Patients' Beliefs about Medications, Adherence to Treatment, and Drug-Drug Interactions in the Management of Heart Failure: A cross-sectional Study at Ayder Comprehensive Specialized Hospital, Northern Ethiopia.

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A Thesis Submitted to the Department of Pharmacology and Toxicology, School of Pharmacy, Mekelle University in Partial Fulfillment of the Requirements for the Degree of Master of Science in Pharmacology and Toxicology.

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The full title of the Study	Patients' Beliefs about Medications, Adherence to Treatment, and Drug-Drug Interactions in the Management of Heart Failure: A cross-sectional Study on at Ayder Comprehensive Specialized Hospital, Northern Ethiopia.
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DECLARATION

I, Asmelash Araya Welecheal, hereby declare that this thesis entitled "Beliefs about Medicines, Adherence and Drug-Drug Interactions in Heart Failure Management: A cross-sectional Study at Ayder Comprehensive Specialized Hospital, Northern Ethiopia" is my original work. It has been carried out under the supervision of Mr. Abera Hadgu, Dr. Abraha Hailu, Mr. Meles Tekie, and Dr. Samuel Brhane, who have provided invaluable support and guidance throughout this research.

I confirm that this work has not been submitted for any other degree or qualification at any other institution. All sources used in the preparation of this thesis have been duly acknowledged, and I take full responsibility for the content of this document.

This research was conducted in compliance with ethical standards and was approved by the Institutional Review Board (IRB) of Mekelle University. I appreciate the cooperation of the participants and the support of the staff at ACSH Department of Internal Medicine, Cardiology unit, which made this study possible.

Signature: ----------

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CERTIFICATE

This is to certify that the thesis submitted in partial fulfillment of the requirements for the Degree of Masters of Science in Pharmacology and Toxicology by 'Asmelash Araya', entitled "Beliefs About Medicines, Adherence and Drug-Drug Interactions in Heart Failure Management: A Study at Ayder Comprehensive Specialized Hospital, Northern Ethiopia" complies with the regulations of the University and meets the accepted standards concerning originality and quality.

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Contents

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List of Abbreviations or Acronyms

ARB	Angiotensin Receptor Blockers
ACEI	Angiotensin-Converting Enzyme Inhibitors
ACSH	Ayder Comprehensive Specialized Hospital
BMQ's	Beliefs About Medication Questionnaires
CD	Cardiac Disorder
CVDs	Cardiovascular Diseases
DDI	Drug-Drug Interaction
DDInter	Drug-Drug Interaction Database
DM	Diabetic Mellitus
Dx	Diagnosis
HF	Heart Failure
IHD	Ischemic Heart Disease
IRB	Institutional Review Board
MMAS	Morisky Medication Adherence Scale
NSAID	Non-Steroidal Anti-Inflammatory Disease
PTHN	Pulmonary Hypertension
SC	Specific Concern
SD	Standard Deviation
SN	Specific Necessity
SPSS	Statistical Package For The Social Sciences

Abstract

Background: Heart failure (HF) is the heart's inability to pump blood effectively due to structural or functional impairments. Patients' beliefs about medications, adherence, and drug-drug interactions are critical factors in heart failure managements and understanding these can enhance HF management and outcomes.

Objective: To assess beliefs about medications, adherence levels, and the prevalence of drug-drug interactions in heart failure treatment.

Method: A cross-sectional study was conducted from June 15 to August 30, 2024, with 314 HF patients selected via convenience sampling methods. Data was collected using the Beliefs about Medicines Questionnaire, Morisky Medication Adherence Scale-8, and DDInetr software. The analysis was performed in SPSS 27 using descriptive statistics, Mann-Whitney U, and Kruskal Wallis H tests ($p < 0.05$, 95% CI).

Results: Among 314 participants, the median (IQR) age was 51.5 (32-65) years, 51.9% were female. The median treatment duration was four years. The mean score for specific necessity (20 ± 3.19), specific concern (15 ± 3.396), overuse (11.05 ± 2.297) and harm (9.03 ± 2.47) was scored. A majority of participants (79.3%) were classified as ambivalent, with a necessity-concern differential of +5.1. Non-adherence was observed in 41.4% of participants, with forgetfulness cited as the leading reason (37.6%). Significant correlations were found between adherence and both specific necessity ($r = +0.27$, $p < 0.001$) and harm beliefs ($r = -0.27$, $p < 0.001$). A total of 993 drug-drug interactions were identified, with moderate interactions being the most common and enalapril with Spironolactone was the drugs with sever interaction. These interactions were more prevalent among older patients and those experiencing polypharmacy.

Conclusion: Overall heart failure patients have strong necessity belief than concern about their medication where 84.7% knows the benefit of their medication. Over half of the participants were adherent to their medication due to high necessity belief, low concern, and forgetfulness. Severe DDIs were less common (6.95%) but requires medical treatment. Collaborative healthcare efforts are key to improving positive beliefs, and adherence, and reducing DDIs for better HF outcomes.

Keywords: Adherence, Belief about Medicine, Drug-Drug Interaction, Heart Failure, Heart Failure Medication

1. INTRODUCTION

1.1. Background

1.1.1. Heart failure

Heart failure (HF) is a serious cardiovascular disease (CVD) characterized by structural or functional limitations that impair the heart's ability to pump or fill blood effectively, resulting in various symptoms and clinical manifestations (1,2).Patients with this disease can be with systolic, diastolic, left-side, or right-side heart failure. It can be categorized based on the ejection fraction, disease prognosis, and symptoms. Ejection fraction classifications categorize heart failure into reduced, mid-range, and preserved types, indicating the heart's pumping ability (3). Prognostic classifications further divide the condition into stages A through D, reflecting the progression and severity of the disease(4). Additionally, the New York Heart Association functional classes I to IV assess the impact of heart failure on a patient's daily activities and quality of life (5).

CVD is a major worldwide health challenge, responsible for over 17 million deaths per year, which accounts for 32% of total global deaths (6). As of 2021, approximately 56.5 million cases of HF were reported worldwide, enlightening a notable gender disparity, 27.3 million cases were among women and 29.2 million among men and its prevalence varies, from 1% to 3%, with estimates in diverse populations typically falling between 2.01% and 2.5% (2,7). Furthermore, the lifetime risk of developing HF has risen to about 24%(8,9). For example, studies in Bangladesh indicate a 2.1% prevalence of HF (10) while research in the Czech Republic shows a significant increase in HF prevalence, from 1679.4 in 2012 to 2689.0 per 100,000 population in 2018 (11).

Studies done in Ethiopia highlight, that the prevalence of CVD is estimated at 5% and that a significant portion of the population is affected by this condition, reflecting a growing public health concern where non-communicable diseases (NCDs) are increasingly contributing to the burden of disease(12). Among patients visiting healthcare facilities, especially those in cardiology clinics, the prevalence of HF is significantly higher, with some studies reporting rates between 10-20%, 10 to 20 times higher than the global prevalence (2,7,13–15). The prevalence of HF in Ethiopia was reported as 43.4% and 46.5% in low and middle-income respectively(16). In comparison to the international statistics of HF prevalence, study data in Ethiopia reveals that while CVD is a leading

cause of death worldwide, the specific context in Ethiopia presents unique challenges. The high mortality rates from conditions such as Ischemic heart disease (IHD) and stroke, coupled with the significant proportion of at-risk populations (e.g., hypertensive patients), indicate that Ethiopia is facing a pressing public health challenge that necessitates tailored approaches to mitigate the impact of cardiovascular diseases (14,15).

The prevalence of HF in Tigray reflects significant clinical challenges and risk factors. In a study at Ayder Comprehensive Specialized Hospital (ACSH), Tigray, 39.1% of patients with structural heart disease were diagnosed with HF, primarily due to rheumatic heart disease (RHD) and IHD (17). Approximately 30% of patients attending cardiology clinics were diagnosed with HF which is an alarming statistic that emphasizes the urgent need for targeted cardiovascular health interventions in the region to address this public health crisis. The prevalence of heart failure in the region is influenced by high rates of hypertension, ischemic heart disease, and limited access to healthcare services (18).

CVD is also a major health problem in the Tigray region (ACSH), in which IHD, stroke, and hypertensive heart disease are leading causes of mortalities where IHD accounts for 45% of CVD fatalities, followed by stroke at 34% (19). HF is one of the CVD, mostly prevalent among individuals with co morbid conditions such as hypertension and diabetes and these co morbidities contribute significantly to the burden of it (20).

Managing HF and its co morbidities, both cardiac and non-cardiac, is complex due to the intricate interplay of various therapeutic challenges (21). HF patients with or without co morbidity or determinants can be treated effectively through medications like diuretics, anticoagulants, antiplatelet, calcium channel blockers, Angiotensin receptor blockers (ARB), Beta-blockers, anti-diabetics, nitrates, statins, Angiotensin-converting enzyme inhibitors (ACEI), anti-arrhythmia and other medication based on the type of HF and its co-morbidities (22).

1.1.2. Patients' beliefs about medicines

Patients' beliefs about medication encompass their cognitive and emotional perceptions regarding how medications work, their effectiveness, safety, and necessity. These beliefs significantly influence medication adherence and health outcomes across various chronic conditions. Patients often

weigh the perceived necessity of medication against concerns about side effects (23). Approximately 50% of patients do not adhere to medication instructions provided by healthcare professionals. This can worsen the disease condition and increase hospital cost of care due to the decreasing patient adherence level. The United Kingdom Clinical adherence guideline recommends adding patient perception of their medication as a part of counseling because studies show the Necessity-Concerns Framework identified individual beliefs about their medication as playing a key role in adherence(24).

The beliefs of patients toward their medication use, its side effects, and the above-listed cognitive and emotional perceptions have an extensive correlation with patients' preference in taking medication, which directly can affect their adherence level. Improving patients' positive perception of medication can improve their adherence and due to an increase in adherence level, the patient's therapeutic outcome also increases (25).

Most patients with chronic disease prefer medication to treat their disease condition and maintain their health, but they perceive medication as unsafe, unaffordable, unavailable, ineffective, improperly prescribed, or dispensed, so understanding medication belief is mandatory. Questionnaires have been developed to assess individual patients' medication beliefs where the most common framework is necessity-concern. Patients with high necessity and less concern are considered as adherent to their medications. This framework helps to know the main factor for nonadherence even doesn't elaborate on individual perceptions that fall out of the framework and that may also affect adherence(26).

Belief about Medication questionnaires (BMQ) is a tool used to evaluate the beliefs of patients about their medication by addressing general and specific medication beliefs (27,28).

BMQ is valid for all age above 18 years patients suffering from chronic disease. While the focus on medication belief is crucial, it is essential to recognize that some patients may turn to alternative therapies when they feel their concerns are not addressed, indicating a complex relationship between belief, trust in healthcare, and treatment choices (26).This tool was validated and used in different languages such as German, Spanish, Danish, Norwegian, Swedish, French, Portuguese, and Maltese(29).

1.1.3. Medication adherence

Medication adherence is the extent to which a patient follows the medication orders by physicians or the prescribed medication dosing regimen, or takes their prescribed medication as agreed with the doctor (30,31). A patient is considered adherent to the prescribed medication if they take 80% of the prescribed medication(31).Medication non-adherence can be deliberate and unintentional where understanding these factors can help to pinpoint them to identify strong non-adherence, adherence obstacles, and personalized adherence-improving ways of treatments) (30). Over 50% of global chronic disease patients including HF patients have been associated with increased mortality, hospitalizations, and healthcare costs due the non-adherence to medication(32).

Medication adherence can be affected by socioeconomic, medical-related, patient-related, medication-related, and healthcare system-related factors(31,33). Patient-related medication adherence factors may include sex, education level, marital status, age, average monthly income, and perception of medication. Patients not encouraged by family members, adverse effects, duration, frequency, quantity of medications, counseling, patient-physician communication regarding medicine, and drug interactions are other factors that could impact a patient's adherence(30,34).Their understanding of the necessity, concern, overuse, and harm of the medication (general and specific medication beliefs), was highly associated with medication adherence (35), and this is mainly affected by age, gender, religion, and cultural beliefs(36).

Patients level of adherence to their medication can be measured by self-report questionnaires (Morisky medication adherence scale (MMAS), Medication Adherence Questionnaire, Medication Adherence Report Scale, and Patient Activation Measure), electronic monitoring devices, pill counts, and biochemical markers(37,38).MMAS-8 is more valid and reliable when used in various patient populations with HF, diabetes, asthma, hypertension, renal disease, obesity, and others(38).

1.1.4. Drug-Drug interactions

Drug-drug interactions (DDIs) refer to the phenomenon where the effects of one drug are modified by the presence of another drug, potentially leading to altered pharmacokinetic or pharmacodynamics profiles. This alteration can result in increased or decreased drug efficacy, emergence of new

effects altogether, or potentially adverse outcomes (39,40). This type of drug effect is common in HF patients due to the complicated process of treating patients with HF medication. HF patients prescribed more than two drugs or multiple drugs may lead to DDI through pharmacokinetic and pharmacodynamics interaction resulting in an increased risk of hospitalization, and cost of drugs(41).

Studies indicate that a significant proportion of HF patients experience potential DDIs, with various factors contributing to this risk. High Prevalence of DDIs In a study of 985 HF patients, 239 were found to have an average of 6.2 potential DDIs per patient, with 7.28% classified as major interactions(42). Another study reported a staggering 96.4% prevalence of potential DDIs among 385 left ventricular failure patients, with 48.9% of these interactions categorized as major(43). In cardiothoracic intensive care units, 84.2% of patients experienced at least one DDI, with anticoagulants involved in 33.5% of cases(44). Age and the number of medications prescribed are significant predictors of DDIs, with older patients and those on polypharmacy at higher risk(43,45). The presence of co morbidities further exacerbates the likelihood of harmful interactions(43).

Currently, DDI is assessed using several databases. Lexicomp, Medscape, and physiologically-based pharmacokinetic modeling are commonly used in clinical decision support and research. The online drug-drug interaction database DDinter, which we utilized for this study, may be considered a viable alternative, as it is robust and free of charge (39,46,47).

1.2. Literature Review

1.2.1. Cardiovascular patients' beliefs about medicines

Research on heart failure patients' beliefs about medication is quite limited, with only a few articles exploring their perspectives and attitudes toward both specific and general medications. The fact that there is only a single study conducted at a hospital in China specifically focused on the beliefs of cardiovascular patients on their medication. This highlights a notable gap in our understanding of how HF patients view their medicine (26)

In this study done in cardiac patients over 40 years patients at Frontier Lifeline Hospital, china of a total of 205 outpatient participants result of the descriptive analysis indicates mean specific necessi-

ty, specific concern, general overuse, and general harm score of 17.61±5.1, 13.49±5.1, 12 ±3.6, and 11.18 ±3.8 respectively. Disagreement with certain BMQ reported as follows: “My medicine prevents my disease from becoming worse” (46.8%), “Without my medicine, I would be very ill” (20.4%), “My medicine is a mystery to me”(50.7%),” my medicine disrupts my life”(46.3%), and “having to take medicine worries me”(37.5%). Bivariate regression analysis of the study shows a significant correlation between BMQ subscales(26).

A cross-sectional study conducted in Malaysia involved 238 hypertensive patients (25), while another study at King Mill Hospital, London with a total sample of 328 rheumatoid arthritis patients(48). Descriptive analysis revealed the mean score of BMQ as specific necessity 3.35±0.79, specific concern 3.32±0.81), overuse 3.25 ±0.79, and general harm 2.9± 0.82. The summed mean score for Specific-necessity and concern were 16±3.95 and 16.60±4.05 respectively while the general medication belief scored 13.01 ± 3.15 and 11.78 ± 3.30 for overuse and harm consequently. The study also shows a positive significant correlation between the duration of hypertension and the general overuse subscale($r=0.132, p=0.046$)(25). In the King Mill Hospital study, a response rate of 74.3% strongly agreed or agreed that their medication was necessary. Additionally, 47.7% were concerned about potential side effects and 80% were concerned about long-term adverse effects. The average necessity and concern score was 19.92 ± 3.13 and 15.84 ± 3.53 consecutively resulting in a differential score of +4.08 with a p-value <0.001 (48). Carvedilol or metoprolol European trial conducted in Swedish included 302 participants of the cohort prospective study who responded that 94% believed their medication made them feel better(49). A cross-sectional study done at Gold Coast, Australia which assessed the impact of patient perception of medication resulted in a significantly higher median necessity score in the adherent group compared to the non-adherent group ($p = 0.0272$). Patients with a strong necessity score also had significantly higher self-reported adherence compared to patients with a strong concerns score ($p = 0.006$)(35).

