



**RESEARCH ARTICLE**

**PREVALENCE OF POLYPHARMACY IN ELDERLY CARDIAC PATIENTS AT KING FAHAD CARDIAC CENTER KFCC IN KING KHALID UNIVERSITY HOSPITAL KKHU- RIYADH SAUDI ARABIA**

**Mohamed N. Al-Arifi\*, Hessa Othman Al-Husein\*\*, Mostafa Q. Al Shamiri\*\*, Ragab Said\*, Syed Wajid \*,  
Salmeen D. Babelghaith\***

\*Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

\*\*College of Medicine King Saudi University, Riyadh, Saudi Arabia

**ARTICLE INFO**

**Article History:**

Received 12<sup>th</sup>, May, 2014

Received in revised form 19<sup>th</sup>, May, 2014

Accepted 17<sup>th</sup>, June, 2014

Published online 28<sup>th</sup>, June, 2014

**Key words:**

Cardiac inpatients, Medications, Polypharmacy, Prevalence,

**ABSTRACT**

Polypharmacy was defined as a taking more than 4 medications per single patients (minor polypharmacy), patients who are taking more than 10 medications we considered as a major polypharmacy. This study was aimed to evaluate the prevalence of polypharmacy in elderly Saudi cardiac patient. A retrospective observational study was carried out at the department of CCU & cardiology unit of the King Fahad cardiac centre (KFCC) in King Khalid university hospital from May, 2012 to October, 2012. All Parameters was analyzed by using Statistical Packages for Social Science (SPSS) to conclude the result; Tests of association were performed using the chi-square statistic. The mean age of patients was  $70.1 \pm 7.75$  years, more than half 83 (51.6%) were males. The highest frequency of chronic diseases found were hypertension (91.0%) followed by, dyslipidemia (74.9%), and diabetes mellitus. Results shown that 82% had polypharmacy (>4 drugs) during the study period, and 47.9% had major polypharmacy. The incidence of inappropriate drug use was found to be higher with men than female ( $p = 0.984$ ). In conclusion this study revealed that high prevalence of polypharmacy and potentially inappropriate medications in elderly Saudi cardiac inpatients

© Copy Right, IJRSR, 2014, Academic Journals. All rights reserved.

**INTRODUCTION**

The continuous use of multiple medications leading to a specific problem of pharmacological therapy in elderly patients, which create exponentially increasing medical, social and age related problems (Garfinkel *et al.*, 2007). Many studies state that elderly people are the largest per capita consumers of medications (Lammy, 1980). Most of them (up to 80%) suffer from chronic diseases (Lammy, 1980). Many elderly patients have at least one reasonably detectable chronic illness, e.g. cardiac condition, diabetes, and so forth, that is the focal point of treatment, these results in polypharmacy. With increasing age, multi-morbidity becomes more common, leading to higher incidence of medication use and higher risk of adverse drug events due to polypharmacy (Beers *et al.*, 1995). This phenomena continues to be a significant problem in Saudi Arabia and all over the world

Even though being a well recognized problem in the elderly population, a universally accepted, formal definition for polypharmacy has yet to be established (Fulton and Allen, 2005; Jyrkka *et al.*, 2006). Several studies have categorized polypharmacy into different levels based on the number of medications taken (Fulton and Allen, 2005; Viktil, 2007; Bjerrum, 1997). Multiple definitions used in this study such as two or more drugs for 240 days or more (Veehof *et al.*, 2000) concurrent use of two or more drugs, use of four or more medications (Bjerrum, 2003), use of five or more different prescription medications (Bikowski *et al.*, 2001). European studies defined polypharmacy according to the number of

medications taken (Fillit *et al.*, 1999), whereas the studies conducted in the United States defined polypharmacy according to whether a medication was clinically indicated (Fillit *et al.*, 1999). World Health Organization defined Polypharmacy as "Use of more medications than clinically necessary"(11). (Rational use of medicines by prescribers and patients., 2004)

Polypharmacy can be "Appropriate polypharmacy", when a patient takes several concomitant drugs, all of which are for recognized indication and "Inappropriate polypharmacy", when a patient really takes more drugs than necessary (Lim W.K, & Woodward M.C., 1999).

