## **Original Article**

# **Polypharmacy among the Elderly**

Seyed Reza Hosseini, Ali Zabihi<sup>1</sup>, Seyedeh Roghayeh Jafarian Amiri<sup>1</sup>, Ali Bijani

Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, <sup>1</sup>Nursing Care Research Center, Babol University of Medical Sciences, Babol, Iran

**Introduction:** Older people are at risk for polypharmacy due to multiple chronic diseases. Considering the lack of information in this regard, the aim of this study was to investigate the state of polypharmacy among the elderly in the city of Amirkola in northern part of Iran. Materials and Methods: This descriptive/ analytical cross-sectional study is a part of Amirkola Health and Aging Project that was conducted on 1616 individuals aged 60 years and over. The data about medications were gathered through interviews and observation of prescriptions and medications consumed by patients. The data were analyzed by SPSS software version 18, and  $P \leq 0.05$  was regarded significant. **Results:** In this study, 1616 individuals including 883 men (54.6%) and 733 women (45.3%) were investigated. The average age of individuals was  $69.37 \pm 7.42$ . Among the investigated individuals, 526 including 368 men (41.7%) and 158 women (21.6%) consumed no medications. The prevalence of polypharmacy in this study was 23.1%, which was 32.7% in women and 15.2% in men (odds ratio = 1.51, 95%confidence interval: 1.10–1.93). The most prevalent group of medications used in both genders was cardiovascular drugs. Conclusions: Regarding the considerable prevalence of polypharmacy among the elderly, especially in aged women, serious efforts are required to manage polypharmacy. Provision of educational programs for physicians, personnel of pharmacies, and the staff of health-care centers in order for appropriate and safe consumption of medications in aged people is absolutely necessary.

**Keywords:** Chronic disease, medication consumption, polypharmacy, the elderly

## **INTRODUCTION**

O ccurrence and concurrency of chronic diseases increase with age, and therefore, the amount of medication use increases correspondingly.<sup>[1,2]</sup> A serious problem in pharmacotherapy in elderly patients is the concurrency of consumption of several medications. Polypharmacy is a state in which five medications or more are consumed concurrently (regardless of dosage form and duration of consumption)<sup>[3-5]</sup> which leads to decreased quality of life, physical problems, increased drug interactions, side effects, and medical problems<sup>[6,7]</sup> and also increases the cost of treatment.<sup>[8]</sup> Moreover, polypharmacy increases the incidence of fall, number and rate of hospital stay, length of stay, frequent hospitalizations, and the death rate in elderly population.<sup>[9]</sup>

Access this article online				
Quick Response Code:	Website: www.jmidlifehealth.org			
	website. www.jinidineneattr.org			
	DOI: 10.4103/jmh.JMH_87_17			

The proper medications for aged people are prescribed according to the history of disease, drug resistance, physical and mental health, physical ability, memory, and family support.<sup>[10]</sup> It seems that the risk of drug complications and interactions is more due to pharmacokinetic or pharmacodynamic changes caused by age-related physiological changes in elderly people. Inattention to different metabolic changes of medications such as their absorption, distribution, and excretion in elderly people's body compared to middle-aged people is regarded as an important factor in incidence of unwanted side effects in elderly people.<sup>[11]</sup>

Address for correspondence: Dr. Ali Zabihi, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran. E-mail: zabihi\_alii@yahoo.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Hosseini SR, Zabihi A, Jafarian Amiri SR, Bijani A. Polypharmacy among the elderly. J Mid-life Health 2018;9:97-103.

Different factors affect polypharmacy in elderly people including age, gender, level of education, frequent visit to doctors, and types and number of diseases.<sup>[12]</sup> Aging and undergoing different diseases increase the need to consume medications in a way that in diabetic patients and patients with coronary artery, the number of medications consumed may reach up to 6–9. Visiting different physicians and hospitalization increases the risk of polypharmacy because new medications may be prescribed for the patient. Low levels of literacy and information in patients are one of the most common causes of polypharmacy.<sup>[13,14]</sup> Moreover, in most of the studies, polypharmacy in women was more than in men.<sup>[15,16]</sup>

