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Evaluation of Drug-Therapy Problems in Cardiovascular Disease Management: Implications for Future Clinical Practice

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Abstract: Drug-therapy problems (DTPs) are a major concern in cardiovascular disease (CVD) management, particularly among older adults exposed to polypharmacy, drug-drug interactions (DDIs), non-adherence, unnecessary drug therapy, and adverse drug reactions (ADRs). This prospective observational study, conducted in the cardiology unit of Saidu Group of Teaching Hospital (SGTH), Swat, Pakistan, evaluated 350 inpatients admitted from January to March 2022. Data were analyzed using SPSS v26 and GraphPad Prism v5.01, employing chi-square tests, t-tests, and binary logistic regression ($p < 0.05$). A total of 323 patients (92.29%) experienced at least one DTP, accounting for 1,252 events. DDIs were the most common DTP, followed by unnecessary drug therapy and ADRs. Age was a significant predictor, with the highest odds of DTPs observed in patients aged 61–70 years; a slight, non-significant increase was noted among females and those with polypharmacy (>5 medications). DTP frequency correlated positively with age and the number of prescribed medications, particularly among individuals aged 31–70 years. The findings indicate a high burden of preventable DTPs in CVD management, dominated by DDIs and unnecessary drug therapy. The incorporation of multidisciplinary medication-review teams, strengthened clinical decision support systems (CDSS), and routine prescription audits is recommended to mitigate DTPs and enhance the safety and precision of cardiovascular pharmacotherapy.

Keywords: DTPs; CVDs; DDIs; ADRs; Unnecessary drug therapy

1. Introduction

CVDs are the foremost cause of premature deaths worldwide and significantly increase the health-care costs. It is one of the chief public health issues usually seen in people of middle and older age groups. The frequently expected underlying cause of CVDs is atherosclerosis, and other common risk factors include smoking, sedentary lifestyle, stress, obesity, high cholesterol level, excessive intake of salt, alcohol, saturated fats and carbohydrates, diabetes mellitus (DM), age, gender, family history, race, genetics, etc. (Shareef et al., 2014). The incidence of CVDs has increased globally among all races, cultures and ethnic groups in recent decades (Vonbach et al., 2023). In 2015, the World Health Organization (WHO) report showed that about 17.7 million people died every year from CVDs worldwide (Dunbar et al., 2018). In 2011, WHO reported that CVDs accounted for approximately 17.1 million deaths annually, representing about 30% of all global deaths. Of these, an estimated 7.3 million deaths were attributed to coronary heart disease, while 6.2 million were due to stroke and other heart diseases (Cosselman et al., 2015).

Reducing the morbidity and mortality linked to CVDs requires optimal use of cardiovascular medications. Even though pharmacotherapy plays an important role in the improvement of the wellbeing of cardiovascular patients, these medications also expose the patients to DTPs (Seid et al., 2020). Drug therapies are essential for the treatment of many diseases, including CVDs; nevertheless, if not used appropriately, they may have

unfavorable effects (Joel et al., 2025). The treatment of CVDs is still difficult in clinical practice because of complicated medication regimens, a large variety of therapeutic products available, various comorbidities, polypharmacy, advanced age, and a lack of application of evidence-based guidelines (Nielsen et al., 2021).

Any unfavorable incident that a patient experiences while receiving drug treatment that genuinely or potentially gets in the way of accomplishing the aims of therapy and needs to be resolved by a professional is referred to as a DTP (Kim et al., 2016). Based on Cipolle's method, DTPs are classified into seven major categories. DTPs include polypharmacy, old age, inadequate medication, need for extra medication therapy, ineffective drug therapy, non-adherence, and ADRs (Babirye et al., 2023). Globally, DTPs have significant social, economic, and humanistic impact. From a social perspective, DTPs can undermine public confidence in healthcare systems and healthcare providers, which may lead to reluctance in seeking medical care (Kim et al., 2016). Economically, due to longer treatments, hospital readmissions, lost productivity, and legal expenses, DTPs have a negative financial impact on healthcare. Furthermore, these problems can cause patients and their loved ones to experience emotional distress in addition to physiological impairment, suffering, and even death (Babirye et al., 2023; Seid et al., 2020). The frequency of DTPs in individuals with CVDs varied from 29.8 to 91%. Previous studies found that DTPs accounted for 28% of all emergency department admissions, with 70–90% of those admissions likely avoidable (Sin et al., 2022).

The escalation in availability of medications, their use and the complexity in their regimen results in more adverse drug events, interactions and complications in follow-up. The availability of a large number of drugs as well as the consistent emanation of new information makes it difficult for the healthcare professionals to update themselves in all aspects (Gandapur et al., 2016). It is a common situation that occurs in chronic non-communicable diseases like CVDs (Shareef et al., 2014). It can occur at each stage of the treatment process like prescription, transcription, dispensing, patient use and follow-up of medication management. Unnecessary drug therapy is used for non-valid indications at this time, or multiple medications are used when a single medication is suitable, or non-medication therapy is best to treat the disease (Nielsen et al., 2021).

