IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Rising Tide Of Polypharmacy And Drug-Drug Interactions In Geriatric Patients

[1] Mahima Sharma, [2] Dr. Dharmendra Ahuja, [3] Shagufta Naaz, [4] Anshul Saini, [5] Sarila

[1] Mahima Sharma M Pharm (PCO) Student, [2] Prof Dr. Dharmendra Ahuja dean and director of FPS at (JVWU), [3] Shagufta Naaz M Pharm (PCO) Student, [4] Anshul Saini (Associate Prof), [5] Sarila (Asst. Prof)
Faculty of Pharmaceutical Science, Jayoti Vidyapeeth Women's University, Jaipur (Rajasthan)

Abstract

When five or more than five used on regular bases that is defined as polypharmacy, and the interactions/ adverse drug reaction occur by using these multiple medications is defined as drug-drug interactions. This study possess the risk of DDIs are rising because of multimorbidity and age related changes, which can cause organ toxicity, organ failure, and can be a reason for hospitalization. In this study we had found that in India, 25% of the total population are in older age in which 49% have no sign of polypharmacy but other 51% include 26% of men's and 24% of women's which shows high prevalence of polypharmacy. In this study we also go through the strategies to call out the risk associated with polypharmacy and various common drug-drug interaction (DDIs) with clinical implications and geriatric risks.

Keywords: Polypharmacy, Drug-drug interactions, Geriatric patients, Adverse drug reactions, Medications, Over the counter (OTC)

Introduction

The existing studies on polypharmacy tend to concentrate primarily on drug-drug interactions (DDIs), particularly between two or more than five medications. Adverse drug events (ADEs) are frequent, expensive side effects of medical treatment that are increasingly accounting for hospitalizations as well as ER or outpatient visits. Although they can happen at any age, ADEs and major damages are more common in older persons. Multimorbidity, frailty, the incidence of polypharmacy, and age-related alterations in pharmacokinetics and pharmacodynamics are the causes of this susceptibility. (1) The FDA defines a drug-drug interaction as a reaction between two or more medications that results in an unanticipated adverse effect. For instance, consuming meals high in tyramine while taking monoamine oxidase inhibitor antidepressants (MAOIs) might result in an abrupt and potentially fatal hypertensive crisis. The following variables may make medication interactions more likely: Age: Drug interactions may be impacted by the physiologic changes that occur with aging. Polypharmacy: The likelihood of an interaction is increased while taking numerous medications. (2) The World Health Organization (WHO) defines polypharmacy as taking many drugs at the same time. It is frequently described as a patient taking five or more drugs on a regular basis. We call this syndrome inappropriate polypharmacy. (3)

Recent data indicate that Polypharmacy is highly prevalent among Indian geriatric populations, with an overall pooled prevalence of approximately 49%. This means nearly half of older adults in India take multiple medications. Significant regional variations exist, with the Northeast reporting the highest prevalence, around 65%. The complexity and difficulties related to polypharmacy have increased in tandem with the rise in the number of prescription drugs and the incidence of chronic conditions. Despite significant advancements in pharmacogenomics (the study of how genes influence a person's response to medications) and genomic medicine

(tailoring healthcare to each person's unique genetic makeup), these approaches are not commonly integrated into clinical practice. This limited adoption can be attributed to factors such as high costs, limited accessibility, and a lack of awareness, which have hindered the widespread use of pharmacogenomics testing. (4, 5)

How do we define polypharmacy?

Many people consider polypharmacy to be a serious public health concern. It increases the likelihood of negative consequences, which can significantly affect health outcomes and raise medical costs. Setting a rigid numerical threshold to identify polypharmacy may not always be beneficial, even when taking many drugs at once might increase the risk of adverse outcomes. As demonstrated by the secondary prevention of myocardial infarction, which usually entails four different kinds of medications—a beta blocker, a statin, an antiplatelet drug, and an ACE inhibitor—polypharmacy can occasionally be both beneficial and required. According to WHO Polypharmacy is the concurrent use of multiple medications. (1)

For example, a 65-year-old retired school principal from Jaipur was diagnosed with type 2 diabetes three years prior and initially received a prescription for metformin. When his blood glucose levels remained uncontrolled, a sulfonylurea was added to his treatment. He then developed swelling and breathlessness, leading to a diagnosis of heart failure, prompting the start of therapy with a beta-blocker, ACE inhibitor, and diuretic. Rising levels of creatinine indicated chronic kidney disease, and he was later diagnosed with hypertension, which required the addition of a calcium channel blocker. By the time he turned 67, he was taking six different medications and coping with side effects such as dizziness and hypoglycemia due to the complicated dosing schedule. Following a review of his medications, his doctor substituted the sulfonylurea with a safer DPP-4 inhibitor, adjusted his diuretic dosage, and streamlined his treatment with combination pills. His journey shows how diabetes can cascade into multiple chronic conditions, necessitating careful management of polypharmacy to ensure safety and adherence.

