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A Cross Sectional Observational Study Conducted to Analyse Drug-Drug Interactions in a Tertiary Care Hospital

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ABSTRACT

AIM: To analyse the drug-drug interactions of various departments in a tertiary care hospital. **OBJECTIVES:** To assess the prevalence of drug-drug interactions. To evaluate the mechanism of action and severity of DDIs. To identify different variables contributing to DDIs. **METHODS:** This study was a cross-sectional, observational study conducted for a period of 6 months from September 2017 to March 2018. The medications in the patient profile forms were then entered into the MICROMEDEX® software. The DDIs were classified based on the severity, mechanism of actions and different variables were also determined**. RESULTS**: From 100 patients, 69% males were more prone to DDIs than females that are 31%. Majority of the patients belongs greater than 60 years of age. A total of 100 prescriptions were analysed of which 743 prescriptions had DDIs. Most of the DDIs were pharmacodynamic (249%) followed by pharmacokinetic (69%) and unknown (27%). A severity assessment showed that majority of the DDIs were moderate (363) followed by major (310), minor (35%) unknown (27%) and contraindicated (8%). Based on the different variables, co-morbid conditions and total number of drugs prescribed were statistically significant with DDIs. **CONCLUSION**: The chances of occurrence of drug-drug interactions are more prevalent in the current hospital settings. Our study helped to understand the most prone age group, common mechanisms and severity and different variables that affect the patient's disease condition.

INTRODUCTION

Drug interaction is the modification, increase or decrease in the effects of one drug by another drug when they are administered simultaneously which can leads to severe adverse effects.[1] The prevalence of drug-drug interactions in elderly patients is 13-55%.[2] DDIs may compromise patient safety or increase hospital stay and hospital costs thereby affects the patient's quality of life. There are two types of mechanisms by which drug interaction occurs and they are pharmacokinetic and pharmacodynamic interactions. Pharmacokinetic interactions are those that can affect the processes by which drugs are absorbed, distributed, metabolized and excreted also called as ADME interaction. Pharmacodynamic interactions are those where the effects of one drug are changed by the presence of another drug at its site of action.[3,4] According to the description of Micromedex®, drug interactions are classified on the basis of documentation-levels and severity-levels. According to the severity levels, the DDIs were divided into major, moderate, minor and contraindicated. Major is defined as it may be life threatening and/or require medical intervention to minimize or prevent adverse effects. Moderate severity level is the interaction which may results in exacerbation of the patient condition and/or requires an alteration in therapy. Minor severity level is the interaction which would have limited clinical effects and generally would not require a major alteration in therapy.[5] Based on the documentation levels, it is divided into different types such as Excellent, Good and Fair. Excellent is defined as the controlled studies have clearly established the existence of the interaction. Good documentation strongly suggests the interaction exists but well controlled studies are lacking. In fair documentation the available documentation is poor, but pharmacologic considerations leads to clinicians to suspect the interaction exists or documentation is good for a pharmacologically similar drug.[5] The DDIs can be prevented by developing a therapeutic relationship with the patient and caregiver to assess attitudes, preferences and drug compliance.

DRUG INTERACTION RATING SCALE [6]

RATING	DESIGNATIONS	EXPLANATIONS
D	Major	Consider therapy modifications—the interaction may be life-threatening/require medical interventions to prevent adverse events
C	Moderate	Monitor therapy—the interaction may result in exacerbation of the patient's conditions/or to require alteration the therapy
B	Minor	No actions needed—the interaction would have limited clinical effects. May include an increase in the frequency or severity of the side effects, but generally, it would not require a major alteration in the therapy.

METHODOLOGY

Study design: This study was a cross sectional observational study done in 100 sample size to estimate the prevalence of Drug-drug interactions, to evaluate the mechanism of action and severity of DDIs and to identify different variables contributing to DDIs in a tertiary care hospital at Trivandrum from march 2017 to September 2018 after obtaining ethical approval from institutional ethical committee.

Inclusion and exclusion criteria: we included patients at 20 years and older of both genders and patient details were collected from 5 departments such as neurology, cardiology, general medicine, gastroenterology and respiratory medicine. We excluded patients who are taking less than five medications, pregnant and paediatric patients, incomplete medication profiles without any relevant data.