A study carried out in Gondar in 2015 included 227 CVD patients, of whom 63.4% faced at least one DTP (Gandapur et al., 2016). Likewise, a study conducted in Ethiopia in 2015 showed that among 130 CVD patients, 72% of cases experienced at least one DTP (Belayneh et al., 2018; Cosselman et al., 2015). Similarly, a prospective observational study was carried out in Ethiopia, showing that among 147 cases, 75.5% faced at least one DTP (Belayneh et al., 2018). Additionally, a study conducted in Ethiopia showed that out of 76 CVD patients, 90.69% faced at least one DTP (Vonbach et al., 2023). The need for additional drug therapy and for different drug products, too low dosage, ADRs, non-compliance, DDIs and polypharmacy are the most identified DTPs reported in many studies (Cosselman et al., 2015; Gandapur et al., 2016; Sin et al., 2022).

A number of researchers have attempted to highlight DTPs in various hospitals around the world with cardiovascular ailments but no such study was found to report such complications in this part of Pakistan. Therefore, this study aims to report the assessment of DTPs with CVDs and the strategies behind achieving the positive outcomes in a tertiary care hospital.

2. Methods

2.1 Study Design, Setting, and Duration

A prospective concurrent observational study was conducted at the cardiology unit of SGTH, Swat, Khyber Pakhtunkhwa, Pakistan. Patients were enrolled consecutively using a non-probability convenience sampling technique, ensuring that all eligible patients admitted during the study period were included. The study was conducted for three months from January to March 2022, representing a sample of DTPs with a refill cycle as most cardiovascular medications are prescribed for 30–90 days. This duration also balanced the feasibility and adequacy of data collection within constrained resources and helped minimize potential bias related to seasonal variation.

2.2 Data Collection

The data for this study were collected by a skilled intern of the Pharm.D program on a special proforma designed by the Department of Pharmacy, Shaheed Benazir Bhutto University Sheringal, Dir Upper. The special proforma for data collection was designed based on a review of existing studies on DTPs, an evaluation of current DTP classifications, and consultations with experts such as pharmacists and researchers. Data collection for identifying DTPs in CVD patients was conducted by interviewing patients to obtain demographic information, medication compliance, and clinical data. Clinical data included complete medication history, prescribed drugs, family history, and ADRs, which were supplemented by reviewing patients' medical charts. All parameters were recorded on the prescribed proforma. The prescriptions were evaluated for DTPs by assessing whether the indications, drug safety, and medication effectiveness were appropriate, and by comparing

each patient's medication therapy with evidence-based guidelines to identify dosage- and effectiveness-related issues.

2.3 Study Population and Eligibility Criteria

All the CVD patients admitted to the hospital during the study period who fulfilled the inclusion criterion were included (n = 350). The exclusion criteria are also presented as follows:

Inclusion criteria: Patients of all ages having CVDs who stayed for more than two days in the hospital. The inclusion criteria ensured the relevant patient population and sufficient stay in hospital for data collection for precise analysis and active patient engagement. Only the patients with complete medical records and those who actively participated in the study were included.

Exclusion criteria: (a) Patients who stayed only for one day in the hospital or were referred to other hospitals. (b) Patients who expired during their hospital stay. (c) Patients who did not respond, or could not be interviewed due to their illness and those who had no caregivers that facilitated the communications or were not willing to participate. (d) Patients whose prescriptions had inadequate data. The exclusion criteria minimized the biases from short-term hospital stays, loss to follow-up in case of referrals to other hospitals, biases related to patient death, issues related to data quality in case of inadequate prescription data and biases related to patients like unwillingness or inability to participate.

2.4 Data Analysis

Data were analyzed using GraphPad Prism version 5.01 and SPSS version 26.0. Descriptive statistics (mean ± standard deviation, frequency, and percentage) were used to summarize data. Chi-square tests assessed categorical associations (e.g., DTPs vs. age/gender). Independent t-tests compared means between groups. Binary logistic regression identified predictors of DTPs while controlling for confounders. A p value < 0.05 was considered statistically significant at a 95% confidence interval (CI). The discrepancies between different tools were addressed by evaluating each interaction across all tools and comparing the results to validate the interaction data. When variations occurred in the reported severity of interactions, the highest severity classification was adopted, and primary literature was consulted to ensure accuracy.

3. Results

A total of 350 patients who were admitted in the Cardiology Ward in SGTH, Swat, Pakistan, were included in the present study for the three-month assessment of DTPs.

3.1 Patient Demographics and Clinical Characteristics

As shown in Table 1, the patients with known cardiovascular ailments included 171 males (49%) and 179 females (51%). Those aged 51–60 years were more prone to developing CVDs and accounted for 36.00% (n = 126), followed by those aged 61–70 years with a proportion of 24.29% (n = 85). Furthermore, it can be observed that the prevalence of CVDs was the lowest in the group aged 1–10 years.

