



PREVALENCE AND DETERMINANTS OF POLYPHARMACY AMONG PATIENTS WITH CHRONIC DISEASES, MINISTRY OF HEALTH (MOH), AL-AHSA, SAUDI ARABIA, 2020

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ABSTRACT

Purpose of the study: The purpose of this study was to determine the prevalence of polypharmacy and its risk factors among the chronic disease patients attending the different ministry of health Primary health care centers of Al-Ahsa.

Introduction: Polypharmacy is defined as a phenomenon in which there is cumulative use of five or more drugs in the last two weeks. Polypharmacy is a common health problem for many patients worldwide resulting in negative effects on health status and pharmaceutical spending. Studies have shown that there were different risk factors associated with polypharmacy which included sex (females more common), ageing, being separated/divorced/widowed, educational level as lack of education, higher body mass index, decreased physical activity, being bedridden during the last two weeks and self-medication. Therefore, recognition of polypharmacy and its risk factors is the first step toward prevention of irrational use of medicines.

Material and Methods: It was a cross sectional study conducted in Al-Ahsa District of Saudi Arabia. All the Adults attending Ministry of health Primary Health Centers of Al-Ahsa, were the study population. Systematic random selections of the PHCs. were done while sample was then selected from each center randomly. The calculated sample size was 290 subjects. Data were collected using structured questionnaires. The questionnaires consisted of Socio-demographic details of the subjects. BMI, smoking status, chronic and associated diseases, number of medications, self-medications, last medical consultation time, another health care service follow up and health satisfaction. The data were entered in the Statistical Package for Social Sciences (SPSS) software version 21 and the same was used for data analysis & inference. Confidence interval (CI) 95% was chosen & the level of significance was set at < 0.05 throughout the study.

Result: Two hundred and fifty out of two hundred ninety participants took part in this survey constituting 86% of the main study sample. The mean age of the participants was **56.27** years (± 18.08 SD). More than fifty one percent of the participants (N=128) were male. Approximately two-third (N=158) of them were married, nearly one-half of the participants (N=112) were unemployed and the majority of the participants (97.6%) were Saudis. Forty two percent of the participants (95% CI 41.01-42.99, N=105) (N=105) were using four and more medicines. The adjusted ORs (AORs) and 95% CIs from multivariable logistic regression on polypharmacy has identified: age (OR= 2.70 95% CI 1.40-4.238), male gender (OR= 2.47 95% CI 1.089-4.680) and coexisting chronic conditions (DM+HTN) (OR= 3.62 95% CI 1.245-8.651). Polypharmacy was more likely among older patients than the younger adult (OR=1.65 95% CI 1.23-1.89). Hypercholesterolemia, depression/anxiety, heart diseases and hypothyroidism were all significantly associated polypharmacy. For example patients with diabetes and hypertension with hypercholesterolemia (OR=4.56 95% CI 2.765-6.452), with depression/anxiety (OR=1.023, 95% CI 0.97-3.43), and with hypothyroidism (OR=3.423, 95% CI 2.31-4.34)

Conclusion: A significant proportion of male patients especially in the older age group with chronic diseases and comorbid conditions such as heart diseases, hypercholesterolemia, depression/anxiety and hypothyroidism were more exposed to polypharmacy in our study. Smoking, Obesity, patients on self-medication as well as those patients who had medical consultation more than 3 months were other risk factors of polypharmacy in our study. Medication reviews are needed to reduce significant polypharmacy related issues in older patients.

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INTRODUCTION

Polypharmacy is a common health problem for many patients worldwide resulting in negative effects on health status and pharmaceutical spending.^[1] Therefore, recognition of polypharmacy is the first step toward prevention of irrational use of medicines. The World Health Organization (WHO) (2017) considers polypharmacy as one of the most important key of its Third Global Patient Safety Challenge,^[2] There is no universal definition of the polypharmacy. Literally

polypharmacy is defined as a phenomenon in which there is cumulative use of five or more drugs in the last two weeks^[3]. Excessive polypharmacy is defined as the use of ten or more drugs in the last two weeks. Self-medication is another drug related problem where patient uses drugs without a prescription.^[1] There are two types of polypharmacy, the first one is quantitative polypharmacy in which the patients use five or more drugs and the second one is qualitative polypharmacy in which at least one drug is considered potentially inappropriate for older adults. The presence of

