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ORIGINAL RESEARCH

Prevalence of Medication Associated with QTc Prolongation Used Among Critically Ill Patients

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Background: Acquired prolonged corrected QT (QTc) interval can lead to life-threatening Torsade de Pointes (TdP) arrhythmia. Multiple risk factors including medications, comorbidities, and electrolyte imbalances contribute significantly to acquired manifestations of the QTc prolongation. Critically ill patients are particularly more vulnerable to TdP due to complex medical conditions, aging, and polypharmacy.

Objective: This study aimed to assess the prevalence of TdP-associated medication prescribing, identify risk factors for QTc prolongation and TdP, and determine primary predictors of high TdP medication usage in critically ill patients in Jordan.

Methods: We conducted a retrospective cross-sectional analysis of electronic medical records for patients from King Abdullah University Hospital who were admitted to Intensive Care Unit (ICU) between (July 2012-July 2022). We collected data on patients' demographics, clinical characteristics, comorbidities, laboratory results, and prescribed medications. Medications were categorized into three TdP risk levels according to CredibleMeds® assessment tool. Data were analyzed using descriptive statistics and a binary logistic regression model.

Results: Of the 13,300 patients (58.2% male, median age 62 years). Prescribing prevalence for medications with known TdP risk was 19%, possible risk (24.7%), conditional risk (21.6%), and confirmed conditional risk (8.3%). Common comorbidities included hypertension (40.9%), diabetes (33.3%), and cancer (15.4%). Drugs with known TdP risk included citalopram, amiodarone, clarithromycin, and ciprofloxacin. A binary regression model revealed that as age increased, the odds of TdP associated medication prescribing decreased (OR = 0.989, $p < 0.001$), while patients on more than five medications had higher odds (OR = 4.281, $p < 0.001$).

Conclusion: The study identified a notable prevalence of prescribing for medications with QTc prolongation/TdP risk in critically ill patients. Healthcare providers in the ICU should exercise caution to minimize the inadvertent prescription of TdP associated medications especially among older patients and those with polypharmacy.

Keywords: torsade de pointes, QTc interval, critically ill patients, Jordan, intensive care unit

Introduction

The prolonged QTc interval is a pathological cardiac condition detectable via electrocardiogram (ECG), characterized by an extended ventricular repolarization phase. This anomaly is associated with the potential development of a specific and life-threatening ventricular cardiac arrhythmia called Torsade's de Pointes, which can result in critical scenarios, including sudden cardiac arrest.[1] A prior comparative investigation conducted in the USA reported a substantial prevalence of QTc prolongation among acutely ill patients, with approximately 24% of these patients exhibiting this abnormality. Additionally, this study revealed that Torsade de Pointes accounted for 6% of in-hospital cardiac arrests.[2] QTc prolongation and the subsequent development of Torsade de Points can arise from congenital or acquired conditions. The predominant contributory factor to acquired Torsade remains the administration of medications with diverse pharmacological effects that are known to prolong the QTc interval. Such medications include antiarrhythmic agents,

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antiemetics, antibiotics, and neuroleptic drugs.[3] Other risk factors do encompass aging, female gender, thyroid gland disorders (hypothyroidism or hyperthyroidism), diabetes, electrolyte disturbances (hypokalemia and hypomagnesemia), and presence of cardiovascular conditions.[4–6]

Critically ill patients exhibit a heightened susceptibility to an elevated risk of developing QTc interval prolongation and concomitant occurrence of Torsade de Points flares compared to other segments of the patient population.[7,8] Proarrhythmic complications encountered in critically ill patients typically stem from various factors beyond the administration of medications with recognized arrhythmogenic potential. These patients often contend with polypharmacy defined as the concurrent use of five or more medications,[6] renal and hepatic disease conditions, electrolyte imbalances and other chronic comorbidities all of which are established higher incidence of proarrhythmic events.[5] A study assessing critically ill patients in the Intensive Care Unit (ICU) reported that approximately 69% of these patients met the criteria for QTc interval monitoring as outlined by the American Heart Association (AHA) criteria. These criteria encompassed the use of medications known to carry a risk of QTc interval prolongation, bradyarrhythmia, and the presence of electrolyte disturbances specifically low levels of potassium and/or magnesium in the bloodstream.[9]