Table 1. Age-wise distribution of patients

Age (Years)	Male	Female	Total	Percentage
01-10	1	0	1	0.29%
11-20	2	1	3	0.86%
21-30	5	1	6	1.72%
31-40	7	6	13	3.72%
41-50	22	28	50	14.29%
51-60	54	72	126	36.00%
61-70	43	42	85	24.29%
71-80	20	21	41	11.71%
81-90	13	7	20	5.71%
91-100	4	1	5	1.43%
Total	171	179	350	100%

A total of 788 cardiovascular illnesses and 334 non-cardiovascular illnesses were diagnosed. As shown in Table 2, the incidence of MI (n = 237) was the highest, followed by ACS (n = 226), HF (n = 82), HVD (n = 42), CAD (n = 36), CMP (n = 31), arrhythmias (n = 21) and stroke (n = 8). Other illnesses (n = 105) included Tetralogy of Fallot (TOF), Complete Heart Block (CHB), Cor pulmonale, hypotension, etc. Among the

non-cardiovascular comorbidities, DM (n = 121) was the most prevalent, followed by IRF (n = 90), respiratory disorders (n = 71), anemia (n = 24) and thyroid disorders (n = 6). Other illnesses (n = 22) included polycythemia, osteoarthritis, rheumatoid arthritis, dementia, etc. These demographic or clinical characteristics may include exposure to risk factors, advancing age, obesity, family history, smoking history, poor diet, physical inactivity, lower socioeconomic status and the clustering of diabetes, hyperlipidemia and hypertension (HTN).

Table 2. Distribution of cardiovascular and non-cardiovascular comorbidities

Cardiovascular Illness	
Type	Frequency
Coronary Artery Disease (CAD)	36
Acute Coronary Syndrome (ACS)	226
Myocardial Infraction (MI)	237
Heart Failure (HF)	82
Arrhythmia	21
Cardiomyopathy (CMP)	31
Stroke diseases	8
Hypertensive Vascular Disease (HVD)	42
Others	105

3.2 Medication Use and Cardiovascular Risk Profiles

The results reveal that in study participants, the frequency of cardiovascular drugs prescribed was 1208 (51.58%) and that of non-cardiovascular drugs was 1134 (48.42%). Furthermore, it shows that the most common prescribed class of cardiovascular drugs (Table 3) was antiplatelets that include aspirin and clopidogrel with a frequency of 346, followed by anticoagulants (n = 182), anti-hyperlipidemic agents (n = 174), diuretics (n = 120), nitrates (n = 99), thrombolytics (n = 70), beta blockers (n = 59), cardiac stimulants (n = 51), ACE inhibitors (n = 48), CCBs (n = 21), ARBs (n = 16) and others (n = 22). While in non-cardiovascular drugs, the most common prescribed class was GI drugs with a frequency of 298, followed by analgesics (297), anti-DM (n = 144), antibiotics (n = 119), inhalers (n = 113) and others (n = 163).

The common risk factors that may be involved in developing CVDs in study participants were identified and grouped in Figure 1. The past history of illness of HTN was the most frequent risk factor (n = 275), followed by other cardiac disorders like MI, HF, dilated CMP, angina, etc. (n = 148), DM (n = 106), family history (n = 84), smoking (n = 12), diet (n = 3), congenital conditions (n = 1), and laboratory findings indicating elevated cardiac hormones, enzymes, cholesterol levels, etc.

Table 3. Class-wise distribution of prescribed drugs in patients

Drugs	**Class**	**Male**	**Female**	**Total**	**Percentage**
Cardiovascular drugs	Thrombolytics	41	29	70	5.80%
	Antiplatelets	169	177	346	28.64%
	Anticoagulants	93	89	182	15.07%
	Nitrates	51	48	99	8.20%
	Diuretics	63	57	120	9.93%
	Beta blockers	28	31	59	4.88%
	Calcium Channel Blockers (CCBs)	7	14	21	1.74%
	Angiotensin-Converting Enzyme (ACE) inhibitors	27	21	48	3.97%
	Angiotensin II Receptor Blockers (ARBs)	7	9	16	1.32%
	Anti-hyperlipidemic agents	87	87	174	14.40%
	Cardiac stimulants	22	29	51	4.22%
	Others	10	12	22	1.82%
	Total	605	603	1208	100%
Non-cardiovascular drugs	Anti–DM	68	76	144	12.70%
	Antibiotics	74	45	119	10.49%
	Analgesics	168	129	297	26.19%
	Gastrointestinal (GI) drugs	157	141	298	26.28%
	Inhalers	66	47	113	9.97%
	Others	93	70	163	14.37%
	Total	626	508	1134	100%

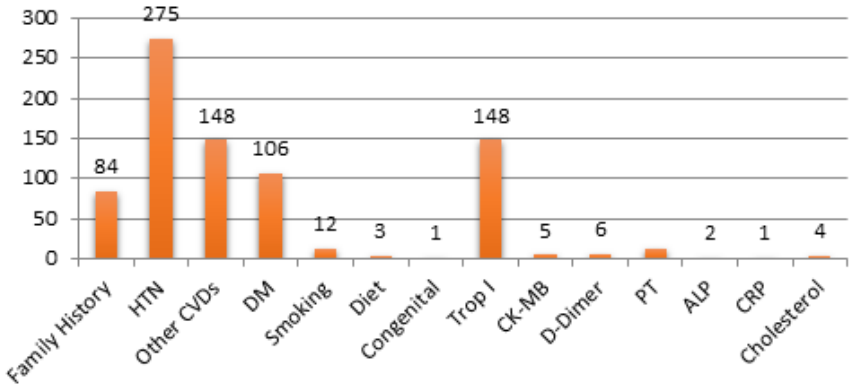

Figure 1. Gender-wise distribution of risk factors

Various dosage forms were prescribed to hospitalized patients (Table 4). The most prescribed dosage form among the study participants was injectable with a frequency of 1652 (48.53%), followed by tablets (n = 1348; 39.60%), inhalers (n = 305; 8.96%), and capsules (n = 43; 1.26%), among others.

