Impact of Medication Therapy Management Interventions on Drug Therapy Problems, Medication Adherence, and Treatment Satisfaction among Ambulatory Heart Failure Patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2019

By

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This is to certify that thesis prepared by Abate Wondesen entitled "impact of medication therapy management intervention on drug therapy problems, medication adherence, and treatment satisfaction among ambulatory heart failure patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia"**.** It is submitted in partial fulfillment of the requirements of Master of Science Degree in Pharmacy Practice complies with the regulations of the University and meets the accepted standards to originality and quality.

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Abstract

Impact of Medication Therapy Management Interventions on Drug Therapy Problems, Medication Adherence, and Treatment Satisfaction among Ambulatory Heart Failure Patients at Tikur Anbessa Specialized Hospital.

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Addis Ababa University, Ethiopia, June 2020

Medication therapy management (MTM) interventions are a promising way to manage a complex disease like heart failure (HF). Medical therapy of HF has become increasingly complex which make HF patients are at high risk for developing drug therapy problems (DTPs) and medication non-adherent. This study aimed to assess the impact of MTM intervention on DTPs, medication adherence, and treatment satisfaction among ambulatory HF patients. A quasi-experimental study was conducted among 423 HF patients. Cipolle et al. DTP classification schemes used to classify DTPs. Medication adherence was determined using the eight-item Morisky medication adherence scale, and drug-drug interactions were assessed using Micromedex drug interaction checkers. The data were entered in Epidata version 4.2.0 and analyzed using SPSS version 25.0 statistical software. Descriptive statistics such as mean, percent, and frequency were used to summarize patients' characteristics. Univariable and multivariable linear regression was used. In the pre-intervention phase, 288 DTPs were identified with a mean (SD) of 1.3±1.1. A significant reduction of DTPs (0.67± 1.1, $p<0.001$) was observed in the post-intervention phase compared to the pre-intervention phase. The most frequently identified DTPs in the pre-intervention phase were drug-drug interactions (47.6%) and non-adherent (37.3%). In the post-intervention phase, medication adherence improved from 73% to 89 % (95% CI of difference (1.17, 1.43), t= 20.17, $p<0.001$). This study found MTM interventions significantly reduced DTPs, and improved medication adherence and treatment satisfaction among HF patients.

***Keywords*:** Heart Failure, Medication Therapy Management, Drug Therapy Problem, Medication Adherence, Treatment Satisfaction, Tikur Anbessa Specialized Hospital

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Abbreviations and Acronyms

ACC	American College of Cardiology
ADE	Adverse Drug Event
AHA	American Heart Association
BMI	Body Mass Index
BP	Blood Pressure
CHD	Coronary Heart Disease
CI	Confidence Interval
CMP	Cardiomyopathy
CMR	Clinical Medication Review
CMR	Comprehensive Medication Review
CP	Clinical Pharmacist
CVD	Cardiovascular Disease
DALYS	Disability Adjusted Life Years
DDI	Drug-Drug Interaction
DTP	Drug Therapy Problem
ED	Emergency Department
HF	Heart Failure
HMIS	Health Management Information System
HR	Hazard Ratio
IHD	Ischemic Heart Disease
IHME	Institute for Health Metrics and Evaluation
LVEF	Left Ventricle Ejection Fraction
MAP	Medication Related Action Plan
MMAS-8	Morisky medication adherence scale
MTA	Medication Therapy Assessment
MTM	Medication Therapy Management
MTR	Medication Therapy Review
MUR	Medicines Use Review

NCD	Non-Communicable Disease
NHLBI	National Heart, Lung, and Blood Institute
NYHA	New York Heart Association
OR	Odd Ratio
PMR	Personal Medication Record
RHD	Rheumatic Heart Disease
SATMED-Q	Treatment Satisfaction with Medicines Questionnaire
SSA	Sub-Saharan Africa
WHO	World Health Organization

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1. Introduction

1.1 Background

Heart failure (HF) is a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood (Mann and Chakinala, 2018). It is the structural and functional impairments that leads to activation of compensatory responses to maintain circulation, which results in the cardinal symptoms of HF (fluid retention, fatigue, and dyspnea) and signs of HF (limit exercise tolerance, peripheral edema, and rales) (Mann and Chakinala, 2018, Parker et al., 2017).

In worldwide HF is affected by greater than 20 million people. HF prevalence rising with age follows an exponential pattern and affects 6-10% of people aged >65 years. But, in developed countries, HF prevalence in the adult population is 2% (Mann and Chakinala, 2018).

Though there is a lack of population-based incidence and prevalence of HF studies in sub-Saharan Africa(SSA) countries, hospital prevalence studies indicate that HF was responsible for 9.4% to 42.5% of all medical admissions and 25.6% to 30.0% of admissions into the cardiac units(Okechukwu S. Ogah, 2019).

In Ethiopia, according to World Health Organization (WHO) report based on Institute for Health Metrics and Evaluation (IHME) of 2015 data; ischemic heart disease (IHD), stroke, and hypertensive heart disease (HHD) are the second leading cause of premature death and disability (6,458 per 100,000 age-standardized disability-adjusted life year (DALYs) of cardiovascular diseases (CVDs)(WHO, 2018).

HF is now broadly categorized into HF with a preserved ejection fraction(EF) (HFpEF; formerly diastolic failure), HF with a reduced EF (HFrEF; formerly systolic failure), and patients with left ventricular (LV) EF between 40 and 50% have been considered as having a borderline or mid-range EF (Mann and Chakinala, 2018, Anderson and Vogel Anderson, 2018).

Following a diagnosis of HF, treatment depends on type, etiology, and severity of HF. The goals of HF therapies are to improve or maintain quality of life, reduce or eliminate signs or symptoms, prevent acute HF hospitalizations, and improve survival by slowing disease progression (Ponikowski et al., 2016, Bonow et al., 2012). These goals are achieved predominantly by HF medications and lifestyle modifications (Felker, 2014, Kraus et al., 2016).

The most common precipitating factors of HF include myocardial ischemia (MI), atrial fibrillation (AF), non-adherence to medication, drug discontinuation, poor diet adjustment, and pulmonary infection, which cause compensated HF patients to become decompensated. In addition to this, drugs also precipitate or exacerbate HF through direct cardiotoxicity, negative inotropic effect, and increased sodium and fluid retention(Wells et al., 2017). HF patients experience complications in their clinical course due to the presence of co-morbidity and poly-pharmacy.

Medication therapy management (MTM) interventions are used to achieve clinical outcome of HF patients by lifestyle modification and pharmacotherapy (Wittayanukorn et al., 2013, Amaral et al., 2018). MTM is group of services or a distinct service that optimize the therapeutic outcome for individual patients (Roane and McLin, 2018). It is designed to optimize therapeutic outcomes by identifying and resolving drug therapy problems (DTPs) and improve medication non-adherent. It is also used to help patients to take an active role in self-management (Christensen et al., 2007, Melaku et al., 2018, Ai et al., 2014).

The five core elements of MTM service models established in 2008 were a medication therapy review (MTR), a personal medication record (PMR), a medication-related action plan (MAP), intervention and/or referral for DTPs, documentation, and follow-up (Anne Burns, 2008, McGivney et al., 2007). MTM intervention is effective for patients who have multiple chronic conditions, high prescription costs, complex drug therapies, and multiple prescribers (Anne Burns, 2008, Pellegrino et al., 2009). In fact, for patients with HF, pharmacists have become a necessary part of the management team due to the increasing complexity of disease management and drug regimens (Santschi et al., 2011).

DTP is an undesirable event or circumstance experienced by a patient that involves, or is suspected to involve drug therapy and that interferes with achieving the desired goals of therapy (Cipolle et al., 2012). Different research groups classify DTPs into different classification systems. According to the Cipolle textbook of pharmaceutical care practice, there are 7 categories of DTP that fall into indication, effectiveness, safety, and compliance(Cipolle, 2014). Numerous studies showed that clinical pharmacist intervention had a positive impact on reducing DTPs among ambulatory HF patients (Al-Dhawailie, 2011, Barber et al., 2003, Poudel et al., 2015, Diaz Gomez et al., 2013, Lada and Delgado, 2007).

HF patients develop multiple co-morbidities and they have to take a complex regimen of drug treatment. Thus, patients often have difficulty adhering to current guideline-recommended medications (Lee et al., 2015a).

Medication non-adherent is defined in the pharmaceutical care practice model as the patient's unwillingness or inability to take a drug regimen that the practitioner has clinically judged to be indicated, efficacious, and able to produce the desired outcomes (Cipolle et al., 2012). In addition, the rate of medication non-adherent is high in HF patients who have a co-morbid disease and those who took poly-pharmacy (Knafl, 2014, Lam and Fresco, 2015).

Treatment satisfaction is a patient-reported outcome that provides useful insights into the patient's perspective on willingness to continue their current treatments (Revicki, 2004, Cardosi et al., 2018). It helps to show the consistent and correct use of drug therapy over time (Liberato et al., 2016, Asadi-Lari et al., 2003, Ruiz et al., 2008).

1.2 Problem Statements

Globally, HF is a major public health problem and causes morbidity, mortality, recurrent hospitalization, and consume high healthcare costs (Wenying Zeng, 2017). The overall cost of HF continues to rise. The costs associated with treating HF co-morbidities and exacerbations in adults are significant, totaling nearly $1 billion, and maybe rising (Benjamin et al., 2019).

In SSA countries, HF affected young and middle-aged adults unlike in developed countries, which is a disease of the elderly (North America, Western Europe, and Japan) (Okechukwu S. Ogah, 2019).

Medical therapy of HF, in contrast to too many other diseases, has been largely an "add-on" phenomenon. Therefore, optimal HF therapy has become increasingly complex (Urbina et al., 2015, Allen et al., 2015, Snyder et al., 2014, Mastromarino et al., 2014). As a result, many patient factors should be also considered when selecting HF medications. These factors include compelling indications, co-morbid disease states, concomitant medications use, cost of medications, and medication adherence (Anderson and Vogel Anderson, 2018).

HF risk factors appear to differ by HF subtype. Dietary and lifestyle factors also have an impact on HF risk. A study including 20,900 male physicians in the physicians' health study showed that the lifetime risk of HF was higher in males with hypertension compared to physicians with healthy lifestyle factors (cereals consumption of breakfast, normal weight, not smoking, physically active, moderate alcohol intake, and vegetables and fruits used were related to lower risk of HF) (Djousse et al., 2009).

Most HF patients have also co-morbid problems (Mastromarino et al., 2014, Jaarsma, 2005) and took poly-pharmacy. As a result, HF patients are at high risk of developing DTPs. Several studies done in different countries showed that there was a high prevalence of DTPs in HF patients, ranging from 29.8% (Urbina et al., 2014) to 88.66% (Tegegne et al., 2015).

Thus, DTPs cause worsening of HF disease, reduces quality of life, augments the risk of mortality, and morbidity (Shareef, 2015). Furthermore, it causes a major reason for hospital admission and ED visits. However, the majority of those negative clinical outcomes were preventable (Gastelurrutia et al., 2011, Nivya et al., 2015, Baena et al., 2006).

Hence, MTM interventions are a promising way to manage complex diseases like HF. MTM services should be considered when the patient takes at least two or more medications and the patient have actual and potential DTPs (Viswanathan et al., 2015).

MTM interventions are used to reduce DTPs, increase patients' medication adherence level, assisting physicians in identifying opportunities to eliminate drug-drug interactions(DDI), and reduce patients' pill burden (Prescription Drug Benefit Manual, 2006, Ernst and Grizzle, 2001, McGivney et al., 2007, Melaku et al., 2018, Viswanathan et al., 2015, Wittayanukorn et al., 2013, Ai et al., 2014).

On the other hand, the American Heart Association(AHA), the European Society of Cardiology(ESC), and the American College of Cardiology(ACC) guidelines implore medication adherent in HF patients due to its reductive potential in mortality and morbidity (Rehman et al., 2019).

Various studies suggested that HF patients who adhere to their medication are associated with improved survival, fewer ED visit, fewer HF exacerbations, and use lower health care expenditure (Wu et al., 2009, Murray et al., 2009, Hope et al., 2004). However, HF patients who are non-adherent to their medication regimens have poor clinical outcomes, frequent use of urgent care, and inpatient hospital services as compared to patients with similar medical conditions who have adherent to their medications (Roebuck et al., 2011).

According to the WHO report in developed countries, the average rate of medication adherence was 50% among patients with chronic disease (Lam and Fresco, 2015). On the other hand, the studies done by Bitton et al (2013), patients who had more than 80% adherent to their prescribed medications had better clinical outcomes than those who did not have.

