EMERGENCY ADMISSION AMONG CARDIOVASCULAR DISEASE PATIENTS; OUTCOME, RISK FACTORS AND DRUG-RELATED ADMISSION, AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA: A PROSPECTIVE OBSERVATIONAL STUDY.

By; Hikma Husein

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Co-advisor: Dr. Merahi Kefyalew (Assistant Professor of Emergency and Critical Care Medicine)

A Thesis Submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfillment for the Requirements of Master of Science Degree in Pharmacy Practice.

February, 2024

Addis Ababa, Ethiopia

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List of abbreviations and acronyms

ADR; Adverse drug reactions

ADHF; Acute Decompensated Heart Failure

AF; Atrial Fibrillation

AOR; Adjusted Odd Ratio

AHR; Adjusted Hazard Ratio

CHF; Congestive Heart Failure

COR; Crud Odd Ratio

CVD; Cardio Vascular Disease

CRVHD; Chronic Rheumatic Valvular Heart Disease

DCMP: Dilated Cardio Myopathy

DREA; Drug-Related Emergency Admission

DRHA; Drug-Related Hospital Admission

DRP; Drug-Related Problems

ED; Emergency Department

HCP; Health Care Professional

HF; Heart Failure

IHD; Ischemic Heart Disease

MI; Myocardial Infarction

TASH; Tikur Anbessa specialized Hospital

Abstract

Background: In Ethiopia, the prevalence of cardiovascular diseases is rising, with varying prevalence from 1 to 20 percent across the nation. Moreover, drug-related hospital admissions are a common issue among these patients because of the greater number of medications required, the multiple issues caused by cardiovascular illnesses, and the usage of pharmaceuticals with a limited therapeutic index.

Objective: This study aims to evaluate the results of cardiovascular patients treated in the emergency room of Tikur Anbessa Specialized Hospital, as well as the frequency of drug-related emergency admissions and the factors linked to both the drug-related admissions and the patient's outcome.

Methodology: A prospective observational study was conducted from September to December 2022 on patients with cardiovascular illness who came to Tikur Anbessa Specialized Hospital's adult emergency department. All patients who visited ED during this time and met the requirements for inclusion was counted in the study. A questionnaire was used to gather data, and SPSS version 25 was used for analysis. While factors associated with drug-related emergency admission were identified by logistic regression analysis, cox regression analysis was used to estimate factors associated with emergency department survival.

Result: In total, 401 patients made up the study; 51.1% of the patients were male and the median age was 50. Of the patients admitted to the emergency room, 9.5% passed away during the study period. Poly-pharmacy, diagnosis with dilated cardiomyopathy and atrial fibrillation, and history of smoking are associated with a higher mortality rate in these patients. 23% of all admission was due to drug related problems, with non-adherence being the most common cause.

Conclusion: A mortality rate of 9.5% was found in cardiovascular disease patients, and the prevalence of drug related emergency admission among cardiovascular disease patients was 23% in this study.

Key words: cardiovascular disease, survival, drug-related emergency admission, Ethiopia

1. Introduction

1.1. Background

Cardiovascular disease (CVD) is an umbrella term of conditions affecting the heart and blood vessels that also encompasses deep vein thrombosis, pulmonary embolism, rheumatic heart disease, peripheral arterial disease, and cerebrovascular disease. With an anticipated 17.9 million deaths from CVDs in 2019, or 32% of all deaths worldwide, CVDs are the leading cause of death worldwide. Furthermore, in low- and middle-income nations, CVD deaths account for more than 75% of all fatalities. In 2019, CVDs were responsible for 38% of the 17 million premature deaths (before the age of 70) caused by non-communicable diseases(1).

In developing nations like Africans, the prevalence of CVD is rising dramatically, primarily as a result of diseases linked to atherosclerosis, which is brought on by continual changes in dietary habits. This comes on by gradual transitions to a westernized diet, which is rich in sugar and saturated fats, and a more sedentary way of life. Additional factors linked to increased CVD epidemiology in these regions include increased cigarette use and greater rates of hypertension(2).

In a retrospective cross-sectional study to determine the prevalence of CVD in our country, hypertension was shown to account for the majority (62.3%) of CVDs among patients who had followed up at Gonder University Hospital's outpatient chronic disease clinic, followed by heart failure (HF) (23.9%). According to this study, hypertensive heart disease and rheumatic heart disease are the two most common CVDs after hypertension and HF(3). Additionally one systematic review and meta-analysis estimated the pooled prevalence of CVD as 5%, with the prevalence range of 1%to 20% in nine different cross-sectional studies(4).

Although drugs are usually prescribed to achieve an optimal therapeutic outcome, the growing number of drug products, an increase in the numbers of the disease being recognized, many patients needing health care service, and poly-pharmacy lead to the occurrence of numerous drug-related problems (DRP). These problems would contribute to hospital admission and affect the optimal drug therapy outcome. Furthermore DRPs leads to

additional morbidity, mortality and health related cost due to the need for further management, investigation and hospital stay(5–8).

DRP is "An event or circumstance involving a patient's drug treatment that actually or potentially interferes with the achievement of an optimal outcome." As defined by Hepler–Strand. Additionally, they divided DRPs into the following categories: untreated indications, poor drug selection, sub-therapeutic dosage, failure to get medications, overdosing, adverse reactions, drug interactions, and drug usage without an indication(9).

A drug-related hospital admission (DRHA) is a hospital admission brought on by any unfavorable clinical symptom that develops as a result of or is motivated by the use of a particular medication. DRHA is caused by avoidable(preventable) medication errors or unavoidable(non-preventable) adverse drug reactions (ADR)(10). Drug therapy has advanced significantly over the last few decades, which improved patient care for better health-related quality of life. However, on the other hand it significantly increased DRHA (5).

Over time, there is a significant increment in the overall rate of DRHA, a problem within the health care system. DRHA significantly impacts consultations and intervention for patients in the emergency department (ED) and ward admissions; this results in an additional complication on the health care system by increasing drug-related morbidity and mortality(11,12). A number of studies on DRHA estimated that DRP caused 5–10% of hospital admissions, and around 50% of which might have been prevented(12). Furthermore an investigation carried out at a university hospital in Saudi Arabia found the preventability of DRP as high as 70 %, indicating that the clinical pharmacist's role is significant enough(13).

According to nationwide surveillance data collected in the different ED in United States (US), approximately 4 ED visits for drug-related adverse events (ADE) were reported annually per 1000 people. About 60% of ED visits for ADE involved the use of anticoagulants, diabetes medications, and opioid analgesics(14). A study conducted to estimate the number of emergency hospital admissions linked to ADR in England over six years demonstrated-that the burden of ADRs is increasing; (from 1.2% in 2008/2009 to 1.6% in 2014/2015). This study shows CV medications are third most typical cause of ADRs after neoplastic substance and analgesics(15).

DRHA is also a common problem among CVD patients due to the higher number of medications to be taken, a number of complications associated with these diseases, and the

use of medicines with a limited therapeutic index, like warfarin or digoxin. Patients with CVD are particularly vulnerable to adverse DDIs; one in ten hospitalized patients with CVD may have a DDI that contributed to their hospitalization. Therefore, DDI-related injury may be a huge global burden(16).

One systematic review on DRHA in 2013 in India, found CV drugs as the most common causes of DRPs (7 out of 15 articles), along with anti-neoplastic and CNS medications(5 out of 15 pieces each). Out of the seven studies that indicated CV medications as the cause of DRPs, 2 of them showed diuretics being the main substance responsible for issues like electrolyte imbalance, according to this review(5).

The purpose of this study is to assess the outcome of CVD patients and related factors in the ED as well as the prevalence of DREA, and factors affecting DREA in CVD patients at the ED of Tikur Anbessa Specialized Hospital (TASH).

1.2. Statement of the problem

Non-communicable diseases are now becoming the primary cause of premature mortality and morbidity in both industrialized and developing nations. A mortality trend analysis estimated that 17.8 million individuals worldwide died from CVD in 2017 (233.1 per 100,000 persons). While the rate in wealthy countries has decreased since 1990, it has stayed constant in low- and middle-income nations, according to this analysis(17).

In sub-Saharan African nations, CVDs account for 37% of non-communicable diseases and 13% of all deaths. The high cost of cardiac drugs, a lack of cardiac specialists, a lopsided budget, and inadequate healthcare infrastructures are some of the factors contributing to the increased prevalence of CVDs in these nations(18). In Ethiopia the prevalence of CVD ranged from 1 to 20% (the pooled prevalence was 5%), according to a systematic review and meta-analysis that includes nine institutional and community-based research (95% CI: 3–8%) (4).

Furthermore, a retrospective observational study was carried out at ED of TASH from March 2018 to 2020, to evaluate all-cause mortality, after separating the cause of death as traumatic and medical causes. According to this study CVDs accounted for a total of 84 deaths

(16.6%); CVD was comorbid in 70 deaths (13.68) and it was immediate cause of death in 80 patients (15.8%)(19).

Studies have shown that the prevalence of DRP in patients with CVD ranged from 69 to 78%. (20). Patients with CVD are more susceptible to DRHA for a variety of reasons, including poly-pharmacy, having numerous comorbidities, and using drugs with a limited therapeutic index. According to a study done in our country by Demessie MB and Berha AB, CV medications were the most frequent class associated with DRHA (21).

Although the CVD patient outcome and the prevalence of DRHA/DREA were done previously at the national and international level, a further study which investigates the mortality, DREA and its associated factors related only to CVD patients are needed. This will help in reducing drug-associated morbidity and mortality in these patients by applying different preventive strategies.

As a result, this study investigated the ED mortality rate and DREA specific to CVD patients to bring evidence for potential rooms related to minimizing cost, morbidity and mortality by assessing the predisposing factors for the drug-related admission.

1.3. Significance of the study

This study evaluated the outcome of CVD patients and associated factors at ED of TASH, so that it will inform healthcare professionals (HCP) on how to minimize mortality and morbidity among these patients, by controlling the modifiable associated factors identified. This study also determined the prevalence of DREA among CVD patients, which will help all HCP to be acquainted with the extent of DREA among these patients. The study also identified potential factors that are associated with DREA and its preventability status at ED of TASH, which will give insight to HCP on how to prevent DREA and manage the factors accounted for this admission.

Finally, this study can serve as a baseline data to look for possible alternative solutions to improve and prevent DRP and enhance the clinical service capacity with a joint effort of the hospital staff and patients. The overall benefit will be the improvement of CVD management by modifying factors associated with poor CVD outcome at ED and preventing DREA that will help minimize medication-related morbidity, mortality and additional healthcare expenditure.

2. Literature review

2.1. ED outcome among CVD patients and associated factors

A descriptive cohort research on patients with hypertensive emergency or urgency at a tertiary referral hospital in Tanzania found that the in-hospital death rates for both conditions were 26.8% and 3.1%, respectively. The severity of the illness, existing comorbidities, and the inability to give critically ill patients advanced care owing to a lack of resources are all recognized as contributing causes to mortality in these individuals.(22).

