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### **Research Article**

### Prevalence and Characteristics of Drug-Related Problems Among Hospitalized CVD Patients in Aden, Yemen. A-retrospective cross-Sectional Study

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#### Abstract:

**Background**: Drug-related problems (DRPs) have become a major public health concern globally, contributing to enlarged morbidity, mortality, and healthcare expenses. Cardiovascular diseases (CVDs) are a foremost cause of death worldwide, and Yemen is no exception. This study aimed to evaluate the incidence and characteristics of DRPs in hospitalized patients with CVDs in Aden city.

**Methods**: This observational cross-sectional study conducted a retrospective investigation of medical records from various hospitals in Aden city. Data collection occurred over a two-month period, from January 2024 to February 2024. Patients admitted exclusively for CVD treatment were included. The Pharmaceutical Care Network Europe (PCNE) DRP classification system. served as the standardized tool for identifying and documenting DRPs. A clinical pharmacist and students reviewed the collected data, with data analysis conducted using SPSS 26 software.

**Results**: A total of 113 participants were enrolled in the study, with 84 (74.3%) males and 29 (25.7%) females. The mean age (SD) was  $62.5 \pm 13$  years. Notably, 88.5% of the study population experienced at least one DRP during their hospitalization. A total of 167 DRPs were identified among 100 patients, with an average of 1.67 DRPs per patient. The most frequently reported DRPs were possible adverse drug events (45.5%), followed by unnecessary drug treatment (21.6%). Effect of drug treatment not optimum VII (20.3%) and untreated indications (12.6%). Polypharmacy appeared as the primary risk factor associated with DRPs.

**Conclusion**: This study exposed a high prevalence of DRPs in hospitalized CVD patients in Aden, Yemen. These findings emphasize the importance of implementing strategies to identify and address DRPs in this population. Further research is needed to explore the specific types and causes of DRPs in Yemeni CVD patients and evaluate the effectiveness of interventions aimed at reducing DRPs and improving patient outcomes

Keywords: Prevalence, Drug-related problems (DRPs), Cardiovascular (CVD) patients, Aden



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### INTRODUCTION

According to the World Health Organization (WHO), cardiovascular diseases (CVDs) are the primary cause of death worldwide and are regarded as one of the major health problems.[1]. In Yemen specifically, coronary heart disease deaths reached a staggering 30,158 in 2020, accounting for 19.39% of all deaths. This translates to an adjusted death rate of 278.48 per 100,000 population, placing Yemen 14th globally in CVD mortality [1]. Pharmacotherapy plays a crucial role in managing CVDs and reducing associated morbidity and mortality. However, the benefits of medication can be hampered by drug therapy problems (DTPs), which also known as drug-related problems (DRPs). DRPs are described as "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" [2]. These issues might arise during the prescription, transcribing, dispensing, and administering phases of the drug use process. [2]. DRPs pose a significant safety concern for hospitalized patients since it negatively impacts patient outcomes in various ways, including reduced life quality, extended hospitalization, and raise healthcare expenses [3].

Prevalence of DRPs in cardiovascular disease varies globally. According to some study findings, the frequency of DRPs in patients with CVD has ranged from 30.8% to 78%. [4][5] In the (USA) the average frequency of DRPs in cardiovascular diseases, particularly coronary artery disease CAD, is over 60% of DRPs, leading to various negative outcomes like a lower quality of living, elevated rates of hospitalization, and higher healthcare costs.[6] In Saudi Arabia the frequency of DRPs among CVD predominantly geriatric patients was 29% which dropped to 14.9% following the pharmacist-led intervention. [7]

While a study in Ethiopia [8] found a high prevalence of DRPs in hospitalized heart failure patients. Over two-thirds of patients experienced at least one DRP, with most problems related to medication effectiveness and safety. Factors like chewing khat, prolonged hospital stays, comorbidities, and polypharmacy were linked to a higher chance of DRPs.

A study by Abdul-Ghaffar et al [9] investigated DRPs in patients with both pulmonary hypertension (PH) and valvular heart disease (VHD). Notably, all participants (100%) had at least one DRP. therapeutic efficiency (59.1%) and safety (33.4%) were the most common issues. Factors contributing to these DRPs included inadequate medication monitoring (18.6%), inappropriate drug combinations (10.3%), incorrect dosing (17.1%), and improper administration timing (7.7%).

