Research Article

Assessment for the Risk Factors of Polypharmacy in Elderly Patients

Mustafa Majed Helayeel[1], Dhuha Ahmed Majeed[2], Noor Mohammed Falih[3], Inam Sameh Arif[4], Amani Anees Abbody[5]

[1]Graduate Student, [2]Graduate Student, [3]Graduate Student, [4]Assistant Professor, [5]Assistant lecturer, Department of Pharmacology and Toxicology, College Of Pharmacy, Mustansiriyah University, Baghdad, Iraq

Abstract

Polypharmacy is typical clinical issue in elderly people, it includes prescribed medications, over-the-counter (OTC) and herbal preparations.

A total of 173 Iraqi elderly patients of age 60 years and above, were enrolled in this study. Data were collected using structured, cross-sectional questionnaire-based survey. List of required data were recorded by interviewing patients during admission to Baghdad teaching hospital, Al-Yarmouk teaching hospital and 3 community pharmacies in Baghdad governorate. From August - September 2019 in Baghdad-Iraq. Data were analyzed using SPSS software (version 25). Relationships between daily drug consumptions (DDC) and other continuous variables were examined using spearmen's correlation. For between-group comparisons of daily drug consumptions, Student's t-tests were performed. For categorical variables with more than 2 categories, multi-factor ANOVA (Analysis of variance) was performed.

Significant number of the older Iraqi patient population has a high prevalence of polypharmacy with a high prevalence of consumption of lipid modifying drugs, proton pump inhibitor, oral antidiabetic drugs, and angiotensin II receptor antagonist. according to this study. The findings of this study showed that the higher DDC was significantly associated with hypertension alongside higher number of comorbidities, ADRs and PIM. Intraclass polypharmacy was highly associated with anti-hypertensives and lipid modifying drugs, suggesting revision of the drug-dispensing policy among older Iraqi population.

Keywords: *Daily drug consumption, potentially inappropriate medicines, Beers criteria, Adverse Drug Reactions, Hypertension.*

Introduction

Polypharmacy is typical clinical issue in elderly people, it includes prescribed medications, over-the-counter (OTC) and herbal preparations. Polypharmacy characterized in the health care setting as taking at least 5 medications. However, there is no thusly standard meaning of polypharmacy, Kaufman suggested that the utilization of an excess of 5 medications implies polypharmacy. Also, Kaufman assembled polypharmacy into four groups <4, 5-9, 10-14 and >15 medication [1,2]. The incidence of polypharmacy in elderly patients issue is predicted to rise up due to multiple factors:

A. The world population faces a demographic shift with the proportion of older population.

B. epidemiological information shows that multimorbidity increases particularly with age.

Corrosponding Author:
Amani Anees Aboddy
Assistant Lecturer, Department of pharmacology and toxicology, college of pharmacy, Mustansiriyah University. E- mail: amanyanees87@gmail.com , Tel: +9647707272227

Causes of polypharmacy includes:

A. Prescribing cascade: prescribing cascade starts while a side effect or unfavorable drug reaction of a medicine is misinterpreted as a new health condition, thus resulting in the prescription of a new medication. After which this new drug may lead to new consequences and then the cycle keeps going.

B. Uncoordinated care: all people aged 65 and older have at least 3 medical diagnosis and according to Kaufman G. study, one fifth have 5 or more clinical conditions [2].

C. Self-medication: self-medication taking issue arises from the availability of enormous over-the-counter drugs, which may exacerbate polypharmacy. However, the foremost effective way to solve this issue is by informing patient regarding the drug they are taking, and to not dispense it in any case if not necessary [3].

The aims of this study are:

Assess DDC (daily drug consumption) and investigate the sociodemographic and health related risk factors for higher DDC among older adults.

A. To evaluate the prevalence of drug classes among polypharmacy (PP) (5–9 medicines) and excessive polypharmacy (EPP) (10+ medicines) groups.

B. To assess the relationship between DDC and PIMs, using Beers criteria, of the 2015 American Geriatrics Society Criteria.

Methods

Sample size and study design

The study involved cross-sectional questionnaire-based survey of older Iraqi patients, by a nonprobability convenient sampling method. A 173 Patients were involved in this study, patients were interviewed during admission to Baghdad teaching hospital, Al-Yarmouk teaching hospital and 3 community pharmacies in Baghdad governorate.