The University of Teaching Hospital (UPTH) in Nigeria undertook a retrospective cross-sectional study to assess the pattern and result of medical emergencies presenting to the facility. This study showed that CVDs are 15.5% prevalent at ED and hypertension-related heart disease (18.1%) was the major contributors for mortality, following HIV-related infections. There is no significant difference in proportion of mortality by gender and age, according to this study(23).

Another retrospective cohort study conducted in New York evaluated weather more ED visits and hospital admissions are related to more fragmented ambulatory care. According to this study, high fragmentation increased the risk of an ED visit by 1.4%, and the supplementary logistic model estimated that high fragmentation increased the risk of an ED visit by 1.4% for every 0.1-point increase in the fragmentation score. These findings were adjusted for age, gender, and the number of chronic conditions. But they discovered no link between the fragmentation score and the risk of hospital admission(24).

According to a cohort study conducted at the Karolinska University Hospital in Solna and Huddinge, Sweden which examined the potential links between ED-measured blood pressure (BP) and acute atherosclerotic cardiovascular disease (ASCVD), myocardial infarction (MI), or stroke over the long term; the ASCVD, MI, and stroke were all related to both systolic and diastolic blood pressure. Systolic blood pressure levels above180 mmHg were associated with a 6-year cumulative incidence of ASCVD of 12% compared to 2% for normal levels, with a progressively higher risk for systolic blood pressure in hypertension grades 1, 2, and 3 (HR, 1.15 [95% CI, 1.06-1.24], 1.35 [95% CI, 1.25-1.47], and 1.63 [95% CI, 1.49-1.77])(25).

N-terminal pro-brain natriuretic peptide (nt-proBnP) and high sensitive troponin t (hs-tnt) serum levels were evaluated in a single-center cohort research to determine their prognostic value for mid-term mortality in patients presenting with symptomatic atrial fibrillation (AF)

to an ED. This study found that the risks for mortality increased with each quartile of NT-proBNP by 1.53 (HR; 95% CI 1.27 to 1.83; p0.001) and with each quintile of hs-TnT by 1.31 (HR; 95% CI 1.10 to 1.55; p=0.002)(26).

In Denmark, between 2005 and 2014, a second countrywide register-based follow-up cohort study was conducted on AF 30-day discharge survivors. During a 1-year follow-up period starting 30 days after release following the patient's initial hospitalization for AF, the study looked at relationships between the socioeconomic position of the patient and a number of outcomes (mortality, re-hospitalization, and others). According to this study, the lowest socioeconomic position is linked to higher 1-year death from all causes and from presumptive cardiovascular disease.(27).

Another prospective cohort study done in Ontario, Canada compared outcomes of HF patients visited an ED between patients who were received hospital admission and patients discharged out of the ED without hospital admission. According to this finding the mortality rate after 7days and 30 days among patients released from the ED without being admitted was 1.3% and 4.0%, respectively; for the hospitalized group, the death rate was 5.7% after 7 days and 12.3% after 30 days. However the 90 day mortality rate was higher for discharged group. Finally they concluded that patients with HF who are discharged from the ED have substantial risks of early death, which, in some cases, may exceed that of hospitalized patients(28).

A retrospective cohort study was performed on AF patients presented to ED of hospitals in China, from Nov 2008 to Oct 2011, to identify the impact of multi-morbidity and poly-pharmacy on clinical outcomes in these patients. According to this study, high and moderate morbidity groups had a significantly increased risk of dying from all causes (HR 2.083, 95%CI 1.482-2.929; HR 1.713, 95%CI 1.198-2.449); and dying from CVD (HR 2.457, 95%CI 1.526-3.954; HR 1.974, 95%CI 1.206-3.232). However, among these outcomes, they could not find any statistically significant data for the poly-pharmacy subcategory(29).

2.2. Prevalence of drug related hospital admission in CVD patients.

According to a prospective, observational study done at the ED of King Abdulaziz Medical City, Riyadh, Saudi Arabia, the prevalence of DRHA was found to be 14.7%. Of these, 9.5% were due to a definite DRP, while 5.2% were due to a possible DRP. ADRs (24.5%), drug overdose (11.3%), and failure to receive prescriptions (47.2%) were the most frequent definite causes of DRHA, as mentioned by this study. Among the identified DRPs in the

definite DRP group, 83.0% were definitely preventable, 3.8% were possibly preventable, and 13.2% were non-preventable(30).

Another cross-sectional observational study on DREA at a tertiary care hospital in India, that sought to quantify the prevalence, severity, preventability, and financial burden of medication-related issues discovered that DREA was present in 2.97% of patients. Sub-therapeutic dose (12%), ADR (10.5%), and non-adherence (71%) were the three categories with the most DRPs according to the study(31).

According to one systematic review done at Gondar University, the average prevalence of DRHA is 15.4%, but ranges from 1.3% to 41.3% and 2.7% of hospitalized patients also died as a result of DRPs. Antithrombotic and antihypertensive medications, both used in patients with CVD, were found to be the drugs that were frequently reported as causing drug-related admissions, followed by other classes of medication. Approximately one-third of DRHA were definitely preventable, and more than 40% were also potentially preventable, according to this review(32).

ADRs leading to hospital admission were found to be 7.8% in older people, and the majority of these ADRs were preventable (91%), according to a study done to determine the prevalence of these events. Furthermore, this study mentioned CV side effects of the CVD medications (falls brought on by the increased antihypertensive drug impact and arrhythmias), as the most common ADRs(33).

A literature review evaluated hospitalizations and ED visits due to DDIs causing adverse drug outcomes and found that 0.054% of ED visits and 0.57% of ED hospitalizations were brought on by DDIs. The authors said "Although the percentages are modest, the number of adverse outcomes due to DDIs is substantial because of the large numbers of ED-visits". According to this review, NSAIDs and CV medications were the substances most frequently found in DDI. GI tract bleeding, hypertension or hypotension, and heart rhythm abnormalities were the most common reasons for hospitalization or ED visits, as mentioned by this review(34).

According to a prospective study conducted to determine the characteristics and cause of admission at ED in decompensated HF patients, poor compliance / inappropriate medication accounts for (43.4%) of ED admission in these patients. Poor compliance/inadequate medication was characterized in the study as noncompliance with water and salt restriction or

the prescribed medication, inadequate use of the drugs (inadequate dose or administration), and usage of substances or drugs that could potentially result in to decompensating (35).

Another observational study was done on ADRs caused by DDIs leading to hospitalization in CVD patients, at a University Clinical Hospital Center. According to this study, hospital admissions caused by ADRs associated to DDIs were common (9.69%), and the majority of these ADRs had an impact on cardiac function (41.07% on heart rate or rhythm), followed by bleeding and an equally distributed influence on blood pressure(17.86%)(16).

According to a cross-sectional study conducted at the Mbarara Regional Referral Hospital, medication-related factors account for four out of every five ED admissions. The most common of these factors is drug therapy that is inefficient (53.3%), which is followed by medication non-adherence (42.9%) and adverse drug reactions (3.8%). According to the study's findings, 27.8% of medication non-adherence was caused by high drug costs and 34.4% by a failure to understand the patient's prescription schedule. 10% are different doctor diagnoses, 8.9% are medication forgetfulness, 8.9% are medication availability issues, and 2.2% are medication refusal (36).

In August 2018, a prospective observational study was conducted in the ED of an apex tertiary care facility to estimate the prevalence of medication-related ED visit, which was found to be 27.1%. According to the findings of this study, failure to receive medications or noncompliance (47.5%), sub-therapeutic dosage (25%), and ADR (16.7%) were the most frequent causes of medication-related visits. Antihypertensive were most frequently implicated (34.1%), followed by oral hypoglycemics (20.8%), and anticonvulsants (15.8%)(37).

2.3. Factors associated with DREA in CVD patients

According to a study conducted to evaluate the prevalence of ADRs leading to hospitalization in elderly patients, Ischemic heart disease (OR = 4.50; 95% CI = 1.36–14.88) followed by depression (OR, 2.49; 95% CI, 1.08–5.77) and HF (OR, 2.08; 95% CI, 1.13–3.81) were the most common patient-related factors predicting ADRs leading to hospitalization. According to this study, patients with four comorbid conditions and poly-pharmacy (taking 6 drugs/day) were also associated with a higher proportion of ADRs (33).

Female gender (AOR = 4.31 [1.43, 13.03 at 95% CI]; P-value = 0.010]) and a history of tobacco use (AOR = 9.58 [1.14, 80.28 at 95% CI]; P–value = 0.037) were found to be the factors associated with DRHA among patients admitted with cardiovascular conditions in a cross-sectional study conducted at the Mbarara Regional Referral Hospital on predictors of medication-related ED admissions among patients with CVD. DRHA occurred around 4.3 times more frequently in female individuals than in male participants. Participants who had previously used tobacco were around 9.5 times more likely than non-users to suffer DRHA, according to this study(36).

Another prospective observational study conducted to recognize the characteristics of patients who are more likely to develop DRP while being treated in a cardiology ward found that poly-Pharmacy (OR=1.228; 95%, CI=1.153–1.308), with a 22% risk increase for each extra drug, female sex (OR=1.496; 95% CI=1.026–2.180), and first admission (OR=1.494; 95% CI=1.005–2.221) were associated with at least 1 DRP in these patients(38).

According to a systematic review on the prevalence of DRHA, which identified CV drugs as the ones most linked to the condition; poly-pharmacy, advanced age, and female sex were mentioned as determinants for DRHA by a number of studies. However, other factors like the presence of multiple co-morbidities, a lower level of education, functional dependence, young age, and male sex were mentioned as factors linked to DRHA in some studies only(32).

In 2013, an analysis of studies from Europe was conducted on the prevalence of DRPs in India. According to this systematic review, the main causes of developing DRPs were poly-pharmacy and older age, with holy physician, non-compliance, and prescription errors as secondary causes(5).

3. Objectives

3.1. General objectives

- ❖ To assess ED admission outcome, drug-related admissions and associated factors among cardiovascular patients at Tikur Anbessa Specialized Hospital from September to December, 2022.

3.2. Specific objective

- To assess the outcome of emergency admission among cardiovascular disease patients
- To identify the risk factors associated with the mortality of cardiovascular disease patients.
- To evaluate the prevalence of drug related emergency admission among cardiovascular disease patients.
- To assess factors associated with drug related emergency admission among cardiovascular disease patients.

4. Methods

4.1. Study setting

TASH was established in 1972 in the capital Addis Ababa, and it is the sole largest-Referral and teaching hospital in Ethiopia. The hospital is structurally under Addis Ababa University, College of Health Science. There are 14 schools under the college, including the school of medicine, school of pharmacy, school of public health science fields. Therefore, it is a teaching-learning and practice-center for all those disciplines. Additionally, practically all regional referral and federal hospitals in Addis Ababa and the surrounding areas are linked to the many schools, clinical services, and training facilities of the college and the hospital. The hospital has 800 beds. According to the management sources, the hospital has 3000 health professionals (169 specialists). Excluding residents, nurses account for the majority followed by physicians. The hospital provides emergency, ambulatory, surgical and different in-patient ward services; like internal medicine, psychiatry, pediatrics, neonatal, surgical, gynecology and obstetrics, cardiology, oncology, and orthopedics. The study was carried out in the emergency department of this hospital. The hospital continues to act as a Center of Excellence for a number of grant-funded initiatives.

