Journal of Young Pharmacists, 2024; 16(3):570-577.
https://www.jyoungpharm.org

Original Article

Prevalence of Drug-Related Problems in Patients with Acute Heart Failure Admitted to the Intensive Critical Care Unit

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ABSTRACT

Background: Drug-Related Problems (DRPs) are prevalent among patients with acute heart failure, potentially leading to adverse outcomes. Understanding the prevalence and nature of DRPs is crucial for improving patient care and outcomes. **Purpose:** This prospective observational study aimed to assess the prevalence of DRPs among patients with acute heart failure admitted to the Intensive Critical Care Unit of a Tertiary Hospital. **Materials and Methods:** Data were collected from 150 patients using a standardised DRP Data Collection form. The Cipolle Classification was used to assess Drug-Related Problems. Statistical analysis was conducted using SPSS version 28.1.1, with Pearson Chi-Square employed for p-value calculation. **Results:** Comorbidities were present in 96% of patients, with 56% prescribed between 11 and 20 drugs. Hospitalisations lasting 4 to 6 days were reported in 41.3% of cases. DRPs were identified in 92% of patients, totalling 344 instances. Adverse drug reactions and unnecessary drug therapy, particularly involving diuretics and antiplatelets, were the most common types of DRPs. Polypharmacy demonstrated a significant association with an increased risk of DRPs. **Conclusion:** This study highlights the common occurrence of DRPs among hospitalised heart failure patients. The findings underscore the need for pharmacist interventions to mitigate DRPs and improve patient outcomes. By contributing to the optimisation of pharmaceutical care in this patient population, this study provides valuable insights for healthcare providers aiming to enhance the quality of care for patients with acute heart failure.

Keywords: Acute Heart Failure, Adverse Drug Reaction, Antiplatelets, Diuretics, Drug-Related Problems, Polypharmacy.

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Received: 17-01-2024;
Revised: 16-02-2024;
Accepted: 05-05-2024.

INTRODUCTION

Heart Failure (HF) is defined universally as a clinical condition characterized by symptoms and signs resulting from a cardiac abnormality, either structural or functional, supported by elevated natriuretic peptide levels and/or objective indications of pulmonary or systemic congestion.[1] "Congestive Heart Failure" refers to evidence of peripheral and lung congestion.[2] Acute Heart Failure (AHF) is characterized by the sudden or gradual onset of symptoms and/or severe signs of heart failure that require immediate medical attention. It is a leading cause of hospitalization in those over 65 and has high rates of rehospitalization and mortality.[3] Drug-Related Problems (DRPs) refer to any undesirable events associated with drug therapy that interferes with treatment goals. Like other medical issues, DRPs require prompt identification and resolution.[4] Studies have revealed that polypharmacy and comorbidities are significant risk factors for DRPs, particularly among heart failure outpatients.[5,6] CVD-hospitalized patients also showed a higher frequency of drug-related problems compared to outpatients.[7] The significance of this study emerges from the intricate challenges posed by comorbidity and polypharmacy in heart failure care, which escalates the susceptibility to Drug Therapy Problems (DTPs). Polypharmacy, prevalent in heart failure, exacerbates risks such as drug interactions and non-adherence.[8,9] Notably, studies have reported alarmingly high rates of DTPs, reaching up to 83.5% of heart failure cases.[10]

A Spanish study found prevalent issues among heart failure outpatients, such as ineffective treatment and inappropriate dosing regimens.[11] Polypharmacy leads to recurrent hospitalizations, adverse drug events and patient non-compliance.[12,13] Pharmacists' participation in the therapeutic hospital team can increase awareness of DRPs.[14]

Collaborative interventions by clinical pharmacists and physicians have effectively mitigated drug-related problems among ambulatory heart failure patients.[15,16]

DOI: 10.5530/jyp.2024.16.71

Publishing Partner : EManuscript Tech. [www.emanuscript.in]

The findings of Shareef *et al.* underscore the significance of a pharmacist's role within a multidisciplinary healthcare team. Their research emphasizes the necessity of pharmacists' regular drug therapy reviews to identify and address drug-related problems, ultimately leading to enhanced therapeutic outcomes and improved patient care.[17] Thus, this study aims to assess DTP frequency, ascertain prevalence and identify risk factors in heart failure patients. The findings will aid pharmacists in proactively identifying, resolving and preventing these issues.