In a systematic review carried out in the Middle East from 11 articles, 30% of studies found a negative correlation between overuse beliefs and adherence, highlighting the need for healthcare providers to address these perceptions. Harm beliefs significantly affect adherence, with 65% of studies showing a negative association between harm beliefs and medication adherence(50).

Belief in medication's necessity and concern impact adherence as a study done in Gonder in 2022 shows the mean standard score was 3.7 from eight (8) and three (3) out of five (5) with 60.6% and 49.3% of prevalence respectively for necessity and concern. Of those who are concerned about their medication, 43.6% are worried that taking medication for a long time will be harmful (51). The patient who has a positive belief in the necessity and a negative belief of concern are strongly adherent to their medication (35).

1.2.2. Adherence to Heart Failure Medication

Different studies on adherence to HF medication, have varied proportion rates from 10% to 98% depending on the definition, different factors, and measurements used to assess and analyze (52). Based on the adherence studies done by the General Medication Adherence Scale (GMAS), it is mainly affected by gender, age, education level, marital status, patient income, cost of medication, presence of comorbidity, health literacy of patients, medication side effects, patient-physician discussion, and supportive family(34,53).

In a research study in the University Hospital of Thailand on 180 HF patients using MMAS-8, adherence was recorded as 38.3%, 50.0%, and 11.7% for high, medium, and low respectively. The median ± IQR (7.0 ±1.2), and mean ±SD (7.1±1. 0) of total MMAS-8 were scored and factors such as age, sex, number of co morbidities, income, employment status, marital status, educational level, and health insurance don't have any association with adherence(54). In other similar studies designed involving 300 patients conducted at Mazandran Heart Center, Sari, Iran results indicate a 5.82 ±2.54 mean adherence score which is highly correlated with education level($p=0.012$), co morbidities($p=0.002$) and number of medications per patient($p=0.001$) but not correlated with gender, age, employment, place of residence, and income level(55).

In a cohort study involving 300 CVD patients at Alsader Teaching Hospital and Misan Cardiac Center, Iraqi, adherence was assessed as dichotomous and three levels. Results of the study showed 54.1% high,27.7% medium, and 18.2% low whereas based on the binary category of adherence 81.8% were adherent to their medication. The association assessment of this study shows, gender ($p=0.507$), and age ($p=0.484$) whereas the number of medications prescribed ($p=0.001$, Odds ra-

tio=1.947 of 95% CI). The mean number of medications taken by non-adherent was 6.53 ± 1.63, higher than the adherent group (3.38±2.07). Based on the non-adherent data 72.3% are intentionally nonadherent, due to the release of medication side-effects, inconvenience of taking, financial cost, and patients' belief(56).

An MMAS-4 research by cross-sectional design including 427 patients at the University of Jordan and, clinical trials in Saudi Arabia involving 94 participants highlights that IHD, hypertension, diabetes Mellitus (DM), and depression are the most prevalent co morbidities that significantly impacted medication adherence of HF patients with prevalence rates of 64.2%, 77.1%, and 61.2% respectively (57,58).

In other cross-sectional studies using GMAS includes 164 participants done at Jordan University in 2023, the prevalence of medication adherence to HF medication was 33.5% high adherence,19.5% good adherence, and 47% poor adherence in which study variables with good to high adherence are significantly associated with < 60 years, having insurance, high school and above, being married, and never been admitted to hospitals (34) while, another cross-sectional study involving 286 sample using GMAS showed that medication adherence is heavily affected by the medication history of HF patients ($p<0.01$), sex ($p<0.05$), and health education ($p<.05$). The duration of patients on treatment of HF also affects adherence. Based on the study result patients who take medication for less than five years are 4.5 times more adherent than those who take it for more than five years (59).

Research studies at North Shewa Public Hospital, Ethiopia, on HF patients, indicate more than half of the 337/603 (56%) patients have good adherence levels (95% CI, 52.1%, and 60% for high and moderate respectively) and 44% adherence. The overall participants of the study were 51.1%, 24.9%, 43.1%, 27.3% 35.3%, 73% forgot to take, missed without reason for more than two weak, forgot to bring when traveling, stopped taking when feeling worse, stopped taking when feeling better, took medication yesterday, and sometimes forget to take all their medication respectively. Based on the logistic regression analysis of the study, various factors such as who can read and write (no formal education (AOR: 1.97, 95%CI;1.34,3.67)), occupational status, health insurance, co morbidity(AOR: 1.72, 95%CI;1.18,2.52) and number of drugs(AOR: 2.11;95% CI;1.35,3.31),

were associated with medication adherence (31). In another study carried out in Addis Ababa, Ethiopia in 2020 using a prospective cross-sectional study on 423 participants to assess drug therapy problems, patient satisfaction, and associated factors, was found that 26.2% of the participants did not comply with their primary prescribed medication. The study showed that more than half of the participants followed their prescribed medication, but 80% of them experienced worsening symptoms after stopping the medication. Moreover, only 39.4% of participants forgot to take their prescribed medication. In summary, the study revealed that 64.86% of the participants adhered to their prescribed medication (60,61)

1.2.3. Potential Drug-Drug Interactions in Heart Failure

HF treatment is complex and challenging because of the presence of co morbidities and DDI. A review of different studies indicates a proportion of 58.3% of drugs prescribed for HF has interaction. There were also various studies done in different corners of the world show significant DDI in the treatment of HF and its co-morbidities with a prevalence of 56% in Bangladesh using Microsoft® Office and Microsoft® Excel 2007 software (with the most common interaction clopidogrel with omeprazole, and furosemide with cephalosporin)(62), 74.06% moderate,17.33% major and 8.61% minor in Pakistan using Lexicomp Interact® (shows 8.5 per patient),(63),77.29% in India (aspirin/clopidogrel, pantoprazole/clopidogrel, aspirin/heparin and aspirin/metoprolol are the most) using Medscape drug interaction checker (64) and 67.8% with 54.5% major interaction in Brazil using Micromedex DrugReax software(65).

Studies were also conducted at Jimma University, Ethiopia, on cardiac patients to examine the drug therapy problem and DDI using prospective observational design on a total of 200 cases. The investigators found that 77.4% of the HF patients in the study experienced DDI and factors such as the number of medications the patients were taking, their older age (p=0.027), and the length of their hospital stay (p=0.024). Furthermore, the study discovered that 45% of the overall sample of 200 patients developed moderate drug interactions. Additionally, one-third of the 74.4% of patients who developed DDIs were found to have severe drug interactions(66).

1.3. The Present Study

1.3.1. Statement of Problem

HF is one of the most prevalent CVDs affecting 56.19 million individuals internationally in 2024 (67) and in the next years from 2012 to 2030 in the United States, it is expected that the prevalence rate will increase by about 46%, this will cause to increase the hospital service cost by 127%. In the developing world, the prevalence rate is increasing due to the epidemiologic transition, and poor diagnostic and treatment alternatives(68).

The burden of HF medication non-adherence and DDI in Africa, Ethiopia, and Tigray has indeed been a significant concern. HF patients often require lifelong therapy with multiple medications. However, medication non-adherence is a common problem among these patients. Factors contributing to medication non-adherence include negative medication beliefs, poor involvement of patients in therapeutic decision-making, the complexity of medication regimens, age, polypharmacy (taking multiple medications), and the presence of co morbidities are the factors increasing the burden of heart failure treatment outcomes.

Furthermore, patients with HF are at an increased risk of DDI interaction because these patients are on multiple drugs due to co morbid disease conditions. DDI is prevalent among ambulatory HF patients, and inpatients (69).Factors that affect adherence may also contribute to DDI. The impacts of these factors on HF management are not enough studied globally (70).

The presence of co morbidity and multiple medications coupled with the patient's belief and attitude towards treatment pose adherence problems and poor treatment outcomes (70).Factors like patient belief in medication, drug interaction, and multiple drug's contribution to patient adherence are not well studied in ACSH,Tigray,and Ethiopia as well in the continent. The specific incidence of potential DDIs in HF patients is also not well-documented. These interactions can lead to adverse events, worsen cardiac conditions, reduce treatment efficacy, and increase healthcare utilization. However, the lack of comprehensive research on DDIs in the context of HF limits our understanding of their prevalence and consequences, impeding efforts to ensure patient safety and optimize treatment outcomes. Finally, the relationship between DDIs and medication adherence in HF patients has not been adequately explored.

1.3.2. Significance of the Study

Studies assessing HF patients 'adherence and beliefs about their medication are not enough in the country in general and are lacking in ACSH in particular. Furthermore, understanding patients 'beliefs about their medications helps professionals to identify barriers and factors that influence adherence among patients with HF and to develop targeted intervention strategies leading to reduced hospital admission and improved overall patient well-being. The finding of this study serves as a valuable reference for another healthcare setting beyond ACSH and contributes to existing body knowledge on factors influencing patient adherence.

Assessing the prevalence of potential DDIs in these patients is crucial for guiding healthcare providers in prescribing practices and adjusting medication regimens. Healthcare providers can make informed decisions regarding combination medications and adjust medication regimens to minimize the occurrence of harmful interactions. This assessment would serve as a guide for healthcare providers, ensuring that they prioritize patient safety and optimize treatment effectiveness. So assessing the prevalence helps to guide healthcare providers in prescribing such combination of medication or adjusting medication regimens to minimize the occurrence of harmful interactions thereby promoting patient safety and optimizing treatment effectiveness. Therefore, this study assesses HF patients' adherence to their treatment, their beliefs about the medication they take, factors influencing adherence, and beliefs about medication-taking behaviors and potential DDI. The findings of this study can serve as a valuable reference for another healthcare setting beyond ACSH and would contribute to existing body knowledge on HF pharmacotherapy.

2. OBJECTIVES

2.1. General Objective

This research aims to determine the level of medication adherence among heart failure patients, examine the extent of their beliefs regarding medications, and identify potential drug-drug interactions in heart failure treatment.

2.2. Specific Objectives

- To determine the level of medication adherence among HF patients.
- To determine the level of medication belief of heart failure patients
- To assess patient medication beliefs among the different socio-demographic and clinical characteristics of HF patients.
- To identify potential drug-drug interactions (DDIs) within patient treatment regimens.
- To determine the prevalence of the pharmacological class of drugs that have DDI
- To determine the prevalence of DDI among clinical and socio-demographic characters

3. METHODOLOGY

3.1. Study Period and Area

The study data was collected from June 15, 2024, to August 30, 2024, at ACSH cardiac clinic, Mekelle City with an overall duration of study from February 1st, 2024 to February 30, 2025. The hospital is located in the Tigray Regional State of Mekelle City, Ethiopia. It is located around 780 kilometers north of the capital Addis Ababa. ACSH commenced rendering its referral and non-referral services in 2008 to the 8million population in its catchment areas of the Tigray, Afar, and South-eastern parts of the Amhara regional States. It provides a broad range of medical services to both in and outpatients of all age groups. As such, the Hospital can be designated as the most advanced medical facility by all accounts in the Northern part of the country and it stands as the second largest hospital in the nation with a total capacity of about 500 inpatient beds in four major departments and other specialty units. The hospital has 108 internal medicine beds and the cardiology unit has five cardiologists, six nurses, one cardiac catheterization laboratory, resting ECG, stress ECG, Holter ECG, and blood pressure monitors. ACSH is also used as a teaching hospital for the College of Health Sciences, at Mekelle University.

3.2. Study Design

An institutional-based cross-sectional study was conducted.

3.3. Source and Study Population

3.3.1. Source population

The source population was all patients who visited the cardiac clinic of ACSH

3.3.2. Study population

All HF patients who visited the hospital's cardiac clinic at the time of the data collection period and fulfilled the inclusion criteria

3.4. Inclusion and Exclusion Criteria

3.4.1. Inclusion criteria

Patients aged 18 years or older with a confirmed diagnosis of HF on medication, with follow-ups of more than six (6) months, and having a complete medical record were included. Those taking more than one (>1) medications only were included in the potential DDI study.

3.4.2. Exclusion criteria

HF patients severely sick (unable to stand for participation), those who cannot speak Tigrigna, and less than six (6) months of follow-up were excluded. Study participants with prescription/medical records were hard to read, didn't include HF medication, and involved non-systemic were not considered for the DDI study.

3.5. Sample Size Calculation and Sampling Process

The sample was drawn from patients taking HF medication, with or without additional treatments for co morbidities, at ACSH. Participants were selected using a convenient sampling method. The sample was calculated using a single proportion sample size calculation method n = (Z^2 * p * (1 - p)) / (E^2) where: n = sample size, Z = desired level of confidence, p = estimated proportion of the population, E = margin of error, CI=95%, proportion=50 %, margin of error=5% then n=384. The final sample was calculated using a finite population correction formula.

$$n_f = \frac{n_i}{1 + \frac{n_i}{N}} = \frac{384}{1 + \frac{384}{1650}} = 312 + 5\% \text{ non response} = 328$$

Where; N=total population, nf=final effective sample size, and ni=initial number of respondents

3.6. Study Variable

Medication adherence, Beliefs about medication, and Potential DDI were considered as the dependent variable and socio-demographic,(age, sex, economic level, marital status, religion, education level, and residence),number of medications prescribed, severity of drug interaction, duration of the disease since diagnosis, and disease co morbidity were considered as the independent variables.

3.7. Data Collection Tools and Process

Structured questionnaires were used to collect relevant data that meet the objective of the study and the questionnaires were universally validated tools (70,71)such as BMQ MMAS -8,medication registry form, and other socio-demographic and clinical factor registry form was used. The questionnaires were prepared in English language and translated to the local language (Tigrigna). It was administered to the participants in the Tigrigna version then later after data was collected back-translated to English after the necessary information was obtained from the participants. The questionnaires were self-administered but the data collector had read the questionnaires for those who couldn't read and write and there were no right or wrong responses, their responses were based on their way of medication-taking behavior or belief in medication.

Training for data collectors was given for the day and after the training, each data collector got practical practice on, how to (administer the questionnaires, contact patients, administer the questionnaires), what information should be collected, specific protocols that need to be followed, proper questioning techniques, maintaining participant confidentiality, and ensuring accurate recording of responses. Supervisors continuously monitored the data collection process to identify any potential issues. During the process of data collection, timely feedback was provided/received, and guidance to the data collectors to maintain data quality.

The tool contains five (5) sections MMAS, BMQ, medication registry form, special-demographic, and health-related factors, and was first pretested on 16 participants to prove the understanding of the patient for the translated tool. Then two nurses trained in data collection collected the data by directly administering the questionnaires of MMAS-8 and BMQ-18 for self-reporting by the patients but the clinical character questions and potential DDI data were gathered by data collectors (For the clinical characteristics and DDI data was collected from patient's charts).

In BMQ-18tools, it contains 18 questions, 1-5 as Specific-Necessity,6-10 for specific concerns, 11-14 for general overuse, and 15-18 for general harm assessments, each item was scored on a 5-point Likert scale, ranging from 5 (strongly disagree) to 1 (strongly agree).

In MMAS -8 responses to questions 1- 7 were scored as 1 for no and 0 for yes for questions 1,2,3,4,6, and 7, but question 5 was rated as yes "1" and no as"0" because these items (variables) typically uses dichotomous response and positive adherence measure were rated as highest score(1). MMAS -8 of items 1-7 measures adherence as yes as negative and only the fifth item measures adherence as yes as positive. Then the 8th question measures the patient's subjective belief about medication with a five-point Likert-type question response with Never/rarely (1), Once in a while (0.75), Sometimes (0.75), usually (0.25), and all the times (0).

The medication recorded on the chart was collected parallel to the above information then every medication was inserted into the online database DDIneter (https://ddinter.scbdd.com/inter-checker/) where it takes two months from September 01 to October 30, 2024. During the feeding of the medication, the DDIneter allows a maximum of five and a minimum of two medications, so the prescription of patients with more than five medication interactions was checked by replacing each other. Finally, interaction result was recorded on the medication recording prepared form as severe, moderate, or low, list of interaction type, and total interaction.

