Int. J. Pharm. Investigation, 2025; 15(4):1304-1310.
https://www.jpionline.org

Original Article

Assessment of Probable Drug-Drug Interactions in IPD Geriatric Patients at Tertiary Care Teaching Hospital

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ABSTRACT

Background: Older adults are at a higher risk of experiencing drug-drug interactions due to their tendency to use several medications simultaneously, which may include prescription medications, over-the-counter products and dietary supplements. The presence of polypharmacy among older adults complicates treatment, raises healthcare costs and poses challenges for healthcare organizations. This systematic review explores how pharmacist-led interventions can effectively address and reduce polypharmacy, considering the changing responsibilities of pharmacists in patient care. **Materials and Methods:** The research was a prospective observational study conducted over a period of six months, focusing on inpatients at Vivekananda General Hospital. Micromedex was employed to evaluate drug-drug interactions. **Results:** In this research, 200 elderly people were examined, in which 109 were males and 91 were females. The participants in the study were 69.5 (±5.0) years old on average. In the general population, 191 (95.5%) Comorbidities among the individuals were reported. The most prevalent chronic diseases were hypertension (53.4%), Next in line is type 2 diabetes (31.3%) and hypothyroidism was the least common condition (1.6%). The subjects were analysed for DDI'S using Micromedex, among which 132 (66%) patients were observed with 154 Drug-Drug Interactions. Majority were found in female 82 (62.12%) followed by 50 (37.87%) males. Based on severity, the discovered DDIs were divided into three categories: severe, moderate and small. Among 154 drug-drug interactions identified, 89 (57.79%) were discovered to be major, 36 (23.37%) were identified to be moderate and 7 (4.54%) were determined to be minors. **Conclusion:** Our research underscores the significance of managing drug-drug interactions in elderly patients. It is crucial to provide targeted care to this population to prevent these interactions, particularly given the prevalence of comorbidities, polypharmacy and low health literacy.

Keywords: Drug-Drug interactions, Geriatrics, Polypharmacy.

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Received: 27-03-2025;
Revised: 08-05-2025;
Accepted: 11-07-2025.

INTRODUCTION

Older adults are more susceptible to Drug-Related Problems (DRPs) due to changes in Pharmacokinetics and Pharmacodynamics (PK-PD) that occur with aging (Nyamangoud S. B. *et al.*, 2024). Over time, the number and percentage of older individuals are rising in every country around the globe. Population aging is an inevitable demographic fact that comes with improvements in health and systems of healthcare. The report from the Expert Committee on Population Projections for India and States (2011-2036) indicates that there was an increase of nearly 34 million seniors in 2021 compared to the 2011 Population Census, with a projected rise of more than 56 million elderly individuals by 2031. India has been labelled an "Aging Nation" because 7.75% of its population is over 60 years old and 75% of the elderly reside in rural regions (Dong, P. T. X. *et al.*, 2022). ((National Statistical Office [NSO], 2021). The population of elderly individuals is expected to reach approximately 324 million by 2050, driven by advancements in medical technology, which will have a considerable effect on society, financial systems and health care planning (Ramanath and Nedumballi, 2012).

Changes in one medication's toxicity or efficacy brought about by taking another medication at the same time are referred to as drug-drug interactions. This change is primarily quantitative, meaning that the response to a medication can either be intensified or diminished. Drug-drug Interactions (DDIs) can arise from pharmacokinetic processes. This means that the administration of one drug can be affected by another drug, or it can occur due to pharmacodynamic processes, where both drugs interact with the same or related targets, leading to either synergistic or antagonistic effects. Clinically significant drug-drug interactions

DOI: 10.5530/ijpi.20250334

can happen with medications that have a steep dose-response curve or a limited therapy index, those that cause or suppress the enzymes found in microorganisms and drugs that follow zero-order elimination kinetics. These interactions are also more likely in severely sick patients, individuals with significant renal or hepatic impairment and elderly patients who are taking multiple medications (Tripathi, 2013).