Patient criteria

Inclusion criteria:

· Elderly patients who are aged above 60 years and their caregivers if present.

Exclusion criteria:

· Elderly patients who are aged below 60 years.

· Elderly patients or caregivers who are unable to provide the required information.

Data Collection

Data was collected using structured, questionnaire-based survey used by articles from similar studies. Hospital visits were conducted as face to face interview, data was collected from patients between August - September 2019 in Baghdad-Iraq.

Medicine definition

Medication use was defined as regular use (every day or every week). We classified medications according to the WHO Anatomical Therapeutic Chemical (ATC) classification system [4].

Dependent variable

The DDC was the dependent variable. Which was obtained by so-called "brown bag" method in which the patient was asked to bring up a bag with all the medicine that he/she was currently using (whether it was prescribed or over-the-counter medications). The Temporary medicines were excluded later. Also we reclassified the DDC into groups for statistical analysis of drug classes among polypharmacy groups, the polypharmacy groups are: no polypharmacy, polypharmacy, and excessive polypharmacy, each term was defined according to other studies [5, 6].

· **Excessive polypharmacy (EPP):** concurrent use of ten or more different drugs.

· **Polypharmacy (PP):** the use of five to nine drugs.

· **No polypharmacy (NPP):** taking four or less drugs (included those taking no medicines).

Independent variables

which included:

· **Sociodemographics characteristics:** The demographic characteristics were age, gender, school education and patient monthly income. Age was treated as both continuous and categorical variable while gender was a dichotomous variable (male, female). Another predictor involved was smoking which was also dichotomous variable.

· **Health conditions:** Patients medical history was taken through medical patients records. These health conditions were reclassified taking in consideration other studies. and was recorded in the data base of the research as dichotomous variable (Yes and No) while the number of was treated as continuous variable, all of these predictors are listed below:

§ Heart diseases (medical history related to various cardiovascular diseases including hypertension).

§ Hypertension.

§ Diabetes mellitus.

§ Dyslipidemia.

§ Joint disease.

§ Eyeconditions(Farsightedness,nearsightedness, age-related macular degeneration, glaucoma, cataracts, cataract surgery or other eye diseases).

§ Number of comorbidities.

· **Number of ADRs:** the patient was asked upon each medication in his/her "brown bag" whether any side effect has been felt during the course of the treatment then cumulative number of the reported ADRs was recorded.

· **Potentially Inappropriate Medications:** The PIMs was treated as continuous variable, and was identified for each patient according to American Geriatric Society (AGS) 2015 updated Beers criteria , by recording any medicine that fall in the following criteria: medications to avoid for most older adults, and or medications to be used with caution, in the organ system, therapeutic category, drug(s) table only.

Results and Discussion

Table 1. Sociodemographic data.

Variables		N (%)	DDC	
			Mean ±SD	P value
Total		173 (100%)	5.32±(2.7)	
a Age	60 - 65	80 (46.2%)	5±(2.6)	NS
	66 - 70	33 (19.1%)	5.97±(3.2)	
	71 - 75	17 (9.8%)	6.41±(2.5)	
	76 - 80	20 (11.6%)	4.8±(1.4)	
	> 80	23 (13.3%)	5.13±(3.0)	

Cont... **Table 1. Sociodemographic data.**

b Gender	Female	89 (51.4%)	5.62±(2.6)	NS
	Male	84 (48.6%)	5±(2.8)	
a School Education	Low/No school education	85 (49.1%)	5.39±(2.5)	NS
	6-11 Years of education	39 (22.5%)	5.56±(3.1)	
	≥12 years of education	49 (28.3%)	5±(2.7)	
a Monthly Income	Low	26 (15.0%)	5.58±(2.5)	NS
	Medium	51 (29.5%)	5.71±(3.0)	
	High	96 (55.5%)	5.04±(2.6)	
b Residency	With family	91(52.3%)	5.18±(2.5)	NS
	Alone	82 (47.1%)	5.48±(2.9)	
b Smoking	Not smoking	151 (87.3%)	5.23±(2.6)	NS
	Smoking	22 (12.7%)	5.95±(3.2)	
NS = Nonsignificant a Factor was statically analyzed by multi-factor ANOVA. b Factor was statically analyzed by student's test.				

