Polypharmacy in older adults and its implications on frailty syndrome

Polifarmácia em idosos e suas implicações na síndrome da fragilidade

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Abstract

Introduction: Frailty is a state of physiological vulnerability associated with aging, and the use of polypharmacy can exacerbate this condition. Objective: To identify the prevalence of polypharmacy and its relationship with frailty syndrome among older adults. Materials and Methods: This observational, cross-sectional study included 376 older adults (≥60 years old) registered at PHC Health Units in Foz do Iguaçu, Paraná, Brazil. Data were collected through individual interviews using a self-reported frailty screening instrument and the question: "Do you regularly use five or more different medications daily?" The chi-square test (χ^2) was used for data analysis to assess differences between groups and associations among categorical variables. Numerical variables were analyzed using means and standard deviations. Results: Polypharmacy was identified in 27% of participants and was more prevalent among women and those aged 60 to 69 years. Polypharmacy was also associated with cognitive impairment, reduced gait speed, falls, incontinence, use of sleep medications, and a higher prevalence of chronic conditions, including endocrine, circulatory, musculoskeletal, and mental disorders. Conclusion: Physiological changes inherent to aging, when combined with polypharmacy, can significantly compromise autonomy, independence, and quality of life in older adults, contributing to the development of frailty syndrome. In this context, healthcare teams need to act proactively through multidimensional assessments, with a focus on identifying and adequately managing polypharmacy and frailty syndrome.

Keywords: vulnerability; aging; polypharmacy; frailty

Resumo

Introdução: A fragilidade é um estado de vulnerabilidade fisiológica relacionado à idade, e o uso de polifarmácia agrava esse quadro. Objetivo: identificar a prevalência da polifarmácia e sua relação com a síndrome da fragilidade em idosos. Materiais e Métodos: estudo observacional, transversal, com 376 idosos (≥60 anos), cadastrados em Unidades Básicas de Saúde de Foz do Iguaçu-PR. A coleta de dados foi realizada por meio de entrevista, utilizando um instrumento de triagem de fragilidade autorreferida e a pergunta: Você faz uso regular de cinco ou mais medicamentos diferentes todos os dias? Para análise dos dados, foi aplicado o teste qui-quadrado (X2) para testar diferenças entre grupos nas associações entre variáveis categóricas. As variáveis numéricas foram analisadas por meio da média e desvio padrão. Resultados A polifarmácia foi identificada em 27% dos idosos, sendo mais prevalente em mulheres e na faixa etária de 60 a 69 anos. Além disso, a polifarmácia esteve associada ao comprometimento da cognição, velocidade da marcha, quedas, incontinência, uso de medicamentos para dormir, e maior prevalência de doenças crônicas, sistema endócrino, circulatório, musculoesquelético e transtornos mentais. Conclusão: As alterações fisiológicas, inerentes ao processo de envelhecimento, quando associadas à polifarmácia, comprometem significativamente a autonomia, a independência e a qualidade de vida dos idosos, contribuindo para o desenvolvimento da síndrome da fragilidade. Nesse contexto, é fundamental que a equipe de saúde atue de forma proativa, abordando essas questões por meio de uma avaliação multidimensional, com foco na identificação e manejo adequado da polifarmácia e da síndrome da fragilidade.

Palavras-chave: : vulnerabilidade; envelhecimento; polifarmácia; fragilidade

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Introduction

The aging process is irreversible, universal, and non-pathological, affecting each individual uniquely [1]. As people age, the differences between individuals tend to become more pronounced. Therefore, promoting autonomy and independence among older adults—while considering their limitations—is essential for supporting active and healthy aging, ultimately contributing to improved physical health outcomes [2].

From this perspective, health in older adults is defined as the individual's ability to meet biopsychosocial needs, regardless of age or illnesses. Therefore, understanding the illnesses that affect older adults is just as important—if not more so—than understanding the determinants of health, functionality, level of dependence, and frailty [3].

As aging progresses, age-related multimorbidities affect individuals who increasingly require care. The presence of multiple health conditions is associated with greater use of health services and a higher risk of iatrogenesis, disability, institutionalization, and even death. Older adults who are polymedicated—often receiving multiple prescriptions with varying classifications and purposes—are at increased risk of drug interactions, which can negatively impact their quality of life [4, 5].

