

Original research article**Serial QT estimation in ECG of patients admitted in critical care at tertiary care center****¹Surbhi, ²Mukesh K Sarna, ³Puneet Rijhwani, ⁴Sudha Sarna, ⁵Shubham Mehtani, ⁶Mohammed Shoib**¹Resident, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India²Professor and Unit Head, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India³Professor and Head, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India⁴Professor and Head, Department, of Palliative Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India⁵Assistant Professor, Department of General Surgery, NIMS Medical College and Hospital, Jaipur, Rajasthan, India⁶Assistant Professor, Department of Pharmacology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India**Corresponding Author:**Dr. Mukesh K. Sarna (Email: mukeshsarna@gmail.com)**Abstract****Background:** Hospital based prospective cross sectional study conducted at a tertiary care center on Estimation of Serial QT on day of admission, day 3rd, day 5th and day 7th in ECG of patients admitted in critical care at tertiary care centre.**Materials and Methods:** An observational, cross-sectional with prospectively collected data, From January 2021-April 2022 in adult patients admitted to medical (M), surgical (S), and emergency (E) ICUs, and HDU in a Mahatma Gandhi Medical Hospital, Jaipur. All study patients signed an Informed Consent Form. During the study period, all patients of both genders, over 18 years-old, admitted to the ICU were invited to the study.**Result:** In current study, the mean QTc value more than 500ms were found in patients with CAD with ischemic disease, CKD, Pneumonia with Sepsis, HF, TB with ATT, Seizure with metabolic abnormality, and patients taking Trimethoprim-Sulfamethoxazole drug on day of admission, 3rd day, 5th day and 7th day.**Conclusion:** The prevalence of prolonged QTc interval is high in Indian emergency medical patients. There was no difference in hospital mortality though on subgroup analysis, patients with markedly prolonged QTc interval had significantly more episodes of in-hospital ventricular tachycardia and hospital mortality. A variety of factors including certain comorbidities, biochemical abnormalities and drugs were associated with QTc prolongation. Based on findings of index study, it would be prudent to closely monitor QTc interval, especially in patients with certain comorbidities and biochemical abnormalities, avoid medications associated with QTc prolongation.**Keywords:** Prospective cross sectional study, Serial QTc, ECG, ICU's**Introduction**

The QT-interval, the length of time between the beginning of the QRS complex and the end of the T-wave of the electrocardiogram (ECG), is a marker of the duration of ventricular repolarisation. Its prolongation might lead to Torsade de Pointes (TdP), a rare polymorphic ventricular tachycardia. Although QT prolongation is asymptomatic in most cases, but TdP can result in sudden death^[1]. This arrhythmia is the consequence of a longer duration of action potential in most ventricular myocardial cells, caused by a reduction of external repolarising currents and/or an increase of internal currents^[2].

QT-interval prolongation, known as the long QT syndrome (LQTS), may have a congenital or an acquired etiology. Several mutations have been described that cause changes in sodium and potassium ionic currents, leading to a prolonged action potential and to the LQTS^[3]. Acquired causes include electrolyte abnormalities, sinus node dysfunction, high-grade atrio ventricular block, myocardial ischemia and injury and medication use^[4]. The latter was the most common reason for QT-interval monitoring (57%) in a study performed in an Intensive Care Unit (ICU)^[5].

Critically ill patients are at increased risk of developing LQTS because they frequently receive pro-arrhythmic drugs, in addition to commonly having other risk factors for TdP, such as renal or hepatic

impairment, electrolyte disturbances and bradyarrhythmia's^[6]. In a study conducted in an Intensive Care Unit (ICU), approximately 69% of critically ill patients had at least one of the three American Heart Association criteria for QT-interval monitoring: use of drugs that are known to cause QT-interval prolongation, cardiac arrhythmias causing severe bradycardia, and hypokalemia or hypomagnesaemia^[5]. Prospective studies in ICUs have shown prevalence's of LQTS of 24%^[5], 46.6%^[7], 27.9%^[8], 39%^[9], 61%^[10] and 52%^[11]. Although LQTS is a frequent finding in critically ill patients and administration of QT-prolonging medications in the ICU setting is common, only a small number of prospective studies aimed at the accurate characterization of this problem have been published. In the last 10 years, only 10 studies on acquired LQTS in intensive care are found in the literature. Those studies were often based on retrospective data or had small sample sizes. Many of the published studies on QT interval prolongation are reviews or case reports. Studies that have focused on drug-induced LQTS commonly have rather simple statistical analyses, as they disregard the influence of other risk factors and study only the medications already reported in the literature as being associated with LQTS, without considering other drugs.

