

## Association Between Polypharmacy and Frailty in Elderly Patients Receiving Care at a Public Hospital in South India

Shalini Tulasedas<sup>1</sup>, Mohana Vishnu Varadhan Sivakumar<sup>1</sup>, Gurulakshmi Ayyanar<sup>1</sup>, Naveena Nagarajan<sup>1</sup>, Sivasubramaniam Balaji<sup>2</sup>, S Arthi<sup>3</sup>, Sivasankaran Ponnusankar<sup>1</sup> and Hunsur Nagendra Vishwas<sup>1</sup>

<sup>1</sup>Department of Pharmacy Practice, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, India; <sup>2</sup>Department of General Medicine, Government Medical College & Hospital, Ooty, The Nilgiris, India; <sup>3</sup>Department of Pharmacology, Government Medical College & Hospital, Ooty, The Nilgiris, India

### Correspondence:

Hunsur Nagendra Vishwas,  
M Pharm, (Ph D), Department of  
Pharmacy Practice, JSS College  
of Pharmacy, JSS Academy of  
Higher Education & Research,  
Ooty, Nilgiris- 643001, Tamil  
Nadu, India.  
E-mail: vishwas@jssuni.edu.in;  
vishpharm@gmail.com

Received: November 26, 2024;  
Revised: September 5, 2025;  
Accepted: September 12, 2025

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### ABSTRACT

**OBJECTIVE** This study analyses the impact of polypharmacy on frailty among the elderly patients visiting the public sector hospitals. The present study was done to assess the frailty status of the elderly patients and to see whether the individuals with polypharmacy exhibited more frailty when compared to those without polypharmacy.

**METHODS** This is a case-control study that included 488 participants age 60 years and above who visited the general medicine department of Public Hospital Ooty, India. Polypharmacy was defined as the concomitant use of 5 or more medications. Frailty status of the participants was assessed using the Tilburg Frailty Indicator.

**RESULTS** Polypharmacy was found to be present in 34.42% of cases. The prevalence of frailty was significantly higher in the polypharmacy group, affecting 41.07% of the study participants. Finally, three variables emerged as influential predictors of polypharmacy namely, 3 or more diseases (AOR 6.303, CI 4.009-9.911,  $p < 0.0001$ ), unsatisfied sleep status (AOR 1.669, CI 1.068-2.606,  $p = 0.01$ ), and people taking frailty causing drugs (AOR 4.328, CI 2.628-7.128,  $p = 0.003$ ). Additionally, there was a moderate relationship between modified lifestyle (smoking, alcohol consumption) and polypharmacy.

**CONCLUSIONS** The results suggest that polypharmacy is linked with frailty among the elderly population, highlighting the importance of clinician awareness of these factors.

**KEYWORDS** elderly, frailty, polypharmacy, Tilburg Frailty Indicator, prevalence

### INTRODUCTION

Across the world the elderly population is growing rapidly, both in absolute size and as a proportion of the total population. The term “geriatric” describes a population with a chronological age of at least 65 years in developed nations and at least 60 years in developing na-

tions (1). According to the population projection report of India, the population of people aged 60 and above is expected to expand from 101.5 million in 2011 to 227.4 million by 2036 (2).

Previous studies indicate that elderly individuals are at increased risk of taking multiple medications, primarily due to their higher prevalence

of chronic diseases. This is because in geriatrics the body physiology changes with time, further increasing the risk of both adverse drugs reactions and adverse outcomes (3). Polypharmacy—commonly defined as the use of five or more medications, including prescription, over-the-counter, and complementary products—is associated with adverse outcomes such as drug interactions, non-adherence to instructions for using the medications, reduced functional capacity, and frailty (4). A recent South Indian study reported the prevalence of hyper-polypharmacy ( $\geq 10$  drugs), major polypharmacy ( $\geq 5$  drugs), and minor polypharmacy (2–4 drugs) as 3.46%, 81.31%, and 15.22%, respectively, with higher rates among males (1).

Frailty, being a multifaceted disease, is highly correlated with aging and is marked by a depletion of reserves and an elevated risk of adverse consequences following the stressful events (5). A longitudinal cohort study in Italy found that the risk of frailty was 55.00% higher in participants taking 4–6 medications, and 147.00% higher in those taking  $\geq 7$  medications (6). Substantial evidence shows that frailty is strongly linked to negative health outcomes, including hospitalization, falls, disability, mortality, and higher health-care costs (4). Previous research suggests that frailty may arise from alterations across multiple interconnected physiological systems (7). Unsurprisingly, since the prevention of frailty among the elderly is a global priority, it is of the utmost importance to find the potential risk factor behind this. Several epidemiological studies have reported that frail or pre-frail elderly adults prescribed more than five medications are more likely to have emergency department visits (8–10). This study aims to evaluate the frailty status of elderly patients and to assess whether people with polypharmacy exhibit more frailty when compared to those without polypharmacy.

