

Comparative Analysis of Electrocardiographic Indices in Metabolically Healthy and Metabolically Unhealthy Obese Adult Males

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Abstract:

Background: Obesity is associated with structural and electrophysiological alterations of the heart, increasing the risk of ventricular arrhythmias and sudden cardiac death. However, cardiovascular risk varies among obese individuals according to their metabolic status. Metabolically healthy obesity (MHO) and metabolically unhealthy obesity (MUO) represent distinct phenotypes with potentially different electrocardiographic (ECG) characteristics. Limited evidence is available comparing ECG-derived indices between these two groups.

Objectives: To compare QT interval, corrected QT interval (QTc), and QT dispersion between metabolically healthy obese and metabolically unhealthy obese adult males

Methods: This prospective case-control study included 110 adult obese males aged 30–50 years, comprising 55 participants with MHO and 55 with MUO. Metabolic status was classified according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. Anthropometric measurements, blood pressure, fasting biochemical parameters, and standard 12-lead electrocardiograms were obtained. QT interval, QTc (Bazett's formula), and QT dispersion were measured manually. Statistical analysis was performed using independent-samples t-tests. A p value <0.05 was considered statistically significant.

Results: QT interval (p=0.016), QTc interval (p<0.001), and QT dispersion (p=0.05) were significantly higher in participants with MUO, whereas heart rate did not differ significantly between the groups.

Conclusion: Metabolically unhealthy obesity is associated with significantly prolonged ventricular repolarization indices compared with metabolically healthy obesity, suggesting a higher risk of ventricular arrhythmias and sudden cardiac death. ECG-derived QT indices may serve as simple, non-invasive markers for early cardiovascular risk assessment in obese individuals, particularly those with metabolic abnormalities.

Keywords: Obesity; Metabolically healthy obesity; Metabolically unhealthy obesity; Electrocardiography; QT interval; QTc interval; QT dispersion.

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Introduction

Overweight and obesity have become significant public health concerns in recent years. As per the World Health Organization (WHO) 2022 data, over 2.5 billion (43%) adults aged 18 and older were overweight, of these 890 million (16%) are obese.[1] Obesity has reached epidemic proportions in India in the 21st century. According to the National Family Health Survey-4 (NFHS-4) in 2015-16, conducted by the Ministry of Health and Family Welfare (MOHFW) in India, the percentage of men and women aged 15–49 years who were obese was 19% and 21%, respectively. [2]

Obesity is defined in adolescents as body mass index (BMI) $\geq$ 95th percentile by age and gender percentile distribution. [3] In clinical terms a BMI between 25 to 29.9 kg/m² is called overweight and

BMI $\geq$ 30 kg/m² is called obese. [4,5]

Recently, concepts of metabolically healthy obesity (MHO) and metabolically unhealthy obesity (MUO) or metabolic syndrome have been put forth. [6] MHO is defined as the absence of metabolic disturbances including insulin resistance, impaired glucose metabolism, type 2 diabetes and dyslipidemia in an individual with a BMI $\geq$ 30Kg/m². [6,7]

As per NCEP ATP-III guidelines, metabolically unhealthy obesity or metabolic syndrome was defined as having three or more of the following five criteria: [8]

- 1) Abdominal obesity male waist circumference $\geq$ 90 cm; 2) Elevated fasting serum triglycerides $\geq$ 150

mg/dL or; 3) Low high-density lipoprotein cholesterol ≤ 40 mg/dL; 4) Increased blood pressure (BP) ≥ 130 mm of Hg or diastolic BP ≥ 85 mm Hg; 5) High fasting plasma glucose ≥ 100 mg/dL;

10-30% of obese individuals belong to MHO and 70-90% of obese individuals belong to MUO category. (6) Obesity is associated with risk of sudden cardiac death which is due to problems of ventricular repolarization. QT indices are an ECG parameter which when prolonged indicates the abnormalities of ventricular depolarization and repolarization. [9,10] Obesity is also associated with abnormal QT indices i.e. prolonged QT interval and corrected QT interval. [11]

Patients with abdominal obesity exhibit deranged ECG abnormalities. For the first time, the relationship between obesity and QT length was described. [12] The fatal arrhythmias in obese individuals are correlated with a prolonged electrocardiographic interval between Q and T waves (QT). One of the ECG abnormality is prolonged QTc interval, which hallmarks delayed ventricular repolarization representing a risk factor for the development of ventricular tachyarrhythmia's, syncope, sudden cardiac death. [13,14]

Several studies have looked at QT interval and QTc interval in MHO. [15] However, the data available is inconclusive. Other research has also found QTc prolongation in MUO (metabolic unhealthy obesity). [16] There is, however, relatively little evidence comparing ECG-derived indices in the MHO and MUO groups.