An ECG which is taken for all patients in an ICU is a tool which can provide valuable information. The ECG represents the electrical activity of the heart. The QT interval, related to ventricular function, if prolonged has been shown to have associations with poor ICU outcomes. It is seen that in acutely ill patients the prevalence of a prolonged corrected QT interval (QTc) is much higher than one might expect. These may be due to an underlying cause which may be correctible.

Cardiac arrest due to torsades de pointes (TdP) is a rare but catastrophic event in hospitals. Patients admitted to cardiac units are at higher risk of drug-induced QT interval prolongation and TdP, due to a preponderance of risk factors. Few data exist regarding the prevalence of QT interval prolongation in patients admitted to cardiac units or the frequency of administering QT interval-prolonging drugs to patients presenting with QT interval prolongation.

Therefore, we plan to conduct a prospective study aimed at the investigation of the prevalence and risk factors for acquired LQTS in patients admitted to critical care unit and an assessment of the risk of LQTS associated with the prescribed medications. The aim of the study is to determine the prevalence of prolonged QTc at admission and assess associated outcomes in patients admitted to a tertiary care center with the following Objectives:

- Identify the incidence and predictors of QTc prolongation in medical (M), surgical (S), and emergency (E) ICUs and HDU patients.
- Investigate the prevalence and risk factors of acquired long QT syndrome (LQTS) on admission to a general Intensive Care Unit (ICU) and HDU.
- To assess the risk of LQTS associated with prescribed medications.

Material and Methods

From January 2021-April 2022, study conducted an observational, cross-sectional with prospectively collected data, in adult patients admitted to medical (M), surgical (S), and emergency (E) ICUs, and HDU in a Mahatma Gandhi Medical Hospital, Jaipur. This study was approved by the Research Ethics Committee of Mahatma Gandhi Medical Hospital, Jaipur and all study patients signed an Informed Consent Form. During the study period, all patients of both genders, over 18 years-old, admitted to the ICU were invited to the study.

Inclusion criteria of study: Patients who are willing to give consent, All patients of both genders, in age group 18-65 years old admitted to the ICU were invited to the study, Hospitalization >48 hours.

Exclusion criteria of study: Patients with congenital LQTS, with complete left bundle branch block or other cardiac conduction defect disallowing QT-interval measurement, with an implanted pacemaker, who were admitted for less than 48 hours for routine monitoring after a diagnostic or therapeutic procedure, or who were admitted after elective surgery.

Results

This prospective cross sectional study included 101 patients with various illnesses admitted in intensive care unit of Mahatma Gandhi medical College, Jaipur, a tertiary care hospital over a period of 12 months. There were 63 (62.4%) males and 38 (37.6%) were females. The mean age of current study was 47.11 ± 16.3 years (Range 21 years-83 years).

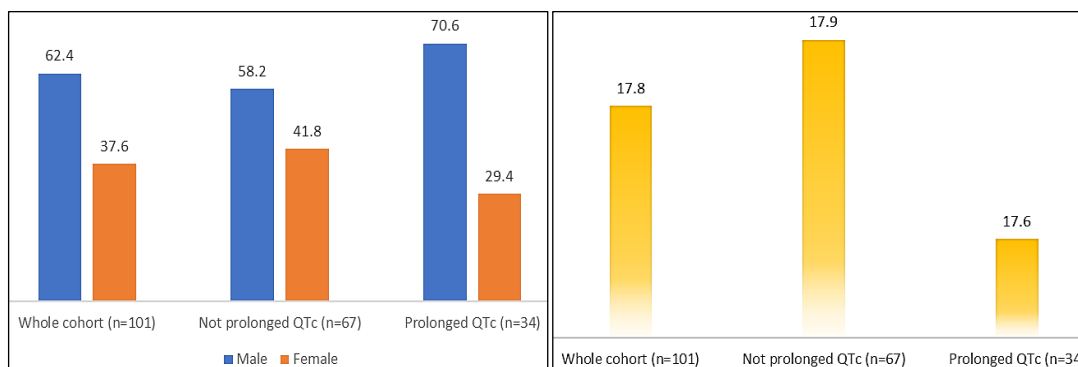


Fig 1: Comorbidities distribution in study population according to prolong QTc interval and non-prolong QTc interval group **Fig 2:** Hospital mortality in study population according to prolong QTc interval and non-prolong QTc interval group

