

**POLYPHARMACY AND DRUG-DRUG INTERACTION IN ELDERLY PATIENTS
HAVING PULMONARY DISEASES**Meenu Pandey^{1*} and N. K. Meera¹¹Department of Pharmacy Practice, Visveswarapura Institute of Pharmaceutical Sciences, Bangalore-560070, Karnataka, India.***Corresponding Author: Meenu Pandey**

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ABSTRACT

Polypharmacy indicates use of multiple medications than clinically necessary. It is most common in the elderly due to occurrence of altered pharmacokinetics, pharmacodynamics, physiological changes and also presence of multiple morbidities. Poly-pharmacy in the elderly increases the potential for drug-drug interactions and potentially inappropriate medication. Hence, an optimal drug therapy to improve the quality of life of the elderly patients is one of the major challenges for a healthcare provider. **Method:** A prospective, observational study was conducted in elderly patients of age >65 years for a period of three years in the department of pulmonary medicine of a tertiary care hospital in Bangalore, India. Patient details regarding demographics, all relevant clinical data including past medical history, medication usage, pulmonary function test report were documented in a well-designed and internally validated case report form based on data obtained from medical records of patients, self-reporting by patient or the care giver and laboratory reports. Drug interactions were analyzed using Lexicomp database. **Result:** Among 418 elderly inpatients recruited during the study, the mean age was 70.02±5.55 years. Polypharmacy (>5 medications/day) was found in 411 patients (98.3%). Out of total drug interactions, 90.4% were pharmacodynamics while 62.7% were pharmacokinetic in nature. Severity assessment showed, 18.7% major, 92.3% moderate while 56.7% minor drug interactions. **Conclusion:** Polypharmacy in the elderly is a common practice and a concern with respect to the poor clinical outcome. Medication appropriateness in this vulnerable group is the challenge for healthcare team.

KEYWORDS: Polypharmacy, Drug interaction, Pharmacokinetics, Pharmacodynamics.**INTRODUCTION**

According to World Health Organization for every nine people there is one elderly individual of age >60 years which is expected to be increase to one in five by 2050. In India, elderly people population is expected to reach 324 million by 2050.^[1] WHO defines polypharmacy as “use of more medications than clinically necessary”^[2] However, the term polypharmacy has varied definitions.^[3] “Poly” in Greek means many, pharmacy refers to drugs.^[4] Polypharmacy indicates multiple number of drugs prescribed most often in the ranges of 5 to 10.^[5]

Polypharmacy is most common in the elderly population, due to multiple morbidities and altered pharmacokinetics, pharmacodynamics, physiological changes that occur with the age. As a result, elderly patients are at the greater risk of potential drug interactions, adverse drug reactions and poor compliance which in turn lead to decreased quality of life, physical problems, as well as increase in the length of stay in

hospital and cost of treatment. The choice of appropriate medications for the elderly is based on the medical history, drug resistance, physical & mental health including cognition, family support, etc. The pharmacokinetic changes involving the absorption, distribution, metabolism and elimination of the drugs are important factors in the occurrence of altered drug response by the elderly.^[6] Hence in order to provide good quality of life for the elderly, healthcare providers face several challenges regarding the choice of the appropriate drug, drug dose, dosage form, dosing schedule and equally important the medication adherence by the elderly.^[5]

Poly-pharmacy in the elderly increases the potential for drug-drug interactions and the possibility of “prescribing cascades”. A drug-drug interaction (DDI) is defined as a clinical response to a medication that occurs with the co-administration of another medication or an interaction between two medications while prescribing together. DDI are classified as either pharmacokinetic or pharmacodynamics interactions and based on the

severity, they are classified as major, moderate and minor. Polypharmacy exposes the elderly to potentially inappropriate medications (PIMs).^[7] Very few studies have been reported on polypharmacy and its impact in the elderly, hence this study was carried out to assess for polypharmacy and drug-drug interactions in the elderly patients diagnosed with pulmonary diseases.

MATERIALS AND METHODS

A prospective, observational study was conducted for a period of three year (August 2018 to July 2021) in the department of pulmonary medicine of a tertiary care hospital in Bangalore, India. Elderly inpatients (>65 years) diagnosed with pulmonary diseases were enrolled in the study. The study received the approval from the Institutional Ethics Committee and written informed consent was taken from the enrolled patients. Non-consenting patients and patients who were shifted to respiratory intensive care unit (RICU) were excluded from the study. Patient details regarding demographics, all relevant clinical data including past medical history, medication usage, pulmonary function test report were documented in a well designed and internally validated case report form based on data obtained from medical records of patients, self-reporting by patient or by the care giver and laboratory reports. The enrolled patients' cases were followed up from the day of admission until discharge. Drug interactions were analyzed for mechanism, severity, reliability rating and risk level using Lexicomp database. The severity was categorized into major, moderate and minor, mechanism was classified into pharmacokinetic and pharmacodynamics, reliability rating was defined as fair, good, excellent and

poor, while risk level was categorized into 5 categories: category A no known interaction, category B no action needed, category C monitor therapy, category D therapy modification while category X avoid combination.