The link between polypharmacy and frailty is complex, and understanding it from both the clinical and the public health perspective has become the key challenge (11). Since polypharmacy is recognized as an important predictor of adverse outcomes in the elderly, our team decided to investigate this issue further. Moreover, there is very little research exploring the link between polypharmacy and frailty, particularly in India and within public health settings. Hence, it was

decided to determine whether polypharmacy is associated with frailty or not among the elderly patients visiting the public health sector.

## METHODS

### Study design

A prospective, case control study was conducted among an elderly population aged  $\geq 60$  years. This single-center study was performed in a public hospital in Ooty, India. Participants were recruited using consecutive sampling from the general medicine outpatient and inpatient departments.

### Study population

Sample size was calculated using the EPITOOLS software. Based on a previous meta-analysis of Indian studies (2002–2020), the expected prevalence of polypharmacy among controls was 49.00% (12). The sample size for each group was determined to be 133, and the overall sample size for a case control study was found to be 266 at a power of 0.8 with the confidence interval of 95% (95%CI).

Elderly patients of either sex, aged  $\geq 60$  years and with polypharmacy were considered as case groups and patients of either sex, aged  $\geq 60$  years without polypharmacy were considered as the control group. Elderly patients with physical disability who had been treated at wards other than general medicine were excluded from the study. Prior to the data collection, written informed consent was obtained from all eligible participants. This study was conducted over a period of 6 months, from December 2023 to May 2024, in South India. During the course of study, data was collected from 488 patients, exceeding the initially determined sample size of 266.

### Ethical consideration

The protocol approval for this study was issued by the Institutional Ethics Committee of Government Medical College and Hospital, The Nilgiris (Ref no IRBGMCO033). Confidentiality of the participant data was strictly maintained.

### Study measures

*The Tilburg frailty indicator questionnaire*

The Tilburg Frailty Indicator (TFI) is a self-reporting questionnaire consists of 15 set of

questions covering physical, psychological and social components which was used for assessing the multidimensional frailty among the study participants. A TFI score of  $\geq 5$  is considered to be Frail as per previous research studies (13).

#### *Modified Kuppaswamy Socioeconomic Scale 2023*

Scoring of the 2023 edition of the Modified Kuppaswamy socioeconomic scale is primarily based on education, occupation and monthly income. The Modified Kuppaswamy Scale categorizes socioeconomic status into five distinct groups, ranging from lower to upper class, based on a scoring system of between 3 and 29. The score is then calculated and analysed to determine the socioeconomic class of each subject (14).

#### **Data collection**

The research work was explained and the consent form was given to the elderly patients who met the study criteria. Once voluntary consent was obtained, participants received a brief explanation about the items to be filled in the data collection form. The patient's sociodemographic, socioeconomic status, medical history, medication history, including a detailed list of their current drugs including over-the-counter medications, prescription drugs, and dietary supplements, lifestyle factors and comorbidities were collected from the medical records and from interviews with the participants. Data was analysed using appropriate statistical tests. The elderly participants were then subjected to a 'frailty assessment' with the help of the TFI. All test observations were documented in the data collection form. The information related to frailty was suitably noted in the data collection form for further segregating of the elderly into frail and non-frail categories.

#### **Statistical analysis**

The statistical analysis was performed using SPSS Version 16.0. Polypharmacy was considered the dependent variable, and demographics and socioeconomic status were considered as the independent variables. For the comparison of variables, Mann-Whitney U test and Pearson  $\chi^2$  test were used for continuous and categorical variables, respectively. Characteristics of the polypharmacy group, being a continuous variable, are

presented as mean  $\pm$  standard deviation. The impact of demographic variables on polypharmacy was evaluated using bivariate analysis, and adjusted associations were subsequently identified through regression analysis, with polypharmacy as the dependent variable. Additionally, Pearson's correlation was used to examine the relationship between the number of medications and TFI scores. Statistical significance was defined as a "p" value of less than 0.05.

#### **RESULTS**

Table 1 shows the demographic and clinical characteristics of the 488 participants. Out of those participants, 51.43% were male and 48.56% were female. Among the study participants who had polypharmacy, 41.07% were frail and 58.92% were non-frail.