In present study, most common comorbidities were diabetes mellitus (23.8%), hypertension (23.8%) and CAD (21.8%). The prevalence of other concurrent illness were following presented in study population; chronic liver disease (11.9%), chronic renal disease (10.9%), pneumonia (12.9%), sepsis (10.9%), cerebrovascular accident (7.9%), chronic obstructive pulmonary disease (4.9%) and heart failure (6.9%). In current study, the mean hospital stay of study population were 7.0 (IQR 4.1-8.8) day, mean Charlson comorbidity index were 5.34±2.13, mean SAPS II Score were 40.4±19.6 and mean SOFA score 6.33±4.14.

After the ECG performed, there were 67 (66.33%) were had normal QTc interval and 34 (33.67%) had prolong QTc interval in study population. In this study, 38(37.6%) patients had sinus tachycardia, 17 (16.8%) had MI, 8(7.9%) had LVH, 2 patients had sinus bradycardia, 2 had BBB and one had AV block. The mean QTc interval in study population were 438.73±46.4 and 5(4.5%) patients were had ventricular tachycardia. Seventeen patients (16.8%) had markedly prolonged QTc interval (QTc >500 ms).

After taking the drug history from study population, four patients were on ondansetron, trimethoprim-sulfamethoxazole, frusemide and norfloxacin, 3 patients were on trimethoprim-sulfamethoxazole, frusemide and norfloxacin, 2 patients were taking haloperidol and domperidone, one were on amiodarone, one were on terfenadine, one were on ranolazine, one on quinidine, one were on clopidogrel and one was taking amitriptyline at admission in ICU. So 15 patients were on QTc prolongation medication in study population. After the laboratory investigation in 101 study participants, 43.6% were found to have serum albumin <3.5 mg/dl (Hypoalbuminemia), 26.7% patients had deranged kidney function, 34.7% had hypophosphatemia (serum phosphorus <4.5mg/dl), 22.8% hypocalcemia, 16.8% hypokalemia, 15.8% hyponatremia, and 27 (26.7%) patients had hypermagnesemia (Serum magnesium <1.7 mg/dl) at diagnosis. The frequency of patients of these abnormal blood investigations were significantly higher in prolong QTc group than non-prolong QTc group. (p<0.05)