Polypharmacy is classified into three levels: mild, moderate, and severe. Mild polypharmacy refers to the concurrent use of two to three medications; moderate, four to five medications; and severe, more than five medications. The impact of polypharmacy is associated with high medication costs, recurrent hospitalizations, poor treatment adherence, and drug interactions [6].

Therapeutic planning involving medication use must be centered on the individual, with a focus beyond the disease itself, enabling effective and safe treatment [7]. In this context, inappropriate prescriptions—those with an unfavorable risk-benefit ratio that may trigger the so-called iatrogenic cascade—can have detrimental effects on treatment and overall therapy outcomes [14].

According to the World Health Organization (WHO), 50% of medications are misused, including over-the-counter drugs, which are often popularized through advertising. It is important to note that older adults frequently experience minor symptoms—such as muscle or joint pain and digestive discomfort—that lead them to self-medicate with over-the-counter products. This practice can contribute to or worsen adverse reactions and drug interactions. Therefore, a more cautious and attentive approach to medication use in this age group is essential [7].

In this context, frailty syndrome—which compromises the autonomy and independence of older adults—can be accelerated or intensified by polypharmacy [7], contributing to a decline in overall health and quality of life. This condition may increase the risk of falls, fractures, hospitalizations, and even death [5]. Such a cascade of adverse outcomes calls for multidisciplinary interventions that rely on effective identification, prevention, and recovery methods while prioritizing the physical and mental well-being of the individuals affected [8].

Given the previous discussion, this study aimed to identify the prevalence of polypharmacy and its association with frailty syndrome among older adults in a municipality in southern Brazil. Expanding scientific research in this area supports a deeper understanding and more effective identification of the harms and adverse effects associated with polypharmacy.

Material and Method

This observational, cross-sectional study was conducted in Foz do Iguaçu, a tri-border region in the far west of Paraná State,

Brazil. The study population consisted of adults aged 60 or older who received care through the Brazilian Unified Health System (SUS) and were enrolled in primary care services at local health units.

Older adults were stratified by age group and geographic allocation within each of the five health districts (North, South, East, West, and Northeast) to determine the sample size. The calculation used a 5% margin of error, a 5% significance level, and an assumed prevalence of 50% in each stratum based on a total population of 20,321 older adults. As a result, the required sample size was 376 individuals, with an additional 10% added to account for potential losses.

Study design and sample

The Institutional Review Board of the University of São Paulo at Ribeirão Preto, College of Nursing (CEP, EERP/USP) approved the study under protocol No. 79408317.4.0000.5393. It is part of a larger research project titled "*Identificação da fragilidade em idosos em região de tríplice fronteira: estratégia para a promoção do envelhecimento ativo*" [Identification of frailty among older adults in a tri-border region: a strategy for promoting active aging] [9].

Research design

Data were collected in 2018 through individual interviews conducted with older adults or their guardians, either at their respective health units or in their homes, after obtaining written informed consent.

A cognitive assessment was performed using the Mini-Mental State Examination (MMSE), which included questions on temporal and spatial orientation, calculation, memory, and language to identify potential deficits that could compromise the reliability of responses. If an individual was deemed cognitively unfit, the interview was conducted with a caregiver who was at least 18 years old and had lived with the older adult for a minimum of three months. Individuals who lacked the cognitive capacity to respond and did not have an eligible caregiver were excluded from the study.

The interview began with questions addressing sociodemographic information, followed by a subjective assessment of physical frailty syndrome using a self-reported screening instrument adapted and validated for use in Brazil [13]. The instrument included five measurable components: unintentional weight loss, fatigue, reduced strength, reduced walking speed, and low physical activity. Based on this classification, individuals who scored in three or more components were considered "frail"; those who scored in one or two were classified as "pre-frail"; and those who did not score in any component were considered "non-frail."

Furthermore, polypharmacy was assessed using the following question: "Do you regularly use five or more different medications each day?" The data were then organized in a spreadsheet and analyzed descriptively.