3.8. Data Quality Control

The quality of data was assured by pre-testing the data collection tool on 5% of the sample size in similar patient groups to see the consistency and reliability of the questionnaires. There was regular supervision of the data collectors and the data collection process and open and honest discussions with data collectors were done on challenges in collecting data. Daily review and checkup of the collected data for completeness before data entry and cleaning was done by running a simple frequency distribution of the questionnaire to see for missing values and inconsistency with the patient response.

3.9. Data Analysis

Data was entered and analyzed using the SPSS version 27.0 statistical package. The collected data was checked for completeness, and missed values using frequency distribution and then manually cleaned up on such indications. Internal consistency was determined using Cronbach's alpha to ensure inter-relatedness and Cronbach's alpha was 0.597and 0.64for general BMQ and specific BMQ

respectively. If items such as “my medicine is a mystery to me” and “my medicine disrupts my life” were deleted Cronbach's alpha values increased to 0.68 and 0.653 respectively. For general BMQ the internal reliability alpha value increased to 0.652 if “doctors prescribe too much medicine” were removed. The interrelatedness of Cronbach's alpha value of MMAS-8 was 0.684 and deleting any of the eight items wouldn’t increase the alpha value.

The data was summarized as, median, mean, variability (standard deviation, variance, and range), frequencies, and percentages. Inferential Statistics include non-parametric tests (Mann-Whitney (U-test), kruskal-wallis, post-hoc, and chi-square tests) to analyze relationships and associations between variables. P-value <0.05 was used as statistically significant.

The scores of 314 target samples for the BMQ-specific (Necessity and specific concerns) and BMQ-general (overuse and harm scale) were calculated by summing the responses to the respective items. The total score for specific (Necessity and concerns) was 5-25 and for BMQ-general scored from 4-20(48). The differential analysis was done as the belief of patients about medication was considered positive when the mean of the sum of 5-item specific necessity was greater than the mean of the sum of specific concerns. In addition, higher scores in general harm and overuse than specific concern indicated the overall negative perception of medications whereas a higher score of specific concern than general harm and overuse shows potential adverse effects of HF or HF co morbidities medications. In this analysis necessity was considered as benefit and concern as cost, this analysis can be also called cost-benefit analysis. Further analysis was done by categorizing into four quadrants of high(>12.5)/low(<12.5) specific necessity and high (>12.5) /low (<12.5) specific concern by cross-tabulation as ambivalent, accepting, skeptical, and indifferent(29,48,72).

In the analysis of MMAS-8, the responses of 314 respondents were summed as no as “1” for 1-7, yes as “1” for item five, and never as “1” for item eight then the sum of each positive respondent scored as 8 for those who responded all 1-8 items as positive and categorized as 0-6, ≥6-7, and ≥7-8 low, moderate and high adherence respectively(73–76). In other ways, adherence was categorized as nonadherent (0-6) and adherent(≥6-8)(55,56,77).

Then the baseline character data and online interaction database results were entered into SPSS and analyzed. Finally, data was analyzed as low, moderate, and high drug interaction. In addition, the three pillars of analysis most common drug interaction, total interaction, and positive correlation factor to drug interaction were presented. Results were summarized in the form of tables, graphs, and as a statement for the variables of interest.

3.10. Operational Definitions

BMQ-18; the score below half of the sum of specific necessity was a negative belief, whereas half of the sum of specific concern was seen as a positive belief. Similar to concern sum less than half (<10) for overuse and harm was considered a positive belief.

MMAS-8; the sum of the score categorized 0-6, ≥6-7, and ≥7-8 as low, moderate, and high or good adherence but also non-adherent (0-6) and adherent (>6-8).

Drug-drug interaction (DDI): is defined as the pharmacokinetic, pharmacodynamics, or pharmaceutical effect of one drug over the other that can affect the safety and efficacy, and even cause severe adverse effects.

Sever DDI: this is a severe type of interaction that requires medical treatment to prevent severe adverse effects unless it may lead is life-threatening.

Moderate DDI: this type of interaction may result in exacerbation of the medical condition of the patient and/or a change in therapy.

Low DDI: a type of interaction that may decrease the therapeutic effect of the other medication.

Total DDI: is the burden of a drug interaction that occurs in a single patient.

3.11. Ethical Considerations

Ethical approval for this study was obtained from the IRB of MU-CHS with the reference number MU-IRB 2209/2024), and permission was also obtained from the School of Pharmacy, the cardiology unit, and the medical director of ACSH.

Before commencing data collection, informed consent was obtained from study participants. This consent ensured that all individuals involved in the study were fully aware of the nature of the research, their involvement in it, and any potential risks or benefits. Furthermore, it was crucial to

emphasize that the identities of the participants were kept confidential and used exclusively for the research study.

Our commitment to obtaining legal and ethical approval, seeking appropriate permissions, and obtaining informed consent underscores our dedication to conducting responsible and ethical research. By adhering to these principles, we uphold the integrity of our study and ensure the well-being and rights of all participants involved.

4. RESULTS

4.1. Response Rate

A study was conducted on 314 respondents of the initially assigned 328 participants to study HF patients on medication adherence, beliefs about medication, and potential DDI. As only 314 were the responsible respondents a very small number of intended respondents, 4.26% were not included in the study due to incomplete information (14). Most of the incomplete data was on the BMQ section (8) where the rest six participants unable to fill their socio-demographic or MMAS-8.The data of missed respondents were cleared due to the incomplete information or data on the sections of socio-demographic, BMQ, and MMAS with seven, three, and four respectively.

4.2. Socio-demographic Characteristics of HF Patients

The overall distribution of demographic characteristics of respondents shows that the age of the participants was mainly concentrated in the middle-aged group, particularly those aged 40-59 years, and the median (IQR) was 51.5 (32-65) years. The gender distribution was closely balanced with females 163/314 (51.9%), the majority of respondents 227/314 (72.3%) live in an urban, a high percentage 232/314 (73.9 %) were married, and 214/314 (68.2%) get their medication for free. Table 1

Table 1: Baseline characteristics of adult HF patients in ACSH, Mekelle, Tigray, Ethiopia, 2024 (n=314)

Characteristics	Level		Frequency/average (n= 314)	Percent
Gender	Male		151	48.1
	Female		163	51.9
Age	Mean ± SD		49.62 ± 17.68	
	Median (IQR)		51.5(32-65)	
	18-39 years		100	31.8
	40-59 years		103	32.8
	60-74 years		91	29.0
	75-87 years		20	6.4
Place of residence	Urban		227	72.3
	Rural		87	27.7
Level of education	No formal education		101	32.2
	Primary school		71	22.6
	Secondary school		91	29.0
	Collage and above		51	16.2
Religions	Orthodox		300	95.5
	Muslim		12	3.8
	Catholic		2	0.6
Marital status	Married		232	73.9
	Single		39	12.4
	Divorced		20	6.4
	Widowed		23	7.3
Monthly income in birr	Average ± SD		5219.79 ± 2913	
	Median (IQR) in birr		4322.5 (3000-7325)	
	<5000		195	62.1
	5000-10000		99	31.5
	>10000		20	6.4
Employment status	Unemployed		95	30.3
	Employed	Governmental	86	27.4
		Private	63	20.1
		Farmer	70	22.3
Medication cost coverage	Paid		89	28.3
	Free		214	68.2
	Insurance		11	3.5

IQR=Interquartile range, SD= standard deviation

4.3. Clinical Characteristics of HF Patients

The clinical characteristics of these adult HF patients were studied and the most prevalent underlying condition was valvular heart disease (VHD) affecting around 149 (47.5%) of individuals and 80.6% had co morbidities with an average of co morbidities per patient being one where pulmonary hypertension (PHTN) was the most common, affecting 60 (19.1%). The median year of treatments for HF was four years suggesting that most of the HF patients were relatively new to treatments because the study result proves 211 (67.2%) had been under treatment for less than five years. Patients had a median of four medications and five medication types per patient were the maximum number recorded. Table 2

Table 2; Clinical characteristics of HF adult patients (n=314) in CSH, Mekelle, Tigray, Ethiopia, 2024

Clinical characteristics		Frequency (n=314)	% from n=314
Underling disease	VHD	149	47.5
	IHD	57	18.2
	HHD	62	19.7
	AV channel defect	1	0.3
	ASD	3	1.0
Years of treatment	Average ±SD	4.52 ±3.3	
	Median (IQR)	4.0(2-6)	
	< 5 year	211	67.2
	6-10 year	87	27.7
	>10 year	16	5.1
Presence of co morbidity	Yes	253	80.6
	No	61	19.4
Number of co morbidities	Mean ±SD	1±0.637	
	Median (IQR)	1.0(1-1)	
	One	198	63.1
	Two	51	16.2
	Three	4	1.3
Main co morbidity	PHTN	60	19.1
	DM	18	5.7
	HTN	13	4.1
	Thyrotoxicosis	6	1.9
	HTN,and DM	6	1.9
	AF	2	0.6
	Epilepsy	1	0.3
	HTN and dyslipidemia	1	0.3
	HTN and asthma	1	0.3
	Dyslipidemia	2	0.6
	CKD	1	0.3
	HTN and Thyrotoxicosis	1	0.3
Number of medication	Mean ±SD	3.76 ±1.057	
	Median (IQR)	4 (3-5)	
	One	2	0.6
	Two	42	13.4
	Three	84	26.8
	Four	88	28.0
	Five	98	31.2

HTN=hypertension, PHTN=pulmonary hypertension,CKD=chronic kidney disease,HHD=hypertensive heart disease, AV=Atrioventricular canal defect, ASD= Atrial Septal Defect, AF=atrial fibrillation

4.4. Belief of Heart Failure Patients about Medicine

4.4.1. BMQ Evaluation

The BMQ data of HF patients indicates a strong perception of the benefit of medication among the respondents. Out of the total target, 142/314(45.2%) strongly agree and 119/314(37.9%) agree that life would be impossible without their medicine, resulting in a total of 83.1% confirming its importance. Similarly, 263/314 (83.7%) believe that they would be very sick without their medication, highlighting the perceived critical benefits of their medication contributing to their health. The highest score of respondents on the necessity was recorded on the perception of their health, at present, depends on medicines which is the sum of agree and strongly agree scored as 286/314 (91.1%) affirms that a deep-seated belief in their importance. Further "My medicines protect me from becoming worse" was the second highest score 280/314 (89.2%), underscoring the trust patients place in their medication. However, the final item of the necessity was recorded 245/314 (78%), their health depends on medication but a lower percentage had uncertainty about long-term reliance.

The concern of HF patients about medication of the respondent was a mix of anxiety and acceptance. From the target sample, 180/314 (57.4%) agreed on "sometimes worry about the long-term effects of their medication" with 22% strongly agreeing and 35.4% agreeing. However, only 38.9% of the sample agreed on "Having to take medicines worries them "but 53.5% disagreed with this statement. Concerns about dependency were also presented with 52.9% agreeing.

Regarding the overuse of medication perception of these patients only 9.6% believe that "If doctors had more time with patients, they would prescribe fewer medicines", this result indicates skepticism about the impact of consultation time on prescribing behaviors, with 43.3% disagreeing. Respondents scored a disagreement of 184/314 (58.6%) on "Doctors prescribe too many medicines" and this highlights more than half of the study participants have a belief that the doctors that prescribed medication were the right medication that belongs to their disease condition. A noteworthy 62.5% express disbelief regarding the doctor's trust placed in medications ("Doctors place too much trust in medicines")**,** while 66.2% disagree that natural remedies are safer than conventional ones. Additionally, just 10.2% believe that "medicines do more harm than good", with 64.6% confirming their

benefits. The idea of "People who take medicines should stop their treatment for a while now and again" was largely rejected, with 70.4% disagreeing, and the belief of "Most medicines are addictive "was 21.3%. Table 3

Table 3; Evaluation of medication beliefs of HF patients based on BMQ-18 (n=314) in ACSH, Mekelle, Tigray, Ethiopia

Beliefs about Medicines Questionnaire(BMQ)					
BMQ –specific	Strongly Agree (%)	Agree (%)	Uncertain (%)	Disagree (%)	Disagree Strongly (%)
BMQ Specific Necessity(BMQ-SN)					
My life would be impossible without my medicine	142(45.2)	119(37.9)	27 (8.6)	24(7.6)	2(0.6)
Without my medicines, I would be very sick	136(43.3)	127(40.4)	36(11.5)	15(4.8)	0(0)
My health, at present, depends on my medicines	141(44.9)	145(46.2)	16(5.1)	12(3.8)	0(0)
My medicines protect me from becoming worse	124(39.5)	156(49.7)	19(6.1)	13(4.8)	0(0)
My health in the future will depend on my medicines	103(32.8)	142(45.2)	35(11.1)	34(10.8)	0(0)
BMQ Specific Concern (BMQ-SC)					
I sometimes worry about the long-term effects of my medication	69(22.0)	111(35.4)	42(13.4)	87(27.7)	5(1.6)
Having to take medicines worries me	30(9.6)	92(29.3)	24(7.6)	162(51.6)	6(1.9)
I sometimes worry about becoming too dependent on my medication	38(12.1)	128(40.8)	35(11.1)	108(34.4)	5(1.6)
My medicine disrupts my life	24(7.6)	103(32.8)	24(7.6)	151(48.1)	12(3.8)
My medicines are a mystery to me	44(14.0)	133(42.4)	23(7.3)	91(29.0)	23(7.3)
BMQ General Overuse					
If doctors had more time with patients, they would prescribe fewer medicines	30(9.6)	57(18.2)	71(22.6)	136(43.3)	20(6.4)
Doctors prescribe too many medicines	12(3.8)	41(13.1)	77(24.5)	169(53.8)	15(4.8)
Doctors place too much trust in medicines	63(20.1)	133(42.4)	48(15.3)	52(16.6)	18(5.7)
Natural remedies are safer than medicines	11(3.5)	16(5.1)	26(8.3)	208(66.2)	53(16.9)
BMQ General Harm					
Medicines do more harm than good	2(0.6)	30(9.6)	46(14.6)	203(64.6)	33(10.5)
People who take medicines should stop their treatment for a while now and again	4(1.3)	18(5.7)	28(8.9)	221(70.4)	43(13.7)
Most medicines are addictive	5(1.6)	62(19.7)	21(6.7)	192(61.1)	34(10.8)
All medicines are poisons	6(1.9)	38(12.1)	46(14.6)	168(53.5)	56(17.8)

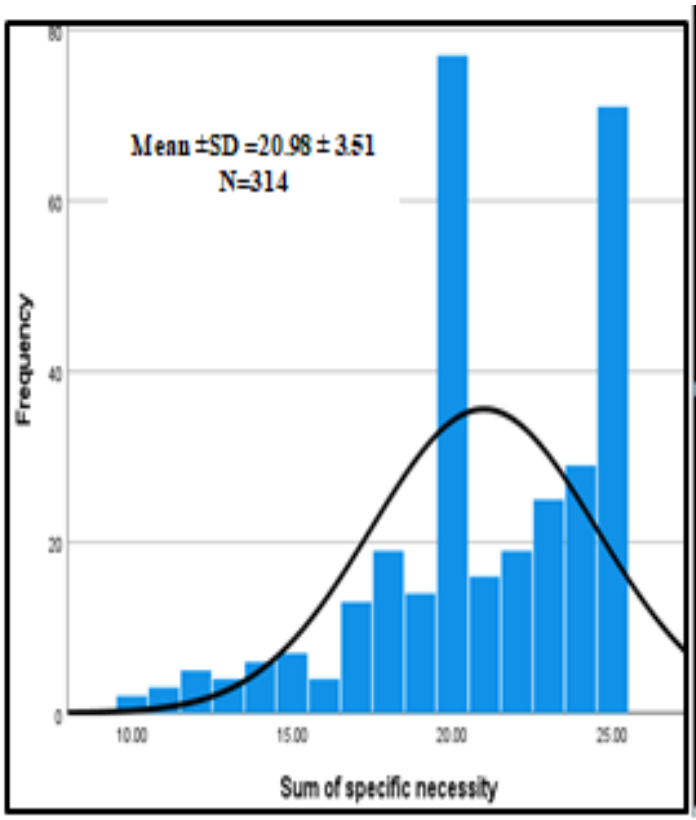
4.4.2. HF Patient's Specific and General Beliefs about Medicines