Inappropriate polypharmacy in the elderly is related to patient demographics, Female sex, increasing age, and low education increase the risk of polypharmacy (Fourrier *et al.*, 1993; Lassila *et al.*, 1996). Two other factors frequently encountered in the elderly population are self medication with over the counter drugs, and borrowing medications from friends and family members (Whitaker *et al.*, 1995). Some studies states that (Linjakumpu *et al.*, Jyrkka *et al.*, 2006) Polypharmacy has been associated with increased age, with specific diseases; including hypertension, cardiovascular diseases, rheumatic diseases and Ischemic heart disease (Bjerrum *et al.*, 1998).

Health professional's often use various strategies to evaluate the incidence of polypharmacy some of this includes the utilization of Beers' criteria (Beers, 1997). In the US, the Beers' criteria have become the most popular and accepted explicit tool used for evaluating potentially inappropriate

\* Corresponding author: **Syed Wajid**

Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

medication (PIM) prescribing. The Beers' criterion is used to help identify and target elderly members at risk of adverse drug events (ADEs) associated with PIM prescribing. In 1991, Beers and colleagues published the first set of explicit criteria for determining potentially inappropriate medication (PIM) use in nursing home residents (Beers, 1997). The criteria divided potentially inappropriate drugs into three categories: drugs that generally should be avoided in older adults; doses, frequencies, or durations of specific therapies that vary from those generally accepted as appropriate use in elderly persons; and drugs to be avoided in combination with a specific comorbidity. Beers' criteria were again updated in 2003 (Beers *et al.*, 1991).

In accordance with the World Health Organization, European countries have decided to strengthen health care system (who, 1978). Ministry of Health (MOH) is the main authority responsible for the provision of health care in Saudi Arabia. Although Earlier studies on drug prescribing in Saudi Arabia showed patterns of overprescribing and extensive use of antibiotics, hypertensive's Beta-blockers (Sebaie, 1985; Sebaie, 1980). However, the subject of drug prescribing patterns in Saudi Arabia has not been studied sufficiently (Asiri and Al-Arifi, 2011). Therefore the present study was carried out to determine the prevalence and characteristics of unnecessary drug use in Saudi cardiac patients (> 60 year old) at King Khalid University Hospital (KKUH) Focus on patient with the high prevalence of multiple (>4) drugs.

**METHODOLOGY**

A retrospective observational study was carried out at the department of CCU & cardiology unit of the King Fahad cardiac centre (KFCC) in King Khalid university hospital from May, 2012 to October 2012. Participants of this study were geriatric patients who satisfied all the inclusion criteria in this study.

**Table 1** Shows Demographic characteristic, number of medications per prescription and predictors of poly pharmacy

Scio demographic characteristics	Number (n)	Percentage (%)
Gender		
Males	78	48.4%
Females	83	51.6%
Mean ±std age	70.1 ± 7.75	
Number of medications		
4-6	31	18.6%
7-9	80	47.9%
More than 10	33	19.8%
Predictors of poly pharmacy		
Dose	141	84.4%
Medication only in nurse sheet	155	92.8%
Sub therapeutics	155	92.8%
Generally contra indicated for >60 year patients	131	78.4%
Treatment side effects of other medicines	122	73.1%
Contra indicated according to stoop criteria	125	74.9%
Unnecessary therapeutics duplications	158	94.6%
Medicines not use full at all	166	99.4%
Dose unsuitable >60 for patients	164	98.2%
Drug disease interactions	160	95.8%
Duration	146	87.4%
Drug-drug interactions	74	44.3%

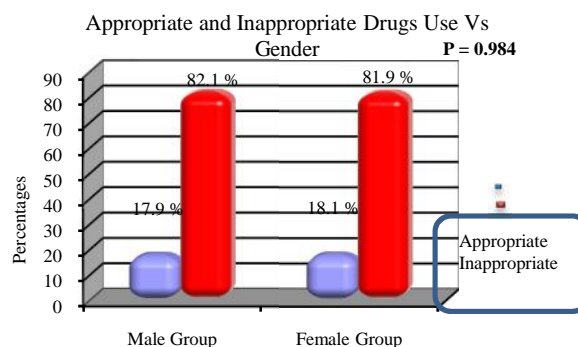
**Inclusion and exclusion criteria**

**Criteria for inclusion were:** Older patients admitted with acute cardiac illness to a university teaching hospital. Only patients

who were >60 years old, and were admitted at KFCC in KKUH, and talking more than (> 4) medications were enrolled. The exclusion criteria included patients who died during their stay in hospital as well as those whose medical records were not sufficient for our study, and those transferred to another hospital were excluded.

