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Assessment of the Prevalence of Drug–Drug Interactions in the Medical Intensive Care Unit of a Tertiary Care Teaching Hospital in India

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ABSTRACT

Background: Drug interaction refers to modification of response to one drug by another when they are administered simultaneously or in quick succession with the increase in the number of patients, multiple diseases, and complex therapeutic regimens, polypharmacy becomes unavoidable in Intensive Care Unit (ICU). Polypharmacy increases the risks of drug Adverse Events (AEs), especially the Drug-Drug Interactions (DDIs), and that leads to elevated healthcare costs, morbidity and mortality. **Methods:** A prospective observational study was conducted for duration of 3 months to assess the prevalence of potential DDIs in medical Intensive Care Unit (MICU) of a tertiary care teaching hospital located in Telangana, India by using Lexi Comp interaction checker. **Results:** A total of 112 patients were included in the study out of which 68 (60.71%) were males and 44 (39.28%) were females. 84 (75%) patients were found to be with drug interactions and 28 (25%) patients were found without any drug interactions. The average length of the stay of the patients in the hospital was 6 days. A total of 248 interactions were found showing an average of 2.95 drug interactions per patient. Furosemide followed by phenytoin, aspirin, atorvastatin and clopidogrel are the most frequently interacting individual drugs. Antiplatelet /anticoagulant agents have a prominent role in the development of interactions in ICU in our study. **Conclusion:** All the health providers must be trained so that they should be able to identify and classify DDIs, and know how to manage/prevent them. In ICUs, clinical pharmacist should take the responsibility of monitoring DDIs and notifying them to prescriber/physician about potential problems. This kind of practice will increase the patient safety.

INTRODUCTION

Drug interaction refers to modification of response to one drug by another when they are administered simultaneously or in quick succession. The modification is mostly quantitative, i.e. the response is either increased or decreased in intensity, but sometimes it is qualitative, i.e. an abnormal or a different type of response is produced. The possibility of drug interaction arises whenever a patient concurrently receives more than one drug, and the chances increase with the number of drugs taken [(1)]. Drug–drug interactions (DDIs) in the intensive care unit (ICU) are associated with longer ICU stays, adverse drug events and end-organ damage [2–4]. However, the decision to prescribe two drugs simultaneously is sometimes intentional, with the aim of obtaining a specific pharmacological synergism [5].

About 5% of all adverse drug reactions in hospitals are caused by DDIs, and the majority of which are avoidable [6]. With the increase in the number of patients, multiple diseases, and complex therapeutic regimens, polypharmacy becomes unavoidable in ICU. Polypharmacy increases the risks of drug AEs, especially the DDIs, and that leads to elevated healthcare costs, morbidity and mortality [7]. Within the context of above facts, it is important to investigate potential DDIs in ICUs.

Drug interactions are generally classified based on the severity as major, moderate and minor. Based on the mechanism they are classified as Pharmacokinetic and Pharmacodynamics interactions. In certain cases, however, the mechanisms are complex and may not be well understood. Few interactions take place even outside the body when drug solutions are mixed before administration [(1)].

MATERIALS AND METHODS

A prospective observational study was conducted for duration of 3 months in the medical intensive care unit of a 373 bedded tertiary care teaching hospital located in Telangana, India.

Patients aged above 18 years and who were admitted in the MICU for more than 48 hours were included in the study. Data is collected in a specially designed proforma. Patient demographic details, diagnosis, drug prescribed and administrated were recorded. The DDIs in the medicine chart were assessed by using Lexi Comp interaction checker.

The drug interactions were classified based on severity, risk rating and reliability as below:

Severity:

Major: Effects may result in death, hospitalization, permanent injury, or therapeutic failure.

Moderate: Medical intervention needed to treat effects; effects do not meet criteria for major.

Minor: Effects would be considered tolerable in most cases; no need for medical intervention.

Risk Rating:

Risk Rating	Action	Description
A	No known interaction	Data have not demonstrated either pharmacodynamic or pharmacokinetic interactions.
B	No action needed	May interact with each other, but there is no evidence of clinical concern.
C	Monitor therapy	The benefits of concomitant use of these two medications usually outweigh the risks.
D	Therapy modification	Assess whether the benefits of concomitant therapy outweigh the risks or not.
X	Avoid combination	The risks associated with concomitant use outweigh the benefits.

Reliability:

The reliability in documentation of DDIs was categorized as excellent, good, fair and poor documentation.

Drug interaction between the drugs which are administered together and which are identified by the Lexi comp interaction checker are included in the study.