Pharmacological treatment in older adults is especially complex and difficult. This patient group is at a higher risk for drug interactions and adverse effects from inappropriate drug combinations due to the presence of three key predisposing factors: advanced age, multiple comorbidities and polypharmacy. For many years, ensuring patient safety throughout the treatment process has been a crucial aspect of the effective operation of healthcare systems globally. As a result, various preventive strategies have been implemented to mitigate factors that negatively impact therapeutic outcomes. One type of preventable medical error is drug interactions. Estimates suggest that one in six older patients may be at risk for a serious drug interaction. Therefore, understanding the mechanisms and causes of drug interactions in older adults, along with the potential consequences, is essential for effectively planning pharmacotherapy (Błeszyńska *et al*., 2020). The prescriber needs to evaluate the potential benefits and risks of introducing a new medication, while also determining the suitable dosage for each individual. This assessment should take into account factors such as age, comorbidities, current medications, frailty and the patient's functional and cognitive status. In older adults with multiple health conditions, polypharmacy is frequently already established (Zhou *et al*., 2023).

Prescribing medications that are more harmful than beneficial, particularly when safer options are available, is a concern: Prescribing an unsuitable dose or duration of medication; Failing to prescribe Possibly helpful drugs; Significant drug-drug interactions, Drug-Disease Interactions (DDIs) and the duplication of medications (Rasool *et al*., 2020).

MATERIALS AND METHODS

This six-month study, which involved inpatients at Vivekananda General Hospital, was a prospective observational study. The Institutional Ethical Committee granted ethical clearance for this study KLECOPH/IEC/2022-23/04.

Inclusion Criteria

Patients above the age of 60, Both male and female patients, Patients who were hospitalized for at least 48 hr.

Exclusion Criteria

Patients below the age of 60, Outpatients, those who were not willing to participate

Sample Size

The total sample was 200

$$N = \frac{[Z_{1-\alpha/2}]2\ p\ (1-p)}{d2}$$

Where, Z is critical value

d is allowable error

p is sample proportion

α is level of significance.

Data Collection

Patient case files, test results, prescription charts, clinical progress charts, interactions with the patient and their carer and interactions with medical experts were among the sources from which the data was gathered. Various data collection forms were used as part of the study protocol to document the data. Throughout the trial, forms for patient profiles, Drug interactions, medication history intervention, clinical pharmacist intervention reporting, patient counselling and recordkeeping were all used.

Using IBM Micromedex, probable drug-drug interactions were identified. To store the data gathered during the investigation, an Excel database was utilised. descriptive statistics in which the frequencies and percentages of categorical variables are displayed. Standard deviation and mean are used to display continuous values. The data was extracted for observational analysis, organised and structured using pivot analysis.

RESULTS

Demographics of study population

In all, 200 senior citizens participated in the study. Among these, 109 (55.5%) were males and 91 (45.5%) were females. The study participants' average age was 68.5 (±5.0) years. 106 (53.2%) of the participants were between the ages of 60 and 69. The research also examined the literacy rate, finding that 138 people (69%) were illiterate or lacked a formal education, while 62 people (31%) were literate. They were mostly living in rural areas. 117 (58.5%), while the others came from cities 83 (41.5%). Taking societal customs into account, 71 (35.5%) were discovered to possess at least one social habit. Out of this, 13 (6.5%) exhibited diverse patterns of social habits, whereas 30 (14.9%) were discovered to be alcoholics and the remaining 28 (14%) were discovered to be smokers. Among the overall population, 191 (95.5%) comorbidities were reported for the individuals. The most prevalent chronic conditions were hypertension 134 (70.10%), type 2 diabetes mellitus 66 (34.55%) and hypothyroidism 5 (2.60%) (Table 1).

Distribution of Probable Drug-Drug Interaction Based on Gender

200 patients were analysed during the study period. in which 132 (66%) patients were observed with 154 probable Drug-Drug

Interactions. Majority were found in female 82 (62.12%) followed by 50(37.87%) males same as shown in Table 2.

