Original Article

Assessment of Potential Drug-Drug Interactions and their Clinical Significance Among Critically Ill Patients in A Tertiary Care Setting

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ABSTRACT

Introduction: Drug-drug interactions (DDIs) are common in critically ill patients due to polypharmacy and complex therapeutic regimens in the intensive care unit (ICU). These interactions may result in therapeutic failure, adverse drug reactions, prolonged hospitalization, and increased healthcare costs. This study aimed to evaluate the prevalence, mechanisms, and clinical significance of potential DDIs in ICU inpatients of a tertiary care hospital.

Materials & Methods: This observational cross-sectional study was conducted over six months (November 2024–April 2025) in the ICU of a tertiary care hospital in western India. A total of 300 prescriptions involving 1,994 drugs were analyzed. Potential DDIs were screened using the Drugs.com interaction checker and "Drug Interaction Facts" reference. Prevalence of drug-drug interactions in the ICU and their classification based on mechanism (pharmacokinetic or pharmacodynamic) and severity (major, moderate, minor). Descriptive statistics were used for data analysis.

Results: Out of 300 prescriptions, 214 (71.3%) had at least one DDI, with 683 total interactions identified, averaging 2.28 DDIs per prescription. Pharmacodynamic interactions predominated (65%) compared to pharmacokinetic (34.9%), with metabolism-related interactions being the most frequent among the latter. Regarding severity, moderate interactions were most common (75.25%), followed by minor (12.88%) and major (11.85%) interactions.

Conclusion: This study demonstrates a high prevalence of potential DDIs among ICU patients, with moderate-severity interactions being predominant. Continuous prescription audits, integration of clinical decision-support systems, and active involvement of clinical pharmacists are essential to reduce preventable adverse outcomes and improve patient safety.

Keywords: Drug-drug interactions, Intensive care unit, Pharmacodynamic, Pharmacokinetic, Prescription audit.

INTRODUCTION

Drug interactions (DDIs) occur when the pharmacological effect of a drug is altered by the presence of another substance, which can be another drug, food, or an environmental factor. Among these, drug–drug interactions are particularly significant, as they can lead to therapeutic failure or increased drug toxicity. DDIs occur when one drug affects the absorption, distribution, metabolism, or excretion (pharmacokinetic interactions) or the pharmacodynamic properties of another drug, leading to altered therapeutic effects. These interactions can result in adverse drug reactions (ADRs), increased hospitalizations, prolonged treatment duration, and higher healthcare costs.[1]

Drug–drug interactions (DDIs) are highly prevalent in intensive care units (ICUs), primarily due to polypharmacy, complex treatment regimens, and the critical nature of patients' conditions. Studies have reported DDI prevalence rates in ICUs ranging from 28% to 96%, indicating a significant risk in these settings.[2]

While several studies have quantified the prevalence of potential DDIs in ICU settings, there remains a significant gap in the literature concerning the detailed categorization of these interactions based on their underlying mechanisms — whether pharmacokinetic or pharmacodynamic and their clinical severity. The study aims to address this need by not only estimating the prevalence of potential DDIs in ICU patients but also categorizing them by mechanism and severity, thus contributing to more informed and safer pharmacotherapy practices in critical care.

Aim: To assess drug-drug interactions (DDIs) through prescription analysis among inpatients in the ICU of a tertiary care teaching hospital.

Objective: To evaluate the potential for drug-drug interactions in the prescriptions of patients admitted to the ICU and categorize drug-drug interactions based on the mechanisms involved and their severity.

MATERIALS AND METHODS

Study site and study period: The study was conducted for a period of 6 months from 1st Nov 2024 to 30th April 2025 in the Intensive Care Unit of a tertiary care hospital in western India.

Regulatory approval: Necessary approval by The Scientific Review Committee and Institutional Ethical Committee of Human Research (Approval No: N-EC/2019/SC/07/103) was received before proceeding for the study.