RESULTS AND DISCUSSION

A total of 112 patients were included in the study out of which 68 (60.71%) were males and 44 (39.28%) were females. 84 (75%) patients were found to be with drug interactions and 28 (25%)

patients were found without any drug interactions. The average length of the stay of the patients in the hospital was 6 days.

A total of 248 interactions were found showing an average of 2.95 drug interactions/ patient. The incidence of the major drug interactions was found to be 0.71 DDI/patient and for moderate it was 2.1 DDI's/patient (Figure 1). In our study the occurrence of DDI per patient is less than the study conducted by Abideen et al.[8] whose study had an occurrence rate of 3.08 DDI per patient. 18 drug interactions (3-major, 14-moderate, 1-minor) were the highest number of interactions found in a single patient.

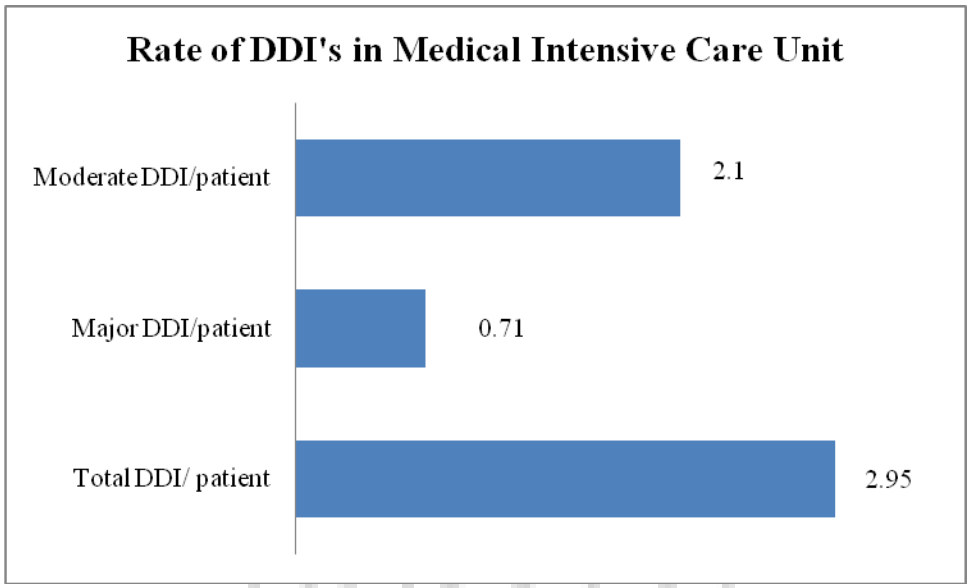

Figure 1: Rate of occurrence of drug interactions in Medical Intensive Care Unit

Of 248 interactions 60 (24.19%) were major, 177 (71.37%) were moderate and 11 (4.43%) were minor (Figure 2). The severity of the drug interactions were in accordance to the study conducted by Abideen et al.[8] whose study showed more of moderate (32.88%) interactions than major (67.11%) interactions.

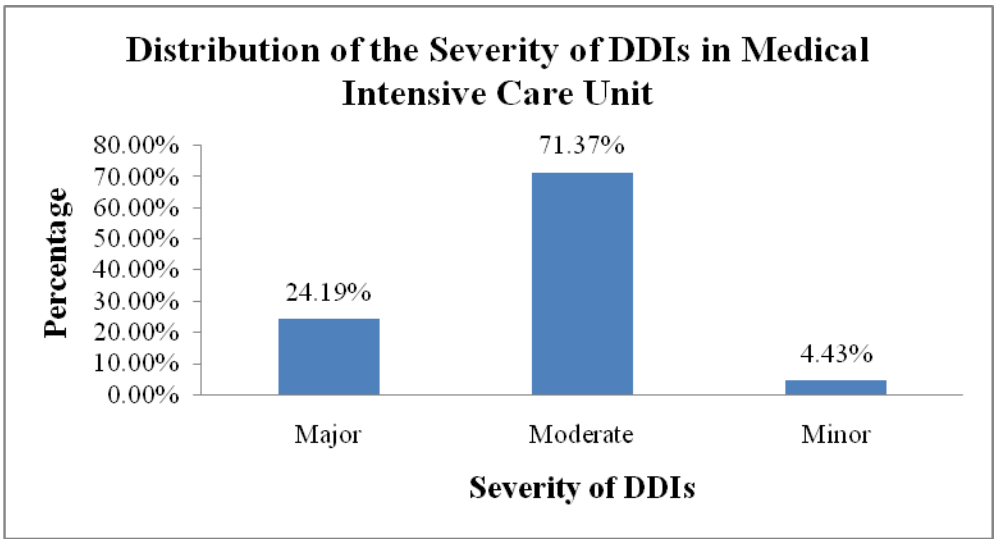

Figure 2: Distribution of severity of various DDIs found in Medical Intensive Care Unit

In terms of the risk rating of the 248 interactions, no action needed (B), combination must consider therapy modification (D) and combination which must be monitored (C) were found to be 11.29% (28), 17.33% (43) and 71.37% (177) respectively (figure 3). Abideen et al. [8]conducted an investigation to assess the DDIs in ICU using the Lexi Comp drug interact found that category X is 7.20%, C is 57.21% and D is 35.59%. It reveals that our study group is less in risk when compared to the above population in ICU.