Absolute and relative frequencies (proportions) were used for data analysis, and the Chi-square test (χ^2) was applied to assess differences between groups and associations between categorical variables. The significance level (α) was set at 5%. For numerical variables, the mean and standard deviation were calculated. Data analysis was performed using Jamovi, version 2.2.5.

Inclusion and exclusion criteria

The analysis included 555 older adults registered in Primary Health Care in Foz do Iguaçu, PR, Brazil, across 26 health units distributed among the five health districts. Most participants were female, aged 60 to 69, retired, had 5 to 9 years of education, lived with family members, and reported a family income of up to twice the minimum wage.

Results

The average age of participants was 70 years (±7.45), ranging from 60 to 99 years. The mean per capita family income was 1.2 times the minimum wage (±0.9), and the average educational level was six years (±4). Polypharmacy was reported by 27.4% of participants, predominantly among the younger older adults (aged 60 to 69). However, proportionally, the highest prevalence was observed among the oldest group (80 years and older), with 37.1% reporting polypharmacy. Higher proportions were also noted among women and retired individuals (Table 1). Although proportional differences were observed across categories, none of the variables showed a statistically significant association with polypharmacy.

Table 1. Distribution of the sample according to sociodemographic characteristics and polypharmacy among older adults enrolled in Primary Health Care in Foz do Iguaçu, Paraná, Brazil - 2018

| VARIABLES (p-value)* | RESPONSE OPTIONS | POLYPHARMACY | | | |
| | | NO | | YES | |
		n	%	n	%
AGE (years) (0.130)*	60-69	220	74.8	74	25.2
	70-79	139	72.8	52	27.2
	80 ≥	44	62.9	26	37.1
SEX (0.514)*	Female	245	71.6	97	28.4
	Male	158	74.2	55	25.8
DISTRICT (0.141)*	Northeast	49	72.1	19	27.9
	South	58	85.3	10	14.7
	East	112	70.0	48	30.0
	West	77	68.8	35	31.3
	North	107	72.8	40	27.2
RETIRED (0.160)*	Yes	289	71.0	118	29.0
	No	114	77.0	34	23.0
SCHOOLING (years) (0.163)	No formal education	66	12	24	4
	1 to 4 years	104	19	48	9
	5 to 9 years	154	28	60	11
	≥ 10	79	14	20	3
LIVING ALONE (0.657)*	Yes	81	74.3	28	25.7
	No	322	72.2	124	27.8
FAMILY INCOME ** (0.189)*	0 to 2 times MW	262	47	87	15
	3 or more times the MW	141	26	65	12
TOTAL		403	72.6	152	27.4

Source: Study data (2018).
Legend: *X^2 test for independent variables; **Current minimum wage: R$954.00 (Decree No. 9.255/17 regulating Law No. 13.152/15 dated December 29, 2017). MW: Minimum Wage.

Polypharmacy was identified in 27% of participants, predominantly among younger older adults (aged 60 to 69), women, and retired individuals. Regarding clinical conditions, the most frequent findings—when variables were analyzed individually—were circulatory system diseases (n = 389; 70.1%) and mood disorders (n = 330; 59.5%), along with the use of sleep medications (n = 434; 78.2%).

Most clinical conditions were associated with polypharmacy. Notably, 40.3% of individuals with reduced walking speed reported polypharmacy, as did 40.4% with a history of falls. Polypharmacy was also prevalent among individuals with five or more chronic conditions (57.9%), endocrine disorders (41.4%), mental health conditions (48.0%), and musculoskeletal disorders (41.0%).

A total of 269 individuals (48.5% of the sample) reported dry mouth, 33.8% of whom were polypharmacy users. Sleep medications were used by 78% of participants, with 24.2% of these individuals classified as polypharmacy users. These

findings may be related to the 70.8% of older adults who reported being satisfied with their sleep quality, of whom 23.7% used sleep medication. Thus, reports of good sleep quality may be influenced by the use of these medications.