The current study compares ECG derived indices in two groups of metabolically healthy obese (MHO) and metabolically unhealthy obese (MUO) males. The research may contribute valuable insights into the specific ECG indices that differ between these two groups. So, we have undertaken this study to compare QT interval, corrected QT interval, corrected QT dispersion values in metabolically healthy obese (MHO) males with age matched metabolically unhealthy obese (MUO) males.

Aims and Objectives

Aim: To study ECG derived indices in metabolically healthy and metabolically unhealthy obese males.

Objective: To compare QT interval, corrected QT interval and QT dispersion in metabolically healthy and metabolically unhealthy obese males.

Material and Methods

Study Design and Setting: This prospective case-control study was carried out over a two-year period from March 2022 to February 2024 after obtaining approval from the Institutional Ethics Committee.

Sample size: calculated by using formula [17]

$$n = 2 \times \left(\frac{z^2 \sigma^2}{E^2} \right)$$

$$n = 2 \times \frac{(1.96)^2 (25.8)^2}{(10)^2}$$

$$n = 51.4 = 52 \text{ cases in each group}$$

The calculated minimum sample size was 52 participants per group. To improve statistical power and compensate for possible exclusions, 55 participants were recruited into each group, resulting in a total study population of 110 obese males.

Study Population: Participants were classified into two groups:

- Group A: Metabolically Healthy Obese (MHO) males (n = 55)
- Group B: Metabolically Unhealthy Obese (MUO) males (n = 55)

Participants fulfilling the eligibility criteria were recruited consecutively after obtaining informed written consent.

Inclusion Criteria: Group A (Metabolically Healthy Obese):

- Male participants
- Age between 30 and 50 years
- Body mass index (BMI) 30.0–49.9 kg/m²
- Absence of metabolic syndrome according to NCEP ATP III criteria: [8,18]

Group B (Metabolically Unhealthy Obese):

- Male participants
- Age between 30 and 50 years
- Body mass index (BMI) 30.0–49.9 kg/m²
- Presence of three or more NCEP ATP III criteria for metabolic syndrome: [8,18]
 - Waist circumference ≥ 90 cm
 - Serum triglycerides ≥ 150 mg/dL
 - HDL cholesterol < 40 mg/dL
 - Blood pressure $\geq 130/85$ mmHg
 - Fasting plasma glucose ≥ 100 mg/dl

Exclusion Criteria: Participants were excluded if they had:

- History of smoking or chronic alcohol consumption
- Known structural heart disease
- Congenital or acquired cardiac conduction abnormalities
- History of diabetes mellitus (MHO group)
- Hypertension (MHO group)
- Current use of medications known to prolong the QT interval, including antiarrhythmic agents, antipsychotics, antidepressants, antihistamines, or other QT-prolonging drugs

- Any acute or chronic systemic illness likely to influence ECG parameters

Anthropometric Measurements: Height was measured without footwear using a wall-mounted stadiometer to the nearest 0.2 cm.

Body weight was measured using a calibrated digital weighing scale with participants wearing light clothing and no footwear.

Body mass index (BMI) was calculated as:

$$\text{BMI} = \text{Weight (kg)} / \text{Height}^2 (\text{m}^2)$$

Classification of obesity for Indian population based on BMI [19]

Classification	BMI (kg/m ²)
Underweight	<18.5
Normal range	18.5-24.99
Overweight	25-29.99
Pre-obese	23-24.9
Obese I	30-34.99
Obese II	35-39.99
Obese III	≥40

Blood pressure was recorded in the sitting position after at least 10 minutes of rest using a calibrated mercury sphygmomanometer. Three measurements were obtained, and the average value was considered for statistical analysis.

Biochemical Investigations: After an overnight fast of 9–12 hours, venous blood samples were collected for estimation of:

- Fasting plasma glucose
- Total cholesterol
- High-density lipoprotein (HDL) cholesterol
- Low-density lipoprotein (LDL) cholesterol
- Serum triglycerides

All biochemical investigations were performed using standard laboratory methods.

Electrocardiographic Assessment: Standard resting 12-lead electrocardiograms were recorded using a Bionet CardioCare 2000 ECG machine at a paper speed of 25 mm/s and calibration of 10 mm/mV. Participants rested comfortably in the supine position for 10 minutes before ECG recording in a quiet, temperature-controlled environment. All ECG recordings and measurements were performed by a single trained investigator to minimize inter-observer variability.

Measurement of QT Interval:

The QT interval was measured manually from the onset of the QRS complex to the end of the T wave in Lead II or Lead V5, whichever demonstrated the clearest T-wave morphology. Measurements were obtained from several consecutive cardiac cycles, and the longest QT interval was selected for analysis. U waves were excluded from QT interval measurements.

