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TO ESTIMATE THE INCIDENCE AND TO IDENTIFY THE PREDICTORS OF POTENTIAL DRUG-DRUG INTERACTIONS IN PATIENTS ADMITTED TO CRITICAL CARE UNITS OF A TERTIARY CARE HOSPITAL AT JSS, MYSURU

Dr. Juneeta Anna Benny*, **Dr. V. Hemanth**, **Dr. Stanly P. Abraham**, **Dr. Chinmay Meher**, **Dr. M. Ramesh**
Nirmala College of Pharmacy, Ernakulam, Kerala – 686661.

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ABSTRACT

Background: Drug interactions are estimated to occur between 3% and 5% in patients to whom few drugs are prescribed and 20% among those who use 10 to 20 drugs simultaneously. In critical care units (CCUs), patients are at increased risk for the development of drug interactions due to use of more medications to treat multifaceted conditions of patients. **Aim:** To estimate incidence and to assess the predictors involved in causing potential drug-drug interactions in patients admitted to critical care units of a tertiary care hospital at Mysuru. **Methodology:** It was a prospective interventional study. All the patients who satisfied the study criteria were included in the study and patients were followed till their discharge. All the required data were collected and documented. Each prescription was subjected for review in order to identify the drug - drug interactions by using the standard references such as Micromedex, Medscape and Stockleys drug interaction. The incidence was estimated. The predictors of PDDIs were determined by using logistic regression analysis. **Results:** Of the 500 patients, a total of 591 potential drug – drug interactions (PDDIs) were identified from 257 patients. The incidence of PDDIs was 51.4%. Anti – infectives for systemic use [n = 962] was widely used class of drugs. In most cases, Asprin (41.9%) and Furosemide (37.5%) were observed to be the index and interacting agent respectively. Age and multiple drug therapy were the predictors of PDDIs. **Conclusion:** The incidence of potential drug – drug interactions was high. As elderly patients and polypharmacy were observed to be predictors of PDDIs, cautious use of medicines in elderly population especially in patients receiving multiple drug therapy is warranted to prevent or minimize the PDDIs in critical care units.

Corresponding author

Dr. Juneeta Anna Benny

Assistant Professor,
Nirmala College of Pharmacy,
Ernakulam, Kerala – 686661
+91- 9886610218
juneetabenny070693@gmail.com

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INTRODUCTION

Drug therapy is one of the major interventions adopted in treating the various ailments. One among them is the presence of other medications taken by the patients at the same time. A drug interaction occurs when the effects and/or toxicity of a certain drug are altered by another drug^[1]. Regardless of whether they result in positive or negative, the interactions are generally unpredictable and undesirable in a pharmacotherapy provided to the patients. "Potential drug-drug interaction" (PDDIs) is the term that is used to refer to the possibility a drug where it can alter the effects of another drug when they are simultaneously administered. Such interactions may occur either before their administration (physical-chemical interaction or incompatibility) or after their administration^[2]. Various studies showed that drug - drug interactions (DDIs) due to polypharmacy and impaired renal and hepatic functions are the main reasons for the poor drug response and development of adverse drug reaction^[1]. The mortality and morbidity are increased in such patients because the therapeutic effects are decreased and toxic effects are amplified due to the presence of concomitant medications. Studies have demonstrated a positive correlation between polypharmacy and Drug Interactions (DI)^[1]. With the continued development of new drugs and subsequent prescriptions with increasingly more complex combinations, it has become difficult for physicians and pharmacists to be familiar with all potential interactions. Drug – drug interactions has received a great deal of recent attention from the regulatory, scientific, and health care communities worldwide. Risk of occurrence and severity of drug – drug interactions rest upon several factors, including the number of drugs prescribed, duration of treatment, patient age and stages of disease. Patients that require a large number of drugs, long time of treatment, with physiological aging changes or certain diseases such as renal failure, shock, hepatic disease such as cirrhosis or acute viral hepatitis, are considered of high risk for severe drug interactions^[3].

The patients admitted to the Critical Care Units (CCUs) of Hospital are always prescribed with multiple medications and are usually exposed to prolonged treatment regimen due to their serious and multiple co - morbid conditions^[4]. Studies have reported a high prevalence of drug interactions in ICU, and found that the number of drugs taken, the duration of stay in ICU, and the types of drugs used were the most important factors that has contributed to drug – drug interactions^[5].