Data Collection: In this study**,** we did a cross sectional observational of 100 patients in which the power was kept as 80%, response distribution as 50%, while confidence interval and margin of error was kept as 95% and 5% respectively. We collected data's from patient profile form which includes patient's age, gender, hospital stay, no of drugs prescribed, provisional diagnosis, relevant laboratory data's and all prescribed drugs including their dosage, route of administration and frequency during his/her stay at the hospital from September 2017 and potential DDIs were screened over a period of 6 months by using MICROMEDEX (Truven Health Analytics). The drug interactions were confirmed with the physician and taken recommended actions for the management and prevention of drug interactions.

DATA ANALYSIS

Frequencies and percentages were used to represent gender, age group and the number of drugs taken by the patients. Median and ranges are also used accordingly. Mann Whitney U test was used for independent two samples comparison. Spearman s correlation is used to determine the association of occurrence of potential drug-drug interactions with specific risk factors including age and number of drugs prescribed. P-value of 0.05 or less was considered as statistically significant. All analyses were performed using SPSS for windows version 20 (SPSS, Inc., Chicago, I, USA).

RESULT

Table No. 1: Prevalence of drug-drug interactions

DRUG-DRUG INTERACTIONS	PERCENTAGE (%)
Present	**95%**
Absent	**5%**

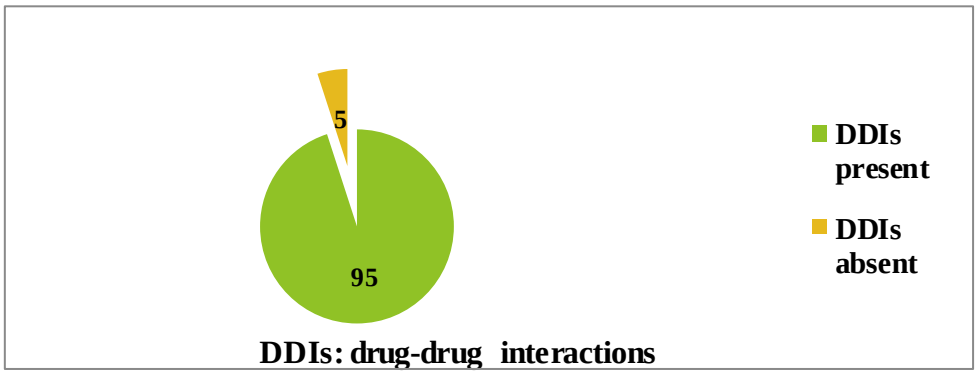

Figure No. 1: prevalence of drug-drug interactions

Table 1 show that about 95% of the prescriptions had at least one drug-drug interaction and the remaining 5% prescriptions indicated rational prescribing.

Table No. 2: Categorization of potential drug-drug interactions based on MOA

BASED ON THE MECHANISM OF ACTION

MECHANISM OF ACTION	NUMBER OF POTENTIAL DRUG-DRUG INTERACTION (N=345)	PERCENTAGE (%)
Pharmacokinetic	69	20.00
Pharmacodynamic	249	72.10
Unknown	27	07.82

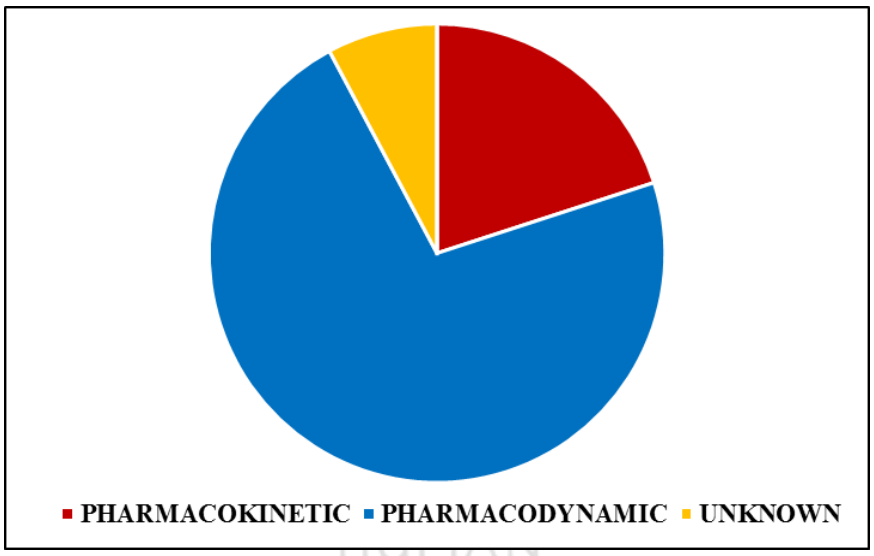

Figure No. 2: Categorization of potential drug-drug interactions based on MOA

In our current study, based on the mechanism of action as shown in table 2, the majority of the interactions were occurring due to pharmacodynamics (72.10%) followed by pharmacokinetic (20.00%), unknown (07.82%).