Comorbidities require consumption of more medications.<sup>[17]</sup> The results of a study showed that elderly people with several comorbidities are more exposed to the risk of polypharmacy. The average number of diseases in aged people was 7.7, and the average number of medications consumed was 4.9, inasmuch as the number of medications consumed and prevalence of polypharmacy was 5.2 (51%) in hypertension, 5.6 (58%) in hyperlipidemia, 5.8 (61%) in myocardial infarction, 5.6 (54%) in diabetes, 5.1 (52%) in dementia, and 7 (73%) in depression.<sup>[18]</sup> Regarding the high prevalence of polypharmacy, its importance, and its adverse effects on the elderly's health and considering the fact that there has not been a comprehensive study on polypharmacy in the elderly in Iran, the present study aims at investigating the state of polypharmacy among the elderly in the city of Amirkola.

## MATERIALS AND METHODS

The present study is a part of Amirkola Health and Aging Project (registry number: 892917)<sup>[19]</sup> that is being conducted as a cohort study on all people aged 60 years and older in the city of Amirkola in north of Iran since 2011. Amirkola's population is 26,232 and about 2200 of them are over 60 years old. The city of Amirkola has two health care centers in which the list of all elderly people can be found. Elderly people are invited to participate in and are given the required information about the project through phone calls and home visits. The required information are gathered by a trained person using standard questionnaires. Pharmaceutical information including number, type, and duration of consumption are gathered through self-report as well as observing the patient's consumed medications and prescriptions. The concurrent use of five or more medications at least for 1 day is regarded as polypharmacy. Dosage form and duration of consumption are not considered in counting the numbers.<sup>[3-5]</sup> Medications that have been consumed periodically are also added to the number of medications. The type of drug category has no effect in assessing polypharmacy. The prevalence of consumption of different drug categories is also investigated.

The presence or absence of chronic diseases in an aged person was determined by asking him/her if he/ she has ever been told by a doctor that he/she has a certain disease. If the aged person reported that if he/ she had a specific health problem, his/her medical records were investigated and if he/she had no medical records, the answer to the question was considered negative. Moreover, in this study, the presence of some diseases and disorders such as cognitive impairment, depression, thyroid disorders, hypertension, and diabetes was determined through questionnaire, examination, and laboratory tests. Osteoporosis was also diagnosed through bone densitometry.

The Mini–Mental State Examination (MMSE) was used to investigate the cognitive state. Maximum and minimum MMSE score is 30 and 0, respectively. If a person obtains a score of 25 or more, he or she is considered normal. Scores of 21–24, 10–20, and <9, respectively, indicate a mild, moderate, and severe cognitive impairment.<sup>[20,21]</sup> In a study in Iran, a cutting point of 22 gave a sensitivity of 90% and specificity of 93.5%.<sup>[22]</sup> The same cutting point was used in the present study.

To assess depression, 15-item version of Geriatric Depression Scale which is a yes/no questionnaire was used. The clinical validity of the scale is proved. In this scale, the patients are divided into several groups based on their obtained scores. A score of 0–4 was considered as normal, 5–8 as mild depression, 9–11 as moderate depression, and 12–15 as severe depression.<sup>[23]</sup> The psychometric properties of the Persian version are verified.<sup>[24]</sup>

The collected data were statistically analyzed after they were entered into SPSS Statistics version 18 and after running different tests including Chi-square test, independent samples *t*-test, and logistic regression. Logistic regression model is used to investigate affective variables on polypharmacy.  $P \le 0.05$  was considered statistically significant.

## RESULTS

In the present study, 1616 individuals including 883 men (54.6%) and 733 women were investigated. The average age of participants was  $69.37 \pm 7.42$  (70 ± 7.7 in men and  $69.7 \pm 7.00$  in women). Among all participants, 1377 individuals (85.2%) were married, 65.8% were illiterate, 82.2% possessed insurance, 6.6% lived alone, 6.6% were unemployed, 39.7% were

homemakers, 21.7% were retired, and 31.1% were employed. A number of 1434 individuals (88.8%) had comorbidities. Moreover, MMSE was normal in 1103 participants (68.4%), and 700 individuals had symptoms of depression.