Condition	Medications	Total Medications	Issues Faced	Adjusted Treatment
Type 2 Diabetes	Metformin	1	Uncontrolled blood sugar, mild hypoglycemia	Replaced sulfonylurea with DPP-4 inhibitor
Heart Failure	Beta-blocker, ACE inhibitor, Diuretic	3	Swelling, breathlessness, dizziness from diuretic	Adjusted diuretic dose, continued heart failure treatment
Chronic Kidney Disease	Diuretic (adjusted dose)	1	Swelling, kidney function monitoring	Optimized diuretic dose for kidney protection
Hypertension	Calcium channel blocker	1	Dizziness, low blood pressure	Adjusted blood pressure medications
Total	Metformin, Sulfonylurea, Beta-blocker, ACE inhibitor, Diuretic, Calcium Channel Blocker	6	Polypharmacy issues, side effects like dizziness and hypoglycemia	Simplified regimen with combination pills and DPP-4 inhibitor

Table 1. This chart summarizes the progression of old man's health conditions and medications, highlighting the journey to polypharmacy and the necessary adjustments made to simplify his treatment.

Furthermore, there are disagreements on how long therapy should last and whether OTC drugs, as well as complementary and alternative therapies, belong in the criteria. However, it is essential to carefully check all drugs the patient is taking, including over-the-counter (OTC) items, as well as conventional and alternative

treatments, in order to reduce medication-related damage. There are two types of polypharmacy: suitable polypharmacy and improper polypharmacy.

Appropriate polypharmacy happens when: (10)

1. Every prescription drug is used to achieve certain therapeutic objectives that have been discussed and agreed upon with the patient.
2. These treatment goals are either being fulfilled or have a good chance of being accomplished.
3. To lower the risk of adverse drug reactions (ADRs), the prescription schedule is improved.
4. The patient has the drive and ability to follow the recommended course of action.

On the other hand, inappropriate polypharmacy occurs when one or more drugs are given needlessly, for example:

1. When the reason for usage has passed, the dosage is higher than necessary, or there is no evidence-based justification.
2. When drugs are unable to produce the desired therapeutic effects.
3. When drugs, either alone or in combination, cause adverse drug reactions (ADRs) or put the patient at high risk for them.
4. When a patient cannot or will not take one or more prescription drugs as directed.(10)

The key differences in both appropriate and inappropriate polypharmacy are Appropriate polypharmacy is well-managed, with each medication providing a clear therapeutic benefit, and the patient is monitored to prevent harm whereas Inappropriate polypharmacy is often a result of prescribing errors, lack of proper oversight, or failure to regularly assess the patient's medication needs, leading to potentially harmful consequences. Regular medication reviews, involving both the patient and healthcare providers, are crucial for ensuring that polypharmacy remains appropriate. Polypharmacy can be stringently defined by evaluating each prescribed medication against ten criteria outlined in the Medication Appropriateness Index :(11)

1. Is there a legitimate indication for the medication?
2. Is the intended condition properly treated by the medication?
3. Is the recommended dose appropriate?
4. Are the usage instructions accurate and clear?
5. Can the patient actually follow the instructions?
6. Are there any noteworthy interactions between drugs?
7. Are there any notable interactions between drugs and conditions or diseases?
8. Does one drug needlessly overlap with another?
9. Does the length of therapy fit the condition?
10. Among medications with comparable benefits, is this the most affordable choice? (11)

If any question is answered negatively, the medication is considered inappropriate, indicating polypharmacy. For research purposes, the first three questions—focusing on indication, effectiveness, and dosage—are prioritized to guide clinicians in evaluating these key aspects. Polypharmacy is categorized into minor, major, and excessive forms based on the number of concurrent medications. Minor polypharmacy, involving two to four medications; Major Polypharmacy, involving five or more medications; and Excessive or Extreme polypharmacy, defined as the concurrent use of ten or more medications. Extreme polypharmacy is often linked to socio-demographic factors and specific conditions such as cancer. Inappropriate polypharmacy, also known as high-risk polypharmacy, refers to situations where the prescribed classes of medications pose unnecessary risks to the patient's health due to misuse or lack of appropriateness. The causes of polypharmacy are diverse and include factors such as patient use of multiple healthcare providers, adherence to complex disease guidelines, prescribing cascades, and direct-to-consumer medication advertising. When patients see multiple providers, poor communication can lead to duplicate or unnecessary prescriptions. Prescribing cascades occur when side effects of medications are mistaken for new conditions, prompting additional prescriptions. Patients' use of over-the-counter drugs and supplements without informing providers further increases risks of drug interactions. Similarly, utilizing different pharmacies limits oversight of potential drug-drug interactions. (11)