Geriatric patients with multiple comorbidities constitute a substantial proportion of ICU admissions. A previous investigation revealed that individuals aged 65 and above accounted for 45.7% of total ICU admissions.[10] Aging itself is correlated with an increased incidence of cardiac arrhythmias, primarily attributed to physical and functional alterations in cardiac muscle and the electrical conduction system. These changes contribute to higher occurrence of age-related cardiac arrhythmias. Additionally, aging associated changes in the cardiac function play a role in promoting arrhythmias during the aging process.[11]

In response to the imperative need for safer medication usage and the prevention of QTc interval prolongation, which can lead to TdP events, CredibleMeds® (www.crediblemeds.org)[12] has introduced an online tool to classify and assess drugs with potential to induce prolongation and TdP. This tool categorizes medications associated with TdP flare into three distinct groups: drugs with a known risk of TdP, drugs with a possible TdP risk, and drugs with a conditional TdP risk.

The primary objective of this study is to investigate the prevalence of prescribing of TdP associated medications among critically ill patients admitted to ICU. The secondary objective is to evaluate the associated factors that can increase the risk of QTc interval prolongation and TdP in this group. Finally, to identify the main predictors associated with higher level of TdP associated medication prescribing in these patients.

Methods

Study Design, Sample Characteristics, and Data Collection

A retrospective cross-sectional study was conducted at the Intensive Care Unit (ICU) of King Abdullah University Hospital (KAUH) in Jordan. All patients admitted to ICU at KAUH during the period of 10 years (from July 2012 – July 2022) were included in the study for further analysis. A total number of 13,300 electronic medical records were evaluated and assessed, respectively. Data was gathered by collecting patients' medication records that have demographic data, clinical characteristics, past medical history, relevant biomedical lab results, and prescribed medications for all patients, co-existed comorbidities, and length of stay (LOS) duration in the ICU. Risk factors that are correlated positively with TdP occurrence were identified through evaluating patients' age, gender, presence of structural or conduction related cardiac diseases, hypothyroidism, diabetes, liver and/or kidney impairment, and medication polypharmacy. Drugs associated with TdP and QTc prolongation risks were assessed and further categorized into three main categories according to the most updated CredibleMeds online QT-Drug List (August 20th, 2023).[12] First, medications with "known risk category" which includes all medications with substantial body of evidence linking them to definite risk of causing QTc interval prolongation and risk of TdP when used as directed in the drug leaflet. Second, medications with "possible risk" category which includes all medications with substantial body of evidence linking them to possible risk of causing QTc prolongation but with inadequate evidence that such drugs, when utilized as directed in the drug leaflet, have a risk of TdP. Third, conditional risk category which include all medications with substantial body of evidence linking them to risk of causing QTc prolongation and developing TdP, but only under certain known circumstances (eg, use with

concomitant QTc/TdP associated drug, use of excessive dose, their use could lead to hypokalemia and/or hypomagnesemia).

Statistical Analysis

Data were gathered and analyzed using both Microsoft Excel and SPSS (version 28). Descriptive statistics were employed to describe the demographics and other characteristics of the patients. Categorical variables were represented as frequencies (%), while continuous variables were expressed as medians (95% confidence interval). The primary focus was on determining the prevalence of drugs associated with TdP. Patients' data were entered into a database to extract key variables, including the prevalence of TdP-inducing drugs, the distribution of TdP categories for each drug, and the examination of connections between various risk factors and different levels of medication-related TdP risk (encompassing known risk, possible risk, conditional risk, and confirmed conditional risk). A binary logistic regression model was constructed to determine factors linked to the usage of at least one drug with TdP risk. The independent variables were age, gender, length of stay, polypharmacy, and number of comorbidities. Statistical significance was determined at a p-value <0.05.