When HF patients are compliant with their treatment regimen and performed symptom monitoring and self-care at home, approximately half of the hospital readmissions could be prevented (Wenying Zeng, 2017).

Treatment satisfied patients are more adherent to prescribed therapeutic regimens, take an active role in their self-care, and improve their quality of life compared to treatment unsatisfied patients (Liberato et al., 2016, Asadi-Lari et al., 2003).

1.3 Rational of the Study

The involvement of pharmacists in HF care teams, improve HF outcomes by medicine management intervention, medication adherence intervention, or a combination of both. Therefore, there are no studies regarding MTM interventions in ambulatory HF patients in Ethiopia. Thus, the present study assessed the impact of MTM interventions on DTPs, medication adherence, and treatment satisfaction among ambulatory HF patients. The finding of the study mainly helps to provide valuable insights for the Federal Ministry of Health(FMoH), non-governmental health organizations(NGO), different health institutions, and healthcare providers in Tikur Anbessa Specialized Hospital and other health institutions to know the impact of MTM intervention on DTPs and medication adherence in HF patients. The data can also serve as a benchmark for researchers and academic institutions to do research.

Finally, the results of the study provide baseline information about the problem of DTPs, medication non-adherent, and treatment satisfaction in HF patients, and how MTM interventions could be used to alleviate this situation.

2. Literature Review

2.1 The Impact of Medication Therapy Management Intervention on Heart Failure

Clinical pharmacists play a vital role in HF clinics, ranging from patient education and support to involvement in patients' treatment plans.

A retrospective cohort study performed in Australia to assess the effectiveness of collaborative medicine reviews in delaying time to next hospitalization in HF patients, from January 2004 to July 2006. The study, included 273 patients in the home medicine review exposed group and 5,444 in the unexposed group. There was a, 45% reduction in delaying time to next hospitalizations in exposed groups compared to the unexposed groups (Roughead et al., 2009).

A systematic review and meta-analysis done on pharmacist involved care for patients with HF showed that all-cause hospitalization reduced and the prescription rates of ACEI (OR 1.43; 95% CI, 1.07–1.91) and BB (OR 1.92; 95% CI, 1.24–2.96) were significantly higher in the pharmaceutical care group compared to the usual care group (Kang et al., 2016).

2.2 The Impact of Medication Therapy management Intervention on Drug Therapy Problems

DTPs have profound medical and safety consequences for HF patients (Hutchison et al., 2014). DTPs prevalence reported among ambulatory HF patients, range from 29% in Minnesota (Ramalho de Oliveira et al., 2010) to 83.5% in Jimma university specialized hospital, Ethiopia (Niriayo et al., 2018).

A hospital-based prospective interventional study done in India (n=112) to assess DTPs in CVD patients, which carried out for 7 months. There were, 53 DTPs identified (55.35%) from 44 study participants. The most common reported DTPs are DI (49.05%), ADR (18.86%), and not received drugs (9.43%). Discontinued drugs (24.52%), changed

frequency of drugs (22.64%), and changed drug dose (20.75%) interventions make by intervening pharmacists. The rates of acceptance of pharmacist interventions were high (96.21%) (Shareef, 2015). Likewise, another prospective interventional study done in Badalona, Spain (n=97) to assess the impact of a pharmacist in a multidisciplinary HF clinic. Inappropriate [(dose, drug regimen, and/or duration) (22%)], adverse drug effects (16%), medication non-adherent (14%), need additional drugs (45 %), ineffective drug (24%), and drug have safety problem (33.5%) the common identified DRPs from study participants. From those DRPs, 94% of them were preventable and the rates of acceptance of pharmacist interventions were 86%. This study also showed a positive relationship between a number of drug taking with a number of DRPs (Gastelurrutia et al., 2011).

A prospective interventional study conducted in the USA to assess the impact of pharmacists' medication therapy counseling and disease state education. The study, included (n= 139) in the control group and (n=140) in the intervention group. There were, 198 interventions made by pharmacists (mean = 1.41 interventions per patient), and 185 (93.4%) interventions were accepted. Discontinued medication, changed the dose, and initiated additional drug are the most common performed interventions (Sarangarm et al., 2013).

A prospective cohort study done in Saudi Arabia conducted from November 2010 to December 2011 (n=337), revealed that clinical pharmacists provide 419 interventions (add drug=68, dose adjustment=76, discontinue drug=52, make 223 counseling session for drug, smoking, and diet) (Bahmaid et al., 2016).

On the other hand, a pre-post quasi-experimental study done at Memphis in Egypt included (n=432) patients in the control group and (n=369) patients in the intervention group, both groups followed for 1 year. Clinical pharmacists did 565 interventions on 216 HF patients. Which includes discontinued medications (318), changed medications (104), changed medication dose (43), needed addition of drugs (38), changed medication frequency (27), and changed dosage form (16). The rates of acceptance of pharmacists' interventions were 85.3% (Hutchison et al., 2014).

Clinical pharmacists provided interventions could reduce the risk of ADR and drug-drug interactions. A prospective interventional study done in Nepal (n=445) to assess impact of educational intervention on drug-drug interactions. There were 53% and 41% of DDIs identified (with the average number of drugs per patient was 8.53 and 7.32) in the pre-intervention and the post-intervention phases, respectively. Sixty four percent of DDIs were moderate level of severity. Cardiovascular drugs accounted 36% of DDIs in pre-intervention phase and 33.2% in post-intervention phase. Furosemide was the highest risk drug of DDIs in both pre and post-intervention phases. DDIs were observed frequently between amlodipine and atenolol (4.82%) in the pre-intervention phase and between furosemide and aspirin (5.20%) in the post-intervention phase (Bista et al., 2009).

Coming to our country Ethiopia, a hospital-based cohort study was conducted in Felege Hiwot referral and Jimma university specialized hospital (n=97) to assess DTPs and contributing factors among patients with CVD. There were, 164 DTPs identified with a mean of 1.69±0.993 per patient. Need additional preventive or prophylactic therapy 56(65.12%), untreated indications 43(53.75%), more effective drug available 12(13.95%), need synergistic or potentiating action 7(8.14%), ADR (undesirable effect 16(18.6%), and dose too high (wrong dose 9 (10.46%) were the common identified DTPs. Number of co-morbidities and a patient with HF were significant factors to develop DTPs (Tegegne et al., 2015).

Furthermore, a cross-sectional study was performed at Harar, Ethiopia (n=216) to assess DTPs among patients with CVD. There were, 131(60.65%) DTPs identified. Need additional drug therapy 76 (58%), unnecessary drug therapy, and non-compliance (both of which accounted for 16 (12.2%)) were the common identified DTPs. Study participants receiving ≥ 3 drugs was a risk factor contributing to develop DTPs(Gelchu and Abdela, 2019).

A study done by Niriayo et al (2018) in Jimma university specialized hospital, Ethiopia (n=340) to assess the prevalence and contributing factors of DTP among ambulatory HF patients. There was, 83.5% of DTPs identified with a mean of 2.6 ±1.8 DTPs per patient. The common identified DTPs are; increased dosage (27.8%), changed ineffective drug

(27.6%), and needed additional drug (27.4%). Most commonly implicated drugs in developing DTPs are BB (34.4%), ACEI (24.8%), statins (16.5%), and anti-thrombotic (13.1%). Determinants associated to DTPs are number of medicines ≥ 5, number of co-morbidities ≥ 2, negative medication belief, poor involvement of patients in therapeutic decision making, and age >50 years. On the other hand, a cross-sectional study done in Gonder, Ethiopia (n=227) to assess DTPs in patients with CVD. There was, 265 DTPs identified. The most common identified DTPs are inappropriate selection of [drugs (36.1%), dose (24.8%), and drug use process (14%)]. Presence of poly-pharmacy and increased number of prescribed drugs are risk factors to develop DTPs (Abdela et al., 2016). Although those researches done in Ethiopia, researchers got different results.

2.3 The Impact of Medication Therapy Management Intervention on Medication Adherence

Rate of medication non-adherent among HF patients ranging from 22.1% in Texas, USA(Lee et al., 2015a) to 46.4% at Felege Hiwot referral hospital and Jimma university specialized hospital, Ethiopia (Tegegne et al., 2015).

Clinical pharmacist interventions in HF patients have important effects to increase medication adherence. Adhering to prescribed medication is a key behavior in HF self-care (Ruppar et al., 2016).

A prospective interventional randomized control trial conducted in the USA included (n=122) in the intervention group and (n=192) in the usual care group to assess pharmacist intervention to improve medication adherence in HF patients showed, 67.9% and 78.8% of medication adherence in the usual care and the intervention groups, respectively. The number of prescribed drugs and co-morbid conditions are determinants of medication adherence (Murray et al., 2007). In addition, a prospective interventional study conducted in the USA to assess the impact of pharmacists' medication therapy counseling and disease state education. The study included (n= 139) in the control and (n=140) in the intervention group. The study participants had, 58.5% and 75.7% of medication adherent in the control and the intervention group, respectively (Sarangarm et al., 2013).

There are multiple and complex factors that make HF patients fail to adhere to the prescribed medication regimen(Shah et al., 2015). A prospective cohort study conducted in the USA (n=242), to assess what puts HF patients at risk for poor medication adherence. The study found, 28.9% of patients had poor medication adherence. The main identified contributing factors of medication non-adherence are a higher number of co-morbid conditions, a higher number of daily medicines use, and being old age(Knafl, 2014). Likewise, a prospective study conducted in the USA (2015) to assess factors associated with medication adherence among HF patients. Forgetfulness(50%), having other medication to take (20%), and being symptom-free (20%) were the most commonly identified factors associated with medication non-adherent (Aggarwal et al., 2015).

A retrospective cohort study was done by Lee et al in the USA (n=357) to assess non-adherence in at-risk HF patients. The study identifies 79 (22.1%) and 278 (77.9%) patients' who had non-adherent and adherent to their medication regimens, respectively. The rate of HF admission was higher in the non-adherent patients comparing to adherent patients [mean (SD); 3.1± 0.5 vs. 2.8 ± 0.4, $p < 0.05$]. Age and sex were significant factors associated with medication non-adherent (Lee et al., 2015a). A cross-sectional study was done in Iran (n=300) to assess negative clinical outcomes associated with DTPs in HF. The study participants had 5.82 ±2.54 mean scores of treatment adherence. Educational level, co-morbidity, and the number of drugs used per day are significantly associated factors to medication adherence (Amininasab et al., 2018).

A meta-analysis and systematic review of 48 studies reported that medication adherence interventions in HF patients reduced mortality risk and hospital readmission (Ruppar et al., 2016).

2.4 The Impact of Medication Therapy Management Intervention on Treatment Satisfaction

The level of patient treatment satisfaction is often used as a marker of performance for both health care organizations and personnel. A prospective interventional study conducted in the USA included (n= 139) in the control and (n=140) in the intervention

groups participants had 54.6% and 69.3% of treatment satisfied in the control and the intervention groups, respectively (Sarangarm et al., 2013).

Patients who reported being treatment satisfied with particular services are more likely to remain members of health care organizations and adhere to prescribed medical regimens(Holsclaw et al., 2005).

Additionally, a study was done at Texas, USA (n=60) to assess patient treatment satisfaction with a pharmacist-provided telephone MTM program. The study found that most of the participants' had treatment satisfied with their telephonic MTM care. There was a, 80% of treatment satisfaction rate (Moczygemba et al., 2010).

A cross-sectional survey conducted by Holsclaw SL et al (2005) (n=491) to assess patient treatment satisfaction with telephone and mail interventions provided by a clinical pharmacy a cardiac risk reduction service. The study found, 94.6% of study participants had treatment satisfied.

2.5 Conceptual Framework

Based on reviewed works in the literature, different factors are affecting DTPs, medication adherence, and treatment satisfaction in HF patients. These factors are categorized as patient related factors, drug-related factors, disease-related factors, and MTM intervention-related factors (McGivney et al., 2007, Bluml, 2005, Kang et al., 2016). Figure 1 is constructed based on reviewed literatures and shows their relationships(Ramalho de Oliveira et al., 2010, Roane and McLin, 2018).

