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Original Research Article

A Retrospective, Observational Study Effect of Polypharmacy and Drug Interactions in Elderly Patients

Asal Tanhaei Saeid[1], Fereshteh Jaferi[1], AR Mahesh[2*], Ali Alipour[3], Komal Kulkarni[1]
[1] Dayananda Sagar College of Pharmacy, Bengaluru, Karnataka, India
[2]Assistant Professor, College of Pharmaceutical Sciences, Dayananda Sagar University, Bengaluru, Karnataka, India
[3]Karnataka College of Pharmacy, Bengaluru, Karnataka, India

***Corresponding author:** AR Mahesh
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Abstract

As the age increase the comorbidities also increases and also chance of polypharmacy. Polypharmacy is termed as the concurrent use of multiple medications (5 or more drugs), whether prescription or over-the-counter, by a single patient. The use of multiple drugs increases the risk of inappropriate prescribing and significantly lowers adherence to drug regimens and results in DDIs. The main aim of study to find drug interactions in elderly patients as a result of polypharmacy and also determine the drug use. A retrospective, observational study was carried out to find among elderly in-patients age above or equal to 60 years for over a period of 3 months. Data was collected from medical record department (MRD) in a pre-designed format which includes demographic details, drugs prescribed, drug per prescription and drug- drugs interactions (DDIs) encountered, DDIs are calculated using drugs.com. during the study we found that average number of drugs are 8.9 (±5.6) and mean age was 70.69 ± 6.89 year between the range 60 -88 years. Drugs involving moderate drug interaction (66.95%) were predominately seen when compared to minor (20.87%) and major (12.18%) drug interactions. The study reveals that there is statistically significant ($p<0.05$) between the number of drugs per prescription and frequency of drug interactions. Highest number of inappropriate drug combinations are seen between aspirin and anticoagulants like enoxaparin and heparin. Polypharmacy is a risk factor in elderly which will results in serious consequences like ADRs and DDIs. These problems can be overcome by strictly monitoring which will helps in maintaining the quality of life in elderly.

Keywords: Polypharmacy, DDIs, Drug Interactions, Prescription, ADRs.

INTRODUCTION

The increase in the number of healthcare set up at rural area, health insurance policy and advanced screening techniques has significantly increased the life expectancy of elderly populations. By the end of 2015 the predicted life expectancy in Indian by 2025 is 69.8 for men and 72.3 for men [1].

In elderly patient's pharmacokinetics and pharmacodynamics differ from the adults which could be due to many reasons. Factors which account for ADME (absorptions, distribution, metabolism, and elimination) changes are altered gastric emptying, decreased intestinal surface area, GI blood flow, variations in plasma-protein binding, reduction in renal function which effects the clearance of drugs, decreased hepatic blood flow, concentrations in metabolic enzymes will be affected [2]. Differences in concentration of drugs at the site of action(sensitivity), modification in drug receptor interaction, in post receptor events, homeostatic responses are causes for pharmacodynamics deviations in geriatric populations [2, 3].

As the age increase the comorbidities also increases and chance of polypharmacy. Polypharmacy is termed as the concurrent use of multiple medications (5 or more drugs), either prescription or over-the-counter, by a single patient. Problems associated with the polypharmacy are adverse drug reactions (ADR), non-compliance to medications, functional status, cognitive impairment, falls, use of herbal medications, nutrition and drug-drug interactions (DDIs) [4, 5].

Drug-drug interactions is the pharmacologic or clinical response to the administration of a drug combination differing from that anticipated from the known effect of the 2 agents [6].

Classifications of DDIs based on their severity.

- Major – This type reaction is life threatening, requires withdrawal of drug involved in the reaction.
- Moderate – Results in the worsening of the clinical condition of patients may require alliteration in therapy.
- Minor – This interaction results in the nominal clinical effects. Doesn't require change in therapy but may need monitoring [7].