Table 2. Correlations between continuous variables and DDC.

Variables	Correlation coefficient	P value
Age	-0.034	0.661
PIM Number	0.442**	0.000
Number of ADRs reported	0.266**	0.000
Medical History (Number of Chronic Disease/s)	0.345**	0.000
**Correlation is significant at the $p < 0.01$		

The mean DDC in the whole sample was 5.32±2.7. In a retrospective cross-sectional analysis of more than 4000 profiles in Riyadh – Saudi Arabia [7], the average number of medications was 5.31±2.8, while the mean DDC in cross-sectional study of a total of 1000 patients in Istanbul was 4.63±3.51 [8]. Suggesting regional similarities.

Female's DDC was slightly higher than of males which is similar to the result of a descriptive analysis study of elderly patients in Kurdistan – Iraq [9] in which the prevalence of polypharmacy was found to be a 54.88% in females and 45.12% in males, suggesting similarities among Iraq-governorates one possible explanation, women are both consult a physician more frequently and participate more often in research studies. However, the relationship between gender and DDC was found to be insignificant risk factor in our study.

The age of the patients ranged from 60 to 89 years, with mean of 67.89±6.72 years. The DDC among age groups showed no significant differences whether age was treated as categorical or continuous variable (table 2), which was similar to the findings of a cross-sectional study of elderly Kuwaiti patients [10] and Istanbul studies [8]. The rest of sociodemographic factors (shown in table 1) were found to be non-significant at both univariate and multivariate level of analysis.

Table 3. Health conditions.

Related health condition		DDC	
		Mean±SD	P value
Heart diseases	No	4.6±(1.9)	0.024
	Yes	5.61±(2.9)	
Hypertension	No	4.24±(2.2)	0.000
	Yes	5.98±(2.7)	
Asthma	No	5.2±(2.7)	0.023
	Yes	7.09±(2.0)	
Diabetes mellitus	No	4.93±(2.5)	0.009
	Yes	6.03±(2.8)	
Dyslipidemia	No	4.85±(2.4)	0.000
	Yes	6.49±(2.9)	
Joint disease	No	4.96±(2.2)	0.031
	Yes	5.86±(3.2)	
Eye condition	No	5.04±(2.7)	NS
	Yes	5.53±(2.6)	
Note: All P-values were adjusted by FDR.			

Table 4. The risk factors for higher DDC after Stepwise linear regression.

Variables	Unstandardized Coefficients		95% Confidence Interval for B		P value
	B	Standard Error	Lower Bound	Upper Bound	
PIM Number	0.683	0.131	0.342	5.195	0.000
Medical History (Number of Chronic Diseases)	0.393	0.133	0.204	2.952	0.004
Number of ADRs	0.221	0.066	0.217	3.340	0.001
Hypertension	0.884	0.354	0.161	2.496	0.014

In this study, four factors remained significant at the end of stepwise linear regression analysis: Number of comorbidities, Number of ADRs reported, Hypertension and number of PIMs found per patient shown in table 4.

The mean number of chronic diseases for single patient was 2.9±1.4 and according to spearman's correlation there was a significant association with higher DDC (correlation coefficient = 0 .345, P <0.001). Patients with comorbid medical conditions always require several drugs to treat each diagnosis, taking in consideration the changes in evidence-based recommendations and the introduction of new specific drugs for the management of certain conditions or diseases.

Hypertension was found to be strong predictor of increased number of DDC in this study (P value = 0.014(. Patient with hypertension is easily prescribed more than one medication if treated according to accepted guidelines making them all appropriate for the same individual. Hypertension was the most common diagnosis in PP and EPP group by 86.7% and 88.6% respectively. The prevalence of hypertension in the whole Iraqi population was 40% according to WHO [11]. A possible explanation of high blood pressure in older adults is the blood vessels naturally harden with age, losing elasticity, leading to cardiovascular consequences which one of them is the hypertension [12].