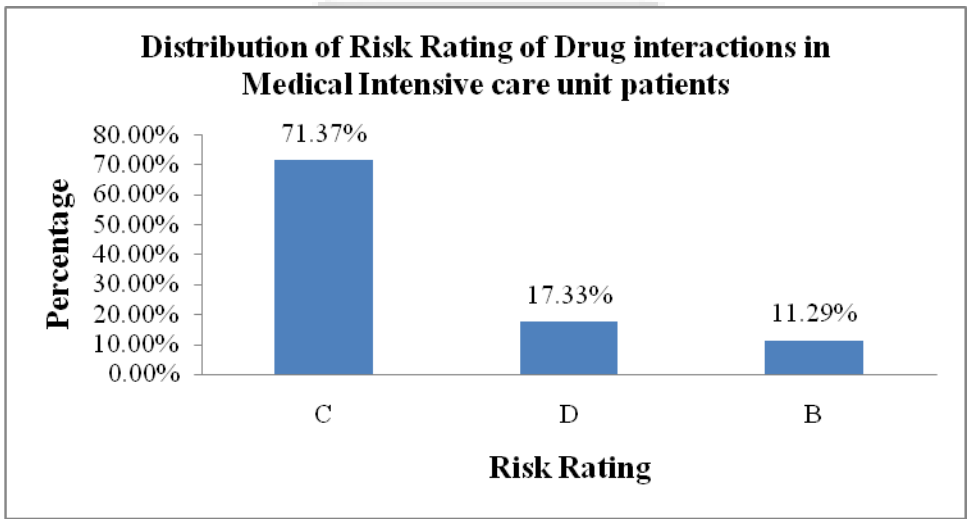

Figure 3: Distribution of Risk Rating of drug interactions in Medical Intensive Care Unit patients

C-Monitor Therapy, D-Therapy modification, B-No action needed

With respect to the reliability of the DDIs, 61.69% (153) DDIs were with fair documentation, followed by 26.61% DDIs with good documentation, 9.27% (23) with poor documentation and 2.41% (6) of DDIs had excellent documentation (figure 4).

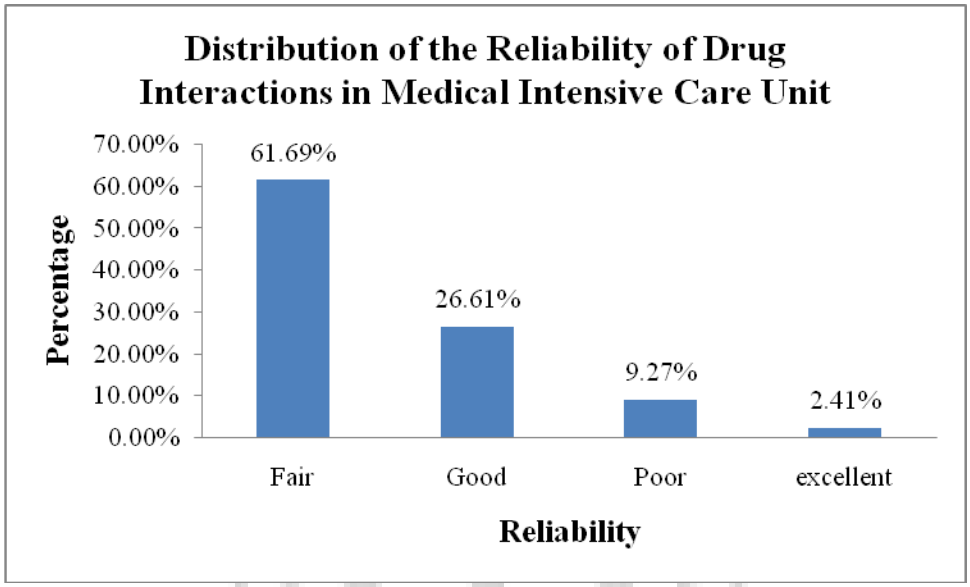

Figure 4: Distribution of Reliability of Drug Interactions in the Medical Intensive Care Unit Patients

Furosemide followed by phenytoin, aspirin, atorvastatin and clopidogrel are the most frequently interacting individual drugs found in our study. Table 1 shows 10 most frequent interacting individual drug, number of drugs interacted, number of interactions and percentage, severity, risk and its reliability. The present study shows that furosemide is one of the principal individual drug interacted with other 14 drugs and lead to the development of a total of 19 (7.66%) interactions.