Other study conducted in Vietnamese [10] discovered that patients with coronary artery disease (CAD) had a significant prevalence of DRPs. Patients had at least one DRP in more than 60% of cases. with the most common issues being inappropriate dosage and frequency of use. One of the biggest risk factors for DRPs was the number of prescription drugs, especially for frequency and interactions.

Given the high prevalence of cardiovascular diseases (CVDs) in Yemen, it is crucial to investigate drug-related problems (DRPs) in this population. Despite the significance of DRPs in healthcare, research on this subject is limited in Yemen, particularly among CVD patients. This study aims to address this knowledge gap by determining the frequency and features of DRPs in patients with CVD in Aden, Yemen.



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### **METHODS**

### Study design and setting

This represented a cross-sectional, retrospective observational study that was carried out in a number of public and private healthcare institutions located within Aden city. The data collection period spanned from January 2023 to January 2024.

### Participants

Inclusion criteria: Patients with CVD older than 18 years who had taken cardiovascular drug therapy and have been hospitalized in Aden hospital from Jan.2023 to Jan.2024 for at least one day or more. Exclusion criteria: Patients who hadn't admitted with cardiovascular diseases or received less than three CVD medications.

### Data collection procedure

Data for hospitalized CVD patients were collected from medical records using data collection form which was adapted from the Pharmacotherapy Review (CP2) form that was modified from Guideline of Ward Pharmacy Activities 2023 [11]. Collected data involved Sociodemographic variables, including age and gender, Clinical variables such as primary diagnosis, comorbidities, medication history, polypharmacy (the consistent use of five or more prescription drugs), laboratory results, and duration of hospital stay were also documented. Patients' therapies were compared to the most recent clinical practice guideline recommendations (American Health Association) and British National Formulary in order to identify DRP. Subsequently a tool created using the PCNE version 9.1 categorization scheme for DRPs [12] utilized to divide the DRP problem areas into three basic categories (P1: treatment effectiveness, P2: treatment safety, and P3: additional issues), which then will be divided more based on classification in each domain.

### Sample Size

Study Sample Based on a study conducted in Ethiopia [13], regarding the prevalence of DRP, the prevalence rate of DRP among CVD patients was found to be (52%) so we can take the 52% as a previous prevalence rate and using a single proportion formula with 95% confidence level and desired margin of error d of 10% using this formula:  $n = Z^2 * P(1 - P) / d^2$  where: n = sample size Z = statistic for level of confidence (1.96 for 95% confidence) P = expected prevalence (0.52 for 52%) d = margin of error (0.1 for 10%) Plugging in the values:  $19 n = (1.96^2) * 0.52 (1 - 0.52) / (0.1)^2 n = 3.8416 * 0.5 * 0.5 / 0.01 n \approx 95$ 

### Data Analysis

The Statistical Package for the Social Sciences (SPSS) version 26.0 was used for all data analysis. Data was presented as the average value (mean) with its variability (standard deviation). For categorical data (like gender or polypharmacy), Chi-square tests were used to identify associations between patient characteristics and the presence of DRPs. In cases where the data within a category



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was limited (less than 5 expected values for over 20% of the data), Fisher's Exact Test was employed for a more reliable analysis. Throughout the analysis, a p-value less than 0.05 was considered statistically significant.

### **Ethical** Approval

The study protocol was examined and approved in all respects by Medical Research Ethics Committee (MREC) at UST University number MEC/ AD010.

### **RESULTS**

### Socio-demographic characteristics of the study participants

This study included 113 patients admitted for CVD treatment inAden City, Yemen. The average age was 62.4 years (SD=13), with a range of 30 to 95 years. The majority of participants were male (84, 74.3%), with females making up the remaining 29 (25.7%). Table 1

Sociodemographic characteristics measures	Frequency (%)
Gender	
Male	84 (74.3)
Female	29 (25.7)
Age, years (mean ±SD)	62.5 ±13
Minimum	30
Maximum	95
Age group	
$\leq$ 45	13 (11.5)
46-65	35 (31.0)
>65	65 (57.5)

### Clinical characteristics of study participants

Among the diagnosed CVDs, Ischemic Heart Disease (IHD) was the most common (71, 62.83%), followed by Cerebrovascular Accident CVA at 20 (17.7%), HF at 11 (9.73%), and other CVDs at 11 (9.73%). Comorbidities were prevalent, affecting 94 patients (83.2%). The most frequent comorbidity was Arterial Hypertension AHT at66 (58.4%), followed by IHD at 56 (49.6%) and Diabetes Mellitus DM at 54 (47.8%) out of total population (n=113). Regarding hospitalization duration, a majority of 26 patients (67, 59.3%) stayed less than 4 days. Polypharmacy was observed in 107 patients (94.7%). Table 2