MATERIALS AND METHODS

Study Sample

The prospective cross-sectional study took place at a Tertiary Care Hospital, lasting six months, with prior approval from the hospital's review board (VH/IEC/Pharm D/003-2023). Participants aged 45-85 diagnosed with heart failure as per ACC/AHA guidelines and admitted to the ICCU were included after informed consent. Exclusion criteria covered incomplete records, liver disorders, active malignancy, critical illness, stroke, cognitive impairment, pregnancy, or non-compliance. A study by Tigabu *et al.* reported a 73.5% prevalence of Drug-Related Problems (DRPs),[18] guiding our aim for a similar rate within a 95% CI and 10% precision. One hundred sixty-eight patients were initially recruited for the study, which was later narrowed down to 150, as shown in Figure 1. No dropouts were reported during the study, ensuring the data set's integrity and completeness.

Data Collection

The study analyzed drug interactions and adverse reactions using Drugs.com's database and Clinirex Software. Cipolle's classification assessed DRPs. Upon confirmation of DRPs, treatment regimens were modified based on clinical insights and evidence-based practices. Despite its observational nature, confirmed DRPs were communicated to healthcare professionals, prompting necessary drug therapy adjustments. Documentation of detailed decision rationale, considering clinical stability, patient preferences and therapeutic efficacy. This approach underscored clinical adaptability to evolving patient needs and therapeutic goals.

Statistical Analysis

The data collected was entered into Microsoft Excel and analysed using SPSS version 28.1.1. Pearson chi-square tests were conducted to calculate *p*-values to determine statistical significance. A *p*-value of >0.05 was considered statistically significant.

RESULTS

The study involved 150 heart failure patients admitted to the intensive critical care unit, with 62% male and 38% female (Table 1). The age distribution showed 44.66% between 45 and 60 years, 26% between 61 and 69 years, 21.33% between 70 and 79 years and 8% over 80 years (Table 2), with no significant age-DRP association (*p*-value: 0.895). Comorbidities were prevalent, with hypertension (74%) and diabetes mellitus (56.6%) being the most common (Figure 2). Smoking (10%) and alcohol consumption (18.6%) were reported, while 70% had no social habits. Various types of heart failure were observed, with ADHF being predominant (72%). During the study, 27 patients had a hospital stay of less than three days, accounting for 18% of all cases. For 62 patients (41.33%), hospitalization lasted four to six days, while 35 (23.33%) required seven to nine days. Twenty-six patients (17.34%) had a hospital stay exceeding ten days (Table 2). Hospitalization duration did not correlate significantly with DRPs (*p*-value: 0.37).

Among the 150 patients studied, 15 (10%) were prescribed ten or fewer drugs, 84 (56%) received between 11 and 20 drugs and 51 (34%) were prescribed 21 or more drugs (Table 3). A total of 2,748 drugs were prescribed during the hospital stay, with diuretics being the most frequently used class for heart failure (5.45%) (Figure 3). Among the patients, 92% experienced Drug-Related Problems (DRPs), with the most common type being Adverse Drug Reactions at 50%. Other kinds of DRPs included Unnecessary Drug Therapy (23.8%), Needs Additional Drug Product and Different Drug Products (8.4%) and non-compliance (5.5%) (Table 3). Polypharmacy significantly correlated with DRPs (*p*-value: 0.018) (Table 4).

The drug analysis (Figure 4) revealed notable contributors to drug-related issues, with antiplatelets, antidiabetics and diuretics being significant. Adverse reactions, accessed via the Naranjo scale (Figure 5), showed varying severities: 3.7% definite, 25.3% probable, 54.7% possible and 16.1% unlikely. Drug

Table 1: Distribution-Based on the Demographic details of the study participants.