Ethical Approval

This study was approved by the Institutional Review Board (IRB) at Jordan University of Science and Technology (JUST) and affiliated King Abdullah University Hospital (KAUH). Approval Number was 56/162/2023. The patient's medical records were assessed retrospectively and for study purposes only. Hence, the requirement for informed consent was waived by the Institutional Review Board (IRB) committee at JUST/KAUH.

Results

A total of 13,300 patients were included in the study (58.2% Male), with a median age of 62 (62–63) years old. The median length of stay for patients in the ICU was 4 (4–5) days. The median polypharmacy count was 6 (6–7) medications. Additionally, patients had a median of 1 (1–2) comorbidity (Table 1). A range of comorbidities are also documented in Table 1. The most occurrences were hypertension, diabetes, and cancer (40.9%, 33.3%, and 15.4% respectively). In contrast, the least common comorbidities were coronary artery diseases (0.3%), Parkinson (0.5%), anemia (0.7%).

Table 2 outlines the frequency distribution of various blood test parameters categorized as "Low", "Normal", and "High". The majority of the patients had a normal value of ALP (93.1%), ESR (91.6%), total bilirubin (91.3%). In contrast, many patients had high values of neutrophils count, urea, and creatinine (46.5%, 33.6%, and 24.7% respectively).

Crucial electrolytes are also presented in Table 2. Regarding magnesium, 85.6% of patients exhibit results within the normal range, while 10.6% display low levels, and 3.9% exhibit elevated levels. Similarly, the distribution of potassium illustrates that 81.4% of patients have levels considered normal, 8.5% have lower levels, and 10.1% have higher levels. Calcium levels also primarily appear to fall within the normal range, as 77.6% of patients show values within the expected range, 21.6% show lower values, and 0.8% show higher levels.

Table 3 provides an in-depth overview of medications categorized based on their potential risks related to TdP. These medications are grouped into "Known Risk of TdP", "Possible Risk of TdP", and "Conditional Risk of TdP".

Regarding drugs with known risk of TdP, a subset of patients (ranging from 0.1% to 8.1%) are prescribed drugs such as amiodarone, ciprofloxacin, citalopram, and others that have a recognized risk of TdP. The number of drugs taken within this category varies, with the majority of patients (79%) taking no such drugs, while a smaller portion was on one (19%), two (1.9%), or three or more (0.1%) drugs with known TdP risk.

The "Possible Risk of TdP" category includes medications like 5-fluorouracil, alfuzosin, and bicalutamide, which could potentially be linked to TdP, although this association is not as firmly established. Seventy-two percent of the patients were not taking such drugs, while 24.7% were on one, 2.9% on two, and only 0.4% were on three or more.

Table 1 Demographics and the Disease Profile of the Enrolled Patients

	Frequency (%) or Median (95% CI)
Age	62 (62–63)
Gender	
Female	5559 (41.8%)
Male	7741 (58.2%)
Length of Stay	4 (4–5)
Polypharmacy	6 (6–7)
Number of comorbidities	1 (1–2)
Anemia	96 (0.7%)
Asthma	243 (1.8%)
Atrial fibrillation	613 (4.6%)
BPH	226 (1.7%)
CAD	42 (0.3%)
Cancer	2044 (15.4%)
Chronic kidney disease (CKD)	769 (5.8%)
COPD	248 (1.9%)
Diabetes	4425 (33.3%)
DVT	217 (1.6%)
Epilepsy	253 (1.9%)
ESRD	432 (3.2%)
Gout	228 (1.7%)
Hyperlipidemia	321 (2.4%)
Hypertension	5439 (40.9%)
Hypothyroidism	368 (2.8%)
IHD	1874 (14.1%)
Obstructive sleep apnea OS	114 (0.9%)
Osteoporosis	158 (1.2%)
Parkinson	67 (0.5%)
Stroke/ CVA	1243 (9.3%)

Similarly, the "Conditional Risk of TdP" group features medications like abiraterone amantadine sulfate, amisulpride, and others, with varying levels of confirmed conditional risk, with the majority taking none (90.5%), followed by patients using one (8.3%), two (1.1%), and three or more (0.1%).

