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## Polypharmacy among patients with diabetes: a cross-sectional retrospective study in a tertiary hospital in Saudi Arabia

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# BMJ Open Polypharmacy among patients with diabetes: a cross-sectional retrospective study in a tertiary hospital in Saudi Arabia

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**Abstract** Patients with diabetes are at high risk for polypharmacy (ie, use of multiple medications) for treatment of diabetes, associated comorbidities and other coexisting conditions. This study aims to estimate the prevalence of polypharmacy and factors associated with polypharmacy among adult patients with diabetes.

**Methods** A cross-sectional retrospective observational study of adults with diabetes, who visited the outpatient clinic of a tertiary teaching hospital in Saudi Arabia, was conducted. Data were extracted from the Electronic Health Record database for a period of 12 months (January–December 2016). Polypharmacy was defined as the cumulative use of five or more medications. Polypharmacy among adults with diabetes was measured by calculating the average number of medications prescribed per patient. A multivariable logistic regression model was used to examine the factors associated with polypharmacy.

**Results** A total of 8932 adults with diabetes were included in this study. Of these, nearly 78% had polypharmacy which was more likely among women as compared with men and more likely among older adults (age  $\geq 60$  years) as compared with the adults. Also, polypharmacy was two times as likely among patients with coexisting cardiovascular conditions (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 categories.

**Conclusions** Polypharmacy is common among patients with diabetes, with an even higher rate in older adults patients. Healthcare providers can help in detecting polypharmacy and in providing recommendations for simplifying medication regimens and minimising medications to enhance the outcome of diabetes care.

## INTRODUCTION

Diabetes is a highly prevalent chronic condition among adults in Saudi Arabia; between 21% and 24% of adults are estimated to have diabetes.<sup>1,2</sup> It is projected that 27% of adults in Saudi Arabia will have diabetes by 2035.<sup>3</sup> Diabetes is 1 of the top 10 causes of morbidity

## Strengths and limitations of this study

- This study has provided a real insight into the current prevalence and predictors of polypharmacy among patients with diabetes in Saudi Arabia including a large study population of patients with diabetes.
- Around 9000 patients were included in this study which allowed us to identify the prevalence of polypharmacy among a subgroup of patients.
- This study has not controlled for the severity of diabetes using the Diabetes Complications Severity Index which may affect the rate of polypharmacy.
- This study used a 12-month period to measure multiple medications use which is not concurrent use and may have resulted in a very high rate of multiple medications uses.
- It has to be noticed that not all polypharmacy is harmful; however, future studies to assess inappropriate medications associated with polypharmacy is warranted.

and mortality worldwide.<sup>4</sup> Patients with diabetes often have coexisting chronic health conditions such as hypertension, dyslipidaemia, coronary artery disease, depression and chronic kidney disease, which requires the use of multiple medications to treat those coexisting chronic conditions.<sup>5</sup> All of this put patients with diabetes at high risk of polypharmacy,<sup>6,7</sup> with an estimated prevalence of 57%–84% of patients with diabetes using five or more medications.<sup>8</sup> A study among adults with diabetes in the USA documented that the 54% of adults with diabetes have polypharmacy.<sup>9</sup> A multicentre cross-sectional survey conducted in Italy reported that 57% of patients with diabetes use five or more medications.<sup>10</sup> In addition, polypharmacy was reported among 84% older adults patients with diabetes.<sup>8</sup> In Saudi Arabia, a cross-sectional study among 766 adults who visited outpatient's clinic at a tertiary care centre,

reported that the prevalence of polypharmacy among patients with diabetes was 71%.<sup>11</sup>