In this investigation, 526 individuals (32.54%) were consuming no medications, while 23.1% of the participants had polypharmacy which was significantly more prevalent in women (32.7%) than in men (15.2%)(P = 0.007) [Figure 1]. The average age of people without polypharmacy was  $69.92 \pm 7.54$  and the average age of people with polypharmacy was  $69.66 \pm 7.00$ , which had no significant difference. The average number of medications consumed in people without polypharmacy was  $1.38 \pm 1.45$  and in people with polypharmacy was  $6.63 \pm 1.60$ . The percentage of people with comorbidities was 88.8. The average number of comorbidities in people with polypharmacy  $(4.23 \pm 1.89)$ was significantly more than in people Without it (2.26  $\pm 1.79$ ) (P = 0.000). The average MMSE score in the group with polypharmacy was  $24.74 \pm 4.21$  and in the group without polypharmacy was  $25.57 \pm 9.55$ , which means that there was no significant difference between the two groups.

The most prevalently consumed group of medications in both genders was cardiovascular-hypertension group, inasmuch as 35.4% of men and 50.05% of women used it. The second most prevalently consumed medications were analgesic, anti-inflammatory, and rheumatic medications, inasmuch as 32.7% of men and 46.1% of women used this group of medications. The third most prevalently consumed group of medications was antilipid medications in men (13.6%) and gastrointestinal medications in women (27.1%) [Figure 2].

Among the chronic comorbidities, depression, hypertension, and heart diseases (angina, myocardial infarction, and heart failure) were the most prevalent diseases among the participants. Moreover, polypharmacy increases significantly with the presence

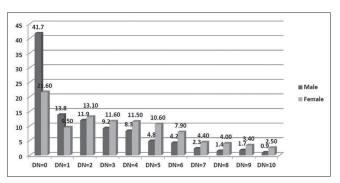


Figure 1: Percentage of drug users in terms of drug number (DN: Drug number) and sex in the elderly of Amirkola

of comorbidity. Heart diseases, diabetes, and pulmonary diseases, respectively, had the most number of polypharmacy (P = 0.000) [Table 1].

Among the investigated variables, being married, being in the age group of 60–69 years and 75–79 years, having comorbidity, being female, being retired, and being employed apart from homemakers had a significant role in increasing polypharmacy [Table 2].

#### **DISCUSSION**

Results of the present study indicate the relatively high prevalence of polypharmacy (23.1%) in people aged 60 years and older. Other cross-sectional studies showed that this amount was 39.4 in Italy,<sup>[25]</sup> 32.5 in Taiwan,<sup>[26]</sup> and 29.5 in New Zealand.<sup>[27]</sup> Moreover, another study in Italy indicated that the prevalence of polypharmacy was 46% in the elderly aged 65 years and older.<sup>[28]</sup> The results of Blozik *et al.*'s study also showed that, like in our study, the incidence of polypharmacy (17%) and consumption of potentially inappropriate medicines (21%) were high in the elderly of Switzerland and were followed by consequences such as hospitalization, decreased performance, and

Table 1: Distribution of comorbidities and the								
percentage of polypharmacy associated with each disease								
Comorbidity	n (%)	Polypharmacy, n (%)	Р					
Diabetes								
Yes	378 (23.4)	68 (44.4)	0.000					
No	1237 (76.5)	206 (16.7)						
Hypertension								
Yes	667 (41.3)	258 (38.7)	0.000					
No	948 (58.6)	116 (12.2)						
Hypothyroidism								
Yes	67 (4.1)	28 (41.8)	0.000					
No	1548 (95.8)	346 (22.4)						
Myocardial infarcti	on							
Yes	91 (5.6)	49 (53.8)	0.000					
No	1524 (94.3)	325 (21.3)						
Angina								
Yes	285 (17.6)	145 (50.9)	0.000					
No	1330 (82.4)	229 (17.2)						
Heart failure								
Yes	38 (2.3)	23 (60.5)	0.000					
No	1577 (97.6)	351 (22.3)						
Arthritis								
Yes	316 (19.5)	107 (33.9)	0.000					
No	1299 (80.4)	267 (20.6)						
Depression								
Yes	700 (43.3)	224 (32.0)	0.000					
No	912 (56.4)	150 (16.4)						
Pulmonary disease								
Yes	121 (7.4)	49 (40.5)	0.000					
No	1494 (92.5)	325 (21.8)						

death.<sup>[4]</sup> The higher prevalence of polypharmacy in most of other studies might be because the age of seniority was considered over 65 years. On the other hand, the incidence of polypharmacy has obviously increased in the population, especially the elderly, during recent decades. Factors that caused this increase might be enhanced life expectancy, presence of chronic diseases that require long-term treatment, greater use of health services, and production of new medications.