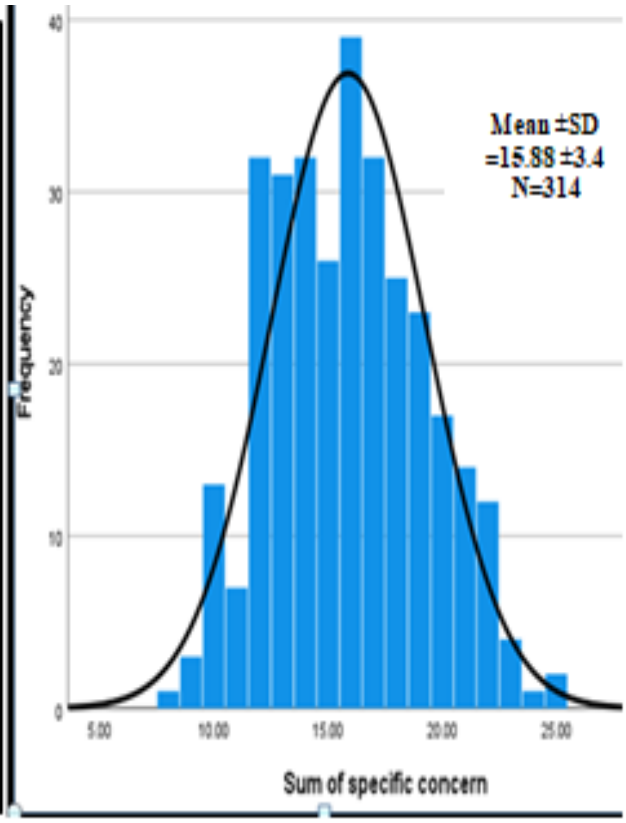
Overall the mean of the specific necessity (SN) score of the respondents was 20 ± 3.19, while the mean specific concern (SC) score was lower at 15±3.396. The study also found that general over-use had a score greater than ten (>10), with the mean harm belief score being 9.03 ± 2.47. The differential of SN and SC (SN-SC=NCD) was positive value (20.98- 15.88=+5.1). Another differential of the same way of calculation for SC and General –harm scored as +6.85 (15.88-9.03). Table 4, Figure 2, and Figure 3

Table 4; Specific and general beliefs about medication of HF patients in ACSH, Mekelle, Tigray, Ethiopia (n=314)

Subscale	Mean ± SD	Median (IQR)	Frequency (%)		Mini-Max (Range)
			Low	High	
Specific–necessity (SN)	20.98 ±3.519	21(24)	10(3.2%)	304(96.8%)	10-25(15)
Specific-concern (SC)	15.88 ± 3.396	16(18)	56(17.8%)	258(82.2%)	8-25(17)
General –overuse	11.05 ± 2.297	11(13)	70(22.3%)	244(77.7%)	5-17(12)
General –harm	9.03 ±2.469	8(10)	205(65.3%)	109(34.7%	4-18(14)
NCD	5.1 ± 4.9	5(8)	---	-----	-12 to 16
Concerned	----	-----	30(9.6)		-----
Know the benefit of medication	---	-----	266(84.7)		-----
Neither concerned nor know the benefit of medication	---	----	18(5.7)		-----

Note:NCD=necessity –concern differential, Mini-Max=Minimum-Maximum, ---- = not feasible to measure


Mean ±SD =20.98 ± 3.51
N=314
Frequency
Sum of specific necessity


Mean ±SD
=15.88 ±3.4
N=314
Frequency
Sum of specific concern

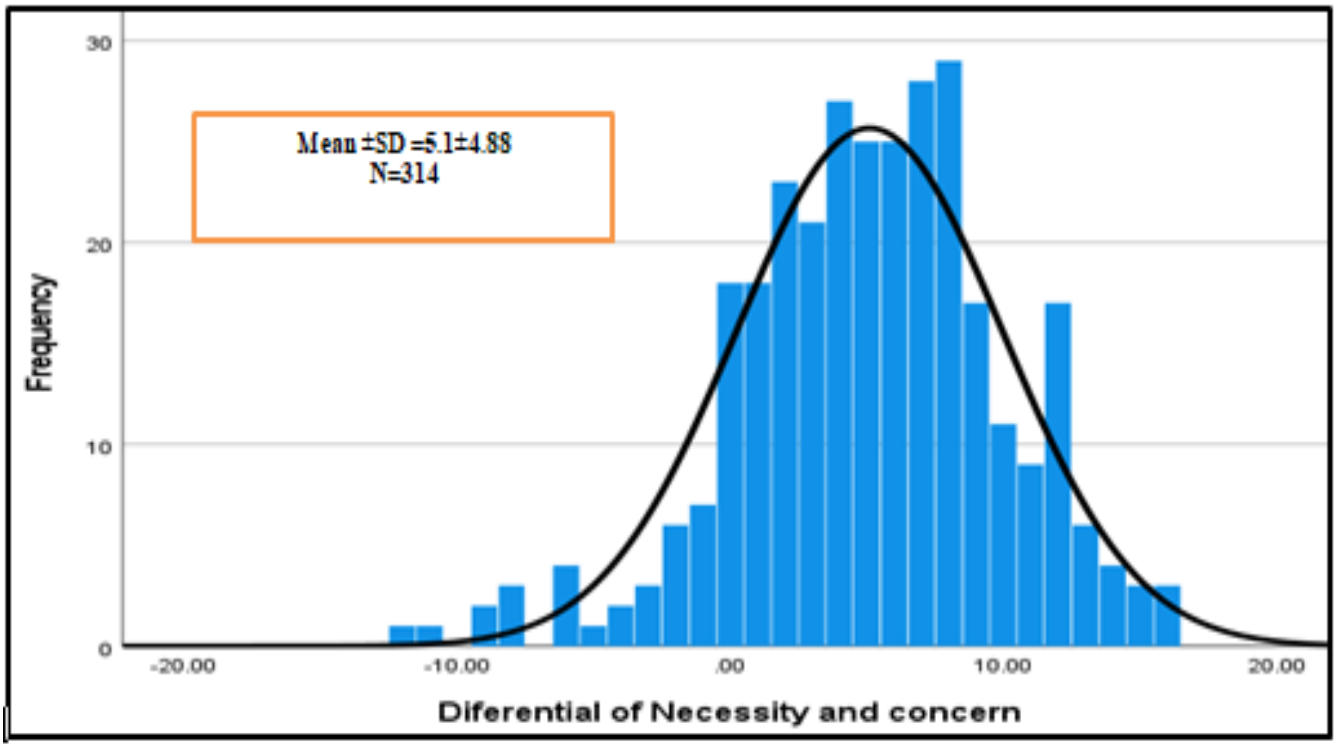

Mean ±SD =5.1±4.88
N=314
Frequency
Diferential of Necessity and concern

Figure 1: Histogram plot of the frequency distribution of SN and SC with their differentials

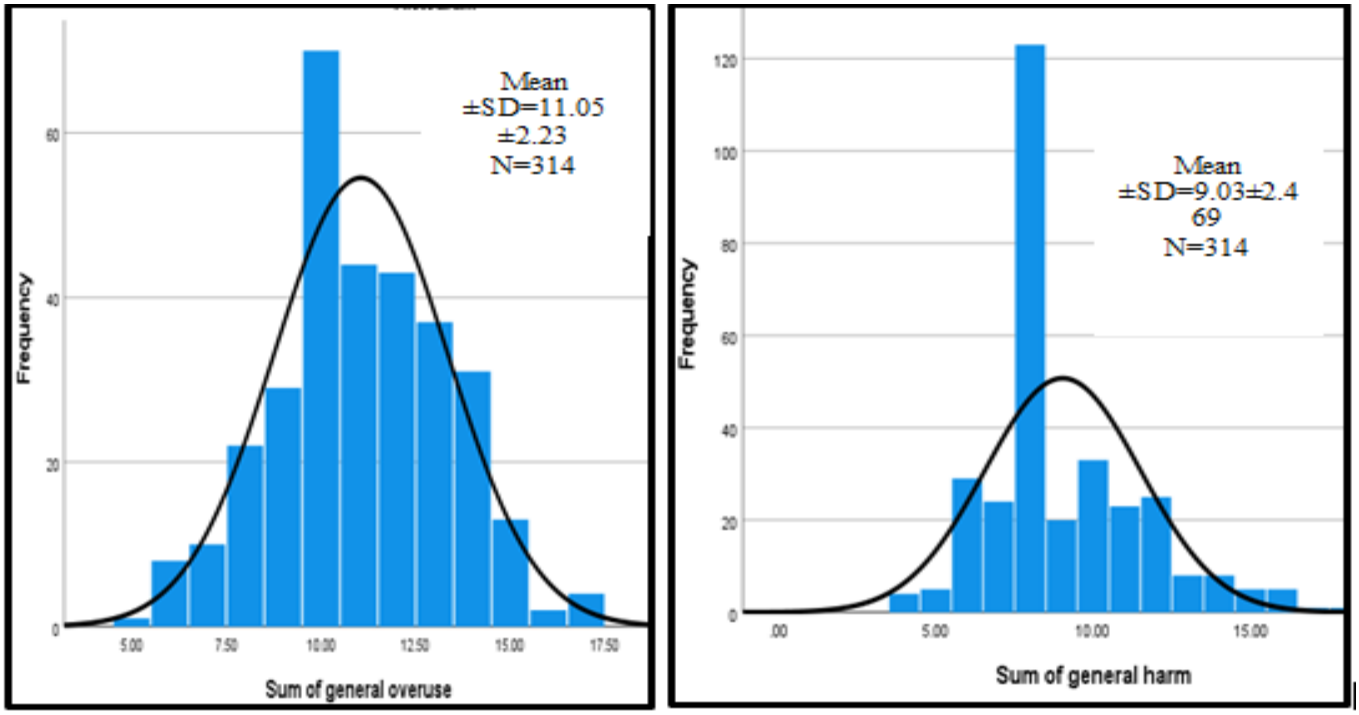


Figure 2: Histogram plot of the frequency distribution of general overuse and harm

4.4.3. Attitudinal Analysis of BMQ of HF Patients

A very small respondent of 1/314 (0.318%) placed under the disengaged/differential category (low necessity/low concern) didn't believe that their medication was important and also expressed no concern. In contrast, 9/314 (2.866%) respondent's fall into the Skeptical category, believing their medications weren't essential while simultaneously worrying about side effects. Out of the total sample, 55/314(17.5%) lay under the axis of low concern/high necessity. Finally, the majority of the study participants were under the category of Ambivalent, 249/314(79.3%) responded results were within the quadrant of high concern /high necessity. Figure 4

Table 5; Attitudinal analysis of BMQ-10 ofHF patients (n=314) in ACSH, Mekelle, Tigray, Ethiopia.

	Level	Specific concern		Total
		Low	High	
Specific necessity	Low	N=1(0.318%)	N=9(2.866%)	10(3.2%)
	High	N=55(17.5%)	N=249(79.299%)	304(96.8%)
Total		56(17.8%)	258(82.2%)	314

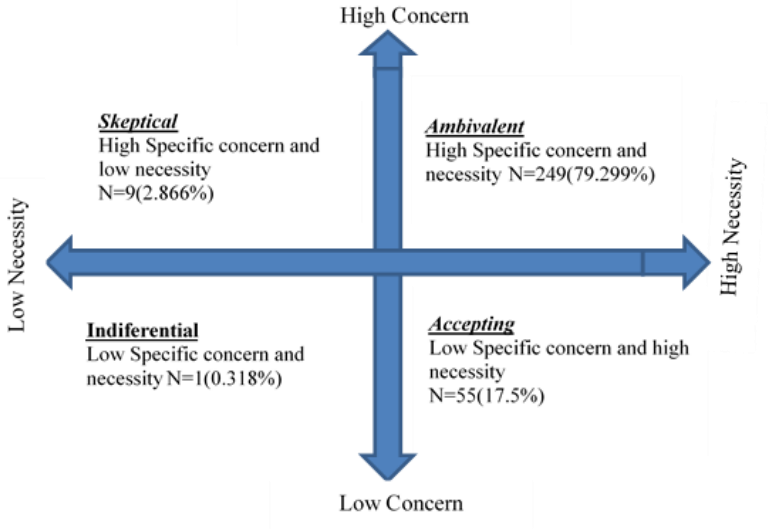


Figure 3: Four quadrant frequency distribution of specific necessity and concern

4.4.4. Distribution of Socio-Demographic and Clinical Characteristics with Beliefs about Medications in HF Patients

Among individuals aged 18-39, an impressive 99 out of 100 (99%) reported high SN, with 74 out of 100 (74%) expressing high concerns about overuse. The gender analysis reveals that 158 out of 163 females (96.9%) had high SN, while 127 out of 151 males (84.1%) indicated high levels of concern, suggesting a similar perception of necessity across genders. Additionally, residence plays a significant role, as rural residents showed a lower percentage of high SN (94.3%), compared to urban residents at 97.8%. However, the scores for SC, overuse, and harm between the two residences were relatively close, with no more than 2.2% differences.

Table 6; Distribution of socio-demographic and clinical characteristics across medication belief subscales of HF Patients at ACSH, Tigray, Ethiopia, 2024(n=314)

Characteristics	Level	SN		SC		G. Overuse		G.Harm	
		Low /%	High /%	Low /%	High /%	Low /%	High /%	Low /%	High /%
Age in years	18-39	1/1	99/99	18/18	82/82	26/26	74/74	68/68	32/32
	40-59	5/4.9	98/95.1	16/15.5	87/84.5	8/17.5	85/82.5	65/63.1	38/36.9
	60-74	3/3.3	88/96.1	20/22	71/78	23/25.3	68/74.7	62/68.1	29/31.9
	75-87	1/5	19/95	2/10	18/90	3/15	17/85	10/50	10/50
Gender	Male	5/3.3	146/96.7	24/15.9	127/84.1	37/24.5	114/75.5	96/63.6	55/36.4
	Female	5/3.1	158/96.9	32/19.6	131/80.4	33/20.2	130/79.8	109/66.9	54/33.1
Residence	Rural	5/5.7	82/94.3	16/18.4	71/81.6	18/20.7	69/79.3	58/66.7	29/33.3
	Urban	5/2.2	222/97.8	40/17.6	187/82.4	52/22.9	175/77.1	147/64.8	80/35.2
Marital status	Single	0/0	39/100	4/10.3	35/89.7	12/30.8	27/69.2	26/66.7	13/33.3
	Married	9/3.9	223/96.1	43/18.5	189/81.5	51/22	181/78	149/64.2	83/35.8
	Widowed	1/4.3	22/95.7	7/30.4	16/9.6	3/13	20/87	14/60.9	9/39.1
	Divorced	0/0	20/100	2/10	18/90	4/20	16/80	16/80	4/20
Education	No formal	7/6.9	94/93.1	24/23.8	77/76.2	29/28.7	72/71.3	71/70	30/29.7
	Educated	3/1.4	210/98.6	32/15.0	181/85	39/18.5	172/81.5	134/63	79/37
Religion	Orthodox	10/3.3	290/96.7	55/18.3	245/81.7	69/23	231/77	195/65	105/35
	Muslim	0/0	12/100	1/8.3	11/91.7	1/8.3	11/91.7	9/75	3/25
	Catholic	0/0	2/100	0/0	2/100	0/0	2/100	1/50	1/50
Employee	Unemployed	2/2.1	93/97.9	19/20	76/80	24/25.3	71/74.7	62/65.3	33/34.7
	Employed	8/3.6	211/96.4	37/16.7	182/83.1	46/21	173/79	143/65	76/35
M.Income in birr	<5000	9/4.6	186/95.4	40/20	155/79.5	41/21	154/79	129/66.2	66/33.8
	≥5000-10000	1/1	98/99	13/13.1	86/86.9	24/24.2	75/75.8	64/64.6	35/35.4
	≥10000	0/0	20/100	3/15	17/85	5/25	15/75	12/60	8/40
Duration of HF Dx	<5 years	134/63	77/36.5	37/17.5	174/82.5	48/22.7	163/77.3	134/63.5	77/36.5
	≥5-10 years	58/66.7	29/33.3	15/17.2	72/82.8	20/23	67/77	58/66.7	29/33.3
	≥10 years	13/81.3	3/18.8	4/25	12/75	2/12.5	14/87.5	13/81.3	3/18.8
presence of co morbidity	Yes	165/65	88/34.8	42/16.6	211/83.4	50/19.8	203/80.2	165/65.2	88/34.8
	No	40/65.6	21/34.4	14/23	47/77	20/32.8	41/67.2	40/65.6	21/34.4

M.Income=monthly income in birr, SN=specific necessity, SC= specific concern,G.harm=general harm, G.overuse=general overuse and low/p=frequency distribution and percentage of low (SN,SC,G.harm and G.overuse

4.4.5. Evaluation of BMQ with HF Patient Baseline and Clinical Characteristics

Specific necessity of HF patients was significantly correlated at 95% CI with monthly income, and years of treatment started. Factors like residence and the number of types of medication they take per day had very little difference and correlation on specific medication beliefs of patients whereas, age, gender, employee statuses, source of medication, and presence of co morbidities didn't have any difference among their groups on affecting medicine beliefs.