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multiple comorbidities was identified as the main factor associated with the prescription of both quantitative and qualitative poly-pharmacy.^[4] Accordingly, the term 'appropriate polypharmacy' is defined as the optimization of medications for patients with complex and/or multiple conditions where medicine usage agrees with best evidence.^[5] The use of polypharmacy medications has been associated with an increased risk of potentially inappropriate medication (PIM) which can have adverse reactions for these patients without having sufficient evidence of their benefits. Inappropriate medication prescribing in older adults has become a public health concern due to its high prevalence, associated negative outcomes, including morbidity, hospitalization, health services use, and increased cost.^[6] Proper and effective Medicines are a primary factor in patient safety. With extensive use of drugs, the medication errors become a major problem in health care systems and patient safety. The medication errors are most preventable cause of patient harm, so prevention of medication errors should have high priority in health care system worldwide.^[7]

Various studies done in different parts of the world have shown the prevalence of polypharmacy ranged between 8% and 85%. The highest prevalence of polypharmacy was documented in a Portugal study.^[8] While the lowest in Brazil.^[9] These studies also showed that there were different risk factors associated with polypharmacy. Some studies showed that age was the most significant risk factor associated with polypharmacy, while other studies showed that polypharmacy is associated with many risk factors: sex (females more common), ageing, being separated/divorced/widowed, educational level as lack of education, higher body mass index, decreased physical activity, being bedridden during the last two weeks and self-medication.

The cross sectional study done in Brazil^[9] (2019) on Patient safety in primary health care and polypharmacy, showed that the prevalence of polypharmacy (consumption of four or more medications) was 37.6%. The prevalence ratio analyses identified independent variables associated with polypharmacy such as age, economic strata, way of medication acquisition through a combination of out-of-pocket and Brazilian public health system, diabetes and hypertension (2.11), comorbidities (coronary artery disease 2.26) and hospital admission (1.73). In the analyses, inappropriate drug use of the 278 patients (≥ 65 years) was associated with polypharmacy (prevalence ratio 4.04).^[2]

A similar study done in Germany (2018) on older patients with chronic diseases has shown that risk factors for polypharmacy was significantly associated with frailty (OR 1.45; 95% CI 1.22-1.71), more than 8 diagnoses (OR 2.64; 95% CI 2.24-3.11), high BMI (≥ 30) (OR 1.18; 95% CI 1.02-1.38), decreased physical health (OR 1.47; 95% CI 1.26-1.72), and decreased mental health (OR 1.33; 95% CI 1.17-1.59). Age ≥ 85 years (OR 0.83; 95% CI 0.70-0.99) led to a significantly lower risk for excessive polypharmacy.^[10]

In a recent study done in Saudi Arabia (2018) which was done on patients with diabetes in a tertiary hospital has found that 78% of the chronic disease patients had polypharmacy which was more likely among females as compared with males and more likely among elderly (age ≥ 60 years) as compared with the adults. Also, polypharmacy was two times higher among patients with coexisting cardiovascular conditions compared to diabetic patients (adjusted OR (AOR)=2.89; 95% CI 2.54 to

3.29), respiratory disease (AOR=2.42; 95% CI 1.92 to 3.03) and mental health conditions (AOR=2.19; 95% CI 1.74 to 2.76), and three times as likely among patients with coexisting musculoskeletal disease (AOR=3.16; 95% CI 2.31 to 4.30) as compared with those without these coexisting chronic conditions.

However no such study has been done in this region of Saudi Arabia with the best of our knowledge. This study was the first of its kind in this region of Saudi Arabia. This study was done to calculate the prevalence of polypharmacy and related risk factors.

