Original Article

Prevalence and associated factors of polypharmacy among adult Saudi medical outpatients at a tertiary care center

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ABSTRACT

Objective: The objective of this study was to assess the prevalence of polypharmacy (PP) and the associated factors in medical outpatients. **Materials and Methods:** A cross-sectional, observational, descriptive study was carried out in adult medical outpatients attending internal medicine clinics at King Abdulaziz Medical City, Riyadh, Saudi Arabia from 1 March 2009 to 31 December 2009. PP was defined as the concomitant use of ≥5 medications daily. The number of medications being currently taken by patient was recorded. Effect of patients' age, gender, educational level, number of prescribers, disease load and disease type on PP was assessed by multivariate analysis using Statistical Package for Social Sciences Incorporated (SPSS Inc) Version 18. **Results:** Out of 766 patients included in the study, 683 (89%) had PP. The mean number of prescribed medications, oral pills and doses was 8.8, 9.6 and 12.1, respectively. Factors significantly associated with PP included age (≥61 years), disease load and the number of prescribers. Gender had no impact on PP while education beyond primary education significantly decreased PP. Hypertension, diabetes mellitus and dyslipidemia alone and as a cluster increased PP. **Conclusion:** We found an extremely high level of PP in medical outpatients at our tertiary care center. The impact of PP on medication compliance and control of underlying diseases in Saudi Arabia is unknown and needs to be studied at different levels of care.

Key words: Medical, medications, outpatients, polypharmacy

INTRODUCTION

One of the greatest challenges facing health systems globally in the 21st century is the increasing burden of chronic diseases.[1] The aging population with multiple chronic diseases has led to a rising prescription of medications.[2-4] As a result, the use of multiple medications or polypharmacy (PP) has become common. PP, defined as the use of multiple medications and/or the administration of more medications than is clinically indicated, often represents unnecessary use of medication.[5] However, there is a lack of consensus regarding the actual number of concomitant medications taken by a person to be rated as PP. This is because different investigators have defined PP as the simultaneous use of two or more,[6] three or more,[7] and four or more medications.[8] Most of the recent studies from Europe and Australia have defined PP as concurrent use of five or more medications.[9-14] When guided by evidence-based-medicine, most of the medications used are rational and beneficial to the patients. Despite the differences in definition, PP is often associated with poor adherence to medications, adverse drug reactions, drug interactions, hospital admissions or readmissions, medication cascade effect and increasing costs.[15-18] PP is also associated with poor nutritional status,[19,20] as well as poor clinical outcomes.[21,22]

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Although a previous study from a primary health care center in Riyadh, Saudi Arabia, found a PP prevalence of 21.1% as defined by the use of 4 or more medications,[8] there is little information about its prevalence and associated risk factors in hospital settings. The aim of the present study was to assess the prevalence of PP and its associated factors in medical outpatients in a tertiary care setting in Riyadh, Saudi Arabia.

MATERIALS AND METHODS

Setting

This was an observational, cross-sectional, descriptive study of patients followed up in internal medicine outpatient clinics in the period between March 1, 2009 and December 31, 2009, at King Abdulaziz Medical City, Riyadh, Saudi Arabia. This hospital is a tertiary care teaching hospital affiliated to King Saud Bin Abdulaziz University for Health Sciences and caters for the medical needs of employees of the National Guard and their families in Saudi Arabia. After approval from the hospital research and ethical committee, patients eligible on the basis of explicit inclusion and exclusion criteria as described below participated in the study.

Inclusion and exclusion criteria

Criteria for inclusion were: Aged 12 years or over, signed an informed consent, 2 or more visits made to the clinic and taking any prescription or non-prescription medication. The exclusion criteria included patients who were not taking any medication, diagnosed with dementia, on palliative care for any malignancy and bedridden patients on nasogastric or percutaneous endoscopic gastrostomy feeding.

Definition of terms

PP was defined as the concurrent use of ≥5 medications daily for at least 3 months. This definition was adopted from many large European and Australian studies.[9-14] We defined prescription medications as medications prescribed by any of the doctors at this hospital or its affiliated clinics and dispensed from the affiliated pharmacies. The non-prescription medications were defined as any medication bought by the patient over the counter without a prescription. All oral, topical, inhaled and injectable medications taken on a daily basis were covered by this definition.

Medication count

All prescription or non-prescription medications being taken by the patient were counted as a medication. These included tablets, capsules, creams, ointments, drops, syrups, liquids, suppositories, inhalers, injections and nebulized medications. Tablets and capsules were counted as pills while other medications were counted as non-pills.