4.2. Study design and study period

A prospective observational study was conducted at the ED of TASH, between September, and December, 2022.

4.3. Population

4.3.1. Source population

All adult cardiovascular disease patients attending ED of TASH.

4.3.2. Study population

All adult cardiovascular disease patients admitted at ED of TASH during the study period

4.4. Inclusion and exclusion criteria

4.4.1. Inclusion criteria

- Patients who provided informed consent, (the informed consent was provided by attendants for patients younger than 18 years old and unconscious patients.)

- Patients with at least one CV medications and
- Patients older than 13 years old were included in the study.

4.4.2. Exclusion criteria

- Patients who are < 3 months since diagnosed with CVD

4.5. Sample size determination and sampling technique

All CVD patients who presented to adult ED of TASH between September and December 2022 were included. Patients who met the eligibility criteria and volunteered to participate in this study were enrolled in the study.

4.6. Study variables

4.6.1. Dependent variables

- Emergency admission outcome
- Drug-related admission

4.6.2. Independent variables

- Socio-demographic characteristics
- Disease and medication-related factors: Duration of disease, Type of CVD, Comorbidity, number and type of drugs

4.7. Data collection and management

A data abstraction tool was used to collect data, which was developed by examining researches carried out in various nations(21,29,36) to include all the pertinent information on the patient demographics and clinical data, including chief compliant, past medication history, medical history, current diagnosis, comorbidity, laboratory investigations. Patient's information was obtained by interviewing patients and care givers. Finally, clinical pharmacists collected the data after trained by the investigator on the data abstraction tool. The investigator had been giving continuous follow-up and support to ensure the quality and accuracy of data collection.

4.8. Data analysis

SPSS version 25 was utilized to perform the data analysis. Descriptive statistics was used to summarize study participants' socio-demographic and clinical variables. The outcome of ED

admission in CVD patients, and the prevalence of DREA were calculated using percentage. Cox regression analysis was done to determine factors associated with ED survival time, which was then expressed in hazard ration. The logistic regression analysis is used to determine factors associated with DREA using a p-value of less than 0.05% significance level and adjusted odds ratio to assess the strength of associations between the variables. Variables with a P-value of less than 0.25 are used in multivariate regression analysis for both cox and logistic regression.

4.9. Ethical approval

The research was conducted upon receipt of complete ethical permission from the Institutional Review Board (IRB) of Addis Ababa University's School of Pharmacy. Then the IRB letter was shared with TASH's ED directors. Furthermore, informed consent was given by each study participant before they were enrolled.

4.10. Operational definition

Drug-related hospital admission (DRHA): a hospital admission is considered as drug-related when the presentation is unequivocally related to the presenting chief concern and /or physicians findings or laboratory results that can be categorized under one of the seven predefined categories of drug therapy problems (non-adherence, Adverse drug reaction, needing additional drug therapy, supra therapeutic dosage, sub-therapeutic dosage, ineffective medications and unnecessary medications*)*

The WHO's definition was used for ADRs and all other terms were defined using the Hepler and Strand Classification(39–41).

ADR*:* Included all reactions to drugs administered at appropriate dosages, and those associated with abnormal laboratory values.

Supra-Therapeutic Dosage*:* Any noxious, unintended, or undesirable effect caused by excessive drug dose or duration for a given indication.

Ineffective Medication: Any noxious, unintended, or undesirable effect caused by the administration of ineffective medicine.

Sub-Therapeutic Dosage: Any noxious, unintended, or undesirable effect caused by failure to receive sufficient drug dosage or duration for a given indication.

Inappropriate Medication: Any noxious, unintended, or undesirable effect due to the use of the drug not optimal in the treatment of a confirmed indication.

Untreated Indication*:* Any noxious, unintended, or undesirable effect resulting from the failure to treat a known indication.

Medication Non-Adherence: Any noxious, unintended, or undesirable effect caused by failing to receive a drug as prescribed by health care providers.

Adult; starting from the age of 13 years, as TASH's adult emergency accepts patients aged > 13 years

Outcome; deceased, survived

5. Result

5.1. Socio-demographic Characteristics of the Study Participants

In this study a total of 401 patients were included. More than half (51.1%) of the participants in the study were male with a mean age of 49 years (SD: ± 19 years) and 8.7% of the participants were younger than 18 years old. Two-thirds of the participants were married, and 22.7% of the study participants don't have formal education. Almost three fourth of the study participants reside in urban area and 83% had monthly income of 4000ETB and above, with a mean of 6759 (SD: ± 3087 ETB). Table1 shows the socio-demographic characteristics of the participants. Regarding to the substance use history of the participant, 14.5% of them were smokers and 41.1% had alcohol use history as shown in Fig.1

Table1; the socio-demographic characteristics of adult CVD patients admitted in TASH.

Variable	Category	Freq.	Percent
Sex	Male	205	51.1
	Female	196	48.9
Age	14 to 24	53	13.2
	25 to 39	72	18.0
	40 to 64	177	44.1
	> 65	99	24.7
Education level	No formal education	91	22.7
	Primary	175	43.6
	Secondary	113	28.2
	College and above	22	5.5
Marital status	Single	72	18.0
	Married	263	65.6
	Divorced/widowed	66	16.5
Residency	Urban	287	71.6
	Rural	114	28.4
Monthly income	1000-1500	10	2.5
	2000-2500	27	6.7
	3000-3500	31	7.7
	≥ 4000	333	83.0

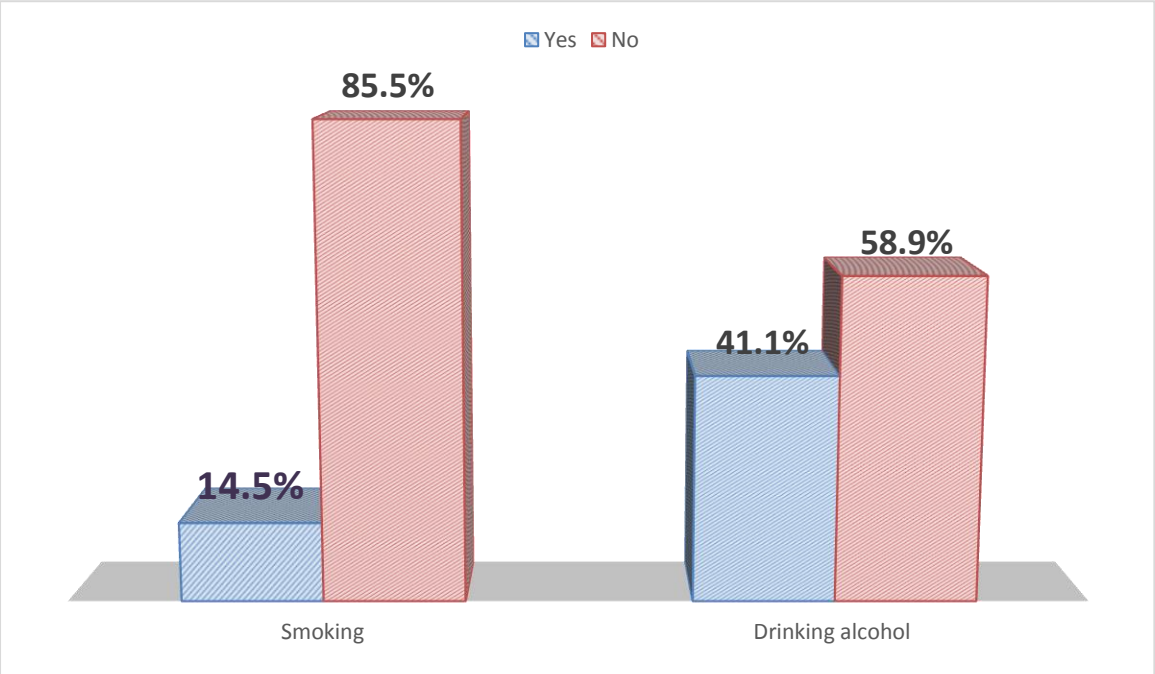

Figure 1. Substance usage characteristics of the study participants

5.2. Clinical Characteristics of the Study Participants

5.2.1. Past medical history

Hypertension was found to be the most common initial diagnosis (47.4%) followed by CRVHD (22.2%) and CHF (10%) when we referred the past medical history of the participants. CVDs were classified it two major groups as primary vascular and primary cardiac looking at the previous diagnosis, and participants are equally distributed into the two groups as shown in Fig. 2 and Fig.3 below.

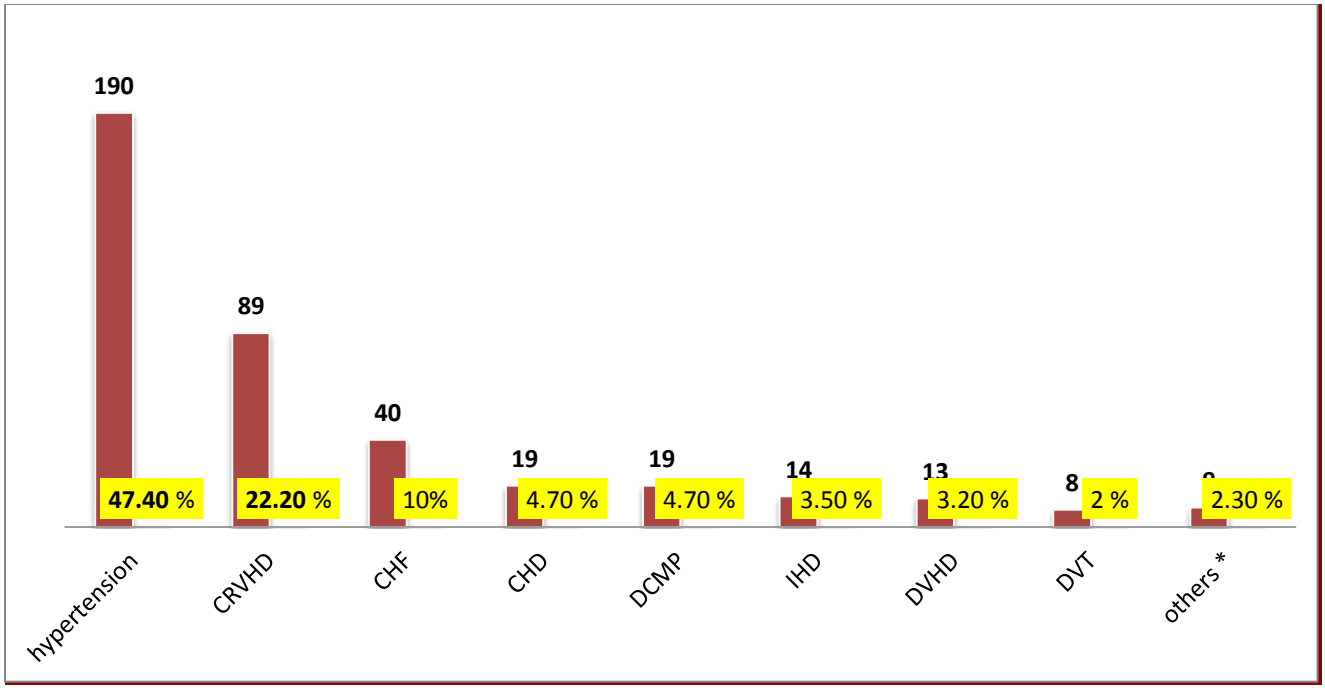

Figure 2: The distribution of cardiac disease among the study participants

*** Aortic aneurism, post TB pericarditis, coarctation of aorta, arrhythmia**

Abbreviations; CRVHD: chronic rheumatic valvular heart disease, CHF: chronic heart failure, CHD: congenital heart disease, DCMP: decompensated cardiomyopathy, IHD: ischemic heart disease, DVHD: degenerative valvular heart disease, DVT: deep vein thrombosis.

