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Prevalence of polypharmacy in heart failure patients: A retrospective cross-sectional study in a tertiary hospital in Saudi Arabia

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ABSTRACT

Background: Cardiovascular disease is the leading cause of death and disability worldwide. It is a general term used to describe a group of disorders that affect the heart or blood vessels. This study aimed to evaluate the prevalence and predictors of polypharmacy in patients with heart failure.
Methods: We conducted a cross-sectional study in a tertiary hospital in Saudi Arabia. Data was extracted from an electronic database between January 2019, and December 2022. The study included all adult patients with heart failure who visited outpatient clinics; individuals with cancer were excluded. The outcome variable in our study was "polypharmacy" which was defined as the use of eight or more medications. Descriptive analysis was performed using frequencies and percentages for categorical variables. In addition, Multivariate logistic regression was used to assess the covariates associated with polypharmacy.
Results: A total of 331 patients with heart failure were included in this study. The prevalence of polypharmacy among our HF population was 39.88 %. Most participants were male (60.73 %), and 60 years or older (68 %). The most frequently used medications were beta-blockers (67.98 %) and diuretics (58.31 %), whereas the least frequently used medications were hydralazine and histamine H2 blockers (5.74, and 3.02 %, respectively). Polypharmacy was likely to be a non-significantly higher in individuals aged between 60 and 69 years (adjusted odds ratio (AOR) = 1.52; 95 % confidence interval (CI) 0.78–2.98) and suffering from hypertension (AOR = 1.48; 95 % CI 0.83–2.64). However, patients with heart failure and diabetes mellitus had a significant six-fold higher of polypharmacy than those without diabetes mellitus (AOR = 6.55; 95 % CI 3.71–11.56).
Conclusion: Patients with heart failure often use multiple medications. Patients with heart failure together with diabetes have a higher risk of polypharmacy. Therefore, healthcare professionals should manage polypharmacy to improve the outcomes in patients with heart failure.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide. This generic term describes a group of disorders that affect the heart or blood vessels. Heart disease, which includes heart failure (HF) and ischemic heart disease, is one of the leading causes of death and disability worldwide (Ndindjock et al., 2011). Due to the significant public health and clinical challenges and the complex nature of this disorder, patients with CVDs are more vulnerable to multimorbidity. When receiving therapy from multidisciplinary care providers, they are prone to taking many medications and are exposed to polypharmacy-related risks (Hovstadius et al., 2010). There is no standard definition of polypharmacy, but it typically refers to patients who take five or more medications, while hyperpolypharmacy is the use of ten medications or more (Masnoon et al., 2017; Kennel et al., 2019).

The high prevalence of polypharmacy increases the potential risk of

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drug-drug interactions (DDIs) that are life-threatening and may require medical treatment or intervention to minimize or prevent severe adverse effects (Sheikh-Taha and Asmar, 2021). Furthermore, polypharmacy may raise the possibility of adverse drug events (ADEs), which worsen the patient's condition (Assiri et al., 2018). The prevalence of CVD is expected to increase rapidly, reaching 17 million deaths by 2030 (Ndindjock et al., 2011). Polypharmacy, widely prevalent in clinical practice, can be found in up to 37 % of outpatients and 92 % of hospitalized patients (Hanlon et al., 2006). In Saudi Arabia, nearly 20 % of primary healthcare facilities and 89 % of tertiary hospitals are involved in polypharmacy prescription (Salih et al., 2013). Polypharmacy presents a heavy economic burden on the healthcare system and patients. It is estimated to cost more than $50 billion annually, according to the U.S. Center for Medicare and Medicaid Services. In addition, the direct and indirect costs of CVD in the United States are estimated to approach $400 annually (Juneja et al., 2013).

There are multiple factors that have been shown to be linked with polypharmacy in CVD, such as the occurrence of complications, the occurrence of numerous illnesses, long-term conditions, and aging (Veehof et al., 2000; Jyrkkä et al., 2009; Volpe et al., 2010). Another study identified variables that could increase the prevalence of polypharmacy among the European population and associated factors, including female patients, the elderly, people with an excessive body mass index (BMI), and other illnesses (Molino et al., 2022). The elevated risk of serious DDIs in an elderly American patient receiving cardiology care was found to be related to polypharmacy (Sheikh-Taha and Asmar, 2021). Patients with polypharmacy-related CVD may be at risk of kidney problems (Chao et al., 2015). African patients who attend outpatient settings in specialized hospitals have high prevalence of cardiovascular polypharmacy, and factors such as a family history of heart disease contribute to the growth of this problem (Tefera et al., 2020). In Saudi Arabia, the prevalence of polypharmacy is high, which could affect treatment plans for patients with illnesses (Balkhi et al., 2021; Aljawadi et al., 2022). In addition, other studies among individuals with diabetes and cancer have shown a higher prevalence of polypharmacy, which may lead to negative drug outcomes (Alwhaibi et al., 2018; Alwhaibi et al., 2020). The occurrence of ADEs was high in governmental and non-governmental Saudi hospitals, which could be a reason for polypharmacy (Aljadhey et al., 2013; Aljadhey et al., 2016).

