

A Study on Polypharmacy and Potential Drug-Drug Interactions among Elderly Patients Admitted in Department of Medicine of a Tertiary Care Hospital in Puducherry

KARTIK JANARDAN SALWE¹, DHARANI KALYANSUNDARAM², YOGESH BAHURUPI³

ABSTRACT

Introduction: The proportion of elderly population has been constantly increasing over last few years. Polypharmacy is unavoidable in the elderly as they often suffer from multiple co-morbidities. Potential drug-drug interaction due to polypharmacy and potential inappropriate medication among the elderly must be carefully assessed.

Aim: To find out polypharmacy and potential drug-drug interactions among elderly patients admitted and discharged in Department of Medicine.

Materials and Methods: This study was carried out on 100 patients above 65 years of age both males and females. Data was collected through review of case sheets. Polypharmacy was observed based on admission and discharge prescriptions.

Frequently occurring drug-drug interactions were assessed using online checks.

Results: Mean number of drugs prescribed to patients on admission (7.61 ± 3.37) was more than that on discharge (5.48 ± 2.46). More than half of these patients received 5 to 9 number of drugs. On admission 52.69% potential drug-drug interactions were observed and on discharge 52.91%. Most common drug interactions observed in both the groups were of moderate grade.

Conclusion: From the present study we can conclude that polypharmacy leads to more potential drug-drug interactions. To improve drug safety in this high-risk population, appropriate prescribing is very important.

Keywords: Admission, Discharge, Elderly, Interactions

INTRODUCTION

The ageing process is a biological reality which has its own dynamic, largely beyond human control. Ageing is a natural process. In other words age is an incurable disease. Discoveries in Medical science and improved social condition during past few decades have increased the life span of man. The worldwide estimated number of elderly population of 605 million in year 2002 is expected to rise beyond 1.2 billion by 2025, with about 840 million representing developing countries [1]. In India, size of elderly population is growing rapidly; from 5.6% of total population in 1961, it is projected to rise to 12.4% by year 2026 [2].

As compared to young adults, elderly persons have more illnesses, as ageing seldom comes alone is often being accompanied by chronic diseases, co-morbidity, disability and social isolation. Also, they are the most common group to be admitted in hospitals. Hence it is not surprising that both the frequency of drug therapy and average number of drugs taken per person progressively increase with age.

Multimorbidity leads to use of multiple drugs, a condition known as polypharmacy. Polypharmacy has no standard definition. A simple definition would be the administration of more medicines than are clinically indicated [3]. In some studies, authors have defined the concomitant ingestion of four or more as Polypharmacy While some other studies mentioned the use of five and more medications as polypharmacy [4-7]. The chances of unintended adverse drug reactions due to drug-drug interactions are greater in geriatric patients because an assortment of different drugs may be administered to a patient depending on the disease or symptoms.

Drug interactions refer to modification of response to one drug by another when they are administered simultaneously or in quick succession. When a patient is prescribed more than one drug in the same prescription, the possibility of drug interactions arises which increases with the number of drugs. Although, the severity of these interactions in most of the cases is unpredictable [8].

Inappropriate medications can be defined, in terms of older people, as "medications or medication classes that should generally be avoided in persons 65 years or older because they are either ineffective or they pose unnecessarily high risk for older persons and a safer alternative is available" [9].

Over the last 20-30 years, problems related to ageing, multimorbidity and polypharmacy have become a prominent issue in global healthcare. The consequences of polypharmacy and drug interactions in elderly patients have already been documented by many researchers particularly in western countries [10,11]. In India however, few studies have emphasized the role of polypharmacy and drug interactions among admitted elderly patients [12,13].

AIM

The present study was planned to find out prevalence of polypharmacy, drug interactions and potentially inappropriate drugs among elderly patients admitted in Department of Medicine of a tertiary care hospital in Puducherry.

MATERIALS AND METHODS

A prospective hospital based cross-sectional study (prescription audit) was conducted in the Department of Medicine of a tertiary

care hospital. This study was carried out on elderly patients (above 65 years of age) both males and females between April-June 2013. In view of duration and considering total number of admitted elderly patients (above 65 years) in the previous year in Department of Medicine, and their eligibility as study subjects, approximately 120 elderly patients were recruited for the present study (Expecting 20% non-response and calculated sample size of 96). Elderly patients willing to participate and who signed informed consent were included.

Exclusion criteria

1. Incomplete patient case sheet.
2. Emergency and intensive care unit patients.
3. Patients with malignancy.
4. Death of patient before being discharged.