Population, Inclusion, and Exclusion criteria

The study included patients who were admitted to the intensive care units and were prescribed two or more medications. The study population comprised individuals of both genders, aged above 18 years, who had given informed consent. Patients who were excluded from the study included outpatients, those with a history of drug abuse, individuals who had undergone surgical procedures, pregnant and lactating women, and those who did not provide consent.

Sample size determination

The sample size was determined using the formula:

$$n = Z^2 \times P \times (1 - P) / d^2$$

where *n* is the required sample size, *Z* is the Z-statistic corresponding to the desired level of confidence, *P* is the expected prevalence or proportion (expressed as a decimal), and *d* is the margin of error (precision), also expressed as a decimal. For a 95% confidence level, the Z-score is 1.96, and the margin of error (d) is set at 5% (0.05). In this study, an expected prevalence (*P*) of 75% was assumed based on previous published literature[3] which reported 76.5% of ICU patients had potential DDIs.

Substituting the values into the formula:

$$n = (1.96)^2 \times 0.75 \times (1 - 0.75) / (0.05)^2 = 288$$

Therefore, a total of 300 prescriptions of patients admitted to the intensive care unit (ICU) were included in the study to assess drug-drug interactions.

Study design & data collection:

This was an observational cross-sectional study, carried out in the intensive care unit of a tertiary care hospital. After getting approval from the institutional ethics committee data was collected from case sheets, medical records of patients admitted in ICU and a documentation form for collecting information on drug-drug interaction was used. Drug-drug interaction documentation form included the patient details, diagnosis, drugs prescribed and clinical outcome.

Data were analyzed in the following manner:

1. Prevalence of drug-drug interactions in ICU
2. Screening for the potential drug-drug interactions was done by using the drug interaction checker within www.drugs.com database [4] and a reference book of "Drug Interaction Facts" published in 2011.[5] Drug interactions were categorized based on the mechanism as pharmacokinetic or pharmacodynamic interactions. The pharmacokinetic drug interactions were further categorized into interactions based on absorption, distribution, metabolism and elimination.
3. The severities of the interactions were assessed and categorized as major (can cause permanent damage or life risk), moderate (can cause harm and treatment is required) or minor (can cause small or no clinical effect, with no treatment required).

Statistical analysis:

The data was entered and statistically analysed in Microsoft Excel 2007. The mean, standard deviation, frequency, and percentage were used to describe the data.

RESULTS

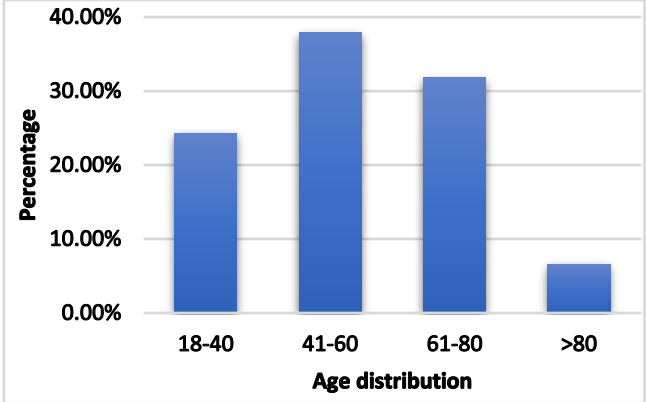

Figure 1: Age Distribution of Patients in ICU with Drug-Drug Interactions

In the present study, the majority of drug-drug interactions (DDIs) were observed in patients aged 41–60 years (37.85%), followed by those in the 61–80 years group (31.77%). Younger patients aged 18–40 years accounted for 24.29% of DDIs, while the least were seen in patients above 80 years (6.54%). This indicates that middle-aged and elderly patients are more vulnerable to DDIs compared to the extremes of age.