For the counting of pills, a tablet or capsule was considered as one if it was used as whole or in part (1/2 or 1/4). To count the doses of medications, the medication used on a weekly, bi-weekly or monthly basis were not included. The doses of medications taken regularly were counted as such, while the doses of Pro re nata (P.r.n) medications were taken as 50% of the maximum doses prescribed daily.

After an informed consent, eligible patients had their demographic and relevant information recorded on a special form designed for this study. This information included patients' hospital identification number, age, gender, education level, number of diseases, number of prescribers, number of drugs being used, number of doses and the number of prescription or non-prescription drugs.

Data was collected by interview, chart review and a check of all drugs being used by the patient and the tracking of their current computerized drug prescriptions. Only prescriptions filled by the patient within 1 week of being seen in the clinic were used. Patients were only included once in the study and any duplicate follow-up forms were excluded by checking the patient's unique identification number.

Statistical analyses

The Statistical Package for Social Sciences Incorporated, Version 18 (SPSS, Inc. Chicago, Illinois, U.S.A) was used for data entry, management and analysis. Data were summarized by number and percentage or mean and standard deviation (SD), as appropriate. The association between PP and categorical variables was determined by using the Chi-square test, whereas the *t*-test was used to assess the association with continuous variables. Odds ratios (OR), 95% confidence intervals (CI) and *P* values were calculated using a multivariate analysis. Alpha of 0.05 was used as an indication of statistical significance.

RESULTS

During the study period, 766 patients were eligible for inclusion in the study. Of this number, 332 (43.3%) were male and 434 (56.7%) were female, with a mean age of 60.4 (SD 14.1) years. Most of the patients, 492 (64.2%), were illiterate. The prevalence of PP was 89.1% (683 patients). Mean (SD) of the number of prescribers and number of diseases per patient was 1.69 (0.97) and 3.86 (1.39) respectively. The mean number, SD and Range (R) of prescription drugs, non-prescription drugs, number of pills, doses of pills and doses of non-pills used per patient was 8.84 (3.86, 1-24), 0.4 (0.275, 0-5), 9.56 (4.43, 1-35), 12.07 (5.90, 1-35) and 2.90 (3.12, 0-24) respectively [Table 1].

After adjustment for the confounding factors using a multivariate analysis, PP was significantly correlated with age ≥61 years compared with age ≤60 years (OR 6.33, 95%

CI 3.55-11.30, $P < 0.0001$). Gender was not a significant factor for PP (OR 0.90, CI 0.56-1.42, $P = 0.62$). Taking illiterate patients as a reference, PP was not significantly related with education to the primary level (OR 0.73, 95% CI 0.36-1.50, $P = 0.40$), but it had a significant inverse relationship to secondary school level (OR 0.22, 95% CI 0.12-0.43, $P < 0.0001$) or university level of education (OR 0.12, 95% CI 0.07-0.23, $P < 0.0001$) [Table 2]. PP was also significantly associated with the number of diseases, with the level of significance improving as the disease burden rose to two or more diseases. PP increased with two prescribers after which statistical significance level decreased with a further increase in prescriber numbers [Table 3]. By multivariate analysis of individual diseases, patients suffering from dyslipidemia (DLP), hypertension (HTN), diabetes mellitus (DM), osteoarthritis, bronchial asthma, osteoporosis, heart failure and coronary artery disease had significantly higher odds of having PP than patients who did not have these diseases. Hypothyroidism and stroke were not associated with a higher PP compared with patients who did not have these diseases [Table 4]. A cluster of diseases including DLP, HTN and DM was present in 58% of the patients and was significantly associated with PP (OR 21.4, 95% CI 8.55-53.52, P <0.0001).

DISCUSSION

We found PP in 89% of our patients. The predictors of

Table 1: Characters of medications in patients with and without PP as mean and standard deviation

Parameter	All patients (*n*=766)	PP (*n*=683)	No PP (*n*=83)	*P* value
Prescription drugs	8.84 (3.86)	9.56 (3.42)	2.88 (1.14)	<0.0001
Non-prescription drugs	0.04 (0.28)	0.04 (0.28)	0.05 (0.27)	0.79
Pill burden	9.56 (4.43)	10.29 (4.05)	3.52 (2.23)	<0.0001
Doses of pills	12.07 (5.90)	13.00 (5.47)	4.47 (3.24)	<0.0001
Doses of non-pills	2.90 (3.12)	3.17 (3.15)	0.65 (1.51)	<0.0001