The average number of diseases reported per participant was 1.87 (±1.3), with a minimum of 0 and a maximum of 6. These conditions were grouped according to the International Statistical Classification of Diseases and Related Health Problems – ICD-10 [16]. Circulatory system diseases were the most prevalent (71%), including essential (primary) hypertension, with 25% of this group using polypharmacy. Endocrine, nutritional, and metabolic diseases were also common, reported by 37% of participants, with 16% of them using polypharmacy; diabetes mellitus was the most frequent condition in this category, affecting 27% of the sample. Only 4% of participants had five or more chronic diseases (Table 2).

Table 2. Clinical variables and polypharmacy among older adults enrolled in Primary Health Care in Foz do Iguaçu, Paraná, Brazil - 2018

VARIABLES (p-value)*	POLYPHARMACY			
	NO		YES	
	n	**%**	**n**	**%**
INSTRUMENTAL ADLs (0.060)*				
Not impaired	331	74.4	114	25.6
Impaired	72	65.5	38	34.5
BASIC ADLs (0.057)*				
Not impaired	389	73.4	141	26.6
Impaired	14	56.0	11	44.0
COGNITION (0.043)**				
Not impaired	273	75.4	89	24.6
Impaired	130	67.4	63	32.6
MOOD (0.095)				
Not impaired	172	76.4	53	23.6
Impaired	231	70.0	99	30.0
GAIT SPEED (0.015)**				
Not impaired	366	74.2	127	25.8
Impaired	37	59.7	25	40.3
FALLS (0.003)**				
No	350	75.1	116	24.9
Yes	53	59.6	36	40.4
INCONTINENCE (0.024)**				
No	262	75.9	83	24.1
Yes	141	67.1	69	32.9
DRY MOUTH (0.001)**				
No	225	78.7	61	21.3
Yes	178	66.2	91	33.8
SLEEP QUALITY SATISFACTION (0.002)**				
Yes	300	76.3	93	23.7
No	103	63.6	59	36.4
USE OF SLEEPING MEDICATION (0.001)**				
No	74	61.2	47	38.8
Yes	329	75.8	105	24.2
FIVE OR MORE CHRONIC DISEASES (0.002)**				
No	395	73.7	141	26.3
Yes	8	42.1	11	57.9
DISEASES OF THE ENDOCRINE SYSTEM (<0.001)**				
Absent	271	81.9	60	18.1
Present	132	58.9	92	41.1
MENTAL DISORDERS (<0.001)**				
Absent	377	74.7	128	25.3

VARIABLES (p-value)*	POLYPHARMACY			
	NO		YES	
	n	**%**	**n**	**%**
Present	26	52.0	24	48.0
DISEASES OF THE CIRCULATORY SYSTEM (<0.001)**				
Absent	152	91.6	14	8.4
Present	251	64.5	138	35.5
MUSCULOSKELETAL DISORDERS (0.004)**				
Absent	357	74.8	120	25.2
Present	46	59.0	32	41.0
RECENT HOSPITALIZATION (0.468)*				
No	381	72.3	145	27.7
Yes	22	78.6	6	21.4
TOTAL	403	72.6	152	27.4

Source: Study data (2018).

Legend: *X^2 test for independent variables; ** Statistically significant at $p < 0.05$.

Analysis of the relationship between frailty syndrome and polypharmacy revealed that older adults using polypharmacy were most frequently classified as frail (n = 78; 14%). Moreover, the prevalence of polypharmacy increased with frailty levels (Table 3).

Table 3. Assessment of frailty among older adults enrolled in Primary Health Care in Foz do Iguaçu, Paraná, Brazil - 2018

VARIABLES (p-values)	POLYPHARMACY			
	NO		YES	
	n	%	n	%
FRAILTY (<0.001)				
Not frail	82	82.8	17	17.2
Pre-frail	193	77.2	57	22.8
Frail	128	62.1	78	37.9
TOTAL	403	72.6	152	27.4

Source: Study data (2018).

Finally, 17.8% of the sample was classified as non-frail, 54.1% as pre-frail, and 37.1% as frail. Notably, the prevalence of polypharmacy increased with higher levels of frailty: 3% among non-frail individuals, 10% among pre-frail, and 14% among frail participants.