DDC association with PIMs and ADRs

ADRs number showed direct correlation with DDC at bivariate level of analysis (table 3-5, P = 0.000), and remained significant at the last stepwise linear regression analysis (P value = 0.001). A Pakistani study [13] showed that ADRs among elderly patients with polypharmacy was 2.3 times more than those of NPP . This could be explained by the fact that elderly patients have increased sensitivity to drug effects. Thus, more prone to adverse drug reactions,

PIM was treated as independent risk factor of DDC. A direct correlation between DDC and PIM were resulted from bivariate correlation analysis (table 3-5, P = 0.000). Confirming the result of Weng M. et.al. [14] that showed the patients who were prescribed five or more drugs had a 5.4 fold higher PIM risk than those prescribed two or fewer drugs.

Table 5. Medications used by the patients.

Drug classes	N= 173 (100%)
Lipid modifying agents	52 (30.06%)
Proton pump inhibitors	47 (27.17%)
Oral antidiabetic drugs	46 (26.59%)
Histamine 2 receptors antagonist	18 (10.40%)
Bronchodilator	16 (9.25%)
Antihypertensives	
Agents acting on the angiotensin system Angiotensin II receptor antagonist Angiotensin converting enzyme inhibitor	 44 (25.43%) 14 (8.09%)
Beta Blockers (selective)	33 (19.08%)
Calcium channel blockers	26 (15.03%)

Table 6. Proportions of drug users in the therapeutic classes reported by polypharmacy groups.

Drug classes	No Polypharmacy (0 - 4)	Polypharmacy (5 - 9)	Excessive Polypharmacy (≥10)	Total
	N=78 (100%)	N=84 (100%)	N=11 (100%)	N=173 (100%)
Lipid modifying agents	12 (15.38%)	31 (36.90%)	9 (81.82%)	52 (30.06%)
Angiotensin II receptor antagonist	15 (19.23%)	24 (28.57%)	5 (45.45%)	44 (25.43%)
Proton pump inhibitors	21 (26.92%)	23 (27.38%)	3 (27.27%)	47 (27.17%)
Oral antidiabetic drugs	21 (26.92%)	21 (25.00%)	4 (36.36%)	46 (26.59%)
Beta Blockers	9 (11.54%)	19 (22.62%)	5 (45.45%)	33 (19.08%)

Cont... **Table 6. Proportions of drug users in the therapeutic classes reported by polypharmacy groups.**

Calcium channel blockers	6 (7.69%)	15 (17.86%)	5 (45.45%)	26 (15.03%)
Bronchodilator	2 (2.56%)	11 (13.10%)	3 (27.27%)	16 (9.25%)
Histamine 2 receptors antagonist	5 (6.41%)	10 (11.90%)	3 (27.27%)	18 (10.40%)
Angiotensin converting enzyme inhibitor	7 (8.97%)	7 (8.33%)	0 (0.00%)	14 (8.09%)