Previous study suggested that 6.8% of hospital admissions are due to DDIs. Reasons for hospitalisation could be due to increased risk of bleeding, QT interval prolongation and hyperkalaemia [8].

Polypharmacy can be overcome by reviewing the drug regimen and optimising the drug use in elderly patients. Optimisations of drug can be done making drug regimen simple, know the protentional ADRs of medications and each drug has an indication with therapeutic goal [4].

The objective of present study to find drug interactions in elderly patients as a result of polypharmacy and also determine the drug use.

Materials and Method s

Study Design and Settings:

A retrospective, observational study was carried out among elderly patients equal or above 65 years of in-patients department of Sagar Hospital, Bengaluru for over a period of 3 months.

Inclusion Criteria:

- Patients age equal or above 60 years.
- Medical record of in-patients is taken for study.
- Drugs above or equal to 5.

Exclusion Criteria:

- OPD patients are excluded.

Sample Size

A total of 149 patients were include based on their inclusion & exclusion criteria. The sample size exceeds minimum of 100 as per the WHO criteria for obtaining the more reliable results.

Data Collection

The data is collected from the medical record department, source of data includes patient case sheets, drugs chart, lab reports and daily progress chart. Data is collected in pre-designed format which included the demographics details (age, sex and gender), comorbidities, diagnosis, drugs prescribed, number of drugs per prescription and drugs interaction encountered.

Analysis

Drug interactions were found using drugs.com. statistical analysis was performed using graph pad prism 8. One-way ANNOVA was used to find the statistical differences. Percentage (%) and ±SD used to express the data.

Results & Discussion

Polypharmacy is major problem associated with the elderly patients due to their comorbidity conditions. This study found that polypharmacy was common in majority of the population, but previous studies showed a less incidence (20 – 30%) [9, 10].

The present the study included the 149 medical records based on their inclusion and exclusion criteria. The average mean (± SD) of patients was 70.69 ± 6.89 year between the range 60 -88 years.

Among the study populations male (71.14%) were predominately high compared to female (28.86%) was supported by study in Maharashtra [1] and which was contradictory to study conducted in Hyderabad [11]. Usually women will leave longer than the men, as men are being more exposed to health risk (Table-1 & Figure-1).

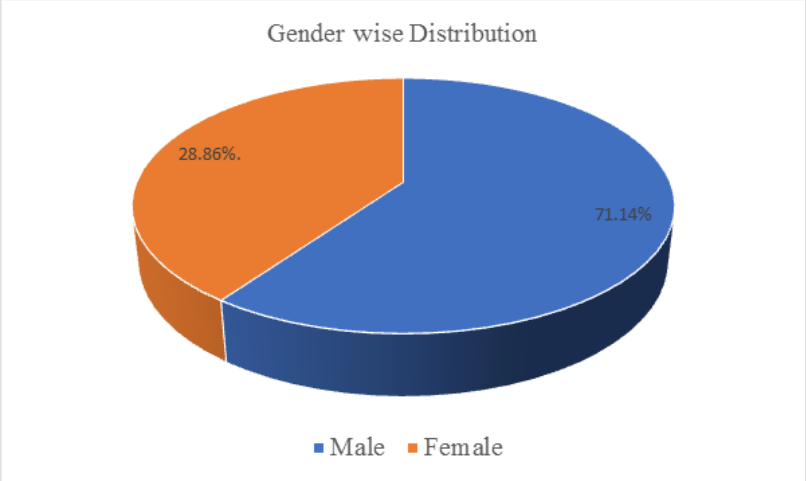

Fig-1: Gender wise distribution of study population

Table-1: Gender wise distribution of study population

Gender	Number (n=149)	Percentage (%)
Male	106	71.14
Female	43	28.86

The study population was categorised into five groups 60-65, 66-70, 71-75, 76-80 and >80 years. The greater number of patients were seen between the age group 60-65 years 28.30% followed by between 71-75 years (23.58%) can be compared with older study [1], as life expectancy was patients in 2018-19 is 68.3 -69.9 years (Table-2 and Figure-2)