Prevalence of drug-drug interactions in ICU:

Prevalence (%) = [Number of prescriptions with ≥1 DDI¸ Total prescriptions] x 100 = 71.33 %

Average number of drug-drug interactions per prescription

Average DDIs per prescription =Total number of DDIs¸ Total prescriptions

= 683¸ 300 = 2.28

In this study, a total of 300 prescriptions comprising 1994 drugs were analyzed. The average number of drugs per prescription was 6.65. Among these, 683 potential drug-drug interactions (DDIs) were identified. A total of 214 prescriptions (71.3%) had at least one DDI, with an average of 2.28 DDIs per prescription**.**

Among the pharmacokinetic interactions (n = 239; 34.9 %), metabolism was the most frequent component, accounting for 145 interactions (60.6 %; $P < 0.05$ compared with absorption**,** distribution, or excretion)**,** followed by absorption with 61 (25.5 %)**,** excretion with 24 (10.0 %), and distribution with just 9 (3.7 %). Pharmacodynamic interactions totaled 444 (65 %), significantly exceeding the pharmacokinetic category ($P < 0.01$).

Table 1: Categorization of drug-drug interactions based on Mechanism

Mechanism of drug-drug interaction	Number of interactions	Percentage	P value
Pharmacokinetic	239	34.9%	-
Absorption	61	25.5%	-
Distribution	9	3.7%	-
Metabolism	145	60.6%	P < 0.05
Excretion	24	10%	-
Pharmacodynamic	444	65%	P<0.01

P < 0.01 compared with Pharmacokinetic drug interactions; P < 0.05 compared with absorption, distribution, excretion mediated drug interactions.

Table 2: Categorization of drug-drug interactions based on Severity

Severity of drug interactions	Number of drug interactions (n = 683)
Major	81 (11.85%)
Moderate	514 (75.25%)*
Minor	88 (12.88%)
*p value < 0.01 compared with Major and Minor drug interactions	

Moderate severity interactions accounted for514 out of 683 cases (75.25 %; p < 0.05 vs major and minor), while major interactionsnumbered81 (11.85 %) and minor interactionstotalled88 (12.88 %). The predominance of moderate severity is clearly reflected in these frequencies (severity categories defined as major, moderate, minor based on clinical impact)

Table 3: Percentage Distribution of Major Drug-Drug interactions, Mechanism and Outcome

Drug-drug interaction combinations	Mechanism	Outcome	Frequency N (%)
Aspirin and Enoxaparin	COX-1 inhibition + Antithrombin III activation (Pharmacodynamic)	↑ Bleeding risk	12 (14.81%)
Heparin and Streptokinase	Antithrombin III activation + fibrinolysis (Pharmacodynamic)	↑ Bleeding complications	10 (12.35%)
Norepinephrine + Vasopressin	Dual vasoconstriction synergistically reduce blood flow to peripheral tissues (Pharmacodynamic)	-Risk of tissue ischemia and necrosis	9 (11.11%)
Methotrexate + Cotrimoxazole	Synergistic inhibition of folate metabolism (Pharmacodynamics)	- Risk of bone marrow suppression	9 (11.11%)
Amiodarone and Ondansetron	Synergistic QT prolongation via potassium channel blockade (Pharmacodynamic)	↑ Arrhythmogenic potential	6 (7.41%)
Ondansetron and Linezolid	MAO inhibition + ↑ serotonergic tone (Pharmacodynamic)	Serotonin Toxicity	6 (7.41%)
NSAIDS + Ramipril	¯Glomerular Filtration Rate (Pharmacodynamic)	Potential for Acute Kidney Injury	5 (6.17%)
Digoxin + Pantoprazole	Pantoprazole raises pH, increasing digoxin absorption (Pharmacokinetics)	Digoxin Toxicity	4 (4.94%)
Spironolactone and Potassium Chloride	Additive effect on potassium retention (Pharmacodynamic)	Cardiac arrhythmias, muscle weakness & cardiac arrest	3 (3.7%)
Fluconazole and Phenytoin	CYP2C9/2C19 inhibition → ↓ phenytoin clearance (Pharmacokinetic)	↑ Phenytoin toxicity	2 (2.46%)

In 35 major drug-drug interactions, 10 different interacting drug combinations were identified and are given in Table 3 with their outcomes.

