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Potential drug interactions in hypertensive outpatients – A cross sectional study

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Abstract: *Hypertension is a predominant public health challenge all across the globe. Presence of comorbid conditions and increasing age makes the management of hypertension complex. The objective of this study wasto assess the pattern of potential drug interactions in hypertensive outpatients. This was a prospective cross sectional study conducted in a tertiary care hospital in India. A total of 255 patients were enrolled and the list of drug interactions in them was analysed using drug interaction checker software. A total of 411 potential drug-drug interactions (PDDIs) were found, with an average of 2.36 drug interactions per patient. Of these, 55.47% were pharmacodynamic in nature and 40.87% were pharmacokinetic in nature. Amlodipine- Metformin was the most common drug pair causing drug interaction. The prevalence of PDDI among hypertensive patients in our study was high. Hence, early detection of harmful drug combinations and careful monitoring of these patients can prevent the occurrence of drug interactions.*

Keywords: *Druginteractions , Hypertension, Hypertensive patients, Medscape drug interaction checker, Potential drug-drug interactions*

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I. Introduction

Cardiovascular diseases contribute to a major part of all morbidities and mortalities worldwide. It has been estimated that, by the year 2020, the worldwide cardiovascular diseases burden will be amplified by almost 75%.[1]Hypertensionis a predominant public health challenge all across the globe.[2]It is accountable for 57% of all stroke and 24% of all coronary heart disease mortalities in India. [3]As the drug therapy is growing more complex, making an appropriate decision on drug therapy is increasingly challenging.[4] Every year, severalnumber of antihypertensive drugs are being introduced, thus the possibility of interactions between medicationsis increasing day by day, leading to increased risk of hospitalization and healthcare costs. [5]

Drug-Drug Interactions (DDI) are observed when effects of one drug are modified by the concurrent administration of another drug.[6]Drug interactions can be either pharmacokinetic or pharmacodynamic. Pharmacokinetic interaction is said to occur when one drug modifies the effect of another drug by changes in absorption, distribution, metabolism or excretion. On the other hand, pharmacodynamicinteraction is seen when the two drugs either exhibit synergism or antagonism in their mechanism of action. [7]Hypertensive patients are commonly prescribed multiple drugs to control their blood pressure. Comorbidities and increasing age are also likely to contribute to the concurrent use of several drugs in these patients. In view of the routine use of multiple drugs, the risk of DDIs is increased in these patients. [8]

One of the threats to the adequate clinical management of hypertension is the significant risk of DDIs among the hypertensive patients. A rational and informed approach to drug interactions,canreduce the chance of adverse effects and improve patient outcomes. Hence, the present study was undertaken to find out the pattern of potential drug interactions in hypertensive patients.

II. Objective

To assess the pattern of potential drug interactions in hypertensive outpatients

III. Materials and Methods

This was a cross-sectional observational study conducted in a tertiary care hospital in India. The study subjects were patients with a diagnosis of hypertension attending medicine outpatient department of the hospital. The study was carried out over the duration of six months. It was approved by the Institutional Ethics Committee.

Inclusion Criteria

- Hypertensive patients above the age of 18years of either sex
- Patients on 2 or more drugs
- Hypertensive patients with comorbidities

Exclusion criteria

- Patients suffering from acute medical condition

Sample size-255

A written informed consent was taken from each patient enrolled in this study. Relevant data (patient demographic details, diagnosis,list of prescribed medications) weredocumented in a case record form. The potential drug-drug interactions were analysed using Medscape Drug interaction checker tool (http://reference.medscape.com/drug-interactionchecker).

The drug interactions detected by the software were documented. Data were analysed using mean, frequency, percentage. SPSS software version 23 was used.

IV. Observations and Results

A total of 255 patients were included in the study. A majority of patients were in the age group of >60 years. (Table 1)The study population consisted of 135 males (53%) and 120 females (47%) (Figure 1) Most of the patients 72(28.32%) were prescribed 3 drugs per prescription. (Table 2)

Table 1: Table depicting the distribution of patients according to age.