Table 4 provides a comprehensive overview of different risk factors and their associations with varying levels of medication risk concerning TdP. Drugs with known risk were more commonly prescribed to patients exhibiting polypharmacy (taking five or more medications), followed by patients with electrolyte disturbances, as well as those with impaired liver or kidney function (25.8%, 23.9%, and 23.6% respectively). Regarding drugs with possible risk, they

Table 2 Blood Test Parameters of Study Patients

	Low Frequency (%)	Normal Frequency (%)	High Frequency (%)	Median (IQR)
ALT	–	11,738 (88.2%)	1563 (11.8%)	20.1 (11.9–41.4)
Albumin	2737 (20.6%)	10,529 (79.2%)	35 (0.3%)	32.9 (26.7–38.9)
ALP	–	12,389 (93.1%)	912 (6.9%)	124 (82–206)
AST	–	11,038 (83%)	2263 (17%)	29.3 (18.1–63)
Calcium	2869 (21.6%)	10,322 (77.6%)	110 (0.8%)	2.11 (1.94–2.26)
Creatinine	2280 (17.1%)	7740 (58.2%)	3281 (24.7%)	90 (62–169.24)
Direct bilirubin	–	11,244 (84.5%)	2057 (15.5%)	4.3 (2.4–10.1)
HCO3	2996 (22.5%)	9004 (67.7%)	1301 (9.8%)	21.7 (17.7–25.5)
Hgb	5983 (45%)	7125 (53.6%)	193 (1.5%)	10.8 (9–12.8)
Lymphocytes (%)	7075 (53.2%)	6029 (45.3%)	197 (1.5%)	9.4 (5.2–16.8)
Magnesium	1407 (10.6%)	11,380 (85.6%)	514 (3.9%)	0.79 (0.7–0.9)
MPV	11 (0.1%)	10,509 (79%)	2781 (20.9%)	9.3 (8.4–10.4)
Neutrophils (%)	862 (6.5%)	6257 (47%)	6182 (46.5%)	83.3 (72.8–89.7)
Pco2	2444 (18.4%)	9420 (70.8%)	1437 (10.8%)	37 (30.7–45)
PH	2174 (16.3%)	10,006 (75.2%)	1121 (8.4%)	7.38 (7.31–7.44)
Phosphorus	781 (5.9%)	11,230 (84.4%)	1290 (9.7%)	1.2 (0.94–1.56)
PLT	2182 (16.4%)	10,354 (77.8%)	765 (5.8%)	222 (152–296)
Po2	2904 (21.8%)	8580 (64.5%)	1817 (13.7%)	74.65 (51–113.1)
Potassium	1125 (8.5%)	10,826 (81.4%)	1350 (10.1%)	4.25 (3.8–4.79)
RBC	4264 (32.1%)	8678 (65.2%)	359 (2.7%)	3.87 (3.22–4.54)
Sodium	1793 (13.5%)	10,201 (76.7%)	1307 (9.8%)	139 (135–143)
Total bilirubin	129 (1%)	12,144 (91.3%)	1028 (7.7%)	10.6 (6.5–20.6)
Total protein	2477 (18.6%)	10,795 (81.2%)	29 (0.2%)	61.1 (53.3–68.3)
Urea	202 (1.5%)	8634 (64.9%)	4465 (33.6%)	8.13 (4.8–15.85)
WBC	293 (2.2%)	7960 (59.8%)	5048 (38%)	11.8 (8.4–16.5)
GLU	90 (0.7%)	11,644 (87.5%)	1567 (11.8%)	8.4 (5.9–13.81)
ESR	–	12,185 (91.6%)	1116 (8.4%)	47 (21–80)
Creatine kinase	227 (1.7%)	12,061 (90.7%)	1013 (7.6%)	153 (69–446)