**Table 2** indicating the most common medical conditions of Saudi cardiac patients

Diagnosis listed	Number (n)	Percentage (%)
Dyslipidemia	125	74.9%
CRF	4	2.4%
Peripheral arterial disease (PAD)	4	2.4%
Transient ischemic attack (TIA)	167	100%
Left ventricular dysfunction (LVD)	3	1.8%
Heart failure (HF)	60	35.9%
Atrial fibrillation (AF)	20	12%
Valvular heart disease	7	4.2%
Post valve replacement	4	2.4%
S/p cabg Status post (Coronary artery bypass graft )	14	8.4%
Ischemic heart disease (IHD)	89	53.3%
Diabetes mellitus (DM)	101	60.5%
Hypertension (HTN)	152	91%
Other	17	10.2%



**Figure 1** representing the percentage of appropriate and inappropriate drug use vs gender

**Table 3** indicates the most commonly prescribed medications

Drug class	Number (n)	Percentage (%)
Anti lipemic agent	127	76%
B-Blockers	125	74.9%
Aspirin	114	68.3%
Diuretics	108	64.7%
ACEI	84	50.3%
ARBS	45	26.9%
Vasodilators	6	3.6%
Nitrates	53	31.7%
Insulin	39	23.4%
Oral hypo glycemc agents	72	43.1%
Anti psychiatric agents	4	2.4%
Clopidogrel	42	25.1%
warfarin	47	28.1%
enoxaparin	3	1.8%
Calcium channel blocker	43	25.7%
Digoxin	34	20.4%
Proton pump inhibitors	51	30.5%
H2RAS (Histamine -2-receptor antagonist )	17	10.2%
Others	74	44.3%

In this study polypharmacy was defined as a taking more than 4 medications per single patients (minor polypharmacy), patients who are taking more than 10 medications we considered as a major polypharmacy. The following data were recorded for each patient: demographic information like age,

weight and gender: most common medications used by patients, number of medications used, Information on whether the patient was mobile or not, drug use appropriate and drug use inappropriate, causes of inappropriate drug use ,identified as potential predictors of Polypharmacy, ischemic heart disease, arterial hypertension, heart failure, atrial fibrillation, diabetes mellitus, chronic obstructive pulmonary disease or bronchial asthma, psychiatric diagnoses. Each patient with four or more of the diagnoses stated was considered as Polymorbid.

**Table 4** indicates the predictors of inappropriate medications

Variables	Number (n)	Percentage (%)
Dose	141	84.4%
Medication only in nurse sheet	155	92.8%
Sub therapeutics	155	92.8%
Generally contra indicated for >60 year patients	131	78.4%
Treatment side effects of other medicines	122	73.1%
Contra indicated according to stoop criteria	125	74.9%
Unnecessary therapeutics duplications	158	94.6%
Medicines not use full at all	166	99.4%
Dose unsuitable >60 for patients	164	98.2%
Drug disease interactions	160	95.8%
Duration	146	87.4%
Drug-drug interactions	74	44.3%

Assessment of unnecessary drug use was determined by clinical pharmacists applying the criteria of the Medication Appropriateness Index (MAI) and rating for Indication Effectiveness, therapeutic duplication was defined as unnecessary.