Distribution of Probable Drug Interactions Based on Severity

Out of 200 prescriptions, 132 (41.5%) 154 probable DDIs were discovered in prescriptions. With IBM Micromedex software, every probable drug-drug interaction was evaluated. Based on severity, the identified probable DDIs were divided into three categories: Severe, Moderate and Small. Of the probable 154 DDIs that were found, 89 (57.79%) were classified as major, 36 (23.37%) as moderate and 7 (4.54%) as minor (Figure 1).

Genderwise Distribution of Probable Drug-Drug Interaction Based on Severity

Out of 154 probable drug-drug interactions 37 male patients and 52 female patients were having major probable drug-drug interactions, 8 male patients and 28 female patients were having moderate probable drug-drug interactions and 5 male patients and 2 female patients were having minor probable drug-drug interactions (Figure 2).

The most common probable drug-drug interactions were aspirin+furosemide 20 (18.1%), aspirin+clopidogrel 13 (11.8%) and metronidazole+ondansetron 10 (9.09%), all of which had significant side effects. The moderately severe aspirin+metoprolol 5 (4.54%) and the mildly severe furosemide+theophylline 4 (3.36%) came next.

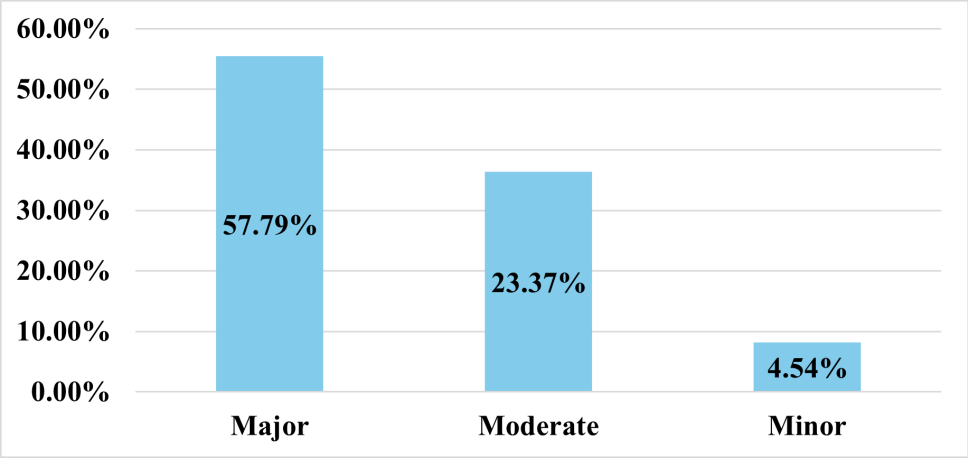

Figure 1: Distribution of probable drug-drug interaction based on severity.

Table 1: Demographic details of the study populations.

Sl. No.	Categories	Sub-categories	No of Participants (*n*=200)
1	Gender	Male Female	109 (55.50%) 91 (45.50%)
2	Age	60-69 70-79 80-89 90-99	106 (53.00%) 73 (36.50%) 15 (07.50%) 6 (02.80%)
3	Residence	Rural Urban	117 (58.50%) 83 (41.50%)
4	Social habits	Smoking Alcoholic Mixed	13 (06.50%) 30 (14.90%) 28 (14.00%)
5	Literacy	Literate Illiterate	62 (31.00%) 138 (69.00%)
6	Comorbidity	Hypertension Type 2 DM Hypothyroidism	134 (70.10%) 66 (34.55%) 05 (02.60%)

Probable Drug-Drug Interactions

The most often found probable drug-drug interaction was aspirin+furosemide 20 (18.1%), which was followed by A total of 132 (66%) of the 200 individuals had 154 probable DDIs. Using software from IBM Micromedex, all probable drug-drug interactions were evaluated. The severity of the discovered probable DDIs was classified as major, moderate and small. Six (3.89%), 40 (25.78%) and 108 (70.13%) of the 154 probable DDIs that were discovered were classified as minor, moderate and major, respectively (Table 3). The most commonly found probable drug-drug interactions were aspirin+furosemide 18 (11.6%), aspirin+clopidogrel 12 (7.79%) and metronidazole+ondansetron 9 (5.8%) with significant severity. The moderately severe aspirin+metoprolol 4 (2.6%) and the mildly severe furosemide+theophylline 2 (1.3%) came next. Severity (Table 3).

