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Polypharmacy and Adverse Drug Reactions in Older Adults: A Hospital-Based Cross-Sectional Study.

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Abstract

Background: Polypharmacy—commonly defined as the concurrent use of five or more medications—is increasingly prevalent among older adults owing to multimorbidity and age-related physiological changes, and it is a major, potentially preventable driver of adverse drug reactions (ADRs). Objective: To determine the prevalence of polypharmacy, estimate the frequency and pattern of ADRs, and examine the association between polypharmacy and ADRs among hospitalised older adults. ***Methods:*** A hospital-based cross-sectional study was conducted among 400 patients aged ≥65 years admitted to the general medicine wards of a tertiary-care hospital. Medication histories and clinical data were collected using a structured proforma. Polypharmacy was defined as ≥5 medications and hyper-polypharmacy as ≥10. Suspected ADRs were identified and causality was assessed using the Naranjo algorithm. Data were analysed using descriptive statistics, the chi-square test, and multivariable logistic regression, with $p<0.05$ considered significant. ***Results:*** The mean age of participants was 71.8 ± 6.4 years; 54.5% were male. Polypharmacy was present in 62.5% and hyper-polypharmacy in 21.0% of patients. At least one ADR was documented in 27.5% of participants. Cardiovascular agents, antidiabetics, and NSAIDs were the most frequently implicated drug classes. After adjustment, polypharmacy (adjusted OR 3.42, 95% CI 1.98–5.91) and the presence of ≥3 comorbidities (aOR 2.11, 95% CI 1.24–3.59) were independently associated with ADRs. ***Conclusion:*** Polypharmacy is highly prevalent among hospitalised older adults and is strongly and independently associated with ADRs. Structured medication review, application of explicit prescribing criteria, and deprescribing initiatives are warranted to reduce medication-related harm in this vulnerable population.

Keywords: polypharmacy; adverse drug reactions; older adults; potentially inappropriate medications; deprescribing; medication safety.

INTRODUCTION

Global population ageing has produced an unprecedented rise in the number of older adults living with multiple chronic conditions. Multimorbidity frequently necessitates the concurrent prescription of several medicines, a phenomenon termed polypharmacy. Although numerous definitions exist, a systematic review by Masnoon et al. found that the most commonly applied and pragmatic threshold is the concurrent use of five or more medications, with "hyper-polypharmacy" often defined as ten or more [1]. The absence of a universally accepted definition has historically complicated comparison across studies, but the numerical five-medication cut-off remains the operational standard in clinical research [1].

Polypharmacy is not inherently harmful; in many older patients, several medications are clinically appropriate and evidence-based. However, as the number of medicines increases, so does the risk of harm. Older adults are particularly susceptible because ageing alters pharmacokinetics (reduced renal and hepatic clearance, altered volume of distribution) and pharmacodynamics (heightened sensitivity to central-nervous-system and cardiovascular agents) [2]. These changes narrow the therapeutic window and predispose to adverse drug reactions (ADRs)—responses to a medicine that are noxious and unintended and occur at doses normally used in humans.

The clinical consequences of polypharmacy are well documented. A narrative review by Wastesson et al. linked polypharmacy to increased risks of ADRs, drug–drug interactions, falls, cognitive impairment, hospitalisation, and mortality [2]. A systematic review of reviews by Davies et al. similarly reported consistent associations between polypharmacy and adverse clinical, safety, and economic outcomes in older people [3]. ADRs are a frequent and often preventable cause of hospital admission in this age group; Parameswaran Nair et al. highlighted that ADR-related hospitalisation in older patients is common and warrants predictive and preventive strategies [4].

A closely related concept is potentially inappropriate medication (PIM) use—prescribing in which the risk of harm outweighs the expected benefit. Explicit screening tools have been developed to identify PIMs, most notably the American Geriatrics Society (AGS) Beers Criteria, updated in 2023 [5], and the STOPP/START criteria, now in their third version [6]. In low- and middle-income settings, the burden appears substantial: a meta-analysis by Bhagavathula et al. reported a high pooled prevalence of polypharmacy, hyper-polypharmacy, and PIM use among older adults in India [7].

Despite this evidence, real-world data quantifying polypharmacy and its relationship to ADRs in hospitalised older adults remain limited in many settings, and locally generated data are essential to inform stewardship and deprescribing programmes. Accordingly, the present study was undertaken to determine the prevalence of polypharmacy, characterise the frequency and pattern of ADRs, and evaluate the association between polypharmacy and ADRs among older adults admitted to a tertiary-care hospital [1–4].

MATERIALS AND METHODS

This was a hospital-based, observational, cross-sectional study conducted in the Department of General Medicine of a tertiary-care teaching hospital over a period of twelve months. The department was selected because it admits a high volume of older adults with multimorbidity, providing a representative sample for the study objectives.

Study population. Patients aged 65 years and older admitted to the general medicine wards during the study period were eligible. Inclusion criteria were: age ≥65 years, admission for at least 24 hours, and willingness to provide informed consent (from the patient or an authorised attendant). Patients with incomplete medication records, those admitted for elective procedures only, and those unwilling to participate were excluded.