Overall, the prevalence of polypharmacy was higher among males ( $p = 0.06$ ), former alcoholics ( $p = 0.02$ ), participants aged  $\geq 75$  years ( $p = 0.08$ ), past smokers ( $p = 0.004$ ), those with poor sleep satisfaction ( $p = 0.01$ ), individuals with  $\geq 4$  comorbidities ( $p = 0.0001$ ), and those with body mass index (BMI)  $< 18.5$  ( $p = 0.09$ ) (Table 2).

When comparing frailty scores (TFI), participants with polypharmacy had a higher mean score ( $5.64 \pm 3.45$ ) than those without polypharmacy ( $4.48 \pm 2.51$ ), a statistically significant difference. This indicates that participants with polypharmacy were more likely to be frail than those without.

#### **DISCUSSION**

Geriatric syndrome is a multifactorial health condition resulting from the accumulation of impairments that affect multiple body systems and their functions. Frailty is defined as a geriatric syndrome that leads to a decrease in physical reserve and increased vulnerability to stressors. Aging is significantly associated with comorbid chronic conditions, which place the older population at increased risk of polypharmacy (3). Frailty affects social well-being and leads to increased utilisation of health care and greater health care costs (15).

Polypharmacy is generally defined as the concurrent use of five or more medications, whether clinically necessary or not (16). Studies worldwide have shown that elderly individuals typically use an average of 2 to 9 medications per day (17). In

**Table 1.** Demographic distribution (N = 488)

Characteristics	n (%)
Age	
60-64	201 (41.14)
65-69	114 (23.36)
70-74	90 (18.44)
≥ 75	83 (17.00)
Body mass index	
< 18.5	33 (6.76)
18.5-24.9	219 (44.87)
25-29.9	175 (35.86)
≥ 30	61 (12.50)
Living condition	
Own home	479 (98.15)
Nursing home	8 (1.63)
Senior care home	1 (0.20)
Marriage status	
Widow/divorced	203 (41.59)
Married	280 (57.37)
Unmarried	5 (1.02)
Physical activity	
Yes	427 (87.50)
No	61 (12.50)
Alcoholic	
Yes	36 (7.37)
No	356 (72.95)
Former alcoholic	96 (19.67)
Smoking	
Yes	42 (8.60)
No	353 (72.33)
Former smoker	93 (19.05)
Sleep (satisfaction)	
Yes	197 (40.36)
No	291 (59.63)
SES	
Lower (< 5)	214 (43.85)
Upper lower (5-10)	240 (49.18)
Lower middle (11-15)	23 (4.71)
Upper middle (16-25)	9 (1.84)
Upper (26-29)	2 (0.40)
Disease	
1	149 (30.53)
2	196 (40.16)
3	101 (20.69)
≥ 4	42 (8.60)
Gender	
Male	251 (51.43)
Female	237 (48.56)

SES, Socioeconomic status (Modified Kuppaswamy Scale 2023)

this population, polypharmacy is influenced by factors such as age, gender, education level, and the type and number of comorbidities. Several earlier studies have reported that the prevalence

of polypharmacy among older adults ranged from 23.10% to 59.10% (18-20). Polypharmacy can lead to negative health outcomes such as increased morbidity, higher economic burden, more hospitalizations, decreased quality of life, and higher rates of readmission. As the number of prescribed medications increases, the potential for drug-drug interactions also rises, further exacerbating adverse outcomes. Age-related changes in renal clearance and metabolism contribute to this problem by increasing drug exposure and susceptibility to drug side effects (21). For that reason, polypharmacy is recognized as a significant and growing concern in clinical practice.

The study team chose to focus on the impact of polypharmacy on frailty because of the growing elderly population, the high prevalence of polypharmacy in this group, and its complex relationship with frailty. In our study, frailty was assessed using the self-reported TFI questionnaire.

We chose to use the TFI scale over other assessment instruments because it conceptualizes frailty as a multidimensional construct, encompassing physical, psychological, and social domains of functioning in the elderly. The TFI scale is widely regarded as a tool with strong validity, reliability, and internal consistency. Individuals with a score of ≥ 5 were considered frail in our study, according to standard scoring criteria. There are only a few studies from India reporting the use of the TFI.

A long-term cohort study in Italy examining the association between polypharmacy and frailty showed that, at the 11-year follow-up, the probability of frailty increased with each additional medication reported at baseline (6). Similarly, a study conducted in Australia found that each additional medication was associated with a 13.00% higher risk of frailty, an 8.00% higher risk of disability, and a 9.00% higher risk of mortality (22).