DISCUSSION

Issues related to drug use are increasingly recognized as a significant public health challenge. Older adults, in particular, are especially susceptible to drug-related problems due to various factors, including the use of multiple medications and improper prescribing practices (Freyer *et al.*, 2018).

Recognizing and preventing the occurrence of Drug-Related Problems (DRPs) in this demographic is essential. In our research, we found that 81.5% of geriatric patients experienced DRPs. This finding is consistent with a study by Ramanath K *et al.*, conducted

Table 2: Distribution of DDI'S based on Gender.

Sl. No.	Gender	Number of subjects
1	Male	50 (37.87%)
2	Female	82 (62.12%)

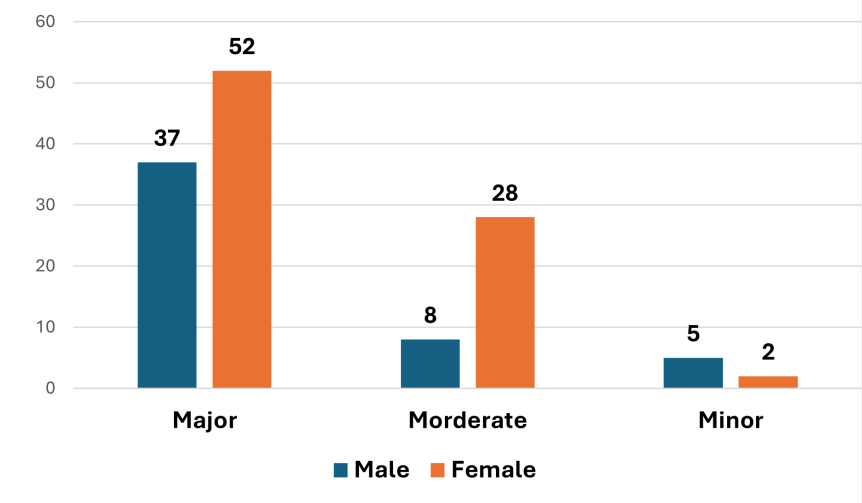

Figure 2: Assessment of severity based on gender.

Table 3: Drug-Drug Interactions.

Sl.No	Suspected Interactions	Severity	Adverse Effects	Frequency
1	Azithromycin+Ondansetron	Major	QT interval prolongation	5
2	Amlodipine+Clopidogrel	Major	Decrease anti-platelet effect and increased risk of thrombotic events	7
3	Cal gluconate+Ceftriaxone	Major	Formation of ceftriaxone-calcium precipitates	1
4	Azithromycin+Ciprofloxacin	Major	QT interval prolongation	2
5	Ciprofloxacin+Tramadol	Major	Respiratory depression	3
6	Calcium gluconate+Ciprofloxacin	Major	Decrease ciprofloxacin efficacy	1
7	Ranitidine+Tramadol	Major	Respiratory depression	1
8	Dexamethasone+Tramadol	Major	Reduced tramadol exposure	2
9	Aspirin+Furosemide	Major	Salicylate toxicity and nephrotoxicity,	18
10	CPM+Ondansetron	Major	Increases serotonin syndrome	2
11	Metronidazole Ondansetron	Major	QT interval prolongation	9
12	Aspirin+Metformin	Major	Increased risk of Hypo-glycemia.	5
13	Aspirin+Tirofiban	Major	Risk of bleeding.	2