Patients with HF were highly suspected of using four to five medications based on the most recent clinical guidelines (Heidenreich et al., 2022). In North America, polypharmacy among elderly hospitalized patients with HF was increasing and could lead to death (Unlu et al., 2020; Perreault et al., 2022). Additionally, due to hyperpolypharmacy, hospital admissions frequently have a high influx of individuals with HF (Minamisawa et al., 2021). The use of numerous medicines as a consequence of polypharmacy in the Japanese population has led to the readmission of patients with HF (Ozasa et al., 2023). In Saudi Arabia, no study has specifically examined polypharmacy in people with HF and its associated predictors; however, there have been other studies in people with diabetes, cancer, or the general population (Alwhaibi et al., 2018; Alwhaibi et al., 2020; Balkhi et al., 2021; Aljawadi et al., 2022). Therefore, this study aimed to evaluate the prevalence and predictors of polypharmacy in patients diagnosed with HF, in an outpatient clinic. Because of the high prevalence of HF in Saudi Arabia and the fact that polypharmacy in patients with CVD is one of the factors causing several treatment problems and unnecessary drug expenditures, this issue needs to be addressed (Volpe et al., 2010).

2. Methods

2.1. Study design

This is an observational retrospective cross-sectional study conducted on outpatients at a tertiary teaching hospital in Saudi Arabia.

2.2. Data source and data extraction

Data was extracted from the electronic medical record (EMRs) database for the time period beginning January 1, 2019, and ending December 31, 2022. The data included information on patient age, sex, medical history, and medications used.

2.3. Study population and settings

The study included all adult patients who were diagnosed with heart failure, who treated in outpatient clinics and received prescription medications at King Fahad University Hospital in Khobar, Saudi Arabia. Individuals with cancer diseases and inpatient visits typically take more medications, due to the complexity of their situation (Lu-Yao et al., 2020). Therefore, they were excluded from our study, along with patients whose information was missing or who were dead.

2.4. Study variables

2.4.1. Dependent

The outcome variable in our study was "polypharmacy" which was defined as the use of eight or more medications. This definition was based on previous studies that have been published in the literature (Sganga et al., 2015; Verdiani et al., 2015). The prevalent medications among adults with HF was determined by the sum of each medication group over the study population. We included all prescription drugs that were listed in each patient's medical recorders.

2.4.2. Independent

The independent variables in our study were sociodemographic data, which included age, gender, heart failure reduced ejection fraction, and the patients' comorbidities such as hypertension, coronary artery disease, ventricular arrhythmia, ischemic heart disease, atrial fibrillation or flutter, diabetes, and chronic kidney disease.

2.4.3. Statistical analysis

Descriptive statistical analysis was conducted to study the baseline characteristics of HF patients. The frequency in percentage were calculated for the categorical variables. The comparison of each covariate was performed between individuals with polypharmacy compared to those without polypharmacy by using the χ^2 test for categorical data.

Multivariate logistic regression was conducted to identify the potential predictors of polypharmacy (dependent variable), after adjusting for age, sex, HF reduced ejection fraction, hypertension, coronary artery disease, ventricular arrhythmia, ischemic heart disease, atrial fibrillation or flutter, diabetes, and chronic kidney disease. A p value < 0.05 was considered statistically significant. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

A total of 513 patient records were identified from January 1, 2019, to December 31, 2022. We excluded 182 individuals for not meeting our criteria, and the final number of patients included in our analysis was divided into two groups: patients without polypharmacy (199) and patients with polypharmacy (132) **(**Fig. 1**).**

3.1. Description of baseline demographic and clinical characteristics of patients with heart failure

As shown in Table 1, majority of the participants in our study with or without polypharmacy were male (60.73 %), aged 60 years or older (68 %), and those without HF reduced ejection fraction (66.47 %) without significant differences between the groups (without polypharmacy and with polypharmacy). The majority of patients with HF in our study had