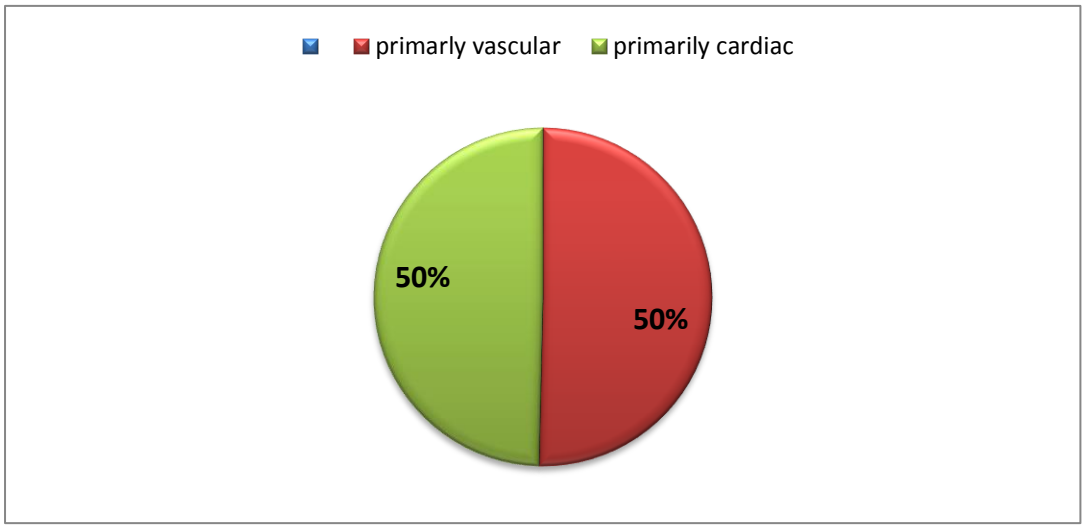

Figure 3: previous diagnosis category of the participants.

5.2.2. The current diagnosis

Majority of the study participants were admitted to ED with a diagnosis of CHF/ADHF (37.4%) followed by hypertension (26.2%), and AKI/CKD (15.5%), AF (9.5%). Table 2 shows the distribution of ED admission diagnosis of the participants.

Table 2; participants' admission diagnosis

Diagnosis of the study participant at admission (n=401)	**Frequency**	**percent**
CHF/ADHF	150	37.4
HTN	105	26.2
AKI/CKD	62	15.5
Atrial fibrillation	38	9.5
Stroke	29	7.2
CRVHD (complicated)	14	3.5
DVT	10	2.5
cardiogenic shock	9	2.2
MI/IHD	8	2.0
others*	11	2.7

***** VSD, PSVT, ACS, warfarin over coagulation, chronic subdural hematoma

Abbreviations; ACS: acute coronary syndrome, ADHF: acute decompensated heart failure, AKI: acute kidney injury, CHF: chronic heart failure, CKD: chronic kidney disease, CRVHD: chronic rheumatic valvular heart disease, DVT: deep vein thrombosis, HTN: hypertension, IHD: ischemic heart disease, MI: myocardial infarction, PSVT: paroxysmal supraventricular tachycardia, VSD: ventricular septal defect.

Looking at the past medical history of study participants, most of patients admitted with the diagnosis of CHF/ADHF were initially diagnosed with other CVDs as shown in Table 3 below.

Table 3; past medical history of patients admitted with CHF/ADHF

Past medical history (n=401)			**Currently diagnosed with CHF/ADHF (n=150)**	
Diagnosis	Frequency	Percent	Frequency	percent
Hypertension	190	47.3	23	15.3
CRVHD	89	22.2	48	32
CHF	40	10	26	17.3
DCMP	19	4.74	12	8
CHD	19	4.74	15	10
IHD	14	3.5	10	6.7
DVHD	13	3.24	10	6.7
Others*	17	4	6	4.0

* Aortic aneurysm, post TB pericarditis, coarctation of aorta, DVT

5.2.3. Comorbidities

During current admission majority of the participants had a comorbid disease (60%), and only 16 patients (4%) admitted with 2 comorbidities while the rest had no any comorbidity. From the identified comorbidities DM took the first place with a frequency of 84 patients (20.9%) followed by infectious disease (14.5%), and cancer (5.2%), as shown the table 4. below.

Table 4; participants' comorbidities during admission

Comorbidities	**Frequency**	**Percent**
DM	84	20.9
Infectious disease	58	14.5
Cancer	21	5.2
Hepatic disease	13	3.2
Electrolyte disturbance	13	3.2
Asthma	12	3
Gastro intestinal illness	10	2.5
TB	10	2.5
RVI	7	1.7
Epilepsy	5	1.2
Others*	10	2.4

* BPH, thrombosis, autoimmune diseases

Abbreviations; BPH, benign prostate hyperplasia, DM: diabetes mellitus, RVI: retroviral infections, TB: tuberculosis

5.2.4. Chief Compliant of the Patient during ED Admission

Most of the participants visited the ED during the study period with the compliant of shortness of breath (SOB) (33.9%) with or without other compliant, followed by easy fatigability (14.2%), generalized body swelling (GBS) and cough (13.5%), (13%), respectively. Fig. 4 below shows the chief compliant of the participants.

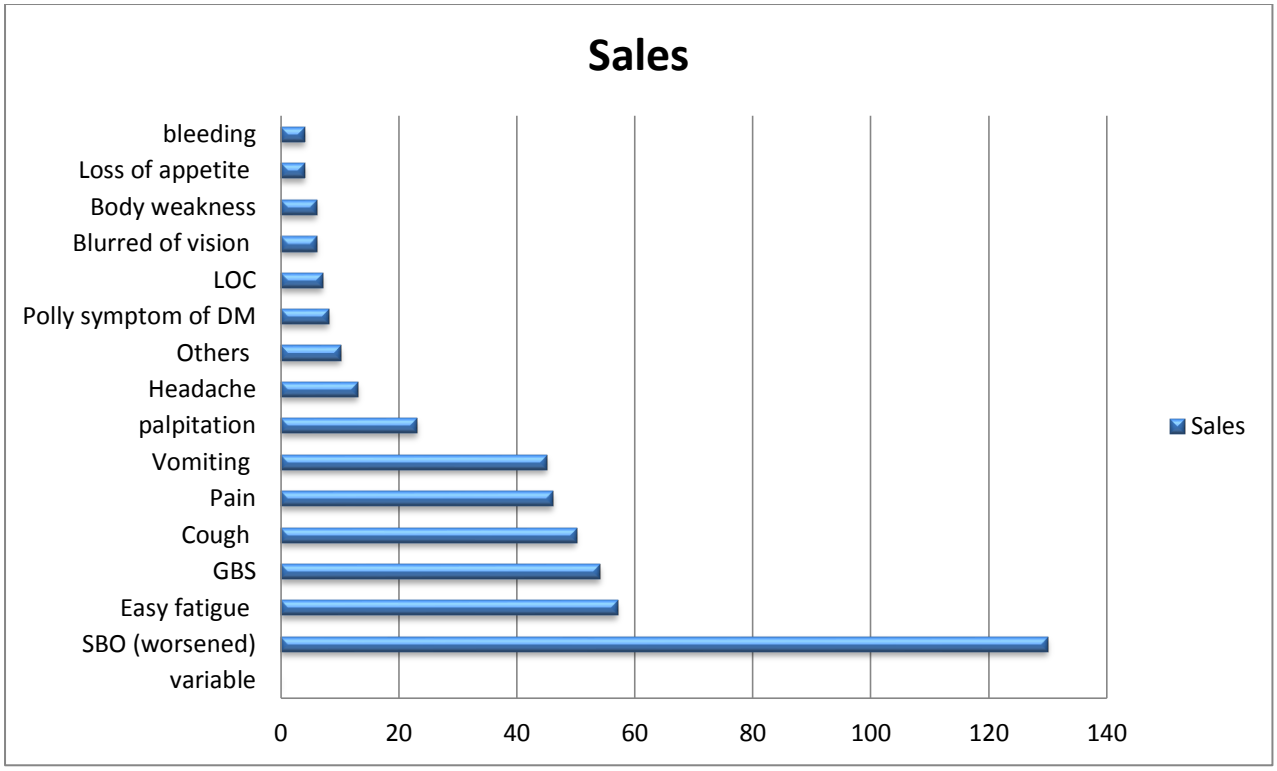

Figure 4: chief complaints of participants during admission.

5.2.5. Medication Characteristics of the Study Participants

5.2.5.1. past medication history

The number of medications patients were taking before current admission ranged from 1 drug to 10 drugs, with a median of 2 drugs (IQR 2-4) and most of the patients had been taking 2 drugs (26.4%), while 8.5 % of the participants were taking unspecified medication. Table 5 below shows the number of drugs patients were taking before current admission.

Table 5: number of participants past medications

Number of medication (n=401)	**Frequency**	**Percent**
Unspecified	34	8.5
1 drug	80	20
2 drugs	106	26.4
3 drugs	74	18.4
4 drugs	59	14.7
5 or more	48	12

5.2.5.2. Medication during ED admission

During the current admission all participants took at least 1 medication and ranging up to a maximum of 11 drugs. The median was 4 (IQR; 3-5). Fig. 5 shows number of medication patients had been taking during ED stay.