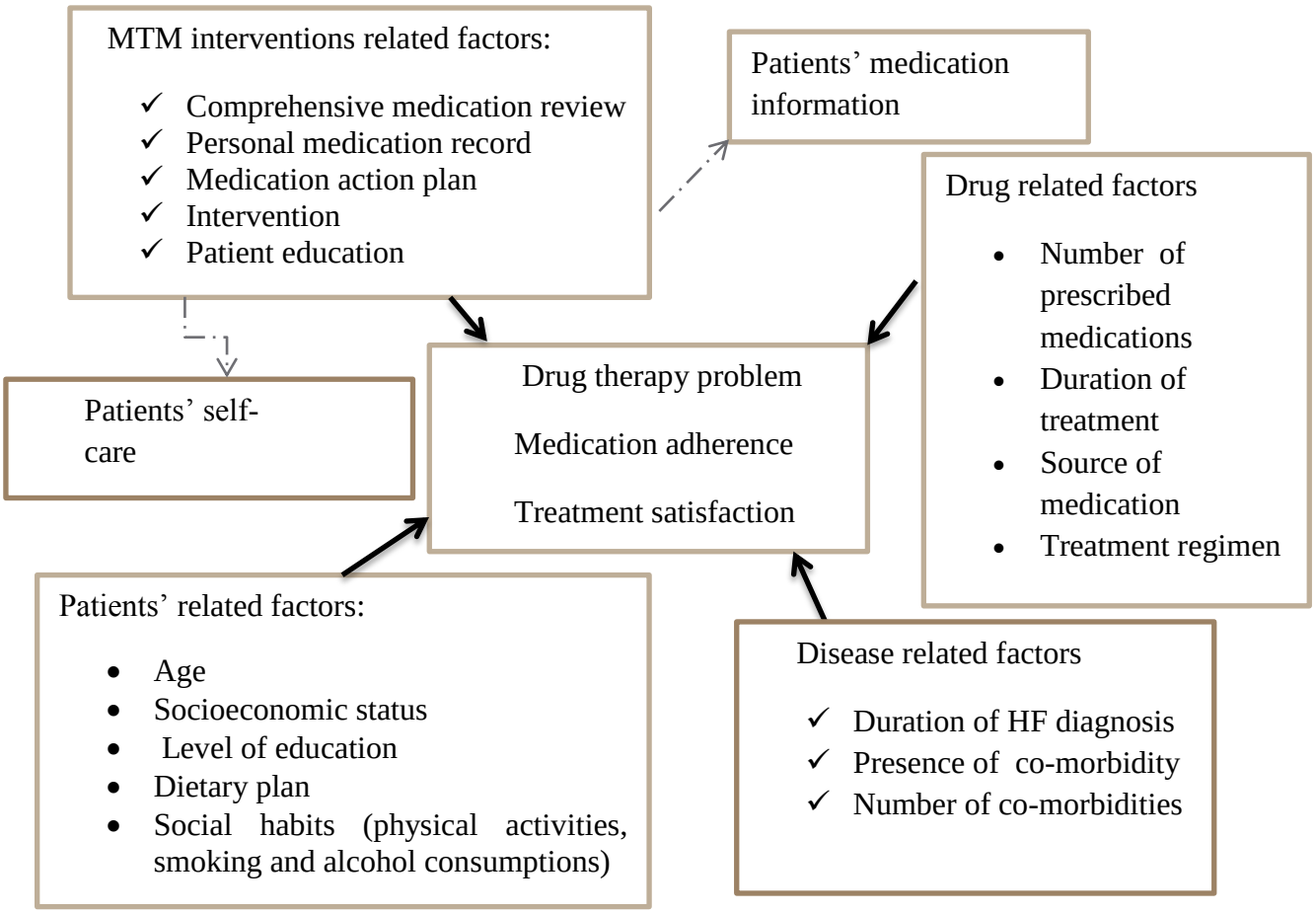

Figure 1. Conceptual framework showing factors involved in drug therapy problems, medication adherence, and treatment satisfaction

3. Objectives

3.1 General objective

To determine the impact of medication therapy management interventions on drug therapy problems, medication adherence, and treatment satisfaction among ambulatory heart failure patients attending the cardiac clinic of Tikur Anbessa Specialized Hospital(TASH), Addis Ababa, Ethiopia, 2019

3.2 Specific Objectives

- ✓ To determine the impact of MTM interventions on DTPs among ambulatory HF patients in the cardiac clinic
- ✓ To determine the impact of MTM interventions on medication adherence among ambulatory HF patients in the cardiac clinic
- ✓ To identify determinants for DTPs among ambulatory HF patients in the cardiac clinic
- ✓ To identify determinants for medication adherence among ambulatory HF patients in the cardiac clinic
- ✓ To determine the impact of MTM interventions on treatment satisfaction among ambulatory HF patients in the cardiac clinic

4. Methods

4.1 Study Setting

The study was conducted at TASH, which is the only tertiary specialized hospital in Ethiopia. The hospital located in Lideta Sub-City, Addis Ababa, Ethiopia, and established in 1972 with a bed capacity of 700 and serves as a teaching specialized hospital for undergraduate and postgraduate medical students, dentists, nurses, midwives, pharmacists, medical laboratory technologists, and radiology technologists. In 1998, the Federal Ministry of Health transferred TASH to Addis Ababa University, and it has since become a University teaching hospital. In addition, almost all regional and federal hospitals in Addis Ababa use this hospital as a referral unit and training site. Specialized clinical services are rendered to the whole nation when clinical services not available in other public or private institutions. The various departments, faculty members and residents under specialty training in the School of Medicine provide patient care in the hospital. The major services provided by the hospital are internal medicine, emergency medicine, surgery, gynecology and obstetrics, pediatrics, oncology/chemo-radiology, radiology, psychiatry, and dermatology. The pharmacy services in the TASH are organized for outpatient, emergency, and inpatients(Addis Ababa University College of Health Sciences, 2020).

Among the specialty clinic in TASH, the adult cardiac clinic is one of them and provides comprehensive cardiac care including HF treatment and follow up. Cardiologists, cardiology fellows, residents, and nurses have manned the clinic. The clinic provides the cardiac service four days per week (except Thursday).

On average, 105 patients were served per day and 10080 patients were visiting the clinic within the study period.

4.2 Study Design and Study Period

This one group pretest-posttest quasi-experimental study was aimed to evaluate the impact of MTM as an intervention in improving the care of HF patients in the cardiac clinic of TASH. The study was conducted from 1st July 2019 to 30th December 2019.

4.3 Population

4.3.1 Source Population

The source population of the study was all ambulatory HF patients who attended adult cardiac clinic of TASH for the management of HF.

4.3.2 Study Population

The study population consisted of all ambulatory HF patients attending TASH within the study period and who fulfilled the inclusion criteria.

4.4 Inclusion and Exclusion Criteria

4.4.1 Inclusion Criteria

- ✓ HF patients ≥ 18 years old
- ✓ HF patients who had medical records
- ✓ HF patients who were willing to participate in the study
- ✓ HF patients took at least two or more medications for at least six months

4.4.2 Exclusion Criteria

- ✓ Patients who could not stand the interview (for example, too sick to be interviewed).
- ✓ HF patients with cognitive impairment
- ✓ Lost appointment date
- ✓ Change follow up site

4.5 Sample Size Determination and Sampling Technique

4.5.1 Sample Size Determination

The sample size was estimated using a single population proportion formula (Kasiulevičius et al., 2006).

$$n = \frac{Z_{\frac{\alpha}{2}}^{2} \, p(1-p)}{d^2}$$

Where: n is the minimum sample size required for a large population (≥ 10,000).

Z α/2 is the critical value for a 95% confidence interval (= 1.96 from Z- table).

p is the proportion of medication therapy management interventional studies in HF patients. Since there were no previous studies in Ethiopia, p was assumed to be 50% (0.5).

d degree of accuracy desired (the margin of error 5% = 0.05). Hence; estimated minimum sample size

$n = (1.960)^2 \times 0.5(1-0.5)/ (0.05)^2 = 384.16 \sim 384.$

The total number of source population in the study period (N), based on the average number of patients coming to the clinic in four days in a week with a total of 24 weeks was 10080 (per day on average 105 patients were coming to the clinic). In 24 weeks, there were 96 working days (96x105). Therefore, the study population was greater than 10,000; we had not used an estimated sample size using the reduction formula.

Taking 10% contingency for incomplete medical records and patients refused to participate in the study provided a final sample size of 423 HF patients.

4.5.2 Sampling Technique

A systematic random sampling technique was used to recruit samples for the study in each day of the data collection technique. The total number of the study population varied in different data collection days. Therefore, the actual sampling fraction (k) also varied in the different days of data collection. As a result, it was calculated by dividing the number

of study populations available at each data collection day by the maximum possible number of patients' that could be interviewed and intervened on the same day. The first study participant was selected by simple random sampling from one to k value. Then, every k^{th} patient (ranging from, 4 to 6) was selected.

The flowchart of study participants' recruitment is summarized in figure 2.

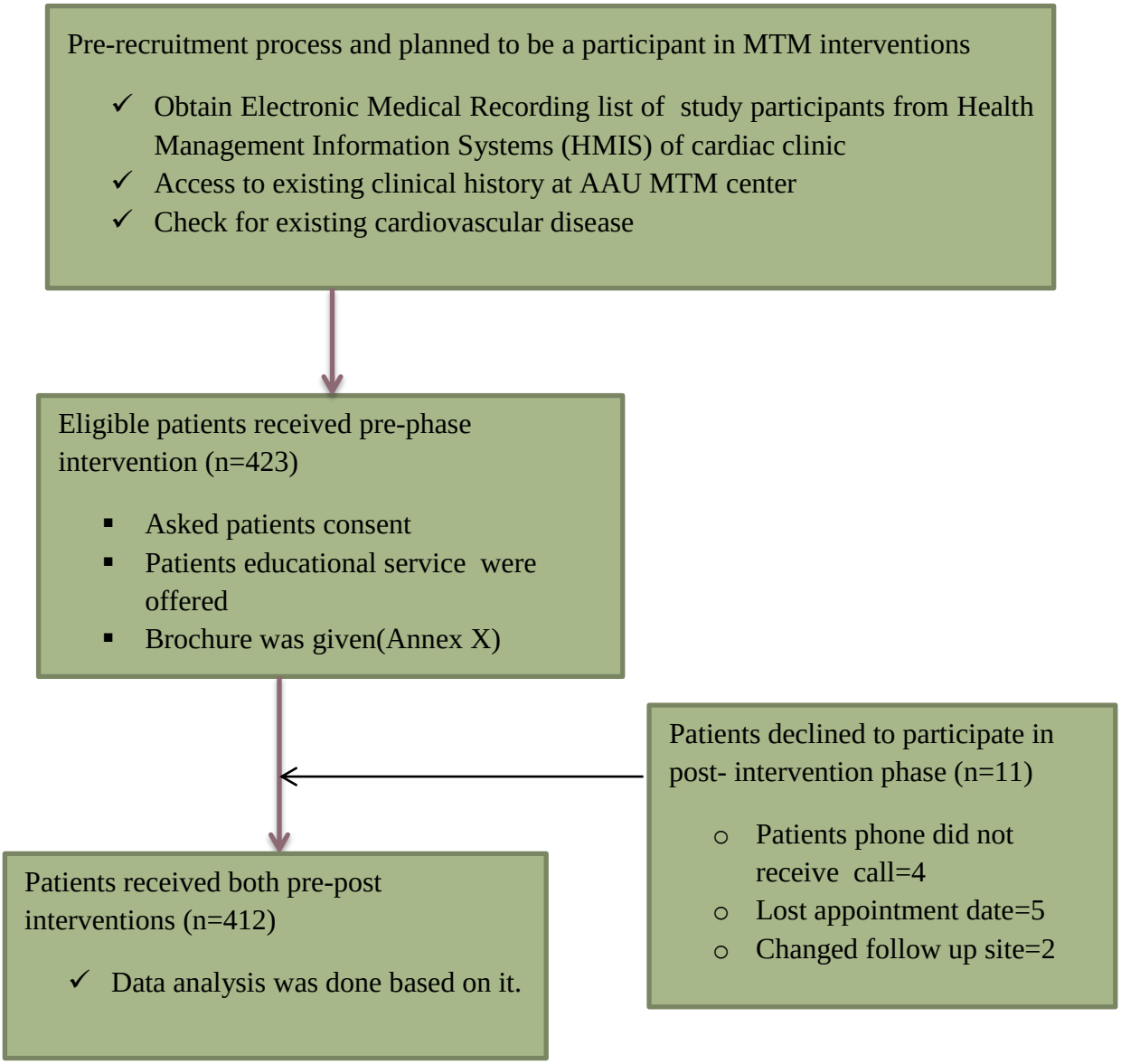

Figure 2. Study participants' recruitment flowchart.