Statistical analysis

The documented data was entered in MS Excel version 2019. The socio-demographic parameters, co-morbidities, number of drugs prescribed were analyzed using descriptive statistics and reported in terms of frequency, percentage, and mean \pm standard deviation. The data were analyzed for comparing variables like age, gender, co-morbidities vs polypharmacy. Level of significance was fixed at 5%. Chi square test was applied to analyze the qualitative data.

RESULTS AND DISCUSSION

Table 1 describes the socio-demographic details, gender and age, presence or absence of comorbidities, comparison of age, comparison of gender to polypharmacy, age with polypharmacy, presence of comorbidities to polypharmacy. 70% of the study populations were in the age group of 65-70 years, 185 in 71-75 year age group and 5.5% were aged between 76-80 years and 6% were above 80 years of age. Overall, 42.1% of elderly patients had different comorbidities. Polypharmacy of more than 5 medications per day was seen in 98.3% of the study group amongst them 46.4% received 6-10 medications per day, 42.8% received 11-15 medications per day and 9.1% received more than 15 medications per day. Majority of the patients in the age group of 71-75 years and greater than 80 years were administered with 11-15 medications per day.

Table 1: Demographics and Correlation between polypharmacy with gender, age and comorbidities amongst study population.

Socio-demographic details			
Gender	N(%)		Age (years)- Mean \pm SD
Male	176 (42.1%)		70.01 \pm 5.51
Female	242 (57.9%)		70.04 \pm 5.56
Total	418		70.02 \pm 5.55
	Patient with Comorbidities	Patient without Comorbidities	
Total	176(42.1%)	242(57.9%)	
Gender wise	Patient with Comorbidities	Patient without Comorbidities	P Value
Male	34.09%	65.9%	P = 0.0001
Female	47.93%	52.07%	P = 0.5208
Gender vs Polypharmacy			
	Male N(%)	Female N(%)	P value
6-10 drugs (N/%)	104(59.1)	90(37.2)	P < 0.0001
11-15 drugs (N/%)	62(35.2)	117(48.3)	P = 0.0076
>15 drugs (N/%)	10(5.7)	28(11.6)	P = 0.0388
Age vs Polypharmacy			
	No. of patients (N)		
Age (years)	6-10 drugs N(%)	11-15 drugs N(%)	>15 drugs N(%)

65-70	144(49)	115(39.1)	28/9.5
71-75	24/31.6	42(55.3)	10/13.2
76-80	14(70)	6(30)	-
>80	9(36)	16(64)	-
Comorbidities vs Polypharmacy			
	Patient with Comorbidities	Patient without Comorbidities	P Value
6-10 drugs (N/%)	45(25.6)	149(61.6)	P < 0.0001
11-15 drugs (N/%)	106(60.2)	73(30.2)	P < 0.0001
>15 drugs (N/%)	25(14.2)	13(5.4)	P = 0.0020

Level of significance at 5% ($P < 0.001$)

During the study, overall 2386 drug interactions were identified and they were assessed for mechanism, severity, risk category and reliability rating. Table 2, depicts these findings.

Table 2: Characteristics of identified drug-drug interaction.

	N	%
Mechanism of drug interaction		
Pharmacokinetic	769	32.2
Pharmacodynamic	1617	67.8
Severity of drug interaction		
Major	120	5.03
Moderate	1954	81.9
Minor	312	13.1
Risk category		
B (No action needed)	972	40.8
C (Monitor therapy)	1123	47.1
D (consider therapy modification)	236	9.9
X (Avoid combination)	55	2.3
Reliability rating		
Fair	1836	76.9
Good	398	16.7
Excellent	142	6.0
Poor	10	0.4

DISCUSSION

Among 418 elderly inpatients recruited during the study, the female study population was higher compared to males. Most of the patients were under age group of 65-70 years while very few of them were above 80 years of age. The socio-demographic pattern found in this study is similar to other study reports wherein the female patients dominated.^[8] This is suggestive of the anatomical and hormonal differences as well as the poor attention towards medication adherence as the suspected factors to be greater in females than males.^[9,10]