Age	Frequency	Percentage
31-45 years	15	5.88%
46-60 years	98	38.43%
>60 years	142	55.69%
Total	255	

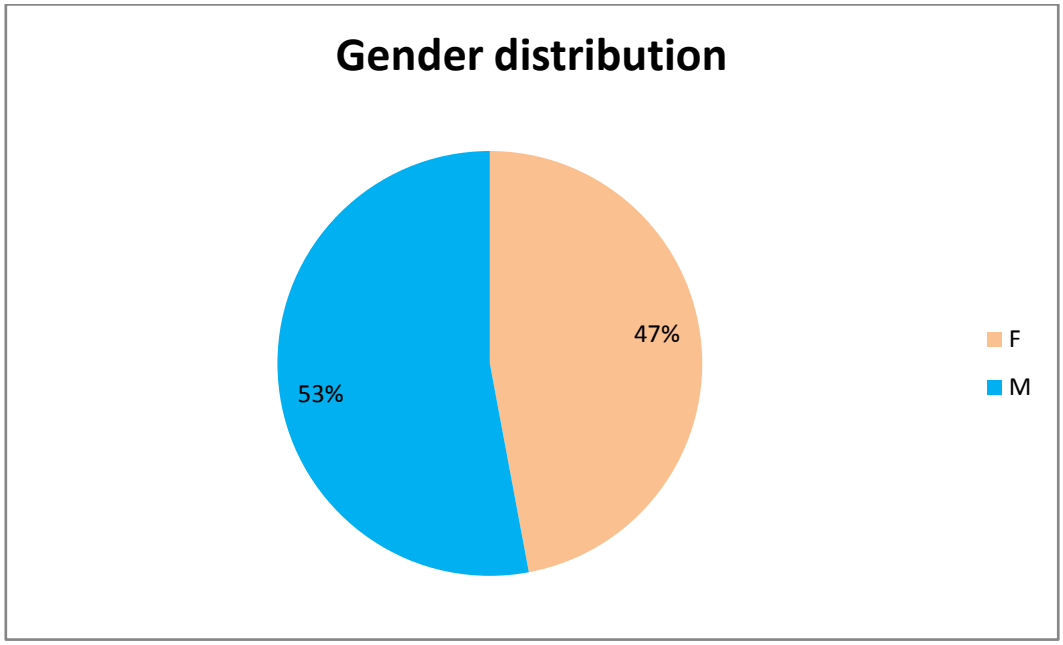

Figure 1: Pie chart depicting the gender distribution

No. of drugs per prescription	No. of patients
2	55
3	72
4	69
5	27
6	24
7	4
8	4

Table 2: No. of drugs per patient

Co-morbid conditions: The following co-morbid conditions were seen in the study subjects.(Figure 2)