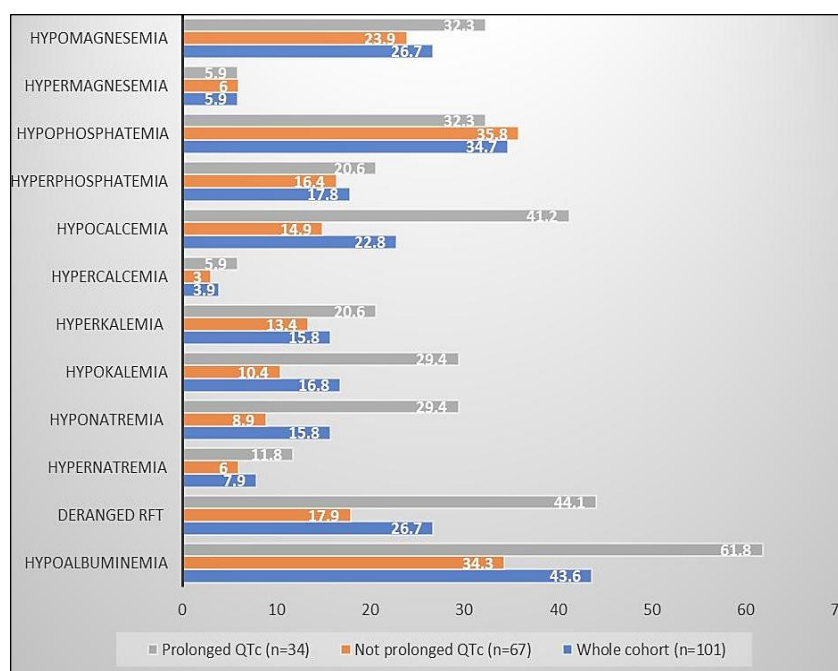


Fig 3: Comparison of Laboratory investigations in 101 patients

ECG pattern in study population and this study found that sinus tachycardia were presented in 37.6% patients, MI features in 12.9%, LVH in 7.9%, sinus bradycardia, ventricular tachycardia in 7.9% patients and BBB in 2 patients while AV block were diagnosed in one patient. MI and LVH diagnosed patients were significantly higher in prolong QTc group than non-prolong QTc group. ($p < 0.05$)

The mean QTc interval in study population were 438.73 ± 46.4 ms. in the mean QTc interval were significantly higher in prolong QTc group than non-prolong QTc group (483.87 ± 21.1 ms vs 413.90 ± 33.7 ms; $p = 0.000$).

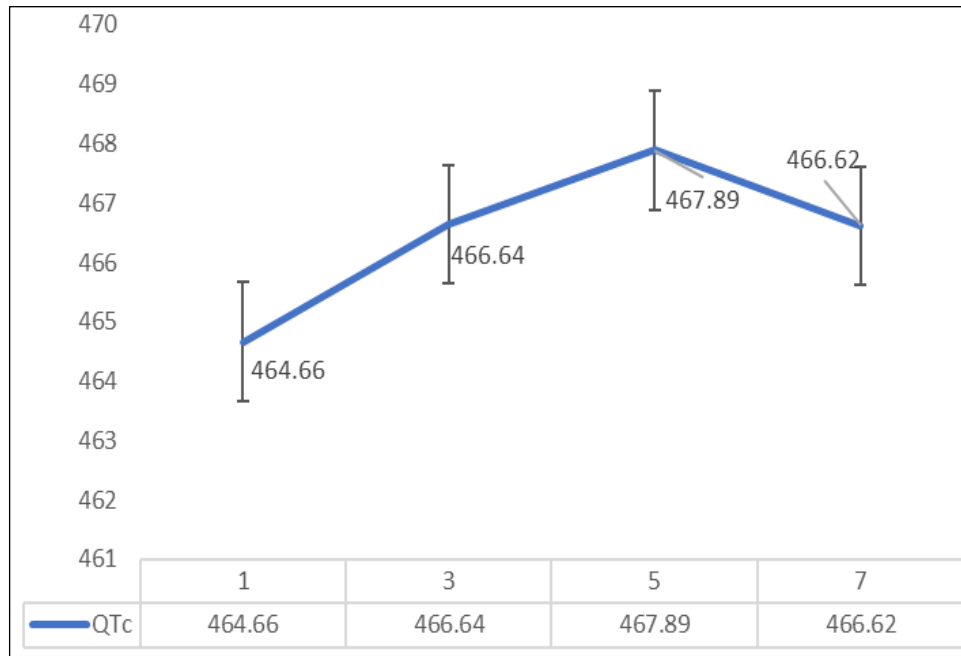


Fig 4: ECG pattern and QTc mean interval in 101 patients with prolong QTc interval and Non-prolong QTc interval