**Table 5** showing the most common medical conditions and drug classes of Saudi cardiac patients

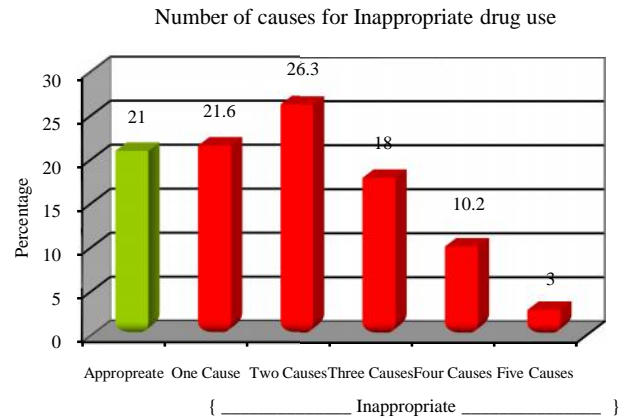
Drug classes	HTN (n=152)	DM (n=101)	Dyslipidemia (n=125)	IHD (n=89)	HF (n=60)	AF (n=20)
ACEI	79(51.97%)	47 (46.5 %)	68 (54.4 %)	46 (51.7 %)	34 (56.7 %)	8 (40 %)
ARBS	43 (28.3 %)	30 (29.7 %)	34 (27.2 %)	27 (30.3 %)	17(28.33%)	4 (20 %)
B-BLOCKERS	119(78.3%)	72 (71.3 %)	98 (78.4 %)	69 (77.5 %)	45 (75 %)	14 (70 %)
VASODILATOR	6 (3.95 %)	4(3.96 %)	5 (4.0 %)	4 (4.49 %)	3 (5 %)	
NITRATES	49 (32.2 %)	37 (36.6 %)	43 (34.4 %)	43 (48.3 %)	24 (40 %)	1 (5 %)
INSULIN	37 (24.3 %)	37(36.6 %)	32 (25.6 %)	30 (33.7 %)	16 (26.7 %)	
ORALHYPOGLYSEMIC AGENTS	67 (44.1 %)	63 (62.4 %)	55 (44.0 %)	41 (46.1 %)	22 (36.7 %)	5 (25 %)
ANTI PSYCHIATRI	4 (2.6 %)	3 (2.97 %)	3 (2.4 %)	1 (1.12 %)	1 (1.7 %)	1 (5 %)
ASPIRIN	107(70.4%)	78 (77.2 %)	90 (72.0 %)	73(82.02%)	41(68.33%)	6 (30 %)
CLOPIDOGREL	41(26.97%)	28 (27.7 %)	35 (28.0 %)	30 (33.7 %)	19 (31.7 %)	2 (10 %)
WARFARIN	44(28.95%)	19 (18.8 %)	37 (29.6 %)	17 (19.1 %)	11(18.33%)	16 (80 %)
ENOXAPARIN	3 (1.97 %)	2 (1.98 %)	3 (2.4 %)	3 (3.4 %)	2 (3.33 %)	
CALCIUM CHANNEL BLOCKER	42 (27.6 %)	29 (28.7 %)	31 (24.8 %)	16(17.98%)	17(28.33%)	11 (55 %)
DIURETICS	103(67.8%)	68 (67.3 %)	84 (67.2 %)	61 (68.5 %)	48 (80 %)	11 (55 %)
DIGOXIN	34 (22.4 %)	19 (18.8 %)	27 (21.6 %)	19(21.35%)	16 (26.7 %)	11 (55 %)
LIPID LOWERING AGENT	123(80.9%)	82 (81.2 %)	76 (60.8 %)	76 (85.4 %)	48 (80 %)	14 (70 %)
PPI	47 (30.9 %)	36 (35.6 %)	42 (33.6 %)	35(39.33%)	20 (33.3 %)	5 (25 %)
H2RAS	17 (11.2 %)	10 (9.9 %)	15 (12.0 %)	13 (14.6 %)	10 (16.7 %)	1 (5 %)
OTHERS	71 (46.7 %)	49 (48.5 %)	56 (44.8 %)	46 (51.7 %)	28 (46.7 %)	9 (45 %)

Data was collected from, patients medical records , consists of patient name, file number , diagnosis, age, weight, gender, medication name, strength, frequency, time of prescription . Data collected from the patient's files and computer system, the result of the study will be compared to updated beer's criteria 2002. The data was revised by clinical pharmacist & medical cardiac team of physicians to evaluate the unnecessary drug use & Medication Appropriateness Index (MAI). All Parameters was analyzed by using Statistical Packages for Social Science (SPSS) to conclude the result; Tests of association were performed using the chi-square statistic.

**RESULTS**

The total number of patients aged 60 years and over attending

during this period was 167, of them 161 fulfils the requirements for enrolled in the study. The demographic characteristics of the respondents were summarized in Table 1.Of the respondents 78 were females (48.45%) and 83 (51.6%) were males.



**Figure 2** representing the percentage of number of causes of inappropriate drug use

The age range was from 60 to 98 years, with a median age± SD in all of the patients studied was 70.1 ± 7.75 years. Results shown that 82% had polypharmacy (>4 drugs) during the study period, and 47.9% had major polypharmacy. In comparison to percentage of appropriate and inappropriate drug use between gender, men used more appropriate drugs with a (p = 0.984) Fig. 1.