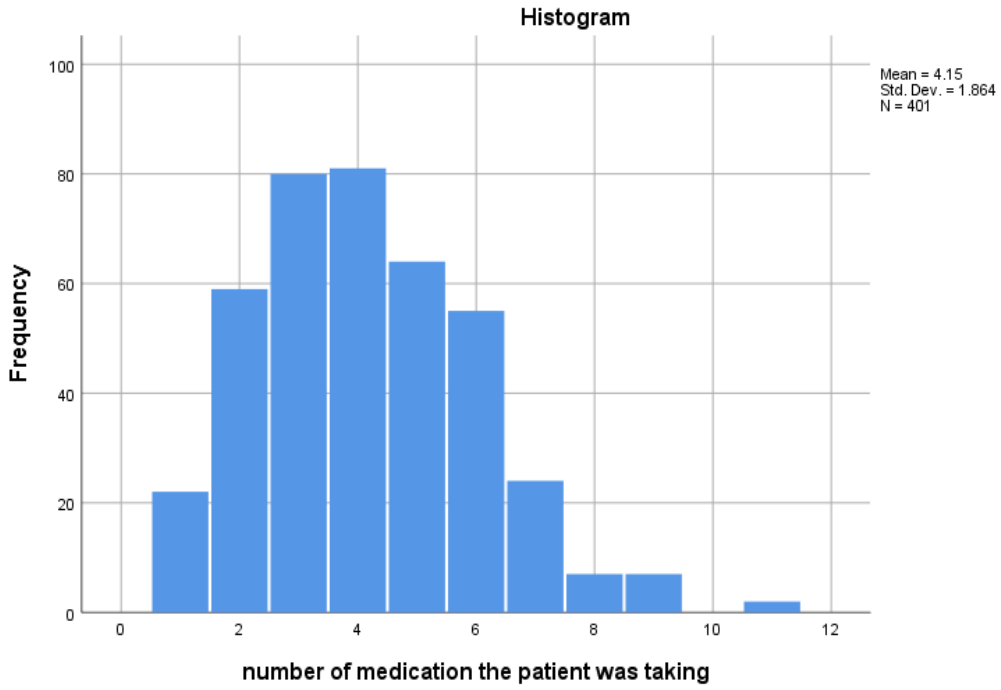

Figure 5; number of medications patients took during ED admission

Regarding to class of medication they received, majority of the study participant took diuretics (70%), followed by BB (36%) and CCB (29.4%). Further coming to specific drug, furosemide was taken by 252 participants (63.3%) followed by spironolactone (27.7%), amlodipine (24%), metoprolol and enalapril (22.6% each), digoxin (20%), and atorvastatin (18%) as shown in the table 6 below.

Table 6: The study participants' medication characteristics of after admission

Medication class	Specific drug	Frequency	Percent
Diuretics	Furosemide	252	**63.3**
	Spironolactone	111	**27.7**
	Hydrochlorothiazide	38	9.5
ACEIs or ARBs	Enalapril	91	**22.6**
	Losartan	12	3.0
	Valsartan	4	1.0
	Candesartan	2	0.5
BBs	Metoprolol	91	**22.6**
	Atenolol	14	3.5
	Propranolol	12	3.0
	Carvedilol	12	3.0
	Labetalol	11	2.7
	Bisoprolol	8	2.0
CCBs	Amlodipine	96	**24**
	Nifedipine	22	5.5
Cardiac glycoside	Digoxin	80	**20.0**
Statins	Atorvastatin	72	**18**
Anti-platelets	Aspirin	53	13.2
	Clopidogrel	7	1.7
Anticoagulants	Warfarin	41	10.2
	Unfractionated Heparin	16	4.0
Penicillin	Benzathine Penicillin	50	**12.5**
Others *		12	3

* Methyldopa, Noradrenaline, Hydralazine, Adenosine

Abbreviations; ACEIs: angiotensin converting enzyme inhibitors, ARBs: angiotensin II receptor blockers, BB: beta blockers, CCB: calcium channel blockers

5.3. Length of ED stay and duration of CVD

The median length of ED stay for study participants was 5 days (IQR: 4-6), with the minimum and maximum days of 1 and 13 days respectively. The median duration of CVD was 4 years (IQR: 2-6 years), with a minimum of 3 months and maximum of 30 years. Majority of the participants have 1to 5 years duration of CVD. Table 7 shows the LOS in ED and CVD duration categorized by frequency.

Table 7: length of ED stay and duration of CVD for patients admitted at ED of TASH

Variables	Categories	Frequency	Percent
LOS	1-3 days	95	23.7
	4- 8 days	272	67.8
	≥ 9 days	34	8.5
Duration of CVD	< 1 year	98	24.4
	1 to 5 years	175	43.6
	6 to 10 years	85	21.2
	>10 years	43	10.7

LOS; length of stay

5.4. Outcome of Emergency Admission

9.5% (n=38) of CVD patients who were admitted to ED during the study period had died (figure 6). Of this, 23.7% (n=9) is secondary to DRP. ADHF accounted for 50% of deaths, followed by hypertension (23.7%), and atrial fibrillation (18.4) as shown in figure 7. Table 8 demonstrates the ED admission diagnosis with respect to the outcomes.

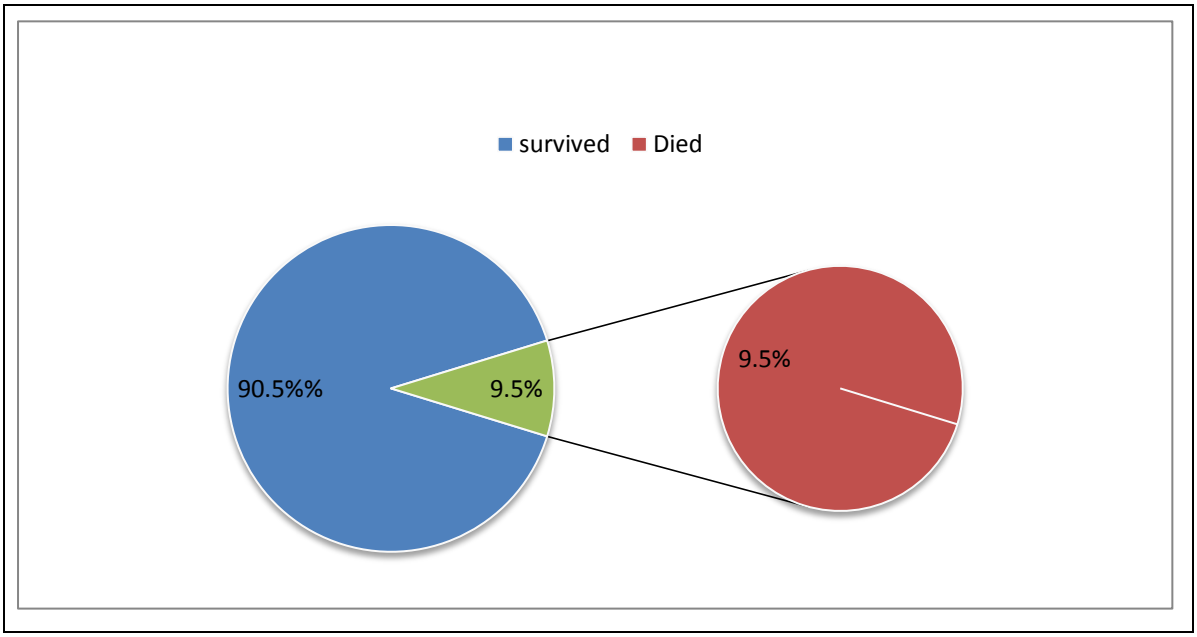

Figure 6; outcome of emergency admission.

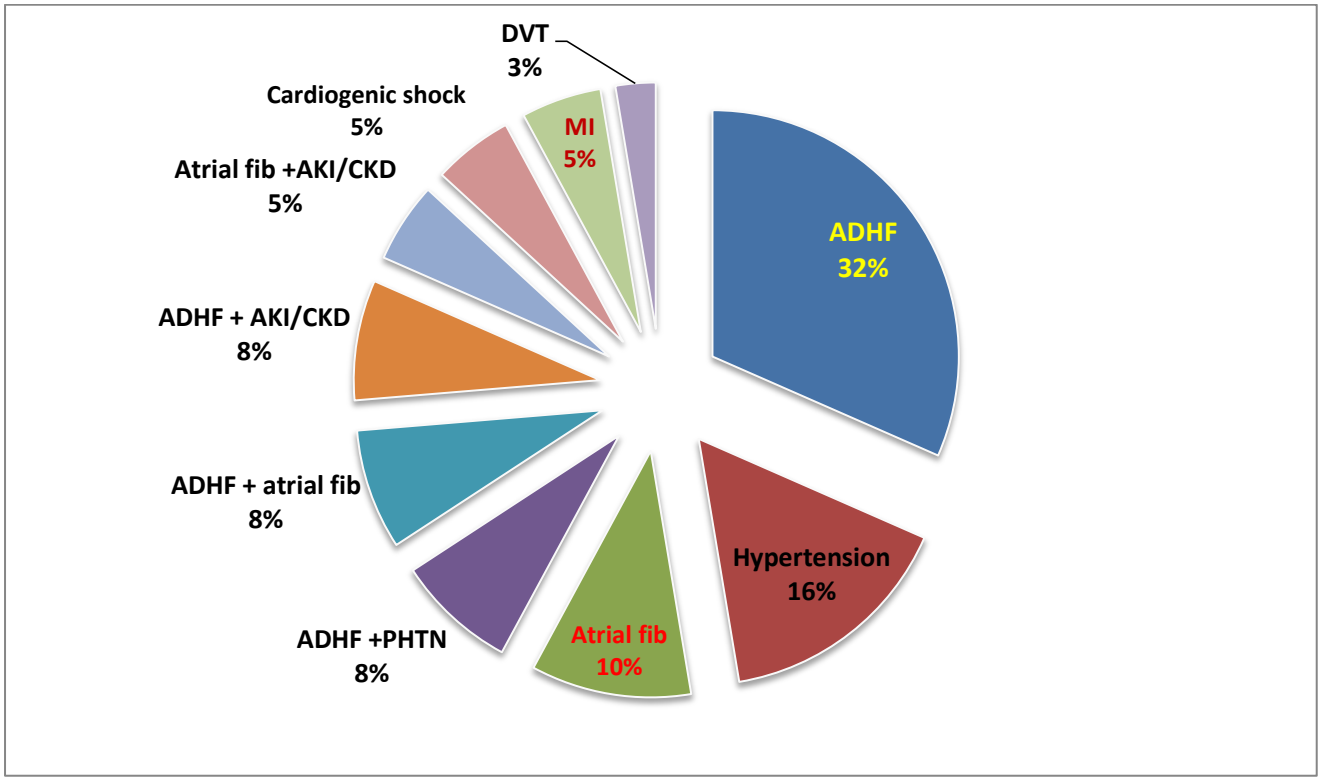

Figure 7; diagnosis distribution of died participants

Table 8; ED admission diagnosis with respect to ED admission outcome.

Outcome of ED admission	ADHF	HTN	AF	MI	CS	DVT	CRVHD	AKI	stroke	Others
Died(n=38)	19	9	7	2	2	1	0	5	0	0
survived	131	96	31	9	7	9	11	57	26	10

CS: cardiogenic shock

* NB; some patients admitted with more than one diagnosis.