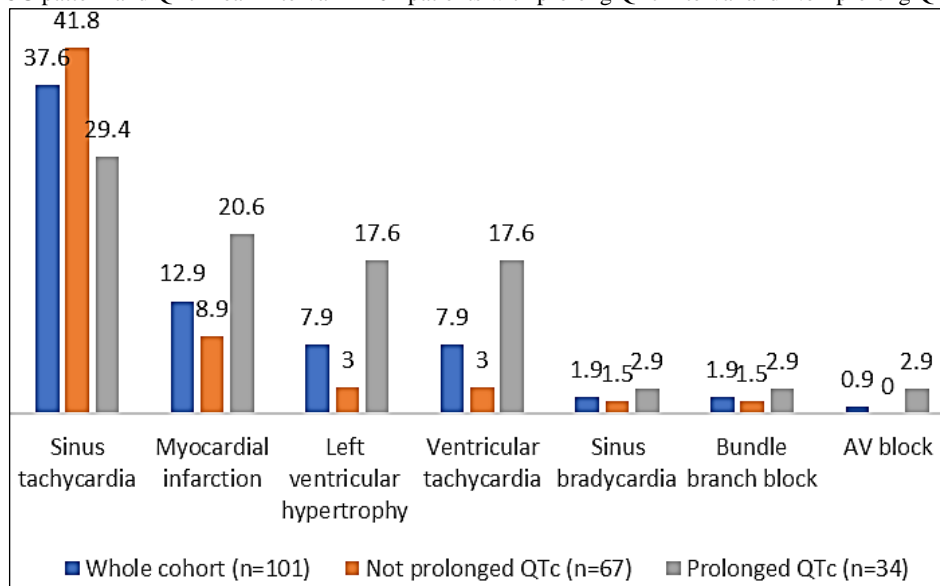


Fig 5: Mean QTc value on day of admission, day 3rd, day 5th and Day 7th

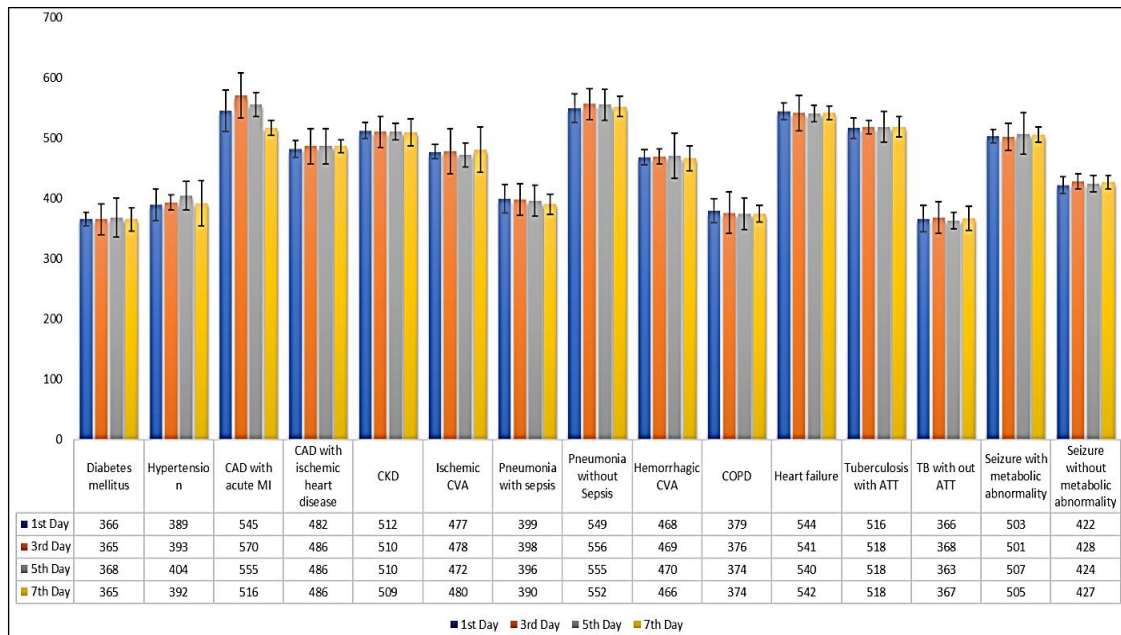


Fig 6: Mean QTc value on day of admission, day 3rd, day 5th and Day 7th and association with comorbidities in study population