Table No. 3: Categorization of potential drug-drug interaction based on severity

BASED ON THE SEVERITY

SEVERITY	NO OF DRUG-DRUG INTERACTIONS (N=743)	PERCENTAGE (%)
Major	310	41.72
Moderate	363	48.85
Minor	35	04.71
Contraindicated	8	01.07
Unknown	27	03.63

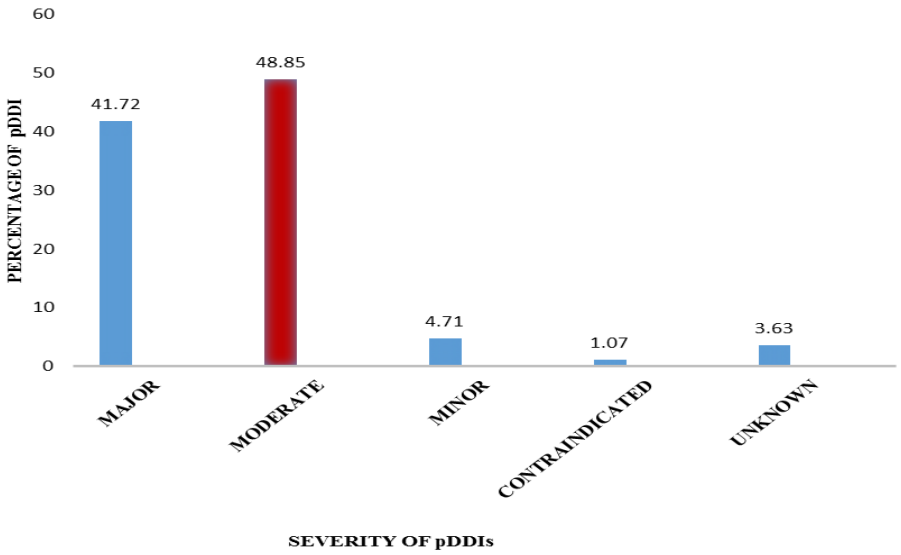

Figure No. 3: Categorization of potential drug-drug interaction based on Severity

Based on the severity level of interactions (table 2), the study found that about half of the interactions were moderate (48.85%) followed by major (41.72%), minor (4.71%), unknown (3.63%) and contraindicated (1.07%).

Table No. 4: Categorization of potential drug-drug interactions based on documentation

BASED ON THE DOCUMENTATION

DOCUMENTATION	NUMBER OF POTENTIAL DRUG-DRUG INTERACTION (N=345)	PERCENTAGE (%)
Fair	258	74.78
Excellent	23	06.66
Good	64	18.55

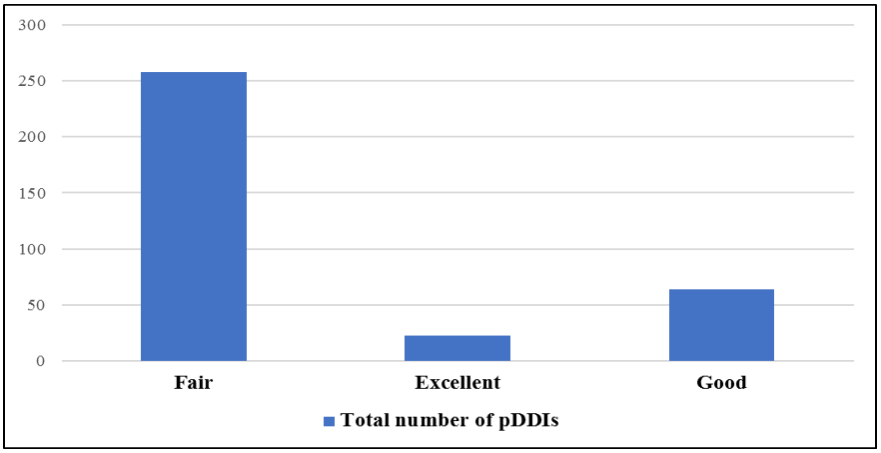

Figure No. 4: Categorization of potential drug-drug interactions based on documentation

When categorizing according to the documentation of interactions as depicted in figure 4, three-fourth of the interactions were documented as fair (74.78%) followed by excellent (6.66%) and good documentation (18.55%).