Table 1: Individual drugs frequently interacted

S No	Drug Name	Interacting With	Total Interactions (%)	Major	Moderate	Minor	Risk Rating	Reliability
1	Furosemide	14	19 (7.66%)	0	19	0	C-19	Good-4 Fair-15
2	Phenytoin	13	21 (8.46%)	10	9	3	D-14 B-2 C-5	Good-5 Fair-16
3	Aspirin	11	33 (13.3%)	0	29	4	B-5 C-28	Good-10 Fair-23
4	Atorvastatin	10	48 (19.35%)	20	28	0	C-28 B-16 D-4	Poor-18 Good-16 Fair-14
5	Clopidogrel	10	55 (22.17%)	19	36	0	D-19 B-16 C-20	Fair-33 Good-22
6	Ondansetron	9	22 (8.87)	5	17	0	C-17 D-5	Fair-18 Good-4
7	Hydrocortisone	9	13 (5.24%)	0	13	0	C-12 D-1	Good-6 Fair-7
8	Telmisartan	8	20 (8.06%)	0	20	0	C-20	Fair-17 Good-3
9	Pantoprazole	6	48 (19.35%)	46	1	1	C-23 D-24 B-1	Poor-22 Fair-24 Good-1 Excellent-1
10	Amlodipine	5	18 (7.25%)	0	18	0	C-17 D-1	Fair-15 Good-3

D: Combination must consider therapy modification, C: Combination which must be monitored, B: No action needed.

Phenytoin is also another important drug found in our study interacting with 13 drugs and lead to the development of 21 (8.46%) interactions. Two studies conducted by Rafiei *et al*. reveals that phenytoin is one of the major drug which leads to most interactions [9,10]. The results suggest the prescriber to take a special precaution while administering these drugs with other interacting drugs in the ICU setup to avoid potential DDIs.

Assessment of most frequently seen interactions was done. Table 2 shows 10 most commonly seen interactions in our study. Interaction between Clopidogrel and Pantoprazole was most commonly seen interaction contributing a percentage of 7.66% (19), followed by Atorvastatin-Pantoprazole 7.25% (18), Clopidogrel-Atorvastatin 6.45% (16), Aspirin-Piracetam 4.83% (12), Clopidogrel-Piracetam 3.22% (8).

Table 2: Most commonly seen drug interactions

S no	Drug 1	Drug 2	Total interactions	Severity	Reliability	Risk Rating	Outcome
1	Clopidogrel	Pantoprazole	19 (7.66%)	Major	Fair	D	Pantoprazole may decrease serum concentration of the active metabolite of Clopidogrel.
2	Atorvastatin	Pantoprazole	18 (7.25%)	Major	Poor	C	Proton pump inhibitors may increase the serum concentrations of HMG-CoA reductase inhibitors.
3	Clopidogrel	Atorvastatin	16 (6.45%)	Moderate	Good	B	Atorvastatin may diminish the antiplatelet effect of Clopidogrel.
4	Aspirin	Piracetam	12 (4.83%)	Moderate	Fair	C	Piracetam increases the Adverse effects of Salicylates. Increased risk of bleeding may result.
5	Clopidogrel	Piracetam	8 (3.22%)	Moderate	Fair	C	Agents with antiplatelet properties may enhance the antiplatelet effect of other agents with antiplatelet properties.

6	Amlodipine	Telmisartan	7 (2.82%)	Moderate	Fair	C	Hypotensive agents may enhance the adverse effects of other hypotensive agents.
7	Metronidazole	Ondansetron	6 (2.41%)	Moderate	Fair	C	Qtc prolonging agents may enhance the QTc-prolonging effect of moderate risk QTc-prolonging agents.
8	Pantoprazole	Phenytoin	5 (2.01%)	Major	Fair	???	Phenytoin may increase metabolism of Pantoprazole.
9	Enoxaparin	Aspirin	5 (2.01%)	Moderate	Fair	C	Agents with antiplatelet properties may enhance the anticoagulant effect of other antiplatelet agents.
10	Ondansetron	Atorvastatin	5 (2.01%)	Moderate	Fair	C	Atorvastatin increases serum concentration of ondansetron.