Sample Size: In absence of reference data, prevalence of polypharmacy was assumed to be 50%.

$$\text{Sample size } N = (Z_{1-\alpha/2})^2 * pq / I^2$$

Hypothesized % frequency of outcome factor in the population, (p): 50%

Confidence limits as % of 100(absolute +/- %) (I): 5%

$Z_{1-\alpha/2}$ value for 95% confidence interval: 1.96

$N \approx 96$

Data collection procedure: Data was collected through review of case sheets of all elderly patients admitted in Department of Medicine. Case sheets of all the admitted elderly patients discharged or to be discharged from the hospital were reviewed each day during the study period. Such review of case sheets were considered only once for each patient during one single admission. Elderly patients admitted more than once during the study period was considered as a separate admission.

A total of 137 patient case sheets were collected within three months. Out of these 14 patients were excluded due to unreadable patient's admission forms, 7 patients of inpatient group died in hospital and 16 patients had incomplete data and were consequently excluded. Thus, 100 patients were included for final evaluation.

Information regarding name, age, sex, date of admission, diagnosis, date of discharge, name and number of drug prescribed at the time of admission and discharge etc. were collected. Polypharmacy was ascertained based on admission and discharge prescriptions. As polypharmacy has no standard definition, we followed definition given by Kaufman and grouped prescribed medications into four groups < 4, 5-9, 10-14 and >15 in admitted and discharge prescriptions [6].

Further, considering admission and discharge prescription prevalence and frequency of occurrence of drug-drug interactions and potentially dangerous drug interactions were assessed using computer based checks online available on the internet (drugs.com interaction checker) [14]. Drug interactions observed in the study were entered in database with following information:

1. Name of the Drug
2. Drug interacting with
3. Severity of Drug interaction as
 - a) **Mild:** Minimally clinically significant. Minimize risk; assess risk and consider an alternative drug, take steps to circumvent the interaction risk and/or institute a monitoring plan.
 - b) **Moderate:** Moderately clinically significant. Usually avoid combinations; use it only under special circumstances.
 - c) **Severe:** Highly clinically significant. Avoid combinations; the risk of the interaction outweighs the benefit.

In addition, 'Potentially inappropriate medicines being used as first line treatment was explored in each prescription using American Geriatric Association updated 'Beers Criteria' [9].

STATISTICAL ANALYSIS

Collected data was entered in Microsoft_Office_Excel 2010 and analysed using SPSS. Inc statistical software version 17.0. Descriptive statistics explained using proportion and percentages and mean±SD. Z-test for two proportions was used to assess statistical significance. Statistical significance was considered at p-value <0.05.

Ethical Clearance: Ethical permission to conduct the hospital based study was obtained from Institution Ethics Committee before commencement of the study (IHEC: UG/2013/06 dated 19th Aug 2013). Subject confidentiality was maintained during and after data collection.

RESULTS

Out of 100 elderly patients admitted in the hospital during study period 62 (62%) were males and 38 (38.0%) were females. Mean age of patients was 71.64 ± 6.51 year [Table/Fig-1]. Total admitted elderly patients were classified into three age groups 65-74, 75-84 and ≥85. Most common elderly patients admitted during study period were between age group 65-74 year followed by 75-85 year and represents 70% (N=70) and 21% (N=21) of total study population respectively. Elderly patients >85 year were admitted in less number and represents 9% (N=9) of total study population [Table/Fig-2].

In all age group mean number of drugs prescribed on admission were more than at discharge. On admission, number of drugs prescribed increased as age of patient increased. Mean number of drugs prescribed on admission of age group 65-74, 75-84 and ≥85 was 7.40±3.32, 8.10±3.30 and 8.11±4.19 respectively while mean number of drugs prescribed at discharge of age group 65-74, 75-84 and ≥85 was 5.56±2.56, 5.62±1.83 and 4.56±2.96 respectively [Table/Fig-3].

Mean number of drugs prescribed to patients on admission (7.61 ± 3.37) was more than that on discharge (5.48±2.46). More than half of admitted and discharged elderly patients received drugs between 5 to 9.

	Number	Percent	Mean Age (Y)
Males	62	62.0%	71.05 ± 6.067
Females	38	38.0%	72.00 ± 6.792
Total	100	100.0%	71.64 ± 6.51

[Table/Fig-1]: Sex wise distribution of patients admitted under department of Medicine.

Age Group (Yr)	Number	Percent
65-74	70	70.0%
75-84	21	21.0%
>85	9	9.0%
Total	100	100.0%
Minimum Age	65	
Maximum Age	87	

[Table/Fig-2]: Age wise distribution of elderly patients admitted in department of Medicine.