An examination of polypharmacy among patients with diabetes is important because polypharmacy increases the probability of the adverse drug events,<sup>12 13</sup> drug–drug interactions,<sup>14</sup> duplication of therapy,<sup>15</sup> decreases compliance to antidiabetic medications<sup>16</sup> and leads to suboptimal glycaemic control.<sup>17</sup> The presence of polypharmacy is also associated with prescribing cascade, in which adverse drug events are misinterpreted as new medical conditions which can result in the prescription of new medications to treat those conditions.<sup>18</sup> Polypharmacy has other negative health consequences such as increased risk of hospitalisation and medication error,<sup>19 20</sup> higher risk of fall,<sup>21</sup> poor functional status,<sup>22</sup> poor quality of life and high healthcare cost.<sup>23 24</sup> Polypharmacy among patients with diabetes is often associated with many factors. These include age,<sup>11</sup> sex,<sup>10</sup> coexisting conditions,<sup>10</sup> rurality,<sup>11 25</sup> diabetes complications<sup>10</sup> and aggressive diabetes treatment.<sup>26 27</sup>

To date, limited studies have examined the prevalence of polypharmacy among adults with diabetes living in Saudi Arabia on a large scale, and assessed the specific factors that put patients at risk of polypharmacy. Identifying the prevalence and the subgroup of patients at high risk of polypharmacy will facilitate pharmacovigilance efforts in clinical practice settings. Therefore, the primary objective of this observational study is to examine the prevalence of polypharmacy among adults with diabetes in Saudi Arabia and to identify the factors that are associated with polypharmacy, specifically the association between coexisting chronic conditions and polypharmacy.

## METHODS

### Study design

A cross-sectional retrospective observational study was conducted in a tertiary teaching hospital in Saudi Arabia. This hospital is one of the largest tertiary teaching hospitals in Riyadh, Saudi Arabia, with a 1200-bed facility and all general and subspecialty medical services. The hospital provides primary, secondary and tertiary care services. The patient population is composed predominantly of local citizens as well as residents, from Northern region in Riyadh; the hospital also serves the entire country as a referral centre.

### Data source and data extraction

This study used data retrieved from the Electronic Health Record (EHR) database for the period from 1 January 2016 to 30 December 2016. Strict confidentiality of the data was maintained throughout the research process. The data from EHR were derived from demographics file, clinical diagnosis file and prescription drug file. The demographics file contained information about the patients' date of birth, gender, marital status, nationality and encounter type. The clinical diagnosis file provided information about the clinical diagnosis from

inpatient and outpatient visits. Physicians reported clinical diagnosis using the International Classifications of Diseases, ninth edition, Clinical Modification (ICD-9-CM) codes, ICD-10th edition, CM codes or the Systematised Nomenclature of Medicine diagnosis codes. The prescription drug file contained information about the medications used. The demographics, clinical diagnosis and prescription drug files were merged into one file using the encrypted patient medical record number. The completeness and the validity of the data from EHR in this tertiary teaching hospital in Saudi Arabia has not been studied before; however, the researchers of this study examined the completeness of this data and found that 91.0% of the patients had a complete data (ie, have information on the age, gender, marital status, nationality, encounter type and clinical diagnosis) and 85.0% of the patients had complete medication-related information.

### Study population

The study population comprised all adult patients with diabetes (type 1 and type 2) (age ≥18 year) (n=8932) who received their treatment at the outpatient's setting in the tertiary teaching hospital during a 1-year period. No exclusion criteria were applied to the study population.

### Patient and public involvement

Patients and public were not involved in the design or conduct of this study.

### Measures

#### Dependent variable

In our study, the dependent variable was 'polypharmacy'. There are different approaches in the literature to measure polypharmacy such as simultaneous, cumulative and continuous. Also, there is no consensus on the thresholds regarding the number of medications above which we consider the existence of polypharmacy.<sup>28</sup> In the current study, we defined polypharmacy as the cumulative use of five or more medications during a 1-year period, this threshold has been used more than others.<sup>25 28 29</sup> Using this definition, the prevalence of polypharmacy among adults was measured by the sum of unique therapeutic medication classes administered over a 12-month period. There is no consensus on the medications that should be included in the measurements of the polypharmacy. Also, all the prescription and the non-prescription/over-the-counter (OTC) medications categories were included in our definition of polypharmacy.