Polypharmacy Prevalence

The prevalence of polypharmacy has been reported to range between 5% and 78%, with the rate increasing significantly due to an aging population, having quintupled between 2000 and 2010. Elderly individuals are particularly vulnerable to polypharmacy, as they typically take more medications than younger populations due to the presence of multiple comorbidities. Furthermore, aging is associated with physiological changes that increase the risk of side effects, including diminished organ function and heightened susceptibility to stress. In India, elderly people aged 65 and above make up about 7% of the total population. According to the 2011 Indian Census, there were nearly 104 million elderly individuals, with a slight gender imbalance, as 51 million were men and 53 million were women. The prevalence of polypharmacy in india among this age group was found to be 25%, with men (26.1%) slightly more likely to experience polypharmacy compared to women (24.2%). (10)

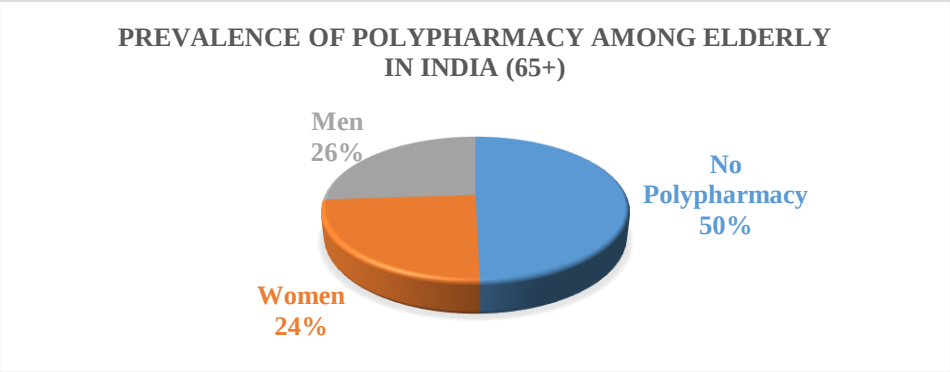

Figure no.: 1 Data indicating the prevalence of polypharmacy among individuals over 65 years of age in India reveals that 26.1% of men and 24.2% of women experience polypharmacy, while 49.7% of the elderly population do not have polypharmacy.

In a study examining polypharmacy in elderly patients, the majority had multiple comorbidities, with 81.8% of the participants reporting between two to five diseases. Specifically, 36.9% had two conditions, while only 4.4% of participants had five or more chronic diseases. The most commonly prescribed number of medications was seven (17.9%), and the overall average was 7.4 medications per patient. This data highlights the significant burden of both multiple chronic diseases and medications among the elderly. (10)

Risk from polypharmacy

Due to the lengthy drug lists of patients with one or more chronic illnesses, polypharmacy is particularly noticeable in older persons. Polypharmacy is especially dangerous for older persons who have no main care physician and several subspecialist doctors. In addition to being more vulnerable than those living in the community, those in long-term care institutions are also at danger due to their numerous medical conditions, cognitive impairment, and other conditions that frequently call for medication. In long-term care, up to 91% of patients use five or more drugs a day. (12)

Multiple therapies and modalities may result in polypharmacy in younger individuals with developmental impairments or persistent pain, such as fibromyalgia, particularly if they also have other chronic medical illnesses. In younger individuals, polypharmacy is also linked to diabetes, heart disease, stroke, and cancer.

Patients with mental health disorders are a demographic that is frequently disregarded when discussing polypharmacy. Psychotropic drugs with negative side effects are frequently provided to these individuals, and other drugs may be added to reduce side effect profiles. In order to attain optimal functioning and avoid illness sequelae, individuals with long-term mental health and medical conditions may need to take many drugs; yet, this reasonable polypharmacy might nonetheless raise the risk of adverse drug events. (12, 13)

High risk group categories

Compared to younger persons, elderly women and men are affected by polypharmacy in distinct ways. For example, older adults react differently to some medications. A person over 55 may take drugs differently from someone 30 years of age because of differences in their body composition. Additionally, older folks may not be included as test subjects for new medications before they are put on the market, so manufacturers may not always be able to easily identify these changes.