	Age Group (Yr)	Number of Drugs prescribed (Mean ± SD)
Admitted	65-74	7.40 ± 3.32
	75-84	8.10 ± 3.30
	>=85	8.11 ± 4.19
	Total	7.61 ± 3.38
Discharged	65-74	5.56 ± 2.56
	75-84	5.62 ± 1.83
	>=85	4.56 ± 2.96
	Total	5.48 ± 2.46

[Table/Fig-3]: Number of drugs prescribed to specific age group of elderly patients admitted in department of Medicine.

Drugs	Admitted		Discharged	
	Frequency	Percentage	Frequency	Percentage
<=4	20	20.0%	40	40.0%
5-9	53	53.0%	55	55.0%
10-14	25	25.0%	5	5.0%
>=15	2	2.0%	0	0%
Total	100	100.0%	100	100.0%
Mean	7.61 ± 3.38		5.48 ± 2.46	

[Table/Fig-4]: Number of drugs prescribed to elderly patients admitted in department of Medicine.

Day Stayed		Number admission	Number discharge
	Pearson Correlation	0.296**	0.095
	Sig. (2-tailed)	0.003	0.346
	N	100	100

[Table/Fig-5]: Correlation between days stayed and increase in number of medications.

**p <0.05 value statistically significant

	Admitted		Discharged	
	Frequency	%	Frequency	%
Drugs acting on Gastrointestinal System	121	15.90%	90	16.42%
Drugs acting on Respiratory System	104	13.67%	81	14.78%
Cardiovascular drugs	94	12.35%	69	12.59%
Antimicrobial drugs	91	11.96%	56	10.22%
Drugs acting on Endocrine system	87	11.43%	62	11.31%
Analgesics & anti-inflammatory drugs	67	8.80%	49	8.94%
Drugs acting on Haematological system	65	8.54%	43	7.85%
Vitamins, minerals & dietary supplements	63	8.28%	43	7.85%
Drugs acting on Central Nervous System	33	4.34%	26	4.74%
Hypolipidaemic Drugs	27	3.55%	25	4.56%
Others*	9	1.18%	4	0.73%
Total	761	100%	548	100.00%

[Table/Fig-6]: Number of drugs prescribed to admitted and discharged elderly patients in Department of Medicine.

*Antihistamines, DMARDs, Drugs for glaucoma, Antioxidants, Immunosuppressant, Antipruritic Drugs and Ectoparasiticides.

	Admission	Discharge
Number of drugs prescribed	761	548
Total number of drug-drug interactions	401 (52.69%)	290 (52.91%)

[Table/Fig-7]: Proportion of potential drug-drug interactions out of total drugs prescribed in elderly patients admitted in department of Medicine.

	Admitted	Discharge	p-value
Total number of drug-drug interactions	401	290	-
Mild drug-drug Interactions	65 (16.2%)	50 (17.24%)	0.72
Moderate drug-drug Interactions	308 (76.80%)	230 (79.31%)	0.44
Severe drug-drug Interactions	28 (6.98%)	10 (3.44%)	0.044

[Table/Fig-8]: Proportion of Severity of Potential drug interaction out of total drug Interactions in elderly patients admitted in department of Medicine.

Among 40% of discharge patients and 20% of admitted patients prescribed number of drugs was between 0-5. While, 25% of admitted patients and 5% on discharge were prescribed drugs between 10-14 in number.

None of the patients discharged was prescribed ≥ 15 drugs while 2 admitted elderly patients were prescribed ≥ 15 drugs. Also, we observed that more than 5 drugs were prescribed for 80% were of admitted & 60% of discharged patients [Table/Fig-4].

	Admission	Discharge
Number of drugs prescribed	761	548
Total number of PIM	48 (6.3%)	27 (4.9%)

[Table/Fig-9]: Proportion of Potential inappropriate medicines (PIM) prescribed in admitted and discharged elderly patients.

PIM on Admission	Number	%
Alprazolam	12	25.00%
Aspirin	7	14.58%
Zolpidem	5	10.42%
Nifedipine	4	8.33%
Chlorpheniramine maleate	4	8.33%
Insulin	4	8.33%
Theophylline	3	6.25%
Spiroglactone	2	4.17%
Others	7	14.58%
Total	48	100.00%

[Table/Fig-10]: Potential inappropriate medicines (PIM) prescribed in admitted elderly patients.