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Table 2 Clinical	characteristics in	study partici	pants (n=113)
	characteristics in	focuary purcher	punto (n=115)

Clinical characteristics measures	Frequency (%)
Diagnosis	
IHD	71 (62.8)
CVA	20 (17.7)
HF	11 (9.7)
Other	11 (9.7)
Comorbid condition (mean)	2.04 ± 1.3SD
Yes	94 (83.2)
No	19 (16.8)
Duration of stay at hospital	
1-3	67 (59.3)
4-9	36 (31.9)
$\geq 10$	10 (8.8)
Polypharmacy	
Yes	107 (94.7)
No	6 (5.3)

### Drug-related problems data

Among 113 participants a significant proportion of patients (100, 88.4%) had as a minimum one DRP throughout the study period. Figure 1



Figure 1 Prevalence of drug related problems among CVD patients

A total of 167 DRPs were recognized, with an average of 1.6 DRPs per patient. The greatest frequently encountered DRPs was possible adverse drug events P2.1 at 76 cases (45.5%), followed by unnecessary drug treatment P3.1 (36 cases, 21.6%), suboptimal treatment effect P1.2 (34 cases, 20.3%), and untreated symptoms or indications P1.3 (21 cases, 12.6%). Table 3



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Problem	Frequency	Percentage
Adverse drug event (possible) occurring (P2.1)	76	45.5
Unnecessary drug treatment (P3.1)	36	21.6
Effect of drug treatment not optimal (P1.2)	34	20.3
untreated symptoms or indications (P1.3)	21	12.6
Total	167	100

**Table 3** Problem Frequencies among participants (n=167)

### Causes of the problem

Our analysis of 167 DRPs in 100 patients with CVD yielded 167 distinct causal causes. Only one error was identified to be the leading cause of each DRP registered. Dose selection errors C3 were the most frequent cause, accounting for 81 cases (48.5%). This highlights the importance of implementing strategies to improve medication prescribing practices and ensure accurate dosing regimens for CVD patients. Drug selection itself C1 emerged as the second most prevalent cause with 61 cases (36.5%), suggesting a potential need for further evaluation of medication choices and optimization of treatment plans. Treatment duration issues C4 were identified in 10 29 cases (5.9%), indicating the importance of monitoring treatment adherence and ensuring medications are continued or discontinued as per established guidelines.

Causes	Frequency	Percentage
Drug selection (C1)	61	36.52
Drug form (C2)	3	1.8
Dose selection (C3)	81	48.5
Treatment duration (C4)	10	5.98
Dispensing C5	3	1.8
Other (C9)	9	5.4
Total	167	100

 Table 4 Causes Frequencies (n=167)

### Analysis of Drug Selection causes

A deeper analysis of drug selection errors C1 revealed further insights into the specific types of prescribing issues encountered. The most prevalent subcategory was "too many drugs prescribed for the indication" C1.6, accounting for 30% of these errors. This was followed by "indication for drug treatment not identified" C1.5 at 21.4% and "inappropriate drug according to guidelines" C1.1 at 17.1%. Notably, cases of "no indication for drug" C1.2 comprised 14.3% of this category. Inappropriate drug combinations C1.3 and unsuitable duplication of therapeutic group or active component C1.4 were less frequent, collectively representing 17% of



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Figure 2 drug selection errors

### Analysis of dose selection causes

An evaluation of medication dosing practices revealed discrepancies between prescribed regimens and recommended guidelines in 81 patients, representing 48.5% of the total causes (Figure 4.5). Underdosing (C3.1, 28.7%) was slightly more common than overdosing (C3.2, 25.5%). Notably, dosing frequency issues dominated, with excessively frequent regimens (C3.4, 39%) outweighing infrequent administration (C3.3, 1.6%). Additionally, 4.9% lacked therapeutic drug monitoring (C3.5).



Figure 3 Classifications of dose selection causes and their percentage

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### Medications with DRPs

Among the medications investigated, Antiplatelet agents were the most problematic medication class, with 48 associated DRPs. Antibiotics and statins had moderate numbers of DRPs (27 and 24 cases, respectively). Anticoagulants had fewer DRPs (13 cases), piracetam, and digoxin had (10 cases each) while diuretics had the lowest number (4 cases).