Demographics	Characteristics	Number (%)
Gender	Male	93 (62%)
	Female	57 (38%)
Age	45-60 years	67 (44.66%)
	61-69 years	39 (26%)
	70-79 years	32 (21.33%)
	>80 years	12 (8%)
No. of Comorbidities	0	6 (4%)
	1-2	65 (43.33%)
	3-5	77 (51.33%)
	>6	2 (1.4%)

The table summarises the distribution of comorbidities among the study participants. Of 150 patients, 4% had no comorbidities, 43.33% had 1-2, 51.33% had 3-5 and only 1.4% had more than six comorbidities. (Reproduction size: at Column width).

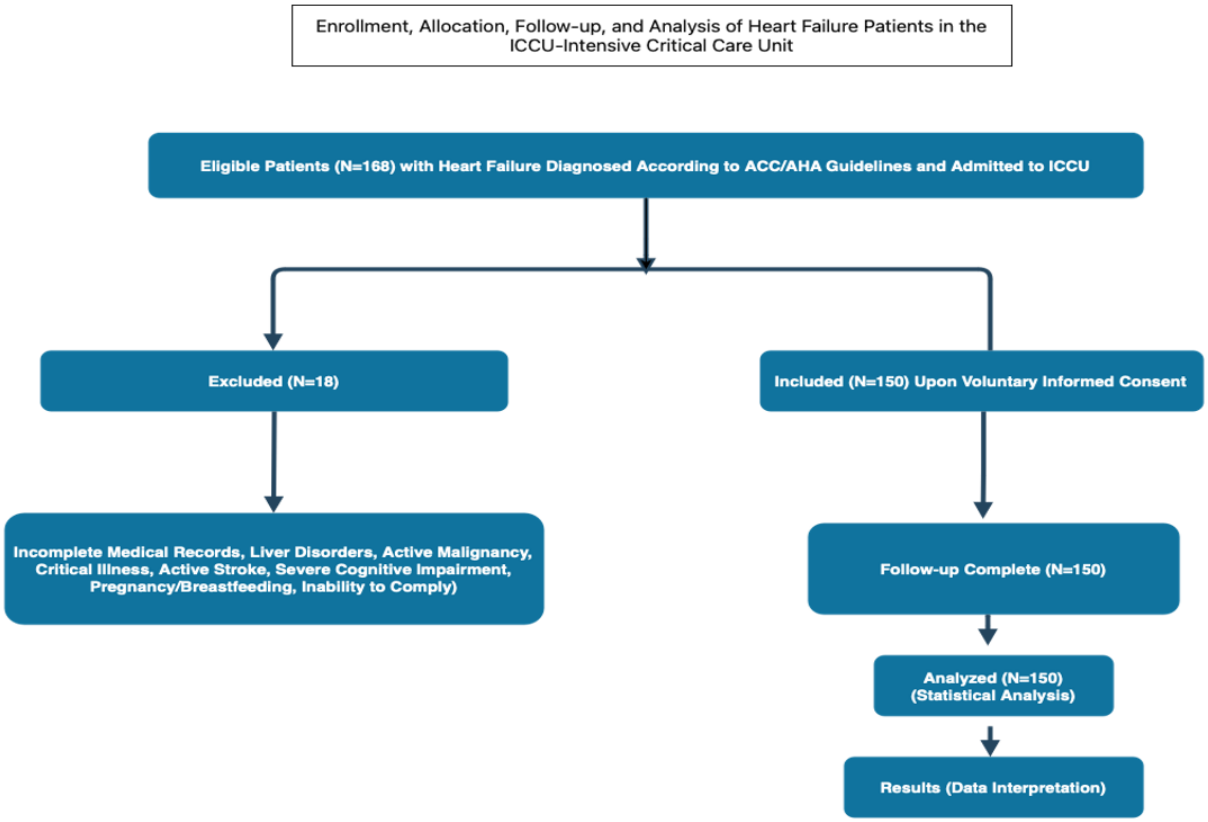

Figure 1: Enrolment, Allocation of Heart Failure Patients.