The distribution of respondents highlights ten out of 314 respondents had a low necessity score (0-12.5) and 304/314 high necessity score (13-25). In addition out of the total 87 respondents that laying the range of 6-10years of treatment, all of them were in the range of 13-25 SN scores. A small number of respondents (16/314) were treated above ten years as clinically confirmed HF patients and all had a strong belief in their treatments (13-25 scored). HF patients with 6-10-year years of treatment tend to have the highest mean rank, and the post-hoc analysis suggests that participants in this group perceive their SN more strongly (Kruskal Walliesp=0.024,Table 7)compared to those with a shorter duration (less than 5 years) or a longer duration (greater than 10 years). Overall the duration of their treatment had a positive correlation (r =+0.169), with SN at 95% CI (P=0.003).

The SN of patients had a positive correlation (r=+0.144, p=0.011,Table 7)with their income. The result shows a statistically significant (p=0.024,Table 7)difference in the mean ranks of SN across different monthly income categories. The posthoc analysis identifies two homogeneous subsets: the first subset includes the group earning less than 5000 birr, while the second subset consists of the 5000-10000 and greater than 10000 groups, indicating that these two latter groups share similar average ranks with Kruskal Walliesp-values of 0.533 and 0.375, suggesting no significant differences among the groups in each subset. Therefore, only the less than 5000 birr group shows a significant difference compared to the higher income categories. The patients under an income level of <5000 birrs per month had the lowest mean rank, indicating that lower income is less associated with SN as compared. Table 7

The SC was affected by marital status, educational status, and monthly income. The patients of divorced (18/20) and single (35/39) had the highest mean rank value as compared to the others with a

p-value of 0.041. Overall, the study result highlights notable differences in SC across marital status with single and divorced individuals showing a higher level of concern towards their medication as compared to their married counterparts. Table 7)

General overuse had a significant positive correlation (p=0.03, 0.001, and 0.018) with age, SC, and SN respectively. Similarly, general harm also had a positive association with SC and overuse (p=0.001) but negative correlations (rho=-0.135) with SN.

Table 7; Spearman and Kruskal Wallies correlation analysis BMQ with clinical and baseline characteristics (n=314) in ACSH, Mekelle, Tigray, Ethiopia.

Variable		Levels	N	KruskalWallies/U-test		Spearman Correlation	
				Mean rank	p-value	Coefficient	P-value
Specific necessity	Monthly income in birr	<5000	195	147.19	0.024	+0.137	0.015
		1000-10000	99	177.39			
		>10000	20	159.53			
		Average income				+0.144	0.011
	Duration of HF Rx	<5 years	211	148.13	0.024	+0.143	0.011
		6-10 years	87	179.23			
		>10 years	16	162.88			
	Duration of HF Rx					+0.169	0.003
Specific concern	Marital status	Married	232	149.87	0.041		
		Single	39	185.82			
		Divorced	20	191.08			
		Widowed	23	157.22			
	Educational status	No formal	101	143.91	0.222		
		Primary	71	155.5			
		Secondary	91	166.35			
		Diploma or above	51	171.41			
	Monthly income	<5000	195	149.09	0.084	0.114	0.043
		1000-10000	99	173.94			
		>10000	20	158.13			
		Average income				+0.114	0.043
	General Overuse	Low score	70	125.08	<0.001	+0.192	<0.001
		High score	244	166.80			
	General harm	Low score	205	140.51	<0.001	+0.258	<0.001
		High score	109	189.45			
General overuse	Age					0.137	0.015
	Place of residence	Urban	227	150.1	0.018	----------	----------
		Rural	87	176.81			-
	Educational status	No formal	101	160.84	0.965	----------	---------
		Primary	71	157.92			
		Secondary	91	155.65			
		Diploma or above	51	153.62			
	Specific concern					0.199	<0.001
	Specific necessity					0.134	0.018
	Age					0.123	0.03
General harm	Overuse					0.358	<0.001
	Specific necessity					-0.135	0.017
	Specific concern					0.32	<0.001

P=0.05 or 95%CI for correlation and Kruskal Wallies, r=spearman correlation coefficient,

4.5. Results of Medication Adherence

4.5.1. Medication Adherence and MMAS-8 Frequency Distribution of HF Patients

Forgetfulness was the most common challenge and respondents of this study reported 118/314 (37.6%) forgot to take their medicines. Among the target respondents, a total of 196 (62.4%), 228 (72.6%), 223 (71%), and 231 (73.8%) answered "no" to the first three questions and "yes" to the fourth. The questions included: "Do you sometimes forget to take your medicine?", "Do you sometimes miss taking medicines for reasons other than forgetting?", "When you travel or leave home, do you sometimes forget to bring along your medicine?", and "Did you take all your medicines appropriately the last time they were prescribed for you?" respectively. Overall the median score and inter-quartile range of the participant's MMAS-8 results were recorded as 6.75 and 4.75 up to 7.81 respectively, which showed the participants had non-adherence to their medications.

Based on the respondent's score–above one-third of the participants had consistently followed their HF medication. The comparable number of patients, 130/314 (41.4%) fall into the low adherence; this indicates that these HF patients may be struggling with some aspects of their treatment regimen. More than half 184/314 (58.6%) of the participants were adherent. Table 8

Table 8; Frequency distribution and percentage of Morisky 8-Item Medication Adherence of HF adult patient patients (n=314)

Morisky Medication Adherence Questionnaire-8-Item			Yes	No	
Do you sometimes forget to take your medicine?			118 (37.6)	196(62.4)	
People sometimes miss taking medicines for reasons other than forgetting. Thinking about the last time you took medicines, were there any when you did not take your medicine?			86(27.4)	228 (72.6)	
Have You ever cut back or stopped taking your medicine without telling your doctor because you felt worse on the last date of taking your medication?			54(17.2)	260 (82.8)	
When you travel or leave home, do you sometimes forget to bring along your medicine?			91(29.0)	223(71.0)	
Did you take all your medicines appropriately the last time they were prescribed for you?			231(73.8)	83(26.4)	
When you feel well, do you sometimes stop taking your medicine?			46(14.6)	268 (85.4)	
Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your Treatment plan?			63(20.7)	242(79.3)	
How often do you have difficulty remembering to take all your medication?	Usually	Sometimes	Once in a while	Never/rarely	All times
	18(5.7)	65(20.7)	100(31.8)	131(41.7)	0
	Mean (SD)		6.1 ±1.8		
	Median (IQR)		6.75(4.75-7.81)		

Note: the value/label of yes, no, and Likert scale was elaborated in the methodologies part

Table 9; Three categories of adherence of HF patients based on MMAS-8 in ACSH, Mekelle, Tigray, Ethiopia (n=314)

Adherence	MMAS-8 Score	Frequency	Percent
High	≥7-8	127	41.4%
Moderate	≥6 -7	57	18.2 %
Low	<6	130	41.4 %

Note: The MMAS-8 score is calculated by summing the responses from the eight questions of the MMAS-8 questionnaire, reflecting participants' medication adherence in three levels.

Table 10; Adherent and non-adherent categories of HF patients based on MMAS-8 in ACSH, Mekelle, Tigray, Ethiopia (n=314)

Adherence	MMAS-8 score	Frequency	Percent
Adherent	≥6	184	58.6 %
Non-adherent	<6	130	41.4%

Note: The MMAS-8 score is calculated by summing the responses from the eight questions of the MMAS-8 questionnaire, reflecting participants' medication adherence in two levels.

4.5.2. Impact of Socio-demographic Characteristics on Medication Adherence in HF Management

Younger individuals aged 18-39 years show a concerning trend, with 66/100 non-adherents (66%) compared to 34/100 adherents (34%). However, adherence levels declined further in the older age brackets, where only 14/20 non-adherents (80%) were recorded among those aged 75-87 years. Females exhibit higher non-adherence rates, with 98/163 non-adherents (60.1%) versus 65/163 adherents (39.9%). The impact of residence, the respondents had similar levels of adherence to their medication, specifically 52/87 individuals were non-adherent (59.7%) in rural and 135/227 participants were non-adherent (59.5%).Among the marital status divorced, individuals displayed higher non-adherence rates (70%) followed by single individuals, 25 out of 39were non-adherent (64.1%) and, married individuals showed a lower rate of non-adherence, with 137/232 (59%) but higher than widowed (47%). The adherence levels among employed individuals indicate a more favorable distribution across high adherence categories.

Table 11: Distribution of adherence across different socio-demographic characters of HF patients at ACSH, Tigray, Ethiopia, 2024(n=314)

Characteristics	Level	Adherence		Adherence		
		Non-adherent	Adherent	Low	Moderate	High
Age in years	18-39	66 (66.0%	34(34.0%)	32(32%)	36(36%)	32(32%)
	40-59	56(54.3%)	47(45.6%)	34(33%)	35(34%)	34(33%)
	60-74	51 (56%)	40(43.9%)	30(33%)	27(29.7%)	34(37.4%)
	75-87	14(80%)	6(20%)	8(40%)	7(35%)	5(25%)
Gender	Male	89 (58.9%)	62(41%)	51(33.7%)	52(34.4%)	48(31.7%)
	Female	98(60.1%)	65(39.9%)	53(32.5%)	53(32.5%)	57(34.96%)
Residence	Rural	52(59.7%)	35(40.2%)	29(33.3%)	26(29.9%)	32(36.78%)
	Urban	135(59.5%)	92(40.5 %)	75(33.03%)	79(34.8%)	73(32.2%)
Marital status	Single	25(64.1%)	14(34.9%)	11 (25.83%)	16(23.26%)	12 (24.84%)
	Married	137(59%)	95(41%)	81(34.9%)	73 (31.5%)	78 (33.6%)
	Widowed	11(47.8%)	12(52.2%)	6(26%)	7(30.4%)	10(43.5%)
	Divorced	14(70%)	6(30%)	6(30%)	7(35%)	7(35%)
Education	No formal	60(59.1%)	41(40.1%)	33(32.6%)	32(31.6%)	36(35.6%)
	Educated	127(59.6%)	86(40.4%)	71(33.3%)	73(34.27%)	63(29.6%)
Religion	Orthodox	181(60.3%)	119(39.6%)	101(33.7%)	102(34%)	97(32.3%)
	Muslim	6(50%)	6(50%)	3(25%)	3(25%)	6(50%)
	Catholic	0(0)	2(100%)	0(0%)	0(0%)	2(100%)
Employee status	Unemployed	64(67.4%)	31(32.6%)	32(33.7%)	36(37.9%)	27(28.4%)
	Employed	123(56.2%)	96(43.8%)	72(30.1%)	69(28.9%)	78(32.6%)
Monthly Income in birr	<5000	116(59.5%)	79(40.5%)	69(35.4%)	61(31.3%)	65(33.3%)
	≥5000-10000	58(58.6%)	41(41.41%)	25(25.3%)	40(40.4%)	34(34.3%)
	≥10000	13(65%)	7(35%)	10(50%)	4(20%)	6(30 %)

4.5.3. Exploring Adherence Variability in HF Patients: Clinical Factors

A total of one-fourth of the study participants treated for over ten years only were non-adherent. This trend suggests that as the duration of HF diagnosis increases, adherence tends to improve. Interestingly, study participants with co morbidities display slightly higher adherence, suggesting that co morbid conditions may not complicate treatment regimens and affect adherence negatively. The number of medications also plays a crucial role in adherence. As the number of medications increases, adherence rates fluctuate, with patients on two medications showing 38% adherence and those on three medications at 36.9%. However, adherence slightly increases again with four medications at 43.2% and five medications at 40.8%. This inconsistency may indicate that while more medications can increase complexity, patients may also become more engaged in their treatment as the number of medications rises.

Patients who perceive a low necessity for medication exhibit a stark 100% non-adherence rate. Conversely, those with high beliefs about necessity show adherence at 58.2%. Patients who express low concerns about their medications tend to have higher adherence rates (53.6%). This indicates that if patients trust their medication and have fewer worries about side effects, they will be more likely to take their medications as prescribed. On the other hand, patients with high concern levels are more likely to be non-adherent (62.2%). This suggests that fears about potential side effects of the medication can lead to reluctance in adhering to treatment. A total of 114 non-adherents (55.6%) perceive their medications as posing low harm, while 91 adherents (44.4%) share this view. This indicates that a majority of patients feel confident about the safety of their medications, but have a higher rate of non-adherence. Conversely, among those who perceive high harm, 73 non-adherents (67%) believe their medications could be harmful, while only 36 adherents (33%) share this concern. Examining overuse, 46 non-adherents (65.7%) do not worry about the overuse of medications, compared to 24 adherents (34.3%). This indicates that a substantial portion of non-adherents feel comfortable with their treatment regimens. In contrast, among patients concerned about overuse, 141 non-adherents (57.8%) believe they might be overusing their medications, while 103 adherents (42.2%) share this concern. Finally, the presence of drug-drug interactions (DDI) does not spastically significant to alter adherence, with 41.6% of patients remaining non-adherent

in the presence of DDI, compared to 39.2% who are non-adherent when no DDI is present. This slight difference suggests that while DDI is a concern, it may not be the primary factor affecting adherence compared to other variables like co morbidity and patient beliefs.