Corrected QT Interval (QTc):

The corrected QT interval (QTc) was calculated using Bazett's formula [20]

$$\text{QTc} = \text{QT} / \sqrt{\text{RR}}$$

where RR represents the interval between two consecutive R waves.

QTc was expressed in milliseconds. Bazett's correction was selected because of its widespread clinical acceptance and suitability for heart rates between 60 and 100 beats/minute.

QT Dispersion:

QT dispersion was calculated as the difference between the maximum and minimum QT interval recorded among the twelve ECG leads. Corrected QT dispersion was calculated from the difference between maximum and minimum heart rate corrected QT interval in all lead manually. Normal value of corrected QT dispersion is 30 milliseconds to 60 milliseconds. [21]

Statistical Analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean $\pm$ standard deviation (SD). Comparisons between the two groups were performed using the independent-samples Student's t-test. A p-value <0.05 was considered statistically significant, whereas p <0.001 was considered highly statistically significant.

Results

Baseline Characteristics: A total of 110 obese adult males aged 30–50 years were enrolled in the study. Fifty-five participants were classified as metabolically healthy obese (MHO) and fifty-five as metabolically unhealthy obese (MUO) according to the NCEP ATP III criteria.

Table 1: Comparison of Age and BMI in group A (MHO) and group B (MUO)

Parameter	Group A (n=55) (MHO)		Group B (n=55) (MUO)		t Value	P Value
	Mean	SD	Mean	SD		
Age (Yrs)	39.78	7.16	41.60	5.95	1.45	0.15
BMI	38.99	7.52	40.13	6.41	0.86	0.39

Significant $p < 0.05$, highly significant $p < 0.001$

Table 1 shows that there was no statistically significant difference in age between the two groups ($p > 0.05$), indicating that the groups were age

matched. Body mass index (BMI) was comparable between the two groups because participants were recruited from the same obesity category.

Electrocardiographic Parameters:

Table 2: Comparison of Heart rate, QT interval, corrected QT, QT dispersion in group A and group B

Parameter	Group A (n=55) (MHO)		Group B (n=55) (MUO)		t Value	P Value
	Mean	SD	Mean	SD		
Heart Rate	82.15	16.44	86.27	11.82	1.51	0.13
QT interval	350.55	46.80	369.45	32.63	2.46	0.016
Corrected QT	405.26	46.01	440.37	30.03	4.74	<0.0001
QT dispersion	50.44	12.71	55.96	16.77	1.95	0.05

Significant $p < 0.05$, highly significant $p < 0.001$

Table 2 Shows that there is no statistically significant difference in resting heart rate between the two groups ($p > 0.05$).

The mean QT interval was significantly longer in the MUO group than in the MHO group ($p = 0.016$).

Similarly, the corrected QT interval (QTc) was significantly prolonged among participants with MUO ($p < 0.001$) as compared to MHO, suggesting greater ventricular repolarization abnormalities in metabolically unhealthy obese individuals. QT dispersion was also higher in the MUO group as compared to MHO, and this difference reached statistical significance ($p = 0.05$), indicating increased heterogeneity of ventricular repolarization.

Discussion

Obesity is becoming a global pandemic especially in young population. Obesity has reached epidemic proportions in the industrialized world and is increasing in the developing countries. There are reports showing that obesity may be associated with early electrocardiographic and / or echocardiographic abnormalities even in the absence of clinical symptoms. [22,23]

Extensive review and a comparative study show that Bazett's formula for corrected QT interval has been used in majority of studies. Goldenberg recommended measurement of QT interval in ECG leads of leads II and V5 or V6 with the longest value. [20]

QT dispersion measures the difference in duration between the maximum and the minimum QT interval in all ECG leads. When corrected for heart rate, it is corrected QT dispersion (QTcd). It is a

good noninvasive measurement for quantifying the degree of myocardial repolarization heterogeneity.

A prolonged corrected QT dispersion is thought to be a possible risk factor for arrhythmias and sudden death. In fact, corrected QT dispersion is a more sensitive and useful predictor of ventricular arrhythmias and sudden cardiac death than corrected QT interval prolongation. [15, 24] There are growing evidences which support the fact that prolonged QT interval, corrected QT interval and corrected QT dispersion can predict and precede morbidity and mortality in various diseases including obesity. [25, 26]

The present study compared ventricular repolarization indices (QT, corrected QT, QT dispersion) between metabolically healthy obese (MHO) and metabolically unhealthy obese (MUO) adult males. Although both groups had comparable degrees of obesity, participants with MUO demonstrated significantly prolonged QT interval, corrected QT interval (QTc), and QT dispersion. These findings indicate that metabolic abnormalities, rather than obesity alone, contribute substantially to alterations in cardiac electrophysiology and may increase the risk of ventricular arrhythmias and sudden cardiac death.