Although a good number of studies assessing the DIs in critical care units are available in India, there are variations in the reported incidence rates of potential drug – drug interactions and predictors based upon the regional wise prescribing patterns, type of patients treated at the critical care units along with the type and number of medications used. Studies showed that most of the consequences of the drug interactions were preventable if proper care taken by the health care professionals at the prescribing and monitoring levels. Therefore, the objective of this study was aimed to evaluate potential drug - drug interactions occurring in patients treated at critical care units of a tertiary care hospital, to assess its incidence and the risk factors that increase the occurrence of drug drug interactions.

METHODOLOGY –

STUDY SITE:

He study was conducted in all the critical care units of JSS Hospital, Mysuru. It is an 1800 bed multi-speciality tertiary care teaching hospital, that provides healthcare facilities to people in and around Mysuru district. This hospital consist of 8 critical care units, such as intensive care unit (ICU) having 16 beds, intensive cardiac care unit (ICCU) having 18 beds, coronary care unit (CCU) having 11 beds, Cardio Thoracic and Vascular Surgery unit (CTVS) having 6 beds, paediatric intensive care unit (PICU) having 12 beds, surgery intensive care unit (SICU) having 14 beds and respiratory intensive care unit (RICU) having 10 beds. The average number of patients admitted in critical care units is 10 to 15 per day.

STUDY DESIGN : It was a prospective interventional study.

STUDY CRITERIA

Inclusion Criteria -

- Patients of any age and either gender.
- Patients who were admitted to critical care units of the hospital.
- Patients taking more than one medications.

Exclusion Criteria –

- Patients whose stay at CCUs was less than 24 hours.
- Patients on other system of medications like Ayurveda, Sidha, Unani.

SOURCES OF DATA : All the relevant and necessary data were collected from

- Patients case notes
- Treatment charts
- Lab reports of the patients
- Interacting with the health care professionals

STUDY PROCEDURE

- All those patients who were admitted to the critical care units of the study site were reviewed on daily basis. Those patients who met the study criteria were enrolled into the study.
- All the study specific data were collected and documented in the designed data collection form and each of the enrolled patients were followed up from the day of admission till patients were shifted from the critical care units to the ward.
- The data collected from eligible patients included the patient demographics details, reason for admission, IP number, admission and discharge date, current diagnosis, past medical history, co-morbidities social history, current medications with their dose, frequency, start and stop dates of medication, reason for use of medication, duration of treatment. All the collected data were documented in a designed data collection form.
- Each prescription was subjected for review in order to identify the drug - drug interactions by using the standard references such as Micromedex, Medscape and Stockley's drug interaction Text book and other resources as appropriate.
- Then all the collected data were entered and documented in the online database for the easy storage and retrieval of data, and the data entered were checked for transcribing errors in order to ensure the correctness of the data prior to subjecting them for analysis of various parameters.

DATA ANALYSIS

Patient characteristics -

All the enrolled patients were grouped according to their age, gender, presence of comorbidities and number of medications prescribed, and their respective percentage values were calculated.

Potential drug-drug interactions -

Incidence of the Potential DDIs was calculated by using the following equation.

$$\text{Incidence of Potential DDIs} = \frac{\text{No. of prescriptions with Potential DDIs}}{\text{Total Number of prescriptions reviewed}}$$

Predictors of potential drug-drug interactions -

- The predictors for drug-drug interactions were identified by Logistic Regression Analysis.
- The predictors associated with the potential drug-drug interactions were identified at a p value of <0.05. Student t-test was performed to obtain p value for continuous variables. Chi-square test was performed to obtain p value for categorical variables.

RESULT AND DISCUSSION

During this study period all the patients who were admitted to all the critical care units (ICCU, CCU, MICU, SICU, RICU, PICU and CTVS) of JSS Hospital over a period of six months from October 2015 to March 2016 were followed on a daily basis. A total of 500 prescriptions were reviewed for potential drug-drug interactions. The demographic details of the study population is depicted in Table 1. Majority of the study subjects belonged to the age group 50 – 59 years (17.8 %), followed by 40 – 49 years (14 %) and 60 – 69 years (12.8 %). Mean age of the study population was 50.2 ± 10.6 . In a study conducted by Virendra K Patel^[6], similar results were reported wherein most of the patients belonged to the age group of 51-60 years with a mean age of 57.27 ± 14.6 .