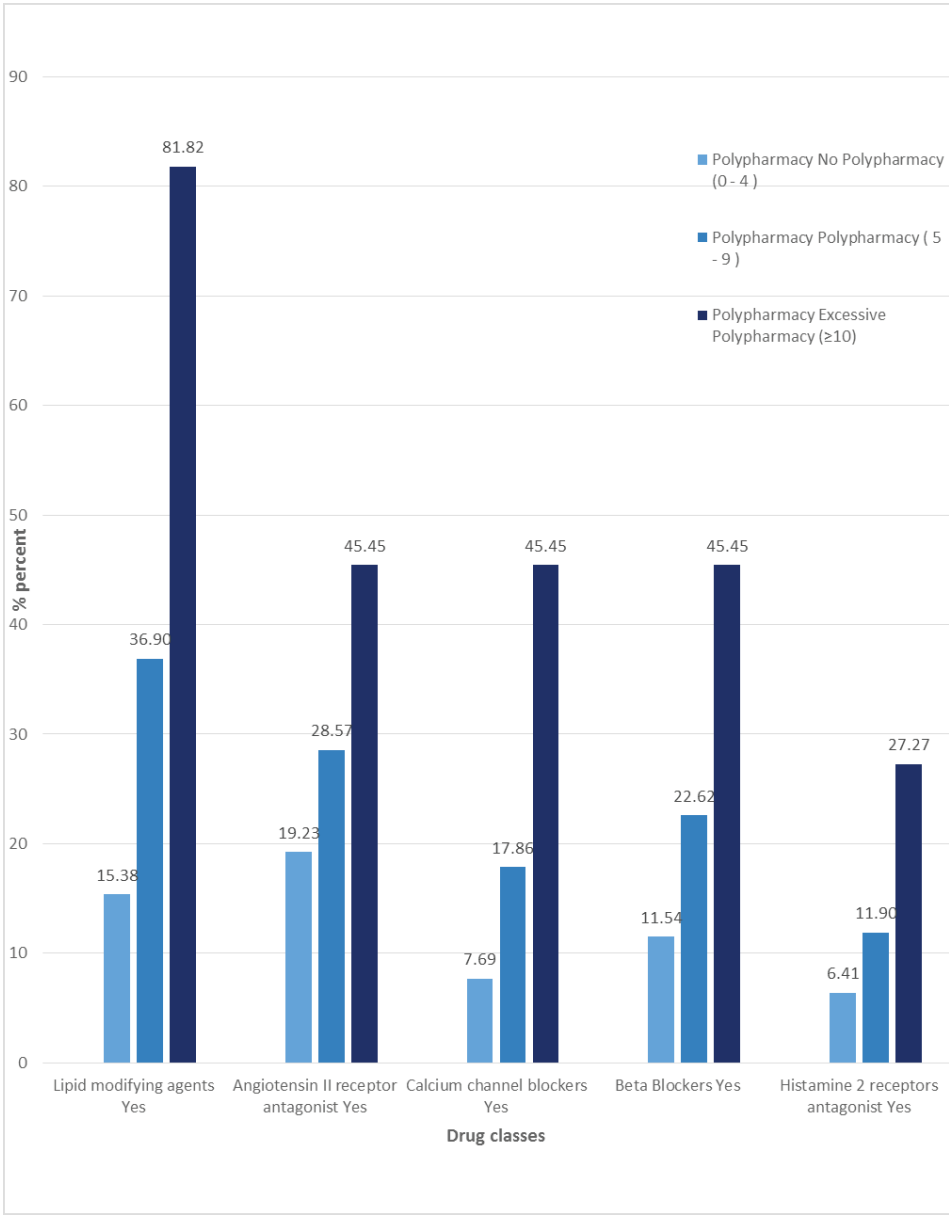

Figure 1. Proportions of drug users in the therapeutic classes reported by polypharmacy groups.

The frequencies of drugs used by our patients, were 30.06% (n = 52) lipid modifying drugs, 27.17% (n = 47) proton pump inhibitor, 26.59% (n = 46) oral antidiabetic drugs, and 25.43% (n = 44) angiotensin II receptor antagonist. For interclass polypharmacy comparison we observed the most frequently used drug in our sample according to table 5 , then nominated them for in-between polypharmacy groups comparison, excluding drug classes that showed no differences among polypharmacy groups and recorded less frequency according to table 5, figure 1. We found that lipid modifying agents and angiotensin II receptor antagonist were the most frequently reported drug in PP and EPP groups in reference to NPP group. According to a retrospective cross-sectional analysis of prescription medications in older adults in Texas/ Mexico [15] agents acting on the renin-angiotensin system and lipid modifying agents were the most frequently prescribed medication by 55.6% (n=55) for both classes of the whole sample.

The limitations of this study:

· We used a nonprobability convenient sampling method with cross-sectional study design.

· PIMs was recoded without applying other categories of 2015 Beers criteria and only PIMs to be avoided and PIMs to be used with caution within "Organ System, Therapeutic Category, Drug(S) Table" only.

· ADRs was recorded by self-reporting in the follow-ups.

· Higher DDC could be a cause as well as consequence or both, according to the situation being studied.

Conclusion

In this study, we confirmed that significant portion of the older Iraqi patient population has a high prevalence of polypharmacy with high consumption of LM, PPI, OA, and ARBs according to this study, and higher DDC was significantly associated with hypertension alongside increasing number of chronic diseases, ADRs and PIMs. Thus, elderly patients are more exposed to the potential hazards of polypharmacy. The findings highlight the need to revise the drug-dispensing policy among older Iraqi population, improve communication between patients and health care providers, initiate programs concerning prescribing issues among older adults, and using of versatile ways to minimize higher DDC to reduce the risk of polypharmacy. Intraclass polypharmacy was highly associated with anti-hypertensives and lipid modifying drugs, therefore health care professionals should be aware of their risk and fully evaluate the prescribing of each drug by evidence-based system with involvement of clinical pharmacists in collaborative care. Also, by simplifying the drug regimen, patients may be better able to understand their treatment and the importance of remembering to take their medications.