Discussion

Polypharmacy is characterized by the use of five or more medications by the same individual, which in this study was found to be 27.4% of the participants (n=152). There is no consensus on polypharmacy among older adults, with differences between different studies, population characteristics, and study location. However, percentages ranged from 18% to 33% [8]. In addition to environmental and social variations, self-medication has been an important component in contributing to polypharmacy and increasing the risk of consumption of medications potentially inappropriate for older people, which can lead to adverse events and consequently reduce quality of life [15].

Self-medication is currently considered a public health concern in Brazil. It is a common practice encompassing various situations, including caregivers determining which medications to administer and how to use them without medical evaluation [5]. According to data from the Brazilian Toxic-Pharmacological Information System, medications have been identified as the main toxic agents capable of altering physiological and biochemical processes in the human body since 1994. Furthermore, self-medication may mask symptoms of progressive diseases and

contribute to the development of iatrogenic conditions, microbial resistance to antibiotics, and increased risks of drug abuse and dependence [10,12].

Younger older adults showed the highest prevalence of polypharmacy. This finding may be explained by an early decline in health status during the initial stages of aging, often due to pre-existing chronic conditions. Age is associated with multimorbidity and can trigger a cascade of adverse outcomes, which may be exacerbated by polypharmacy [13]. However, polypharmacy can also affect individuals aged 75 and older due to the increasing number or severity of chronic conditions associated with the aging process [15].

Several factors are associated with polypharmacy among older adults, including female sex, low educational level, and the presence of chronic diseases [13]. However, with increasing life expectancy and the feminization of aging, there is a growing demand for healthcare services, as women tend to initiate treatment earlier than men, which may explain the higher prevalence of polypharmacy in this group [12, 14, 17]. In contrast, men often demonstrate greater resistance to seeking healthcare services due to fear, lack of time, or even disinterest—factors that may contribute to worsening existing health conditions [18].

Furthermore, the low level of education among older adults regarding polypharmacy stands out, as it negatively affects their health due to difficulties in understanding medical prescriptions, written instructions, and the complexity of the therapeutic regimen. These factors contribute to a higher risk of adverse events related to medication mix-ups and incorrect dosing [17].

Regarding clinical aspects, 18% of older adults using polypharmacy presented with mood disorders, including symptoms such as discouragement, sadness, hopelessness, or a lack of interest or pleasure in daily activities. This loss of motivation for previously enjoyable activities may contribute to cognitive decline and reduced autonomy. It can also lead to the use of psychotropic medications to manage somatic symptoms. This approach has been associated with adverse outcomes such as falls with a risk of fractures, cognitive impairment, delirium, and psychiatric hospitalizations [15].

Furthermore, the integrity of the nervous system is directly linked to gait speed and fall risk. The use of certain medications can interfere with gait, contribute to drug interactions, and lead to adverse effects [20]. One of the common consequences of polypharmacy is dizziness, which—when combined with advanced age—can impair postural stability mechanisms and increase the risk of falls [25,21].

This study found no association between medication use and gait speed. However, it cannot be concluded that medication use did not impact falls, as falls are considered multifactorial events that may be reduced through home safety measures and continuous monitoring [23].

Furthermore, polypharmacy can interfere with both the production and quantity of saliva. The medications most commonly associated with this effect include anticholinergic, antidepressant, and antihypertensive agents. In this study, hypertension was one of the most prevalent circulatory system conditions, suggesting the frequent use of such medications. Complaints of dry mouth or hyposalivation were reported, which leads to imbalances in oral physiology that can impair chewing, speech, swallowing, nutrition, and communication in older adults [19].

Older adults often experience changes in sleep quality, which tends to decline in effectiveness due to neuronal aging. In this study, 70.8% of participants reported being satisfied with their sleep quality, while the remaining 29.2% reported disturbances such as excessive daytime sleepiness and difficulty initiating or maintaining sleep. However, the majority (78%) used some form of sleep-inducing medication, which may have

influenced their perception of sleep quality [19].

A multidisciplinary team should monitor and evaluate pharmacotherapy to ensure its benefits and support successful clinical management. This approach helps prevent dependence, drug interactions, adverse events, and unnecessary costs while also considering the recommended duration of medication use [25].