In the present study, polypharmacy was significantly more prevalent in elderly women (32.7%) than in elderly men (15.2%) (P = 0.007). In most of other studies, likewise, the risk of polypharmacy in elderly

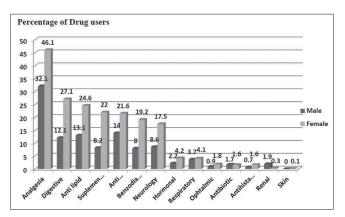


Figure 2: Percentage of drug users in terms of drug and gender in the elderly of Amirkola

women was more than in elderly men.[27-31] Only in Slabaugh et al.'s study, polypharmacy in men was more than in women<sup>[25]</sup> which was due to higher prevalence of chronic diseases in men. In the present study, the percentage of men and women who consumed no medications was, respectively, 41.7% and 21.6%. In Nobili et al.'s study, too, 13.3% of men and 11.1% of women consumed no medications.<sup>[28]</sup> In the present study, the average number of consumed medications in people without polypharmacy was  $1.38 \pm 1.45$  and in people with polypharmacy was  $6.63 \pm 1.60$ . In a similar study, the average number of consumed medications in the elderly without polypharmacy was  $2.6 \pm 1.2$  and in the elderly with polypharmacy was  $(7.1 \pm 2.1)$ .<sup>[32]</sup> Therefore, it is important to educate about the correct use of medications by health professionals and nurses in the families of the elderly, especially elderly women.

In the present study, the average age of participants without polypharmacy was  $69.92 \pm 7.54$  and the average age of participants with polypharmacy was  $69.66 \pm 7.00$ , which had no significant difference. However, the age group of 65–69 years and 75–79 years was significantly associated with increase of polypharmacy (P = 0.005 and P = 0.011). In other studies, polypharmacy consumption pattern was associated with increase of age.<sup>[25,28,33]</sup> In a study in New Zealand, the risk of polypharmacy and hyperpolypharmacy was more in the age group of 80–84 years.<sup>[27]</sup> Moreover, in a study in Taiwan, patients with

	-				
Investigated variables	Polypharmacy, n (%)	OR	OR 95% CI		Р
			Lower	Upper	
Marital status					
Married	21.2	Reference			
Single	34.5	0.596	0.444	0.903	0.015
Age					
60-64	20.2	1.480	1.027	2.124	0.036
65-69	24.4	1.650	1.119	2.427	0.012
70-74	37.6	1.254	0.812	1.931	0.309
75-79	22.8	2.052	1.208	3.486	0.008
$\geq 80$	40.5	0.588	0.222	1.555	0.285
Gender					
Male	15.2	Reference			
Female	32.7	1.515	1.100	1.937	0.007
Comorbidity					
Yes	26.00	1.668	1.547	1.800	0.000
No	0.6	Reference			
Occupational status					
Unemployed	38.9	Reference			
Housewife	31.9	1.461	0.421	1.089	0.039
Retired	19.6	1.638	0.324	0.959	0.011
Employed apart from homemakers	10.9	1.216	0.203	0.603	0.362
Unemployed	30	1.947	0.188	5.117	0.011

 Table 2: Odds ratio and 95% confidence interval of variables effective on polypharmacy in the elderly of the city of Amirkola

OR: Odds ratio, CI: Confidence interval

the highest percentage of polypharmacy were in the age group of 75–84 years.<sup>[26]</sup> According to studies that were mentioned, polypharmacy in the elderly has increased with age and it can be said that since the number of chronic comorbidities and other problems of the elderly increases with age, the incidence of polypharmacy will increase consequently.