Acknowledgment: We are grateful for the assistance and support provided by Al-Yarmouk teaching hospital and three community pharmacies stuff in Baghdad and allow the collection of patient data with complete privacy.

Ethical Clearance: Taken from the ethical and scientific committee in the college of pharmacy/ Mustansiriyah University

Source of Funding: Self

Conflict of Interest: Nil

References

1. Kaufman G. Polypharmacy: the challenge for nurses. Nursing Standard. 2016 May 25; 30(39): p. 52-60.
2. Rathod G, K NG, Nagaral JV, N SG, P D, Prema M, et al. Factors associated with polypharmacy in geriatrics. International Journal of Basic & Clinical Pharmacology. 2017 Nov 22; 6(7): p. 1763-1767.
3. Mortazavi SS, Shati M, Keshtkar A, Malakouti SK, Bazargan M, Assari S. Defining polypharmacy in the elderly: a systematic review protocol. BMJ Open. 2016 Nov 22; 6(3).
4. WHO Collaborating Centre for Drug Statistics Methodology: Norwegian Institute of Public Health; 2014; 2014.
5. Hovstadius B, Hovstadius K, Åstrand B, Petersson G. Increasing polypharmacy - an individual-based study of the Swedish population 2005-2008. BMC Clinical Pharmacology. 2010 Dec 2; 10.
6. O'Dwyer M, Peklar J, Mccallion P, Mccarron

M, Henman MC. Factors associated with polypharmacy and excessive polypharmacy in older people with intellectual disability differ from the general population: A cross-sectional observational nationwide study. BMJ Open. 2016; 6(4).

7. Alsuwaidan A, Almedlej N, Alsabti S, Daftardar O, Al Deaji F, Al Amri A, et al. A Comprehensive Overview of Polypharmacy in Elderly Patients in Saudi Arabia. Geriatrics. 2019 May 15; 4(2): p. 36.
8. Ersoy S, Engin VS. Risk factors for polypharmacy in older adults in a primary care setting: A cross-sectional study. Clinical Interventions in Aging. 2018; 13: p. 2003-2011.
9. Venturini CD, Engroff P, Ely LS, de Araújo Zago LF, Schroeter G, Gomes I, et al. Gender differences, polypharmacy, and potential pharmacological interactions in the elderly. Clinics. 2011; 66(11): p. 1867-1872.
10. Badawy N, Labeeb S, Alsamdan M, Alazemi B. Prevalence and Risk of Polypharmacy among Community-Dwelling, Elderly Kuwaiti Patients. Medical Principles and Practice. 2020 Feb 1; 29(2): p. 166-173.
11. WHO EMRO | Iraq celebrates World Health Day under the theme of hypertension | Iraq-events | Iraq. [Online]. Available from: "http://www.emro.who.int/irq/iraq-events/world-health-day. html .
12. Secora A, Alexander GC, Ballew SH, Coresh J, Grams ME. Kidney Function, Polypharmacy, and Potentially Inappropriate Medication Use in a Community-Based Cohort of Older Adults. Drugs and Aging. 2018 Aug 1; 35(8): p. 735-750.
13. Sato I, Akazawa M. Polypharmacy and adverse drug reactions in Japanese elderly taking antihypertensives: A retrospective database study. 2013 Jun 22.
14. Weng MC, Tsai CF, Sheu KL, Lee YT, Lee HC, Tzeng SL, Ueng KC, Chen CC, Chen SC. The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. QJM: An International Journal of Medicine. 2013 Nov 1;106(11):1009-15,
15. Lawson K, Vinluan CM, Oganesyan A, Gonzalez EC, Loya A, Strate JJ. A retrospective analysis of prescription medications as it correlates to falls for older adults. Pharmacy Practice. 2018 Oct 1; 16(4).