4.6 Study Variables

4.6.1 Dependent Variables

- Drug therapy problems
- Medication adherence
- Treatment satisfaction

4.6.2 Independent Variables

- ✓ Patients' demographic feature includes age, sex, marital status, educational status, and economic status.
- ✓ Study participants social habit (presence of physical activity plan, smoking, alcohol use, presence of dietary plan, and khat chewing)
- ✓ Patients' clinical characteristics (presence of co-morbid disease, number of co-morbidities, and duration of HF diagnosis)
- ✓ Drug related factors
    - Number of prescribed drugs
    - Type of Drug regimens
    - Duration of HF treatment
    - Presence of drug allergy history
    - Source of medication

4.7 Data Collection and Management

4.7.1 Data Collection Instruments

Instruments

Relevant information regarding each patient's demographics and clinical data was collected by a questionnaire (Annex I). Data on patients' clinical characteristics (etiology of HF, co-morbid conditions, pertinent laboratory values, relevant past medical and medication history, current medications, duration of heart failure treatment) were collected by using data abstraction format from patient charts (Annex I). The adequacy of medical therapy of HF was evaluated using the European Society of Cardiology(van der Meer et al., 2019, Ponikowski et al., 2016) and American Heart Association/ American College of Cardiology (AHA/ACC) HF guidelines (Yancy Clyde et al., 2017).

Micromedex® health care series software drug-drug interaction checker was used to identify drug-drug interaction and only absolute contraindications and major drug-drug interactions were selected as significant drug interactions, whereas moderate and minor interactions were omitted.

Finally, DTPs were identified from the collected data using the above guidelines. DTPs were categorized as the need for additional drug therapy, unnecessary drug therapy, ineffective drug, dosage too high, dosage too low, adverse drug reactions, and non-adherence by the Cipolle et al. (2012) classification system. The identified DTPs were recorded and classified by using the DTP registration format, which was taken from Cipolle et al (Annex III).

ADRs were identified from medical charts, which were already recorded by the physicians.

Medication adherence and patient treatment satisfaction were determined using the Morisky medication adherence scale (Annex II) and Treatment Satisfaction with Medicines Questionnaire (SATMED-Q) questionnaires (Annex IV), respectively.

Assessment of Medication Adherence Instrument

Morisky medication adherence scale (MMAS-8): is a validated scale, utilized to collect information necessary to assess medication adherence and reasons contributing to non-adherence. MMAS-8 is part of the WHO case management adherence guideline assessment tools. It consists of eight items focusing on past medication use patterns with closed dichotomies (yes/no) answers. Each 'no' response rated as 1 and each 'yes' response rated as 0 for items 1 to 7, except for item 5, reversed, and 'yes' was rated as '1' and 'no' as '0. A Likert scale was used for item 8 (difficulty to remember taking medications) and scored as "never/rarely = 4, once in a while = 3, sometimes = 2, usually = 1 and always = 0. For this, the code (0-4) was standardized, dividing the result by 4 to calculate the summated score. The total score ranged from 0 to 8 and grouped into high adherence (8 points scored), medium adherence (6 to < 8 points scored), and poor adherence (< 6 points scored).

Assessment of Patient Treatment Satisfaction Instrument

Patient treatment satisfaction was assessed by using Treatment Satisfaction with Medicines Questionnaire (SATMED-Q), which is composed of 17 items with 6 (domains) dimensions (undesirable side effects, treatment effectiveness, convenience to use, impact on daily activity, medical care, and global satisfaction).

Satisfaction with each of the specific domains of treatment was given an ordinal score on a five-point Likert scale; very much satisfied = 4 points, Quite a bit = 3 points, somewhat satisfied = 2 points, a little bit = 1 point and not at all = 0. Summing up the direct scores of the items yields a total composite score ranging between 0 and 68 points. The observed total composite score was transformed to a more intuitive and easier to understand metric with a minimum of 0 and a maximum of 100, using the following expression: Y' = [(Yobs-Ymin) / (Ymax-Ymin)] x100 = Yobs x 1.471, where Ymax = 68 (maximum total score); Ymin = 0 (minimum total score); Yobs = total score obtained by the patient; and Y' = transformed score. A similar expression can be used to change the metric of each dimension.

4.7.2 Data Collection Processes

Data collection had three phases and depicted in Figure 3.

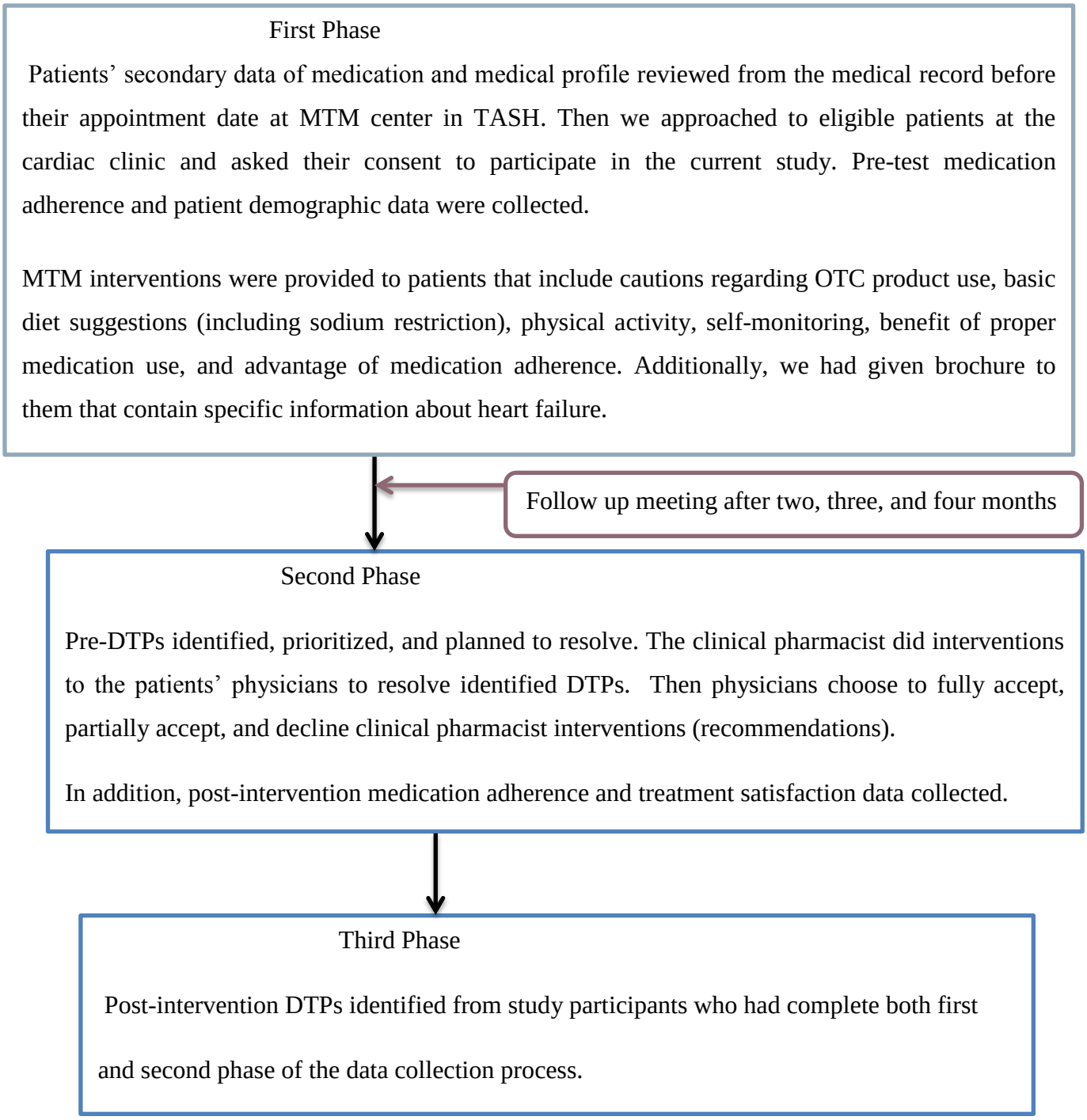

Figure 3. Data collection and medication therapy management interventions process

4.7.3 Recruitment of Data Collectors and Training

The selection of data collectors was based on the educational level and possible familiarity in medical and health research. From TASH, two clinical pharmacists and three nurses took training to carry out the data collection. The clinical pharmacists involved in chart review to identify DTPs and the nurses in patient interviews. Data collectors were trained on strict use of study criteria, explanation of study objective, getting of verbal consents from study participants, implementation of sampling technique, uniform interpretation of questions, patient education material (brochure), and the collected data confidentiality.

4.7.4 Data Quality Assurance

A cardiologist physician assessed the data collection tools (the data abstraction format and questionnaire) about the completeness and clarity of its contents. A pre-test (5%) was done and all necessary adjustments and modifications were incorporated before implementing them in the main study. The principal investigator (PI) gave one-day training to the data collectors on how to collect data from patient charts, how to conduct a patient interview, and how to make interventions. The PI supervised the data collection process and gave feedback and correction daily.

4.8 Data Analysis and Interpretations

The collected data were sorted, cleaned, coded, and entered into Epidata version 4.2.0 and then exported to statistical package for social sciences (SPSS) version 25 software. In addition, data checks and corrections were done. Descriptive statistics was, used to summarize frequencies, means, and percentages. Linear regression analysis was performed to see the relationship between occurrence of DTPs and independent variables as well as medication adherence and independent variables. All variables with $p < 0.25$ in the univariable linear regression analysis were included in the multivariable linear regression analysis, which was performed to determine the potential predictors of DTPs and medication adherence.

Finally, the results were summarized and described using tables and figures. Paired-t-test was used to compare the mean difference between the pre and post-interventions data sets. A p-value of < 0.05 was considered as statistically significant.

4.9 Ethical Consideration

From Addis Ababa University School of Pharmacy Ethical Review Board (ERB/SOP/107 /06 /2019, ethical clearance of the study protocol was obtained. Additionally, permission was sought from the outpatient directorate and cardiac clinic of TASH to conduct the study in the cardiac clinic. Before data collection, study participants were informed about the study, and verbal consent was obtained. Each patient was informed about the objective of the study, assurance of confidentiality, procedures of selection, and their rights to refuse were maintained. To minimize social desirability bias and enhance anonymity no identifiers were used. The privacy of participants was ensured since patients were interviewed in a different room. All information obtained from the participants was kept confidential and the data were used for the research purpose only.

4. 10 Operational Definition of Terms

- **Heart failure**: Is a clinical syndrome characterized by typical symptoms and signs caused by a structural and/or functional cardiac abnormality.
- **Drug therapy problem**: Presence of circumstances involving drug therapy that actually or potentially interferes with achieving the patients' desired health outcomes.
- **Medication therapy management**: A service is given by clinical pharmacists to add values to the care of patients by identifying, resolving, preventing drug therapy problems, counseling patients to improve medication adherence, and treatment satisfaction.
- **Drug interaction**: Only major or clinically significant drug-drug interaction regimens were reported by using Micromedex® health care series software drug interaction checker.
- **Adverse Drug Reaction**: Any undesirable event experienced by a patient whilst taking a medicine, regardless of whether or not the medicine is suspected to be related to the event.
- **Exercising regularly:** Study participants do aerobics physical activity (every day activities, occupational activities, and leisure time activity) or doing other exercises regularly recommended by physician.
- **Alcohol use:** Patients drink three or more alcoholic beverages per week.
- **Co-morbid disease**: The existences of more than one disease condition that causes and/or aggravates heart failure or coexisting alongside a primary diagnosis of heart failure.
- **Medication adherence**: Is a drug-taking behavior of a patient measured with the Morisky scale in which the patient is considered high medication adherent if he/she scores 8 points, medium medication adherent if he/she scores 6 to < 8 points, and poor medication adherent if the patient scores < 6 points.
- **Poly-pharmacy**: Considered when greater than or equal to five drugs are prescribed for the patient.

- **Body Mass Index (in kilograms per square meters):** Interpreted as underweight (BMI<18.5), normal weight (18.5-24.9), overweight (25.0-29.9), and obese (≥30.0).
- **No Formal Education:** Participants who do not have any grade level of education.
- **Unemployed**: Study participants who have not job to obtain money.

5. Results

5.1 Socio-Demographic Characteristics of Study Participants

From 423 study participants enrolled in the current study, 11 study participants were excluded because they fulfill the exclusion criteria. As a result, data of 412 study participants were used for analysis.

The socio-demographic characteristics of the participants are depicted in Table 1. Out of 412 study participants, who were eventually followed up from 1st June until 30th December 2019, the mean(SD) age was 44.57 years (± 17.4) (range 18 to 93 years). The majority of them were within 18-33 years of age (33%) followed by 50-65 years of age (30.6%). More than half (53.6%) of them were females and about two-third (64.3%) were married. About a quarter (26.7%) of them had no formal education and most of them (54.6%) payout of pocket for their medication.