India has the second highest population of elderly in the world. Polypharmacy, is considered as an emerging public health concern in elderly persons due to altered pharmacokinetic and pharmacodynamic factors and presence of comorbidities.^[2,11] The co-occurrence of various health problems, including chronic diseases (eg, diabetes, hypertension, asthma, heart failure), acute conditions (eg, infections), and symptoms (eg, pain),

which dominate with age. The application of evidence-based prescribing guidelines designed in individuals with single disease to individuals with co-morbidity can result in complex drug regimens, which again shows the need for use of multiple drugs in elderly patients.^[12]

As in present study, the number of female patients present with comorbidities was higher in compared to male patients with comorbidities. Similar results were found in a study, where more than 80% of elderly patients were having comorbidities^[13] while in another study, polypharmacy increased significantly with the presence of comorbidities, and the highest incidence of polypharmacy was, respectively, in patients with heart disease, diabetes, and pulmonary disease.^[6]

Ageing comes with presence of multiple diseases which increase the consumption of drugs prescribed and also increase the risk of polypharmacy in elderly.^[4] In the present study, number of drugs prescribed was more in females due to the presence of comorbidities. Several reasons such as the presence of comorbidities, lifestyle, drug adherences, use of many other non-prescription drugs, altered effect of drugs with ageing, contribute to polypharmacy.^[3]

While assessing the practice of polypharmacy, the study population was prescribed with a minimum of 6 drugs to the maximum of 22 drugs, average of 11.09 ± 3.26 (SD). In a similar study, the mean number of drugs prescribed in all the prescriptions was found to be 7.4 ± 2.6 .^[15] Polypharmacy was found more in the age group of 76-80 years followed by 71-75 years. In another study, polypharmacy was found highest in the age group of 76-80 years and next highest with 65-70 years of age group.^[16] In present study, 40% of elderly patients were prescribed with hyperpolypharmacy, where number of drugs prescribed was more than 10. In another study, approx. 23% of admitted patients were prescribed with hyper-polypharmacy.^[17] Medication regimen inappropriateness and polypharmacy are interchangeable.^[18] Polypharmacy is considered inappropriate if the prescribed medications are not indicated, not effective, or constitute a therapeutic duplication.^[19] Moreover, polypharmacy comes with the risk of "overtreatment," or a situation that arises where the risk of adverse reactions far outweighs the expected clinical outcome. However, prescription of multiple

drugs can be clinically acceptable and is not necessarily inappropriate in several clinical situations.^[12]

Drug interactions are the common problems in geriatrics because of their multiple comorbid conditions and associated polypharmacy. In our study, total of 2386 drug interactions were found, out of which, 67.8% were pharmacodynamics while 32.2 were pharmacokinetic. 81.09% were moderate, 13.1% were minor while 5.03% were major in severity. As per, Lexicomp definition of risk category, 47.1% were under category C, 40.8% were under category B, 9.9% were under category D while 2.3% were under category X. According to reliability rating, 76.9% were fair, 16.7% were good, 6.0% were excellent while 0.4% were poor.

Major drug interaction was between clarithromycin and methylprednisolone under category D, which indicated the need for therapy modification and also clarithromycin and budesonide under category C where clarithromycin may increase the serum concentration of corticosteroids. The same was informed to the physician who accepted the recommendations and the modification of the therapy was done by withdrawing the methylprednisolone and budesonide administered as an inhaler, required patient monitoring. In the X category, combination of acebrophylline & aminophylline and bilastine & clarithromycin, were found. This information on the drug interaction was provided to the physicians and the same was accepted. In case of acebrophylline and aminophylline, acebrophylline may enhance the stimulatory effect of theophylline derivatives so theophylline derivatives should not be co-administered with acebrophylline. So the drug was stopped after informing to the physicians. In case of bilastine & clarithromycin, clarithromycin may increase the serum concentration of bilastine. It again depends on renal function of the patients which should be monitored regularly and on informing the physicians, the renal function was monitored closely. Similar findings were reported by various authors with the analysis of DDIs amongst the elderly population with polypharmacy.^[20,21,22,23]

CONCLUSION

In conclusion, our findings showed prevalence of polypharmacy in the study patients, which can be correlated to factors such as age and comorbidities in turn leading to drug interactions and unwanted therapeutic outcomes. Prescribers should therefore consider the use of a therapeutic regimen for achieving a clinically significant outcome for an optimal quality of life in the elderly patients. The clinical pharmacist can actively involve in monitoring the therapy and contribute towards increasing the awareness of the various risk factors associated with polypharmacy in elderly patients.

AUTHORS CONTRIBUTION

Dr. Meenu Pandey conceptualized, gathered and analyzed the data with regard to this work. Dr. N.K

Meera designed the study and provided the required clinical inputs for the conduct of the study. All the authors equally contributed in preparing the manuscript.

CONFLICT OF INTEREST

Conflict of interest declared none.

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