Table 12: Distribution of adherence across different clinical characters and perception of HF patients at ACSH, Tigray, Ethiopia, 2024(n=314)

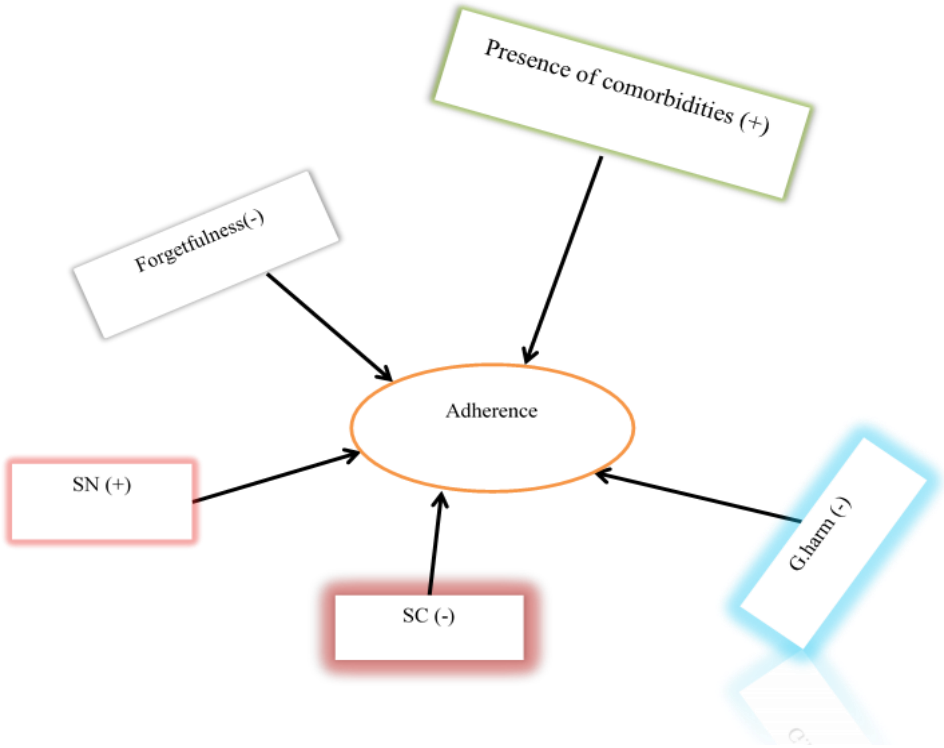
Character	Categories	Adherence		Adherence		
		Non –adherents	Adherents	Low	Moderate	High
Duration of HF Rx	<5 years	128(60.7%)	83(39.3%)	71(33.6%)	73(34.6%)	67(31.8%)
	5-10 years	55(63.2%)	32(36.8%)	32(36.8%)	28(32.2%)	27(31%)
	10 years	4(25%)	12(75%)	1(6.3%)	4(25%)	11(68.8%)
Presence of co morbidity	Yes	145(57.3%)	108(42.7%)	79(31.2%)	81(32%)	93(36.8%)
	No	42(68.8%)	19(31.1%)	25(41%)	24(39.3%)	12(19.7%)
Number of medication	One	0(0%)	2(100%)	0(0%)	0(0%)	2(100%)
	Two	26(61.9%)	16(38%)	16(38%)	15(35.7%)	11(35.7%)
	Three	53(63.1%)	31(36.9%)	23(27.4%)	36(42.9%)	25(29.8%)
	Four	50(56.8%)	38(43.2%)	26(29.5%)	28(31.8%)	34(38.6%)
	Five	58(59.2%)	40(40.8%)	39(39.8%)	26(26.5%)	33(33.7%)
BMQ-SN	Low	10(100%)	0(0%)	9(90%)	1(10%)	0(0%)
	High	177(58.2%)	127(41.8%)	95(31.25%)	104(34.2%)	105(34.5%)
BMQ-SC	Low	26(46.4%)	30(53.6%)	19(33.9%)	11(19.6%)	26(46.4%)
	High	161(62.2%)	97(37.6%)	85(32.9%)	94(36.4%)	79(30.6%)
BMQ-harm	Low	114(55.6%)	91(44.4%)	53(26%)	75(36.8%)	76(37.3%)
	High	73(67%)	36(33%)	50(45.9%)	30(27.5%)	29(26.6%)
BMQ-overuse	Low	46(65.7%)	24(34.3%)	22(31.4%)	29(41.4%)	19(27%)
	High	141(57.8%)	103(42.2%)	82(33.6%)	76(31.1%)	86(35.2%)
Presence of DDI	Yes	97(58.43%)	69(41.6%)	93(33.8%)	89(32.4%)	93(33.8%)
	No	90(60.8%)	58(39.2%)	11(28.2%)	16(41%)	12(30.8%)

4.5.4. Analysis of Demographic and Clinical Factors Influencing Adherence

There were no statically significant relationships between age ($p = 0.67$, 95% CI), gender ($p = 0.883$ 95%CI), and residence ($p = 0.84$, 95% CI) with adherence levels. Marital status also lacked statically significant differences ($p = 0.563$), although widowed individuals demonstrated a higher mean rank in adherence. Other factors, such as employment status, monthly income, and presence of DDI similarly showed no statically significant relationships with adherence. Finally, Individuals with co morbidity don't have a significant association (U-test, $p=0.053$) but it is close enough to imply a potential trend. Importantly, SN ($rho= +0.27$, $p < 0.001$), and general harm perceptions ($rho= -0.27$, $p < 0.001$), emerged as a statically significant factor. Overall, while demographic and clinical characteristics showed limited impact, focusing on specific patient necessities and perceptions of harm could enhance adherence strategies in this population.

Table 13: Factors influencing adherence of HF patients at ACSH, Tigray, Ethiopia, 2024(n=314)

Characteristics	Level	Kruskal wallis/U-test			Correlation	
		N	Mean rank	p-value	rho	p-value
Age in years	18-39	100	154.45	0.67	0.25	0.66
	40-59	103	155.79			
	60-74	91	166.12			
	75-87	20	142.36			
Gender	Male	151	156.73	0.883	----------	----------
	Female	163	158.22			
Residence	Rural	227	158.14	0.84	----------	----------
	Urban	87	155.84			
Marital status	Married	232	155.08	0.563	----------	----------
	Single	39	159.18			
	Divorced	20	153.18			
	Widowed	23	182.28			
Education	No formal	101	155.98	0.076	-0.07	0.22
	Primary	71	179.46			
	Secondary	91	153.00			
	Educated	51	137.98			
Religion	Orthodox	300	155.66	1.00	----------	--------
	Muslim	12	183.88			
	Catholic	2	275.50			
Employee status	Unemployed	95	149.15	0.244	---------	---------
	Governmental	86	151.38			
	Private	63	176.92			
	Farmer	70	158.87			
Monthly In-come in birr	<5000	195	154.08	0.410	0.04	0.505
	≥5000-10000	99	166.88			
	≥10000	20	144.40			
Presence of DDI	Yes	275	156.92	0.761	----------	----------
	No	39	161.6			
Presence of co morbidities	Yes	253	162.32	0.053	----------	----------
	No	61	137.52			
Specific necessity					+0.27	<0.001
General harm					-0.15	<0.007
Duration of HF under treatments					0.037	0.51
Number of co-morbidities					0.046	0.416
Number of types of medication					-0.001	0.979
Specific concerns					-0.097	0.086
Total DDI					0.010	0.853



Note: Positive (+) indicated incresae adherence level and negative (-) decrease adherence level

Figure 4: Factors Influencing Adherence

4.6. Potential Drug-Drug Interaction (DDI) of HF Patient

4.6.1. Analysis of Medication Interactions and Their Severity in HF

The median of medication prescribed was approximately four. The maximum number of DDIs recorded for a single patient was twelve, representing the highest interaction burden observed. In total, there were 993 DDIs among 314 patients, which is equivalent to 316.24% of the sample size, indicating that the total sample experienced interactions averaging three times the sample size, with occurrences ranging from zero to twelve per patient. A significant majority, 275 out of 314 patients (87.6%), experienced DDI, with moderate interactions being the most common at 258 out of 314 (82.2%). Additionally, 69 out of 314 patients (22%) faced severe interactions.

As low DDI was the major interaction, aspirin emerged as the most interactive drug with proton pump inhibitors (PPI), beta-blockers, and diuretics in 192/993(19.3%) of a total drug interaction. Beta-blockers also interact with atorvastatin in addition to aspirin, 99/993(10%) of the interaction

experienced in respondent HF patients. The third most frequent low drug interaction was recorded on diuretics, spironolactone, and furosemide 80/993(8.14%) and 55/993 (5.6%) with different classes of medication respectively.

With the sum of DDI recorded, 665 from a total of 993/314 HF patients had moderate interaction, and the maximum interaction that occurred was nine. Diuretics was the most frequent interaction recorded class of drugs with a wide array of medications in 321/993 (32.32%) of interactions. Following diuretics, beta-blockers were recorded close to it, accounting for 24.67%, notable with diuretics and digoxins.

Lastly 69/993(6.95%) of the total respondents experienced severe DDI with a maximum of two severe interactions per patient recorded. Spironolactone was the most severely interactive drug, particularly with enalapril as more frequent and losartan one time from a total target. Other notable severe interactions were experienced among warfarin with aspirin and clopidogrel, and clopidogrel with omeprazole and warfarin.

Table 14; Evaluation of DDI of HF patients based on DDIneter.com online database in ACSH, Mekelle, Tigray, Ethiopia (n=314)

Medication characteristics	Category	Frequency	Percent
Number of medications per patient	Mean ± SD	3.73 ±1.1	
	Median (range)	4(1-5)	
Presence of drug interaction	Yes	275	87.6%
	No	39	12.4%
Presence of low drug interaction	Yes	166	52.9%
	No	148	47.1%
Presence of moderate drug interaction	Yes	258	82.2%
	No	56	17.8%
Presence of severe drug interaction	Yes	69	22%
	No	245	78%
Multiple drug interactions developed	Low and moderate drug interaction	104	33.1%
	Low and severe drug interaction	2	0.6%
	Moderate and severe drug interaction	11	3.5%
	Low, moderate, and severe drug interaction	46	14.6%
	No or only one type of interaction	151	48.1%
Number of drug interactionsper patient	Mean ± SD	3.13± 2.6	
	Median (range)	3(0-12)	
	Total DDI (n=314)	993	
Drug interaction per patient	One interaction	69	22.4%
	Two interaction	47	15.0%
	Three interaction	46	14.6%
	Four interaction	23	7.3%
	Five interaction	38	12.1%
	Six to twelve interaction	52	16.2%
	No interaction	39	12.4%

Table 15;Low DDI of adult heart failure patients based on DDIneter.com online database at ACSH, Mekelle,Tigray,Ethiopia(n=314 and total interaction =993)

Pharmacologic class		Interaction with	Frequency	Percent
Betablocker		Asprin and ,atorvastatin	99	10.0%
Diuretics	Spirolacton	asprin,digoxin,and warfarin	80	8.14%
	Furosemid	asprin,omeprazole,PTU,and phyntoin	55	5.6%
Digoxin		Spirnolactone ,and cimetidine	27	2.75%
Warfarin		Spirnolactone ,and atorvastatin,	34	3.46%
Asprin		Betabloker ,PPI,and diuretics,	192	19.55%
Statins		Asprin,warfarin,and propranolol	10	1%
PPI		Asprin	7	0.7%
CCB		Enalapril	12	1.2%
Total		Sum from 993(n=314)	262	26.4%
		Mean ± SD (n=314)	0.83 ±0.935	
		Range	0-12	

Note: The sum of DDI is not the sum of frequency in the table rather it is the sum of low interaction per patients

Table 16; Moderate DDI of adult HF patients based on DDIneter.com online database at ACSH, Mekelle, Tigray, Ethiopia (n=314 and total DDI interaction =993)

Pharmacologic class	Interaction with	Frequency	Percent
Betablocker	Digoxin ,diuretics ,NPH, amlodipine, salbutamole, PTU, amiodaron, cimetidine,and glibenclamid	245	24.67%
Diureticts	Digoxin, sildenafil, ACEI, beta-blocker, metformin, PPI, phenobarbital, ceftriaxone, glibenclamide, vancomycin, and prednisolone	321	32.32%
Digoxin	ACEI,diuretics, betablocker, ASA,PTU, PPI, and statins	100	10%
ASA	ACEI, NPH, beta-blocker, CCB, clopidogrel, PPI,digoxin, prednisolone,glibenclamide, methotrexate, and lisinopril	141	14.2%
ACEI	Digoxin, sildenafil, diuretics, ASA, NPH, metformin, heparin,	162	16.3%
Warfarin	PPI, diuretics,benzthin pencillin,valporic acid, and cimetidine	8	0.8%
CCB	Statines, ASA, and beta-blocker,	33	3.32%
Clopidogrel	Heaparin, statine, and ASA	14	1.4%
Statines	CCB, PPI, clopidogrel,azythromycin,digoxin,	31	3.12%
Methotrexate	Folic acid and atorvastatin	2	0.2%
Total	Sum	667	67.2%
	Mean ± SD (n=314)	2.12 ±1.85	
	Range	0-9	

Note: The sum of DDI is not the sum of frequency in the table rather it is the sum of moderate interaction per patient

Table 17; Severe DDI of adult HF patients based on DDIneter.com online database at ACSH, Mekelle,Tigray,Ethiopia (n=314 and total interaction =993)

Pharmacologic class	Interaction with	Frequency	Percent
Spironolactone	Enalapril and losartan	49	4.93%
Clopidogrel	Omeprazole and warfarin	2	0.2%
Warfare	ASA, and clopidogrel, amidarone	13	1.3%
Allopurinol	Enalapril	1	0.1%
Amiodarone	Furosemide and warfarin	1	0.1%
Amlodipine	Simvastatin	1	0.1%
Total	Sum	67	6.67%
	Mean ± SD (n=314)	0.21±.44	
	Minimum –Maximum	0-2	

Note: The sum of DDI is not the sum of frequency in the table rather it is the sum of severeinteractions per patient

4.6.2. Evaluation of Association and Correlation of DDI with HF Patient Sociodemographic Characteristics

Older individuals, especially those aged 60-74, show higher mean ranks for DDI, evidenced by a statistically significant p-value of 0.001 and a positive correlation of +0.367. This suggests that the likelihood of experiencing drug interactions increases with age. Marital status approaches significance with a p-value of 0.055, suggesting a potential trend, but it does not reach the conventional threshold of 0.05. In contrast, gender, residence, education, religion, and monthly income show no significant difference across them on DDI, as evidenced by high p-values (e.g., gender p = 0.165, residence p = 0.517, education p = 0.959, and religion p = 0.980). Table 18

Table 18: Kruskal Wallis and U-test evaluation ofthe association of DDI with the socio-demographic character of HF patients at ACSH, Tigray, Ethiopia, 2024(n=314)

Characteristics	Level	Kruskal-Wallis /U-test			Correlation (rho)	
		N	Mean rank	p-value	Rho	p-value
Age in years	18-39	100	118.48	0.001	+0.367	0.001
	40-59	103	148.71			
	60-74	91	204.55			
	75-87	20	183.8			
Gender	Male	151	164.81	0.165	----	-------
	Female	163	150.73			
Residence	Rural	227	159.54	0.517	------	---------
	Urban	87	152.19			
Marital status	Married	232	162.92	0.055	---------	--------
	Single	39	124.56			
	Divorced	20	140.13			
	Widowed	23	173.73			
Education	No formal	101	158.77	0.959	-0.006	0.917
	Primary	71	154.13			
	Secondary	91	160.65			
	>diploma	51	154.06			
Religion	Orthodox	300	157.69	0.98	-------	----------
	Muslim	12	152.5			
	Catholic	2	158.75			
Monthly Income in birr	<5000	195	155.66	0.814	0.03	0.593
	≥5000-10000	99	158.8			
	≥10000	20	168.63			

4.6.3. Evaluation of Association and Correlation of DDI with HF Patient Clinical Characteristics

The duration of treatment (Rx) shows significant differences across categories, with a p-value of 0.003 indicating that patients on treatment for less than 5 years have a lower mean rank (149.39) compared to those on treatment for 5-10 years (164.29) and over 10 years (227.53). This suggests that longer treatment durations may be associated with a higher likelihood of experiencing DDIs.

The number of medications taken is another critical factor. There is a statistically significant relationship ($p < 0.001$) indicating that as the number of medications increases, the mean ranks sharply

rise, particularly for those on five medications (236.59), suggesting that polypharmacy significantly elevates the risk of DDIs.Additionally, the number of comorbidities shows a significant correlation with DDIs ($p = 0.001$), indicating that patients with more comorbidities were likely to experience higher interaction rates.

The correlation analysis reveals significant relationships between low drug interactions, moderate and severe drug-drug interactions (DDIs), and several factors. Low DDIs are strongly correlated with age ($r = 0.420$, $p < 0.01$), the number of medication types ($r = 0.646$, $p < 0.01$), duration of heart failure treatment ($r = 0.125$, $p = 0.027$), and the number of co morbidities ($r = 0.131$, $p = 0.02$), suggesting that older patients tend to experience more interactions. Additionally, moderate DDIs show a positive correlation with age ($r = 0.319$, $p < 0.01$), years of HF ($r = 0.057$, $p = 0.318$),co morbidities ($r = 0.139$, $p < 0.05$), and number of type of medications ($r = 0.690$, $p < 0.01$), while the total MMAS-8 scores reveal no significant correlation, indicating that adherence does not significantly affected by the frequency of interactions. Finally, a positive correlation was also seen between severe DDI with age ($r = 0.314$, $p < 0.01$), and number of co morbidities ($r = 0.134$, $p < 0.05$) suggesting that older patients are more susceptible. These findings indicate that age and co morbidities are the most relevant factors related to severe drug interactions, while other variables show limited significance.