Table-2: Age wise distribution of study population

Age group	Average age with SD	Males (n=106)		Females (n=43)	
		Number	Percentage (%)	Number	Percentage (%)
60-65	62.90 ± 1.69	30	28.30	12	27.9
65-70	67.77 ± 1.36	24	22.64	11	25.58
71-75	73.26 ± 1.42	25	23.58	10	23.25
76-80	77.87± 1.32	16	15.09	7	16.28
>80	84.08 ± 2.36	10	9.43	3	6.97

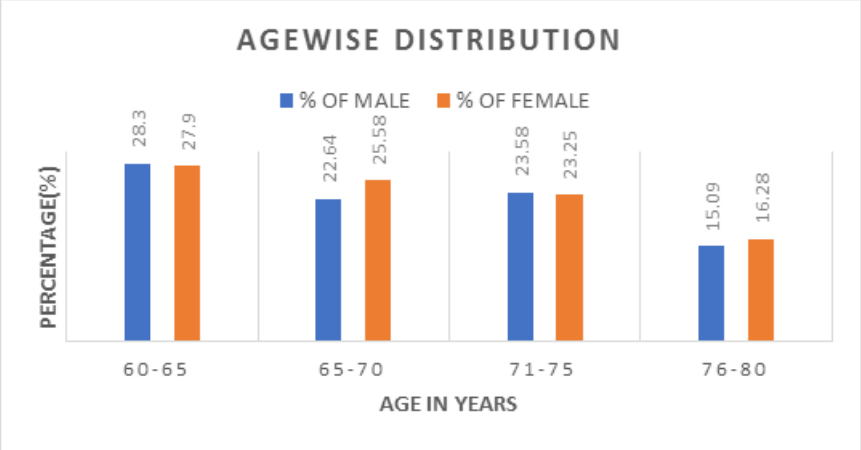

Fig-2: Age wise distribution of study population

The average number of drugs per prescription is 8.9 (±5.9) which deviated from WHO standards of 1.6 – 4.8. Our results similar to the previous study; 9.15 (±0.03) [11] and higher than study conducted in northern Ethiopia, 6 (±4), this may be due to difference in the study set up, pattern of drug use & comorbidities.

In the current study we found that, cardiovascular disease like hypertension (33.82%), IHD (24.63%), MI (6.25%) are majorly seen comorbidities followed by endocrine disorders such as diabetes mellitus (27.57%) and Hypothyroidism (3.66%) (Table-3 and Figure-3). This result can be correlated with the extensive use of antihypertensive agents (23.13%), anticoagulants (17.52%), antihyperlipidemic (8.23%), antiplatelets (6.96%), OHAs (3.37%) in study (Table-4).

Table-3: Comorbidities

Comorbidities	Number (n=272)	Percentage (%)
Hypertension	92	33.82
DM	75	27.57
IHD	67	24.63
Myocardial Infraction	17	6.25
Hypothyroidism	10	3.66
COPD	4	1.47
Asthma	3	1.10
Hyperthyroidism	2	0.74
Parkinsonism	2	0.74