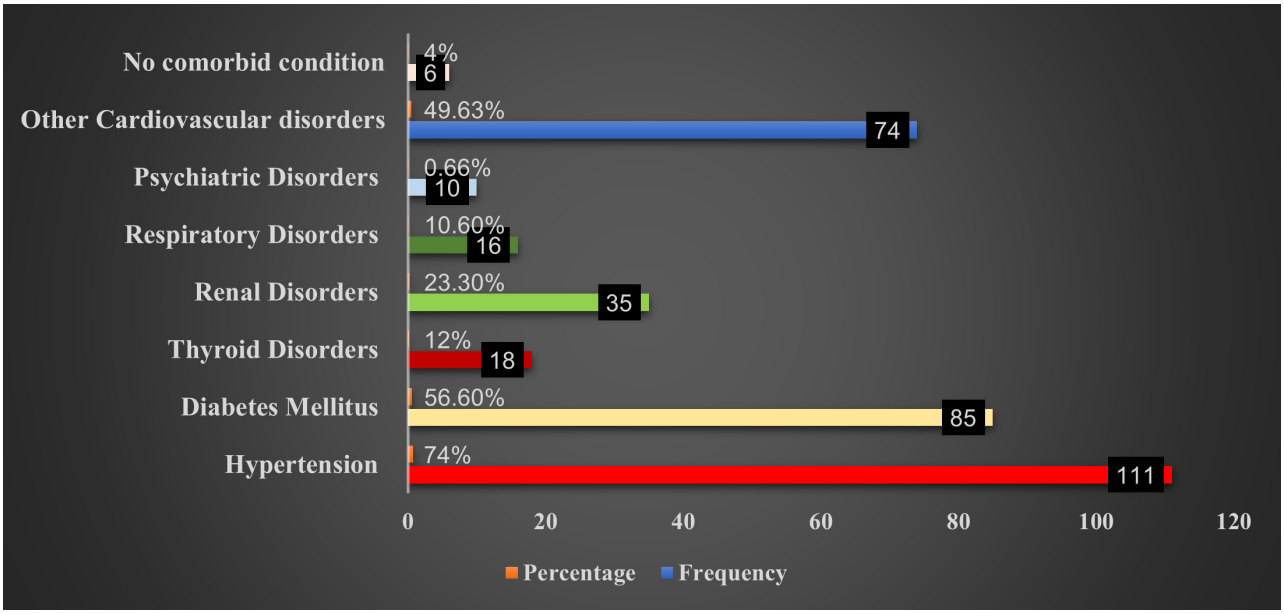

Figure 2: Comorbid Conditions of the Study Participants. The chart depicts comorbidity prevalence among patients. Hypertension is most common (74%), followed by Diabetes Mellitus (56.5%). Other comorbidities include thyroid disorders (12%), renal diseases (23.3%), respiratory disorders (10.6%), psychiatric disorders (0.66%) and other cardiovascular diseases (49.3%). Only 4% of patients had no comorbidities. (Reproduction size: full page width).

Table 2:Duration of Hospital Stay and number of Drugs Prescribed during Hospital Stay.

Duration of Hospital stay	Number (%)	Number of Drugs Prescribed during Hospital Stay	Number (%)
<3 days	27 (18%)	≤10	15 (10%)
4-6 days	62 (41.33%)	11 to 20	84 (56%)
7-9 days	35 (23.33%)	≥21	51 (34%)
>10 days	26 (17.34%)	Total	150 (100%)

The table summarizes hospital stay duration and the number of drugs prescribed to participants. Out of 150 patients, 27 (18%) stayed less than three days, 62 (41.3%) for 4-6 days, 35 (23.33%) for 7-9 days and 26 (17.34%) for more than ten days. Regarding medication burden, 10% received ≤10 drugs, 56% received 11-20 pills and 34% received ≥21 drugs. (Reproduction size: Column width).

Table 3: Frequency and Type of Drug-Related Problems among Study Participants.