### DISCUSSION

The average age of participants (62.5 years) aligns with findings reported by [14]. However, a gender inequality was observed, with a higher proportion of males (74%) compared to the near equal male-female ratio reported in the Spanish study by [15]. This inconsistency might be due to regional variations in demographics and small sample size. The most prevalent CVD in our study was IHD (62.8%), followed by CVA (17.7%) and HF (9.7%). This differs from the findings of [16] in Ethiopia, where hypertension and congestive heart failure were the most common CVDs. Similarly, the prevalence of comorbidities like arterial hypertension AHT, diabetes mellitus, and HF differed from the Ethiopian study by [16], which reported chronic obstructive pulmonary disease, atrial fibrillation (AF), and dyspepsia as the most prevalent. These discrepancies likely stem from variations in study design, sample size composition, and potentially, the underlying regional prevalence of specific CVDs and comorbidities.

Our study identified a concerningly high prevalence of DRPs (88.4%) among hospitalized CVD patients in Aden, with an average of 1.6 DRPs per patient. This result is comparable to another study conducted in Yemen [17] which aimed to assess the prevalence of DRPs among pediatrics. The author concluded that prevalence was 89%. In addition, this finding is analogous to the study carried out in Ethiopia [18], which reported DRPs prevalence of 83.5%. In contrast, studies conducted in 36 Saudi Arabia [7] and Ethiopia [19] reported lower DRPs prevalence (29.6% and 52.7%, respectively). These variations possibly due to heterogeneity in the study communities, sample sizes, or regional disease prevalence. The most frequently encountered DRP in our study was possible adverse drug events ADEs (45.4%), which aligns with the findings of study in Spain by Gastelurrutia [20] who reported a similar percentage of ADEs (45.8%) in their study. However, a study in south west Ethiopia [8] observed a lower prevalence (21%) of possible ADEs. Treatment effectiveness issues were identified in 33% of cases, categorized as suboptimal treatment effect (20.3%) and untreated symptoms or indications (12.6%). This distribution is partially consistent with the findings of study in south west Ethiopia [8] that reported treatment effectiveness problems in 55.48% of cases, with suboptimal drug treatment and untreated indications accounting around 28% and 25%, respectively. Conversely, other study conducted in Southwest Ethiopia at the ambulatory clinic [19] reported a higher rate of treatment effectiveness issues (83%), with suboptimal drug therapy and untreated indications contributing to 55% and 27% of cases, correspondingly. These inconsistencies may result from changes in the sample size, DRP identification and classification techniques, clinical features, locations, people demographics, pharmacological therapy employed, or study design. Our analysis revealed dose selection errors (48.5%) and drug selection errors (36.5%) as the most common causes of DRPs. This is somewhat in line with research conducted in southern India., which reported inappropriate drug selection (34%) and dose selection errors (27%),[21] however, the observed variations in the relative frequency of these error types (dose selection being higher in our study) might reflect potential differences in medication prescribing practices across regional healthcare systems. The most common medications associated with DRPs in our study included antiplatelets,





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statins, antibiotics, digoxin and anticoagulants. These medications have been identified by other studies [14],[22] as potentially contributing to DRPs.

**Limitations:** The study's retrospective design limited its ability to implement interventions and observe clinical outcomes in patients. The small sample size and reliance on medical records may have affected the generalizability and accuracy of the findings. Additionally, the refusal of some hospitals to participate may have limited the diversity of hospital types included in the study.

**Recommendations**: These studies highlight the need for further research to strengthen the understanding of DRPs among CVD patients in Aden city. Ideally, future prospective interventions studies could employ with a larger, more representative sample in multicenter around the country to obtain more comprehensive data.

### CONCLUSION

This research investigated the prevalence of DRPs among cardiovascular patients who has hospitalized in Aden city hospitals, it revealed a high incidence of DRPs with an average of more than one DRP per patient. The most frequent types of DRPs encountered involved potential adverse reactions to medications, followed by instances of unnecessary drug treatment being administered. Notably, a substantial portion of the DRPs identified were associated with suboptimal treatment effects or the existence of untreated symptoms or indications. Additionally, the study's findings highlight that polypharmacy, emerged as a prominent risk factor associated with DRPs. This suggests a potential link between the complexity of medication regimens and the increased likelihood of DRP occurrence.

### Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

### **Conflict of Interest**

There are no financial, personal, or professional conflicts of interest to declare.

### Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript

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