QT Interval and Corrected QT Interval: One of the principal findings of the present study was the significantly prolonged QT and QTc intervals in the MUO group compared with the MHO group. QT interval prolongation reflects delayed ventricular repolarization and is a well-recognized predictor of malignant ventricular arrhythmias, torsades de pointes, and sudden cardiac death. Our findings are consistent with those of Arslan et al. [25] who reported that obesity is associated with QT interval prolongation even in apparently healthy young males, suggesting that excess adiposity alone may

adversely affect myocardial repolarization. Similarly, Schouten et al. [27] demonstrated that prolonged QTc independently predicted long-term cardiovascular mortality in otherwise healthy individuals. Singh P et al. [28] and Ganashree et al. [29] also observed significantly prolonged QT and QTc intervals among obese individuals, supporting the concept that obesity contributes to electrophysiological remodeling. The greater prolongation observed in the MUO group in our study suggests that metabolic syndrome amplifies the adverse effects of obesity on ventricular repolarization. This observation is supported by Ahmad MI et al. [30] who demonstrated a progressive increase in QT interval from metabolically healthy non-obese individuals to metabolically unhealthy obese individuals, indicating that metabolic dysfunction has an additive effect beyond obesity alone.

QT Dispersion: QT dispersion represents the spatial heterogeneity of ventricular repolarization and has been associated with an increased risk of ventricular arrhythmias. In the present study, QT dispersion was significantly higher in the MUO group, indicating greater electrical instability. Similar findings have been reported by Merlyn et al. [31] who observed significantly increased QT dispersion in obese individuals, with improvement following weight reduction. Seyfeli et al. [32] likewise demonstrated increased QT dispersion in obese participants compared with healthy controls. Together, these findings suggest that obesity and metabolic abnormalities contribute to increased dispersion of ventricular repolarization, thereby increasing susceptibility to malignant arrhythmias.

Possible Mechanisms: Several mechanisms may explain the observed prolongation of QT indices in metabolically unhealthy obesity. Chronic systemic inflammation associated with obesity increases circulating concentrations of pro-inflammatory cytokines, including tumor necrosis factor- α , interleukin-6, and interleukin-1 β . These mediators impair endothelial function and promote myocardial fibrosis and electrical remodeling. Insulin resistance and hyperglycaemia increase oxidative stress, reduce nitric oxide bioavailability, and alter ion-channel function, leading to delayed ventricular repolarization. Autonomic dysfunction, characterized by increased sympathetic activity and reduced parasympathetic tone, is another important mechanism. Increased sympathetic activation accelerates heart rate variability abnormalities and contributes to QT prolongation. In addition, visceral fat accumulation promotes myocardial lipid deposition, resulting in cardiac steatosis, left ventricular hypertrophy, and structural remodeling. These changes increase heterogeneity of ventricular repolarization, explaining the greater QT dispersion observed in metabolically unhealthy obesity. Thus,

ventricular repolarization abnormalities appear to arise from the combined effects of structural remodeling, autonomic imbalance, inflammation, and metabolic dysfunction.

Conclusion

The present study demonstrates that metabolically unhealthy obese (MUO) adult males exhibit significantly prolonged QT interval, corrected QT interval (QTc), and QT dispersion compared with metabolically healthy obese (MHO) males despite having a similar degree of obesity. These findings indicate that metabolic abnormalities exert a greater influence on ventricular repolarization than excess body weight alone. The observed prolongation of QT indices suggests an increased susceptibility to ventricular arrhythmias and sudden cardiac death in metabolically unhealthy obesity. Therefore, routine electrocardiographic evaluation, particularly QTc assessment, may serve as a simple, inexpensive, and non-invasive screening tool for early identification of obese individuals at increased cardiovascular risk. Recognition of obesity phenotype, together with assessment of metabolic status and ECG parameters, may facilitate earlier intervention through lifestyle modification, weight reduction, and aggressive management of metabolic risk factors, thereby reducing long-term cardiovascular morbidity and mortality.

Further multicentre prospective studies involving larger and more diverse populations are required to validate these findings and establish the prognostic value of QT indices in different obesity phenotypes.

Clinical Implications: The present findings have important clinical implications.

- 1) Resting 12-lead electrocardiography is inexpensive, non-invasive, and widely available, making it an attractive tool for cardiovascular risk assessment.
- 2) Measurement of QT interval and QTc may help identify obese individuals at increased risk of ventricular arrhythmias before the development of overt cardiovascular disease. Obese individuals with metabolic syndrome may therefore benefit from closer cardiovascular surveillance, aggressive lifestyle modification, weight reduction, and optimization of metabolic risk factors.
- 3) Early identification of ventricular repolarization abnormalities may also assist clinicians in avoiding medications known to prolong the QT interval and in identifying patients who require further cardiovascular evaluation.

Conflict of Interest: There are no conflict of interests.

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