Table 4. Gender-wise distribution of prescribed dosage forms

Dosage Forms	Male	Female	Total
Tablets	663	685	1348
Injectables	813	839	1652
Capsules	21	18	39
Inhalers	153	152	305
Syrups	15	20	35
Suspensions	12	4	16
Gels	1	1	2
Creams	1	0	1
Sachets	0	3	3
Lozenges	1	0	1
Drops	0	2	2
Total	1680	1724	3404

3.3 Prevalence and Types of DTPs

In this study, a total of 1252 DTPs were identified and categorized according to Cipolle's method (Figure 2). In 323 (92.29%) cases out of 350 study participants, one DTP was reported in 24 (8.86%) study cases, two DTPs in 68 (19.43%) study cases, three in 72 (20.57%) study cases, four DTPs in 58 (16.57%) study cases, five DTPs in 36 (10.29%) study cases and six DTPs in 28 (8%) study cases. Furthermore, seven DTPs were reported in 20 (5.71%) study cases, eight DTPs in 8 (2.29%) study cases, nine DTPs in 4 (1.14%) study cases, ten DTPs in 1 (0.29%) study case, eleven DTPs in 2 (0.57%) study cases and twelve DTPs in 2 (0.57%) study cases.

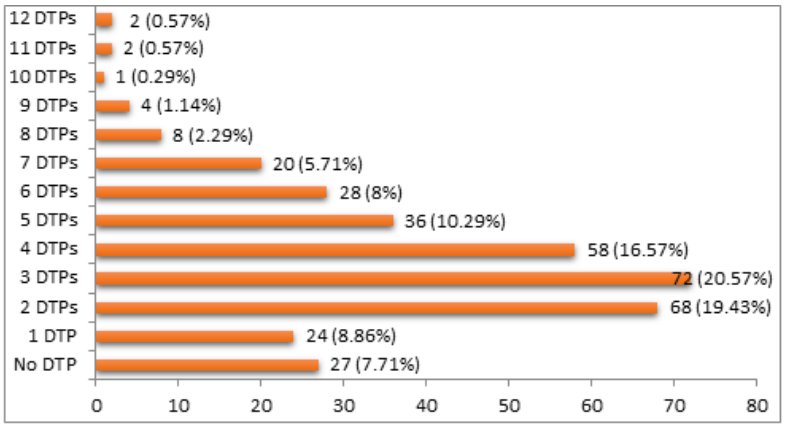

Figure 2. Prevalence of DTPs

Different types of DTPs were noted in the study participants with a frequency of 1252, as shown in Table 5. These results show that the most common DTPs that occurred were DDIs with a frequency of 992 (79.23%), followed by unnecessary drug therapy (n = 109; 8.71%), ADRs (n = 83; 6.63%) and the need for additional drug therapy (n = 51; 4.07%). The need for different drug products (n = 6; 0.48%), non-compliance (n=6; 0.48%), too low dosage (n = 4; 0.32%) and too high dosage (n = 1; 0.08%) were the least observed DTPs.

Table 5. Disaggregation of DTPs

DTP Type	Frequency	Percentage
Unnecessary drug therapy	109	8.71%
Need for additional drug therapy	51	4.07%
Need for different drug products	6	0.48%
Too low dosage	4	0.32%
ADRs	83	6.63%
Too high dosage	1	0.08%
Non-compliance	6	0.48%
DDIs	992	79.23%
Total	1252	100%

3.4 Subtypes of DTPs

3.4.1 Unnecessary drug therapy

Unnecessary drug therapy was identified (Table 6) among the study participants. The drug therapy with no medical indications accounted for 22.94% (n = 25) and the duplicate therapy accounted for 77.06% (n = 84). The most common drugs prescribed with no medical indications were antibiotics (n = 18), followed by anti-allergics (n = 3), inhalers (n = 3) and CNS drugs (1). The most frequently prescribed duplicate therapy was cardiovascular agents (n = 23), followed by cortisones (n = 13), anticoagulants (n = 10), nitrates (n = 5), acid suppressants (n = 5), GI agents (n = 4), sympathomimetics (n = 4), antibiotics (n = 4), diuretics (n = 4), antihypertensives (n = 4), oral anti-DM (n = 3), anti-cholinergics (n = 3), long-acting insulin (n = 1) and anti-arrythmics (n = 1).

Table 6. Frequency of different types of unnecessary drug therapy

Unnecessary Drug Therapy Type	Frequency	Percentage
No medical indication		
Antibiotics	18	16.51%
Anti-allergics	3	2.75%
Inhalers	3	2.75%
Central Nervous System (CNS) drugs	1	0.92%
Sub-total	25	22.94%
Duplicate therapy		
Cardiovascular agents	23	21.10%
GI agents	4	3.67%
Anticoagulants	10	9.17%
Acid suppressants	5	4.59%
Cortisones	13	11.93%
Oral anti-DM	3	2.75%
Anti-cholinergic	3	2.75%
Sympathomimetics	4	3.67%
Antibiotics	4	3.67%
Diuretics	4	3.67%
Antihypertensives	4	3.67%
Long-acting insulin	1	0.92%
Nitrates	5	4.59%
Anti-arrhythmics	1	0.92%
Sub-total	84	77.06%
Grand-total	109	100%

3.4.2 Need for additional drug therapy

The current research shows that the need for additional drug therapy accounted for about 4.07% of DTPs (Table 7). Among these the untreated indications (n = 26), the most common was DM (n = 21), followed by pericarditis (n = 2), RA (n = 1), UTI (n = 1) and leukocytosis (n = 1). The results also show that GI upset was the reported indication that needs prophylactic treatment (n = 25).