The percentage of number of causes for inappropriate medications use was illustrated in Fig. 2. This inappropriate prescribing is mainly due to Drug - Drug Interactions (55.7%), Treatment side effect of other medication (26.9%) Contra indicated according to stoop criteria (25.1%), and 80% had multiple causes. Only 17.9%of the male patients and 18.1% of the female patients are using appropriate medications, inappropriate use of medication is high in both male and female patients (82.1%) .

According to our study one hundred fifty two patients presented with a hypertension (91%), which was the most frequent presenting complaint in cardiac patient. Other presenting complaints were, dyslipidemia (74.9%), diabetes mellitus (60.5%), ischemic heart diseases IHD (53.3%), heart

failure HF (35.9%), and atrial fibrillation (12%) (Table 2). The most commonly dispensing drugs are angiotensin converting enzyme inhibitors 77.2% (ACEI), lipid lowering agents 76%, beta blockers 74.9% and analgesic class of drug aspirin 68.3% these classes of drugs are most responsible for incidence of polypharmacy (Table 3). Cardiac patients are more prone to polypharmacy due to number of medications used, and interactions of different medications. As shown in the table (4) most important predictor of inappropriate medication use of medications were medicine not use full at all (99.4%), dose unsuitable >60 for patients (98.2%), drug disease interactions (95.8%), Unnecessary therapeutics duplications (94.6%), Sub therapeutics (92.8%). Most common medical conditions and drug classes of Saudi cardiac patients were summarized in (Table 5).

## DISCUSSION

The study confirmed a relatively high prevalence of polypharmacy in elderly Saudi cardiac patients. These results were relatively higher than those found in elderly subjects surveyed in other studies (Fulton and Allen, 2005; Bjerrum *et al.*, 1997; Linjakumpu *et al.*, 2002; Hajjar, 2007; Huang, 2004; Anderson and Kerluke, 1996; Joørgensen *et al.*, 2001). The stay in hospital led to an increase in the number of drugs taken. The number of medications used corresponded to the proportions of diagnoses in the evaluated group. The results of the study revealed that, hypertension dyslipidemia and diabetes were strong predictors of polypharmacy this is confirming the role of CV disease in increasing number of medications. However previous studies (Veehof *et al.*, 2000; Bjerrum, 2003; Linjakumpu *et al.*, 2002; Bedell *et al.* 2000; Golden *et al.*, 1999) reported that use of cardio vascular medications (i.e., beta blockers, angiotensin II-converting enzyme inhibitors, calcium channel antagonists, antiarrhythmics) increases the risk of polypharmacy. These results clearly indicate that primary care providers must be vigilant for the development of polypharmacy in clients with co morbidities such as cardiovascular disease.

With regards to gender Study results shown males were found to be more likely exposed to polypharmacy comparing to females. This finding is also consistent with the previous surveys, reported a positive correlation between male sex and polypharmacy (Slabaugh *et al.*, 2010; Chan *et al.*, 2009). Conversely, many studies have reported a correlation between polypharmacy and female sex (Linjakumpu *et al.*, 2002; Bjerrum, 2003; Kaufman *et al.*, 2002; Jyrkka *et al.*, 2009; Rozenfeld *et al.*, 2008). In a longitudinal study, Linjakumpu *et al.* (2002) found that women used more prescription medications than men, with 81% of women using medications compared to 74% of men. Kaufman *et al.* (2002) reported that the highest overall medication use occurred in women. Twelve percent of women aged 65 and older took at least 10 medications, and 23% took at least five prescription medications (Kaufman *et al.*). Such differences among gender could be due to differences in physicians' prescribing attitude toward sexes, as well as to differences between sexes in educational and socioeconomic characteristics (Bierman *et al.*, 2007). Further research exploring the relationship between sex and polypharmacy is necessary.

