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Multimorbidity, medications, and their association with falls, physical activity, and cognitive functions in older adults: multicenter study in Sri Lanka

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This study was aimed to examine the prevalence and associations between multimorbidity, polypharmacy, Falls Risk Increasing Drugs use (FRIDs), Anti Cholinergic Burden (ACB), and adverse health outcomes in older adults attending medical clinics. A cross-sectional study was conducted among 704 older adults attending medical clinics in four tertiary care hospitals. The mean (SD) age of study participants was 73 (5.5) years, and the majority were females (58.7%). Patients 305 (43.5%) reported at least one fall after age of 65 while 220 (31.3%) reported falls in the previous 12 months and 90 (12.8%) reported recurrent falls. The prevalence of multimorbidity was 77.4% while polypharmacy was seen in 51.2%. The use of at least one FRID was seen in 70.5% patients while higher ACB was seen in 5.4%. Multimorbidity, polypharmacy, use of FRIDs and ACB were not associated with negative health outcome ($p > 0.05$). Polypharmacy, however, was associated with high ACB ($p < 0.001$). This study highlights a high prevalence of multimorbidity and polypharmacy among older people in clinical settings. However, negative associations between drugs and multimorbidity with adverse health outcomes indicate that these relationships are complex, potentially influenced by other factors such as poor drug compliance, which can lead to falls.

Keywords Falls, Multimorbidity, Older adults, Polypharmacy, Sri Lanka

Abbreviations

ACB	Anti cholinergic burden
ADL	Activities of daily living
BI	Barthel index
CI	Confidence interval
CNTH	Colombo North Teaching Hospital
CSTH	Colombo South Teaching Hospital
FRIDs	Falls risk increasing drugs
MLR	Multiple logistic regression
NHG	National Hospital Galle
OR	Odds ratio
S.E.	Standard error
SD	Standard deviation

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SPSS	Statistical package of social sciences
TH	KDU-Teaching Hospital-Kotelawala Defense University
USD	United States dollars
WHO	World Health Organization

Falls are prevalent among older adults, and they lead to increased morbidity, mortality and health care cost[1,2]. Nearly one third of older population living in the community experience falls at least once a year while one sixth of them experience recurrent falls[3]. With the expansion of older adult population, falls have become a major public health concern.

Falls are associated with a multitude of factors including medications, comorbidities, impaired mobility, female gender and advanced age[4]. Apart from falls, multimorbidity and polypharmacy are linked with physical dependence and cognitive impairment[5,6].

Multimorbidity, defined as the presence of two or more chronic health conditions at a given time[7], is common among older adults. Multimorbidity leads to complex interactions between diseases and polypharmacy. Furthermore, multimorbidity is associated with high risk of recurrence of falls[8]. Apart from multimorbidity, polypharmacy, the use of five or more drugs[9], is also associated with increased risk of recurrent falls[10,11]. A systematic review reported that polypharmacy can cause 1.5 to 2 times higher risk of recurrent falls[12]. The irrational use of multiple drugs is referred to as inappropriate polypharmacy and attempts must be made to avoid this prescribing habit[13]. Medications such as antihypertensives, diuretics, antidiabetics, psychotropics, hypnotics, antihistamines and several cardiovascular drugs have been recognised as Falls Risk Increasing Drugs (FRIDs) and a study from Pennsylvania in the USA found that multiple FRIDs are an independent risk factor of falls[14]. A Japanese study discovered that taking one or more medications increased the risk of falls during the next three years. This study also reported that even a single FRID in the prescription is associated with an increased risk of falls[15]. Deprescribing FRIDs was an effective strategy in reducing the risk of falls and the greatest benefit was observed with the withdrawal of cardiovascular drugs[16].

Many medications used to treat chronic medical conditions in old age have anticholinergic properties. These drugs exert adverse outcomes by increasing the anticholinergic burden (ACB) which is estimated by adding the ACB of individual drugs in the prescription. Wong et al. have shown an increased risk of falls per unit increase of ACB score[17]. Furthermore, PP with greater ACB is positively associated with 5-year mortality and frailty[18]. Many studies have demonstrated the significant association of polypharmacy and increased ACB with the incidence and recurrence of falls, particularly in frail older adults[19,20]. Besides, several studies have demonstrated the effect of multiple drug use with ACB in cognitive impairment and progression of neurodegenerative disease[21,22].