Table 1. Socio-demographic characteristics of study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Variables	Categories	Number (%)	Mean ±SD	Range
Sex				
	Male	191(46.4)		
	Female	221(53.6)		
Age (years)				
	18-33	136(33)		
	34-49	103(25)	44.57±17.14	18-93 years
	50-65	126(30.6)		
	>65	47(11.4)		
BMI($kg/m^{2)}$		n =340		
	BMI<18.5	29(8.5)		
	BMI 18.5-24.9	203(59.7)	22.9±3.26	
	BMI 25-30	95(27.9)		
	BMI≥30	13(3.9)		
Religion				
	Orthodox	274(66.5)		
	Muslim	81(19.7)		

Table 1(cont.)

Variables	Categories	Number (%)	Mean ±SD	Range
	Catholic	17(4.1)		
	Protestant	40(9.7)		
Marital status				
	Single	121(29.4)		
	Married	265(64.3)		
	Widowed	5(1.2)		
	Divorced	21(5.3)		
Educational status				
	No formal education	110(26.7)		
	Primary	116(28.2)		
	Secondary	96(23.3)		
	Diploma and above	90(21.8)		
Place of residence	Addis Ababa	249(60.4)		
	Out of Addis Ababa	163(39.6)		
Occupation	Governmental Employed	118(28.6)		
	Private employed	105(25.5)		
	Unemployed (house wife, student)	96(23.3)		
	Self-employed (farmer, daily labor, merchant, driver)	59(14.3)		
	Others*	34(8.3)		
Monthly income(Birr) **				
	very low (<860)	79(19.2)		
	low (861-1500)	85(20.6)		
	Average(1501-3000)	145(35.2)		
	Above average (3001-5000)	90(21.8)		
	High(≥5001)	13(3.2)		
Source of medications				
	Free	85(20.6)		
	Paid	225(54.6)		
	Covered by insurance	52(12.6)		
	Covered by family	50(12.1)		

*Retired, Guard, Mechanics (garage)

** Based on the Ethiopian Civil Service monthly Salary scale of Civil Servants

5.2 Clinical Characteristics of Heart Failure Patients

Among the study participants, 34.3% of patients diagnosed with HF for greater than 10 years and 33.5% had been taking HF treatments for 5-10 years. Nonetheless, 56.8% and 43.2% of patients had been taking 2-4 and ≥ 5 drugs, respectively. Only sixteen patients (3.9%) reported that they did experience drug allergy (Table 2).

Table 2. Clinical characteristics of study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Clinical Characteristics	Category	Number (%)	Mean ±SD	Range
Duration of HF diagnosis	< 5years	132(32)		
	5-10 years	139(33.7)		
	>10 years	141(34.3)		
Duration of HF treatment				
	<5 years	134(32.5)	9.45±6.47	1-35 years
	5-10 years	138(33.5)		
	>10 years	140(34)		
History of hospital admission				
	Yes	182(44.2)		
	No	230(55.8)		
Number of drugs				
	2-4 drugs	234(56.8)	4.2±1.71	2-8 drugs
	≥5 drugs	178(43.2)		
Frequency of encountered for MTM intervention				
	≥ 2 months	245(59.47)		
	≥3 months	167(40.53)		
Drug allergy history				
	Yes	16(3.9)		
	No	396(96.1)		

5.2.1 Common Etiology of Heart Failure among Study Participants

The common identified etiologies of HF are CRVHD 231(56%), followed by IHD 69(17%), and then HHD 47(11%) (Figure 4).

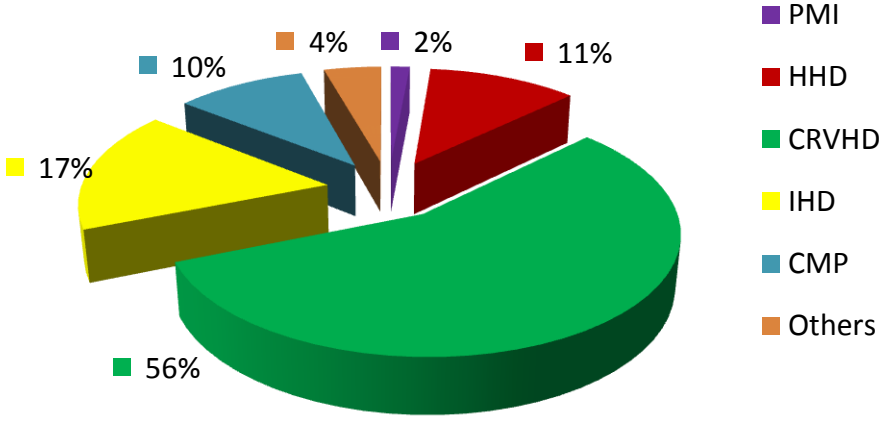

Fig.4 Etiology of heart failure among the study participants

Figure 4: Etiology of heart failure among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

IHD: Ischemic Heart Disease, HHD: Hypertensive Heart Disease, CRVHD: Chronic Rheumatic Valvular Heart Disease, PMI: Previous Myocardial Infarction, CMP: Cardiomyopathy

*Others include; Degenerative Valvular Heart Disease, Cor-pulmonale, Congenital Heart Disease, Constrictive Pericarditis, Left Ventricular Hypertrophy, Third Degree AV Block.

5.2.2 Types of Co-Morbidities among Heart Failure Patients

Among the study population, 126(30.6%) of HF patients did not have co-existing co-morbidities. However, 83(20.1%), 48(11.7%), 58(14.1%), and 97(23.5%) of patients had been diagnosed with one, two, three, and four and above co-morbidities, respectively.

Atrial fibrillation (28%) and hypertension (22%) were accounted higher percentage (Figure 5).

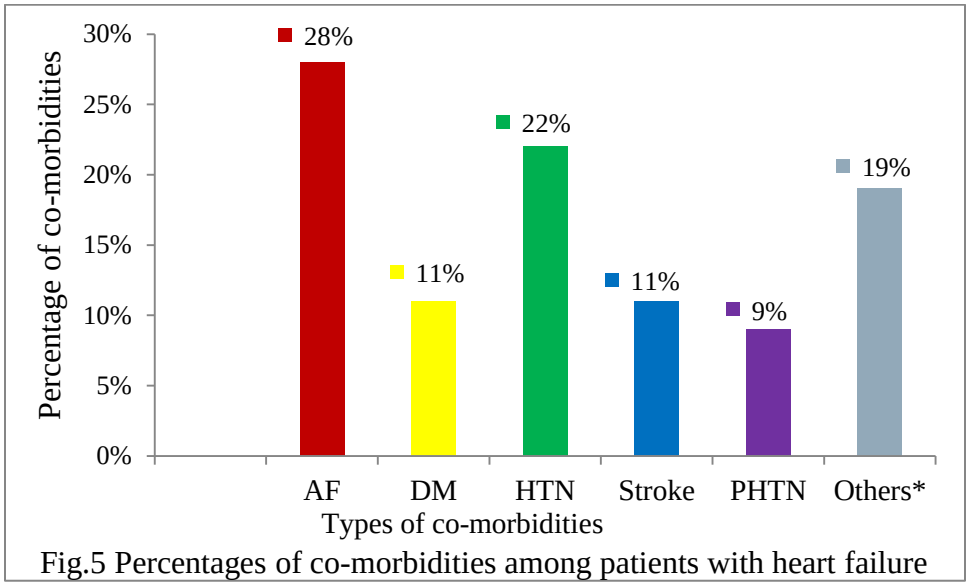

Figure 5. Percentages of co-morbidities among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

AF: Atrial fibrillation, DM: Diabetic, HTN: Hypertension, PHTN: Pulmonary hypertension

*Others: Chronic kidney disease (CKD), dyslipidemia, benign prostate hyperplasia(BPH), bronchial asthma, goutry arthritis, osteoarthritis, peripheral arterial disease (PAD), retroviral infection(RVI), erectly dysfunction, schizophrenia, chronic myeloid leukemia(CML), depression, aortic aneurism, hypothyroidism, left atrial thrombus, severe anemia, cardiac cirrhosis, chronic hepatitis B-virus (HBV), and atria-ventricular-block, bradycardia.

5.3 Management Approaches of Heart Failure Patients

5.3.1 Non-Pharmacological Management Approaches of Heart Failure Patients

Nearly two-third, 262(63.6%) of study participants had no agreed exercise plan with physicians. Majority of study participants 301(73.1%) had agreed dietary plans with physicians (Table 3).

Table 3. Non-pharmacological management approaches of study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Variables	Frequency (%)
Dietary Approaches	
Presence of agreed dietary plan with physicians	
Yes	301(73.1)
No	111(26.9)
Presence of agreed exercise plan with physicians	
Yes	150(36.4)
No	262(63.6)
Cigarette	
Current smoker	2(33.33)
Previous smoker	4(66.67)
Regular coffee intake	
Yes	333(80.8)
No	79(19.2)
Presence of regular alcohol consumption	
Yes	85(20.6)
No	327(79.4)
Recreational drug use / khat chawing	
Yes	14(3.4)
No	398(96.6)

5.3.2 Pharmacological Management Approaches of Heart Failure Patients

A total number of prescribed medications used for HF management were 1662 drugs. The mean (SD) number of drugs use per day was 4.2±1.71 per patient. Commonly prescribed drug classes were diuretics (26%), followed by B-blockers (16%). The most frequently prescribed specific drugs were furosemide (15%), followed by benzathine penicillin (11%), and then warfarin (10%) (Table 4).

Table 4. Profile of prescribed medications for study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Variables	Frequency	Percent
Diuretics	419	
Furosemide	243	15
Spironolactone	149	9
Hydrochlorothiazide	27	2
Beta blockers	266	
Atenolol	132	8
Metoprolol	120	7
Carvedilol	14	1
Anticoagulants	167	
Warfarin	164	10
Rivaroxaban	3	0.1
Angiotensin Converting Enzyme Inhibitor		
Enalapril	150	9

Table 4 (cont.)

Variables	Frequency	Percent
Angiotensin Receptor Blocker		
Losartan	10	1
Cardiac Glycoside		
Digoxin	95	6
Anti-Diabetic Medications		
NPH Insulin	25	2
Metformin	20	1
Glibenclamide	3	0.1
Calcium Channel Blockers		
Amlodipine	53	3
Anti-platelets		
Asprin	119	7
Clopidogrel	12	1
Statins	122	7
Benzathine penicillin	182	11
Others*	19	1
Total number of medications	1662	

*Others: alfuzosin, captopril, amitriptyline, allopurinol, isosorbide dinitrate, amlodipine/valsartan, telmsartan

5.4 Number of Drug Therapy Problems among Heart Failure Patients

The number of identified DTPs was 288 in the pre-intervention phase and 174 in the post-intervention phase, providing prevalence of 70% and 42.2%, with a mean (SD) of 1.3±1.1 and 0.63±0.87 per patient, respectively (Figure 6). One DTP was identified in 95(23.1%), 2 DTPs in 144(35%), and ≥ 3 DTPs in 49(11.9%) patients in the pre-

intervention phase. On the other hand, one DTP was identified in 114(27.7%), 2 DTPs in 36(8.7%), and ≥ 3 DTPs in 24(5.8%) patients in the post-intervention phase (Figure 6).

In the pre-intervention phase, drug-drug interactions, non-adherent to medications, and need additional preventive or prophylactic therapy were the most prevalent DTPs, which accounted for 196/288(47.6%), 154/288(37.3%), and 55/288(13.3%) cases, respectively whilst 36/288(8.7%) patients did not receive the most effective drugs, in 18/288(4.4%) patients the doses used were ineffective. Other DTPs including dose too high, medication use without indication, and duplicate therapy accounted for a relatively low number (Table 5).

However, drug-drug interactions, non-adherent to medications, did not receive the most effective drugs, and need additional drug therapy were decreased by 78(19%), 131(31.7%), 22(5.3%), and 63(15.3%) following interventions, respectively (Table 5).