Table 19: Kruskal Wallis and U-test evaluation of the association of DDI with the clinical character of HF patients at ACSH, Tigray, Ethiopia, 2024(n=314)

Clinical characteristics	Level	Kruskal-Wallis /U-test			Correlation	
		N	Mean rank	p-value	Rho	p-value
Duration of Rx in years	<5	211	149.39	0.003	0.11	0.06
	≥5-10	87	164.29			
	>10	16	227.53			
Presence of co morbidity	Yes	253	151.92	0.025	------	
	No	61	180.64			
Number of medication	One (1)	2	20	<0.001	0.785	<0.001
	Two (2)	42	36.71			
	Three(3)	84	101.35			
	Four (4)	88	183.8			
	Five (5)	98	236.59			
Number of co-morbidities	No (0)	60	---	0.001	0.785	<0.001
	One (1)	199	112.79			
	Two (2)	51	178.85			
	Three (3)	4	204.75			
Number of low DDI					0.763	<0.001
Number of moderate DDI					0.916	<0.001
Number of server DDI					0.508	<0.001

5. DISCUSSION

The majority 304/314 (96.8 %) of HF patients at ACSH reported a strong belief in the necessity of their medications. This finding aligns with a study finding by Ekman I et al, and Maguire et al where 94% of cardiovascular patients(49) and 93% of hypertensive patients (78)believed their medication made them feel better. Other reports of a study in Frontier Lifeline Hospitals by Mohamud Thayub et al noted that 42% of the patients had a strong belief in the necessity of their medication whereas the response rate was decreased by greater than half of the participants in ACSH (26). The higher belief in medication necessity among HF patients at ACSH is primarily driven by increased disease awareness with longer diagnosis and treatment duration, consistent patient education, and a possibly more supportive healthcare environment. This finding underscores the importance of continuous patient engagement and education in improving medication perception. Interestingly, sociodemographic and clinical factors (like age, gender, income, education level) did not affect the patients' belief in medication at ACSH. This could mean that the hospital's structured education or counseling programs were equally effective across all patient subgroups, creating a more uniform perception of necessity.

The studies on medication beliefs among HF patients and those with other chronic conditions reveal significant variations in their necessity. Participants in ACSH had a mean score of 20 ± 3.19 whereas patients in China studied by S MT *et al*.reported a mean score of 17.61 ± 5.1(26), they had lower SN belief of their medication in comparison to HF patients in Ayder, while Malaysian hypertensive patients result in finding of Tan *et al*had the lowest score (16±3.95)(25). In contrast, in rheumatoid arthritis (RA) patients at King Mill Hospital, the study reported by Neame and Hammond showed a necessity score of 19.92 ± 3.13(48) which is comparable to the response rate of HF patients in this study. Overall HF patients at ACSH, Tigray, Ethiopia had a stronger belief in the need for medication for the management of their cases. This highlights a belief that the importance of their medications is better in comparison to others because of HF is a symptomatic and life-threatening condition, and patients often experience a direct link between medication use and symptom relief (e.g., reduced breathlessness, improved energy). This contrasts with conditions like hypertension, which may remain asymptomatic for years, reducing the perceived urgency of adher-

ence. Furthermore, many ACSH patients likely have a longer disease duration and consistent follow-up, allowing for greater exposure to health education and clinical counseling. This repeated engagement reinforces the importance of medication in managing their illness and preventing complications.

In this study on the SC, we found that 82.2% of participants had a high concern which is five times the finding of Mohamud Thayub et al, at Frontier Lifeline Hospitals.Furthermore, Neame and Hammond reported that only 47.7% of their participants were concerned about potential side effects, a figure significantly lower than the concernobserved in our study. The mean score of SC of our study was 15.88 ± 3.4 which is in line with findings from various studies: Mohamud Thayub et al. reported a score of 13.49 ± 5.1 among Chinese HF patients (26), Tan et al. found 16.60±4.05 in Malaysian hypertension patients (25)and Neame and Hammond reported 15.84 ± 3.53 for rheumatoid arthritis patients at King Mill Hospital(48). However, Mohamud Thayub et al.'s study indicated a lower level of concern among patients regarding their medication. The present study shows most of the participants are concerned about their medication even though the mean score is not as high as in other studies. Patients in low-resource settings like ACSH may have less access to detailed pharmaceutical counseling, which could lead to anxiety or uncertainty about medication safety, interactions, and side effects. Additionally, higher concern may stem from personal or community experiences with adverse drug reactions or complications, increasing patients' vigilance and fear. Furthermore, limited healthcare alternatives and financial constraints could amplify concerns about the consequences of continued medication use, especially if side effects arise and options for changing drugs are limited. In contrast, studies like that of Mohamud Thayub et al. reported lower concern (13.49 ± 5.1 and lower percentage overall), possibly due to differences in healthcare delivery models, patient education levels, or cultural perceptions of medication risks. Therefore, the high concern level in this study reflects a combination of clinical exposure, health system limitations, and patient awareness shaped by local realities.

The NCD analysis of this study was +5.1 which is greater than the finding of Neame and Hammond +4.08 and the greater NCD reveals a stronger belief in the benefit of their medication. The scores for general overuse and harm were 77.7% and 34.7% respectively where 3.5 times higher for over-

use and more than two times higher general harm concern than the findings of Mohamud Thayub eat at Frontier Lifeline Hospitals. The difference between the score of harm and SC (SC-harm) reveals that they were worried about the side effects of their medication rather than the long-term effects of their medication.

The four-quadrant analysis of BMQ-specific according to the midpoint of the SN and SC results of participants was distributed under the four quadrants with high SC and low necessity 2.866%, high SC and necessity 79.299%, low SC and necessity 0.318% and Low SC and high necessity 17.5% but, based on Li Wei et al studies, 45% of patients were classified as high SC and necessity /ambivalent/, 45% as 'Low SC and high SN /Accepting', 4% as High SC and low SN/'Sceptical' and 6% as low SC and necessity /Indifferent(72) where the participants under ambivalent were less as compared to our study results but greater accepting groups. This large group acknowledges the necessity of the treatment while also expressing safety concerns. This indicates a complex relationship where patients understand the importance of the treatment for their health but have reservations about its safety. The combination of low necessity/low concern patients indicated they didn't actively participate in their treatment decisions or prescribed regimens, indicating a potential detachment from their treatment. Patients under Skeptical category didn't view their medication as important and were aware of the potential negative impacts of medication but didn't feel sufficiently compelled by benefits to continue treating their HF. This lack of perceived necessity combined with high concern may lead to inconsistent medication adherence and reflect ambivalence (taking medication but lacking confidence in their necessity). Out of the total sample, 17.5% lay under the axis of low concern/high necessity which, understand the benefit of their medication and remain accepting, indicating that they adhere to their regimen, or may not doubt the treatment's effectiveness or safety. figure 4

The majority of the study participants were under the category of Ambivalent. This is the largest group incorporated, indicating a strong belief in the necessity of their medication while also being aware of and concerned about potential side effects, reflecting a realistic understanding of the medication choice involved in treatment so, participant's accepted the necessity of their treatment with awareness of side effects. Figure 4

Medication beliefs of HF patients were different across various factors. This study highlights that the years of treatments significantly affect necessity beliefs among HF patients. Specifically, patients treated for 6-10 years showed a heightened perception of SN (Kruskal-Wallis H, p=0.024, Table 7)) compared to those treated for less than 5 years or over 10 years. Additionally, median SN scores were similar for urban and rural residents (Mann Whitney U-test, p=0.077), with many from both groups reporting high necessity scores, indicating that beliefs in medication necessity were widespread. Marital status also emerged as significant, divorced and single participants exhibited greater levels of concern, highlighting the potential impact of social support on patients' perceptions of their treatments. The income level of respondents also had a weak positive correlation with SN.

A weak direct positive correlation was found between overuse and SC ($p < 0.001$, $r = 0.199$) and between overuse and SN ($p = 0.018$, $r = 0.134$), which is lower than the moderate correlation reported by Wei Li et al., who found a correlation of ($p < 0.001$, $r = 0.49$) between overuse and SC. Additionally, the study result aligns with previous findings regarding the correlation between general harm and SC, with results showing ($p < 0.001$, $r = 0.32$ which is consistent with those of Wei et al. (72).

Medication adherence is an essential component in the management of HF, a complex condition that requires ongoing treatment and lifestyle adjustments. Despite the significance of adherence, many patients struggle to follow their prescribed regimens, leading to adverse health outcomes. This discussion explores the multifaceted nature of adherence, the barriers faced by patients, and potential strategies to enhance compliance. Our study highlights several key findings related to medication adherence among HF patients, MMAS-eight, socio-demographic factors, and beliefs about medications.

The adherence results in this study, with 40.4% of participants showing high adherence and an equal proportion demonstrating low adherence, are relatively balanced but still point to significant challenges in maintaining consistent treatment behavior, as reflected by the mean MMAS-8 score of 6.1 ± 1.8 and median ± IQR of (6.75 ± 4.75 -7.81). This distribution underscores the challenges many patients face in managing their treatment. In comparison, research conducted on HF patients

by Silavanich et al. at a university in Thailand reported a high adherence rate of 38.3%, a moderate adherence rate of 50%, and a low adherence rate of 11.7% (54). Their study also noted, a greater median ± IQR of MMAS-eight (7.0 ± 1.2) (54), suggesting a more favorable adherence profile than that observed in the present study. Furthermore, the research findings of Jarrah et al on HF patients identified three levels of adherence using the GMAS: 33.5% with high adherence, 19.5% with good adherence, and 47% with low adherence (34). This study reveals a low adherence rate similar to the respondents at ACSH of this study. The weak association between co morbidities and adherence indicates that while some patients may become more vigilant about their health due to multiple conditions, others may feel overwhelmed, leading to decreased adherence. Furthermore, the positive correlation between adherence and beliefs in medication necessity highlights the impact of patient attitudes on adherence behavior, as those who view their medications as essential are more likely to comply. Inconsistent findings across studies, particularly regarding socio-demographic factors, underscore the variability in how different populations experience medication adherence, influenced by local healthcare practices and cultural attitudes.

Overall, 41.4% of respondents in this study were classified as non-adherent. This is similar with those reported in studies conducted in northern Shewa Ethiopia(44%) (31). In contrast, a cohort study by Alalaqi et al. involving CVD patients at Alsader Teaching Hospital and Misan Cardiac Center in Iraq reported higher adherence levels, with 54.1% classified as highly adherent, 27.7% as moderately adherent, and only 18.2% as low adherers, additionally binary classification of adherence of Alalaqi et al shows, 81.8% of these patients were found to be adherent to their medications (56). Another study on HF patients conducted by Amininasab et al. reported a non-adherence rate of 60% and a mean ± SD score of 5.82 ± 2.54 on the MMAS-8(55), which is higher than the findings of this study. Finally, our study had a lower non-adherence rate than, Amininasab et al. and Jarrah et al but higher than Alalaqi et al and Silavanich et al studies. (34,54–56,79)

The analysis of the data reveals limited significant relationships between demographic characteristics and health-related factors. It highlights that demographic factors such as age (Kruskal Wallis, p= 0.67), gender (U-testp = 0.883), residence (U-test, p = 0.84), employment status,(Kruskal Wallis, p= 0.24), and monthly income don’t have any association with adherence which are in line with

finding by Silavanich et al and Amininasab et al(54,55). Factors such as Education levels (kruskal Wallis, p = 0.076),andMarital status (Kruskal Wallis, p = 0.563), also showed no significant relationships with adherence. This finding is consistent with MMAS-8 of HF patients by Silavanich et al (54). In contrast, studies by Amininasab *et al* and Hussein et alindicate adherence is highly associated with education level, co morbidities, and the number of medications per patient(31,55).The present study also found that adherence doesn't differ across the presence of DDI (U-test, p = 0.761). The conflicting finding of Jarrah et al studies by GMAS shows adherence is mainly affected by gender, age, educational level, marital status, patient income level, medication side effects, and presence of co morbidities (34).

The presence of co morbidities may had a very weak difference in the adherence level (p=0.053, U-test).Based on the Mann-Whitney U-test the presence of co morbidities may be associated with an increased level of adherence which is inconsistent with a study conducted in northern Shewa, Ethiopia (31). This increment in adherence may be due to an increase in the patient's awareness about their disease status. This finding is inconsistent with other studies where the presence of co morbidities may decrease the level of adherence (55,79).

Finally, the findings of this study indicate none of the socio-demographic patient factors had a significant difference in medication adherence. This is consistent with Amininasab et al findings (55) and inconsistent with the findings by Jarrah et al. studied GMAS.

Patient's adherence level had a positive weak correlation with SN(r=+0.27),whereas another study also proved that adherence level is associated with a strong belief in medication necessity(80)and negative weak correlation(r=-0.10 and-0.15) with SC and general harm is in lined with other studies (35,80). A systematic review study finds consistent results with our study where general medication beliefs are negatively correlated with medication adherence(50).

The present study reveals that 37.6% of respondents sometimes forget to take their medication, lower than the 51.1% reported in other Ethiopian studies (31). Additionally, 27.4% acknowledged missing doses for reasons other than forgetfulness, compared to 24.9% in the other study who missed doses without reason for over two weeks(31). Moreover, 17.2% admitted to cutting back or

stopping their medication without informing their doctor, while 27.3% in northern Shewa, Ethiopia did so when feeling worse(31). About 29.0% sometimes forgot their medication while traveling; significantly lower than 43.1% reported elsewhere. The adherence rate in this study was 73.8%, compared to 73% in the other study. Concerns about the inconvenience of daily medication were noted by 20.7% here, versus 47.3% in the other study(31). Both studies highlight forgetfulness as a common cause of non-adherence, underscoring the need for targeted interventions.

The results of the study on medication adherence among HF patients reveal several underlying factors contributing to the observed adherence levels and patterns. With 41.4% of respondents classified as non-adherent, the complexity of managing HF, which requires continuous medication regimens and significant lifestyle changes, likely plays a significant role. Many patients face challenges such as forgetfulness, misunderstanding medication instructions, or feeling overwhelmed, hindering adherence. Comparisons with studies by Silavanich et al. and Alalaqi et al. showed lower adherence rates in this study, potentially reflecting differences in patient populations, healthcare systems, or educational initiatives. Notably, demographic factors such as age, gender, and income did not significantly correlate with adherence, suggesting that individual beliefs and experiences may be more influential.

Overall, these results demonstrate that medication adherence in HF patients is shaped by a complex interplay of factors, including treatment complexity, patient beliefs, and external support systems, indicating that targeted educational interventions and supportive care strategies may enhance adherence rates and improve health outcomes.

This is the first study conducted in ACSH and Ethiopia using the online database DDIneter among HF patients. In the study, the complexity of medication management became evident through the analysis of DDIs. On average, each patient was prescribed approximately four medications, with a range of one to five. The study recorded a total of 993 DDIs among 314 patients, indicating a staggering interaction burden, as this represents 316.24% of the sample size. This means that, on average, patients experienced over three interactions, with some individuals facing up to twelve but other study shows a higher average DDI per patient (63).

Among the participants, 275 patients (87.6%) experienced some form of drug interaction where this prevalence was higher than study findings in Bangladesh (56%) (62), India (77.29%) (64), and Brazil (67.8%) (65). Another study conducted by Akbar et al, inPakistan (100%)(81), Sahoo and Gupta, India (99%)(82), Khaled et al., Egypt (95%)(83), and Haq et al,Pakistan (94%)(43)reported a higher rate of drug interaction than our study findings. However, none of them had used a similar drug interaction checker with the present study.

In the present study majority of these interactions were moderate, affecting 258 patients (82.2%) higher than findings in Pakistan (74.6%) (63), following moderate drug interaction minor drug interaction was the next highest rate recorded with 166/314(52.9%) which is more than six times (>6x) the finding in Pakistan(63), while 69 patients (22%) faced severe interactions which are higher than found in Brazil (17.33%)(65). Furthermore, 104 patients (33.1%) exhibited both low and moderate interactions, indicating the challenges in managing multiple medications.

A study conducted at Jimma University, Ethiopia reports a 77.41% of HF patients experienced DDI (66) and this is also inconsistent with our findings. The overall prevalence rate of DDI in HF patients of ACSH, Tigray was recorded neither higher nor lower than the other studies conducted worldwide. Even though it is lower than other studies it was driven by limited access to essential medications, economic constraints, and polypharmacy, exacerbated by war conditions in the region. Inconsistent medication availability forces patients to use alternative drugs, while economic hardships lead to self-medication. The prevalence of multiple prescriptions for chronic illnesses further increases the risk of harmful interactions, complicating patient management in a challenging healthcare environment.

Of the medications frequently prescribed for HF, aspirin emerged as the most frequently involved in minor interactions, contributing to 192 of the total interactions (19.3%). It is often used in combination with proton pump inhibitors, beta-blockers, and diuretics, which is consistent with others (64). Beta-blockers also had significant interactions, particularly with atorvastatin, which affected 99 patients (10%). Diuretics, such as spironolactone and furosemide, showed interactions in 80 (8.14%) and 55 (5.6%) cases, respectively. Overall, 262 minor interactions (26.4%) were recorded,

indicating a need for careful monitoring to prevent decreasing the therapeutic effect of the other medication.