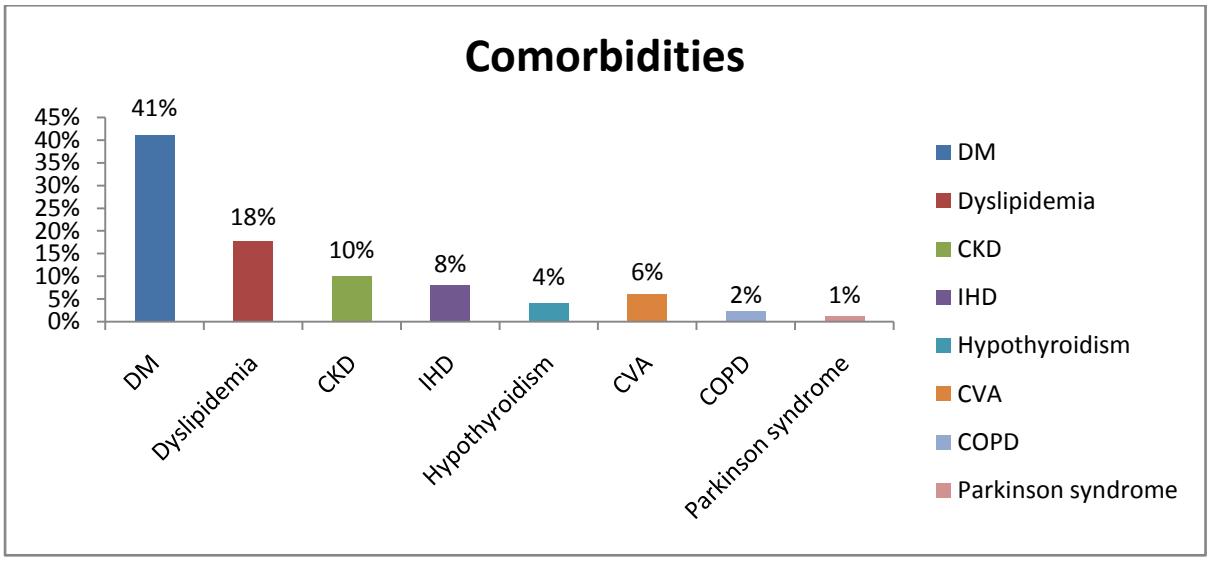

Figure 2: Bar diagram depicting the co-morbidities in the patients

Characteristics of drug-drug interactions

Out of the total subjects, 174 (68.23%) patients showed potential drug-drug interactions. A total of 411 potential drug interactions were noted in the study, of which 228 (55.47%) were pharmacodynamic in nature, 168 (40.87%)were pharmacokinetic in nature and therest 15 were of unspecified nature. (Table 3)

Category	No. of drug interactions
Pharmacodynamic	228
Pharmacokinetic	168
-Absorption	24
-Distribution	19
-Metabolism	40
-Elimination	85
Unknown	15

Table 3.Table depicting the types of potential drug interactions

Drug pair	Frequency
Amlodipine - Metformin	43
Hydrochlorothiazide - Metformin	22
Aspirin - Enalapril	18
Aspirin - Losartan	17
Aspirin - Metoprolol	13
Hydrochlorothiazide - Glimepiride	11

Table 4: Drug pairs showing pharmacodynamic antagonism

V. Discussion

The present study was undertaken to see the pattern of potential drug interactions in hypertensive outpatients. It was found that PDDI could occur in 68.23% of the patients which indicates that the frequency was high. A total of 411 PDDIs were found, with an average of 2.36 drug-drug interactions per patient. In a study done by Kothari *et al* , it was seen that 71.5% of the hypertensive patients had a prescription with PDDI this proportion was same as seen in our study. [9]In another study in Nairobi, which included hypertensive patients in both inpatient and outpatient setting, the frequency was 92.7%.[10] Therefore it is seen that the prevalence of DDI is high in hypertensive patients. In the present study, most of the patients were aged >60 years (55.69%). This is comparable to a study by AravindNC *et al*, which reported that incidence of PPDI was high in elderly age group and also found a direct correlation between the age of the patients and the number of potential drug-drug interactions.In general, elderly patients are at higher risk for DDIs because they are likely to have multiple diseases and polypharmacy that usually occur with an increased duration of disease condition and altered physiology.[11] In our study, 41% of patients had diabetes mellitus. As per previous studies,co-morbidities do have a significant relationship with the occurrence of PDDIs. Therefore, it is necessary to monitor PDDIs especially in elderly patients, who receive multiple drugs due to comorbidities.[4]

In our study, most of the drug interactions were pharmacodynamics (55.47%) in nature followed by pharmacokinetic interactions (40.87%). A study done in Austria has found the similar results.[12]These types of interactions derive from modification of the action of one drug at the target site by another drug, independent of

a change in its concentration. This may result in an enhanced response (synergism), an attenuated response (antagonism) or an abnormal response. [13]This data varies in another study where 62.2% of drug interactions noted were the pharmacokinetic type.[4]Majority of the pharmacokinetic interactions observed were due to interaction with elimination. In our study, the commonly involved drug classes in the occurrence of PDDIs were calcium channel blockers, Antiplatelet drugs, oral hypoglycemic agents, diuretics and beta blockers.

Assessing potential severity of the interaction is important in assessing the risks vs. benefits of therapeutic alternatives. With appropriate dosage adjustments or modification of the administration schedule, the negative effects of most interactions can be avoided. All these findings indicate that it is very much essential for the PDDIs to be assessed and monitored regularly. [11]The major drugs and the drug classes involved in the PDDIs identified in this study would help the health care professionals for further monitoring and evaluating the PDDIs in the future.

VI. Conclusion

The overall incidence rate of potential drug interactions in our study was 68.23%. The DDIs were found to be more common in elderly patients. Early detection of harmful drug combinations and careful monitoring of thesepatients can prevent the occurrence of drug interactions. The knowledge of the prevalence of clinically important potential DDIs will help the practicing physicians to identify patients at higher risk of developing drug interactions thus, promoting rational use of drugs, increasing the therapeutic efficacy, cost effectiveness, and minimizing the adverse effects.

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