Most of the studies pertaining to polypharmacy have been reported from private hospitals and very few from public hospitals. Ours is one such study reporting this important aspect from a public hospital.

Several classes of drugs have been associated with worsening health outcomes, such as falls and frailty. We conducted a PubMed search of previously published studies reporting drugs linked to frailty and falls (23-25). Medications found to exacerbate or contribute to frailty included

**Table 2.** Bivariate analysis of risk factors associated with polypharmacy

Subject characteristic	OR	(95%CI)	p-value
Sex			
Male	1.41	(0.97-2.06)	0.060
Female	1	(Reference)	
Age			
60-64	1	(Reference)	
65-69	0.81	(0.49-1.32)	0.405
70-74	0.91	(0.54-1.54)	0.740
> 75	0.66	(0.41-1.05)	0.080
Alcohol intake			
Former alcoholic	1.60	(1.06-2.42)	0.020
Not Alcoholic	1	(Reference)	
Smoking habit			
Smoker	1.81	(1.206-2.72)	0.004
Non-smoker	1	(Reference)	
Sleep (satisfaction)			
Satisfied	1	(Reference)	
Not Satisfied	1.63	(1.10-2.42)	0.010
Frailty			
Frail	1.7012	(1.15-2.51)	0.008
Non-Frail	1	(Reference)	
NO. of diseases			
1-2	1	(Reference)	
≥ 3	5.81	(3.80-8.87)	< 0.0001
Drugs and frailty			
Drug induced frailty	4.61	(1.68-12.6)	0.003
Non-drug induced frailty	1	(Reference)	
Body mass index			
< 18.5	1.89	(0.89-3.97)	0.090
18.50-24.99	1	(Reference)	
25.00-29.99	1.21	(0.79-1.85)	0.360
> 30.00	1.57	(0.87-2.82)	0.128

benzodiazepines, antipsychotics, anticholinergics, antiepileptic drugs, NSAIDs, and antihistamines. We further verified whether patients in both groups had been prescribed these drugs. In our study, patients in the frail group were more commonly prescribed with drugs such as ibuprofen, fluoxetine, diclofenac, chlorpheniramine maleate, and diphenhydramine, which have been linked to frailty. Benzodiazepines, such as diazepam and clonazepam, commonly used as sedatives, can lead to falls and contribute to the development or worsening of frailty in older adults. The study results demonstrated that patients in the polypharmacy group were more likely to be prescribed these drugs compared to those without polypharmacy. This relationship was also found to be statistically significant.

According to several studies, polypharmacy is a significant risk among the elderly and is commonly associated with factors such as age over

65 years, long-term illnesses, chronic diseases, frequent healthcare visits, and hospitalizations. In our study, we observed several factors to be associated with polypharmacy, including alcohol use, smoking, poor sleep satisfaction, having more than two diseases, and frailty.

With respect to alcoholism, alcohol can damage the liver, impairing its ability to metabolize drugs and lead to increased drug concentrations which may cause liver toxicity and other adverse effects. Additionally, alcohol can exacerbate the side effects of some medications, often necessitating the prescription of additional drugs, thus further compromising overall health in the elderly (26).

This case-control study demonstrated a higher prevalence of polypharmacy among current and former smokers, with an odds ratio of 1.81 (95%CI: 1.206-2.72). Similar results were reported in a 4.7-year follow-up study conducted in Australia, which also showed similar statistically

significant findings (27). Smoking induces elevation of certain liver enzymes, thereby metabolizing drugs more rapidly than in non-smokers. This reduction in drug concentration and efficacy can lead to subtherapeutic dosing, in which case higher doses of medication may be required to achieve the desired therapeutic effects while potentially increasing the risk of adverse effects or toxicity (28).

Sleep disruption becomes more common with age. Older adults often experience altered sleep architecture, an increased risk of sleep disorders, shifted circadian rhythms, and various mental and physical comorbidities related to sleep quality. Quality of life is significantly affected by age-related sleep problems, particularly among those exposed to polypharmacy (29). In comparing individuals with and without polypharmacy, there was a significant difference in the proportion of participants with polypharmacy reporting poor sleep satisfaction. Overall, poor sleep satisfaction was more frequent among participants with polypharmacy.