were more frequently prescribed to patients with polypharmacy (36.1%), followed by diabetic patients (28.6%) and patients with electrolyte disturbances (27.3%). Drugs with confirmed conditional risk were more prescribed to patients with electrolyte imbalances, followed by those with polypharmacy, and then diabetic patients.

Overall, more than half of the patients with polypharmacy and those with electrolyte imbalances were prescribed at least one of the medications categorized as TdP risk drugs (including drugs with known risk, possible risk, and confirmed conditional risk).

Table 3 Medications Categorizing Based on Their Potential Risks Related to TdP

		Frequency (%)
Known Risk of TdP		
Amiodarone		647 (4.9%)
Azithromycin		20 (0.2%)
Ciprofloxacin		233 (1.8%)
Citalopram		1075 (8.1%)
Clarithromycin		237 (1.8%)
Domperidone		132 (1%)
Escitalopram		75 (0.6%)
Flecainide acetate		206 (1.5%)
Fluconazole		44 (0.3%)
Gatifloxacin		53 (0.4%)
Haloperidol		6 (0%)
Hydroxychloroquine		271 (2%)
Levofloxacin		21 (0.2%)
Ondansetron		37 (0.3%)
Oxaliplatin		5 (0%)
Papaverine		19 (0.1%)
Propofol		3 (0%)
Number of taken drugs with known risk	0	10,502 (79%)
	1	2529 (19%)
	2	255 (1.9%)
	3 or more	15 (0.1%)
Possible Risk of TdP		
Alfuzosin		393 (3%)
Bicalutamide		589 (4.4%)
Capecitabine		34 (0.3%)
Carbetocin		216 (1.6%)
Clozapine		62 (0.5%)
5-fluorouracil		2579 (19.4%)
Flupenthixol		10 (0.1%)
Imatinib		71 (0.5%)
Imipramine		2 (0%)
Lapatinib		29 (0.2%)

(*Continued*)

Table 3 (Continued).

		Frequency (%)
Levetiracetam		6 (0%)
Mirabegron		14 (0.1%)
Mirtazapine		20 (0.2%)
Oxytocin		4 (0%)
Remdesivir		14 (0.1%)
Tacrolimus		51 (0.4%)
Tamoxifen		14 (0.1%)
Tizanidine		27 (0.2%)
Tolterodine		40 (0.3%)
Tramadol		27 (0.2%)
Venlafaxine		5 (0%)
Zuclopenthixol acetate		20 (0.2%)
Number of taken drugs with possible risk	0	9571 (72%)
	1	3288 (24.7%)
	2	391 (2.9%)
	3 or more	51 (0.4%)
Conditional Risk of TdP		
Abiraterone		47 (0.4%)
Amantadine sulphate		700 (5.3%)
Amisulpride		1324 (10%)
Amphotericin b liposomal		762 (5.7%)
Clomipramine		5 (0%)
Diltiazem		72 (0.5%)
Esomeprazole		1 (0%)
Famotidine		43 (0.3%)
Fluoxetine		37 (0.3%)
Fluvoxamine		68 (0.5%)
Furosemide		6 (0%)
Hydrochlorothiazide		41 (0.3%)
Indapamide		46 (0.3%)
Itraconazole		8 (0.1%)
Ivabradine		7 (0.1%)
Lansoprazole		33 (0.2%)

(*Continued*)

Table 3 (Continued).