Sample size. Assuming an expected polypharmacy prevalence of approximately 50%, a 95% confidence level, and an absolute precision of 5%, the minimum required sample was 384; this was rounded to 400 participants to account for incomplete data.

Sampling. Consecutive eligible patients were enrolled until the target sample size was reached.

Data collection. After obtaining informed consent, data were collected using a pre-tested, structured proforma. Variables recorded included sociodemographic details (age, sex, residence, education), lifestyle factors, number and nature of comorbidities, complete medication history (prescription and over-the-counter medicines, including herbal preparations), duration of therapy, and relevant laboratory parameters (notably renal and hepatic function). Medication data were verified against prescription charts and pharmacy records.

Operational definitions. Polypharmacy was defined as the concurrent use of five or more medications and hyper-polypharmacy as ten or more, consistent with the most widely applied definitions in the literature [1]. An adverse drug reaction was defined per the World Health Organization as a response to a medicine that is noxious and unintended, occurring at doses normally used for prophylaxis, diagnosis, or therapy. Potentially inappropriate medications were identified with reference to the 2023 AGS Beers Criteria [5] and the STOPP/START criteria version 3 [6].

ADR assessment. Suspected ADRs were identified through patient interview, clinical examination, laboratory findings, and review of case records. The causal relationship between the suspected drug and the reaction was assessed using the Naranjo Adverse Drug Reaction Probability Scale, categorising ADRs as definite, probable, possible, or doubtful. Severity was graded using the modified Hartwig and Siegel scale, and preventability was assessed using the modified Schumock and Thornton criteria.

Statistical analysis. Data were entered into a spreadsheet and analysed using standard statistical software. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. The association between polypharmacy and ADR occurrence was tested using the chi-square test. Variables significant on univariate analysis ($p<0.10$) were entered into a multivariable binary logistic regression model to identify independent predictors of ADRs, with results expressed as adjusted odds ratios (aOR) and 95% confidence intervals (CI). A two-sided p-value <0.05 was considered statistically significant. Was obtained from all participants or their authorised attendants, and confidentiality was maintained throughout.

RESULTS

A total of 400 older adults were enrolled. The sociodemographic and clinical characteristics of the study population are summarised in **Table 1**.

Table 1. Sociodemographic and clinical characteristics of study participants (N = 400)

Variable	Category	n (%)
Age group (years)	65–74	258 (64.5)
	75–84	116 (29.0)
	≥85	26 (6.5)
Sex	Male	218 (54.5)
	Female	182 (45.5)
Residence	Urban	236 (59.0)
	Rural	164 (41.0)
Number of comorbidities	1–2	174 (43.5)
	≥3	226 (56.5)
Mean age (years), mean ± SD		71.8 ± 6.4

The cohort was predominantly in the "younger-old" 65–74 age band (64.5%), with a slight male preponderance (54.5%). Notably, more than half of participants (56.5%) had three or more comorbidities, underscoring the high multimorbidity burden that typically drives polypharmacy in this population.

Table 2. Distribution of medication use and prevalence of polypharmacy (N = 400)

Medication category	Definition	n (%)
No polypharmacy	1–4 medications	150 (37.5)
Polypharmacy	≥5 medications	250 (62.5)
— of which hyper-polypharmacy	≥10 medications	84 (21.0)
Mean number of medications per patient, mean ± SD		6.3 ± 2.7

Polypharmacy (≥5 medications) was present in 62.5% of participants and hyper-polypharmacy (≥10) in 21.0%, with a mean of 6.3 medications per patient. These figures indicate that multiple-medication use is the norm rather than the exception among hospitalised older adults.

Table 3. Frequency, causality, severity, and preventability of adverse drug reactions

Parameter	Category	n (%)
ADR occurrence	At least one ADR	110 (27.5)
	No ADR	290 (72.5)
Causality (Naranjo)*	Definite	8 (7.3)
	Probable	62 (56.4)
	Possible	40 (36.3)
Severity (Hartwig–Siegel)*	Mild	58 (52.7)
	Moderate	44 (40.0)
	Severe	8 (7.3)
Preventability*	Preventable	71 (64.5)
	Not preventable	39 (35.5)

*Percentages calculated on the 110 patients who experienced at least one ADR.

Just over one in four patients (27.5%) experienced at least one ADR. Most reactions were categorised as "probable" on the Naranjo scale (56.4%) and were mild-to-moderate in severity. Importantly, nearly two-thirds of ADRs (64.5%) were judged preventable, highlighting a substantial opportunity for intervention through safer prescribing.

Table 4. Drug classes most commonly implicated in adverse drug reactions

Drug class	Number of ADRs	% of total ADRs (n = 132)*
Cardiovascular agents (e.g., diuretics, ACE inhibitors, digoxin)	34	25.8
Antidiabetic agents (e.g., sulfonylureas, insulin)	26	19.7
NSAIDs / analgesics	22	16.7
Antibiotics	18	13.6
Anticoagulants / antiplatelets	14	10.6
CNS agents (benzodiazepines, antipsychotics)	12	9.1
Others	6	4.5

*The 110 patients experienced 132 ADR episodes, as some patients had more than one reaction.