PP: Polypharmcacy

Table 2: Relationship of age, gender and educational level to PP

Parameter	All patients (*n*=766)	PP (*n*=683)	No PP (*n*=83)	OR	95% CI	*P* value
Age (years)						
Mean (SD)	60.4 (14.1)	62.4 (12.2)	43.7 (17.6)	-	-	<0.0001
≤60 (%)	353 (46.1)	285 (41.7)	68 (81.9)	1 (Ref)	-	-
≥61 (%)	413 (53.9)	398 (58.3)	15 (18.1)	6.33	3.55-11.30	<0.0001
Gender (%)						
Male	332 (43.3)	298 (43.6)	34 (41.0)	1 (Ref)	-	-
Female	434 (56.7)	385 (56.4)	49 (59.0)	0.9	0.56-1.42	0.64
Education (%)						
Illiterate	492 (64.2)	461 (67.5)	31 (37.3)	1 (Ref)	-	-
Primary	131 (17.1)	120 (17.6)	11 (13.3)	0.73	0.36-1.50	0.4
Secondary	78 (10.2)	60 (8.8)	18 (21.7)	0.22	0.12-0.43	<0.0001
University	65 (8.5)	42 (6.1)	23 (27.7)	0.12	0.07-0.23	<0.0001

PP: Polypharmacy; OR: Odds ratio; CI: Confidence interval; SD: Standard deviation

Table 3: Relationship of disease load and prescribers to PP

Parameter	All patients (*n*=766)	PP (*n*=683)	No PP (*n*=83)	OR	95% CI	*P* value
Disease load						
Mean (SD)	3.86 (1.39)	4.10 (1.24)	1.89 (0.88)	-	-	<0.0001
1 disease (%)	34 (4.4)	3 (0.4)	31 (37.3)	1 (Ref)	-	-
2 diseases (%)	86 (11.2)	51 (7.5)	35 (42.2)	15.06	4.27-53.12	<0.0001
3 diseases (%)	186 (24.3)	173 (25.3)	13 (15.7)	137.5	37.02-510.82	<0.0001
≥4 diseases (%)	460 (60.1)	456 (66.8)	4 (4.8)	1178	252.4-5497.7	<0.0001
No of prescribers						
Mean (SD)	1.69 (0.97)	1.73 (0.99)	1.31 (0.62)	-	-	<0.0001
1 prescriber (%)	423 (55.2)	360 (52.7)	63 (75.9)	1 (Ref)	-	-
2 prescribers (%)	224 (29.2)	209 (30.6)	15 (18.1)	2.44	1.35-4.39	0.003
3 prescribers (%)	73 (9.5)	69 (10.1)	4 (4.8)	3.02	1.06-8.57	0.04

PP: Polypharmacy; OR: Odds ratio; CI: Confidence interval; SD: Standard deviation

Table 4: Relationship of ten most prevalent diseases with PP

Disease	Status	Patients (%)	PP (%)	No PP (%)	OR	95% CI	*P* value
Dyslipidemia	No	111 (14.5)	65 (9.5)	46 (55.4)	1 (Ref)	-	-
	Yes	655 (85.5)	618 (90.5)	37 (44.6)	11.82	7.15-19.54	<0.0001
Hypertension	No	177 (23.1)	124 (18.2)	53 (63.9)	1 (Ref)	-	-
	Yes	589 (76.9)	559 (81.8)	30 (36.1)	7.96	4.88-12.98	<0.0001
Diabetes mellitus	No	261 (34.1)	195 (28.6)	66 (79.5)	1 (Ref)	-	-
	Yes	505 (65.9)	488 (71.4)	17 (20.5)	9.72	5.56-16.98	<0.0001
Osteoarthritis	No	475 (62.0)	399 (58.4)	76 (91.6)	1 (Ref)	-	-
	Yes	291 (38.0)	284 (41.6)	7 (8.4)	7.73	3.51-17.01	<0.0001
Bronchial asthma	No	644 (84.1)	565 (82.7)	79 (95.2)	1 (Ref)	-	-
	Yes	122 (15.9)	118 (17.3)	4 (4.8)	4.13	1.48-11.48	0.003
Hypothyroidism	No	662 (86.4)	586 (85.8)	76 (91.6)	1 (Ref)	-	-
	Yes	104 (13.6)	97 (14.2)	7 (8.4)	1.78	0.81-4.01	0.15
Osteoporosis	No	686 (89.6)	605 (88.6)	81 (97.6)	1 (Ref)	-	-
	Yes	80 (10.4)	78 (11.4)	2 (2.4)	5.22	1.26-21.66	0.01
Heart failure	No	695 (90.7)	614 (89.9)	81 (97.6)	1 (Ref)	-	-
	Yes	71 (9.3)	69 (10.1)	2 (2.4)	4.55	1.10-18.92	0.02
Stroke	No	704 (91.9)	624 (91.4)	80 (96.4)	1 (Ref)	-	-
	Yes	62 (8.1)	59 (8.6)	3 (3.6)	2.52	0.77-8.23	0.11
Coronary artery disease	No	714 (93.2)	632 (92.5)	82 (98.8)	1 (Ref)	-	-
	Yes	52 (6.8)	51 (7.5)	1 (1.2)	6.62	0.90-48.52	0.03