5.4.1. Predictors of poor outcome of CVD patients during ED admission

Variables with p-value < 0.25 in the bivariate cox regression analysis were transformed into multivariate cox regression analysis. Marital status, rural residency, smoking history, primarily cardiac disease, having DCMP and IHD as initial diagnosis, comorbid GI illnesses, poly-pharmacy, and admission diagnosis of ADHF/CHF and AF were associated with higher risk of early death in bivariate cox-regression analysis. In the multivariate cox regression; smoking history (AHR=3.71, 95% CI= [1.54, 8.936], P-value =0.002), DCMP (AHR =8.26, 95% CI= [2.43, 28.04], p-value =0.001), GI comorbidity (AHR=8.567, 95% CI= [2.09, 35.123], p-value =0.003), atrial fibrillation (AHR =3.50, 95% CI= [1.32, 9.28], p-value =0.012) , and poly-pharmacy (AHR=2.68, 95% CI= [1.11, 6.46], p-value =0.028) showed strong association with ED survival time (Table 9).

Table 9: bivariate and multivariate COX regression analysis

Variables	Categories	Patients N (%)	Events		Crude HR (95% CI)	Adjusted HR (95% CI)	P value
			N	%			
Marital status	Single	72 (17.9)	8	2.0	0.70(0.28, 1.72)	1.69(0.51, 5.61)	0.38
	Married	263 (65.5)	18	4.5	0.36(0.17, 0.77)	1.11(0.44, 2.817)	0. 812
	D/W	66 (16.4)	12	3.0	1	1	1
Residency	Urban	287 (71.6)	23	5.73	1	1	0.291
	Rural	114 (28.3)	15	3.74	1.93(1.001, 3.72)	1.525 (0.69, 3.339)	
Smoking history	Yes	58 (14.5)	13	3.2	3.57(1.81, 7.05)	3.717 (1.54, 8.936)	**0.002***
	No	343 (85.5)	25	6.2	1		
Previous diagnosis	vascular	202 (50.4)	12	3.0	1	1	0.062
	cardiac	199 (49.6)	26	6.5	2.58(1.30, 5.13)	0.24 (0.05, 1.14)	
DCMP (PD)	Yes	19 (4.7)	6	1.5	6.79(2.79, 16.52)	8.26 (2.43, 28.04)	**0.001***
	No	382 (95.3)	32	8.0		1	
IHD (PD)	Yes	14 (3.5)	4	1.0	3.50 (1.23, 9.95)	1.06 (0.23, 4.85)	0.944
	No	387 (96.5)	34	8.5	1	1	
Hypertension (PD)	Yes	190 (47.4)	8	2.0	0.24 (0.11, 0.52)	0.25 (0.06, 0.99)	**0.050***
	No	211 (52.6)	30	7.5	1	1	
GI illness (comorbidity)	Yes	11 (2.74)	4	1.0	6.47(2.27, 18.42)	8.56 (2.09, 35.12)	**0.003***
	No	390 (97.2)	34	8.5	1	1	
ADHF (AD)	Yes	150 (37.4)	19	4.74	1.65 (0.87, 3.14)	2.03 (0.87, 4.75)	0.100
	No	251 (62.6)	19	4.74	1	1	
AF (AD)	Yes	38 (9.5)	7	1.74	2.82 (1.23, 6.49)	3.50 (1.32, 9.28)	**0.012***
	No	363 (90.5)	31	7.73	1	1	
No of PM (n=367)	<5	319 (86.9)	27	7.3	1	1	**0.028***
	≥ 5	48(13.1)	10	2.7	2.26 (1.08, 4.73)	2.68 (1.11, 6.46)	

AD; admission diagnosis, D/W; Divorced/ widowed, PD; previous diagnosis; PM; past medication

5.5. Prevalence of DREA

A total of 125 DRPs were found in 92 participants with 1.36 DRPs per patient identified in this study and the prevalence of DREA is found to be 23% as shown in the Fig. 8 below. From this drug-related admission, 9.8 % patients (n= 9) have died.

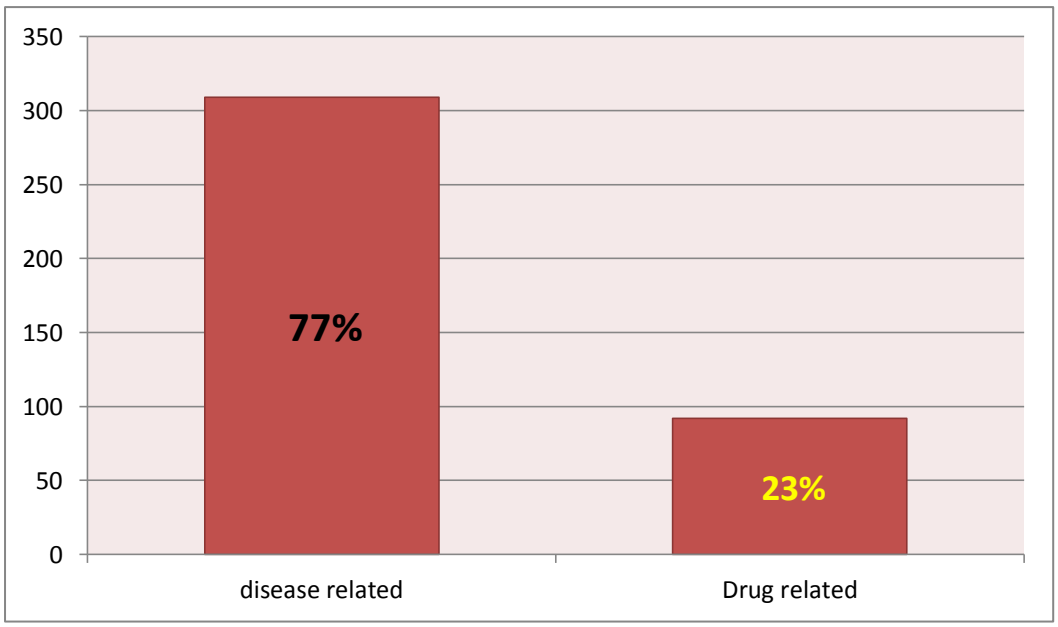

Figure 8; The specific reason of ED admission of the study participants.

5.5.1 Characteristics of DRPs

Of the identified DRPs, 73 (58.4% percent) were ascribed to non-adherence, 16 (12.8%) patients had ADR and from those reaction 5(31.2%) were hyperkalemia. DDI identified by physician in seven patients (5.6%) and 10(8.0%) improper drug selection was found. Inappropriate indication found in 10 patients (8.0%) and Nine (7.2%) in appropriate dose of medication (fig. 10). Most patients with non-adherence discontinued all of the medications they were taking (25), followed by patients discontinued Benzathine Penicillin (10), and metoprolol (8). 80.4% of patients admitted for drug-related reason received intervention by physbicians; with the majority of those interventions resuming their medication (75.7%), as the major problem was non-adherence.