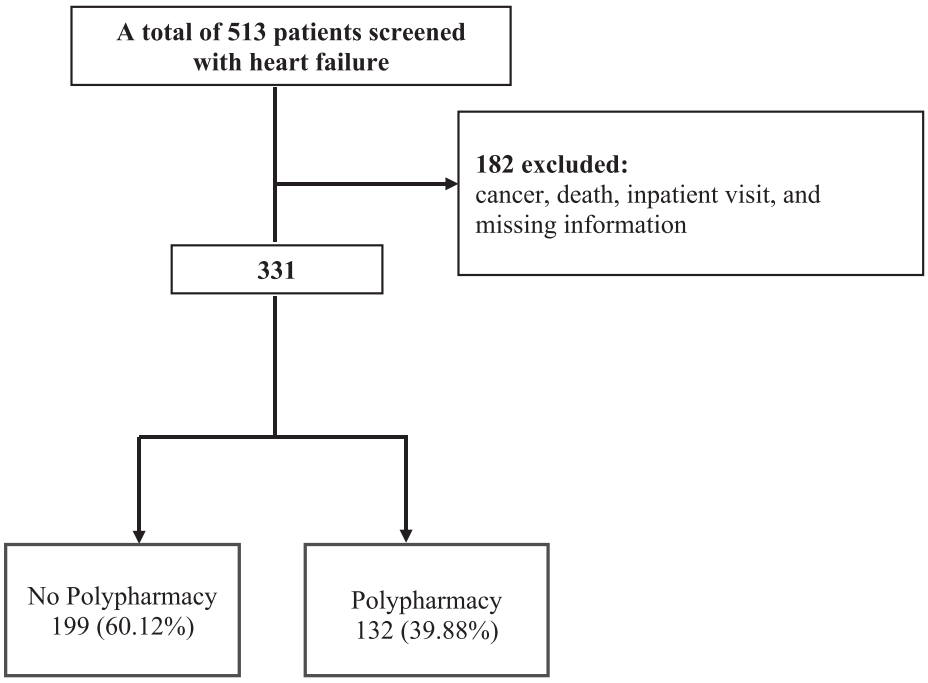

Fig. 1. Study Flowchart of HF Patients With and Without Polypharmacy.

Table 1
Baseline Demographic and Clinical Characteristics of Patients with Heart Failure.

	No polypharmacy (<8 medications)		Polypharmacy (>= 8 medications)		Total		*P*-value*
	N = 199		N = 132		N = 331		
	N	%	N	%	N	%	
Age group							
18–59	71	66.98	35	33.02	106	32.02	0.0834
60–69	45	51.14	43	48.86	88	26.59	
70 and more	83	60.58	54	39.42	137	41.39	
Gender							
Male	121	60.20	80	39.80	201	60.73	1.00
Female	78	60.00	52	40.00	130	39.27	
Heart Failure Reduced Ejection Fraction							
No	132	60.00	88	40.00	220	66.47	1.00
Yes	67	60.36	44	39.64	111	33.53	
Medical History: Hypertension							
No	112	74.17	39	25.83	151	45.62	< 0.0001
Yes	87	48.33	93	51.67	180	54.38	
Coronary Artery Disease							
No	162	64.80	88	35.20	250	75.53	0.0027
Yes	37	45.68	44	54.32	81	24.47	
Atrial Fibrillation or Flutter							
No	172	61.21	109	38.79	281	84.89	0.3506
Yes	27	54.00	23	46.00	50	15.11	
Ventricular Arrhythmia							
No	195	60.00	130	40.00	325	98.19	1.00
Yes	4	66.67	2	33.33	6	1.81	
Ischemic Heart Disease							
No	184	61.74	114	38.26	298	90.03	0.0909
Yes	15	45.45	18	54.55	33	9.97	
Chronic Kidney Disease							
No	176	62.63	105	37.37	281	84.89	0.0292
Yes	23	46.00	27	54.00	50	15.11	
Diabetes Mellitus							
No	133	83.65	26	16.35	159	48.04	< 0.0001
Yes	66	38.37	106	61.63	172	51.96	

* *P*-value < 0.05.

high rates of hypertension and diabetes mellitus (54.38 and 51.96 %, respectively). In addition, approximately 80 % of the population had not been diagnosed with chronic kidney disease or coronary artery disease. Less than 15 % of patients had other comorbidities, including ischemic heart disease, atrial fibrillation, or flutter.

Approximately 49 % of individuals with HF and polypharmacy were between 60 and 69 years of age compared to patients without polypharmacy. There was no significant difference in the incidence of polypharmacy between males and females. Patients with hypertension (51.67 %, p value < 0.0001), coronary artery disease (54.32 %, 0.0027), chronic kidney disease (54.00 %, 0.0292), or diabetes mellitus (61.63 %, < 0.0001) had significantly higher rates of polypharmacy.