No. of Drug-Related Problems	Number (%)	Type of Drug-Related Problem	Number (%)
1	41(29.71%)	Unnecessary Drug Therapy	82 (23.8%)
2	52 (37.6%)	Needs Additional Drug Therapy	42 (12.2%)
3	39 (28.2%)	Needs Different Drug Product	29 (8.4%)
4	6 (4.3%)	Adverse Drug Reaction	172 (50%)
		Non-Compliance	19 (5.5%)
		Dosage too Low	0 (0%)

The data indicates that among participants, 29.71% encountered a single Drug-Related Problem (DTP), while 37.6% experienced two and 28.2% faced three issues. A smaller fraction (4.3%) dealt with four problems. In total, 344 DTPs were identified among 138 individuals, with Adverse Drug Reactions being the most prevalent (50%), followed by Unnecessary Drug Therapy (23.8%), Needs Additional Drug Therapy (12.2%), Needs Different Drug Products (8.4%) and Non-Compliance. (Reproduction size: Column width).

Table 4: Association between Number of Drugs Prescribed and Drug-related Problems.

	Drug-Related Problems			
No of Drugs Prescribed	Yes		No	
≤10	11	4.04%	4	16.67%
11-20	78	28.68%	4	16.67%
≥21	47	17.28%	4	16.67%
Total	138	50.00%	12	50.00%

The p-value of 0.018 indicates statistical significance, given its lower value than the typical significance level of 0.05. Patients prescribed 11 to 20 drugs showed the highest incidence of Drug-Related Problems, suggesting a significant association between medication count (polypharmacy) and Drug-related problems, supported by the p-value of 0.018. (Reproduction size: Column width).

interactions (Figure 6) were identified, with 6.25% minor, 79.16% moderate and 14.59% major cases. Major interactions included Spironolactone and Alprazolam, Furosemide and Amiodarone and Diltiazem and Bisoprolol. Statins exhibited a noteworthy association with comorbidities contributing to DRPs.

DISCUSSION

Our study provides insights into the prevalence, types and underlying causes of Drug-Related Problems (DRPs) in Cardiovascular Disease (CVD) patients, particularly those with heart failure; understanding these issues is crucial for improving patient care and reducing adverse outcomes and healthcare costs associated with managing CVDs (Niriayo *et al.*,2024).[19]

Among the 150 heart failure patients included in our study, we observed a male predominance of 62%, aligning with previous research indicating males' heightened susceptibility to CVDs (Amankwa Harrison *et al.*, 2022).[20] Our study found that heart failure mainly affects older individuals, consistent with previous research by Sefera *et al.*, 2022.[21] The study found no significant age-related association with Drug-Related Problems (DRPs) in Cardiovascular Disease (CVD) patients, consistent with Tsige AW *et al.*, 2021.[22] Drug therapy problems were more common in older people, according to Niriayo YL *et al.*[19]