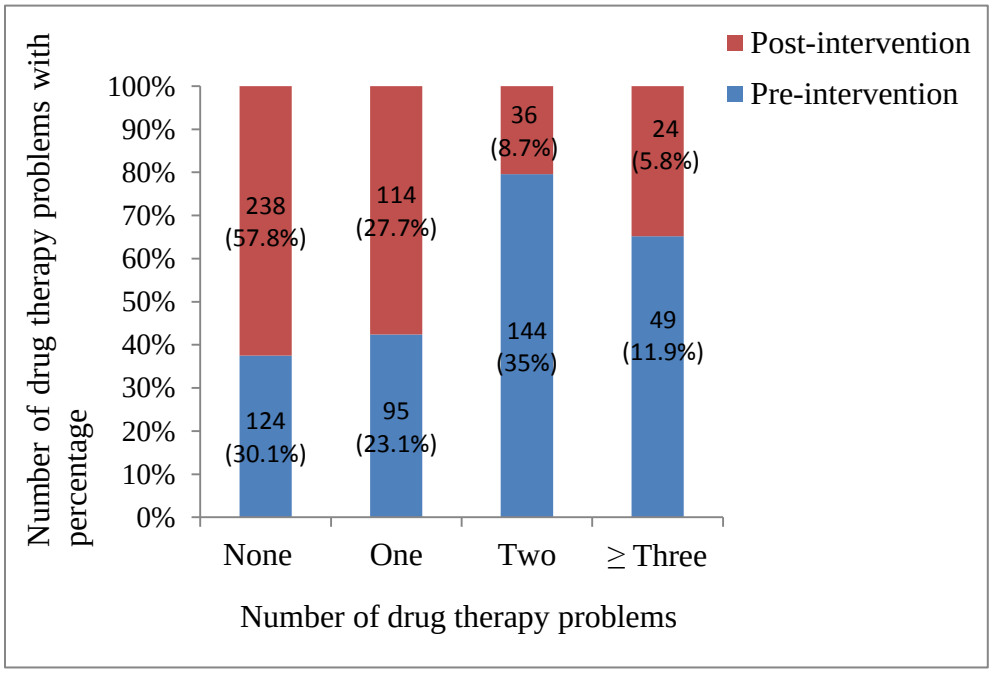

Figure 6. Number of identified drug therapy problems per patient during pre-intervention and post-intervention phases among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

As shown below in Table 5, based on the paired t-test result, there was strong evidence that, number of DTPs were reduced in the post-intervention phase compared to the pre-intervention phase [mean difference (SD) 0.67±1.1 with 95% CI of difference (0.57, 0.78), t=12.4, p<0.001].

Table 5. Drug therapy problems identified and results of Paired sample T-test of identified drug therapy problems during pre and post intervention phases among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Type of DTPs [R]	Specific DTPs	Pre-intervention n(%)	Post-intervention n(%)	Paired sample T-test of DTPs in pre-post interventions		
				Mean difference ± SD	95% CI	P-value*
Unnecessary drug therapy	No indicated medical condition	8(1.9)	1(0.2)	0.67±1.1	(0.57,0.78)	<0.001
	Duplicate therapy	9(2.2)	1(0.2)			
Needs additional drug therapy	Untreated indication	1(0.2)	1(0.2)			
	Preventive or prophylactic	55(13.3)	8(1.9)			
	Synergistic or potentiating	21(5.1)	5(1.2)			
Ineffective drug product	More effective alternative is available	36(8.7)	14(3.4)			

Table 5 (cont.)

Type of DTPs [R]	Specific DTPs	Pre-intervention n(%)	Post-intervention n(%)	Paired sample T-test of DTPs in pre-post interventions		
				Mean difference ± SD	95% CI	P-value*
	Not effective for the condition	10(2.4)	7(1.7)			
	Contraindication present	11(2.7)	2(0.5)			
Dose too low	Ineffective dose	18(4.4)	3(0.7)			
	Frequency inappropriate	0	1(0.2)			
Adverse drug reaction	Undesirable effect not dose related	4(1)	0			
	Unsafe drug for patient	2(0.5)	1(0.2)			
	Drug interaction not dose related	196(47.6)	118(28.6)			
Dose too high	Wrong dose(over therapeutic dose)	5(1.2)	0			
	Frequency inappropriate	1(0.2)	0			

Table 5 (cont.)

Type of DTPs [R]	Specific DTPs	Pre-intervention n(%)	Post-intervention n(%)	Paired sample T-test of DTPs in pre-post interventions		
				Mean difference ± SD	95% CI	P-value*
Non-adherence	Drug interaction	0	2(0.5)			
	Direction is not understood	7(1.7)	2(0.5)			
	No willingness to take the drug	22(5.3)	6(1.5)			
	Patient forget to take the drug	32(7.8)	1(0.2)			
	Cost of medication too expensive	40(9.7)	2(0.5)			
	Patient can’t swallow/administer	10(2.4)	1(0.2)			
	Unavailability of medication	19(4.6)	8(2)			
	Regimen complexity	24(5.8)	3(0.7)			

*****; Using paired T-Test at 5% significance level.

SD=Standard deviation: DTPs= drug therapy problems:

R ; Drug therapy problem classification based on Cipolle et al. classification system

5.4.1 Drug interactions

As shown below in Table 6, 290, drug-drug interactions were identified in the pre-intervention phase among the study participants. Warfarin and benzathine penicillin were the most common interacting drugs accounted for 96(33%) of the total drug-drug interactions, followed by spironolactone and digoxin 46(16%), and then aspirin and furosemide 35(12%) in the pre-intervention phase.

Table 6. Frequency of major drug-drug interacting regimens among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Drugs involved in DDI	Pre-intervention n(%)	Post-intervention n(%)	Severity	Possible effects
Spironolactone + enalapril	31(10)	12(9%)	major	Increased risk of hyperkalemia
Spironolactone + digoxin	46(16)	14(11%)	major	Increased digoxin toxicity
Aspirin +furosemide	35(12)	0	major	Increased risk of nephrotoxicity
Aspirin +metformin	16(6)	3(2%)	major	Increased risk of hypoglycemia
Aspirin + amitriptyline	6(2)	1(0.8%)	major	Increased risk of bleeding
Amlodipine +digoxin	2(0.6)	0	major	increase the risk of bradycardia and complete heart block
Amlodipine +simvastatin	8(3)	1(0.8%)	major	Myopathy
Aspirin +digoxin	4(2)	1(0.8%)	major	Increased serum digoxin level
Aspirin +spironolactone	14(5)	1(0.8%)	major	Increased risk of nephrotoxicity

Table 6 (cont.)

Drugs involved in DDI	Pre-intervention n(%)	Post-intervention n(%)	Severity	Possible effects
Aspirin + HCT	10(3)	4(3.1%)	major	Increased risk of nephrotoxicity
Aspirin +warfarin	7(2)	4(3.1%)	major	Increased risk of bleeding
B.penicillin +warfarin	96(33)	87(67%)	major	Increased risk of bleeding
Atorvastatin + digoxin	3(1)	1(0.8%)	major	Increased digoxin toxicity
Aspirin + clopidogrel	4(2)	1(0.8%)	major	Increased risk of bleeding
Captopril +digoxin	1(0.35)	0	major	Increase risk of digoxin toxicity
Simvastatin +warfarin	2(0.6)	0	major	Increase risk of bleeding and rhabdomyolysis
Digoxin +HCT	2(0.6)	0	major	Increased digoxin toxicity
Azithromycin + warfarin	2(0.6)	0	major	Increased risk of bleeding
Erythromycin +warfarin	1(0.35)	0	major	Increased risk of bleeding

DDI: Drug-drug interaction.

Of the 14 ADR identified, dry cough and bleeding were 7 cases and 5 cases, respectively. On the other hand, hypotension, penicillin allergy, and amenorrhea were the least identified ADRs.

5.4.2 Predictors of Drug Therapy Problems

In the multivariable linear regression analysis, for each daily take of drugs increase by one drug, DTPs were increase by 0.106 times (B=0.106, 95% CI [0.03, 0.15], p=0.001). As the number of co-morbidities increased by one disease, DTPs were increase by 0.104 times (B=0.104, 95% CI [0.03, 0.16], p=0.002) (Table 7).

The study revealed that HF patients with drug-drug interactions were 0.92 times increased DTPs than HF patients who did not have (B=0.92, 95% CI (0.68, 0.91), p<0.001). For each 10 years increase in patients' age, DTPs was decreased by 0.1 times (B= -0.01, 95% CI [-0.01, -0.002], p=0.014). Please note that we are not saying that an increase in patient age is causing lower DTPs (Table 7).

Hence, age, number of drugs, presences of co-morbidity, number of co-morbidities, and drug-drug interactions were the only predictors of DTPs in HF patients. The other patient factors did not have statistically significant relationship with DTPs (Table 7).

Table 7. Univariable and multivariable linear regression analysis of predictors of drug therapy problems among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Variables	Univariable analysis Unstandardized Coefficient(B) (95% CI)	P value	Multivariable Analysis Unstandardized Coefficient(B) (95% CI)	P value
Age(years)	-0.003(-0.01,0.003)	0.3	-0.01(-0.01,0.002)	.014
Number of drugs	0.073(0.02,0.13)	0.014	0.106(0.03,0.15)	0.001
Number of Co-morbidities	0.096(0.03,0.16)	0.003	0.104(0.03,0.16)	0.002
Gender				

Table 7(cont.)

Variables	Univariable analysis Unstandardized Coefficient(B) (95% CI)	P value	Multivariable Analysis Unstandardized Coefficient(B) (95% CI)	P value
Male	1		1	
female	0.11(-0.11,0.32)	0.32	0.13(-0.1,0.36)	0.28
Smoking				
No	1		1	
Yes	-0.68(-1.77,0.41)	0.22	-0.62(-1.6,0.43)	0.25
ADR				
No	1		1	
Yes	0.49(-0.11,1)	0.1	0.34(-0.27,0.9)	0.3
Drug interaction				
No	1		1	
Yes	0.76(0.56,0.97)	P<0.001	0.92(0.68,0.91)	P<0.001
Co-morbid disease				
No	1		1	
Yes	0.42(0.19,0.65)	P<0.001	0.66(0.41,0.9)	P<0.001

5.5 Medication Adherence among Heart Failure Patients

According to the eight-items Morisky medication adherence scale, at pre-intervention phase, 6.3% of HF patients were highly adherent, 54.6% of patients had medium adherent, while 39.1% of patients were poorly adherent to their treatment regimens. However, the adherence scores had greatly improved after the interventions. At post-intervention phase, 36.4%, 61.9%, and 1.7%, of HF patients were highly adherent, medium adherent, and poor adherent to their treatment regimens, respectively (Figure 7).

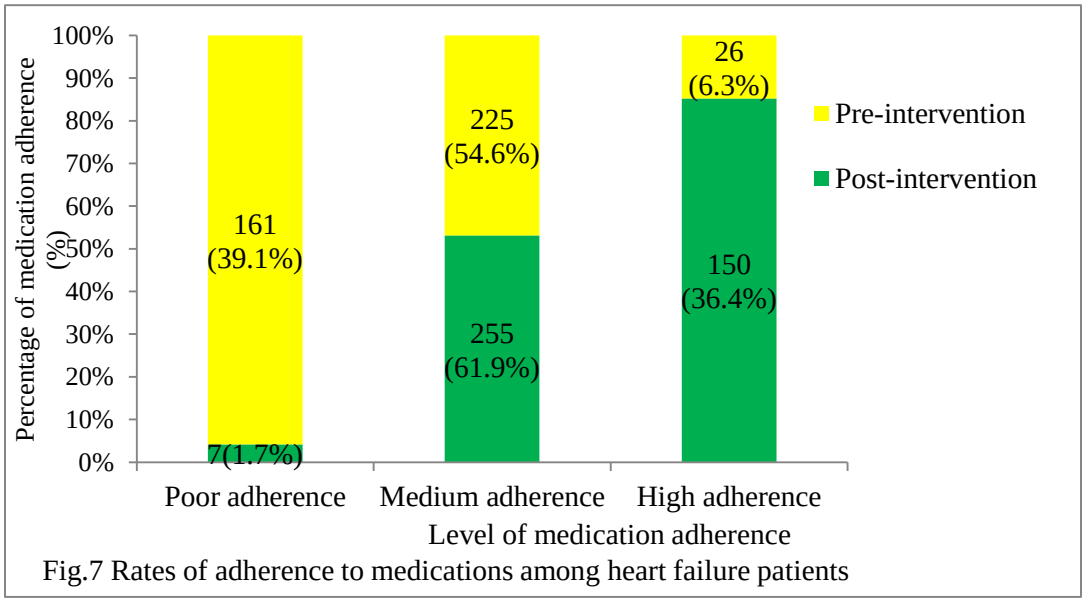

Fig.7 Rates of adherence to medications among heart failure patients

Figure 7. Rates of medication adherence in pre and post intervention phases among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

5.5.1 Paired T-test Results of Pre and Post Medication Adherence Interventions

As shown below in Table 8, the overall medication adherence of Morisky scores revealed that, a statistically significantly higher mean score of medication adherence in the post-intervention phase compared to the pre-intervention phase [mean difference (SD) 1.3±1.31, 95% CI of the difference (1.17,1.43), t= 20.17, p<0.001].