Regarding hospitalizations, 6% of individuals using polypharmacy reported having been hospitalized within the past six months. Older adults who have recently been hospitalized tend to use a more significant number of medications after discharge, with an average of five to twelve prescribed drugs, indicating that hospitalization can lead to or increase polypharmacy [22]. Conversely, polypharmacy itself can contribute to hospitalization, increasing the risk of emergency admissions up to fourfold due to a higher likelihood of adverse drug reactions, which are currently considered a public health concern [3].

The transition from the hospital to the home environment also requires careful attention, and healthcare professionals must be prepared to provide clear guidance at discharge to prevent complications related to prescribed therapies and recommended care.

Frailty can be characterized by a reduced capacity of the body to restore physiological systems, combined with age-related decline, chronic conditions, and the cumulative effects of lifestyle habits such as tobacco and alcohol use, physical inactivity, and obesity [24]. In this study, approximately 37% of participants were identified as frail—a lower prevalence compared to other studies, where frailty has been observed in up to 63% of participants, with 73.9% of those individuals using polypharmacy [27, 25].

The frailty process is intensified when aging is accompanied by multiple comorbidities and medication use, as this increases the individual vulnerability of older adults. Periodic assessment is essential to recognize and detect frailty and to support timely interventions [8].

Several studies have demonstrated an association between polypharmacy and frailty, as chronological age and altered pharmacokinetic responses contribute to the frailty process. Age-related changes in body composition and reduced renal and hepatic function can affect the pharmacokinetics and pharmacodynamics of numerous medications. As a result, older adults become more susceptible to intensified adverse effects or therapeutic responses [8].

Furthermore, an individual's response to medications changes over time, making it difficult to predict outcomes due to age-related physiological changes, the presence of comorbidities, and polypharmacy. In addition, frail older adults—particularly those with multiple disabilities and functional dependencies—are often underrepresented in studies evaluating the efficacy and safety of medications, which contributes to the unpredictability of the therapeutic process in this population [7].

From this perspective, it is important to revisit the concept of quaternary prevention as defined by the World Organization of Family Doctors (WONCA). Quaternary prevention involves actions aimed at identifying individuals and populations at risk of excessive medicalization, protecting them from unnecessary or invasive medical interventions, and ensuring the provision of scientifically and ethically appropriate care [27].

This study did not identify the pharmacological classes used by participants, which represents a limitation. Nonetheless, polypharmacy was associated with numerous adverse effects that impact the well-being of older adults, compromise their autonomy and independence, and increase vulnerability—factors that contribute to the development of multidimensional frailty in this population [29].

The data highlight the severity and scale of the issue, which can pose a significant threat to individual health. Both

prescribing and deprescribing are clinical practices that require skill and judgment, and each can profoundly impact the health of older adults. These processes combine scientific knowledge, clinical experience, and the intention to act in the patient's best interest while navigating the inherent uncertainties of medical care. Such complex decisions must be guided by the ethical principles of non-maleficence and beneficence [7].

This study's limitations include its cross-sectional design, which prevents the identification of cause-and-effect relationships. Because individuals were assessed at a single point in their personal and social trajectories, it is impossible to infer how frailty progressed. Additionally, this study does not allow for the calculation of a precise risk measure associated with the presence or absence of each variable.

Conclusion

This study identified a polypharmacy prevalence of 27.4% among participants, with higher rates observed among women, individuals with lower incomes, and those aged 60 to 79. Additionally, the results showed a statistically significant association between polypharmacy and several clinical variables, including cognitive impairment, reduced walking speed, frequent falls, urinary and fecal incontinence, dry mouth, dissatisfaction with sleep quality, use of sleep medications, the presence of five or more chronic conditions, and diseases related to the endocrine, circulatory, musculoskeletal systems, as well as mental health disorders.

Another finding is that higher levels of frailty are associated with a greater prevalence of polypharmacy, which in turn increases the risk of adverse reactions and iatrogenic events.

These findings reinforce the need for a multidimensional approach to the care of older adults, with an emphasis on identifying and appropriately managing polypharmacy to minimize its negative impact on their health and quality of life.

Primary Health Care plays a crucial role in preventing health complications among older adults who use multiple medications, with a focus on minimizing adverse reactions, drug interactions, and iatrogenic events.

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