Table 7. Frequency of need for additional drug therapy in different types

Need for Additional Drug Therapy	Frequency	Percentage
Untreated indication		
DM	21	41.18%
Rheumatoid Arthritis (RA)	1	1.96%
Pericarditis	2	3.92%
Urinary Tract Infection (UTI)	1	1.96%
Leukocytosis	1	1.96%
Sub-total	26	50.98%
Prophylactic therapy		
GI upset	25	49.02%
Sub-total	25	49.02%
Grand-total	51	100%

3.4.3 Need for different drug products

The results show that there are six indications that need for different drug products to be prescribed, including HF (n = 2), CHB (n = 2), HTN (n = 1) and pneumonia (n = 1). For HF treatment, furosemide 20 mg twice daily (BD) was prescribed in one case, whereas digoxin 250 mcg once daily (OD) was prescribed in another. For CHB, adrenaline 10 mg was administered immediately in one case, while antiplatelets, anticoagulants, anti-hyperlipidemic agents, and nitrates were recommended in the other case. For HTN, antiplatelets, anticoagulants, and anti-hyperlipidemic agents were prescribed; however, no antihypertensive therapy was provided. In the case of pneumonia, Augmentin was prescribed. According to standard treatment protocols, the most effective drug products are available for all mentioned cases.

3.4.4 Dosage-related problems (too low/too high)

The results show that four drugs (metoprolol, sulbactam, meropenem and amoxicillin) were prescribed in too low dosages that required interventions to provide the recommended effective dosages (Table 8).

Table 8. Frequency of too low dosage

Drug	Dosage	Frequency	Percentage
Metoprolol	25 mg ½ BD	1	25%
Sulbactam	1 gm OD	1	25%
Meropenem	500 mg OD	1	25%
Amoxicilin	1.2 gm OD	1	25%
Total	-	4	100%

The current study recorded several drugs prescribed at high doses (Table 9). Only one drug—metformin—was prescribed at a dose considered too high, and it required intervention to adjust it to the recommended safe dosage.

Table 9. Distribution of DDIs

Number of DDIs	Frequency	Percentage
Participants with no DDIs	32	9.14%
Participants with 1 DDI	38	10.86%
Participants with 2 DDIs	84	24%
Participants with 3-5 DDIs	174	49.71%
Participants with 6 DDIs	11	3.14%
Participants with 7 DDIs	5	1.43%
Participants with 8 DDIs	3	0.86%
Participants with 9 DDIs	3	0.88%
Total	350	100%

3.4.5 ADRs

As shown in Figure 3, the study participants experienced many ADRs (n = 83). Among these, the most frequently reported ADR was GI irritation (n = 19), which occurred due to the combination of aspirin and clopidogrel, followed by sleep disturbance due to use of cefoperazone (n = 10), restlessness due to use of digoxin, GI irritation (n = 7) due to the combination of orphenadrine, aspirin and clopidogrel and so on. Proton pump inhibitors (PPIs) like omeprazole and pantoprazole were frequently prescribed in conjunction with aspirin and clopidogrel to minimize the potential for GI irritation and ulceration. H2 receptor antagonists were utilized when patients could not tolerate PPIs, with ranitidine serving as a substitute, though it was less effective in

preventing bleeding from serious lesions. Patients on PPIs showed a notable decrease in GI-related side effects, such as dyspepsia and ulceration. Clinical documentation indicated a reduced frequency of hospital admissions due to GI bleeding in those receiving co-prescribed PPIs. However, concerns were raised regarding the possible interactions between PPIs and clopidogrel, especially with omeprazole, which might compromise clopidogrel's antiplatelet effect. In those scenarios, alternative PPIs, like pantoprazole, were preferred.