Table 8**.** Results of paired sample T-test of medication adherence in the pre and post interventions among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

	Pre-intervention**	Post-intervention**	Mean difference ± SD	95% CI	P-value*
	Mean ± SD	Mean ± SD			
Adherence score [K]	5.8 ±1.1	7.1 ± 0.82	1.3±1.31	(1.17, 1.43)	<0.001

*****; Using paired T-Test at 5% significance level.

SD=Standard deviation

K; HF patient medication adherence based on Morisky questionnaire.

**; The pre and post medication adherences percentage calculated out of the total number of Morisky scores.

5.5.2 Possible Reasons for Medication Non-adherence among HF Patients

Upon evaluation of the reasons for HF medication non-adherent, forgetfulness (40%) was the main reason, followed by inadequate availability of medications, and then the cost of medication too expensive accounted for 29% and 22%, respectively in the pre-intervention phase (Table 9). Nevertheless, cost of medication too expensive 120(50%), inadequate availability of medication 75(31%), and forgetfulness 30(13%) were the main reasons for medication non-adherent in the post-intervention phase (Table 9).

Table 9. Reasons for medication non-adherence in the pre and post-interventions among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Reason for medication non-adherence	Pre-intervention n(%)	Post-intervention n(%)
Cost of medication too expensive	70(22)	120(50)
Inadequate availability of medication	90(29)	75(31)
Drug side effect	3(1)	4(2)
Simply Forgetfulness	125(40)	30(13)
Patients has no support at home	1(0.1)	1(0.1)
Regimen complexity	20(7)	8(3)
Patient prefer not to take	1(0.1)	0
Patients felt worse when take drug	4(1)	1(0.5)

5.5.3 Predictors of Medication Adherence

In the multivariable linear regression analysis, as the number of co-morbidities increased by one disease, the medication adherence score was decreased by 0.12 times (B= -0.12, 95% CI [-0.19, -0.05], p=0.001). HF patients who had drug-drug interactions were 29% lower medication adherent than those who did not have (B= -0.29, 95% CI [-0.52, -0.07], p=0.01). Furthermore, HF patients' drug regimens increased by one drug, the medication adherence score was decreased by 0.17 times (B=-0.17, 95% CI [-0.24, -0.11], p <0.001) (Table 10).

HF patients who had incomes ≥5000 birrs were 0.95 times higher medication adherent than those who had very low income (B= 0.95, 95% CI [-1.32, -0.03], p=0.014). In addition, study participants who had ADRs' were 0.86 times lower medication adherent than those who did not have ADR (B=-0.86, 95% CI (-1.54,-0.17), p=0.014). Therefore, the number of drugs, number of co-morbidities, presences of comorbidity, drug-drug interaction, presence of ADR, agreed dietary plan, and income level of study participants were the only predictors of medication adherence in HF patients (Table 10).

Table 10. Univariable and multivariable linear regression analysis of predictors of medication adherence among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

Variable	Univariable Analysis Unstandardized Coefficient(B) (95% CI)	P value	Multivariable Analysis Unstandardized Coefficient(B) (95% CI)	P value
Age	-0.002(-0.01,0.01)	0.67	-0.01(-0.01,0.003)	0.24
Total number of drugs	-0.19(-0.25,-0.13)	<0.001	-0.17(-0.24,-0.11)	<0.001
Number of co-morbidities	-0.11(-0.18,-0.05)	0.001	-0.12(-0.19,-0.05)	0.001
Gender				
male	1		1	
Female	0.02(-0.24,0.27)	0.91	-0.12(-0.39,0.17)	0.44
Agreed dietary plan				
No	1		1	
Yes	0.55(0.27,0.83)	< 0.001	0.48(0.18,0.79)	0.002
Drug interaction				
No	1		1	
Yes	-0.30(-0.53,-0.08)	0.008	-0.29(-0.52,-0.07)	0.011
Adverse drug reaction				
No	1			
Yes	-1.3(-2.0,-0.63)	<0.001	-0.86(-1.54,-0.17)	0.014
Presence of co-morbidities				
No	1		1	
Yes	-0.72(-0.98,-0.45)	<0.001	-0.69(-1.00,-0.38)	<0.001
Drug allergy history				
No	1		1	

Table 10 (cont.)

Variable	Univariable Analysis Unstandardized Coefficient(B) (95% CI)	P value	Multivariable Analysis Unstandardized Coefficient(B) (95% CI)	P value
Yes	0.31(-0.34,0.97)	0.35	0.24(-0.52,1)	0.53
Income				
Very low income	-0.47(-0.79,-0.15)	0.5	1	
Low income	-0.23(-0.54,0.08)	0.15	0.2(-0.24,0.63)	0.38
Average income	0.18(-0.11,0.44)	0.19	0.38(-0.006,0.77)	0.059
Above average income	0.2(-0.12,0.51)	0.2	0.27(-0.15,0.69)	0.2
≥5000 income	1.2(0.47,1.9)	0.001	0.95(-1.54,-0.17)	0.014

5.6 Acceptance of Clinical Pharmacist Interventions

As indicated in Figure 8, 148(35.92%) of the clinical pharmacist interventions were fully accepted, 68(16.5%) partially accepted, while 38(9.22%) of the interventions were not accepted by the physicians.

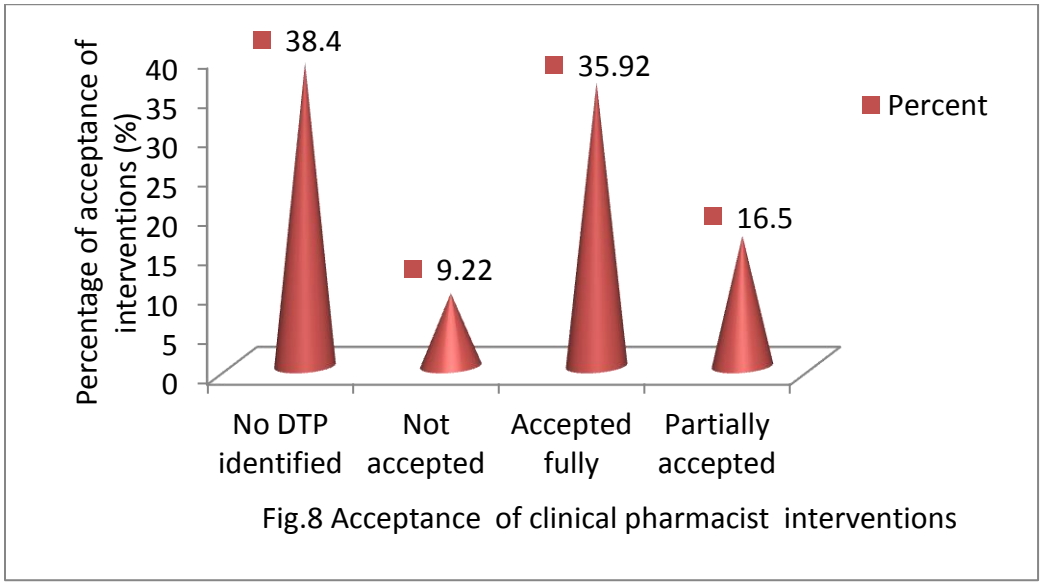

Figure 8. Percentages of acceptance of clinical pharmacist interventions on drug therapy problems among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

5.6.1 Examples of Drug Therapy Problems Identified from Study Participants

Table 11. Examples of drug therapy problems identified from study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

No	Description of DTP	Type of DTP	Intervention
1	A 69 years-old male patient diagnosed with IHD (EF 39) and type2 DM. He currently takes atenolol 25mg PO bid, ASA 81mg PO/d, atorvastatin 40mg PO/d, metformin 500mg PO bid, and NPH insulin. Nevertheless, for patients with HFrEF atenolol is not effective. There are DDI between(ASA with metformin)	• Not the most effective drug (change atenolol to metoprolol succinate 50mg PO bid) • DI	Fully accepted
2	A 46 years-old female patient with NYHA class III, DCMP (EF=10), and AF. She currently takes furosemide 60mg PO tid, spironolactone 25mg PO/d, and warfarin 5mg PO/d. Her BP, PR, and INR were 102/68mmHg, 98 beats/min, and 2, respectively.	Need additional synergistic drug therapy(Start metoprolol succinate 12.5mg PO/day)	Partially accepted
3	A 35 years-old male diagnosed with DCMP(EF=30). He currently takes enalapril 5mg PO/day and atenolol 25mg PO bid. His BP and PR was 110/70 and 78, respectively. The patient has not received the most effective drug. Spironolactone can also be considered in symptomatic patients with HFrEF and LVEF ≤35%.	Need additional synergistic drug therapy (add spironolactone 25mg and ASA 81mg PO/d) Not received the most effective drug (discontinued atenolol and start metoprolol succinate 50mg PO bid).	Accepted fully

Table 11 (cont.)

No	Description of DTP	Type of DTP	Intervention
4	A 46 years-old male patient diagnosed with IHD, type 2 DM, AF, and gout arthritis. Currently he takes metoprolol 25mg PO/d, allopurinol 100mg PO/d, metformin 500mg PO bid, furosemide 60mg PO tid, candesartan 4mg PO/d, warfarin 2.5mg PO/d. His BP was 90/60. However, the guideline recommends statin use for CVD with type 2 DM patients >45years old.	Dose too high (deescalate furosemide 60mg bid). Need additional cardiac preventive drug therapy(add atorvastatin 20mg PO per day)	Fully accepted
5	A 47 years-old male patient presented with IHD and PAD. He is taking ASA 81mg PO/d, simvastatin 40mg PO/d, and metoprolol 25mg PO/d. Unfortunately, ASA is not recommended for patients who had PAD.	Contraindication present (unsafe drug for the patient) discontinue ASA and start clopidogrel 75mg PO/d)	Accepted fully
6	A 48-years-old female patient diagnosed with CRVHD and LVH. She currently takes furosemide 40mg PO bid, spironolactone 25mg, and metoprolol succinate 12.5mg for the past 9 months. Her BP was 110/70 and her pulse was 92 beats/min.	Dose too low(escalate the dose of metoprolol to 25mg PO /d)	Accepted partially

Table 11 (cont.)

No	Description of DTP	Type of DTP	Intervention
7	A 51 years-old male patient diagnosed with IDCMP(EF 15%). He was on furosemide 80mg PO tid, spironolactone 25mg PO/d, atorvastatin 40mg PO/d, enalapril 2.5mg PO/d, metoprolol succinate 12.5mg PO/d, Hydrochlorothiazide 25mg PO/d, and digoxin 0.125mg PO/d. His BP was 70/40mmHg. The dose of furosemide is high and there is a duplication of drug therapy.	• Dose too high (make furosemide 80mg PO bid). • Unnecessary drug therapy [duplication of drug(discontinue HCT)]	Accepted fully
8	A 73 years-old female patient was diagnosed with HHD, type 2 DM, and gouty arthritis. Currently, she is taking allopurinol 100mg PO/d, atenolol 50mg PO/d, glibenclamide 5mg PO/d, simvastatin 40mg PO/d, and ASA 81mg PO/d. With her current drug regimens, her BP is not controlled (170/90 mmHg) since she has compelling indication (DM), enalapril could be considered as synergistic therapy and ASA is not recommended >70 years old.	• Not received the most effective drug (discontinue atenolol and start carvedilol 12.5mg PO bid) • Unsafe drug for the patient (discontinue ASA and start clopidogrel 75mg PO/d) • Need additional drug (start enalapril 5mg PO/d)	Accepted partially

Table 11 (cont.)

No	Description of DTP	Type of DTP	Intervention
9	A 72 years-old male patient diagnosed with HTN, IHD, and LVH. He is taking ASA 81mg PO/d, enalapril 5mg PO bid, atenolol 50mg PO/d, and simvastatin 20mg PO/d. Nevertheless, this patient has not received the most effective drug.	• Not received the most effective drug(discontinue atenolol and start carvedilol 12.5mg PO bid)	Partially accepted
10	A 59 years-old female presented with T2DM, HTN, and IHD. She currently takes amlodipine 5mg, metoprolol succinate 50mg, atorvastatin 40mg, losartan 50mg, metformin 1gm bid, and glibenclamide 5mg. Her BP and PR were 160/80mmHg and 98 beats/min, respectively. She had a history of dry cough during she took enalapril. But, the patient needs an antiplatelet drug for cardiovascular protection.	• Need additional drug therapy(start ASA 81mg PO/d) • Dose too low(escalate the dose of amlodipine to 7.5mg PO/d and metoprolol succinate 50mg PO bid)	Accepted fully
11	A 62 years-old female patient was diagnosed with DVHD, HTN, OA, and drug-related depression. Now she is taking metoprolol succinate 12.5mg not available (atenolol 12.5 mg PO/d), HCT 25mg PO/d, and ASA 81mg PO/d. Her BP and PR was 130/70mmHg and 80 beats/min, respectively. The patient experienced drug-induced depression and the patient forgets to take drugs.	• Received ineffective drug(discontinue HCT and start amlodipine 5mg PO/d) • Patient non-adherent to her medications	Not accepted

Table 11 (cont.)