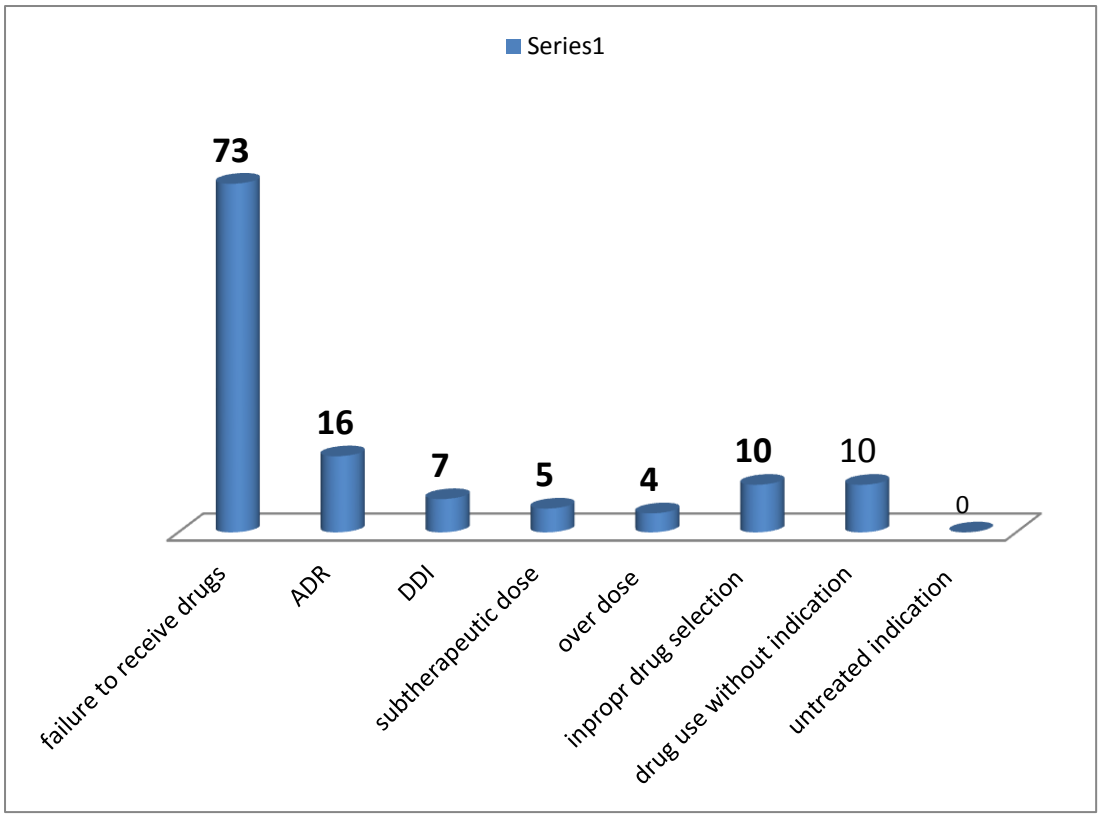

Figure 9; types of DRPs identified

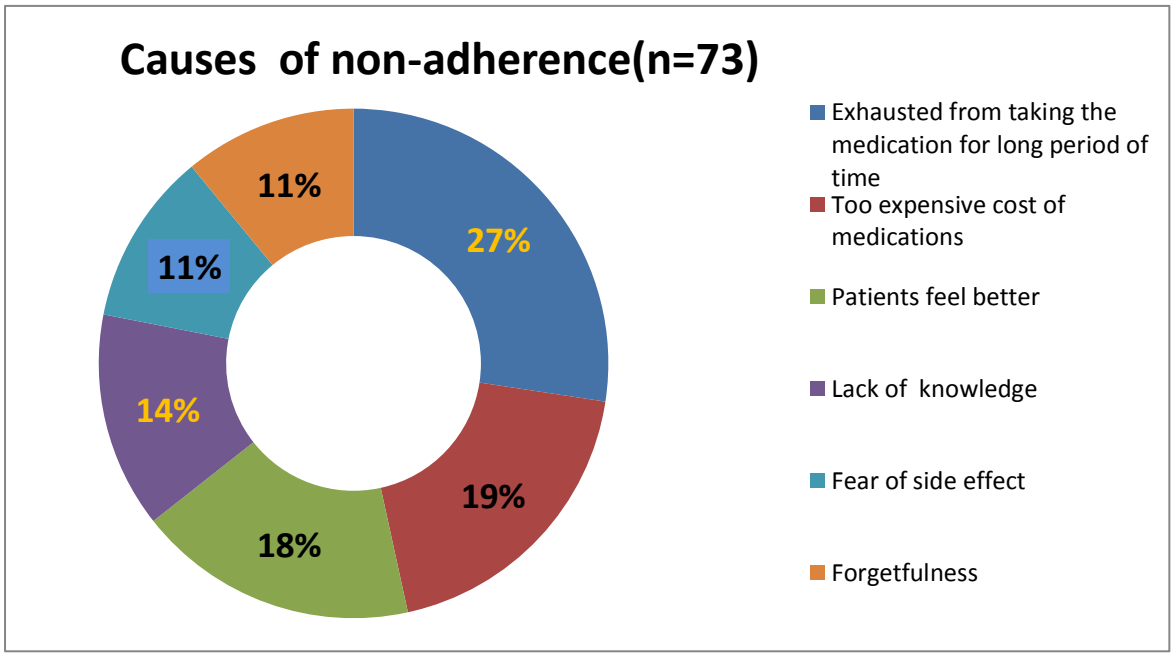

Figure 10; causes of non-adherence

5.4.2. The Determinant Factors Affecting DREA

The bivariate logistic regression analysis showed that age, education level, marital status, monthly income, smoking history, duration of CVD,TB comorbidity, electrolyte disturbance, and poly-pharmacy had an association with DREA(p-value<0,25), hence were included in multivariate logistic regression analysis. Some continuous variables (monthly income) were re-categorized for the purpose of regression analysis. **Marital status, duration of CVD, smoking history, and poly- pharmacy had significant association with DREA (p-value < 0.05).** Smokers have 2 odds of increased risk for DREA than non-smokers (AOR=2.47, 95%CI= [1.07, 5.70] **p-value =** 0.034) and patients who take poly-pharmacy have 8 odds of increase in DREA (AOR=8.54, 95%CI= [3.73, 19.53], p-value=0.000) [table 12].

Table 10: factors associated with DREA using bivariate and multivariate regression.

Variable	Categories	ED admission		P-value	COR with 95% CI	P-value	AOR with 95% CI
		DREA	non-DREA				
Education level	no formal edc	20	71	0.166	0.49 (0.18, 1.34)	0.156	0.38 (0.10, 1.44)
	Primary	41	134	0.191	0.54(0.21, 1.37)	0.206	0.48 (0.15, 1.51)
	Secondary	23	90	0.108	0.91(0.46, 1.78)	0.100	0.34 (0.09, 1.23)
	College +	8	14	1	1	1	1
Marital status	Single	12	60	0.010	0.35 (0.16, 0.78)	**0.000**	0.02 (0.003,0.14)
	Married	56	207	0.012	0.47 (0.27, 0.85)	**0.001**	0.25 (0.11, 0.56)
	divorced/widow	24	42	1	1		1
Smoking history	Yes	24	34	0.000	2.85 (1.59, 5.13)	**0.034**	2.47 (1.07, 5.70)
	No	68	275	1		1	
Monthly Income	1000-2500	13	24	1	1	1	1
	3000-4500	17	53	0.237	0.59 (0.25, 1.41)	0.756	0.84(0.28 ,2.49)
	5000-7000	21	105	0.017	0.37 (0.16, 0.84)	0.195	0.50(0.17, 1.43)
	≥ 8000	32	103	0.164	0.57(0.26, 1.16)	0.396	0.63 (0.22, 1.83)
Duration of CVD	< 1 year	1	9	0.019	0.39(0.18, 0.86)	0.190	0.51 (0.18, 1.4)
	1 to 5 years	12	15	0.005	0.36(0.17, 0.73)	**0.009**	0.28(0.10, 0.72)
	6 to 10 years	7	24	0.115	0.53(0.24, 1.66)	0.183	0.50 (0.18, 1.39)
	> 10 years	72	261	1		1	
TB (comorbidity)	Yes	4	6	0.206	2.30(0.63, 8.32)	0.293	2.44(0.46, 12.86)
	No	88	303	1	1	1	
electrolyte disturbanc	Yes	8	5	0.003	5.8(1.85, 18.2)	0.026	4.85(1.21. 19.44)
	No	84	304	1	1	1	1
No of past medication	< 5 drugs	43	217	1			
	≥ 5 drugs	39	68	0.34	2.89(1.74, 4.83)	**0.000**	8.54 (3.73, 19.5)

6. Discussion

The ED mortality rate of CVD patients was 9.5% and most of the deaths (50%) occurred in ADHF patients in this study. This mortality rate is similar with a study conducted on ADHF patients in Brazil (10%)(35), however, it is lower than a study done in our country at St. Paul hospital, (24.3%) which might be due to the difference in distribution of CVD types in the participants and the study setting, the St. Paul's study included CVD patients admitted to ICU and medical ward of the hospital(42).

Smoking history, which is a risk factor for developing CVDs, also has impact on mortality survival time in these patients in this study (AHR=3.71, 95% CI= [1.54, 8.936], P-value =0.002), as identified by the cox regression analysis. This is supported by some other studies, of which one is cohort study conducted on middle aged males, which compared different lifestyle characteristics over 61 years, and never smoking has a protective effect on coronary heart disease induced mortality (HR=0.73) and heart disease of uncertain etiology induced mortality (HR=0.57)(43). Additionally, a 30-year cohort study on Thai population support this result in that they found a HR=1.32 and HR=1.70, in ex-smokers and current smokers respectively(44).

GI illness is the only comorbid disease factor affecting CVD outcome and survival time in the current study (AHR=8.567, 95% CI= [2.09, 35.123], p-value =0.003). This finding is comparable with the Osaka cohort study, which indicated that constipation is associated with mortality in CVD patients, and one systematic review which showed that inflammatory bowel disease (IBD), ulcerative colitis, and Crohn disease have greater risk of poor CVD outcomes (45,46).

In the current study, DCMP was the type of initial CVD diagnosis that predict survival time in ED. Participants diagnosed with DCMP as their fist CVD diagnosis had higher probability of early death within ED (AHR =8.26, 95% CI= [2.43, 28.04], p-value =0.001), compared to others. In addition, having an admission diagnosis of AF was a predictor of ED survival time (AHR =3.50, 95% CI= [1.32, 9.28], p-value =0.012). However, there is no literature which compared the type of diagnosis with outcome and survival time of CVD patients.

Poly-pharmacy, in the past medication history is another factor predicting the ED survival time of CVD patients according to current study (AHR=2.68, 95% CI= [1.11, 6.46], p-value =0.028). This is proportional with the systematic review and meta-analysis done to evaluate

the effect of poly-pharmacy on the outcome of AF patients, and concluded that it is associated with poor outcome in these patients (47). However it opposed the study done on HFpEF patients which did not found any association between poly-pharmacy and mortality in this patients(48). This difference might come from the difference in the study population; our study included all CVD patients.

In this study sex did not showed any association with survival time in CVD patients which is similar with the UPTH study, which didn't show significant difference in outcome by gender difference (23) and incompatible with the study done in Ontario Canada, which mentioned being male is predictor of mortality. This dissimilarity could be due to difference in study population as the Ontario study relied on HF patients only, which has worsened outcome in male (28).

Socio-economic status also had no significant effect on the ED survival time in this study as opposed with the study on AF patients, which found poor outcome in patients with low socio-economic status(27). The study followed patients after they are discharged from ED, which could be the reason for this difference. Furthermore Age of participants, number of comorbidity, number of current medication, duration of CVD and organ impairment, also did not affect the survival time rate in this study.

The current study found the prevalence of DREA to be 23% in CVD patients, which is comparable with the apex tertiary care facility's study (27.1%) (37). It is higher than the average prevalence of a systematic review conducted at Gondar (15.4%), besides, it is within the range of the prevalence identified in this review (1.3%–41.3%) (32). This prevalence is also higher than the study of King Abdul-Aziz Medical City, Riyadh, Saudi Arabia (14.7 percent) and the Indian study (2.97%)(30,31), and this disparity might be due to the differences in socioeconomic status, patients' medication and disease knowledge, and also due to the difference in the study population. However, it is lower than the Mbarara study, which identified four drug-related admissions out of five ED admissions(36).

Non-adherence was the major DRP identified in this study; among the 126 DRPs 58% is accounted for non-adherence. This is comparable with the apex tertiary care facility's study (47.5%)(37). Moreover, non-adherence caused 73.9% of DREA and 18.2% of the overall admission in our setting. This is comparable with a study conducted in India(71%)(49), and higher than most of studies in this literature(33,35). Besides, it is lower than the St. Paul study, in which drug discontinuation was responsible for 25.5% of admission in CVD

patients(42). The lack of adherence was caused by exhaustion from taking the drugs for an extended period of time, as mentioned by majority of the participants with none-adherence (27%), while others discontinued the drugs because they feel better (18%) and not understanding the regimen well, as it was complicated (14%).

These are an indicator that in our country, patients are not being provided with sufficient information about their disease and medications. This was resulted from HCP's insufficient communication and informational support with their patients; they do not tell them CVD prescriptions are to be taken for significant stretch of time and that they have to be completely adhere to their medicine. In this instance pharmacists are mostly to blame for the issue as, in most cases; they act more like drug sellers than pharmaceutical care professionals and do not offer enough counseling prior to filling prescriptions. Furthermore, 19% of the non-adherence occurred due to financial problem, as some of the CVD medications are expensive and not available in government sector.

ADR was accounted for 12.8% of the DRPs in our study, which was almost similar with the Indian study(10.5%) and higher than the cross-sectional study at the Mbarara Regional Referral Hospital (3.8%) (31,36) however lower than the observational study in the ED of an apex tertiary care center (16.7%) (37). Additionally DDI took 5.6% of the DRP and which was comparable with the Indian study (2.9%), and lower that a study done in Spain (22.1%). This variation could be due to the fact that they include both drug-drug and drug-food interactions.

Divorced/widowed marital status was associated with more DREA in the present study. Single and married participants had lower risk of admission caused by DRPs (AOR=0.02, 95%CI= [0.003, 0.14], p-value= 0.000), and (AOR=0.25, 95%CI= [0.11, 0.56] p-value= 0.001), respectively. This could be explained by the fact that lack of psychological support from spouse or family has impact on medication use pattern, which could result in frequent drug discontinuation. Unfortunately, literatures compared the effect of separation and divorce on the health outcome, did not mentioned their effect on DRPs.

Poly-pharmacy (AOR=8.54, 95% CI= [3.73, 19.5], p-value= 0.00) had significant association with DREA in current study, which is the case in most of the literatures (5,32,33,38). The rationale for poly-pharmacy to cause DRP is that, risk of ADRs and DDI increase as number of pills increase, and patients become non-adherent to the medication for

different reason, of which one is difficulty to remember every regimen, and the other is fear of a number of side effects from different class of medication.

Similarly, smoking history, which was the other predictor of DREA in current study [AOR=2.47, 95% CI= (1.74, 8.95), p-value= 0.001], was also mentioned in the Mbarara study, however the OR for smoking was higher in their study (AOR = 9.58 [1.14, 80.28 at 95% CI]; P–value = 0.037)(32). Not only ingredients in the tobacco interact with the medication reduce the effect of the drug, also addicted patients might be less attentive of other basic needs like their health conditions, and they might spent their money on the substance they are using, which altogether increase the risk of admission due to DRPs.