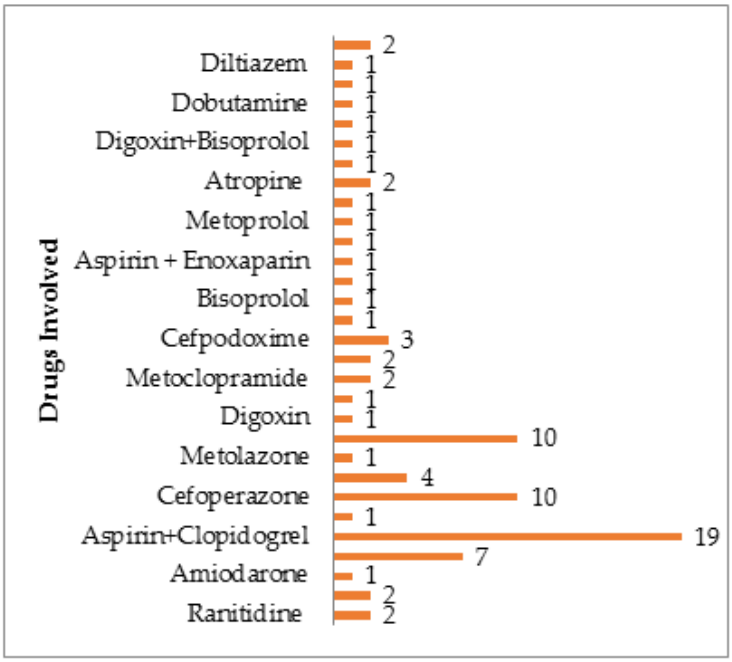

Figure 3. ADRs (n = 83) among cardiovascular inpatients

3.4.6 DDIs

In this study, it was found that the most frequently occurring DTPs were DDIs. All prescriptions were scrutinized for contraindicated, serious and major classes of DDIs, while the rest of the classes like moderate and minor were omitted. Out of 350 study participants, the DDIs were found in 318 (90.86%) participants while no interactions were found in 32 (9.14%) participants. In these study cases, a total number of 992 DDIs of contraindicated, serious and major classes were found, as shown in Table 9. This research classified DDIs based on their severity, which includes major, moderate, and minor DDIs. Major DDIs can lead to significant adverse effects, including bleeding, arrhythmias, or renal dysfunction, and necessitate immediate medical attention. Moderate DDIs require careful monitoring or adjustments to dosage but typically do not result in severe consequences if managed correctly. Minor DDIs are generally of low clinical importance and often resolve without the need for intervention. Consequently, DDIs frequently contribute to the worsening of pre-existing conditions.

3.5 Predictors of DTPs

Regression analysis of multiple variables was conducted to find out the predictors of DTPs based on the research data (Table 10). Results indicate that the odds of having DTPs are significantly higher for most age groups compared to the reference group (1–10 years). The age group of 61–70 years (odds for DPTs are 18.75 times higher, 95% CI: 2.43–144.92, $p = 0.005$) has the highest odds ratio (OR), followed by the age groups of 51–60 (odds for DPTs are 11.60 times higher, 95% CI: 1.60–84.11, $p = 0.02$) and 41–50 years (odds for DPTs are 10.50 times higher, 95% CI: 1.42–77.73, $p = 0.02$), suggesting these groups are at a higher risk for DTPs. Furthermore, the odds of having DTPs are slightly higher (1.16 times) for females compared to males (95% CI: 0.23–5.83, $p = 0.86$). Similarly, patients taking more than five drugs have higher odds of experiencing DPTs (95% CI: 0.42–5.73, $p = 0.51$), compared to those taking fewer drugs. Positive correlations were observed for DTPs between the number of drugs taken and age of patients. The odds of experiencing DTPs increase substantially with age, particularly from 31 to 70 years. Considering the possibility that older individuals are more likely to be prescribed multiple drugs, which could, in turn, increase their risk of DTPs.

Table 10. Regression results of predictors of DTPs

Predictor	Category	DTP Number (%)	No DTPs (%)	OR	95% CI	*p* value
Age, years	1–10	0	1 (100%)	Reference	-	-
	11–20	1 (33.3%)	2 (66.6%)	1.50	0.15–15.21	0.73
	21–30	2 (33.33%)	4 (66.66%)	1.50	0.24–9.41	0.66
	31–40	10 (76.9%)	3 (23.07%)	11.11	1.20–102.87	0.03
	41–50	42 (84%)	8 (16%)	10.50	1.42–77.73	0.02
	51–60	116 (92%)	10 (8%)	11.60	1.60–84.11	0.02
	61–70	81 (94.18%)	4 (5.92%)	18.75	2.43–144.92	0.005
	71–80	36 (87.8%)	5 (12.2%)	7.20	0.93–55.93	0.06
	81–90	13 (65%)	7 (35%)	3.00	0.50–17.90	0.23
	91–100	3 (60%)	2 (40%)	1.50	0.20–11.48	0.70
Sex	Male	167 (97.6%)	4 (2.4%)	Reference	-	-
	Female	174 (97.2%)	5 (2.8%)	1.16	0.23–5.83	0.86
Number of drugs	Less than 5	124 (88.5)	21 (11.5)	Reference	-	-
	More than 5	143 (92.2%)	12 (7.8%)	1.55	0.42–5.73	0.51

4. Discussion

From the complete description of relative studies, it is indicated that CVD patients are at greater risk of developing DTPs due to the presence of comorbidities, complexity in drug regimens, and polypharmacy. The presence of DTPs in CVD patients is associated with adverse health outcomes. Determining the DTPs and their associated factors is critical for preventing DTPs and improving health outcomes. The current research recorded such DTPs among the patients suffering from CVD in a tertiary care healthcare setting. Various studies have reported the CVD in diverse models of research for better understanding (Assegie & Elaraby, 2023) and brought to light important gaps that suggested women were more likely than men to suffer from CVD. The results of this study are consistent with research reported in 2010 that CVD was more prevailent in women (51%) than in men (49%) (Niquille & Bugnon, 2010). In 2018, Timmis et al. (2018) reported that the prevalence rate of DTPs was 48.18% in males and 51.82% in females. Similarly, 52.8% of CVDs in women and 47.2% in men were reported by Ruan et al. (2018). The proportions were 52.7% and 47.3% in women and men, respectively, in a study reported in 2020 (Seid et al., 2020). Moreover, women accounted for 50.3% and men accounted for 49.7% in a study in 2018 (Niriayo et al., 2018). It was in contrast with the findings of Babirye et al. (2023), with women and men accounting for 37% and 63%, respectively. Likewise, in a study in 2016, 59.73% of women and 40.26% of men had CVDs (Al-Azzam et al., 2016), and 28% of women and 72% of men were reported in 2012 (Al-Amin et al., 2012).