Table No. 5: Demographic details of the study population

DEMOGRAPHICS OF STUDY POPULATION

VARIABLES	TOTAL
Gender	
Male	69
Female	31
Age range (years)	
20-45	07
46-60	18
>60	75
Number of drugs prescribed	
05-10	16
11-20	70
21-30	14
Co-morbid conditions	
Hypertension	75
Diabetes Mellitus	67
Dyslipidemia	39
Coronary artery disease	33
Chronic obstructive pulmonary disease	17
Chronic kidney disease	11
Cerebrovascular accident	06
Drug use pattern	
Total number of drugs received by 100 patients	1554
Number of drug per patient	15.54

Table 5 contains the demographic details of the study subjects which include gender, age, number of drugs prescribed, comorbid conditions and drug use pattern.

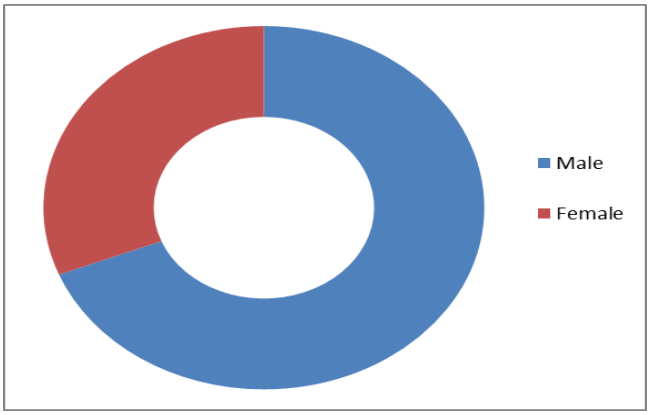

Figure No. 5: Gender Distribution

Among 100 adult inpatients, 69 were males and remaining 31 were female.

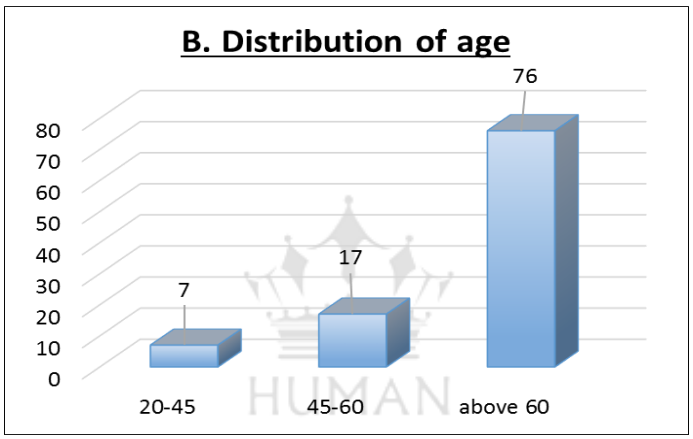

Figure No. 6: Age Distribution

According to the current study, age was categorized into three groups *i.e.* 20-45, coming under the first group, 45-60 under the second group and above 60 in the third group. Most of the study subjects are having the age group above 60 years followed by 45-60 years and 20-45 years.

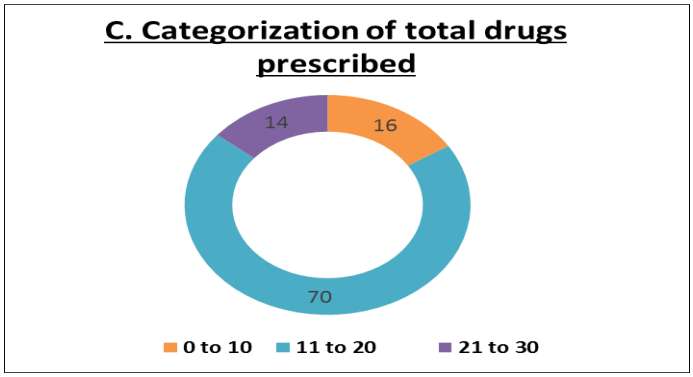

Figure No. 7: Categorization of total drugs prescribed

In terms of total number of drugs prescribed, the majority of the patients had taken 11-20 drugs followed by 0-10 drugs and 21-30 drugs.