14	Aspirin Cilostazol	Major	Risk of bleeding.	1
15	Aspirin Torsemide	Major	Reduced diuretic effect and nephrotoxicity	1
16	Aspirin Glimepiride	Major	Increased risk of Hypo-glycemia.	1
17	Acenocoumarol+Enoxaparin	Major	Risk of bleeding.	1
18	Azithromycin+Metronidazole	Major	QT interval prolongation	2
19	Ondansetron+Tramadol	Major	Increases serotonin syndrome	3
20	Enalapril+Furosemide	Major	Severe hypotension and renal failure.	1
21	Phenytoin+Theophylline	Major	Decrease theophylline or phenytoin exposure.	1
22	Hydrocortisone+Levofloxacin	Major	Increased risk of tendon rupture.	1
23	Theophylline+Levofloxacin	Major	Theophylline toxicity.	1
24	Amiodarone+Carvedilol	Major	Increased risk of bradycardia or heart-block.	1
25	Diclofenac+Heparin	Major	Risk of bleeding.	1
26	Metronidazole+Phenytoin	Major	Risk of phenytoin toxicity.	2
27	Amiodarone+Diltiazem	Major	Increased risk of bradycardia, sinus arrest, or AV block.	1
28	Diltiazem+Metoprolol	Major	Increase risk of hypotension, bradycardia, AV-conduction disturbances.	1
29	Aspirin+Spironolactone	Major	Reduced diuretic effect, hyperkalaemia.	7
30	Furosemide+Enalapril	Major	Severe hypotension and deterioration in renal function including renal failure.	1
31	Ciprofloxacin+Ondansetron	Major	QT interval prolongation.	2
32	Ciprofloxacin+Metronidazole	Major	QT interval prolongation.	2
33	Furosemide+Telmisartan	Major	Severe hypotension and deterioration in renal function including renal failure.	1
34	Aspirin+Digoxin	Major	Increase serum concentration.	1
35	Atorvastatin+Digoxin	Major	Increased plasma level concentration of digoxin.	1
36	Aspirin+Phenytoin	Major	Reduced phenytoin exposure	4
37	Azithromycin+Theophylline	Moderate	Increases serum theophylline concentration	2
38	Cal gluconate+Levofloxacin	Moderate	Decreased oral levofloxacin effectiveness.	2
39	Clopidogrel+Tramadol	Moderate	Reduced efficacy of clopidogrel	2
40	Aspirin+Metoprolol	Moderate	Increased blood pressure	4
41	Acetaminophen+Phenytoin	Moderate	Risk of hepatotoxicity	2
42	Atorvastatin+Azithromycin	Moderate	Risk of rhabdomyolysis	1
43	Furosemide+Hydrocortisone	Moderate	Result in hypokalemia.	2
44	Azithromycin+Theophylline	Moderate	Increase serum theophylline concentration	2
45	Aspirin+Sodium bicarbonate	Moderate	Decreased salicylate effectiveness.	1
46	Azithromycin+Phenytoin	Moderate	Increased serum phenytoin levels	1
47	Folic acid+Phenytoin	Moderate	Decreased folic acid serum levels,decreased phenytoin effects	2
48	Aspirin+Insulin	Moderate	Risk of hypoglycemia	1
49	Phenytoin+Metronidazole	Moderate	Phenytoin toxicity or decreased metronidazole plasma levels	2
50	Diclofenac+Enalapril	Moderate	Renal dysfunction or increased blood pressure	1
51	Metformin+Enalapril	Moderate	Increased risk of hypo-glycemia	1
52	Metformin+Metoprolol	Moderate	Hypo-glycemia or hyperglycemia	1