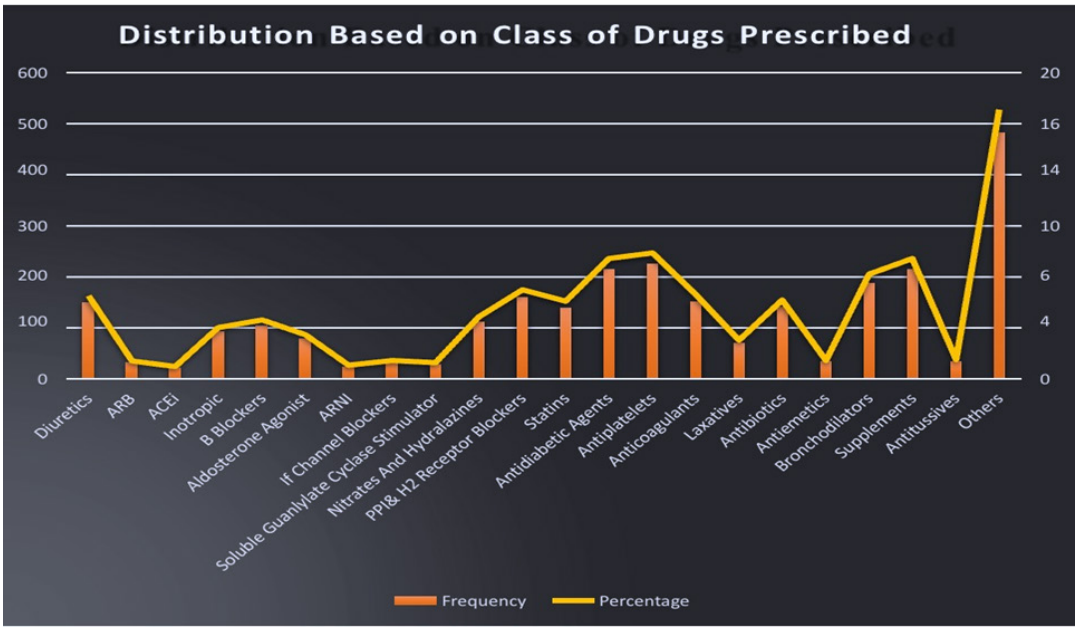

Figure 3: Classes of Drugs Prescribed. ARB: Angiotensin receptor Blocker, ACEI: Angiotensin-converting enzyme inhibitors, B-blockers: Beta Blockers, ARNI: Angiotensin receptor/neprilysin inhibitor, If Channel Blockers: funny current blockers, PPI: Proton pump inhibitors. The bar chart displays medication utilization among participants, primarily cardiovascular drugs. Out of 2748 prescriptions, diuretics comprise 5.45%, the highest among prescribed medications. Antiplatelets (8.22%), antidiabetic agents (7.86%), bronchodilators (6.84%) and anticoagulants (5.53%) follow in utilization. Other medication classes were also prescribed, contributing to the participants' comprehensive treatment. (Reproduction size: at full page width).