Most of the patients (36%) were in the age group of 51-60 years and these findings were lower than the 40.5% reported by Ruan et al. (2018), while were higher than the 26.5% reported by Abdela et al. (2016). It was also much higher than the 24% reported by Seid et al. (2020). In contrast to a study by Vakade et al. (2016) which found that MI (50%) and Unstable Angina (USA) (36.56%) were the most common CVDs, the current study found that ACS and MI were the most common CVDs, accounting for 237 (67.7%) and 226 (64.6%) cases, respectively; HTN (64.6%) and CHF (30.77%) were the most common CVDs, according to a 2017 study by Thomas et al. (2017); HF (31.3%) and Valvular Heart Disease (VHD) (26.9%) were the most common CVDs, according to a study by Abdela et al. (2016); and the research by Argaw et al. (2019) revealed that HTN (51%) was the most common CVD and MI (12%) was the least common. The concomitant non-cardiovascular comorbidities reported in current findings were DM in 121 cases (34.57%) and IRF in 90 cases (25.7%); while the findings reported by Timmis et al. (2018) showed that Chronic Kidney Disease (CKD) occurred in 60% and DM in 50% of the study participants; the study of Niquille & Bugnon (2010) reported that DM was found in 19% of the study population; and findings of Abraham (2014) showed that DM was diagnosed in 46.25% of the study population and Congestive Cardiac Failure (CCF) in 10%.

This study reported a total number of 1797 drugs were prescribed to all study participants with an average number of 5.13 drugs per patient. This value is higher than the study conducted by Niriayo et al. (2024), where the average number of drugs per patient was 4.33; Seid et al. (2020) showed that the number was 4.96 and the study carried out by Tegegne et al. (2015) showed that number was 3.03. But less than the study conducted by Abraham (2014), which showed that the average number of drugs per patient was 13.14; the study by Bhatty et al. (2018) revealed that the number was 8.65 and the study by Vakade et al. (2016) showed that the number was 8.4.

The results of this research revealed that a total number of 1208 cardiovascular drugs were prescribed among the study population with an average of 3.45 drugs per prescription and the most common prescribed classes of cardiovascular drugs were antiplatelets with a frequency of 346 (28.64%) and anti-hyperlipidemic with a

frequency of 174 (14.40%), which is greater than the study carried out by Abdela et al. (2016), which showed that 2.84 cardiovascular drugs were prescribed per patient and the most frequently prescribed classes were diuretics (29.5%) and ACE inhibitors (12.42%), while the study conducted by Sin et al. (2022) showed that the average number of cardiovascular drugs per prescription were 1.95 and the most commonly prescribed classes were ACE inhibitors (44%) and CCBs (44%). A study conducted by dos Reis et al. (2022) showed the average number of cardiovascular drugs per prescription was 1.49 and the most commonly prescribed classes were diuretics (30.35%) and drugs acting on the renin-angiotensin system (21.38%). A total of 1134 non-cardiovascular drugs were used in which the most frequently prescribed classes were GI drugs with a frequency of 298 (26.28%) and analgesics with a frequency of 297 (26.21%). These results deviate from the study done by Sin et al. (2022), which showed that the most frequently used non-cardiovascular drugs were antibiotics (48.93%), followed by GI drugs (19.35%) and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) (17.74%), while the study reported by Tegegne et al. (2015) showed that the most frequent non-cardiovascular drugs was antibiotics (35.1%) and analgesics (7.2%). The most common risk factor of HTN was found in 78.6%, which is less than the findings reported by Yang et al. (2024) where the prevalence of HTN as a risk factor was 99.97%, but more than the 28.8% found by Thomas et al. (2017). The other risk factor reported in this research was family history (24%), which is greater than the 4.6% reported by Dunbar et al. (2018).

Moreover, the present research indicates a total number of 1252 DTPs were identified in 323 cases (n=350), corresponding to 92.29% of all study participants with a rate of 3.58 DTPs per patient, which is lower than 80.73% reported in the study by Tigabu et al. (2014) with a rate of 2.35 DTPs per case; Tegegne et al. (2015) revealed that in 88.66% of the study population had DTPs at the rate of 1.69 DTPs per case; Tegegne et al. (2015) showed that DTPs were occurred in 96.05% cases at the rate of 1.38% per case; Yang et al. (2024) reported that DTPs were found in 81.26% cases with an average number of 4.62 DTPs per case; Dunbar et al. (2018) showed that DTPs occurred in 72% of the study population with a rate of 1.25 DTPS per case; Tigabu et al. (2014) showed that DTPs occurred in 73.5% of the study cases at the rate of 1.23 DTPs per patient; Abdela et al. (2016) showed that in 63.4% participants had DTPs at the rate of 1.17 DTPs per case; and Seid et al., (2020) showed that DTPs accounted for 60.65% of the study participants at a rate of 0.6 DTPs per case. The results reported by Dunbar et al. (2018) revealed that DTPs occurred in 91.7% of the study population at a rate of 3.9 DTPs per case, and Hsu et al. (2016) showed that DTPs occurred at the rate of 5.6 DTPs per participant.