MATERIAL AND METHODS

It was a cross sectional study conducted in Al-Ahsa District of Saudi Arabia between August 1st and December 31st 2020. All the Adults attending Ministry of health Primary Health Centers of Al-Ahsa, Saudi Arabia were the study population during the specified time period. However the pregnant women and PHC that are located in remote area from the main city were excluded from the study. Stratified multistage random sampling from 3 health sectors of Al-Ahsa (Hufuf, Mubarraz, Al-Omran) was done. In the first stage, systematic random selection of the centers within each sector from sample frame was done. Sample was then selected from each center randomly. Simple random selections of the patients were done within the center with chronic diseases. With a total population of 5000 patients with chronic diseases registered at all the selected PHC, we used the Epi info software to calculate the study sample. The calculated sample size was 290 subjects based on a 95% confidence level with additional 25% to compensate the missing data with a presumed prevalence of polypharmacy between 75-85% based on previous research on the same in Saudi Arabia.

Data were collected using structured questionnaires which was verified by consultants and validated by pilot study. The questionnaires were filled by assigned team trained to fill the questionnaires after interviewing the patients. The questionnaires consisted of 2 sections. The first section consisted of Socio-demographic details of the subjects. The second section consisted of BMI, smoking status, chronic and associated diseases, number of medications, self-medications, last medical consultation time, another health care service follow up and health satisfaction. The data were entered in the Statistical Package for Social Sciences (SPSS) software version 21 and the same was used for data analysis & inference. Confidence interval (CI) 95% was chosen & the level of significance was set at < 0.05 throughout the study. The appropriate test for the appropriate variables was conducted. The frequencies data was calculated. The prevalence of polypharmacy was calculated using WHO definition. Institutional Review Board (IRB) & institution-related ethical committee approval was taken before the start of the study. Informed consent was obtained from all participants prior to participation. Participants' privacy & confidentiality was reserved. The purpose of the study was explained to all participants. Any participant had a full autonomy to be involved or no in the study.

RESULT

The number of participants who answered the questionnaires completely was 250 out of 290 in number constituting 86% of the main study sample. The mean age was 56.27 years (± 18.08 SD). More than fifty one percent of the participants (N=128)

were male. Approximately two-third (N=158) of them were married, nearly one-half of the participants (N=112) were unemployed and the majority of the participants (97.6%) were Saudis. Thirty seven percent of the participants (N=92) were uneducated while thirty six percent (N=89), sixteen percent (N=41) and eleven percent (N=38) were intermediate, graduate and post graduate respectively. More than fifty percent of the participants (N=123) were over-weight while more than eighteen percent (N=50) were obese. The details of the demographic characteristics of the participants are shown in table 1.

Table 1 frequencies and percentages of the demographic data

Variables	Number	Percentage
Nationality		
Saudi	244	97.6
Non saudi	6	2.4
Sex		
Male	128	51.2
Female	122	48.8
Age group		
<40 years	68	27.2
41- 50 years	59	23.6
51-60 years	63	25.2
>60 years	60	24
Marital Status		
Unmarried	47	18.8
Married	158	63.2
Divorced	12	4.8
Widow	33	13.2
Level of education		
Uneducated	92	36.8
Secondary	89	35.6
Graduate	41	16.4
Post Graduate	28	11.2
Occupation		
Unemployed	132	44.8
Employed	71	28.4
Retired	47	18.8
BMI		
Underweight	3	1.2
Normal	76	50.4
Over weight	123	49.2
Obese	50	18.4

Forty two percent of the participants (95% CI 41.01-42.99, N=105) (N=105) were using four and more medicines while more than fifty five patients (N=139) were using less than four medicines. The details of the poly pharmacy status is shown in table 2

Table 2 showing frequencies and percentages of polypharmacy

Variable	Number of medicine being used	n	%
How many medications do you take currently?	None	6	2.4
	less than 4	139	55.6
	4 and more	105	42.0
	Total	250	100.0

A total of sixtyeight participants (27.2%) stated that they were taking self-medication and more than twenty five percent of the participants (N=64) were smokers. Approximately one-half of the participants (N=122) stated that they have diabetes and hypertension. More than fifty percent of the participants (N=129) stated that they had associated other diseases. The most mentioned diseases were Stroke (6.52%), Hypercholesteremia (29.46%), Osteoarthritis (13.18%, heart disease (16.28%) and GERD/ Dyspepsia (7.75%). And hypothyroidism (13.18%) More than sixty percent of the participants (N=151) mentioned that the last time they had a

medical consultation was 3 or more months ago. The details of the risk factors are shown in table 3