53	Atorvastatin+Clopidogrel	Moderate	Decreased formation of clopidogrel active metabolite resulting in high on-treatment platelet reactivity.	1
54	Iron sucrose+Pantoprazole	Moderate	Reduced iron bioavailability	2
55	Atorvastatin+Phenytoin	Moderate	Decreased atorvastatin plasma concentration and decreased atorvastatin efficacy	3
56	Clopidogrel+Phenytoin	Moderate	Phenytoin toxicity	3
57	Phenytoin+Levofloxacin	Moderate	Decreased in phenytoin levels.	1
58	Dapagliflozin+Furosemide	Moderate	Increase risk of hypoglycaemia	1
59	Dapagliflozin+Metoprolol	Moderate	Increase risk of hyperglycaemia	1
60	Ferrous sulphate+Pantoprazole	Moderate	Reduces iron bioavailability	1
61	Aspirin+Clopidogrel	Major	Increase risk of bleeding	12
62	Iron folic acid+Calcium	Minor	Decrease iron effectiveness	1
63	Iron folic acid+Sodium bicarbonate	Minor	Decrease iron effectiveness	1
64	Furosemide+Theophylline	Minor	Alteration in theophylline concentration.	2
65	Amikacin+Piperacillin and Tazobactam	Minor	Loss of aminoglycoside efficacy	1
66	Aspirin+Hydrocortisone	Minor	Risk GIT ulceration and subtherapeutic aspirin serum concentration.	1

in a rural tertiary care hospital in India, which reported a prevalence of 83.4% for DRPs (Ramanath and Nedumballi, 2012).

The study consists of a total of 200 participants according to inclusion and exclusion standards. Out of 200 Subjects, 109 (54.5%) were males and 91 (45.5%) were females. We categorized the participants into four age groups, i.e., 60 to 69, 70 to 79, 80 to 89 and >90. Maximum of study participants belong to the age group of 60-69 years 106 (53%) and minimum exists in >90 years of age group 6 (2.85%). The average study population is 69.5 years and majorly the participants reside in rural area. Research conducted by Hailu *et al*., showed similar results, male (54) was predominant, and majority of subjects were found in age group of 60-70 years and (68.5%) majority of participants resides in rural areas (Hailu *et al*., 2020). In our study, a total of 154 probable drug-drug interactions were observed in 132 subjects using IBM Micromedex drug interaction application. Out of which 108 (70.10%) were of major severity followed by 40 (26.1%) moderate severity and 6 (3.89%) of minor severity. The most common probable DDIs observed in our study was Aspirin-furosemide (18) causing salicylate toxicity and nephrotoxicity followed by Aspirin-clopidogrel (12) causing increased risk of bleeding. Probable Drug-drug interactions may be because of greater number of drugs prescribed per prescription, taking multiple drugs at the same time, subjects' unawareness on their health condition and safe use of medicine (i.e., when and how to take the drug). An analogous study attained by Samuel Berihum Dagnew *et al*., the drug-drug interaction 154 (30.61%) were the main type of DRP (Dagnew *et al*., 2022).

CONCLUSION

Drug related problems like drug-drug interactions are more frequent in hospitalized patients who have comorbidities and are taking multiple drugs to treat the diseases. Incidence of DDI's are higher in female than male subjects. Subjects above 60 years of age, polypharmacy, comorbidity, illiteracy and low economic status are the risk factors linked with the occurrence of DDI's. The study results show that the most common drug class and drug involved in DDI's were cardiovascular drugs and Furosemide respectively.

ACKNOWLEDGEMENT

The authors are thankful to the Vice-Chancellor, Registrar and Dean of Pharmacy, KLE Academy of Higher Education and Research, Belagavi.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

DRP: Drug-Related Problems; **ADR:** Adverse Drug Reactions; **DDI:** Drug-Drug Interaction.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee. (KLECOPH/IEC/2022-23/04).

PATIENT CONSENT

Consent was taken verbally while interviewing the patient.

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Cite this article: Purantar AM, Nyamagoud SB, Swamy AHV, Jangliwale BK, Kumar K, Rakshita TP. Assessment of Probable Drug-Drug Interactions in IPD Geriatric Patients at Tertiary Care Teaching Hospital. Int. J. Pharm. Investigation. 2025;15(4):1304-10.