Others: Hyoscine, Ibuprofen, Theophylline, Verapamil, Tramadol, Ibuprofen

PIM on Admission	Number	%
Aspirin	7	25.93%
Alprazolam	7	25.93%
Zolpidem	3	11.11%
Insulin	3	11.11%
Nifedipine	2	7.41%
Others	5	18.52%
Total	27	100.00%

[Table/Fig-11]: Potential inappropriate medicines (PIM) prescribed in discharged elderly patients.

Others: Chlorpheniramine maleate, Glimipride, Ibuprofen, Nifedipine, Verapamil (each one)

We observed a positive correlation between number of days stayed in hospital with an increase in number of drugs. Increased one day stay by an elderly lead to an increase in number of drugs by 0.296 in admitted elderly and 0.095 at discharge. There was statistically significant correlation found in admitted patients [Table/Fig-5].

Prescription pattern in admitted and discharged elderly patients was same. Anti-ulcer drugs were most commonly prescribed drugs in both admitted and discharged elderly patients. Respiratory medicines were prescribed more to discharged patients than admitted while antimicrobial agents were prescribed more to admitted elderly than on discharge [Table/Fig-6].

Out of total 761 medicines prescribed on admission, 401 (52.69%) potential drug-drug interactions were observed. Out of total 548 medicines prescribed on discharge, 290 (52.91%) potential drug-drug interactions were observed [Table/Fig-7].

Most common drug interactions observed in admitted as well as in discharged patients was of moderate grade and was 76.80% (N=308) and 79.31% (230) respectively. Severe drug interactions in admitted patients (6.98%) were more than in discharged patients (3.44%) while mild grade drug interactions were more in discharged (17.21%) elderly patients than admitted (16.2%) elderly patients [Table/Fig-8].

We observed more number of potential inappropriate medicines in admitted (6.3%) than in discharged elderly patients (4.9%) [Table/Fig-9].

Most common Potential inappropriate medicine used was Alprazolam followed by Aspirin, Zolpidem, Nifedipine and Insulin (Sliding scale) on admission [Table/Fig-10], and that on discharge was Aspirin followed by Alprazolam, zolpidem and Insulin (Sliding scale) [Table/Fig-11].

DISCUSSION

In this study majority of patients admitted in department of medicine are between age group 65-75 years. In admitted elderly patients mean number of drugs prescribed was increased as age of patients increased but this was not true for discharged patients in which older elderly patients received less number of drugs. Our study findings are similar to study findings by Baumgartner D. in which there was increase in the mean number of drugs prescribed to admitted elderly (≥ 85 year) but on discharge the mean number of drugs prescribed was less [15]. Our study results are also similar to a study done by Ali A et al., in which less drugs were prescribed to discharged elderly patients [16]. The increase in number of medicines in the admitted elderly patients reveals that these group of patients are diagnosed with new diseases/illness and require prescription of new medication to manage the condition which might be discontinued when they are discharged from the hospital to avoid drug interaction related problems.

More than 80% of the admitted patients and about 60% of the discharged patients were prescribed more than 5 medications. Our study results are similar to the study conducted by Ali A et al., and Schuler Jet al., [16,17]. Both of them observed polypharmacy in more than 55% of admitted elderly. But our study results are contradicting to those of REPOSI's. They found that on 38 internal medicine wards there was a rise (67%) in polypharmacy among discharged elderly patients (52% among admitted patients) [18]. According to Kaufman the use of more than 5 drugs means Polypharmacy [6]. Polypharmacy in our study observed was higher than that reported internationally [3,19]. We also observed proportional relationship between length of stay and number of medications used. This might be because patients do not respond to treatment so more options of drugs are used by the Physician.

There were an extraordinary number of potential drug-drug interactions observed in this study. The drug-drug interactions were found more when more drugs were prescribed to the elderly patients. In our study most common potential drugs interaction were of moderate grade (76.8%). Potentially severe drug interactions are (6.98%) of total potential drug-drug interactions. We found more potential drug-drug interactions when compared to study conducted by Björkman IK et al., in which there were drug interactions in 46% of patients [20]. Also, the study conducted by GosneyM et al., showed potential drug-drug interactions in 33% of all prescriptions in admitted elderly patients [21].