Adults with coexisting chronic diseases, especially those aged 55 and beyond, may take many medications, including:

- Elevated blood pressure
- Diabetes
- Cholesterol
- Having asthma
- Sleeplessness
- The condition of arthritis
- Elevated
- COPD
- Coronary heart disease
- Depression

Nonprescription medications and goods also play a role. Certain nutritional supplements and herbal treatments are heavily promoted to senior citizens with inflated promises and scant scientific support. They may have adverse effects and interfere with prescribed medications. Gingko biloba supplements, for example, may intensify the effects of prescription blood thinners, increasing the risk of bleeding in patients. (14, 15)

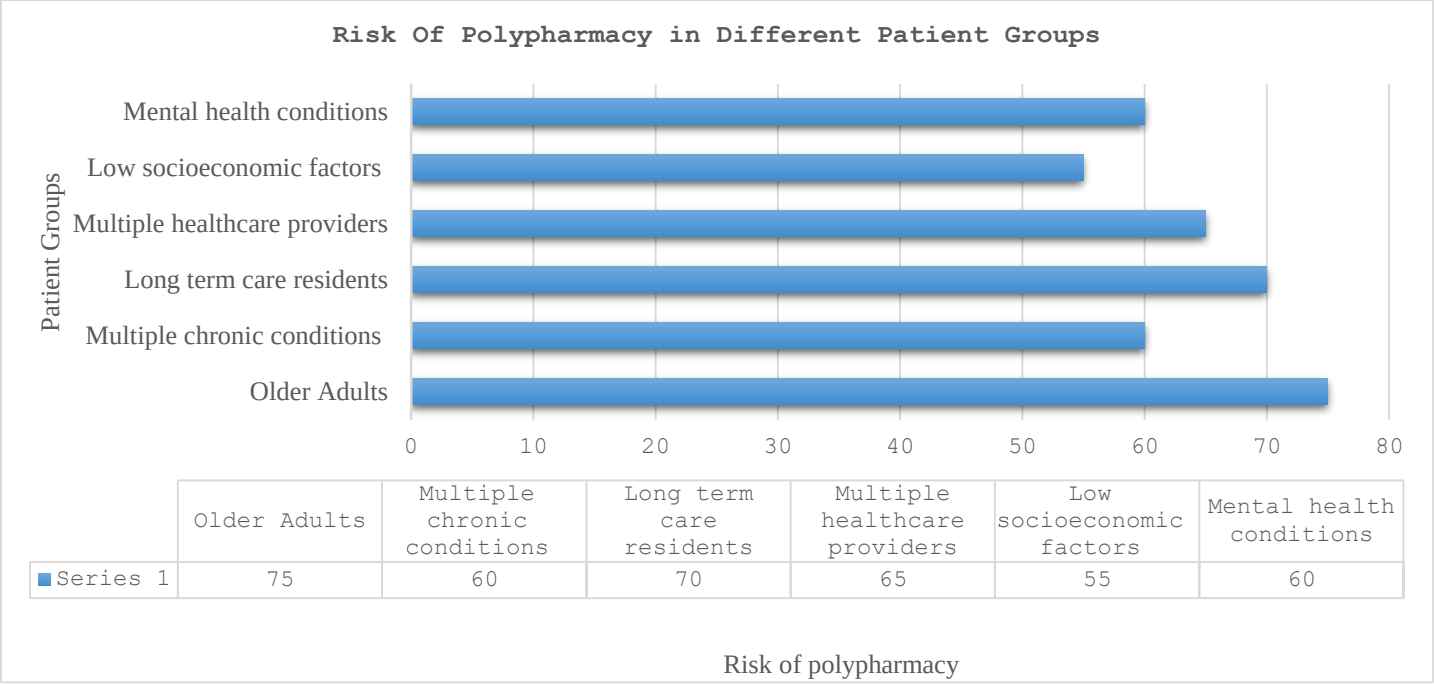

Figure No. 2 Visual representation of how these patient groups are disproportionately affected by polypharmacy risks.