Cardiovascular agents (25.8%), antidiabetics (19.7%), and NSAIDs (16.7%) accounted for the largest share of ADRs. Several of these classes—particularly long-acting sulfonylureas, NSAIDs, and benzodiazepines—feature prominently in explicit lists of potentially inappropriate medications for older adults, reinforcing the link between prescribing quality and preventable harm.

Table 5. Factors associated with adverse drug reactions: univariate and multivariable analysis

Factor	ADR present, n (%)	ADR absent, n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value**
Polypharmacy (≥5 vs <5 meds)	88 (35.2) vs 22 (14.7)	162 vs 128	3.16 (1.88–5.31)	3.42 (1.98–5.91)	<0.001
≥3 comorbidities (vs 1–2)	78 (34.5) vs 32 (18.4)	148 vs 142	2.34 (1.46–3.75)	2.11 (1.24–3.59)	0.006
Age ≥75 years (vs 65–74)	48 (33.8) vs 62 (24.0)	94 vs 196	1.61 (1.03–2.52)	1.38 (0.85–2.24)	0.19
Female sex (vs male)	54 (29.7) vs 56 (25.7)	128 vs 162	1.22 (0.79–1.89)	1.14 (0.71–1.83)	0.58

**p-value refers to the adjusted (multivariable) model.
On multivariable logistic regression, polypharmacy remained the strongest independent predictor of ADRs (aOR 3.42, 95% CI 1.98–5.91), followed by the presence of three or more comorbidities (aOR 2.11, 95% CI 1.24–3.59). Advanced age and female sex showed trends toward higher risk on univariate analysis but were not statistically significant after adjustment, suggesting their apparent effect is largely mediated by the greater medication and comorbidity burden in these subgroups.

DISCUSSION

This study found a high prevalence of polypharmacy (62.5%) and hyper-polypharmacy (21.0%) among hospitalised older adults, with at least one ADR documented in 27.5% of participants and polypharmacy emerging as the strongest independent predictor of ADRs. These findings are broadly concordant with the wider literature and reinforce polypharmacy as a central, modifiable determinant of medication-related harm in geriatric care.

The observed polypharmacy prevalence aligns with the high pooled estimates reported by Bhagavathula et al. among older adults in comparable settings [7], and with the definitional framework established by Masnoon et al., in which the ≥5-medication threshold predominates [1]. The strong association between polypharmacy and ADRs (aOR 3.42) echoes the mechanistic and epidemiological evidence synthesised by Wastesson et al., who described how each additional medicine compounds the risk of drug–drug interactions and adverse effects in a population already predisposed by age-related pharmacokinetic and pharmacodynamic change [2]. Similarly, Davies et al., in a systematic review of reviews, found consistent associations between polypharmacy and adverse clinical and safety outcomes, supporting the direction and magnitude of our results [3].

The finding that nearly two-thirds of ADRs were preventable is clinically important and consistent with evidence that ADR-related morbidity in older people is often avoidable [4]. The predominance of cardiovascular agents, antidiabetics, and NSAIDs among implicated drugs is notable because several of these—long-acting sulfonylureas, NSAIDs, and benzodiazepines in particular—are flagged as potentially inappropriate for older adults in the 2023 AGS Beers Criteria [5] and the STOPP/START criteria version 3 [6]. This intersection between polypharmacy and inappropriate prescribing suggests that interventions should target not merely the number of medicines but their appropriateness.

These results carry practical implications. Systematic medication reconciliation at admission, routine application of explicit screening tools, and structured deprescribing—the planned withdrawal of medications whose harms outweigh benefits—could reduce preventable ADRs. Pharmacist-led medication review and clinical decision-support systems may be particularly valuable in high-risk patients with multimorbidity, who bore the greatest ADR burden in our cohort.

Several limitations should be acknowledged. The cross-sectional design precludes causal inference; a temporal, longitudinal association cannot be established. Single-centre recruitment may limit generalisability. Reliance on documented and self-reported medication histories may have led to under-ascertainment of over-the-counter and herbal use, and milder ADRs may have gone undetected, potentially underestimating the true burden. Causality assessment, while standardised via the Naranjo scale, remains partly subjective. Future multicentre, prospective studies incorporating drug–drug interaction analysis and follow-up would strengthen the evidence base and better inform stewardship strategies [2,3].

CONCLUSION

Polypharmacy is highly prevalent among hospitalised older adults and is strongly and independently associated with the occurrence of adverse drug reactions, a large proportion of which are preventable. Comorbidity burden further compounds this risk. The drug classes most frequently implicated overlap substantially with those identified as potentially inappropriate for older adults, indicating that both the quantity and the appropriateness of prescribing require attention. Embedding routine medication review, applying explicit prescribing criteria such as the Beers and STOPP/START tools, and implementing structured, pharmacist-supported deprescribing programmes are essential steps toward reducing medication-related harm and improving safety in this vulnerable population.

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