		Frequency (%)
Metoclopramide		39 (0.3%)
Metronidazole		111 (0.8%)
Olanzapine		50 (0.4%)
Omeprazole		47 (0.4%)
Piperacillin		33 (0.2%)
Quetiapine		131 (1%)
Ranolazine		27 (0.2%)
Risperidone		20 (0.2%)
Risperidone		20 (0.2%)
Sertraline		9 (0.1%)
Solifenacin succinate		45 (0.3%)
Voriconazole		8 (0.1%)
Number of taken drugs with all conditional risk	0	10,012 (75.3%)
	1	2871 (21.6%)
	2	399 (3%)
	3 or more	19 (0.1%)
Number of taken drugs with confirmed. conditional risk	0	13,217 (90.5%)
	1	1212 (8.3%)
	2	165 (1.1%)
	3 or more	11 (0.1%)

A binary regression model was built to identify variables associated with taking at least one drug with TdP risk. Nagelkerke R Square was 0.23 indicating moderate model fit, and the results revealed that as the age increases the odds of taking at least one drug with TdP risk decreases (OR = 0.989, 95% Cl (0.987–0.991), $p < 0.001$). However, patients taking more than five medications demonstrated an elevated likelihood of using at least one drug with TdP risk (OR = 4.281, 95% Cl (3.935–4.658), $p < 0.001$).

Discussion

This study represents the inaugural effort to ascertain the prevalence of medications, prescribing characterized by definite and potential prolonged QT interval and TdP risks, along with the identification of risk factors contributing to the cumulative burden of TdP in critically ill patients from Jordan. The outcomes of our investigation offer invaluable insights into medication prescribing practices and potential vulnerabilities within this population.

The current study has unveiled a relatively high prevalence of medications prescribing among critically ill patients admitted to ICU encompassing varying levels of TdP risk. Specifically, the prevalence rates for the prescription of at least one drug with a known risk of TdP were 19%, possible risk (24.7%), conditional risk (21.6%), and confirmed conditional risk (8.3%). These prevalence figures exhibit notable disparities when compared to our previous study which was conducted on elderly outpatients and reported lower prevalence rates for drug prescribing with know and possible TdP

Table 4 Medication Distribution According to Both Risk Factors and TdP Risk Category

	Known Risk	Possible Risk	Conditional Risk	Confirmed Conditional Risk	Total (with All Conditional Risk)	Total (with Confirmed Conditional Risk)
Gender (female)	1214 (21.8%)	1476 (26.6%)	1244 (22.4%)	568 (10.2%)	3070 (55.2%)	2452 (44.1%)
Age (≥65)	1259 (20.8%)	1539 (25.5%)	1727 (28.6%)	765 (12.7%)	3506 (58%)	2632 (43.6%)
Structural or conduction related cardiac disease	1425 (21.3%)	1797 (26.8%)	2021 (30.2%)	857 (12.8%)	3996 (59.7%)	2954 (44.1%)
Impaired liver or kidney function	1379 (23.6%)	1558 (26.7%)	1674 (28.7%)	752 (12.9%)	3539 (60.7%)	2702 (46.3%)
Thyroid disease (Hypothyroidism)	77 (20.9%)	90 (24.5%)	96 (26.1%)	43 (11.7%)	200 (54.3%)	151 (41%)
Electrolyte disturbances	956 (23.9%)	1092 (27.3%)	944 (23.6%)	651 (16.3%)	2322 (58.1%)	2058 (51.5%)
Diabetes	979 (22.1%)	1266 (28.6%)	1349 (30.5%)	610 (13.8%)	2734 (61.8%)	2060 (46.6%)
Polypharmacy (≥ 5 medications)	2232 (25.8%)	3130 (36.1%)	2625 (30.3%)	1246 (14.4%)	5966 (68.8%)	4743 (54.7%)