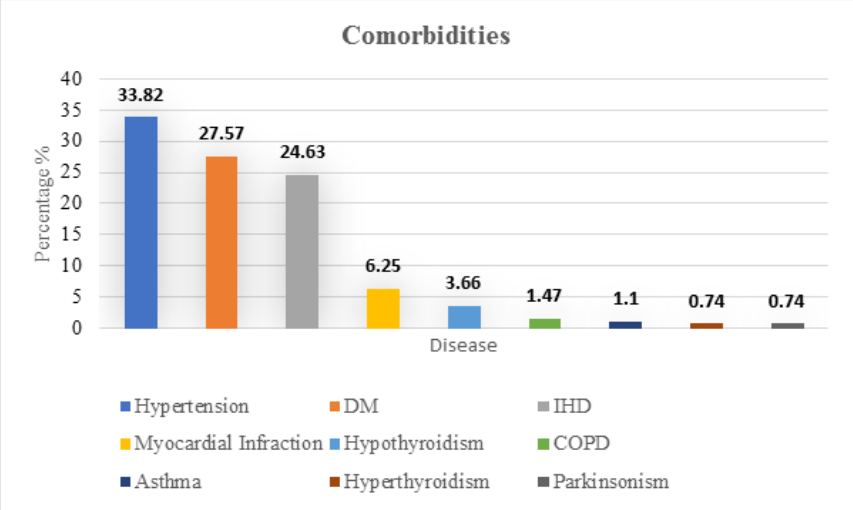

Fig-3: Comorbidities

Table-4: Various classes of drugs

Class	Number (n=1336)	Percentage (%)
Antihypertensive	309	23.13
Anticoagulants	234	17.52
PPI's and H2 receptor antagonists	157	11.75
Antihyperlipidemic	110	8.23
Antibiotics	93	6.96
Antiplatelet	93	6.96
Antiasthmatics	74	5.53
Steroid	48	3.59
OHA's	45	3.37
Vitamins and iron supplements	36	2.69
Antianginals	35	2.62
Analgesics	26	1.95
Antianxiety	24	1.80
Antihistamines	18	1.35
Antiemetic's	15	1.12
Anticonvulsants	9	0.67
Antipsychotics	5	0.37
Antidepressants	5	0.37

Drugs interactions in study was classified based on the severity of interactions. They are categorised are major, moderate and minor. The study showed a greater number of major interactions (66.95%) %) followed by minor interactions (20.87%) and major interactions (12.18%) (Table-5 and Figure-5). This is the favourable observation as moderate interaction can be managed by altering the therapy [12].

Table-5: Drug interactions based on severity

Severity	Number (n=944)	Percentage (%)
Major	115	12.18
Moderate	632	66.95
Minor	197	20.87

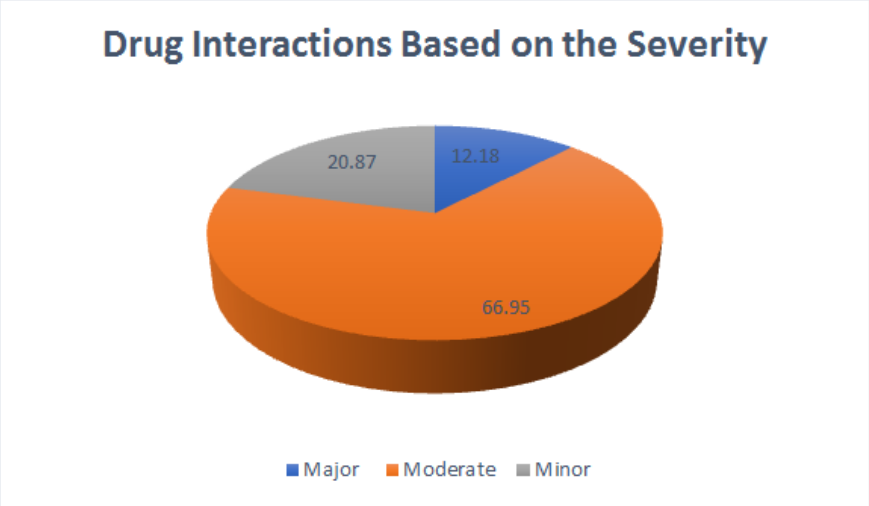

Fig-5: Drug interactions based on severity

We correlated the frequency of drug interaction with the drugs per prescription. We found that results were a statistical signification with $p<0.0035$ ($p<0.05$)), as drug interactions increase with the increase in the number of drugs per prescription. We divide the drugs per prescription into groups 5, 6-10, and >10. More drugs interactions were found in patients with more than 10 drugs (Table-6 and Figure-6) [12].