The study showed that patient's risk of polypharmacy was increased in case of certain particular diseases like

hypertension, heart failure and diabetes mellitus dyslipidemia, ischemic heart disease, often require combined pharmacotherapy. Similar results were obtained in the previous studies (Bjerrum, 2003). Comorbid conditions were considered to be the most significant predictors of polypharmacy, Similar to most other studies (4, Fulton and Allen 2005; Bjerrum, 2003; Anderson and Kerluke, 1996; Viola *et al.*, 2004; Thomas *et al.*, 1999) our study found a strong association between numbers of chronic conditions and risks of polypharmacy. Many have identified that visiting more physicians or lack of regular physician is a major risk factor for polypharmacy (Fulton and Allen, 2005; Veehof *et al.*, 2000; Hajjar *et al.*, 2007; Joørgensen *et al.*, 2001).

The top most frequently prescribed pharmacological classes included in this study, in particular, those that influence the cardiovascular system were anti lipemic agents b-blockers, aspirin, diuretics, ACE inhibitors, ARBS, vasodilators, nitrates, oral hypoglycaemic agents, proton pump inhibitors, calcium channel blockers, in line with the findings of other studies on polypharmacy (Bjerrum *et al.*, 1998; Anderson *et al.* 1996; Kaufman *et al.*, 2002; Wawruch *et al.*, 2008). The high proportion of lipid lowering agents, B-blockers, and ACE inhibitors, represented predominantly and, can be considered as positive, since hypertension was the most frequent diagnosis of cardiac patients. A similarly significant rise in the utilization of this class of drug was described by some other studies (Linjakumpu *et al.*, 2002; Bjerrum *et al.*, 1998; Bedell *et al.*, 2003). Conversely, study results also identified an increase in the prescription of other classes of cardiovascular drugs (Digoxin, nitrates, calcium channel blockers, diuretics, and aspirin). The frequent prescription of oral hypoglycaemic agents in our analysis reflects the preference for this medication in the therapy of diabetes mellitus.

## CONCLUSION

This study found high prevalence of polypharmacy and potentially inappropriate medications in geriatric Saudi Arabian. In addition Hypertension, diabetes mellitus, heart failure and renal diseases were the common morbidities among geriatric inpatients. Consequently, antithrombotic agents and oral hypoglycaemic agents, and antihypertensive agents were the most frequently prescribed medications and were significantly associated with polypharmacy. The study recommended that all health professionals should be knowledgeable and awareness of the number and types of medications prescribed that may cause adverse clinical outcomes in geriatric patients.

This study was the first on impact of polypharmacy and appropriateness of prescribing medications among geriatric in Saudi Arabia. The study has several limitations. Firstly, this study was conducted as a retrospective study, therefore no interventions were provided to decrease the number of medications among geriatric inpatients and reduce polypharmacy cases. Secondly, the present study was focused on patients 60 years old and more who were hospitalized at the department of CCU & cardiology unit of the King Fahad cardiac centre (KFCC) in King Khalid university hospital. Hence, these results may not be generalizable for geriatric population in different locations in Saudi Arabia.