Polypharmacy Signs and Symptoms

Polypharmacy symptoms might include:

- Diminished attentiveness
- Perplexity or cognitive issues
- Accidents and falls
- Dizziness and weakness
- Appetite loss
- Gastrointestinal issues such incontinence, constipation, or diarrhea
- Rashes on the skin
- Depression
- Fear
- The ability to be excited. (16)

Medicines optimization's four guiding principles

Healthcare practitioners must completely embrace the idea of medicine optimization in order to help patients and the general public get the most out of their prescriptions. This approach is underpinned by four core principles, which guide its practical application and define the intended outcomes. All members of the healthcare team participating in a patient's care should embrace these concepts cooperatively, but pharmacists are essential in spearheading and assisting efforts to optimize medications. Beyond guiding frontline healthcare professionals, these principles serve as a framework for designing care pathways and services. Importantly, the four principles align with established national standards and best practices, reinforcing their role. The aim of medicines optimization is to: (16)

- Improve patient results
- Guarantee proper medication usage
- Avoid the use of unnecessary medications
- Reduce medication waste
- Enhance medication safety
- Focusing on promoting the safe and effective use of medicines (17)

That is accomplished by:

- Offering current information and guidance on medicines and treatments.
- Promoting the safe, evidence-based, and cost-effective use of medications.
- Creating local guidelines and care pathways to enhance medication use and condition management.
- Collaborating with hospitals, GP practices, community pharmacies, and healthcare partners to support Medicines Optimization. (17)

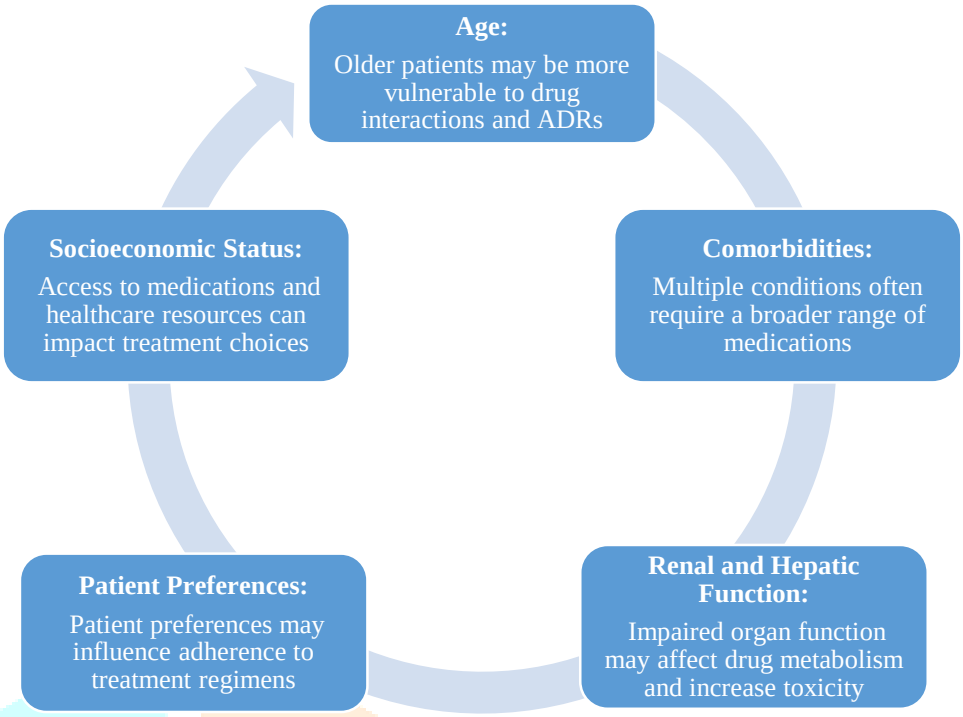

Figure No. 3. The key factors that influence the management of polypharmacy in patients with multimorbidity. Overview of how polypharmacy impacts patients with multimorbidity and outline the strategies to manage it effectively.

Risk Prediction tool

The Beers Criteria, the Drug Interaction Probability Scale (DIPS), the STOPP (Screening Tool of Older Persons' Prescriptions) criteria, and the PRISCUS list of potentially inappropriate medications (PIMs) are the four main tools for this purpose, according to a 2014 systematic review that evaluated the quality of validated risk-prediction tools for adverse drug reactions (ADRs) in people 65 and older. Notwithstanding their potential, these technologies' ability to recognize ADRs is still limited and performs poorly. These tools' relevance to primary care or ambulatory settings, where the majority of long-term care prescriptions occur, has not been fully validated due to the fact that they were mostly created using data from hospital inpatients. There is an urgent need for more efficient risk-prediction models designed for out-of-hospital settings due to the rising incidence of polypharmacy in older populations, especially in primary care. (6)

Drug-Drug Interactions (DDIs)