#### Independent variables

Independent variables included were age groups in years (18–29, 30–39, 40–49, 50–59, 60–69, 70–79, >80), gender, nationality (Saudi, non-Saudi), marital status (married, unmarried) and documented chronic conditions which were classified into five categories (cardiovascular, chronic kidney disease, musculoskeletal, respiratory or mental health conditions) (online supplementary appendix 1). Cardiovascular conditions composed of hypertension, ischaemic heart disease, vascular heart disease, stroke,

heart failure and dyslipidaemia. Musculoskeletal conditions composed of osteoarthritis and osteoporosis; respiratory conditions include asthma and chronic obstructive pulmonary disease (COPD). Mental health conditions include dementia, depression, anxiety and schizophrenia. These conditions have been selected because they are highly prevalent among patients with diabetes and some of them were associated with polypharmacy.<sup>5 30</sup>

### Statistical analysis

Frequency and percentage were used to describe the categorical variables (age, sex, marital status, nationality, coexisting chronic conditions and polypharmacy). Mean and SD were used to describe continuous variables.  $\chi^2$  tests were used to examine the factors associated with polypharmacy. A multivariable logistic regression was used to examine the factors associated with polypharmacy (ie, use of  $\geq 5$  medications) after adjusting for age, sex, marital status, nationality and coexisting chronic conditions. All statistical analyses were carried out using the SAS V.9.2.

## RESULTS

A total of 8932 adult patients were identified during the 12-month period. The majority were Saudi (89.4%), female (62.2%) and 43.3% of the study population were older adults (age  $\geq 60$  years), the mean age of the study population was 57 years old. About half of the subjects (54.1%) had two or more diagnosed coexisting chronic health conditions. Hypertension, dyslipidaemia, asthma, osteoarthritis and anxiety were among the most common chronic conditions in our study population. Characteristics of the study population are presented in [table 1](#).

### Polypharmacy among patients with diabetes

Overall, 77.9% of adults with diabetes have used (cumulative) five or more medications. Also, when we identified the rate of hyperpolypharmacy (ie, taking 10 or more medications), we found that 17.2% of adults have a hyperpolypharmacy. The most commonly used medications in our study population were antidiabetic medications (81.4%), followed by non-steroidal anti-inflammatory drugs (NSAIDs) (72.4%) and antihyperlipidaemic agents (68.8%) ([table 2](#)).

The study population characteristics by polypharmacy status are summarised in [table 1](#). This study found 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%,  $p < 0.001$ ). Women with diabetes had a significantly higher percentage of polypharmacy as compared with men (81.7% vs 71.6%,  $p < 0.001$ ). Moreover, polypharmacy was significantly higher among patients with diabetes with two or more coexisting comorbid conditions versus those with no coexisting chronic conditions (89.6% vs 48.6%,  $p < 0.001$ ). Looking at comorbid conditions closely, polypharmacy was significantly higher among patients with cardiovascular disease (83.4%,  $p < 0.001$ ), chronic kidney disease

(95.2%,  $p < 0.001$ ), musculoskeletal (93.6%,  $p < 0.001$ ), respiratory (89.0%,  $p < 0.001$ ) and mental health conditions (85.4%,  $p < 0.001$ ) as compared with those without those coexisting chronic conditions.

### Logistic regression: factors associated with polypharmacy

The adjusted ORs (AORs) and 95% CIs from multivariable logistic regression on polypharmacy are displayed in [table 3](#). Several factors were identified: age, gender and coexisting chronic conditions. Polypharmacy was more likely among older adults as compared with younger adults. Women were more likely to have polypharmacy compared with men (AOR=1.60; 95% CI 1.43 to 1.79). Cardiovascular diseases, mental conditions, respiratory and musculoskeletal diseases were all significantly associated with polypharmacy. For example, adults with diabetes and musculoskeletal disease were three times more likely to have polypharmacy (AOR=3.16; 95% CI 2.31 to 4.30) as compared with adults with diabetes and without musculoskeletal conditions.