For moderate interactions, 66 of 993 HF patients experienced these, with diuretics being the most frequently interacting class (321 interactions or 32.32%). Beta-blockers were also significant, particularly with digoxin but other studies find beta-blockers the most common interactive drugs with NSAID(45,83) exacerbation of the medical condition of the patient and/or a change in therapy.

Severe interactions, though less common, were still noted in 66 patients (6.64%), with spironolactone being particularly problematic when combined with enalapril and losartan. Other severe interactions involved warfarin with aspirin and clopidogrel and it is consistent with Khaled et al findings(83). These findings underscore the critical need for vigilant monitoring and comprehensive medication management strategies to minimize the risks associated with DDIs in HF patients, ensuring safer therapeutic outcomes and improving overall patient care.

The present study shows different factors had an association with the occurrence of DDIs. Longer treatment durations correlate with higher DDI likelihood ($p = 0.003$). Comorbidities also impact DDIs, with patients having more interactions ($p = 0.025$). Polypharmacy is critical, as increasing medications significantly raises DDI risk ($p < 0.001$). Age, particularly for those 60-74, shows a strong correlation with DDIs ($p < 0.01$). Overall, age and comorbidities are key factors influencing DDIs in patients. These factors are also consistent with other findings as a factor for the occurrence of DDI(66,82,84).

6. LIMITATIONS OF THE STUDY

The study had limitations that should be considered. First, it was conducted at a single center, ACSH,Tigray which may limit the generalizability of the findings to other healthcare settings in Ethiopia and beyond. The cross-sectional design of the study restricts the ability to observe changes in medication beliefs and adherence over time, which could provide a more dynamic understanding of these factors. Additionally, data on medication adherence and beliefs were gathered through self-reported questionnaires, making them susceptible to response bias, as participants might overestimate their adherence and belief due to social desirability. The data was collected after a genocidal war in the region participants misunderstood the questionnaires/ as a form prepared for economic support whereas some of the participants were psychologically affected and responded carelessly.

The evaluation of DDI could also be limited, as it may not encompass all possible interactions, particularly those beyond the common medications prescribed for heart failure. The method for data collection to study DDI was done throw reviewing their medical record from their chart where incomplete medical records were a challenge. Furthermore, the software used to check drug interaction wasn't able to differentiate does dependent interaction among the different medications. For aspirin, 81 mg was mostly prescribed for antiplatelet effect and the software tells as the analgesic dose (300mg) also.

7. CONCLUSION

The study revealed that while patients generally perceive their medications as necessary for managing HF, with a notable percentage expressing high necessity beliefs, concerns regarding potential side effects were also prevalent. This ambivalence may influence their overall attitudes toward treatment, leading to adherence challenges despite acknowledging the importance of medications. However, patients perceive their medication use as excessive, feeling they take too many medications and that others are overmedicated as well. This sentiment may arise from complex treatment regimens and fears of potential drug interactions and side effects. Additionally, it reflects broader societal worries about polypharmacy. Such beliefs can undermine trust in treatment plans, leading to hesitancy in adherence. Overall patient's belief about medication was affected by factors such as monthly income, potential DDI, and years of treatments.

The high rate of non-adherence among HF patients imposes a significant burden on healthcare systems. This study shows socio-demographic, DDI, and clinical characteristics didn't impact adherence but individual perceptions of medication, and forgetfulness play crucial roles in adherence levels among HF patients. Those with high necessity beliefs and low concerns about side effects were more likely to adhere to their treatment regimens. Understanding these factors can help healthcare providers tailor their approaches to encourage better adherence, ultimately leading to improved patient health outcomes and reduced healthcare costs.

Moreover, patients on multiple medications face an increased likelihood of major DDIs, which can lead to adverse outcomes such as hospitalization and higher healthcare costs. Factors such as age, the number of prescribed medications, and the presence of comorbidities play crucial roles in determining the risk of DDIs, particularly among older adults and those requiring polypharmacy. These findings underscore the necessity for healthcare providers to utilize drug interaction checkers and clinical decision support tools, ensuring vigilant monitoring and tailored medication management. Ultimately, addressing DDIs is essential for optimizing HF treatment and enhancing patient safety, warranting further research into effective interventions.

8. FUTURE DIRECTION/RECOMMENDATION

Based on the results of the study, it is essential to develop targeted educational programs that clarify the importance of medications in managing HF, address common misconceptions, and emphasize the consequences of non-adherence. Utilizing the BMQ will allow healthcare providers to assess individual patients' beliefs and concerns, enabling tailored interventions that specifically address these issues. Improving communication between healthcare providers and patients is crucial for fostering trust and understanding regarding medication regimens and their potential side effects. Additionally, establishing a systematic approach to monitor potential DDIs for patients on multiple medications can enhance safety and minimize risks. Developing personalized adherence strategies that consider patients' recall strategy and health literacy will further support compliance. Lastly, conducting further research into the impact of cultural beliefs on medication adherence among heart failure patients in Ethiopia will inform more effective interventions. By implementing these recommendations, healthcare providers can significantly improve medication adherence, reduce the incidence of DDI, and ultimately enhance health outcomes for heart failure patients.

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APPENDICES

Appendix I: Information about the Studies

My name is ……I am a data collector for a master's student Mr Asmelash Araya at the College of Health Sciences, Mekelle University. He is now conducting a study on heart failure management: patient medication adherence, belief on their medication, and the potential drug-drug interaction with their associated factors, in Ayder Comprehensive Specialized Hospital. The main objective of this study is to evaluate the level of patient adherence and belief in heart failure treatments, identify the potential drug-drug interaction, and factors that influence patient adherence, and assess the influence of co morbidities associated with heart failure. The process of this participation is as follows: We ask you a specific question for these things that require participation and we will re-record your answer. Your cooperation also involves allowing us to capture an image of your prescription, which will take less than a minute. Your right not to participate is reserved. Mainly if you do not participate in the study, you will receive equal service with anyone else. Your participation is voluntary. You have the right to ask questions if you don't understand. You reserve the right to leave at any time if you are unhappy with any topic during the question and answer process. However, the knowledge gained from it can be used to find solutions to heart failure management.

We would like to assure you that privacy will strictly be maintained throughout. Your personal information will be maintained through the use of unique identifiers, and through restricting access to the data set to the principal investigator and those working directly with him. The data collected from each participant will be entered into a computer where it will be maintained in password control. Hard copies of completed instruments will be kept in a locked file and will be available only for research study staff.

If you have any questions or would like to receive further information about the study; please contact the following responsible bodies:

Persons to contact:

Asmelash Araya: Project PI

Mob: +251-951148719

E-mail: asmelasharayaashu@gmail.com

My advisor: Mr. Abera Hadgu

E-mail: ahadgu@gmail.com

Consent: I have read the document stated above or it has been read to me by the data collector as I can understand all conditions stated above. Therefore, I:

1. Agree _____
2. Disagree on participation in the study----------
3. Name of the interviewer: _____Sign. _____ Date of interview_____
4. Name of the supervisor: _____ Sign. _____ Date_____

Thank you for your time.

Appendix II: Baseline Characteristics of Study Participants

1. Age
2. Gender A. Male B.Female
3. Place of Residence A. Urbana B. Rural
4. Marital status A. Married B.Single C.Divorced D. Widowed
5. Educational level A.No Formal Education B. primary school B.Secondary Education D. diploma and above
6. Religion A. orthodox B . Muslim C.catholic D. others
7. Employment status A. no work B.gevormental C. Private D.Farmer
8. Average Monthly Household Income ----------
9. Medical bill A. paid B. free of charge C. insurance.
10. Duration of heart failure under treatment in years ----------
11. Presence of comorbidities A. no B. Yes if yes: Specify----------
12. Currently prescribed Medications (to check drug-drug interaction)

S.N	Main diagnosis	Comorbidities coexist	Name of drug
1			
2			
3			
4			
5			
6			

Table 20: Prescribed medication refilling

Appendix III: Beliefs about Medicines Questionnaire:

Here, we would like to ask you about your personal views about medicines prescribed for you. Below are statements ot

S.n	**Beliefs about Medicines Questionnaire**					
	BMQ –specific	Strongly Agree	Agree	Uncertain	Disagree	Disagree Strongly
1.	My life would be impossible without my medicine.					
2	Without my medicines, I would be very sick.					
3	My health, at present, depends on my medicines.					
4	My medicines protect me from becoming worse.					
5	My health in the future will depend on my medicines.					
6	I sometimes worry about the long-term effects of my medication.					
7	Having to take medicines worries me.					
8	I sometimes worry about becoming too dependent on my medication.					
9	My medicine disrupts my life.					
10	My medicines are a mystery to me.					
	BMQ-General	Strongly Agree	Agree	Uncertain	Disagree	Disagree Strongly
11	If doctors had more time with patients, they would prescribe fewer medicines.					
12	Doctors use too many medicines.					
13	Doctors place too much trust in medicines.					
14	Natural remedies are safer than medicines.					
15	Medicines do more harm than good.					
16	People who take medicines should stop their treatment for a while now and again.					
17	Most medicines are addictive.					
18	All medicines are poisons.					

Table 21: BMQ-18

Appendix IV: Morisky 8-Item Medication Adherence Questionnaire

S.n	Morisky 8-Item Medication Adherence Questionnaire	Yes	No
1	Do you sometimes forget to take your medicine?		
2	People sometimes miss taking medicines for reasons other than forgetting. Thinking about the last time you took medicines, were there any when you did not take your medicine?		
3	Have You ever cut back or stopped taking your medicine without telling your doctor because you felt worse on the last date of taking your medication?		
4	When you travel or leave home, do you sometimes forget to bring along your medicine?		
5	Did you take all your medicines appropriately the last time they were pre-scribed for you?		
6	When you feel well, do you sometimes stop taking your medicine?		
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your Treatment plan?		
8.	How often do you have difficulty remembering to take all your medication? A)Never/rarely B) Once in a while C) Sometimes D) Usually E) All the time		

Appendix V: Severity of Potential Drug-Drug Interactions

Interaction Severity and mechanism of interaction ofDDInter checker results

Sn	Type of interaction		Name of medication	Yes	No
1	Sever				
2	Moderate				
3	Low				
4	No				

Table 22: DDI recording formats

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Table 23:□□□□□□□□□□□□□□□□□□□□□□□□

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Table 24: □□□□□□□□□□□□□□□□□□□□□□□□□□

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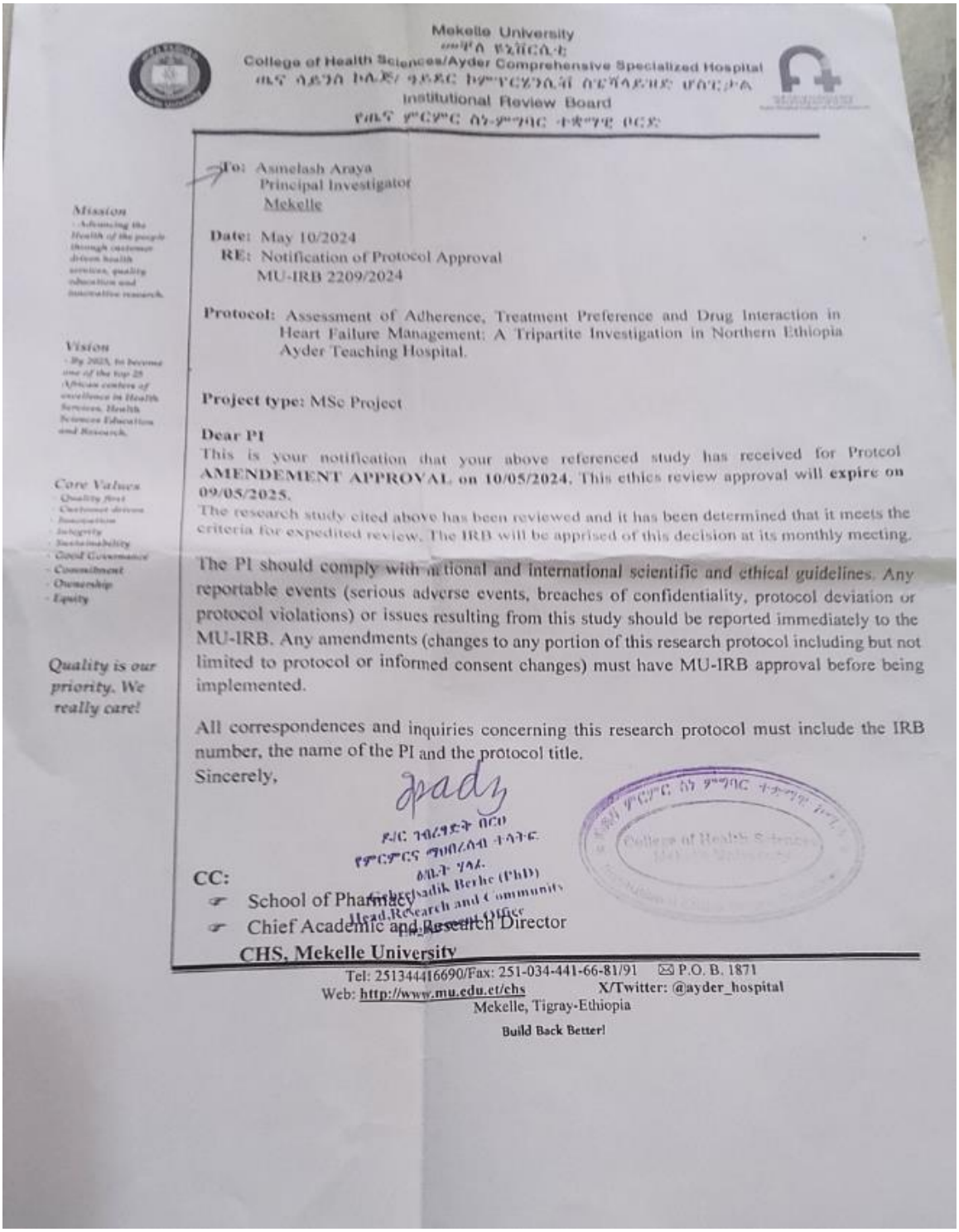
Appendix VI: Ethical Approval Letter



Mekelle University
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College of Health Sciences/Ayder Comprehensive Specialized Hospital
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To: Asmelash Araya
Principal Investigator
Mekelle

Date: May 10/2024
RE: Notification of Protocol Approval
MU-IRB 2209/2024

Protocol: Assessment of Adherence, Treatment Preference and Drug Interaction in Heart Failure Management: A Tripartite Investigation in Northern Ethiopia Ayder Teaching Hospital.

Project type: MSc Project

Dear PI

This is your notification that your above referenced study has received for Protcol **AMENDEMENT APPROVAL on 10/05/2024.** This ethics review approval will **expire on 09/05/2025.**

The research study cited above has been reviewed and it has been determined that it meets the criteria for expedited review. The IRB will be apprised of this decision at its monthly meeting.

The PI should comply with national and international scientific and ethical guidelines. Any reportable events (serious adverse events, breaches of confidentiality, protocol deviation or protocol violations) or issues resulting from this study should be reported immediately to the MU-IRB. Any amendments (changes to any portion of this research protocol including but not limited to protocol or informed consent changes) must have MU-IRB approval before being implemented.

All correspondences and inquiries concerning this research protocol must include the IRB number, the name of the PI and the protocol title.

Sincerely,

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Gebresadik Berhe (PhD)
Head,Research and Community
Engagement Office

CC:
- School of Pharmacy
- Chief Academic and Research Director
  CHS, Mekelle University

Mission
- Advancing the Health of the people through customer driven health services, quality education and innovative research.

Vision
- By 2035, to become one of the top 25 African centers of excellence in Health Services, Health Sciences Education and Research.

Core Values
- Quality first
- Customer driven
- Innovation
- Integrity
- Sustainability
- Good Governance
- Commitment
- Ownership
- Equity

Quality is our priority. We really care!

Tel: 251344416690/Fax: 251-034-441-66-81/91 P.O. B. 1871
Web: http://www.mu.edu.et/chs X/Twitter: @ayder_hospital
Mekelle, Tigray-Ethiopia

Build Back Better!