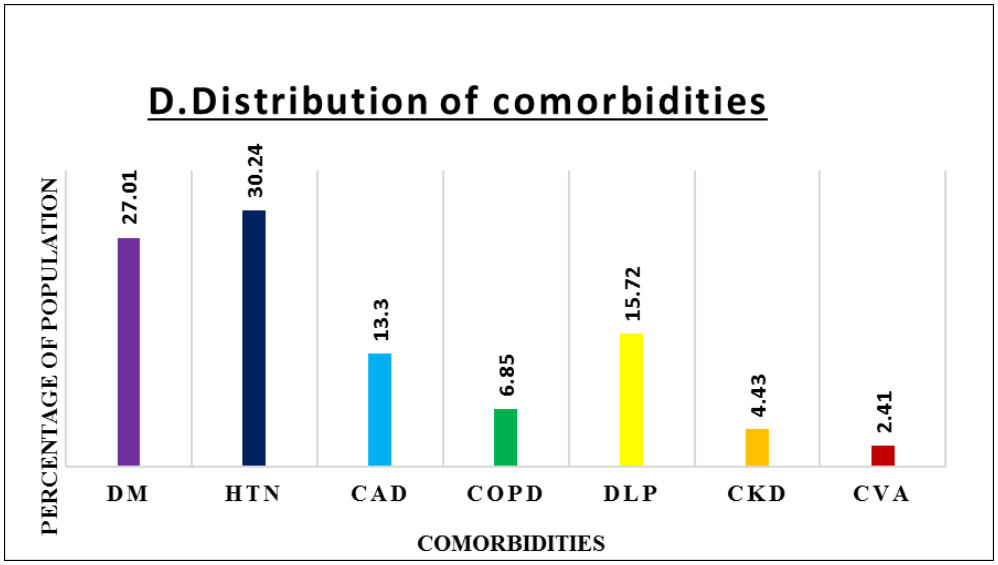

Figure No. 8: Comorbid distribution

DM: Diabetes mellitus, HTN: Hypertension, CAD: Coronary artery disease, COPD: Coronary artery disease, DLP: Dyslipidemia, CKD: coronary artery disease, CVA: Cerebrovascular accident

Hypertension (30.24%) was the most commonly observed comorbid condition followed by diabetes mellitus (27.01%), dyslipidemia (15.72%), coronary artery disease (13.3%), chronic obstructive pulmonary disease (6.85%), chronic kidney disease (4.43%) and cerebrovascular accident (2.41%).

The factors associated with potential drug-drug interactions include age, gender co-morbid conditions and number of drugs prescribed. There is no statistical association between the gender and the drug-drug interactions and there is a correlation between the age with drug-drug interactions but we did not get a statistical significant P-value.

STATISTICAL ANALYSIS FACTORS ASSOCIATED WITH POTENTIAL DRUG-DRUG INTERACTION

ASSOCIATION OF COMORBID CONDITIONS AND DDIs

Table No. 6: Statistical association of Comorbid conditions and DDIs

COMORBID CONDITION		NUMBER OF PATIENTS	MEDIAN	IQR	P VALUE
HTN	Present	75	6	8	0.004
	Absent	25	3	4	
DM	Present	67	6	11	0.000
	Absent	33	3	5	
CAD	Present	33	9	10	0.000
	Absent	67	3	5	
DLP	Present	39	9	13	0.001
	Absent	61	3	5	
COPD	Present	17	7	10	0.177
	Absent	83	5	8	
CKD	Present	11	8	13	0.048
	Absent	89	5	7	
CVA	Present	6	9	13	0.164
	Absent	94	5	7	

DM: Diabetes mellitus, HTN: Hypertension, CAD: Coronary artery disease, COPD: Coronary artery disease, DLP: Dyslipidemia, CKD: coronary artery disease, CVA: Cerebrovascular accident

Among the co-morbidities hypertension, diabetes mellitus, coronary artery disease, dyslipidemia and chronic kidney disease found a significant association with potential drug-drug interactions.