## References

1. Anderson G, Kerluke K. Distribution of prescription drugs exposures in the elderly: descriptions and

- implications. *J Clin Epidemiol* 1996 Aug; 49 (8): 929-35.
2. Asiri YA, Al-Arifi MN. Polypharmacy and patterns in drug prescribing at a primary healthcare centre in the Riyadh region of Saudi Arabia. *Int J Pharm Pract*. 2011 Apr;19 (2):123-8. doi: 10.1111/j.2042-7174.2010.00083.x. Epub 2011 Feb
  3. Bedell, S., Jabbour, S., Goldberg, R., Glaser, H., Gobble, S., Young-Xu, Y., *et al.* (2000). Discrepancies in the use of medications [Electronic version]. *Archives of Internal Medicine*, 160(14), 2129. Retrieved August 28, 2003, from Health and Wellness Resource Center database.
  4. Beers M, Jones T, Berkwits M, Kaplan J, Porter R. *The Merck Manual of Geriatrics*, 2nd Edition. eds. Merck Research Laboratories, Whitehouse Station, NJ,1995: 1516 pp.
  5. Beers MH, Ouslander JG, Rollingher I, *et al.* Explicit criteria for determining inappropriate medication use in nursing home residents. *UCLA Division of Geriatric Medicine. Arch Intern Med*.1991;151 (9):1825–1832.
  6. Beers, M. (1997). Explicit criteria for determining potentially inappropriate medication use by the elderly: An update. *Archives of Internal Medicine*, 157(14), 1531–1537.
  7. Bierman AS, Pugh MJ, Dhalla I, *et al.* Sex differences in inappropriate prescribing among elderly veterans. *Am J Geriatr Pharmacother* 2007 Jun; 5 (2): 147-61
  8. Bikowski R, Ripsin C, & Lorraine V. Physician-patient congruence regarding medication regimens. *Journal of the American Geriatric Society*, 2001: 49(10): 1353–1357.
  9. Bjerrum L, Rosholm JU, Hallas J, *et al.* Methods for estimating the occurrence of polypharmacy by means of a prescription database. *Eur J Clin Pharmacol* 1997; 53 (1): 7-11.
  10. Bjerrum L, Sogaard J, Hallas J, *et al.* Polypharmacy: correlations with sex, age and drug regimen. A prescription database study. *Eur J Clin Pharmacol* 1998 May; 54 (3): 197-202.
  11. Bjerrum L. Pharmacoepidemiological studies of polypharmacy: Methodological issues, population estimates, and influence of practice patterns. Doctoral dissertation, Odense University 65. [Electronic version]. Retrieved August 28, 2003, from <http://www.sdu.dk/health/IPH/genpract/staff/lbjerrum/PHD/PHD.html> (Rational use of medicines by prescribers and patients.,2004)
  12. Fillit H, Futterman R, Orland B, Chim T, Susnow L, Picariello G. *et al* Polypharmacy management in Medicare managed care: Changes in prescribing by primary care physicians resulting from a program promoting medication reviews. *The American Journal of Managed Care*, 1999: 5(5): 587–594.
  13. Fourrier A, Dequae L, Chaslerie A, *et al.* sociodemographic characteristics and polypharmacy in the elderly people: data from the paquid study. *Post mark survey* ,1993: (7)291-8:
  14. Fulton MM, Allen ER. Polypharmacy in the elderly: a literature review. *J Am Acad Nurse Pract* 2005 Apr; 17 (4): 123-32.
  15. Garfinkel D, Zur-Gil S, Ben-Israel J. The war against Polypharmacy: A New Cost-Effective Geriatric-Palliative Approach for improving drug therapy in disabled elderly people. *IMAJ* 2007;9:430-434.
  16. Jyrkka J, Vartiainen L, Hartikainen S, *et al.* Increasing use of medicines in elderly persons: a five-year follow-up of the Kuopio 75+ study. *Eur J Clin Pharmacol* 2006 Feb; 62 (2): 151-8.
  17. Kaufman DW, Kelly JP, Rosenberg L, *et al.* Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. *JAMA* 2002 Jan 16; 287 (3): 337-44
  18. Lammy pp. the health status of the elderly. In: Lammy pp, editors. *Prescribing for the elderly*. Littleton: PSG publishing Co: 1980: 113-7.
  19. Lim W. K, & Woodward M.C. Improving medication outcomes in older people. *Aust J Hosp Pharm*, 1999: 29(2), 103.
  20. Linjakumpu T, Hartikainen S, Klaukka T, *et al.* Use of medications and polypharmacy are increasing among the elderly. *J Clin Epidemiol* 2002 Aug; 55 (8): 809-17.
  21. Rational use of medicines by prescribers and patients. Report by the secretariat. 16. December. 2004. World Health Organization.
  22. Sebaie Z *et al.* A study of three health centers in rural Saudi Arabia. *Saudi Med J* 1980; 1: 197–202.
  23. 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 Dec 1;27(12):1019-28.
  24. Thomas HF, Sweetnam PM Janchawee B, *et al.* Polypharmacy among older men in South Wales. *Eur J Clin pharmacol* 1999 Jul; 55 (5): 411-5
  25. Veehof L, Stewart R, Haaijer-Ruskamp F, & Meyboom-de Jong B. The development of polypharmacy: A longitudinal study. *Family Practice*, 2000;17(3): 261–267.
  26. Wawruch M, Zikavska M, Wsolova L, Kuzelova M, Tisonova J, Gajdosik J, Urbanek K, Kristova V. Polypharmacy in elderly hospitalised patients in Slovakia. *Pharm World Sci*. 2008 Jun;30(3):235-42
  27. Whitaker P, Wilson R, Bargh J Chapman M. *et al.* Use and Misuse of purchased analysis with age. *Pharm J*, 1995: 254: 553-6.
  28. World Health Organization. *Primary Health Care*. Geneva: World Health Organization, 1978.

\*\*\*\*\*