Studies regarding the outcomes of multimorbidity and polypharmacy on the risk of falls among older adults are scarce in Sri Lanka. According to a study done in Northern Sri Lanka, prevalence of polypharmacy among older adults was 58.7%[23]. A study conducted in a tertiary care facility in Sri Lanka assessed the modifiable risk factors linked to falls in older adults and revealed a strong connection between long-term multiple medication use and hospital admissions due to falls[24]. Another Sri Lankan study demonstrated the use of antihypertensive medication or at least one long-term medication was associated with an increased risk of both falls and recurrent falls in older adults[25]. We were unable to find studies that examined the influence of ACB and FRIDs on the incidence of falls among older adults in Sri Lanka.

In Sri Lanka, older adults including those with multimorbidity are being cared in busy clinical settings, not permitting adequate time to review prescriptions. Furthermore, there is a significant gap in geriatrics training for healthcare professionals, who often do not recognize the importance of deprescribing inappropriate medications and the harmful ramifications of PP, especially in older patients.

This study was aimed to investigate the association of multimorbidity, polypharmacy, use of FRIDs and ACB with falls, physical activity and cognitive function in older adults attending medical clinics in Sri Lanka.

Methods

Study design, setting and sample

The study was conducted as a multi-center cross sectional study in medical clinics of four tertiary care centers: National Hospital, Galle (NHG), Colombo South Teaching Hospital (CSTH), Colombo North Teaching Hospital (CNTH) and Teaching Hospital- Kotelawala Defense University (TH-KDU). These were four major tertiary care hospitals, located in highly populated two provinces in Sri Lanka. These four centers were specifically selected since they deliver health care service to a large and diverse population of older adult patients in the country.

The minimum required sample size was determined using the formula $n = p\,(1-p) \times z^2/d^2$, based on the falls prevalence of 34.3% among community-dwelling older adults in the Galle District, Sri Lanka[25,26]. The sample size for each site was allocated proportionally, considering the number of clinic registrants aged 65 years and above.

Data were collected from a total of 720 older adults across all four sites. However, 16 participants were excluded from the analysis due to incomplete questionnaires, resulting in a final sample of 704 individuals. Participants were recruited consecutively from each center, aged 65 years or more, attending two or more clinic visits within the last six months between August 2021 and August 2022.

In order to retain the external validity of data, only those who did not consent to participate were excluded. When patients admitted that they have recall limitations, collateral information was collected from caregivers who accompanied those patients. This was done in nearly 90% of patients, especially those with physical and mental function impairment.

Data collection and tools

Demographic, socioeconomic and anthropometric measurements were obtained using an interviewer administered questionnaire by trained data collectors.

Furthermore, multimorbidity and current medications, particularly FRIDs, and ACB score were recorded. Physical activity based on activities of daily living (ADL) and cognitive function were assessed using the 10 item Barthel Index (BI), Sinhala version[27] and Mini Cog test, which was only a content validated version[28], respectively. The Mini Cog test assessed domains including cognitive function, memory, language, comprehension, visual motor skills and executive functions and further provides a visible record of both normal and impaired performance[29].

A detailed analysis of falls, including any falls after the age of 65 years and falls during the previous 12 months was done. Recurrent falls were defined as two or more falls during the previous 12 months[30]. while multimorbidity was defined as the presence of two or more diseases currently. Polypharmacy was defined as consuming five or more medications including supplements and over-the-counter medications. FRIDs were enlisted using the STOPP Fall tool which included antihypertensives, antiarrhythmics, anticholinergics, antihistamines, antipsychotics, antidepressants, opioids and non-steroidal anti-inflammatory agents etc[31]. The ACB score of current medications was calculated using the online calculator (www.acbcalc.com) and considering all medications[17].

Statistical analysis

Means (SD) or frequency (%), was used to describe the data. Associations between the prevalence of falls and polypharmacy or multimorbidity using Chi square test. Physical activity based on Activities of daily livings (ADL), ACB and cognitive function were compared with polypharmacy, multimorbidity, and the use of FRIDs using either independent t-test or one way ANOVA.

Statistical analyses were performed using Statistical Package of Social Sciences (SPSS) version 26.0. The P value was adjusted for multiple comparisons by Bonferroni method.