CORRELATION OF AGE AND TOTAL NUMBER OF DRUGS PRESCRIBED WITH DDIs

Table No. 7: Correlation of age and the total number of drugs prescribed with potential drug-drug interactions

Sr. No.	VARIABLES	MEAN±SD	SPEARMAN'S RHO CORRELATION COEFFICIENT	P-VALUE
1.	Total number of drugs prescribed Total number of DDI	15.54±7.43 5.165±7.633	0.528*	0.0001
2.	Age Total number of DDI	67.84±7.43 13.61±7.63	0.528**	0.141

The number of drugs prescribed was positively correlated with potential drug-drug interactions and the P-value is 0.0001. This means that the risk of potential drug-drug interactions increases with increases in the number of drugs prescribed in the treatment regimen.

There is a correlation between the age and potential drug-drug interactions but we did not get a statistical significant p-value. Spearman´s correlation test was used to determine the association of occurrence of potential drug-drug interactions with age and numbers of drugs prescribed.

DISCUSSION

A Cross sectional observational study was conducted in a 300 bedded tertiary care hospital from a period of September 2017 to March 2018. In our study, a total of 100 patients were enrolled based on the inclusion and exclusion criteria. Based on the prevalence of potential drug-drug interactions, about 95% of the patients had presence of at least one drug-drug interaction and the remaining 5% of the patients showed rational prescribing and Z. T. Tesfaye *et al.,* also got the similar findings showed that the prevalence of pDDIs among the inpatients was high (78.2%). In our study, the drug-drug interactions were categorized based on the mechanism of action, severity level and documentation. Based on the mechanism of action of drug-drug interaction, pharmacodynamic interactions were (72.1%) followed by

pharmacokinetics (20%) and unknown mechanism (7.82%). Based on the severity level, our current study found that most of the pDDIs had moderate (48.85%) level of severity as that of Henok Get *et al.,* study followed by major (41.72%), unknown (3.63%) and contraindicated (1.07%). In case moderate severity level, management should be monitored regularly to prevent any complications and in case of major interactions, therapy modification should be considered to prevent any adverse effects. Simultaneous administration of two drugs should be avoided if they are contraindicated. According to the documentation of interactions, most of the interactions were documented as fair (74.78%) followed by excellent (6.66%) and good (18.55%). The demographic details of the patients which include gender, age, number of drugs prescribed, comorbid conditions and drug use pattern. Among 100 patients, most interactions were seen in males (69) than in females (31) due to the increased number of medications prescribed to this population and according to Srujana Srithari *et al*., study concluded that the incidence of drug interactions varies with age, gender and affected disease of the patient**.** Based on the age categorization, most of the patients were having the age above 60 years as similar as that of Mateti *et al*., study reporting that DDIs are common in elderly patients who are taking multiple drug regimens. In case of the number of drugs prescribed in our study, majority of the prescriptions had 11-20 drugs and Kapadia J *et al*., study also showed that the number of drugs prescribed increases the number of pDDIs. Hypertension was the most commonly observed co-morbid condition followed by diabetes mellitus and dyslipidemia. Based on the drug use patterns, total number 1554 drugs were being received by 100 patients. A total of 743 Drug-drug interactions in the prescriptions were found out by using MICROMEDEX® software. The current study results found that there was a statistically significant association of potential drug-drug interaction with co-morbid conditions and number of drugs prescribed. The study found that there was a correlation between potential drug-drug interactions with age and number of drugs prescribed the drug-drug interactions was confirmed. Appropriate management were provided for clinically relevant DDIs and reported to both the physician and hospital authority to avoid similar incidents in the future.

CONCLUSION

Our study helped to understand the most prone age groups, gender, common mechanism that can affects the patient's disease condition. The results of this study has revealed the high risk patients such as elderly and those with co-morbid conditions who are more prone to DDIs, thus it is need of time to explore this area in order to promote safe and effective therapies.

Polypharmacy and co-morbid condition are clinically associated with potential drug-drug interactions. The study also helped to define the role of clinical pharmacist in hospitals which will further provide DDIs alerts to prescribers.

ABBREVIATIONS

ADME-Absorption, Distribution, Metabolism and Excretion; CAD-Coronary Artery Disease; CKD-Chronic Kidney Disease; CNS-Central Nervous System; COPD-Chronic Obstructive Pulmonary Disease; CVA-Cerebrovascular Accident; DDIs Drug-Drug interaction; DLP-Dyslipidemia; DM-Diabetes Mellitus; HTN-Hypertension; MOA-Mechanism of Action; pDDIs- Potential Drug-Drug Interactions; SPSS-Statistical Package for the Social Sciences.

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CONFLICTS OF INTEREST

Nil

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