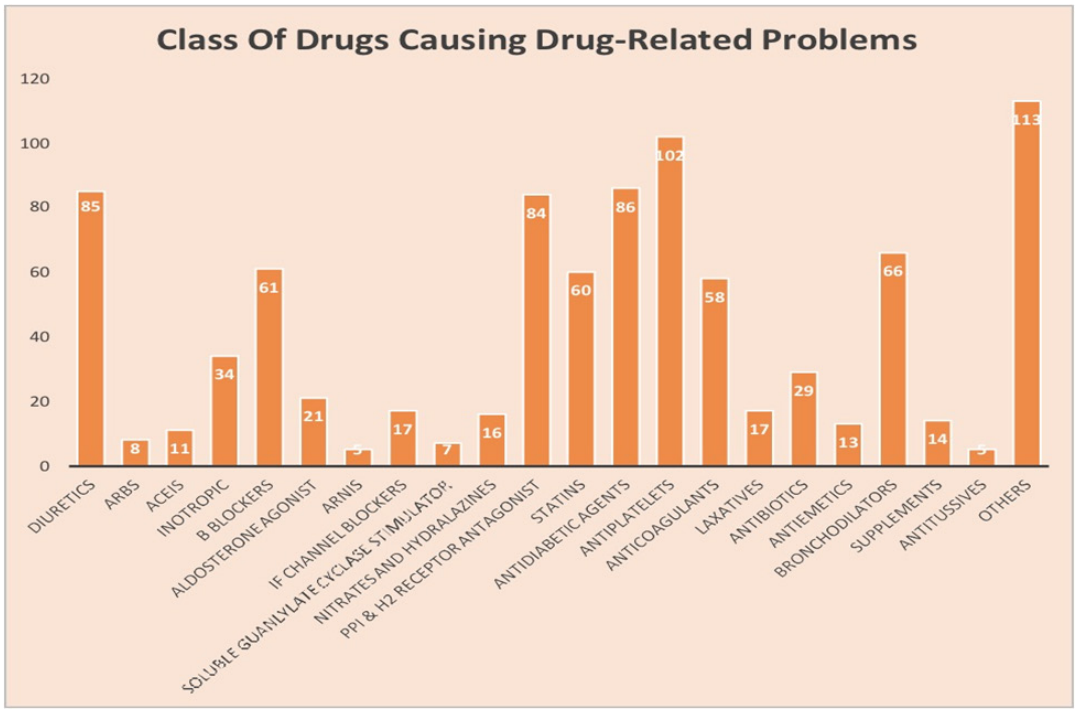

Figure 4: Drug Class Causing Drug-Related Problem. ARB's: Angiotensin receptor Blockers, ACEI's: Angiotensin-converting enzyme inhibitors, B-blockers: Beta Blockers, ARNI: Angiotensin receptor/neprilysin inhibitor, If Channel Blockers: Funny current blockers, PPI: Proton pump inhibitors. The graph depicts drug classes contributing to Drug-Related Problems, including diuretics (9.32%), antiplatelets (11.18%), antidiabetic agents (9.42%) and others (12.3%). Notably, β blockers (6.68%), proton pump inhibitors and H2 receptor antagonists (9.21%) and statins (6.57%) are also prominent. Less frequent contributors include antibiotics (3.17%) and bronchodilators (7.23%). (Reproduction size: full page width).

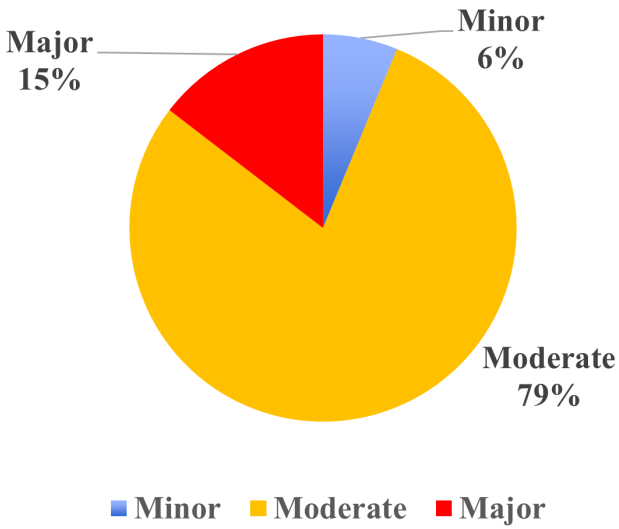

Figure 5: Severity of Adverse Drug Reactions. The Figure illustrates the severity of adverse drug reactions based on corresponding scores in 453 cases. Adverse reactions were categorised as Definite (3.7%, 17 cases), Probable (25.3%, 115 cases), Possible (54.7%, 248 cases) and Unlikely (16.1%, 73 cases). (Reproduction size: at full page width).