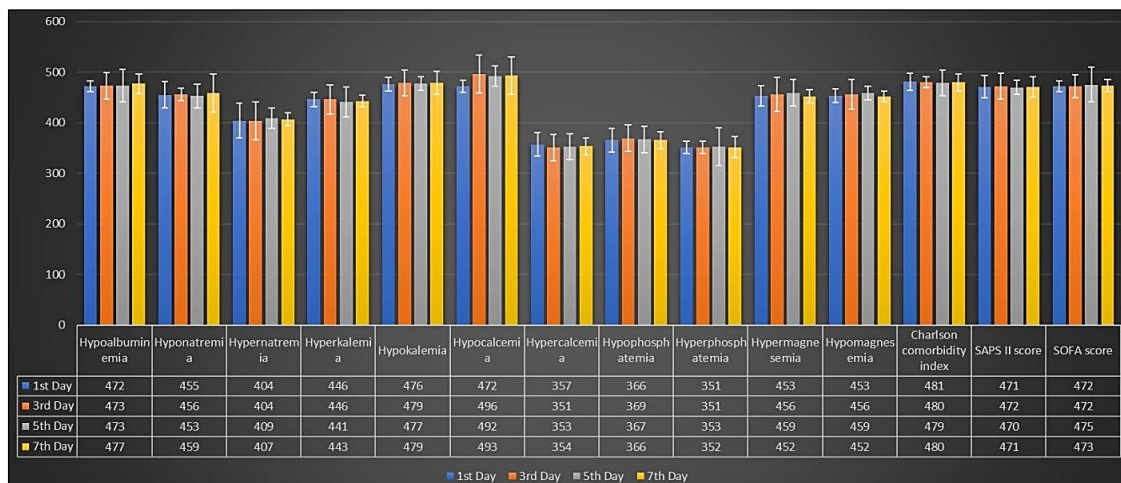


Fig 7: Mean QTc value on day of admission, day 3rd, day 5th and Day 7th and association with abnormal lab investigation in study population

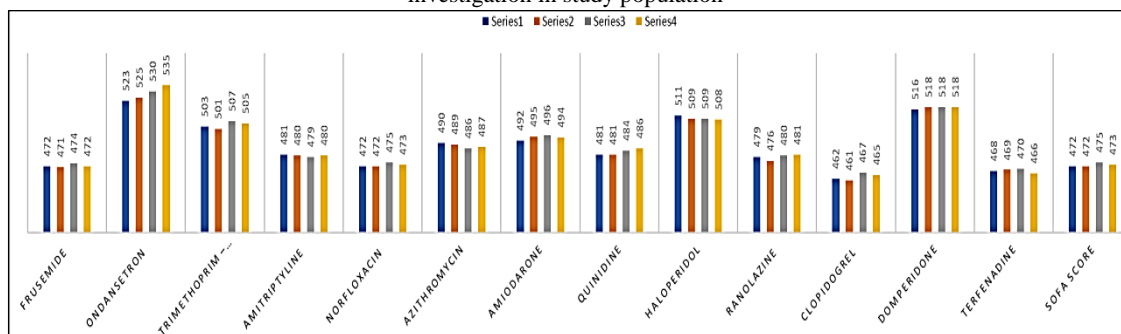


Fig 8: Mean QTc value on day of admission, day 3rd, day 5th and Day 7th and association with Drugs in study population

Logistic regression to assess the associated with abnormal ECG and risk factors significantly correlated with QTc prolongation and except Serum calcium, Serum potassium and serum albuminemia showed positive association with QTc interval prolongation.

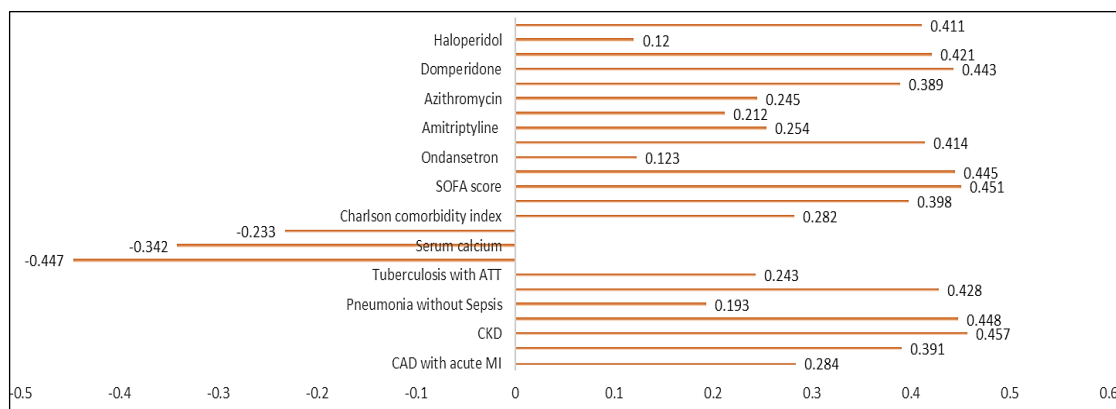


Fig 9: Logistic regression to assess the associated with abnormal ECG and risk factors significantly correlated with QTc prolongation