Table 4: Percentage Distribution of Moderate Drug-Drug interactions, Mechanism and Outcome

Drug-drug interaction combinations	Mechanism	Outcome	Frequency N (%)
Aspirin + Clopidogrel	Both inhibit platelet function, increasing bleeding risk (Pharmacodynamic)	Increased bleeding risk	51(9.92%)
Aspirin + Insulin	Aspirin enhances insulin's glucose-lowering effect (Pharmacodynamic)	Higher chance of hypoglycaemia	46 (8.95%)
Metoprolol + Amlodipine	Additive cardiac suppression, raising bradycardia risk (Pharmacodynamic)	Risk of bradycardia	30 (5.84%)
Atorvastatin + Clopidogrel	Atorvastatin lowers clopidogrel's active metabolite (Pharmacokinetic)	Reduced antiplatelet effect	28 (5.45%)
Furosemide + Carvedilol	Combined blood pressure reduction and electrolyte imbalance (Pharmacodynamic)	Hypotension and arrhythmia risk	25 (4.86%)
Loop Diuretics + Diclofenac (NSAID)	¯Prostaglandin synthesis by diclofenac leading to decreased renal perfusion and attenuated diuretic effect	¯ Efficacy of loop diuretics	20 (3.89%)
Furosemide + Pantoprazole	Increased magnesium loss through urine (Pharmacokinetic)	Risk of low magnesium	19 (3.69%)
Amlodipine + Atorvastatin	CYP3A4 inhibition raises statin toxicity risk (Pharmacokinetic)	Risk of muscle breakdown (rhabdomyolysis)	19 (3.69%)
Fluconazole and Atorvastatin	CYP3A4 inhibition → ↓ statin metabolism	Fluconazole and Atorvastatin	18 (3.5%)
Hydrocortisone and Levofloxacin	Collagen degradation + impaired tendon repair	Hydrocortisone and Levofloxacin	15 (2.91%)

Moderate drug-drug interactions were more common514 (75.25%) than both major and minor interactions. Table 4 represents ten most frequent moderate drug -drug interaction pairings along with their outcomes.

Table 5: Top 10 Minor Drug-drug interaction combinations, Mechanism and Outcome

Drug-drug interaction combination	Mechanism	Outcome	Frequency N (%)
Pantoprazole + Sucralfate	Both act on gastric mucosa — pantoprazole reduces acid secretion, sucralfate forms a protective barrier	Mildly improved ulcer healing	20 (22.72%)
Omeprazole + Clopidogrel	Omeprazole inhibits CYP2C19, reducing clopidogrel activation.	Mild reduction in antiplatelet activity.	18 (20.45%)
Metoclopramide + Acetaminophen	Accelerated gastric emptying ↑ absorption;	Metoclopramide + Acetaminophen	12 (13.63%)
Heparin + IV Nitroglycerin	Nitroglycerin may reduce heparin's anticoagulant response.	Mild reduction in aPTT; monitor anticoagulation.	9 (10.22%)
Aztreonam + Gentamicin	Aztreonam may mildly increase gentamicin serum levels by reducing its renal clearance (Pharmacokinetic)	Slight risk of nephrotoxicity or ototoxicity	6 (6.81%)
Ondansetron + Dexamethasone	Both reduce nausea via different pathways — ondansetron blocks 5-HT3 receptors, dexamethasone	Enhanced antiemetic effects	5 (5.68%)
Miconazole + Tobramycin	Miconazole may inhibit the metabolism and renal clearance of tobramycin	Higher risk of nephrotoxicity or ototoxicity	5 (5.68%)
Amiodarone + Atorvastatin	Amiodarone may increase atorvastatin plasma levels via CYP3A4 inhibition.	Mild myopathy risk	4 (4.54%)
Furosemide + Dobutamine	Dobutamine may counteract hypokalemia caused by furosemide.	Slight alteration in potassium; generally mild.	3 (3.40%)
Metoprolol + Digoxin	Additive AV node conduction delay.	Bradycardia or Atrioventricular block	3 (3.40%)

Out of 88 minor drug-drug interactions more prevalent drug interaction combinations with outcomes are given in Table 5.