PP: Polypharmacy; OR: Odds ratio; CI: Confidence interval

PP were age, the number of prescribers, disease load and having different chronic diseases alone or together as a cluster. It was not associated with a particular gender, while a rise in the educational level beyond primary school was associated with a decrease in PP. The prevalence of PP differs in various studies depending on the definition of PP, the age of patients included and whether the patients were seen in a general practice, hospital practice or on admission. The definition of PP we used was the concomitant use ≥ 5 medications, because this cutoff had been associated with the outcome of medication-related adverse effects for frailty, disability, mortality and falls.[14]

An 89% prevalence of PP found in our study is extremely high compared to other studies that used the same definition. For example, it was 10% in the German study of primary practice health insurance database,[9] 33% in Denmark in a population-based general practice prescription data base,[10] 46% in Italians over 65 years,[11] 47% in Norway in admitted rheumatology and internal medicine patients,[12] and 57% in geriatric patients of 75 years and over in Sweden.[13] The high level of PP recorded by us may be because our study was done at a tertiary care center, where most patients are referred because of complicated diseases or multiple morbidity. It may also be because in other countries patients often have to buy drugs or pay for prescription cost per drug, whereas all medications and supplies in our center are completely free of charge. Compared to European studies,[11,13,15,16] which showed that women used more medications than men, we did not find any significant gender difference in the use of PP. We found the educational level of the patient to be inversely related to PP. This is in agreement with findings from Sweden,[13] but in contrast to a Turkish study.[23]

In general, improving the educational level of the public may decrease PP by better primary prevention, healthy life-style and disease control. In agreement with other studies,[13,23,24] we also found increasing age to be a risk factor for PP. This is not unexpected because increasing age has been linked to increased disease burden and PP.[25] Furthermore, many of the diseases of older age are chronic in nature. PP increases with age and increasing number of chronic diseases.[26] A cluster of diseases defined as two or more concurrent chronic diseases have been found to be associated with PP. In a study of 65 years or older patients admitted to hospitals, a cluster of diseases associated with DM was associated with PP.[27]

We also found a cluster of DLP, HTN and DM to be associated with PP. We observed a slight but statistically significant difference in PP according to the number of prescribers that often results from consultations with multiple physicians. This is in contrast to a Japanese study,[28] that did not find any significant relationship between the number of consultations and number of medications prescribed.

Although the need to decrease PP has been stressed, longitudinal studies have shown an increasing PP over the years.[25,29,30] Patients on PP often do not adhere to prescribed medications. Non-adherence increases linearly with the number of medications used by a patient, being 80% with one medication compared to 20% with six or more medications.[31] Successful strategies to reduce PP have included home visits,[32,33] physician feedback,[34] physician education on the promotion of rational prescribing,[35] medication reconciliation,[36] and fixed dose combinations.[37,38] The use of these strategies needs to be explored in Saudi patients.

Our study had certain limitations. The patients might not have revealed the use of over the counter medications or the medications prescribed from other hospitals. Similarly, they might not necessarily be using the medications prescribed from our hospital. The disease load might have been under-estimated since skin, ear or eye diseases were not counted. The strength of our study includes the definition and explanation of medication numbers, pills and doses prescribed to the study population as this has not been adequately addressed in the literature.

Because of the high prevalence of PP in our center, further studies in the general population, at the primary care level and in other patient groups are needed in Saudi Arabia. A study of the impact of PP on disease control, medication adherence, health-care cost, adverse drug reactions, re-admissions and falls in Saudi Arabia should also be done.

CONCLUSION

We found a very high level of PP in the internal medicine outpatients in our tertiary care center in Riyadh, Saudi Arabia. This was related to age, educational level and number of prescribers and the burden of disease. The impact of PP on compliance to medication and control of underlying diseases in Saudi Arabia is unknown and needs to be studied at different levels of care.

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