Discussion

This was a single-center prospective observational study undertaken in patients with varied medical illnesses admitted in emergency medical services of a tertiary care hospital. Out of 101 patients recruited, 95 (34.1%) were found to have prolonged QTc interval at presentation. Fifteen patients (5.4%) had markedly prolonged QT interval (QTc >500 ms). CKD, CLD, hemorrhagic CVA, and heart failure were the medical conditions associated with QTc prolongation. Among laboratory abnormalities, patients with low hemoglobin, with deranged renal parameters and with hypokalemia had a greater share of patients with prolonged QTc interval. Subgroup of patients with markedly prolonged QTc interval had greater episodes of ventricular tachycardia and also significantly higher in hospital mortality rate. QTc interval is calculated from beginning of Q wave to the end of T wave on surface ECG, and thus it measures the duration of both cardiac depolarization and repolarization.

Corrected QT interval is calculated by using various formulas, of them Bazette's formula is most widely accepted. QTc interval is affected by various factors including increasing age, female gender, several medical conditions, electrolyte abnormalities, and many drugs. Pathogenesis of QTc interval prolongation includes alteration of ion channels and intracellular potassium leading to heterogeneous intra-cardiac repolarization and early after-depolarization. Furthermore, structural alteration in cardiomyocytes and conduction pathways may have added role in causing repolarization abnormalities leading to QTc interval prolongation. Prolonged QTc interval, especially duration of repolarization is well known to cause life-threatening cardiac arrhythmias including TdP and ventricular tachycardia.

Various studies regarding the prevalence and prognostic significance of prolonged QTc interval have been undertaken in selected medical conditions including liver cirrhosis, intracranial hemorrhage, HIV, CAD, but little is known about the prevalence of QTc prolongation in non-selected emergency medical patients having a convergence of many potentially QTc prolonging medical conditions, electrolyte abnormalities, and medications.^{[4],[5],[6]} This study was conducted to find out the prevalence of prolonged QTc interval in emergency medical patients, factors predisposing it and prognostic significance in terms of duration of hospital stay, occurrence of ventricular tachycardia and hospital mortality. The study shows a high prevalence of QTc interval prolongation at the time of presentation to emergency services in patients with varied medical illnesses. This finding is consistent with a retrospective study in non-selected emergency medical patients that reported 35% prevalence rate. In a retrospective review of patients identified through an institution-wide, electronic medical record-based QT alert system, out of 7522 patients with ECG at the emergency department, 93 (1.2%) patients had prolonged QTc interval, triggering electronic QT alert. These patients had more than one QT-prolonging conditions such as electrolyte disturbances in 51%, a QT prolonging condition in 56%, and QT-prolonging drugs in 77% of them. High prevalence of prolonged QTc interval was also reported in a study conducted in medical ICU patients in India. Prevalence of QTc prolongation in index study though was more than reported prevalence of 22.3% in a cross-sectional study conducted at Swiss teaching hospital in medical inpatients. Higher prevalence of QTc prolongation in the study was possibly due to the recruitment of acutely ill patients with a variety of illnesses presenting in emergency medical services who often had one or more risk factors for QTc prolongation including the prescription of QTc prolonging drugs. Prevalence of markedly prolonged QTc interval noted in our study is consistent with findings reported in these older studies^[8,9,10,11].

In this study, rate of ventricular arrhythmias was higher in patients with prolonged QTc interval group patients and patients with markedly prolonged QTc interval had significantly higher hospital mortality rate.

Conclusion

The prevalence of prolonged QTc interval is high in Indian emergency medical patients. There was no

difference in hospital mortality though on subgroup analysis, patients with markedly prolonged QTc interval had significantly more episodes of in-hospital ventricular tachycardia and hospital mortality. A variety of factors including certain comorbidities, biochemical abnormalities and drugs were associated with QTc prolongation. Based on findings of index study, it would be prudent to closely monitor QTc interval, especially in patients with certain comorbidities and biochemical abnormalities, avoid medications associated with QTc prolongation.

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