3.2. Most prevalent therapeutic classes among heart failure patients

The most frequently used medications as per our study were beta-blockers (67.98 %), diuretics (58.31 %), antihyperlipidemics (54.68 %), and antiplatelets (47.73 %), while the least used medications were isosorbide dinitrate, hydralazine, and histamine H2 blockers (9.67 %, 5.74, and 3.02 %, respectively). Further details are shown in Fig. 2.

3.3. Logistic regression of polypharmacy in patients diagnosed with heart failure

The multivariate logistic regression analysis of polypharmacy with HF after adjusting for covariates is presented in Table 2. The covariates studied were age, sex, HF reduced ejection fraction, and baseline medical history. The multivariate logistic regression analysis of polypharmacy with HF after adjusting for covariates is presented in Table 2. The covariates studied were age, sex, HF reduced ejection fraction, and baseline medical history. The multivariate logistic regression analysis yielded a non-significant result since all covariate AOR crossed 1 except for diabetes mellitus which represent a significant finding. More explanation, that patients with HF, and diabetes mellitus had a six-fold higher likelihood of having polypharmacy than those without diabetes mellitus (AOR = 6.55; 95 % CI 3.710–11.56).

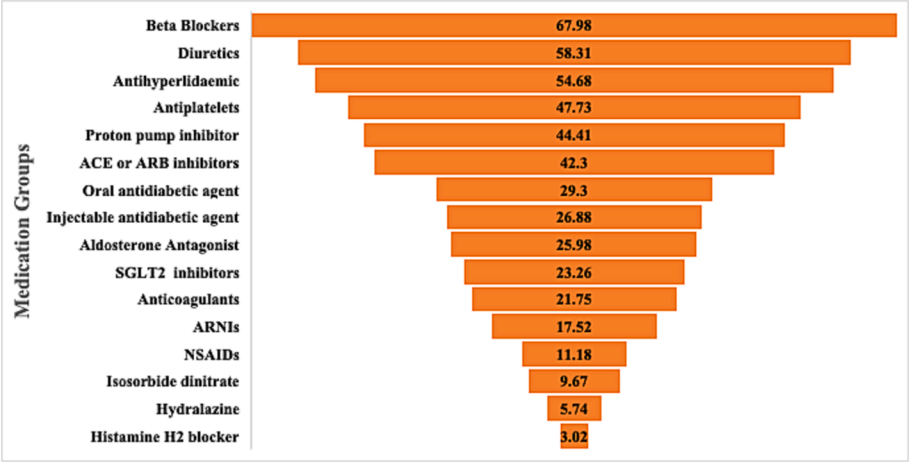

Fig. 2. Percentage of Medication Group Usage Among the HF Population.

Table 2
AOR and 95% CI Logistic Regression on Polypharmacy in HF Patient.

Predictors	AOR	95 % CI	
Age group 60–69 vs 18–59	1.519	0.775	2.977
Age group 70 and more vs 18–59	0.997	0.527	1.887
Sex (female vs. male)	0.951	0.548	1.650
*HFrEF (yes vs. no)	0.976	0.563	1.693
Atrial Fibrillation or Flutter (yes vs. no)	1.090	0.546	2.174
Ventricular Arrhythmia (yes vs. no)	1.111	0.167	7.370
Hypertension (yes vs. no)	1.480	0.831	2.638
Coronary Artery Disease (yes vs. no)	1.355	0.757	2.425
Ischemic Heart Disease (yes vs. no)	1.061	0.470	2.391
Chronic Kidney Disease (yes vs. no)	1.050	0.527	2.089
Diabetes Mellitus (yes vs. no)	6.556	3.710	11.583

* HFrEF: Heart Failure Reduced Ejection Fraction; AOR: Adjusted Odds Ratio, CI: Confidence interval $R^2 = 0.2157$.

4. Discussion

To the best of our knowledge, this is the first study conducted in Saudi Arabia, in patients with HF to examine the prevalence of polypharmacy and its contributing factors. Our study showed that the prevalence of polypharmacy was high among individuals diagnosed with HF. The most frequently used therapeutic classes included antihyperlipidemic drugs, beta-blockers, and diuretics. Patients were also at a high risk of polypharmacy if they additionally had diabetes mellitus.