As reported by studies conducted so far, polypharmacy in the elderly is related to the presence of chronic diseases.<sup>[17,29,34]</sup> Comorbidities require consumption of more medications. Polypharmacy causes drug interactions, adverse drug reactions, decreased patient compliance, and personal and social costs and it affects the quality of life as well.<sup>[17]</sup> In our study, too, it was shown that comorbidities increase with age, and consequently, the chance of occurrence of polypharmacy increases.

In a study, 61.1% of aged patients suffered from more than three chronic diseases, inasmuch as the average number of chronic diseases was 2.8 and was related to polypharmacy.<sup>[35]</sup> The most prevalent diseases in this study were hypertension (75.3%), depression (45.5%), and dementia (39.4%). Moreover, in Sabzwari et al.'s study, the most prevalent chronic diseases among the elderly included diabetes, hypertension, heart disease, and depression.<sup>[36]</sup> In another cross-sectional study by Vyas et al. in the United States, the amount of polypharmacy was variable from 7.2% in patients with pulmonary disease to 64.1% in those who had three concurrent diseases.<sup>[37]</sup> In the present study, too, chronic comorbidities including depression (43.2%), hypertension (41.3%), and heart diseases (25.5%) were the most prevalent diseases in the elderly. Moreover, polypharmacy increased significantly with the presence of comorbidities, and the highest incidence of polypharmacy was, respectively, in patients with heart disease, diabetes, and pulmonary disease (P = 0.000). Furthermore, in the present study, polypharmacy had no significant relation with some chronic diseases such as liver and kidney diseases, peptic ulcer, and hyperthyroid.

study. the most widely consumed In our group of medications in both genders was the cardiovascular-hypertension group, inasmuch as 35.4% of men and 50.05% of women consumed it. The second most prevalently consumed medications were analgesics, anti-inflammatory, and rheumatic medications, inasmuch as 32.7% of men and 46.1% of women consumed this group. Finally, the third most widely consumed medications were antilipid medications in men (13.6%) and gastrointestinal medications in women (27.1%). Like our study, in Nobili et al.'s study, too, cardiovascular medications (66%) were the most prevalently consumed

medications in the elderly, and after that, gastrointestinal medications (42%), antibiotics (41%), and medications for musculoskeletal system (38%) were the most consumed medications.<sup>[27]</sup> In other studies also, the increase of polypharmacy was followed by increased consumption of antidepressant, antidiabetic, and heart medications.<sup>[28,38]</sup> In Sabzwari *et al.*'s study, the most prevalently consumed group of medications in polypharmacy included psychoactive, cardiovascular, nonsteroidal anti-inflammatory, and oral hypoglycemic medications.<sup>[36]</sup> In another study, polypharmacy in European countries was associated with consumption of antidepressant, antithrombotic, anticholinergic, and antipsychotic medications.<sup>[39]</sup>

In the present study, marital status, being retired, or being employed apart from homemakers was significantly associated with the increase of polypharmacy. In Carvalho *et al.*'s study, higher income and being employed were directly connected to polypharmacy in the elderly.<sup>[5]</sup> However, in another study, polypharmacy was associated with poverty.<sup>[28]</sup> In Charlesworth *et al.*'s study, marital status was not related to polypharmacy.<sup>[28]</sup> In our study, there was no significant connection between polypharmacy and level of education. In another similar study, too, participants' level of education had no significant relation with polypharmacy.<sup>[28]</sup> However, in some other studies, the low level of literacy and awareness of elderly patients were the most prevalent causes of polypharmacy.<sup>[12-14]</sup>

In the present study, there was no significant relation between polypharmacy, MMSE score, and Geriatric Depression Scale. In Sganga *et al.*'s study, too, polypharmacy was not significantly associated with MMSE score and Geriatric Depression Scale.<sup>[40]</sup> However, in our study, there was a significant connection between polypharmacy and depression (P = 0.000). In another study, likewise, there was a relation between polypharmacy, depression, and cognitive capacity.<sup>[38]</sup>

## CONCLUSIONS

The results of this study indicate that the prevalence of polypharmacy is high in the elderly people and is associated with demographic factors such as being married, being female, being in the age group of 60–69 and 75–79 years, having comorbidity, being retired, and being employed apart from homemakers. As a result, it is important to plan for specific interventions for rational and correct administration of medications, especially in the elderly with the above-mentioned characteristics. Since it is anticipated that the population of the elderly increase remarkably over the coming decades and be followed by the increase of chronic diseases and polypharmacy, assessment and management of polypharmacy by physicians, pharmacists, and authorities of health-care centers are highly required. Moreover, increase of awareness among physicians, experts, authorities, and families about characteristics of the elderly people and factors affecting polypharmacy can help in the proper and safe use of medications, and as families' awareness increases, it encourages the proper culture for using medications and decreases the negative effects of this problem.