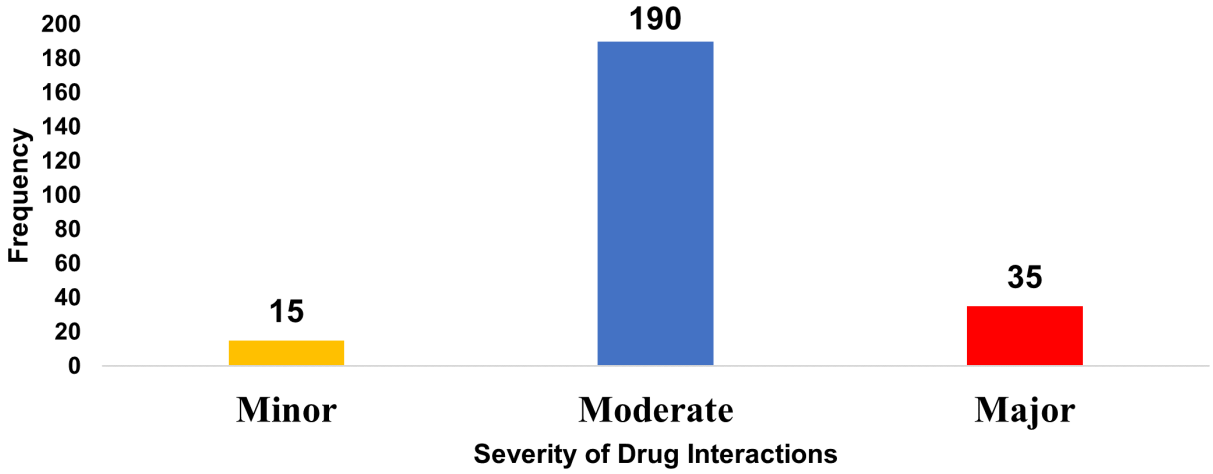

Figure 6: Severity of Drug Interactions. The Figure depicts the severity distribution of Drug Interactions. Out of 240 identified Drug-Drug Interactions, 15 were minor (6.25%), 190 were moderate (79.16%) and 35 were major (14.59%). (Reproduction size: at full page width).

Despite the prevalent comorbidities, including hypertension and diabetes mellitus, among our sample population, we found no conclusive relationship between hospitalization duration and DRPs in heart failure patients (Seid *et al.*, 2022). This underscores the multifactorial nature of DRP occurrence, warranting further investigation into contributing factors (Seid *et al.*, 2022).[23]

Polypharmacy, characterized by the concurrent use of multiple medications, was prevalent in our study population and correlated significantly with increased DRPs, consistent with previous research highlighting the association between polypharmacy and medication-related harm (Yirga *et al.*, 2018; Mohan *et al.*,2018).[10,24]

Out of 150 patients, 138 (92%) experienced Drug-Related Problems (DRPs), aligning closely with a study by Wendie and Angamo findings., 2020 (91.3%).[25] Consistent results across studies show the persistent nature of DRPs in clinical practice. Vigilant monitoring and comprehensive management of medication therapy are critical for patients with CHF due to the high prevalence of DRPs.

Notably, half of the identified DRPs were attributed to Adverse Drug Reactions (ADRs), differing from previous findings where additional drug therapy predominated (Gelchu and Abdela, 2019; Gokcekus *et al.*, 2016).[26,27] The significant contribution of diuretics, beta-blockers, antiplatelet medications and anticoagulants to drug-related issues underscores the importance of tailored

interventions and vigilant monitoring in managing medication regimens for heart failure patients (Yirga *et al.*, 2018).[10]

Our research identified 256 adverse reactions using the Naranjo scale, with most reactions being either possible or probable. A study by Sharma *et al.* reported similar results with probable and possible adverse reactions.[28] Systematic assessment and comparison of adverse reaction findings can enhance patient safety measures. Our study also evaluated adverse reactions and Drug-Drug Interactions (DDIs), revealing variations in severity compared to previous research by Haq *et al.*, 2020 and Straubhaar *et al.*, 2006.[29,30] While our study reported a substantial proportion of moderate DDIs, tailored interventions and proactive management strategies are imperative to optimize medication safety and mitigate patient risks in clinical practice. Understanding these variations can inform targeted approaches for effective DDI management in CVD patients, ultimately improving patient outcomes and healthcare delivery.

CONCLUSION

In conclusion, our study sheds light on the complexity of Drug-Related Problems (DRPs) in Cardiovascular Disease (CVD) patients, particularly those with heart failure. Through thoroughly examining 150 patients, we identified prevalent patterns and underlying causes of DRPs, emphasizing the need for tailored interventions to optimize medication management and improve patient outcomes.

Our findings underscore the importance of a holistic approach to patient care, considering individual characteristics, comorbidities and medication regimens. Vigilant monitoring and proactive management strategies are crucial in mitigating risks associated with DRPs, such as adverse drug reactions and drug-drug interactions. Moving forward, collaborative efforts and continued research are vital to develop effective strategies for identifying, preventing and addressing DRPs in heart failure patients, ultimately enhancing the quality of care for this vulnerable population.

ACKNOWLEDGEMENT

We extend our heartfelt appreciation to all those who contributed to the successful completion of this research. We are grateful for the guidance, mentorship and collaboration of colleagues and research participants.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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Cite this article: Afshi SS, Noor S, Shahbaaz S, Fathima K. Prevalence of Drug-Related Problems in Patients with Acute Heart Failure Admitted to the Intensive Critical Care Unit. J Young Pharm. 2024;16(3):570-7.