Table 3 Showing frequencies and percentages of the risk factors of the study

Variable	Number	Percentage
Are you taking self-medication?		
Yes	68	27.2
No	182	72.8
Are you currently smoking?		
Yes	64	26.6
No	186	73.4
Which chronic disease do you have?		
DM	77	30.8
HTM	51	20.4
DM+HTM	122	48.8
Do you have any associated disease?		
Yes	129	58.6
No	121	41.4
Associated diseases (N=129)		
Stroke	11	6.52
Hypercholesterolemia	38	29.46
Depression/anxiety	15	1.63
Heart diseases	21	16.28
Osteoarthritis	17	13.18
GERD/Dyspepsia	10	7.75
Hypothyroidism	17	13.18
When was the last time you had medical consultation?		
Less than 3 months	99	39.6
More than 3 months	151	60.4

The prevalence of polypharmacy was significantly higher among male than the female (58% Vs. 24.59%, P=.001). Similarly As age progressed the prevalence of polypharmacy increased significantly. It was highest among the age group higher than 60 years and lowest among the age group less than 40 years (80% Vs. 25%, P=0.0001). The prevalence was also higher among the married than the unmarried participants (60.12% Vs.10.63%, P=0.0001). The level of education was not significantly associated with polypharmacy prevalence and so also the and so also the occupation. P=0.0001). However polypharmacy was more prevalent among obese than the normal weight or overweight (70% Vs.26.31% Vs.40.65%, P=0.02).

Table 4 presents the relationship between demographic characteristics and polypharmacy.

Variables	Using 4 and more than 4 medicines N (%)	Using less than 4 medicines N (%)	p value
Gender			
Male	75 (58.59)	53(41.41)	.001
Female	30 (24.59)	92 (75.41)	
Age group			
Less than 40 years	17(25)	51(75)	0.0001
41-50 years	40 (67.80)	19(32.20)	
51 to 60 years	48 (80)	12 (20)	
Marital Status			
Unmarried	5(10.63)	42(89.37)	0.0001
Married	95(60.12)	63(39.88)	
Widow	5 (15.15)	28(84.85)	
Divorced	1 (8.33)	11(91.67)	
Level of education			
Uneducated	45 (45.45)	54(54.55)	0.072
Secondary	17 (47.22)	19(52.78)	
Graduate	26(49.05)	27(50.95)	
Post graduate	14(50.00)	14(50.00)	
Occupation			
Unemployed	58(51.78)	54(48.22)	0.081
Employed	35 (49.29)	36 (50.71)	
Retired	24 (51.06)	23(48.94)	
BMI			
Underweight	0(0)	3 (100)	0.02

Overweight	50 (40.65)	73(59.35)
Normal	20(26.31)	56(73.69)
Obese	35 (70.00)	15(30.00)

** Significant at p<0.05 level.

As far as the relationship between polypharmacy and risk factors is concerned, there was a significant relationship between polypharmacy and self-medication (63.24% vs. 34.07, p=0.002). Similarly there was a significant relationship between polypharmacy and the participants who were smoking (64.07 vs. 34.60%, P=0.001) than the nonsmoker. Polypharmacy was also significantly more among participants with DM+HTN (63.11% Vs. 29.87% Vs. 9.60%,P=0.0001) than those with only DM and only hypertension. The prevalence of polypharmacy was also significant among the participants who were suffering from other diseases (70.07% Vs. 19.20%, P=0.0001).

Patients with diabetic and hypertension and associated Stroke (63.64% Vs. 36.36, P=0.002), hypercholesterolemia (84.21% Vs.15.79%, P=0.0001), depression/anxiety (66.64% Vs. 33.33%, P=0.001), heart diseases(71.43% Vs. 28.57, P=0.001) and hypothyroidism (68.75% Vs. 31.25%, P=.001).

Those participants who had delayed consultation of more than 3 months had significantly higher poly-pharmacy than those with consultation within 3 months (59.95% Vs. 19.20%, P=0.02).The details of the relationship of poly-pharmacy with the risk factors are shown in table 5.