When one medication alters the toxicity, efficacy, or activity of other drug, this is known as a drug-drug interaction (DDI), and it frequently results in different treatment outcomes. Pharmacokinetic or pharmacodynamics interactions may be involved. Pharmacokinetic DDIs alter a drug's plasma concentration and effectiveness by affecting its absorption, distribution, metabolism, or excretion. Antacids and proton pump inhibitors, for example, change the pH of the stomach, which affects the solubility and bioavailability of antibiotics and antifungals. In a similar vein, the cytochrome P450 (CYP450) enzyme system is essential for interactions pertaining to metabolism. While inhibitors like ketoconazole raise medication levels and may cause toxicity, enzyme inducers like rifampin improve drug metabolism and lower plasma levels. Alterations in renal clearance, often mediated by transporter proteins like P-glycoprotein, also influence drug excretion, affecting medications such as digoxin. (8, 9)

Pharmacodynamics DDIs, on the other hand, involve drugs with similar or opposing effects acting on the same physiological pathway. For example, combining anticoagulants such as warfarin with antiplatelet agents like aspirin significantly raises the risk of bleeding, while the concurrent use of beta-blockers and calcium channel blockers can result in excessive bradycardia or hypotension.

Certain populations are at heightened risk for DDIs. Polypharmacy, particularly common among older adults, is a primary risk factor, with up to 50% of seniors at risk for at least one significant DDI. (9)

Drug Combination	PDDI Percentage	Severity	Interaction Mechanism	Clinical Implications & Geriatric Risk
Torsemide + Gentamycin	3% (0.96%)	Moderate	Pharmaco-dynamics (PD), Synergism	Both drugs can contribute to nephrotoxicity, a significant concern in older adults with compromised renal function. Monitor renal function and adjust doses accordingly.
Calcium Gluconate + Gentamycin	4% (1.29%)	Moderate	PD, Synergism	In elderly patients, calcium gluconate and gentamycin may potentiate each other's effects, increasing the risk of renal toxicity and neuromuscular blockade. Monitor renal function closely.
Budesonide + Spironolactone	4% (1.29%)	Moderate	(PK & PD)	Budesonide may decrease spironolactone levels, leading to reduced therapeutic effects. Monitor for fluid retention or electrolyte imbalances.
Diltiazem + Budesonide	4% (1.29%)	Moderate	PD	Diltiazem may increase budesonide levels, increasing the risk of corticosteroid side effects, such as osteoporosis and hyperglycemia, in elderly patients.
Hydrocortisone + Ranolazine	4% (1.29%)	Moderate	PK	Hydrocortisone may reduce ranolazine levels, compromising its effect in elderly patients with cardiovascular disease. Monitor for treatment failure.
Diltiazem + Ivabradine	4% (1.29%)	Moderate	PD, Synergism	Diltiazem can increase ivabradine levels, raising the risk of bradycardia and syncope in elderly patients with slower heart rates.
Ranolazine + Metformin	4% (1.29%)	Moderate	PD, Antagonism	Ranolazine can increase metformin levels, increasing the risk of lactic acidosis, which is particularly dangerous in elderly patients with renal dysfunction
Haloperidol + Ivabradine	4% (1.29%)	Moderate	PK	Haloperidol may increase ivabradine levels, potentially leading to bradycardia. Elderly patients are more prone to cardiac arrhythmias.
Quetiapine + Levodopa	5% (1.61%)	Moderate	PD, Antagonism	Levodopa may antagonize quetiapine's effects, reducing its efficacy. Elderly patients may experience worsened psychiatric symptoms due to inadequate treatment.
Haloperidol + Pramipexole	4% (1.29%)	Moderate	PD, Antagonism	In elderly patients, who are more prone to cognitive and movement-related problems, this combination may decrease the effectiveness of both medications.
Escitalopram + Quetiapine	4% (1.29%)	Moderate	PK	Escitalopram may increase the QTc interval, potentiating the risk of arrhythmias when used with quetiapine in elderly patients. ECG monitoring is recommended.
Spironolactone + Potassium Chloride	4% (1.29%)	Mild	PD	This combination raises the risk of hyperkalemia, which is more prevalent in older adults with kidney impairment. Frequent monitoring of potassium levels is recommended.
Ramipril + Pregabalin	4% (1.29%)	Moderate	PD, Synergism	This combination can cause excessive hypotension in elderly patients, particularly those with renal impairment. Monitor blood pressure and kidney function regularly.
Clonidine + Metoprolol	5% (1.61%)	Moderate	PD, Synergism	Both medications can cause profound hypotension, especially in the elderly, who may be more sensitive