Table-6: Correlation between number of drugs prescribed and frequency of DDIs

No. of drugs prescribed	No. of patients	Frequency of DDIs	
		Number (n=944)	Percentage (%)
5	9	27	2.86
6-10	63	412	43.85
>10	77	505	53.49

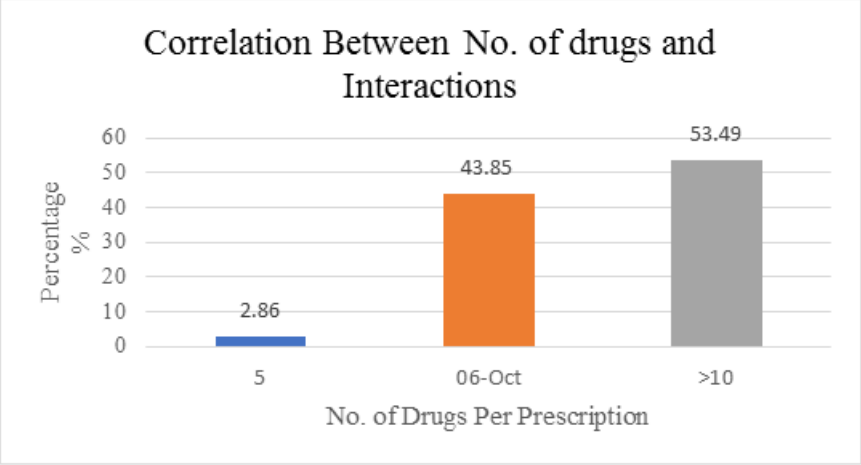

Fig-6: Correlation between number of drugs prescribed and frequency of DDIs

Most frequently seen DDIs in the present study aspirin with pantoprazole (90), Aspirin with anticoagulants such as heparin (82), enoxaparin (60) and enoxaparin with clopidogrel (60) (Table-7). These combinations are preferred in elderly patients as a prophylactic treatment to prevent thrombolytic events [6]. But these combinations may result in serious bleeding as per the studies. However, sometimes these combinations are unavoidable, strict monitoring can be done to prevent the complications [13-15].

Table-7: List of top 10 drug-drug interactions

Drug -drug interaction	Effect	Number (n=944)
Aspirin + Pantoprazole	Reduced bioavailability of aspirin	90
Heparin + Aspirin	Risk of bleeding	82
Clopidogrel + Pantoprazole	Reduced effectiveness of clopidogrel	76
Enoxaparin + Clopidogrel	Increase risk of bleeding	60
Aspirin + Enoxaparin	Risk of bleeding	60
Heparin + enoxaparin	Increase risk of bleeding	60
Furosemide + Pantoprazole	Hypomagnesemia	55
Furosemide + Aspirin	Reduced effects of furosemide	55
Atorvastatin + Clopidogrel	Reduced effects of clopidogrel	46
Digoxin + Pantoprazole	Alter the levels of digoxin	26

The current study reveals that polypharmacy increase risk of occurrence of protentional DDIs in elderly patients. However, the limitations of the studies are: carried out retrospectively which will restrict see the outcomes of DDIs and single centre study.

CONCLUSION

Drug therapy is most important in elderly patients as they are on medications for long term for the management of chronic conditions like hypertension, diabetes mellitus and hypothyroidism. Which ultimately results in polypharmacy. Polypharmacy will increase the cost burden, pill burden which results in non-compliance and occurrence of ADR and DDI's which will increase the frequency as well as length of hospitalisation.

In the present study we found that drugs involving moderated drug interactions (66.95%) were more when compared to minor (20.87%) and major (12.18%) drug interactions. There was significant statistical difference ($p<0.0035$) with number of drugs per prescription and drugs interactions involved. More number of inappropriate drug combinations which indicated towards polypharmacy.

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