
8. Schouten EG, Dekker JM, Meppelink P, Kok FJ, Vandenbroucke JP, Pool J. QT interval prolongation predicts cardiovascular mortality in apparently healthy population. *Circulation*, 1991; 84: 1516-23.
9. Schwartz PJ, Stramba-Badiale M, Segantini A, Austoni P, Bosi G, Giorgetti R, et al. QT interval prolongation and the sudden infant death syndrome, *N Engl J Med*, 1998; 338: 1709-14.
10. Malathi Balamurugan, Balamurugan Maruthamuthu, Gomathi Ramanathan. QT and corrected QT parameters in non-obese young Indian women with polycystic ovary syndrome. *I nternational Journal of Medical Science and Public Health*, 2016; 5: 2493-2497.
11. Malathi Balamurugan, Balamurugan Maruthamuthu, Gomathi Ramanathan. Heart rate variability and lipid profile in non-obese young Indian women with polycystic ovary syndrome. *J Eval Med Dent Sci.*, 2015; 4(24): 4092–109.
12. Malathi Balamurugan, Balamurugan Maruthamuthu, Gomathi Ramanathan. Poincare plot of heart rate variability: quantitative analysis of sympathetic nervous activity in non-obese polycystic ovary syndrome patients. *J. Evolution Med. Dent. Sci.*, 2016; 5(47): 3005-3010.
13. Stramba-Badiale M, Locati EH, Martinelli A, Courville J, Schwartz PJ. Gender and the relationship between ventricular repolarization and cardiac cycle length during 24-h Holter recordings. *Eur Heart J.*, 1997; 18: 1000-6.
14. Stramba-Badiale M, Locati EH, Martinelli A, Courville J, Schwartz PJ. Gender and the relationship between ventricular repolarization and cardiac cycle length during 24-h Holter recordings. *Eur Heart J.*, 1997; 18: 1000-1006.
15. Schwartz PJ, Stramba-Badiale M, Segantini A, Austoni P, Bosi G, Giorgetti R, et al. QT interval

- prolongation and the sudden infant death syndrome, *N Engl J Med*, 1998; 338: 1709-14.
16. Rautaharju PM, Zhou SH, Wong S. et al. Sex differences in the evolution of the electrocardiographic QT interval with age. *Can J Cardiol*, 1992; 8: 690-695.
 17. Makkar RR, Fromm BS, Steinman RT, Meissner MD, Lehmann MH. Female gender as a risk factor for torsades de pointes associated with cardiovascular drugs. *JAMA.*, 1993; 270: 2590-2597.
 18. Lehmann MH, Hardy S, Archibald D, Quart B, MacNeil DJ. Sex difference in risk of torsade de pointes with d,l-sotalol. *Circulation*, 1996; 94: 2535-2541.
 19. Stramba-Badiale M, Priori SG. Gender-specific prescription for cardiovascular diseases?, *Eur Heart J.*, 2005; 26: 1571-2.
 20. Liu XK, Katchman A, Drici MD. et al. Gender difference in the cycle length-dependent QT and potassium currents in rabbits. *J Pharmacol Exp Ther*, 1998; 285: 672-679.
 21. Burke JH, Goldberger JJ, Ehlert FA, Kruse JT, Parker MA, Kadish AH. Gender differences in heart rate before and after autonomic blockade: evidence against an intrinsic gender effect. *Am J Med.*, 1996; 100: 537-543.
 22. Mikiko Nakagawa, Tatsuhiko Ooie Naohiko Takahashi, Yayoi Taniguchi, Futoshi Anan, Hidetoshi Yonemochi, Tetsunori Saikawa. Influence of Menstrual Cycle On Qt Interval Dynamics. *Pacing Clin Electrophysiol*, 2006 Jun; 29(6): 607-13.
 23. Ota T, Takamura T, Hirai N, Kobayashi K. BMI Classification physical status: Preobesity in World Health Organization. Classification involves the metabolic syndrome in Japanese. *Diabetes Care*, 2002; 25(7): 1252-3.