				to blood pressure fluctuations. Close monitoring of blood pressure is essential.
Dexamethasone + Disulfiram	5% (1.61%)	Moderate	PK	Disulfiram may intensify the toxic effects of dexamethasone due to altered hepatic metabolism. Elderly patients with reduced liver function are at higher risk for corticosteroid toxicity.
Clopidogrel + Aspirin + Pantoprazole	5% (1.61%)	Moderate	PD	Pantoprazole reduces the efficacy of clopidogrel in preventing thrombotic events, which can be more detrimental in elderly patients at high cardiovascular risk. Monitoring of platelet aggregation is recommended.
Pantoprazole + Digoxin	6% (1.93%)	Moderate	PK	Pantoprazole may enhance the absorption of digoxin, raising the risk of digoxin toxicity. This is especially critical in older adults, who are more vulnerable to the drug's side effects, such as arrhythmias.
Tramadol + Desloratadine	6% (1.93%)	Moderate	PK	This combination may enhance CNS depression and sedation. Elderly patients are more susceptible to respiratory depression and sedation. Monitor for signs of excessive drowsiness or respiratory issues.
Tramadol + Gabapentin	6% (1.93%)	Moderate	PD	Tramadol and gabapentin enhance CNS depression, increasing the risk of falls, dizziness, and sedation in elderly patients. Careful dose adjustment and monitoring of CNS side effects are required.
Ceftriaxone + Enoxaparin	7% (2.25%)	Severe	PD, Antagonism	Ceftriaxone enhances enoxaparin's anticoagulant effects, heightening the risk of bleeding, which is more critical in geriatric patients who may already be at risk for bleeding disorders. Monitor coagulation parameters.
Quetiapine + Pramipexole	9% (2.90%)	Severe	PD, Synergism	Combined use enhances sedation, increasing fall risk in elderly patients. This combination should be used with caution, especially in those with a history of falls or fractures.
Ceftriaxone + Calcium Acetate	9% (2.90%)	Severe	PD, Antagonism	Calcium salts may increase ceftriaxone toxicity, especially in older patients with impaired renal function. Risk of calcium-phosphate precipitation, leading to renal failure.
Sodium Bicarbonate + Levofloxacin	11% (3.54%)	Severe	PD, Antagonism	This interaction may decrease the absorption of levofloxacin, resulting in reduced treatment effectiveness, especially in older adults who often experience slower digestion and absorption. Monitoring the effectiveness of the treatment is recommended.
Dexamethasone + Ivabradine	11% (3.54%)	Severe	PD, Antagonism	Dexamethasone reduces ivabradine’s effectiveness by altering hepatic metabolism. In elderly patients, decreased hepatic function could exacerbate this effect. Monitor for signs of inadequate heart rate control.
Azithromycin + Heparin	12% (3.87%)	Severe	PD, Synergism	Azithromycin can increase heparin’s anticoagulant effects, which increases the risk of bleeding in elderly individuals with comorbidities such as cardiovascular disease. Regular coagulation testing is advised.

Fludrocortisone + Tolvaptan	14% (5.41%)	Severe	PK	Fludrocortisone may reduce the effectiveness of tolvaptan in older patients by affecting p-glycoprotein function. Monitor fluid and electrolyte balance closely, particularly in those with heart or kidney disease.
Levofloxacin + Ondansetron	16% (5.16%)	Severe	PK & PD	This combination may prolong the QTc interval, increasing the risk of arrhythmias in elderly patients, who are more susceptible to cardiovascular issues. Continuous cardiac monitoring is advised.
Sodium Bicarbonate + Levofloxacin	17% (5.48%)	Severe	PD	Sodium bicarbonate can reduce levofloxacin absorption, potentially leading to sub therapeutic levels. This interaction is more pronounced in older adults with altered gastric pH and slower gastric emptying. Monitor for therapeutic failure.
Nifedipine + Amlodipine	25% (8.06%)	Severe	PD	Both drugs are calcium channel blockers and may enhance hypotension, especially in elderly patients with compromised vascular tone. Careful monitoring for signs of dizziness, lightheadedness, or orthostatic hypotension is recommended.

Table No. 2 Common drug- drug interactions.

Conclusion

In this study, the polypharmacy and various drug interactions (DDTs) faces challenges overseeing in elderly, especially one's with the multimorbidity. High prevalence of polypharmacy and potential DDIs found among geriatric patients, which might be life-threatening to some and for some various different problems may occur. Polypharmacy possess different risks such as ADRs, DDIs, prescribing cascade, and cognitive impairment and so on. Furthermore, Geriatric are among the high risk group categories due to age related changes in them i.e. pharmacodynamics, pharmacokinetics, physiological changes and psychological changes. Ultimately, improving the management of polypharmacy and DDIs will enhance therapeutic outcomes, reduce medication-related harm, and improve the quality of life for geriatric patients.