DISCUSSION

Patients aged 41–60 years are more prone to drug-drug interactions due to polypharmacy from chronic comorbidities and additional ICU medications. Early physiological changes such as reduced renal or hepatic function, further increase their susceptibility to altered drug metabolism and effects.[6]

Mechanism of Drug-Drug Interactions:

In the present study, pharmacodynamic interactions were observed more frequently than pharmacokinetic interactions. In critically ill patients admitted to the ICU, the use of multiple drugs to manage diverse clinical conditions such as pain, sedation, infection, and hemodynamic instability leads to a high risk of pharmacodynamic drug-drug interactions. These interactions arise when medications exert additive, synergistic, or antagonistic effects on the same physiological systems. Additionally, the presence of organ dysfunction, which is common in ICU patients, can significantly alter the pharmacodynamic response to drugs even when drug concentrations remain unchanged. As a result, pharmacodynamic interactions tend to be more clinically significant in this setting than pharmacokinetic interactions.[7]

In the ICU setting, among pharmacokinetic drug-drug interactions, those involving metabolism are significantly more common than those affecting absorption, distribution, or excretion. This can be attributed to the fact that many drugs used in critically ill patients are metabolized by the cytochrome P450 enzyme system, which is highly susceptible to induction or inhibition by co-administered agents.[8]

Major Drug-Drug Interactions:

The present study highlights that the most frequent major drug-drug interactions (DDIs) observed in the ICU involved combinations with antithrombotic agents such as aspirin and enoxaparin (14.81%), heparin with streptokinase (12.35%), and vasopressors like norepinephrine with vasopressin (11.11%). These interactions primarily exhibit pharmacodynamic mechanisms with additive or synergistic effects, resulting in serious clinical outcomes such as bleeding complications and tissue ischemia. The clinical significance of these findings lies in the heightened vulnerability of critically ill patients to such adverse effects due to polypharmacy and organ dysfunction. Prevention strategies include close monitoring of coagulation parameters, renal function, individualized dosing, and the use of clinical decision support tools or automated alerts in electronic prescribing systems.

Similar patterns have been reported in Indian studies. A study by Risvana et al. reported that anticoagulants and antiplatelets were among the most frequently implicated agents in hospitalized cardiology patients, reflecting their high use and narrow therapeutic index.[9] Wagh et al. found a high prevalence of major interactions in ICU patients, with many involving cardiovascular agents, including vasopressor combinations, which can potentiate adverse hemodynamic effects. They also noted interactions between QT-prolonging agents such as ondansetron and amiodarone, posing a substantial risk for arrhythmias.[10]These studies reinforce the need for increased vigilance, protocol-driven therapy, and regular medication review to reduce preventable DDI-related morbidity in ICU settings.

Moderate Drug-Drug Interactions:

Among the moderate drug-drug interactions in the ICU cohort, metabolism-mediated pharmacokinetic interactions were prominent—e.g., amlodipine with atorvastatin and fluconazole with atorvastatin pairing, where CYP3A4 inhibition can raise statin exposure and precipitate myopathy or rhabdomyolysis; atorvastatin with clopidogrel may also blunt clopidogrel activation and its antiplatelet effect. For excretion, combination of furosemide pantoprazole was notable for increased urinary magnesium loss and potential hypomagnesemia. Most of the remaining moderate DDIs were pharmacodynamic, such as metoprolol with amlodipine and aspirin with insulin pairings**.** The hydrocortisone and levofloxacin pair increases tendon-injury risk; avoid in elderly or renally impaired patients when possible, and if necessary, use the shortest effective fluoroquinolone course with renal dose adjustment and prompt evaluation of new tendon pain.