Table 5 Showing the relationship between polypharmacy and risk factor

Risk factors	With less than 4 medicines N(%)	With more than 4 medicines N (%)	P value
Patients on self-medication			
Yes	25 (37.76)	43(63.24)	0.002
No	120(65.93)	62(34.07)	
Patients with smoking			
Yes	23 (35.93)	41(64.07)	0.001
No	121(65.40)	64(34.60)	
Patients having chronic diseases			
DM	54(70.13)	23(29.87)	0.0001
HTN	46 (90.20)	5(9.60)	
DM+HTN	45 (36.89)	77(63.11)	
Patients having other associated diseases			
Yes	35(28.93)	94(70.07)	0.0001
No	80(62.01)	41(37.99)	
Stroke	4(36.36)	7(63.64)	0.002
Hypercholesteremia	6 (15.79)	32(84.21)	0.0001
Depression/anxiety	5 (33.33)	10(66.64)	0.001
Osteoarthritis	11 (64.71)	6(35.29)	0.01
Heart disease	6 (28.57)	15 (71.43)	0.001
GERD/dyspepsia	7 (70.0)	3(30.0)	0.001
Hypothyroidism	5 (31.25)	11(68.75)	0.0001
When was the last time you had medical consultation?			
Less than 3 months	80(80.80)	19(19.20)	0.02
More than 3 months	65(43.05)	86(59.95)	

** Significant at p<0.05 level

Logistic regression: factors associated with polypharmacy:

The adjusted ORs (AORs) and 95% CIs from multivariable logistic regression on polypharmacy has identified: age (OR= 2.70 95%CI 1.40-4.238), male gender (OR= 2.47 95% CI 1.089-4,680) and coexisting chronic conditions (DM+HTN) (OR= 3.62 95% CI 1.245-8.651). Polypharmacy was more likely among older patients than the younger adult (OR=1.65 95% CI 1.23-1.89). Hypercholesterolemia, depression/anxiety,

heart diseases and hypothyroidism were all significantly associated polypharmacy. For example patients with diabetes and hypertension with hypercholesterolemia (OR=4.56 95% CI 2.765-6.452), with depression/anxiety (OR=1.023, 95% CI 0.97-3.43), and with hypothyroidism (OR=3.423, 95% CI 2.31-4.34)

DISCUSSION

This study was meant to determine the prevalence of polypharmacy and the risk factors influencing the polypharmacy among the patients with chronic diseases attending the Ministry of Health Primary health care centers of Al-Ahsa district of Saudi Arabia. This study has found a prevalence of polypharmacy among the chronic patients to be 40% which is higher than that of the similar study done in Brazil^[4] (37.6%), Gaza^[11] (27.6%), Iran^[12] (23.1%),Togo^[13] (22.7%), Spain^[14](21.9%) and Australia^[15] (36.1%) but lower than what found in Greek^[16](53.5%),UAE^[17](89%),China^[18] (72.2%), Jordan^[19](74.9%), Qatar^[20] (75.5%) and another Saudi study^[3] (78%).

In our study the prevalence of polypharmacy among male(58% vs. 24.59%, OR= 2.47 95% CI 1.089-4,680, P=.001)was significantly higher than those of female counterpart. The same result was found in Singapore study^[21] where prevalence of polypharmacy was significantly more among the male. The Brazil study^[4] also revealed that males were significantly more exposed to polypharmacy than the opposite sex. However in Gaza^[11], Jordan^[19], Australian^[15] and in another Saudi Study^[4] Polypharmacy was higher in female than that of male. In Iranian study^[12] also the prevalence of polypharmacy was statistically significant among women than the men (32.7% vs. 15.2%, odds ratio = 1.51, 95% confidence interval: 1.10-1.93). Similar result was found in a Qatari study^[20] where females were 1.18 times more likely to have polypharmacy compared to males (95% CI: 1.03-1.34).