Results

The mean (SD) age of the participants were 72.6 (5.5) years and majority were females 58.7%. The mean (SD) BMI of the study participants was 23.2 (4.2) kg/m^2. Mean (SD) BI and Mini Cog scores were 91.4 (16.3) and 3.4 (1.6) respectively. After 65 years of age, 305 (43.5%) of older adults had fallen at least once, and 220 (31.3%) had fallen in the previous 12 months. Of those who have fallen in the past 12 months, recurrent falls have been experienced by 90 (12.8%) older people. The prevalence of multimorbidity and polypharmacy in the study sample was 546 (77.4%) and 367 (51.2%) respectively. (Table 1).

Characteristic	Subcategory	Mean (standard deviation) or frequency (%)
Falls related information		
Falls after 65 years		305 (43.5%)
Falls in the previous 12 months		220 (31.3%)
Recurrent falls		90 (12.8%)
Number of chronic health conditions	None	37 (5.3%)
	One	125 (17.8%)
	Multimorbidity ((≥ 2)	546 (77.4%)
Number of current medications	None	83 (11.8%)
	One	75 (10.7%)
	Two	151 (21.4%)
	Three	181 (25.7%)
	Four	125 (17.8%)
	Polypharmacy (≥ 5)	367 (51.2%)
Number of fall risk increasing drugs prescribed	None	208 (29.5%)
	One	368 (52.4%)
	Two	67 (9.5%)
	Three or more	60 (8.6%)
Number of drugs with anti-cholinergic burden prescribed	One	163 (23.2%)
	Two	57 (8.1%)
	Three or more	34 (5.4%)
Other characteristics		Mean (SD)
Age (years)		72.6 (5.5)
Female gender		414 (58.7%)
Barthel index score		91.4 (16.3)
Mini Cog test score		3.4 (1.6)

Table 1. Descriptive data of 706 study participants.

Characteristics		Presence of multimorbidity		*P* value *
		No Frequency (%)	Yes Frequency (%)	
History of falls after age of 65	Yes	97 (25%)	301(75%)	0.328
History of falls in the previous 12 months	Yes	114 (23%)	370(76%)	0.612
History of recurrent falls	Yes	141 (22%)	473 (77%)	0.938

Characteristics	Presence of multimorbidity		P value**
	No Mean (Standard Deviation)	Yes Mean (Standard Deviation)	
Physical activity—Barthel Index score	92.7 (13.6)	91.2 (16.8)	0.39
Cognitive function—Mini cognitive test score	3.4 (1.8)	3.1 (1.6)	0.10

Table 2. Association between multimorbidity and falls, physical activity and cognitive function ($n = 706$). *Statistical test: Association of multimorbidity with occurrence of falls and recurrent falls was tested using Chi square test. **Statistical test: Association of multimorbidity with physical activity and cognitive function was tested using independent t test.

Characteristics		Polypharmacy		*P* value*
		No Frequency (%)	Yes Frequency (%)	
Had falls after age of 65	Yes	202(50.7)	196(49.2)	0.404
Had falls in the previous 12 months	Yes	245(50.6)	239(49.3)	0.234

Characteristics	Polypharmacy		P value**
	No Mean (SD)	Yes Mean (SD)	
Age	72.4(5.5)	72.7(5.5)	0.534
Total anti-cholinergic burden score	0.19(0.56)	0.98(1.07)	< 0.001
Physical activity—Barthel Index score	92.0 (19.4)	90.8 (12.3)	0.21
Cognitive function—Mini cognitive test score	3.4 (1.7)	3.4 (1.6)	0.98

Table 3. Association between polypharmacy and falls, anti-cholinergic burden, physical activity and cognitive function ($n = 706$). *Statistical test: Association of polypharmacy with occurrence of falls and recurrent falls was tested using Chi square test. **Statistical test: Association of polypharmacy with age, total ACB, physical activity and cognitive function was tested using one way ANOVA test.

Of the participants, a total of 77% of the participants had multimorbidity, with hypertension being the most common condition, affecting 74.1% of the group. Additionally, 54.7% had dyslipidaemia, and 53.6% were diagnosed with diabetes mellitus. Ischemic heart disease was present in 31% of the participants, while 13.9% had osteoarthritis. Chronic kidney disease and a history of malignancy were reported in 2.6% and 1.6% of the participants, respectively.

Although multimorbidity, polypharmacy and use of FRIDs were prevalent, no significant association was found between them and falls. Furthermore, physical activity and cognitive function were not different between those with and without multimorbidity. Similarly, polypharmacy or the use of FRIDs was not associated with poor physical activity or cognitive functions. However, the presence of polypharmacy has resulted in a significant increase in the total ACB burden < 0.001 in this study population (Tables 2, 3 and 4).