risk equal to 14.9%, and 16.6%, respectively.[13] These discrepancies in prevalence can be elucidated by the nature of the conditions prevailing in each respective healthcare setting. Critically ill patients are more susceptible to polypharmacy and administration of a greater number of medications. This phenomenon is primarily due to the presence of complex comorbidities, infections, and the imperative for intensive therapeutic management during their ICU confinement. Additionally, ICU patients frequently experience electrolyte imbalances, such as low potassium and magnesium levels, which are known triggers for TdP.[14] Furthermore, the therapeutic objectives differ significantly between the two settings. While outpatient services concentrate on enhancing the quality of life and managing disease symptoms, the overarching goal in the ICU is to avert short-term mortality and enhance survival rates. Consequently, the prevention of medication-related issues may not be the foremost priority for ICU physicians during their patient care duties. Hypertension, diabetes, and cancer were the most common conditions found to exist among critically ill patients in this study. The history of hypertension and diabetes have been implicated as definite risk factors for QTc interval prolongation and instigating Torsade arrhythmia. Various reports have identified definite correlations between QTc interval prolongation and cardiovascular diseases and diabetes.[15–18] An early study has found that prevalence of long QTc interval was higher in patients with type 2 diabetes and impaired insulin sensitivity was associated significantly with increased QTc interval among type 2 diabetic patients.[16] On the other hand, a recent large scale epidemiological study has demonstrated that cancer patients had longer QTc interval compared to non-cancer healthy individuals.[19] The same study attributed the reasons behind their note to the prescription pattern of antiemetic medications and pain killers linked to high risk of QTc prolongation in cancer patients.

In this study, citalopram, amiodarone, clarithromycin, and ciprofloxacin emerged as the most frequently prescribed medications with known risk of TdP. Notably, citalopram has been confirmed to prolong QTc interval even at lower doses particularly in geriatric patients with chronic comorbidities and polypharmacy. This finding positions citalopram as a less favorable treatment option when compared to other selective serotonin reuptake inhibitors within this patient population.[20] It has been previously suggested that macrolides antibiotics, especially clarithromycin and erythromycin have the highest ability to induce QTc interval prolongation due to their intrinsic properties of inducing QTc prolongation and their strong inhibitory activity of the cytochrome P450 and metabolism inhibition of other drug linked to QTc interval prolongation.[21]

Exploring other risk factors known to prolong QTc interval and increase the likelihood for TdP development has revealed that more than half of the patients with polypharmacy and those with electrolyte imbalances, including hypokalemia and hypomagnesemia, were prescribed at least one of the medications categorized as TdP risk drugs. Since polypharmacy is often associated with individuals who have multiple chronic conditions, such as hypertension, diabetes, or heart disease.[22] These conditions themselves can increase the risk of TdP independently, in addition to that, medications used to treat these comorbidities may further contribute to the TdP risk. Also, the existence of polypharmacy prescribing could carry greater number of serious drug–drug interactions, especially those boosting the pharmacokinetic availability of many drugs with potential TdP risk in the circulation leading to QTc interval prolongation yonder normal limits.[23] Furthermore, polypharmacy may compromise the body's ability to clear drugs from the system mainly at pharmacokinetic level suggesting more odds for clinically relevant drug–drug interactions.[24]

Limitation of the Study

This study is limited by its retrospective cross-sectional design. Causality relationship measurements were not feasible to assess in this study. The researchers were not able to address whether utilization of drugs with TdP risks was associated clinically with QTc interval prolongation. However, this study included a large sample size to address the prescribing practice among critically ill patients, especially for drugs with potential overlooked life threating consequences including TdP arrhythmia.

Conclusion

In summary, our study indicated a high prevalence of medication administration attributed to long QT prolongation/ Torsade de Points risk among critically ill patients admitted to intensive care unit. This study showed urgent need to assess critically ill patients for their medications administered comprehensively to prevent unnecessary risk of developing life-threatening conditions, including Torsade de Pointes and sudden death.

Data Sharing Statement

Data used to conduct this research will be available from the corresponding author based on reasonable request.

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Disclosure

The authors declare no competing interest in this work.

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