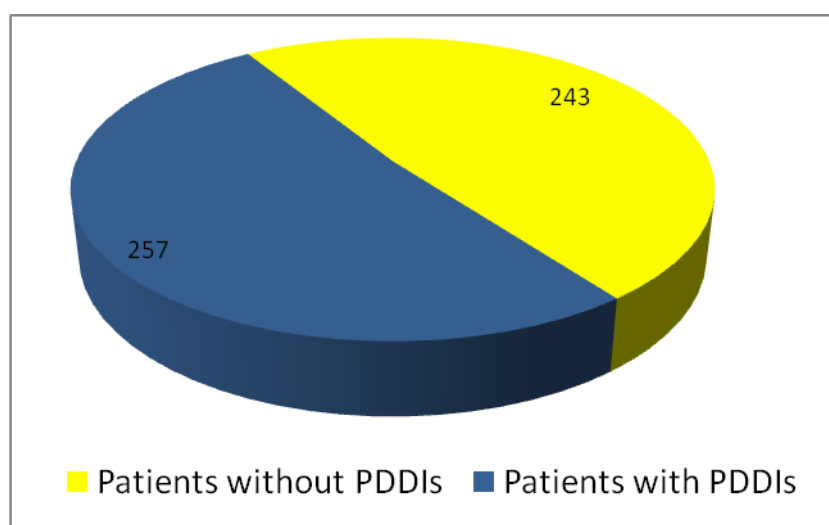
Of the total patients, 64% (n=320) of the study subjects were males. A total of 353 patients had one or more comorbidities. The average number of comorbid condition was 4.12. The most common comorbid conditions observed in our study patients include Hypertension, Diabetes mellitus, Chronic obstructive pulmonary disorder and Ischemic heart disease. Majority (73%) of the study population were receiving 6 to 10 drugs while 21.4% (n=107) of patients were receiving more than 10 drugs. The average number of drugs received by the study patients was 6.95 (range: 5 – 15). Majority of the study patients received multiple medications due to their multiple conditions. It is obvious that the patients with multiple disorders require several medications in treating their disease conditions.

Table 1: Demographic details of the study population.

DEMOGRAPHIC DETAILS		NO. OF PATIENTS (n =500)	PERCENTAGE(%)
Age (in years)	PEDIATRIC -		
	0 – 9	53	10.6
	10 – 18	27	5.4
	ADULT -		
	19 – 29	56	11.2
	30 – 39	60	12
	40 – 49	70	14
	50 – 59	89	17.8
	GERIATRIC -		
	60 – 69	64	12.8
Gender	70 – 79	55	11
	≥80	26	5.2
	Male	320	64
	Female	180	36
	NIL	147	29.4
Number of Comorbidities	1	136	27.2
	2	113	22.6
	3	60	12
	4	22	4.4
	≥5	22	4.4
	1-3	Nil	Nil
	4 – 5	28	5.6
Number of drugs	6 – 10	365	73
	11 – 15	63	12.6
	≥16	44	8.8

INCIDENCE OF POTENTIAL DRUG-DRUG INTERACTIONS -

Out of 500 patients reviewed, 257 patients were found to have had at least one potential drug – drug interactions giving the incidence rate of 51.4% (Figure 1). A total of 591 potential DDIs were identified from 257 patients. The patients admitted to the CCUs are at an increased risk for the development of PDDIs, as their condition is complicated by disease severity and organ failure, both of which can alter the pharmacologic response to medications⁷. The number of prescribed drugs is another important risk factor for the occurrence of PDDIs which was seen in our study population. In a study conducted by Patel et al^[6] at an intensive care unit, reported 388 PDDIs that were identified among 249 patients and the incidence of potential DDI was reported to be 30.67%. The increase in incidence rate of PDDIs is due to the fact that critical care patients have always been found to have a higher chance of having drug-drug interactions compared to other group of patients due to their multiple drug therapy and severity of disease condition.

**Figure 1: Number of patients with and without the PDDIs.**

DISTRIBUTION OF PATIENTS ADMITTED TO VARIOUS CRITICAL CARE UNITS

Higher number of patients were admitted to the Medicine ICU (n =130) followed by ICCU [n= 114] and CCU [n= 89]. Out of which, PDDIs were identified in 77,61 and 59 patients respectively. The incidence of PDDIs was high in CCU (66.2 %) followed by MICU (59.2%), ICCU (53.5 %) and CTVS(45 %). The patients admitted to these CCUs have multifaceted conditions for which multiple drug therapy was prescribed. The number of medications prescribed for such patients who were admitted to CCUs was higher when compared to other intensive care units. The common disease conditions for which patients were treated in these CCUs were Hypertension, Diabetes mellitus, Coronary artery disease, Myocardial infarction, Stroke and poisoning due to pesticides and medicines. The details of distribution of patients admitted to various critical care units are presented in Figure 2.