In variety of studies different computerized drug-drug interaction programmes were used to find out drug interactions. Studies assessing actual drug interactions i.e. with an adverse patient outcome from as a result of drug interaction should be separated from those looking at potential drug-drug interactions [22]. Generally the prevalence of clinically relevant drug interactions is about 6% in patients taking two to four medications, 50% in those taking five and almost 100% in those taking 10 medications. So in our study also we observed potential drug-drug interaction in more than 50% of patients as mean drugs prescribed to both admitted and discharged patients were more than five. Several studies testing the performance of drug interaction software found low levels of sensitivity and specificity but more recent studies indicate that sensitivity and specificity have improved [23]. Beers criteria is a frequently used method for evaluating appropriateness of prescribing in elderly. It was developed in 1999 & recently updated by American geriatric society in 2012 [9].

In our study potential inappropriate medicines prescribed were 6.3% of total prescribed drugs in admitted elderly patients and 4.9% of total prescribed drugs in discharged elderly patient. Study conducted in south India by Haruger A et al., observed potential inappropriate medicines in 22.1% patient at the time of admission, which is higher than our study findings [13]. Also, our study findings contradict the study conducted by Rothberg et al., who observed

at least 1 potential appropriate medicines in 49% patients [24]. But our study findings are similar to study conducted by Veena et al., who observed at least 1 potential appropriate medicines in 4.33 % of patients [25]. One reason for this contradicting results could be the limited population, as those studies were on a large population.

The most common potential inappropriate medications used were benzodiazepine and anti-inflammatory group. Insulin also comes under potential inappropriate medicines but if it is prescribed in Sliding scale. Similarly for Zolpidem intervention or close monitoring might be required. Increased number of medications' use may point to the likelihood of exposure to potential inappropriate medicines, it may not necessarily reflect the irrational use of medicines as in few patients it may be appropriate to use more number of medications.

We found the commonest group of drugs prescribed to admitted as well as discharged patients were Antiulcer drugs, Antiasthma medications, Antimicrobial Agents and Antihypertensives. The antiulcer drugs are commonest prescribed drugs because they are taking many medications at a time so there was need of gastric protection.

This study provides data to assess the prevalence of Polypharmacy, potentially dangerous drug-drug interactions and potentially inappropriate medicines among elderly patients. Polypharmacy is unavoidable as elderly patients usually suffer from many chronic diseases which demand use of multiple drugs resulting in complex regimen. Clinicians remember common drug-drug interactions but it is impracticable for clinicians to remember all the drug-drug interactions and their clinical significance. Though clinician may give such prescriptions by weighing benefits verses adverse effects of drug-drug interaction/s. It warrants time to time updates on such medications. To reduce burden of drug-drug interactions due to polypharmacy, educational programmes should be taken but it may require a considerable amount of time and close monitoring. Additionally, pitfalls may be encountered if a provider attempts to make multiple changes to a regimen at a single point in time [26]. Therefore, a more rational approach to drug discontinuation might involve tapering a single drug at a time with careful monitoring for symptoms of withdrawal and disease exacerbation [27]. As a general rule, healthcare providers should minimize the number of medications prescribed for older adults, keep the dosing schedule as simple as possible, and limit the frequent number of medication changes. This must be followed by periodic review at specific intervals.

Today, most of the hospitals are well connected with information technology. Possibility of dangerous drug-drug interactions can be reduced with the help of regularly updated or online Computer-assisted drug-drug interaction checker software. There is need of increase in awareness of potentially inappropriate medication for elderly patients as listed in the Beers criteria. Harmonizing drug policy and regulatory measures with respect to potentially inappropriate medication use should be a major focus e.g., withdraw harmful medications, establish prescribing limits for the elderly, and approve safer alternatives [28]. Raising physician's awareness and steps to sensitize higher authorities regarding Polypharmacy and dangerous drug interactions may help to curb irrational prescriptions and ensure safety of the elderly.

LIMITATIONS

It was conducted on a small population and was restricted to one specialty. Hence for a better understanding, a detailed prospective hospital based studies involving larger elderly population and involving multiple specialty are necessary to make prescriptions more rational in elderly population.

CONCLUSION

The use of medicines in a disease condition is necessary, but unnecessary load of drugs to patient will increase the safety

problems. Polypharmacy can be avoided by sharing treatment goals and plans. To improve drug safety in this high-risk population, appropriate prescribing might be more important than simply reducing the number of prescribed drugs.

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PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Pharmacology, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth, Puducherry, India.
2. Final year MBBS Student, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth, Puducherry, India.
3. Assistant Professor, Department of Community Medicine, Indira Gandhi Medical College and Research Institute, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Kartik Janardan Salwe,
2E, Type II Staff Quarters, Mahatma Gandhi Medical College and Research Institute, Campus, Pillaiyarkuppam, Puducherry, India.
E-mail : kartiksalwe@outlook.com

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