#### Financial support and sponsorship

This study was conducted with financial support of the deputy of research and technology of Babol University of Medical Sciences.

#### **Conflicts of interest**

There are no conflicts of interest.

#### References

- Kim HA, Shin JY, Kim MH, Park BJ. Prevalence and predictors of zpolypharmacy among Korean elderly. PLoS One 2014;9:e98043.
- Wickop B, Langebrake C. Good prescribing practice in the elderly. Ther Umsch 2014;71:366-73.
- Dovjak P. Tools in polypharmacy. Current evidence from observational and controlled studies. Z Gerontol Geriatr 2012;45:468-72.
- Blozik E, Rapold R, von Overbeck J, Reich O. Polypharmacy and potentially inappropriate medication in the adult, community-dwelling population in Switzerland. Drugs Aging 2013;30:561-8.
- Carvalho MF, Romano-Lieber NS, Bergsten-Mendes G, Secoli SR, Ribeiro E, Lebrão ML, *et al.* Polypharmacy among the elderly in the city of São paulo, Brazil - SABE study. Rev Bras Epidemiol 2012;15:817-27.
- Hofer-Dueckelmann, Christina. Gender and Polypharmacotherapy in the Elderly: A Clinical Challenge. Handbook of experimental pharmacology. 2012;214:169-82.
- Chiang-Hanisko L, Tan JY, Chiang LC. Polypharmacy issues in older adults. Hu Li Za Zhi 2014;61:97-104.
- Santibáñez-Beltrán S, Villarreal-Ríos E, Galicia-Rodríguez L, Martínez-González L, Vargas-Daza ER, Ramos-López JM, *et al.* Economic cost of polypharmacy in the elderly in primary health care. Rev Med Inst Mex Seguro Soc 2013;51:192-9.
- Banerjee A, Mbamalu D, Ebrahimi S, Khan AA, Chan TF. The prevalence of polypharmacy in elderly attenders to an emergency department – A problem with a need for an effective solution. Int J Emerg Med 2011;4:22.
- Campanelli CM. American geriatrics society updated beers criteria for potentially inappropriate medication use in older adults: The American geriatrics society 2012 beers criteria update expert panel. J Am Geriatr Soc 2012;60:616.
- 11. Kaufman G. Polypharmacy in older adults. Nurs Stand 2011;25:49-55.
- Salih SB, Yousuf M, Durihim H, Almodaimegh H, Tamim H. Prevalence and associated factors of polypharmacy among adult saudi medical outpatients at a tertiary care center. J Family Community Med 2013;20:162-7.
- 13. Rambhade S, Chakarborty A, Shrivastava A, Patil UK,

Rambhade A. A survey on polypharmacy and use of inappropriate medications. Toxicol Int 2012;19:68-73.