A quarter of patients were on one drug with anticholinergic properties while another 12% were on more than one drug associated with anticholinergic properties. The total ACB, however, did not show a significant association with falls, physical ADL or mental functions (Table 5).

Discussion

This multi-center study involving 704 older adults attending medical clinics revealed the prevalence of multimorbidity, polypharmacy, use of FRIDs and ACB and their associations with falls, physical activity and cognitive function. Nearly a third of older adults in this study group reported at least one fall within the previous year and nearly half of them reported recurrent falls. Despite the high prevalence of multimorbidity and polypharmacy, no significant association was observed between them and falls, physical activity or cognitive function. Although 70% were on at least one FRID, the number of FRIDs did not show a significant association with falls, physical activity level, or cognitive function.

The high prevalence of multimorbidity and polypharmacy observed in this study is concordant with previous studies on this subject. The prevalence of polypharmacy among older patients in Poland was 53.5% which was primarily attributed to multimorbidity[32]. A recent systematic review across 30 countries revealed that the

Characteristics		FRIDs* Category			*P* value**
		No FRIDs Frequency (%)	One FRID Frequency (%)	≥ Two FRIDs Frequency (%)	
History of falls after age of 65	Yes	84 (27.5)	162 (52.9)	60 (19.6)	0.45
History falls in the previous 12 months	Yes	61 (27.7)	114 (51.8)	45 (20.5)	0.49
History recurrent falls	Yes	24 (26.7)	44 (48.9)	22 (24.4)	0.23

Characteristics	FRID Category			
	No FRIDs Mean (Standard Deviation)	One FRID Mean (Standard Deviation)	≥ Two FRIDs Mean (Standard Deviation)	P value***
Physical activity—Barthel Index score	91.45 (19.27)	90.02 (14.47)	89.69 (16.43)	0.19
Cognitive function—Mini cognitive test score	3.28 (1.73)	3.11 (1.59)	3.01 (1.68)	0.210

Table 4. Association between fall risk increasing drugs with falls, physical activity and cognitive function ($n = 706$). *FRIDS: Falls Risk Increasing Drugs. **Statistical test: Association of FRIDs with occurrence of falls and recurrent falls was tested using Chi square test. ***Statistical test: Association of FRIDs with physical activity and cognitive function was tested using independent t test.

Characteristics		ACB*			*P* value**
		No medication with ACB Frequency (%)	One Medication with ACB Frequency (%)	≥ Medications with ACB Frequency (%)	
Had falls after age of 65	Yes	247(62)	98(24)	53(13)	0.51
Had falls in the previous12 months	Yes	295 (61)	121(25)	67(13)	0.80
Recurrent Falls	Yes	387(63)	149 (24)	77 (12)	0.18

Characteristics	No medication with ACB Mean (SD)	One Medication with ACB Mean (SD)	≥ 2 Medications with ACB Mean (SD)	P value***
Physical activity—Barthel Index score	91.07 (17.69)	91.72 (14.15)	91.98 (13.94)	0.844
Cognitive function–Mini cognitive test score	3.44 (1.64)	3.31 (1.74)	3.41 (1.52)	0.686

Table 5. Association of ACB with falls, ADL, and mental function ($n = 706$). *ACB: Anti-Cholinergic Burden. **Statistical test: Association of ACB with occurrence of falls and recurrent falls was tested using Chi square test. ***Statistical test: Association of ACB with physical activity and cognitive function was tested using independent t test.

prevalence of multimorbidity and polypharmacy ranged from 20–93.1% and 5–85%, respectively in clinical setting and 28.2%–61.4% and 3.6%–31.9% in the community setting[33]. Many studies have linked polypharmacy and multimorbidity with increased incidence of falls and recurrent falls in older adults[5,34]. Moreover, studies have found a close link between multimorbidity to a decline in functional skills and cognitive functions in elderly[35]. Likewise, studies have shown a notable connection between polypharmacy and the decline in physical performance and cognitive functions among older adults[20]. In a Brazilian study, polypharmacy was not independently related to the frequency of falls in older adults but became significant when adjusted to FRID use[36]. Similarly in Rotterdam study falls in older adults were associated with the use of polypharmacy, but only when at least one established FRID was part of the daily regimen[37]. A Japanese study revealed that even a single category of FRIDs could increase the risk of falls, with antihypertensives being the most common type[38]. Furthermore, several studies have reported correlation between polypharmacy and FRIDs with poor physical activity level and cognitive function[39–41].