## DISCUSSION

Our study was set out to examine the prevalence of polypharmacy among adults with diabetes in Saudi Arabia. In this large sample of subjects with diabetes, the rate of polypharmacy was high, as nearly four out of five adults with diabetes were prescribed five or more medications. Similar rates were reported in the literature among patients with diabetes 54%–84%,<sup>8–10</sup> however, to our knowledge, no study has attempted to measure the rate of polypharmacy among all age groups of adults with diabetes, which is a major contribution of our study. A higher rate of polypharmacy among older individuals (age 60 and above) as compared with all age groups was also observed in this study. Studies among adults in the general population have reported that older adults (defined as age  $\geq 60$  or age  $\geq 65$  years) have a higher risk of polypharmacy use as compared with adults.<sup>31 32</sup> One possible reason for the high rate of polypharmacy among this population is the coexistence of other chronic conditions.

Furthermore, a noteworthy finding of the current study is the high prevalence of chronic conditions and the higher rate of polypharmacy among diabetic individuals with coexisting chronic conditions. Previous studies have shown that 90% of patients with diabetes had at least one coexisting chronic condition,<sup>5</sup> our study found that 86% of patients with diabetes had at least one coexisting chronic condition. It is plausible that the high rate of polypharmacy in this study is potentially associated with the number of comorbidities among the study population. The findings of this study support that patients with diabetes with multiple chronic conditions were at higher risk of polypharmacy.<sup>5 33</sup> Although there is a well-documented literature on the relationship between the higher number of coexisting conditions and polypharmacy,<sup>5 10 34</sup> our study extended the literature by analysing the association between the type of chronic conditions

**Table 1** Characteristics of the study population number and row percentage of characteristics by polypharmacy among adults with diabetes, Electronic Health Records database, 2016

	Total		Polypharmacy		No polypharmacy		X <sup>2</sup> value	Significance
	N	%	N	%	N	%		
Total	8932	100.0	6957	77.9	1975	22.1		
# of medications mean(SD)	6.54 (3.50)		8.06 (2.97)		2.85 (1.14)			
Age mean (SD)	57.7 (12.12)		59.7 (11.3)		52.7 (12.68)			
Age group							517.7	***
18–29	198	2.2	74	37.4	124	62.6		
30–39	463	5.2	253	54.6	210	45.4		
40–49	1226	13.7	830	67.7	396	32.3		
50–59	3176	35.6	2521	79.4	655	20.6		
60–69	2434	27.3	1909	78.4	525	21.6		
70–79	1126	12.6	951	84.5	175	15.5		
≥80	309	3.5	269	87.1	40	12.9		
Marital status							76.5	***
Single	957	11.6	635	66.4	322	33.6		
Married	7310	88.4	5769	78.9	1541	21.1		
Gender							122.8	***
Male	3375	37.8	2418	71.6	957	28.4		
Female	5557	62.2	4539	81.7	1018	18.3		
Nationality							6.6	**
Saudi	7957	89.4	6167	77.5	1790	22.5		
Non-Saudi	946	10.6	768	81.2	178	18.8		
Chronic kidney disease							25.8	***
Yes	146	1.6	139	95.2	7	4.8		
No	8786	98.4	6818	77.6	1968	22.4		
Cardiovascular conditions							668.1	***
Yes	7209	80.7	6015	83.4	1194	16.6		
No	1723	19.3	942	54.7	781	45.3		
Musculoskeletal conditions							124.4	***
Yes	787	8.8	737	93.6	50	6.4		
No	8145	91.2	6220	76.4	1925	23.6		
Respiratory conditions							76.8	***

Continued

**Table 1** Continued

	Total		Polypharmacy		No polypharmacy		X <sup>2</sup> value	Significance
	N	%	N	%	N	%		
Yes	961	10.8	855	89.0	106	11.0		
No	7971	89.2	6102	76.6	1869	23.4		
Mental health conditions							27.3	***
Yes	766	8.6	654	85.4	112	14.6		
No	8166	91.4	6303	77.2	1863	22.8		***
# Chronic conditions							1093.8	***
No coexisting conditions	1250	14.0	607	48.6	643	51.4		
Single coexisting condition	2849	31.9	2018	70.8	831	29.2		
≥2 coexisting conditions	4833	54.1	4332	89.6	501	10.4		

Study population comprised 8932 adults with diabetes (age >18 years) who visited outpatient's clinics from a tertiary hospital in 2016. Polypharmacy was defined as the cumulative use of five or more medications during the 1-year period.