As age progressed the prevalence of polypharmacy increased significantly in our study.it was highest among the age group higher than 60 years and lowest among the age group less than 40 years (80% Vs. 25%, P=0.0001).Similar result was found in Gaza study^[11] where the polypharmacy was highest among patients aged 60 - 69 years when compared with other ages categories of study population but not reached to be statistically significant (0.012).In china study^[18] also the odds of polypharmacy prescription increased with patients' age (18-39 years: 1; 40-59 years: OR 1.86, 95% CI 1.28-2.71; and ≥60 years: 2.42, 1.65-3.55),A significantly higher percentage of polypharmacy among older adults as compared with patients with age between 18 and 29 years (84.8% vs. 37.4%, p<0.001) was also found in other Saudi study^[4]. In an Australian Study^[15] the researchers have found highest prevalence of polypharmacy among those aged 80-84 years (43.9%). However in UAE study^[17] the reverse was true and the lowest level of polypharmacy was found in age group above 80 years of age. One possible reason for the high rate of polypharmacy among this age group might be the coexistence of other chronic conditions.

Self-medication has been found as an important risk factor of polypharmacy. The patients on self-medication were significantly associated with polypharmacy in our study. In Jordan^[19], Togo^[13] and Spain^[14] studies the same result were found.

The prevalence of polypharmacy was significantly higher among married patients in our study. In Spain study^[14] polypharmacy was associated with divorced and widow. However most of the mentioned studies including one of American study^[23] did not find any co relation between polypharmacy and marital status.

The prevalence of polypharmacy was significantly higher among obese patients than the normal, overweight and underweight patients in our study. The same result was published by a research done in Europeanunion^[24] countries where being obese (OR 1.18; 95% CI 1.02–1.38) was one of the significant risk factors of polypharmacy. The same result was found in study done on African Americans^[25] where obesity was a risk factor for polypharmacy. In An UK Study^[25] Obesity was found to be significantly associated with polypharmacy (adjusted HR 1.81; 95% CI 1.53 to 2.15, p<0.01). Spain study^[14] also found that High Body Mass Index (BMI) was associated with polypharmacy

A significant association between smoker and polypharmacy was observed in our study. In a similar study in UK no statistically significant association between smoking and polypharmacy (adjusted HR 1.06; 95% CI 0.86 to 1.29, P=0.56) was established. However in a polish study^[26] cigarette smoking was not found a determinant of polypharmacy.

Coexisting chronic conditions (DM+HTN) (OR= 3.62 95% CI 1.245-8.651), Hypercholesterolemia, depression/anxiety, heart diseases and hypothyroidism were all significantly associated polypharmacy. For example patients with diabetes and hypertension with hypercholesterolemia (OR=4.56 95% CI 2.765-6.452), with depression/anxiety (OR=1.023, 95% CI 0.97-3.43), and with hypothyroidism (OR=3.423, 95% CI 2.31-4.34). In a similar study in Saudi Arabia^[3] polypharmacy was found two times as likely among patients with coexisting cardiovascular conditions and mental health conditions as compared with those without these coexisting chronic conditions categories.

A study conducted on Thais population has also found the predictors associated with polypharmacy in the logistic regression model included hypertension (OR = 1.985, 95% CI = 1.420–2.775), anxiety disorder (OR = 4.402, 95% CI = 2.630–7.367) and dyslipidemia (OR = 0.511, 95% CI = 0.325–0.803).^[27] In Greek study^[16] also the independent predictors of polypharmacy were arterial hypertension, coronary artery disease and heart failure

We have seen in our study that older male people on self-medication and with comorbid conditions are more prone to polypharmacy. Healthcare providers need to give more attention on these categories of patients and should monitor them for potentially inappropriate medications, adverse drug events and drug-drug interaction. Furthermore the patients with both hypertension and diabetes and with comorbid conditions, polypharmacy may benefit from multidisciplinary collaborative care model that involves pharmacist follow-up for the patients to assess the medication use and minimize polypharmacy.

Those Patients who had medical consultation for over 3 months' time had significantly higher polypharmacy than those less than 3 months. This might be due to the reason of self-medication.

Conclusion: A significant proportion of male patients especially in the older age group with chronic diseases and comorbid conditions such as heart diseases, hypercholesterolemia, depression/anxiety and hypothyroidism were more exposed to polypharmacy in our study. Smoking, Obesity, patients on self-medication as well as those patients who had medical consultation more than 3 months were other risk factors of polypharmacy in our study. Medication reviews are needed to reduce significant polypharmacy related issues in older patients.

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