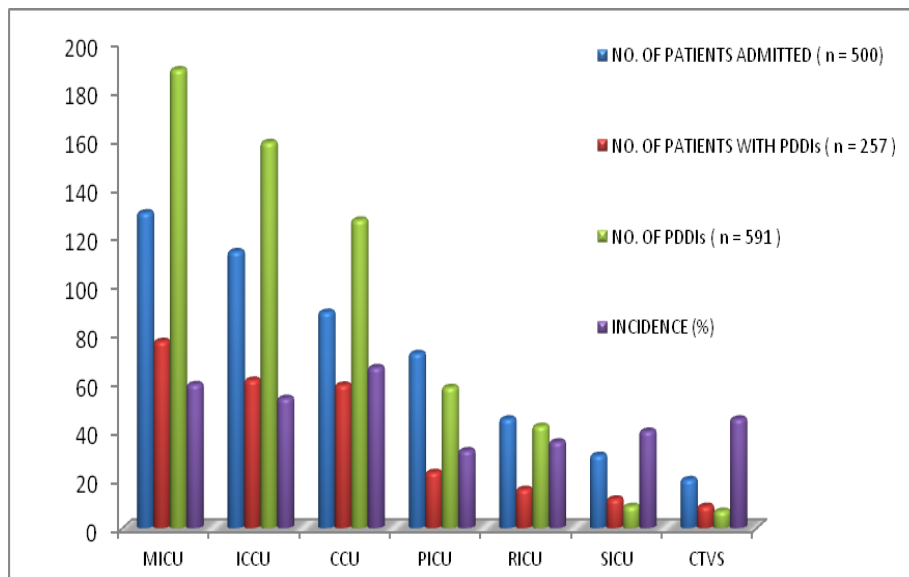


Figure 2: Distribution of patients admitted to various critical care units.

PREDICTORS OF POTENTIAL DRUG - DRUG INTERACTIONS

The bivariate logistic analysis was applied to determine the predictors of drug - drug interactions like age, gender, number of co - morbidities, multiple prescribers and polypharmacy in the study population. It was found that the gender difference was not a significant predictor of PDDIs. The findings also suggested that multiple prescribers and number of comorbidities were not risk factors in developing PDDIs in our study population. A higher incidence was detected in patients who were on polypharmacy and belonging to the age group of ≥ 50 years which was statistically significant [(p= 0.004); odds ratio 1.696]. It is obvious that the risk of PDDIs increases when a patient receives multiple drug therapy. In a study conducted by Kashyap M and et al^[8], studies showed that patients exposed to polypharmacy were at a risk of harmful drug interactions with p value = 0.05 and Odds Ratio 2.6. Advanced age, gender and length of stay in the hospital were not significant risk factors for drug interactions in the above mentioned study. The details of the predictors of PDDIs are presented in Table 2.

Table 2 - Predictors of PDDIs.

Variable	Total number of patients: <i>n</i> = 500		Multivariate	
	Interaction present (<i>n</i> = 257)	Interaction absent (<i>n</i> = 243)	OR (95% CI)	<i>P</i> -value
<i>Patient age (years)</i>				
<i>Pediatric</i>	52	51		
<i>Adult</i>	98	130	1.696	
<i>Geriatric</i>	107	62	(1.191 – 2.416)	0.004
<i>Gender</i>				
<i>Female</i>	101	80	0.758	1.09
<i>Male</i>	156	163	(0.526 – 1.094)	
<i>Number of comorbidities</i>				
<3	110	172	3.237	1.08
≥3	147	71	(2.234 – 4.691)	
<i>Number of drugs</i>				
<10	136	217	1.362 (1.17 – 1.3)	0.004
≥10	120	26		
<i>Number of Multiple Prescribers</i>				
<2	41	63	4.804 (4.187 – 4.86)	1.20
≤2	216	180		

CONCLUSION

The incidence of potential drug-drug interactions was 51.4%. The drug – drug interactions were predominant in females. Of the total PDDIs, majority of interactions were observed in CCU. Majority (42.6%) of PDDIs were observed in elderly patients. Polypharmacy and age of the patient were the predictors of PDDIs.

The incidence of potential drug – drug interactions was high. As the age and polypharmacy were observed to be predictors of PDDIs, cautious use of medicines in elderly population especially in patients receiving multiple drug therapy is warranted to prevent or minimize the PDDIs in CCU.

Can also recommend future research.

ABBREVIATIONS

CCUs	Critical Care Units
CTVS	Cardio thoracic and vascular surgery
DDIs	Drug – Drug Interactions
DI	Drug Interaction
ICU	Intensive Care Unit
ICCU	Intensive Cardiac Care Unit
MICU	Medical Intensive Care Unit
PDDIs	Potential Drug - Drug Interactions
PICU	Pediatric Intensive Care Unit
RICU	Respiratory Intensive Care Unit
SICU	Surgery Intensive Care Unit

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CONFLICT OF INTEREST

There is no conflict of interest.

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