#, Number.

Asterisks (\*) represent significant differences in polypharmacy from X<sup>2</sup> tests.

\*P<0.001, \*\*0.001≤P<0.01.

**Table 2** Most prevalent therapeutic classes among the study population (n=8932)

Medication therapy class	N	%
Oral antidiabetic agent	7270	81.4
Non-steroidal anti-inflammatory drugs	6467	72.4
Antihyperlipidaemic agents	6144	68.8
Proton pump inhibitor	2540	28.4
ACE inhibitor	2321	25.9
Injectable antidiabetic agent	2253	25.2
Calcium channel blocker	2162	24.2
Corticosteroid, local	1892	21.1
Diuretic	1934	21.6
Beta-adrenergic blocker, beta-1 selective	1806	20.2
Angiotensin II receptor blocker	1796	20.1
Thyroid analogue	1355	15.1
Histamine H2 blocker	822	9.2
Anticoagulants	706	7.9
Corticosteroid, systemic	600	6.7
Antiplatelet	357	4.0

and polypharmacy. We observed that the polypharmacy rates differed by the type of coexisting chronic conditions; with the highest use among those with musculoskeletal conditions. This is not surprising because individuals with musculoskeletal conditions such as osteoarthritis use analgesic and NSAIDs to relieve the chronic pain. We also observed that patients with cluster of diseases (diabetes and cardiovascular diseases) have a higher rate of polypharmacy as compared with adults without the cluster of diseases which is consistent with the published literature.<sup>31 35</sup> Patients with diabetes and mental health conditions have also a high rate of polypharmacy as compared with those without mental health conditions. Further studies are required to explore the contributing factors, as there is no supporting evidence in the literature. Polypharmacy was also highly prevalent among patients with diabetes and respiratory diseases, which is consistent with data from previous studies, which showed higher rates of medication use in patients with COPD.<sup>36</sup>

Accordingly, healthcare providers need to routinely monitor these individuals for potentially inappropriate medications, adverse drug events and drug–drug interactions. For instance, in older individuals, comprehensive geriatric assessment has shown effective impact in decreasing the number of medications prescribed.<sup>37</sup> Further, patients with diabetes and polypharmacy may benefit from multidisciplinary collaborative care model that involves pharmacist follow-up for the patients to assess the medication use and minimise polypharmacy. In an open-label, parallel-arm, randomised, controlled study, collaborative care has been associated with improvement in the management of diabetes and

**Table 3** AORs and 95% CIs logistic regression on polypharmacy adults with diabetes, Electronic Health Records Database, 2016

	AOR	95% CI	Significance
<b>Age group</b>			
30–39 vs 18–29	1.48	(1.00 to 2.18)	**
40–49 vs 18–29	2.13	(1.47 to 3.08)	***
50–59 vs 18–29	3.54	(2.46 to 5.11)	***
60–69 vs 18–29	5.11	(3.51 to 7.44)	***
70–79 vs 18–29	7.59	(5.07 to 11.35)	***
≥80 vs 18–29	9.65	(5.69 to 16.38)	***
<b>Marital status</b>			
Single versus married	1.16	(0.96 to 1.40)	
<b>Gender</b>			
Female versus male	1.60	(1.43 to 1.79)	***
<b>Nationality</b>			
Non-Saudi versus Saudi	1.81	(1.50 to 2.19)	***
<b>Cardiovascular conditions</b>			
Yes versus no	2.89	(2.54 to 3.29)	***
<b>Musculoskeletal conditions</b>			
Yes versus no	3.16	(2.31 to 4.30)	***
<b>Respiratory conditions</b>			
Yes versus no	2.42	(1.92 to 3.03)	***
<b>Mental health conditions</b>			
Yes versus no	2.19	(1.74 to 2.76)	***

Based on 8932 adults with diabetes, who visited outpatient's clinics from a tertiary hospital in 2016. Polypharmacy was defined as the cumulative use of five or more medications during the 1-year period.