Polypharmacy was observed in more than 50% of the participants in the study, yet this research did not establish a direct link between falls and polypharmacy. A systematic review that examined polypharmacy and its health outcomes, revealing conflicting results about the relationship between polypharmacy and falls in older adults, supported this conclusion. They observed that studies lacking adequate adjustment for confounding variables were more likely to demonstrate a positive correlation between polypharmacy and adverse outcomes, such as falls[42]. Another systematic review analyzing 220 articles found that taking cardiac medications was a protective factor against falls in older adults[43]. In our study, the majority of older adults (70.5%) were on at least one medication described under FRIDs. Zidoru et al. have also demonstrated that the prevalence of FRIDs is higher among older adults[44]. In the present study, increased number of FRIDs did not show any relationship with occurrence of falls, physical activity or cognitive function. Castaldi et al. have reported similar findings in relation to the association between the number of FRIDs and fall occurrence[45]. This is further supported by IMPROVE FALL trial which demonstrated that deprescribing FRIDs did not provide any advantage in fall reduction[46]. When medications are assessed individually rather than taking the total number of FRIDs, some studies were able to demonstrate associations between individual FRIDs with fall occurrence, physical activity and cognitive function[47,48] and in this analysis we did not investigate the relationship between individual FRIDs and their different dosage with falls or physical and mental functions. A German follow-up study of older persons

with cognitive impairment discovered no link between potentially inappropriate medication or multimorbidity and falls, supporting the current study's negative association[49].

Although not evident in our analysis, the use FRIDs and ACB have been linked with risk of falls and cognitive and physical impairment. A systematic review described a relationship between moderate to high ACB and falls in eight studies[50]. Furthermore, data from literature including a meta-analysis by Pieper et al. found that anticholinergic drug use is associated with an increased risk of dementia and cognitive decline[51]. In a similar manner, studies have revealed a relationship between anticholinergic medications and decreased physical performance as well as cognitive impairment[52] Furthermore, Won et al. have described a positive association between polypharmacy and increased ACB[53] and our data also supported this.

In general, one would expect multimorbidity and polypharmacy to have a negative impact on physical and cognitive function of older adults and the conflicting results across studies suggest that these relationships are more complex and may be influenced by other factors. In this study, falls were self-reported, and it is possible that patients may have underreported falls because of recall limitations. Further, poor adherence to medications, particularly those with adverse effects such as FRIDs and medications with high ACB, is common among older adults. These may have contributed to the negative results we observed in this study.

Strengths and limitations

This study involved several study centers across the country, enhancing the external validity of the findings. The cross-sectional design of the study, however, limits the observation of real time associations between these variables. Cognitive function was assessed using the Mini-Cog and more comprehensive assessments such as Mini Mental score could have provided a more accurate information. For data collection, we had to rely on recall. The study population being older adults may have impaired recall. We minimize this problem by obtaining collateral details from family members present with the patient during the clinic visit, as well as reviewing their medical records.

Conclusion

This study highlights a high prevalence of multimorbidity and polypharmacy among older adults in clinical settings but found no significant associations between them and falls, physical activity or cognitive function. Total number of medications including FRIDs and drugs with high ACB also did not show an association with negative health outcomes. Future research should focus on longitudinal studies to further interpret the relationships between individual drug classes of FRIDs and ACB and adverse outcomes. Broader research is required to develop effective deprescribing strategies to mitigate medication-related risks and improve health outcomes of older adults.

Data availability

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

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Author contributions

W.Z. contributed to design, data collection, data analysis, and manuscript drafting and revision. N.R. involved in design, data analysis and preparing tables. S.M. was involved in data analysis and manuscript drafting. A.L., D.P., S.S., P.J., and C.M. contributed to data collection, guided quantitative data analysis, and manuscript revision. S.L.

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Declarations

Competing interests
The authors declare no competing interests.

Ethics approval
Ethical clearance for this study was obtained from Ethics Review Committee, Faculty of Medicine, University of Ruhuna, Sri Lanka (Reference number; 2021.P.075). All methods were carried out in accordance with relevant guidelines and regulations.

Patient consent statement
All participants provided informed consent to participate, collected via an information sheet and consent form.

Additional information
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