References

1. Bourgeois, F. T., Shannon, M. W., Valim, C., & Mandl, K. D. (2010). Adverse drug events in the outpatient setting: an 11-year national analysis. Pharmacoepidemiology and drug safety, 19(9), 901–910. https://doi.org/10.1002/pds.1984
2. U.S. Food and drug administration (2024). Drug interactions what you should know. Retrieved from https://www.fda.gov/drugs/resources-drugs/drug-interactions-what-you-shouldknow#:~:text=Drug%2Ddrug%20interactions%20occur%20when,you%20take%20a%20nasal%20decongestant
3. Molokhia, M., Majeed, A. Current and future perspectives on the management of polypharmacy. BMC Fam Pract 18, 70 (2017). https://doi.org/10.1186/s12875-017-0642-0
4. Bhagavathula, A. S., Vidyasagar, K., Chhabra, M., Rashid, M., Sharma, R., Bandari, D. K., & Fialova, D. (2021). Prevalence of Polypharmacy, Hyperpolypharmacy and Potentially Inappropriate Medication Use in Older Adults in India: A Systematic Review and Meta-Analysis. Frontiers in pharmacology, 12, 685518. https://doi.org/10.3389/fphar.2021.685518
5. Umaima Farheen Khaiser, Rokeya Sultana, Ranajit Das et al. Exploring Polypharmacy and Drug Interactions in Geriatric Patients: A Cross-Sectional Study from India, 16 July 2024, PREPRINT (Version 1) available at Research Square https://doi.org/10.21203/rs.3.rs-4488300/v1
6. Veehof, L. J., Stewart, R. E., Meyboom-de Jong, B., & Haaijer-Ruskamp, F. M. (1999). Adverse drug reactions and polypharmacy in the elderly in general practice. European journal of clinical pharmacology, 55(7), 533–536. https://doi.org/10.1007/s002280050669

7. Joshi, H., Majumdar, F. D., Patel, S. N., Modi, K. B., Rathod, J., Kanani, P., Shah, K. B., & Malhotra, S. D. (2023). Prescription Analysis and Evaluation of Potential Drug–Drug Interactions among Patients Attending the Geriatric Unit at a Tertiary Care Hospital. Journal of the Indian Academy of Geriatrics, 19(4), 225-231. Retrieved from https://journals.innovareacademics.in/index.php/ajpcr/article/download/37623/22823
8. Cahir, C., Moriarty, F., Teljeur, C., et al. (2014). Adverse drug reactions and polypharmacy in older adults: a systematic review. British Journal of Clinical Pharmacology, 77(4), 710-717.
9. World Health Organization. (2022). Medication safety in polypharmacy. WHO Global Patient Safety Challenge. Retrieved from https://www.who.int
10. University of Arkansas for Medical Sciences (UAMS) College of Pharmacy. Polypharmacy: Definition, Causes, and Solutions. Retrieved from https://agec.uams.edu/polypharmacy/
11. Maher, R. L., Hanlon, J., & Hajjar, E. R. (2014). Clinical consequences of polypharmacy in elderly. Expert opinion on drug safety, 13(1), 57–65. https://doi.org/10.1517/14740338.2013.827660
12. Payne, R. A., & Avery, A. J. (2011). Polypharmacy: one of the greatest prescribing challenges in general practice. The British journal of general practice: the journal of the Royal College of General Practitioners, 61(583), 83–84. https://doi.org/10.3399/bjgp11X556146
13. Vennu V. Polypharmacy Is Associated with Sociodemographic Factors and Socioeconomic Status in United States Adults. Pharmacy. 2024; 12(2):49. https://doi.org/10.3390/pharmacy12020049
14. sang JY, Sperrin M, Blakeman T, et alDefining, identifying and addressing problematic polypharmacy within multimorbidity in primary care: a scoping reviewBMJ Open 2024;14:e081698. doi: 10.1136/bmjopen-2023-081698
15. Johns Hopkins "Polypharmacy in Adults 60 and Older." Retrieved from https://www.hopkinsmedicine.org/health/wellness-and-prevention/polypharmacy-in-adults-60-and-older
16. NSH England. Medicine Optimization. Retrieved from https://www.england.nhs.uk/medicines-2/medicines-optimisation/