- 14. Moradi F. Physicians need more pharmaceutical knowledge. Lakartidningen 2014;111:853.
- Neuner-Jehle S. Less is more How to prevent polypharmacy? Praxis (Bern 1994) 2013;102:21-7.
- Venturini CD, Engroff P, Ely LS, Zago LF, Schroeter G, Gomes I, *et al.* Gender differences, polypharmacy, and potential pharmacological interactions in the elderly. Clinics (Sao Paulo) 2011;66:1867-72.
- 17. Bor A, Matuz M, Doró P, Viola R, Soós G. Drug-related problems in the elderly. Orv Hetil 2012;153:1926-36.
- Mizokami F, Koide Y, Noro T, Furuta K. Polypharmacy with common diseases in hospitalized elderly patients. Am J Geriatr Pharmacother 2012;10:123-8.
- Hosseini SR, Cumming RG, Kheirkhah F, Nooreddini H, Baiani M, Mikaniki E, *et al.* Cohort profile: The Amirkola health and ageing project (AHAP). Int J Epidemiol 2014;43:1393-400.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
- Mitchell AJ, Malladi S. Screening and case finding tools for the detection of dementia. Part I: Evidence-based meta-analysis of multidomain tests. Am J Geriatr Psychiatry 2010;18:759-82.
- Seyedian M, Falah M, Nourouzian M, Nejat S, Delavar A, Ghasemzadeh H. Validity of the farsi version of mini-mental State examination. J Med Counsil of I.R.I., 2008;25:408-14. [Persian].
- Yesavage JA, Sheikh JI. 9/Geriatric depression scale (GDS) recent evidence and development of a shorter version. Clin Gerontol 1986;5:165-73.
- Malakouti K, Fathollahi P, Mirabzadeh A, Salavati M, Kahani S. Validation of geriatric depression scale (GDS-15) in Iran. Res Med 2006;30:361-9.
- Nishtala PS, Salahudeen MS. Temporal trends in polypharmacy and hyperpolypharmacy in older New Zealanders over a 9-year period: 2005-2013. Gerontology 2015;61:195-202.
- Slabaugh SL, Maio V, Templin M, Abouzaid S. Prevalence and risk of polypharmacy among the elderly in an outpatient setting: A retrospective cohort study in the Emilia-Romagna region, Italy. Drugs Aging 2010;27:1019-28.
- Nobili A, Franchi C, Pasina L, Tettamanti M, Baviera M, Monesi L, *et al.* Drug utilization and polypharmacy in an Italian elderly population: The EPIFARM-elderly project. Pharmacoepidemiol Drug Saf 2011;20:488-96.
- Charlesworth CJ, Smit E, Lee DS, Alramadhan F, Odden MC. Polypharmacy among adults aged 65 years and older in the United States: 1988-2010. J Gerontol A Biol Sci Med Sci 2015;70:989-95.
- 29. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK, *et al.* Health outcomes associated with polypharmacy in community-dwelling older adults: A systematic review. J Am Geriatr Soc 2014;62:2261-72.
- Takane AK, Balignasay MD, Nigg CR. Polypharmacy reviews among elderly populations project: Assessing needs in patient-provider communication. Hawaii J Med Public Health 2013;72:15-22.
- Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf 2014;13:57-65.
- 32. Morandi A, Bellelli G, Vasilevskis EE, Turco R, Guerini F, Torpilliesi T, *et al.* Predictors of rehospitalization among elderly patients admitted to a rehabilitation hospital: The role of polypharmacy, functional status, and length of stay. J Am Med

Dir Assoc 2013;14:761-7.

- Lu WH, Wen YW, Chen LK, Hsiao FY. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: A retrospective cohort study. CMAJ 2015;187:E130-7.
- Zelko E, Klemenc-Ketis Z, Tusek-Bunc K. Medication adherence in elderly with polypharmacy living at home: A systematic review of existing studies. Mater Sociomed 2016;28:129-32.
- Bahat G, Tufan F, Bahat Z, Tufan A, Aydin Y, Akpinar TS, *et al.* Comorbidities, polypharmacy, functionality and nutritional status in Turkish community-dwelling female elderly. Aging Clin Exp Res 2014;26:255-9.
- 36. Sabzwari SR, Qidwai W, Bhanji S. Polypharmacy in elderly: A cautious trail to tread. J Pak Med Assoc 2013;63:624-7.

- Vyas A, Pan X, Sambamoorthi U. Chronic condition clusters and polypharmacy among adults. Int J Family Med 2012;2012:193168.
- Jyrkkä J. Drug use and Polypharmacy in Elderly Persons. Publications of the University of Eastern Finland Dissertations in Health Sciences; 2011. p. 47.
- Mannucci PM, Nobili A, REPOSI Investigators. Multimorbidity and polypharmacy in the elderly: Lessons from REPOSI. Intern Emerg Med 2014;9:723-34.
- Sganga F, Landi F, Ruggiero C, Corsonello A, Vetrano DL, Lattanzio F, *et al.* Polypharmacy and health outcomes among older adults discharged from hospital: Results from the CRIME study. Geriatr Gerontol Int 2015;15:141-6.