The present research showed that in 92.29% of the study population, one or more DTPs were reported with a maximum of 12 DTPs, which is greater than the 80.7% reported by Tigabu et al. (2014) with a higher number of three DTPs; Dunbar et al. (2018) showed that this percentage was 72% with a maximum number of three DTPs, and Abdela et al. (2016) found that the proportion was 63.4% with a maximum number of three DTPs. However, Tegegne et al. (2015) showed that in 96.1% of cases, one or more DTPs occurred frequently with a maximum number of four DTPs. Furthermore, the present study revealed that three DTPs occurred frequently. However, in the study reported by Hussein et al. (2014), the frequently occurring was one DTP, and in the study by Tegegne et al. (2015) and Abdela et al. (2016), the number was two DTPs.

In this research, the most frequently observed DTP was DDIs, which accounted for 79.23%, which is consistent with several studies by Hsu et al. (2016) (37% of all DTPs), Abraham (2014) (46.2% of all DTPs), Hussein et al. (2014) (58.7% of all DTPs), Hamsini et al. (2019) (58.6% of all DTPs), and Celin et al. (2012) (25% of all DTPs). However, the study conducted by Hsu et al. (2016) showed the DDIs were the second most frequent DTPs after the need for laboratory tests which accounted for 31% of all DTPs. The most frequently occurring DDIs were enoxaparin + clopidogrel (25.9%) and aspirin + enoxaparin (25.5%), which is higher than aspirin + enoxaparin (10.1% and 11% in the Khyber Teaching Hospital sample and the Hayatabad Medical Complex Hospital sample, respectively) and enoxaparin + clopidogrel (9.7% and 11.7% in the two samples) in the study conducted by Shakeel et al. (2018). The second most frequent DTP in this study was unnecessary drug therapy, which accounted for 8.7% of all DTPs. This is similar to results (30.9%) reported by Belayneh et al. (2018). Ayalew et al. (2015) reported that this category of DTPs was the second least occurring DTP, which accounted for 4.5% of all DTPs and Hamsini et al. (2019) showed the untreated indication was the second least DTP, which accounted for 19.26% of all DTPs.

This study revealed the proportions of ADRs (8.4%), need for additional drug therapy (5.14%), need for different drug products (0.6%), non-compliance (0.6%), too low dosages (0.4%) and too high dosages (0.1%) in all DTPs. These results are different from the findings reported by Al-Amin et al. (2012), which highlighted that too high dosages accounted for 28%, too lower dosages were 10% and contraindications were 23% of all DTPs; Abraham (2014) showed that too high dosages accounted for 17.3%, therapeutic duplication for 11.2% and too low dosages for 10.4% of all DTPs; the study of Ayalew et al. (2015) showed that ADRs were the second most common DTP and accounted for 23% and the need for additional drug therapy for 11.6%; and Saldanha et al. (2020) reported that too high dosages were 14.5%, ADRs were 10% and too low dosages were 9.7% of all DTPs.

4.1 Limitation of the Study

The current study consisted of 350 CVD patients and was executed in a period of three months in a single tertiary care center. Therefore, a pilot study is suggested to report DTPs from the whole health care settings of the country.

4.2 Future Perspectives

A proper system of prescription review teams, including pharmacists, physicians and nurses, could significantly contribute to the mitigation of these DTPs not only in the treatment regimen of CVDs but also DTPs associated with many chronic diseases, including DM, cancer, hepatitis, liver cirrhosis, kidney diseases and psychological disorders, where patient compliance and attribution to patient response are highly admissible factors.

5. Conclusion

In conclusion, DTPs, particularly DDIs and unnecessary drug therapy, are frequent among hospitalized CVD patients. Implementing a multidisciplinary prescription review team (including clinical pharmacists, cardiologists, and nurses) and adopting CDSS-based monitoring can significantly reduce medication errors and enhance therapeutic outcomes. Regular training workshops and prescription audits should also be institutionalized to sustain safe and rational medication practices.

Author Contributions

Conceptualization, R.B and M.E.; methodology, R.B.; software, M.A.A.; validation, M.E.; formal analysis, R.B.; investigation, M.A.A.; resources, M.E.; data curation, M.E.; writing—original draft preparation, M.A.A.; writing—review and editing, R.B.; visualization, M.E.; supervision, M.E.; project administration, M.A.A.; funding acquisition, M.E. All authors have read and agreed to the published version of the manuscript.

Informed Consent Statement

Ethical approval was obtained for this study from Institutional Ethics Committee of Shaheed Benazir Bhutto University Sheringal, Pakistan. This study was conducted following the ethical guidelines. It involved the concurrent collection and analysis of patient data from Saidu Group of Teaching Hospital, Saidu Sharif, Swat, Khyber Pakhtunkhwa, Pakistan. All participants provided written informed consent prior to their inclusion in the study. The research adhered to the ethical standards of the 1964 Helsinki Declaration.

Data Availability

All the necessary data are included in this manuscript. However, additional data are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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