Our study reported that the prevalence of polypharmacy was higher among participants with  $\geq 2$  diseases compared to those with fewer than 2 diseases. Managing multiple chronic conditions often necessitates the use of multiple medications to control symptoms, slow disease progression, and reduce complications. Additionally, the use of medications from different therapeutic classes increases the risk of drug-drug interactions, potentially further worsening the well-being of the elderly (30, 31). The longitudinal Midlife in the United States (MIDUS) study found comparable statistically significant associations between polypharmacy and the prevalence of chronic diseases (16).

The polypharmacy group in this study had a considerably higher prevalence of frailty (41.07%) compared with the non-polypharmacy group (29.06%). Polypharmacy may contribute to the onset of frailty, regardless of the presence of multiple chronic conditions, likely due to the adverse effects of the medications. It is postulated that age-related changes in pharmacodynamics and pharmacokinetics increase the likelihood and severity of adverse drug reactions (ADRs) in older individuals, resulting in more frequent drug-drug and drug-disease interactions (27).

When examining the relationship between frailty and the number of prescribed drugs using Pearson's correlation, a weak positive correlation was observed ( $r = 0.233$ ), which suggests that the risk of frailty increases with the number of drugs prescribed.

Five variables (alcohol intake, smoking status, sleep satisfaction, having three or more diseases, and the use of frailty-associated drugs) were included in the binary logistic regression model after being identified as significant in the bivariate analysis. Finally, three variables emerged as significant predictors of polypharmacy: having three or more diseases (absolute odds ratio (AOR) 6.303, CI 4.009-9.911,  $p < 0.0001$ ), poor sleep satisfaction (AOR 1.669, CI 1.068-2.606,  $p = 0.01$ ), and use of frailty-associated drugs (AOR 4.328, CI 2.628-7.128,  $p = 0.003$ ).

However, such a study has not been conducted or reported in India. Our study is among the limited number of studies that examine the link between polypharmacy and frailty. Its generalizability is limited, as it was conducted in a single hospital in a specific region of South India.

The association between polypharmacy and frailty could be bidirectional, as demonstrated in previous systematic reviews. These studies indicate that frail individuals often develop multiple chronic conditions requiring complex treatment regimens, with frailty being linked to higher medication use as a result of functional decline, multimorbidity, and increased healthcare interactions (11). This highlights the importance of longitudinal studies to determine causality and support interventions such as regular medication reviews in frail populations.

## CONCLUSIONS

The overall prevalence of polypharmacy in our study was lower than that reported in other studies. Several predictors were identified, consistent with findings from international research. A weak positive correlation ( $r = 0.233$ ) between the polypharmacy and frailty scores suggests that frailty risk increases proportionally with medication burden. These results highlight the critical need for regular medication reviews, cautious prescribing practices that consider both the number and type of medications, and the implementation of targeted interventions for elderly patients. In

conclusion, our findings demonstrate that polypharmacy is associated with increased frailty in older adults. Future multicenter studies across India are needed to validate these results and inform standardized guidelines for medication management in elderly populations.

By observing the results of the present study, we are in the opinion that, in a large country like India with limited electronic health records (EHR) integration within the public health sector, hospitals have a challenges of improved coordination and sharing of medical records between institutions which could help minimize the occurrence and adverse consequences of poly pharmacy.

### ACKNOWLEDGMENTS

The study team would like to thank all the elderly patients who participated in the study. The study team is indebted to health care professionals at Government Medical College Hospital, Ooty, Nilgiris. We acknowledge the generous research infrastructure and support from JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, Nilgiris, Tamil Nadu, India.

### FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

### CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

### AUTHOR CONTRIBUTIONS

S.T.: methodology, validation, investigation, formal analysis, writing-original draft, data curation; M.V.V.S.: methodology, validation, investigation, formal analysis, writing-original draft, data curation; G.A.: methodology, validation, investigation, formal analysis, writing-original draft, data curation; N.N.: methodology, validation, investigation, formal analysis, writing-original draft, data curation; S.B.: resources, supervision, project administration, visualization, writing-review & editing; S.A.: supervision, project administration, visualization, writing-review & editing; S.P.: supervision, project administration, writing-review & editing, visualization; H.N.V.: conceptu-

alization, methodology, data curation, software, project administration, writing-review & editing.

All authors have read and agreed to the published version of the manuscript

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### INSTITUTIONAL REVIEW BOARD STATEMENT

The protocol approval for this study was issued was responsible Institutional Ethics Committee of Government Medical College and Hospital, The Nilgiris (Ref no IRBGMCO033).

### INFORMED CONSENT STATEMENT

Written informed consent was obtained from all participants. Confidentiality of the participant data was strictly maintained.

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