These patterns are consistent with Indian ICU studies reporting frequent cardiovascular-class drug-drug interactions and CYP-mediated pharmacokinetic problems alongside clinically important pharmacodynamic pairs. Gupta et al. similarly documented numerous potential DDIs among critically ill inpatients, underscoring the need for proactive monitoring and dose optimization.[11] Findings from Kumar et al. further highlight ICU polypharmacy as a driver of interaction risk.[12] In cardiology inpatients, Risvana et al. reported frequent involvement of antiplatelets and statins, aligning with our moderate-severity pairs that feature CYP3A4 effects on atorvastatin.[9]

Minor Drug-Drug Interactions:

In the present study, a total of 114 minor drug-drug interactions were identified, with the most frequent combinations being pantoprazole with sucralfate (17.5%), omeprazole with clopidogrel (7.0%), metoclopramide with acetaminophen (7.0%), and heparin with IV nitroglycerine (5.3%). Although classified as “minor,” many of these interactions have important clinical implications in critically ill patients, where small pharmacokinetic or pharmacodynamic changes can significantly impact therapeutic outcomes. For instance, omeprazole and clopidogrel interaction results from CYP2C19 inhibition, reducing clopidogrel activation and antiplatelet efficacy. While the COGENT trial reported no significant increase in cardiovascular events with concurrent PPI use, several observational studies have suggested an elevated risk of stent thrombosis and recurrent ischemic events, emphasizing the need for cautious co-prescribing in ICU patients requiring dual therapy.[13] Similarly, heparin with IV

nitroglycerine reduces heparin's anticoagulant effect due to competitive binding at endothelial sites, necessitating close monitoring of activated partial thromboplastin time (aPTT) and dosage adjustments, especially in patients at high thrombotic risk.[14]

The combination of ondansetron with dexamethasone in our study was associated with beneficial pharmacodynamic synergy, enhancing antiemetic efficacy without significant adverse outcomes, aligning with findings from oncology and perioperative studies where this combination remains the standard of care.[15] Conversely, the amiodarone and atorvastatin interaction, though less frequent, warrants attention, as amiodarone-mediated CYP3A4 inhibition can raise statin plasma concentrations, increasing the risk of myopathy and rhabdomyolysis.[16] Clinical guidelines recommend using lower statin doses or switching to pravastatin or rosuvastatin in such cases. Our findings are consistent with previous ICU-based studies where the prevalence of minor DDIs ranged between 18–27%, with gastrointestinal drugs (PPIs, sucralfate, ondansetron) and cardiovascular agents (amiodarone, digoxin, nitroglycerin) being the most commonly implicated.[17]

CONCLUSION

This study demonstrates a high prevalence of potential drug-drug interactions (71.3%) among ICU inpatients, with an average of 2.28 DDIs per prescription. Pharmacodynamic interactions were more frequent than pharmacokinetic ones, and moderate-severity interactions predominated. These findings highlight the need for continuous prescription auditing, early identification of high-risk combinations, and active involvement of clinical pharmacists in ICU medication review. Integration of computerized decision-support systems and adherence to evidence-based prescribing guidelines can play a pivotal role in reducing preventable adverse outcomes and strengthening patient safety in critical care settings.