 24. World Health Organization. Obesity – Preventing and Managing the Global Epidemic: Report of a WHO Consultation on Obesity. Geneva: World Health Organization, 1998.
 25. Lean MEJ, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. *BMJ*, 1995; 311: 158-61.
 26. Measurement method for body size. Human characteristic Dada bare. National Institute for Technology and Evaluation. <http://www.tech.nite.go.jp/human/eng/contents/cmeasurement/uran/neckuran.html>.
 27. Jagadamba Aswathappa, Sumit Garg, Karthiyane Kutty, and Vinutha Shankar. Neck Circumference as an Anthropometric Measure of Obesity in Diabetics. *N Am J Med Sci.*, 2013 Jan; 5(1): 28-31.
 28. Yang GR, Yuan SY, Fu HJ, Wan G, Zhu LX, Bu XL. Neck circumference positively related with central obesity, overweight, and metabolic syndrome in chinese subjects with type 2 diabetes: Beijing community diabetes study 4. *Diabetes Care*, 2010; 33: 2465-7.
 29. William B. White. Heart rate and the rate-pressure product as determinants of cardiovascular risk in patients with hypertension. *American Journal of Hypertension*. February, 1999; 12(S2): 50S-55SS.
 30. Browne KF, Prystowsky E, Heger JJ, Chilson DA, Zipes DP. Prolongation of the QT interval in man during sleep. *Am J Cardiol*, 1983; 52: 55-9.
 31. Bazett HC. An analysis of the time relations of electrocardiograms. *Heart*, 1920; 7: 353-67.
 32. Ilan goldenberg, m. d., arthur j. Moss, m.d., and wojciech zareba. QT Interval: How to Measure It and What Is "Normal".. *Journal of Cardiovascular Electrophysiology*. March, 2006; 17(3): 333-336.
 33. Sioba'n D. Harlowa, Oona M.R. ampbellb. *Br J Obstet Gynaecol*. January, 2004; 111: 6-16.
 34. Abou Zahr C, Vaughn JP. Assessing the burden of sexual and reproductive ill-health: questions regarding the use of disability adjusted life years. *Bull WHO*, 2000; 78: 655-666.
 35. Carl De Créé. Sex Steroid Metabolism and Menstrual Irregularities in the Exercising Female. *Sports Med*, 1998 Jun; 25(6): 369-406.
 36. Tara Sedlak, Chrisandra Shufelt, Carlos Iribarren, and C. Noel Bairey Merz. Sex Hormones and the QT Interval: A Review. *Journal of Women's Health*, 2012; 21: 9.
 37. Nakagawa M, Ooie T, Takahashi N, et al. Influence of menstrual cycle on QT interval dynamics. *PACE*, 2006; 29: 607-613.
 38. Rodriguez I, Kilborn MJ, Liu XK, Pezzullo JC, Woosley RL. Drug-induced QT prolongation in women during the menstrual cycle. *JAMA*, 2001; 285: 1322-1326.
 39. Romhilt D.W., Chaffin C., Choi S.C., Irby E.C. Arrhythmias on ambulatory electrocardiographic monitoring in women without apparent heart disease, *Am J Cardiol*, 1984; 54: 582-586.
 40. Bidoggia H., Maciel J., Capalozza N., et al. Sex differences on the electrocardiographic pattern of cardiac repolarization: possible role of testosterone, *Am Heart J.*, 2000; 140: 678-683.
 41. Bai CX, Kurokawa J, Tamagawa M, Nakaya H, Furukawa T. Nontranscriptional regulation of cardiac repolarization currents by testosterone. *Circulation*, 2005; 112: 1701-1710.
 42. Rautaharju PM, Zhou SH, Wong S, Calhoun HP, Berenson GS, Prineas R, et al. Sex differences in the evolution of the electrocardiographic QT interval with age. *Can J Cardiol*, 1992; 8: 690-5.
 43. Rainer Schimpf a, Christian Wolperta, Fiorenzo Gaitab, Carla Giustettob, Martin Borggrefea. Short QT syndrome. *Cardiovascular Research*, 2005; 67: 357 - 366.