D: Combination must consider therapy modification, C: Combination which must be monitored, B: No action needed.

Table 3 lists the class of drugs which were commonly interacted in our study. Antiplatelet /anticoagulant agents have a prominent role in the development of interactions in ICU. 88 interactions were developed by Antiplatelet /anticoagulant agents contributing a percentage of 35.48% of total interactions. This result is in accordance to the study conducted by Pamela L. Smithburger *et al*. which showed that Antiplatelet/Anticoagulants are most frequently interacting class [(11).]

Table 3: Class of drugs which are responsible for interaction

S no.	Class	Total Interactions (%)	Major	Moderate	Minor	Risk	Reliability
1	Antiplatelet or Anticoagulant Agents	88 (35.48%)	19	65	4	D-19 C-48 B-21	Fair-56 Good-31 Poor-1
2	Statins	53 (21.37%)	24	29	0	C-33 B-16 D-4	Poor-22 Good-17 Fair-14
3	Antacids	49 (19.75%)	46	1	2	C-23 B-2 D-24	Poor-22 Good-2 Fair-24 Excellent-1
4	Diuretics	29 (11.69%)	0	29	0	C-29	Fair-21 Good-8
5	Anticonvulsants	25 (10.08%)	11	12	2	D-15 C-8 B-2	Fair-17 Good-8
6	Antiemetics	22 (8.87%)	5	17	0	C-17 D-5	Fair-18 Good-4
7	Corticosteroids	16 (6.45%)	1	15	0	C-14 D-2	Good-6 Fair-10

Other class of drugs include statins 53 (21.37%), antacids 49 (19.75%), diuretics 29 (11.69%), anticonvulsants 25 (10.08%), antiemetics 22 (8.87%) and corticosteroids 16 (6.45%).

CONCLUSION

A total of 84 (75%) of 112 enrolled patients were exposed to one or more DDIs. We found an average of 2.95 DDIs per patient. The concomitant administration rates of potentially interacting drugs are very high in MICU. The most commonly interacting class of drugs in ICU were Antiplatelet /anticoagulant, statins, antacids, diuretics, anticonvulsants, antiemetics and corticosteroids. DDIs leading to serious adverse effects must be cautiously monitored when multiple drugs are given simultaneously.

All the health providers must be trained so that they should be able to identify and classify DDIs, and know how to manage/prevent them. In ICUs, clinical pharmacist should take the responsibility of monitoring DDIs and notifying them to prescriber/physician about potential problems. This kind of practice will increase the patient safety.

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REFERENCES

1.KDTripathi-Essentials of Medical Pharmacology ; 6th edition;2008
2. Moura C *et al*. Potential drug-drug interactions associated with prolonged stays in the intensive care unit: a retrospective cohort study. *Clin Drug Invest* 2011; 31: 309–316.
3. Plaza J *et al*. Drug interactions and adverse events induced by drugs used in an intensive care unit. *Rev Med Chil* 2010; 138: 452–460.
4. Kopp BJ *et al*. Medication errors and adverse drug events in an intensive care unit: direct observation approach for detection.*CritCareMed*2006; 34: 415– 425.
5.Romac DR, Albertson TE. Drug interactions in the intensive care unit.Clin Chest Med 1999;20(2):385-99, ix.
6.Fijn R, Van den Bemt PM, Chow M, De Blaey CJ, De Jong-Van den Berg LT, BrouwersJR.Hospital prescribing errors: Epidemiological assessment of predictors. Br J ClinPharmacol 2002;53(3):326-31.
7. Plaza J, Alamo M, Torres P, Fuentes A, López F. Drug interactions and adverse events induced by drugs used in an intensive care unit. Rev Med Chil 2010;138:452-60.
8.Abideen S, Vivekanandan K, Mishra P. Assessment of Prevalence of Potential Drug-Drug Interactions in Medical Intensive Care Unit of a Tertiary Care Hospital In India.Asian J Pharm Clin Res2014;8(1):125-130
9. Rafiei H, EsmaeliAbdar M, Amiri M, Ahmadinejad M. The study of harmful and beneficial drug interactions in intensive care, Kerman, Iran. J Intensive Care Soc 2013;14(2):155-8.
10. Rafiei H, Arab M, Ranjbar H, Sepehri GR, Arab N, Amiri M. The prevalence of potential drug interactions in intensive care units. Iran J Crit Care Nurs 2012;4(4):191-6.
11. Pamela L. Smithburger, Sandra L. Kane-Gill and Amy L. Seybert. Drug–drug interactions in the medical intensive care unit: an assessment of frequency, severity and the medications involved. International journal of Pharmacy Practice2012;20:402–408