Asterisks (\*) represent significant differences on polypharmacy compared with the reference group based on logistic regression.

\* $P < 0.001$ , \*\* $0.001 \leq P < 0.01$ .

AOR, adjusted OR.

reduction the healthcare cost.<sup>38</sup> Pharmacists can help other healthcare providers in detecting polypharmacy, drug interactions and in providing recommendations for simplified medication regimens and minimising medications to positively impact health outcomes of diabetes care.<sup>39–40</sup>

We also looked at other related factors for polypharmacy. We observed that women were more likely to have a polypharmacy compared with men, this is consistent with the findings from data among patients with diabetes.<sup>10</sup> In addition, studies have reported that women in the general population have a higher use of prescribed and non-prescribed medications, and higher healthcare utilisation as compared with men.<sup>41–44</sup> This could be because women tend to be more concerned about their health and seek health services more often than men.<sup>45</sup> It has to be noted that the majority of patients with diabetes in our study were women, this is not surprising since the rate of diabetes is higher in women as compared with men in Saudi Arabia.<sup>2</sup>

## Strengths and limitations

This study has some limitations; we defined polypharmacy as the cumulative use of five or more medications during a 1-year period rather than the concurrent use of medications, using this definition may have overestimated the rate of polypharmacy. We did not control for the severity of diabetes using the Diabetes Complications Severity Index, which may affect the rate of polypharmacy. We have also only observed filled prescriptions and not actual use of the medications. By using the EHR data, we cannot eliminate some risk of bias; inaccurate information or missing data related to the use of EHR. Due to the cross-sectional nature of the data, it is difficult to assess any causal relationships. People with the end-of-life care were included in the study, which may have also overestimated the rate of polypharmacy.<sup>46</sup> Moreover, we have included all therapeutic medication classes, including OTC medications and vitamins in our definition, which may have overestimated the rate of polypharmacy. It has to be noticed that not all polypharmacy is harmful; however, we have not assessed if the polypharmacy was appropriate or not. This study was conducted in a tertiary hospital in Riyadh; therefore, the findings from this study cannot be generalised to primary care settings or to other regions in Saudi Arabia. In addition, we cannot exclude selection bias; patients included in this study may be sicker, have severe diabetes and higher rates of comorbidities as compared with individuals seen in primary care settings.

Despite these limitations, this study has many advantages such as the use of large sample size, which allowed us to identify the prevalence of polypharmacy among a subgroup of patients. Furthermore, findings from this study added to the existing literature on the prevalence of polypharmacy among all age groups and identified the individuals who have a high risk of polypharmacy based on their comorbidities. In addition, our results highlighted the need for routine monitoring of high-risk individuals for drug-related problems. Therefore, future studies are required to identify the rate of polypharmacy among other healthcare settings and assess the impact of pharmacist-led interventions on the rate of polypharmacy in patients with diabetes.

## CONCLUSION

Polypharmacy is very common among adults with diabetes; particularly among individuals with multiple chronic conditions. Older adults patients have a higher rate of polypharmacy, which could be due to the increased number of multiple chronic conditions in this population. Moreover, patients with coexisting cardiovascular, mental and musculoskeletal chronic conditions are at a high risk of polypharmacy. Individuals with diabetes may benefit from simplified treatment regimens; thereby enhancing the health outcomes of this population.



## Ethics and data confidentiality

Confidentiality of the data was maintained throughout the research process. Retrieved data were stored and saved as coded excel files. A customised formula was used to generate the study-encrypted identification assigned to each participant and replaced patients' medical record number. Data extracted were stored at the research unit at the tertiary hospital on secured, password-protected and limited accessed computers.

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**Patient consent** Obtained.

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