In our study, patients with HF had a 40 % prevalence of polypharmacy, which is considered an elevated rate. A study among the Saudi population, 60 years and older, found a rate of 51.5 % polypharmacy, which is close to our findings (Aljawadi et al., 2022). In another study conducted on adult and elderly patients found that polypharmacy was relatively high, reportedly 47 % and 66 %, respectively; this is similar to our findings in the adult group (Balkhi et al., 2021). However, the reported rate of polypharmacy among the population in Saudi Arabia, especially in the Riyadh region, in patients with diabetes or cancer, and the general population was 78–89 %, which was higher than that in our study (Salih et al., 2013; Alwhaibi et al., 2018; Alwhaibi et al., 2020). The variation in the rates of polypharmacy across previous studies and the present study, may be due to reasons, such as the fact that our study was conducted in the eastern part of the Saudi Arabian kingdom, that we only included patients with HF, and the time of the study period. A crucial distinction between our investigation and the prior studies (Asiri and Al-Arifi, 2011; Salih et al., 2013; Alwhaibi et al., 2018; Alwhaibi et al., 2020; Balkhi et al., 2021; Aljawadi et al., 2022) is that our study defines polypharmacy as the use of eight or more medications, whereas earlier studies defined it as the use of five medications or more. We defined polypharmacy in our study as use of eight or more medications since there is no standard definition of polypharmacy, and especially for patients with HF, wherein usually four to five medications indicate polypharmacy, based on clinical guidelines (McDonald et al., 2021). Thus, in literature, there is variation in the definition of polypharmacy in patients with HF across different studies, which means there is no cutoff definition for this specific population (Martínez-Sellés et al., 2004; Wawruch et al., 2008; Carroll et al., 2016; Alvarez et al., 2019). However, two studies were in line with our definition of polypharmacy, as the use of eight or more medications (Sganga et al., 2015; Verdiani et al., 2015).

Polypharmacy among elderly individuals was high as per our study, which is consistent with the findings of previous studies (Alwhaibi et al., 2020; Aljawadi et al., 2022). Thus, this specific population requires more care to avoid falls, DDIs, and other negative complications (Dagli and Sharma, 2014; Kurczewska-Michalak et al., 2021; Delara et al., 2022). The use of cardiovascular medications such as beta-blockers and diuretics was high as per our study and as expected; this is consistent with a previous study (Ghimire and Dhungana, 2019). However, the number of proton pump inhibitor prescriptions was higher in our study, which could increase the risk of HF or CVD if patients had been taking them for a prolonged period (Bell et al., 2021). Therefore, medical professionals should warn their patients to avoid taking proton pump inhibitors for an extended period unless necessary (Sheikh-Taha and Dimassi, 2018).

Although sodium glucose cotransporter-2 (SGLT2) inhibitors are considered important treatments for individuals with HF (Heidenreich et al., 2022; Monzo et al., 2023), but we found that their use was limited in our study. This is because our study was conducted on patient records from 2019 to 2022, and updated recommendations for the addition of SGLT2 inhibitors have been provided in the more recent therapeutic guidelines. We observed that individuals with comorbidities, such as diabetes, had a high risk of polypharmacy. The findings of a previous study were consistent with our findings but included all CVDs without distinguishing between them (Alwhaibi et al., 2018). Another study that supported our findings revealed that polypharmacy in patients with diabetes and HF could result in death (Perreault et al., 2022).

4.1. Strengths and limitations

The strength of our study is that it is the first to examine the prevalence of polypharmacy and its contributing factors in this specific population of the Kingdom of Saudi Arabia in patients with HF. Our research will provide policymakers with useful information for improving medication prescription practices. However, there are some limitations of our study that should be mentioned. First, our study was

conducted at a single center in the eastern province of Saudi Arabia; therefore, we cannot generalize our findings to other regions of Saudi Arabia. Second, there could be a risk of bias because data from EMRs may be missing or contain inaccurate information. Third, our study could be suspected of selection bias, since we did not use strategies that could minimize this risk like the propensity scores matching technique. Fourth, we were unable to determine if there was an associated risk with the high use of proton pump inhibitors, as we were unable to verify whether the patients were taking the drug for a short or long term. Fifth, we only considered the prescribed medications, that were documented in the patient's electronic medical record, and we did not include supplements or over-the-counter medications. Therefore, that could lead to underestimate the prevalence of polypharmacy in our study.

5. Conclusion

Based on our findings, the prevalence of polypharmacy among the patients diagnosed with heart failure was relatively high. Additionally, individuals with diabetes were observed to be at a high risk of polypharmacy. Therefore, healthcare providers should carefully manage patient therapy to avoid the possible risk of adverse events or complications since these two diseases are common in Saudi Arabia.

Ethical approval

This study was approved by the Institutional Review Board at Imam Abdulrahman bin Faisal University, Dammam, Saudi Arabia (IRB- PGS-2023–05–018).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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