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REFERENCES

1. Palleria C, Di Paolo A, Giofrè C, Caglioti C, Leuzzi G, Siniscalchi A, et al. Pharmacokinetic drug-drug interaction and their implication in clinical management. J Res Med Sci. 2013 Jul;18(7):601-10. doi:10.4103/1735-1995.115512.
2. Dagdelen MS, Gulen D, Ceylan I, Girgin NK. Evaluation of potential drug-drug interactions in intensive care unit. Eur Rev Med Pharmacol Sci. 2021;25(18):5801-6. doi:10.26355/eurrev_202109_26798.
3. Gupta M, Chincholkar AS, Wagh RJ, Maheshwari N, Siddiqui W. A study of potential drug–drug interactions among critically ill patients at a tertiary care hospital. Int J Basic Clin Pharmacol. 2016;5(4):1281-5. doi:10.18203/2319-2003.ijbcp20161899.
4. Cerner Multum I. Drug Interactions Checker. USA: Cerner Multum, Inc.; 2016 [cited 2016 Jun 12]. Available from: http://www.drugs.com/drug_interactions.html
5. Tatro DS. Drug Interaction Facts: The Authority on Drug Interactions. Philadelphia: Lippincott Williams & Wilkins; 2011.
6. Eissa M, El-Masry R, El-Rashidy F, Abo-Elnaga S, Youssry M, El-Sayed S, et al. Evaluation of potential drug–drug interactions in intensive care unit patients: a cross-sectional study. Ther Clin Risk Manag. 2023;19:1195-206.
7. Zheng M. Pharmacodynamic drug–drug interactions. In: Hock F, Gralinski M, editors. Drug Discovery and Evaluation: Methods in Clinical Pharmacology. Cham: Springer; 2018. p. 1-10.
8. Roberts DJ, Hall RI. Drug absorption, distribution, metabolism and excretion considerations in critically ill adults. Expert Opin Drug MetabToxicol. 2013;9(9):1067-84. doi:10.1517/17425255.2013.803345.
9. Risvana AV, Sona S, Kurup YP, Athira S, George C. A retrospective observational cohort study on drug-drug interactions among hospitalized patients in the cardiology department of a tertiary care hospital. Int J Pharm Res Appl. 2022;7(4):1413-28. doi:10.35629/7781-070414131428.
10. Wagh BR, Godbole DD, Deshmukh SS, Iyer S, Deshpande PR. Identification and assessment of potential drug-drug interactions in Intensive Care Unit patients. Indian J Crit Care Med. 2019;23(4):170-4. doi:10.5005/jp-journals-10071-23147.
11. Gupta M, Chincholkar AS, Wagh RJ, Maheshwari N, Siddiqui W. A study of potential drug–drug interactions among critically ill patients at a tertiary care hospital. Int J Basic Clin Pharmacol. 2016;5(4):1281-5. doi:10.18203/2319-2003.ijbcp20161899.
12. Kumar R, Kaur R, Arora S. Drug–drug interactions in intensive care unit of a tertiary care hospital in India: a prospective observational study. J Clin Diagn Res. 2019;13(4):FC01-4. doi:10.7860/JCDR/2019/39962.12706.
13. Bhatt DL, Cryer BL, Contant CF, et al. Clopidogrel with or without omeprazole in coronary artery disease. N Engl J Med. 2010;363(20):1909-17. doi:10.1056/NEJMoa1007964.
14. Becker RC, Corrao JM, Bovill EG, et al. Intravenous nitroglycerin-induced heparin resistance. Am Heart J. 1990;119(6):1254-61. doi:10.1016/S0002-8703(05)80172-3.
15. López-Olaondo L, Carrascosa F, Pueyo FJ, et al. Ondansetron plus dexamethasone for prevention of postoperative nausea and vomiting. Br J Anaesth. 1996;76(6):835-40. doi:10.1093/bja/76.6.835.
16. Wiggins BS, Saseen JJ, Page RL, et al. Recommendations for managing clinically significant drug–drug interactions with statins. Circulation. 2016;134(21):e468-95. doi:10.1161/CIR.0000000000000456.
17. Patel TK, Patel PB, Tripathi CB. Drug–drug interactions in ICU patients of a tertiary care hospital: a prospective observational study. Indian J Crit Care Med. 2014;18(3):140-6. doi:10.4103/0972-5229.128696.