Coming to duration of CVD, patient lived with CVD between 1 and 5 years experienced lower risk of DREAs compared to patients lived with the disease for more than 10 years (AOR=0.28, 95%CI= [0.10, 0.72], p-value=0.009**).** This suggests that patients with shorter treatment durations—less than a year—experience higher DRP because they are less familiar with their regimen, while those with longer durations—more than five years—may become careless about their sickness as they survived the condition for a longer period of time, they became less attentive. Finally there was no significant association between DREA and age, gender, educational status number of comorbidities, type of medication, and type of CVD.

7. Strength and limitation

7.1. Strength

This is a prospective observational study, in which the data is extracted directly from participants and charts, with lower rate of missed data and due to the fact that this methodology enables data gathering in a real-world scenario, the results have greater external validity. The other strength of this study is it evaluated the overall CVD mortality in ED, and the mortality and morbidity caused by DRP and factors affecting them, so that it could be a base for HCP in order to prevent or minimize these problems, by providing adequate health care services for the patients.

7.2. Limitation

As this study focused only on survival and death while patients are within ED for the sake of time, further study which follows patients' outcome after they are transferred to other wards is needed to generalize the overall outcome of CVD patients came to hospital with emergency cases. Additionally, in our study there was no pharmacists' intervention on identified DTPs, which should be included in further studies.

8. Conclusion and Recommendation

8.1. Conclusion

CVD mortality rate was as big as 9.5% and, there was no survival time difference in patients admitted with DRPs and non DRPs. Smoking history, GI comorbidity, initial diagnosis of DCMP, admission diagnosis of AF and poly-pharmacy increased the risk of early death in these patients. Additionally, the prevalence of DRP in CVD patients was 23%, and smoking history, marital status and poly-pharmacy were associated with higher occurrence of DRPs in CVD patients. As a result, smoking history and poly pharmacy found to be the common risk for both mortality and DRPs in CVD patients.

Furthermore, 79.3% of the DREA were due to non-adherence, which indicates that there is lack of provision of enough patient education by physicians and pharmacists while prescribing and dispensing the medication for the patients, respectively. Patients are not adequately informed about their medication use and the consequence of non-adherence.

8.2. Recommendation

Depending on the result of this study we have the following recommendations

- HCP should provide adequate education for patients regarding their disease and drug conditions, and to be compliant with the pharmacotherapy, particularly for patients with chronic disease like CVD patients, as they have to take medications for long period of time and so that they don't be exhausted and discontinue. Especially pharmacists have big role here, as they are the medication provider and patients make contact with them more often, so they have to provide enough counseling and education
- The responsible health care authority has to train HCPs regarding providing appropriate patient education, in order to minimize the unnecessary lost cost of illness.
- HCP must educate patients more on quitting smoking, as it is associated with poor outcome, DREA, survival time.
- Finally physician better to prescribe single pill preparation of the CVD medication whenever it is available and affordable in order to minimize number of pill burden, hence improve adherence.

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Annex: questioner

This Is A Patient Questionnaire Format Developed By Hikma Husein (Clinical Pharmacy Student) For The Objective Of Data Collection for a Msc Study Titled by " **Emergency Admission Among Cardiovascular Disease Patients; Outcome, Risk Factors And Drug-Related Visit, At Tikur Anbessa Specialized Hospital** ". I Would Like To Thank You For Your Participation.

Part I. Admission profile

1. Card No: _____

2. date of admission _____

3. date of discharge/ death _____

Part II. Socio-demographic characteristics of the study population

1. Sex……..1. Male 2. Female

2. Age in year…….

3. Education level……

1. No formal education 2. Primary, 3 Secondary 4. college and above.

4. Marital status ……..1. Single 2. Married 3.Divorced/widowed

5. Smoking history……..1 yes 2 no

6. Alcohol use history…….1 yes 2 no

7. Monthly income…….

8. residency……1 urban 2 rural

Part III. Clinical data

1. Medical history……

2. Duration of CVD disease ……..

3. Previous diagnosis category… … … … … … … 1 Primarily vascular 2 Primarily cardiac

4. Comorbidities……
……

5. Current diagnosis…….
.

6. Chief compliant
…….

7. past medication history
…….

8. Current medication .....

9. Specific reason for the current complaint 1 drug related 2 disease related

10. is there drug related need in terms of drug efficacy, safety, indication and adherence?

1.No 2.Yes, specify DTP with its cause …….

11.Is there any intervention provided for drug related admission

1. No 2. Yes, specify
……

12. Outcome of emergency admission ……..

1 survived 2. Death

Part IV; characteristics of DRP

1. Did the patient have known drug allergy

1. yes 2 no, 3 not mentioned

If yes specify it……

2.Did the patient have reaction to drug; 1 . y e s

2 no

if yes specify it……

3. Is there any drug interaction identified by physicians

1 yes 2 no,

If yes specify it

……

4. Is there any recorded Dispensing error, Administration error, Prescription error?

1 yes 2 no,

If yes specify……

5. Is there any drug identified as Inappropriate medication

1 yes 2 no,

If yes specify……

6.Is there any identified Inappropriate dose from past medication

1 yes 2 no,

If yes specify

……

7. Is there laboratory monitoring

1 yes 2 no

If yes
specify……

Annex 2: የአሚኮ መጠይቅ

የልብና የደምዝወወር ሥርዓት ሕመምተኞች መጠይቅ

ይህ በ ክሊኒካል ፋርማሲተሚሪ ሂካማሁሴን "በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል፣ የልብና የደምቧንቧ ሕመምተኞች ድንገተኛ መገቢያ (emergency department) ፣ ውጠት፣ የአደጋ መንስኤዎች እና ከመድኃኒት ጋር የተገናኘ ጉብኝት" በሚል ርዕስ ለ Msc ጥናት ሚጃ ማሰባሰቢያ ዓላማየ ተዘጋጀ የታካሚመጠይቅነ ው። ስለተሳትፎህ/ሽ ከልብ ላመሰግንህ/ሽ እወዳለሁ።

ክፍል I

የመገቢያ መለጫ

1. ካርድ ቁጥር
2. የሆስፒታል(ED) የመገቢያ ቀን
3. ከሆስፒታል(ED) መውጫቀን /ሕመምተኛውየ ሞተበት ቀን

ክፍል II ;ስነ -ሕዝብ ባህሪያት

1. 1.ጸታ
    i. ወንድ
    ii. ሴት
2. ዕድሜበዓመት
3. የትምህርት ደረጃ
    i. ያልተማረ
    ii. የመጀመሪያ ደረጃ
    iii. ሁለተኛ ደረጃ
    iv. ከፍተኛ ትምህርት
4. . የጋብቻ ሁኔታ *
    i. ያላገባ
    ii. ያገባ
    iii. የተፋታ
5. አጨስህ ታውቃለህ
    i. አዎ
    ii. አይ
6. 6. አልኮል ጠጥተህ ታውቃለህ
    i. አዎ
    ii. አይ
7. ወርሃዊ ገቢ(ETB) *

8. የመኖሪያ ቦታ *

I. ከተማ

II. ገጠር

ክፍል III :ክሊኒካዊ መረጃ

1. ያለፈውየ ሕክምና ሁኔታ (medical history)
2. የ ካርዲዮቫስኩላር በሽታቆይታ

3. የ ቀድሞየ ምርመራ ምድብ
   i. በዋናነት የደምቧንቧ
   ii. በዋናነት የልብ
4. ተጓዳኝ ህመም
5. የ መግቢያ ምርመራ
6. ዋና ምልክቶች
7. በሽተኛውሲወስዱየቆዩ መድሃኒቶች
8. ወቅታዊ መድሃኒቶች
9. ለአሁኑ ቅሬታየተለየ ምክንያት *
   i. ከመድኃኒት ጋር የተያያዘ
   ii. ከበሽታ ጋር የተያያዘ
10. ከመድሀኒት ውጤታማነት፣ ደህንነት፣ አመላካችነት እና ጥብቅነት አንፃር ከመድሃኒት ጋር የተያያዘ ፍላጎት አለ?
    i. አይ
    ii. አዎ
11. ለጥያቄ ቁጥር 10 መልሱአዎ ከሆነ DTP ከምክንያቱ ጋር ይግለጹ
    .....
12. ከመድኃኒት ጋር በተያያዙ ጉዳዮች ላይ የቀረበ ጣልቃገብነት አለ?
    i. አይ
    ii. አዎ
13. ለጥያቄ ቁጥር 12 መልሱአዎ ከሆነ ፣ ጣልቃገብነቱን
    ይግለጹ.....
14. የ ሕክምና ውጤት
    i. ተረፈ
    ii. ሞተ

ክፍል IV : ከመድኃኒት ጋር የተያያዘ ችግር ባህሪያት

1. በሽተኛውየ መድኃኒት አለርጂን ያውቃል?

   iii. አዎ

   iv. አይ

v. ያልተጠቀሰ

2. ለጥያቄ ቁጥር 1 መልሱ አዎ ከሆነ ይግለጹ ……..

3. በሽተኛውለመድሃኒት ቀዳሚምላሽ ነበረው;

i. አዎ
ii. አይ
iii. ለጥያቄ ቁጥር 3 መልሱ አዎ ከሆነ ይግለጹ .....

5. በሀኪሞች ተለይቶ የሚታወቅ የመድሃኒት ማከተጋብር አለ?

i. አዎ
ii. አይ

6. ለጥያቄ ቁጥር 5 መልሱ አዎ ከሆነ ይግለጹ ……

7. የተመዘገበ የጠፍ ባለመያዎች ስህተትአለ?

i. አዎ
ii. አይ

8. ለጥያቄ ቁጥር 7 መልሱ አዎ ከሆነ ይግለጹ ……

9. ተገቢያልሆነ መድሃኒት ተብሎየተገለጸ መድሃኒት አለ?

i. አዎ
ii. አይ

10. ለጥያቄ ቁጥር 9 መልሱ አዎ ከሆነ ይግለጹ.....

11. ካለፈውመድሃኒት የተወሰደ ተገቢያልሆነ ማጠን ተለይቶ ይታወቃል?

i. አዎ
ii. No

12. ለጥያቄ ቁጥር 11 መልሱ አዎ ከሆነ ይግለጹ ……..

13. መድሃኒት አቋርጠህ ታውቃለህ ?

i. አዎ
ii. አይ

14. ለጥያቄ ቁጥር 13 መልሱ አዎ ከሆነ ፣ ያለመታዘዝ ምክንያቱ ምንድነ ው?

i. የመድሃኒት አለመገኘት
ii. ስለ መድሃኒቱ ጥቅምእውቀት ማጣት
iii. የገንዘብችግር

15 ለታካሚየተደረገ የላብራቶሪ ክትትል አለ?

i. አዎ

ii. አይ

16. ለጥያቄ ቁጥር 15 መልሱ አዎ ከሆነ , የላብራቶሪ ውጤትጋር ይግለጹ ……