No	Description of DTP	Type of DTP	Intervention
12	A 56 years-old female patient comes with CRVHD, AF, and old cardio-embolic stroke. Currently she is taking digoxin 0.125mg PO/d, furosemide 20mg PO/d, spironolactone 12.5 mg, carvedilol 12.5mg, and ASA 81mg. Her PR was 68 beats/min. However, the guideline recommend anticoagulant is superior to antiplatelet drugs for prevention of patients with cardio-embolic stroke with AF.	• Not received the most effective drug (discontinue ASA and start warfarin 5mg PO/d)	Accepted fully
13	A 80 years-old male patient was diagnosed HHD with HTN, sclerotic aortic valve disease, and T2DM. He currently takes enalapril 10mg PO bid and atorvastatin 20mg PO/d. His BP and PR was 160/85mmHg, 60 beats/min, respectively. However, the patient experienced poor BP control.	• Need additional drug(start amlodipine 5mg po/d)	Accepted fully
14	A 24 years-old male patient diagnosed with CRVHD. She currently takes furosemide 40mg PO/d, spironolactone 25mg PO/d, digoxin 0.125mg PO/d, and warfarin 5mg PO/d. His pulse rate was 110 beats/min not controlled by digoxin alone.	• Need addition drug(start metoprolol succinate 12.5mg PO/d)	Not accepted

5.7 Treatment Satisfaction of Heart Failure Patients

The total composite score of treatment satisfaction of the study participants was 80.35%. For medical care service, 93.3% of study participants were satisfied regarding detailed information on drug treatment and disease. Around 9 % of the study participants said that, the undesirable side effects of the medications were interfering with their daily, leisure, and physical activities (Table 12).

Table 12. Treatment Satisfaction among study participants attending cardiac clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July to December, 2019

SATMED-Q-Dimension	Standard value total	Standard value Transformed	Min	Max	Percent	Mean	SD
Undesirable side effect (0-100)	12	18	0	16.2	9	1.6	1.8
Treatment effectiveness(0-100)	12	18	14.7	18	90	16.2	0.8
Convenience of use (0-100)	12	18	14.7	18	90.6	16.3	0.8
Impact on daily living (0-100)	12	18	14.7	18	91.7	16.5	0.82
Medical care(0-100)	8	12	8.8	12	93.3	11.2	0.8
Global satisfaction (0-100)	12	18	13.2	18	91.7	16.5	0.95
Total composite score (0-100)	68	100	72.1	95.6	80.35	80.35	3.84

6. Discussion

In our study, patients' received 1662 medications with a mean (SD) of drugs per day of 4.2±1.71 per patient. This finding is lower than studies done in China(mean=5.08 ±3.02) (Lee et al., 2015b) , Australia (10.2 ± 3.2) (Gastelurrutia et al., 2011), and Taiwan (17.6 ± 2.9)(Hsu et al., 2015). The reason might be attributed to differences in the study area and the study setting (outpatient vs. inpatients); usually admitted patients are exposed to more medications. This can cause the above variations.

Diuretics (26%) were the most widely used drug class in the management of HF followed by B-blockers (16%), and then ACEI (9%). This finding is lower than studies done by Tegegne et al (diuretics accounted 62.5%) (Tegegne et al., 2015) and Niriayo et al [B-blocker (59.1%) and ACEI (71.2%)] (Niriayo et al., 2018). The reason for this lower percentage could be the inaccessibility of medication in the study setting that has a benefit of reducing morbidity and mortality of HF.

B-blockers, ACEIs, diuretics, anticoagulants, cardiac glycosides, and antiplatelet were common drug classes involved in the development of DTPs. This finding is in line with study done in Spain (ACEI/ARB, B-blockers, anti-aldosterone drugs, diuretics, and digoxin) common drug class and/or drugs involved in DTPs (Gastelurrutia et al., 2011).

Based on the paired t-test result, there was a statistically significant difference between mean DTPs of the pre and post interventions (mean difference (SD) = 0.67 ±1.1, $p<0.001$). DTPs reduced from 70% in the pre-intervention phase to 42.2% in the post-intervention phase. This finding is lower than studies done in Indonesia (DTPs mean difference = 5.72 ±1.92 and 88% reduction of DTPs by clinical pharmacist intervention) (Sagita et al., 2018). This finding is also supported by a systematic review and meta-analysis of 59 studies, 68% of HF outcome was associated with better improvement by clinical pharmacist educational intervention and medication management intervention (Altowaijri et al., 2013).

Regarding the type of DTPs encountered in the present study, DDI, non-adherence, and need additional preventive or prophylactic therapy were the most prevalent DTPs in both the pre and

post-intervention phases. DDI was the first most prevalent DTPs in both the pre-intervention (47.6%) and post-intervention phases (28.6%). These findings of DDIs were a 'moderate' level of significance. These problems requiring drug regimen adjustments. This finding is lower than a similar study done in Nepal, 53% in the pre-intervention, and 41% in the post-intervention phases (Bista et al., 2009). A possible explanation could be applying a different standard drug interaction database to identify drug-drug interactions and differences in the classification and operationalization of drug interaction. For example, studies conducted in India, drug-drug interaction operationalized as the result of a drug-drug, drug-food, or drug-laboratory test interaction. However, the present study considers only drug-drug interactions. Although the use of drug combinations is becoming unavoidable and can further increase the risk of DDI, this is often predictable and preventable(Bista et al., 2009).

The most common DDI were between benzathine penicillin and warfarin (33%) followed by spironolactone and digoxin (16%), ASA and furosemide (12%), and then spironolactone and enalapril (10%) in the pre-intervention phase while in the post-intervention phase; warfarin and benzathine penicillin(67%), spironolactone and enalapril(9%), and then spironolactone and digoxin(11%) were accounted in a higher percentage. This finding is inconsistent with studies done in India (antiplatelet agents, antihypertensive, and GI drugs most commonly involved in DDI) (Shareef, 2015) and Nepal (Atorvastatin and azithromycin(10.4%), enalapril and metformin(10.4%), enalapril and potassium chloride(10.4%), atorvastatin and clarithromycin (8.3%), and furosemide with gentamicin (6.3%)(Sharma and Vaishya, 2014). The reason might be due to differences in the study area and health setting. Both the above two studies were done in hospitalized cardiac patients.

Needs additional drug therapy accounted (18.6%) in the pre-intervention phase and (3.3%) in the post-intervention phase. By pharmacist intervention, 15.3% of additional drug therapy initiated. This finding is lower than studies done in Saudi Arabia(35%) (Bahmaid et al., 2016), in Memphis, United States(38%) (Hutchison et al., 2014), and Mexico (38.3%) (Sarangarm et al., 2013).

Patients who had not received the most effective drug were common DTPs both in the pre-intervention phase (8.7%) and in the post-intervention phase (3.4%). Pharmacists' intervention

changed, 5.3% of the ineffective drug to effective drug. This finding is lower than studies done in Australia(45%) (Gastelurrutia et al., 2011), and Jordan, Asia(25.4%) (El-Refae and Abuhamdah, 2017). But, higher than studies done in India(5.6%)(Shareef, 2015) and Spain(2.23%)(Urbina et al., 2014). This difference may be due to unavailability of most effective drugs used to treat HF disease in our resource-limited setting.

Dose too low accounted, 4.4% and 0.9% out of all DTPs in the pre-intervention and the post-intervention phases, respectively. Pharmacists' interventions increased the low dose of drugs by 3.5%. This finding is lower than Taiwan (dose too low=4.1%) (Hsu et al., 2015) and Spain (dose too low =0.45 %). In the current study, ACEIs and evidence-based β-blockers titrated towards established ESC and AHA guidelines recommended target doses. These lead to adequate inhibition of the renin-angiotensin-aldosterone system by ACEI on ventricular remodeling, norepinephrine release, vasoconstriction, sodium and water retention, and preventing myocardial fibrosis, myocyte apoptosis, and cardiac hypertrophy (Stout et al., 2018, van der Meer et al., 2019).

Drugs have no indicated medical condition and duplicate therapy accounted for (4.1%) in the pre-intervention phase and (0.4%) in the post-intervention phase. Pharmacists' intervention discontinued 3.7% of unnecessary drug therapy. The finding is lower than studies done in Jordan, Asia (El-Refae and Abuhamdah, 2017), USA(J Kiel and W Phillips, 2017), Spain(22%)(Gastelurrutia et al., 2011), Memphis ,United State(28.4%)(Hutchison et al., 2014), and Minnesota(12.5%)(Ramalho de Oliveira et al., 2010).

In the multivariable linear regression analysis, the number of drugs, number of co-morbidities, drug-drug interaction, age, and presence of co-morbidities found to be statistically significant relations with DTPs.

As the number of prescribed drugs increased by one drug, DTPs were increased by 0.106 times (B=0.106, 95% CI [0.03, 0.15], p=0.001). The finding of this study is similar to other studies reported that multiple uses of drugs were a significant predictor for developing at least one DTPs (Tigabu et al., 2014, Baena et al., 2006, Niriayo et al., 2018, Urbina et al., 2014, Gastelurrutia et al., 2011, Abdela et al., 2016).

As the number of co-morbidities was increased by one disease, DTPs was increased by 10.4% (B=0.104, 95% CI [0.03, 0.16], p=0.002). This finding is supported by studies done in Jimma, Ethiopia, demonstrated that a number of co-morbidity was a risk factor for the occurrence of DTPs (e.g. studies done by Tegegn et al reported that as the number of co-morbidities was increased by one unit, the number of DTPs was increased by 28.2%)(Tegegne et al., 2015, Niriayo et al., 2018).

The age of study participants, also another factor significantly related with DTPs. This is supported by previous studies done in Spain (Baena et al., 2006), Ethiopia(Tigabu et al., 2014, Niriayo et al., 2018), and Australia (Gastelurrutia et al., 2011). As age, co-morbidity, and the number of drugs increase, this puts patients to an increased risk for developing DTPs.

The study revealed that HF patients who had significant drug-drug interactions were 0.92 times increased DTPs (B=0.92, 95% CI (0.68, 0.91), p<0.001) compared to patients who did not have. This is similar to studies done in Jimma university specialized hospital, Ethiopia(Tigabu et al., 2014). The higher likelihood of having drug-drug interactions may plausibly be due to the complexity of drug regimens in the management of HF.

We have found 14(3.4%) study participants developed ADRs. Seven participants had dry cough while five participants had bleeding. This finding is lower than studies done in Minnesota(34%) (Fischer et al., 2002) and Spain (16%)(Gastelurrutia et al., 2011).

Based on the paired t-test results, the Morisky score result showed a significant improvement in participants' levels of medication adherence. In the pre-intervention phase, > 39 % of study participants had poor medication adherence and < 7% of study participants had high medication adherence. While, in the post-intervention phase, < 2% of study participants had poor medication adherence and >36% of the study participants had high mediation adherence. This finding is higher than studies done in Chicago, USA (medication adherence was 67.9% and 78.8% in the usual care and intervention groups, percentage difference 3.9%)(Murray et al., 2007), Mexico(58.5% and 75.7% in the control and intervention groups (Sarangarm et al., 2013), and USA(28.9% poor medication adherence))(Knafl, 2014). This variation could be attributed to differences in the study setting, methods used to measure medication adherence, study design,

level of health facilities, and physicians' approach to their patients that could bring differences in patients' attitudes for their medication. This finding is supported by a systematic review and meta-analysis done by Ruppar et al reported that pharmacist intervention had significant effects to improve medication adherence among HF patients(Ruppar et al., 2016).

Out of the various reasons behind the non-adherent issue in the pre-intervention phase, forgetfulness (40%), inadequate availability of medications(29%), and cost of medication too expensive(22%) were the main reasons for medication non-adherent. However, in the post-intervention phase cost of medication too expensive (50%), inadequate availability of medication (31%), and forgetfulness (13%) were among the top-ranking reasons for medication non-adherent in HF patients.

Moreover, forgetfulness was the main reasons contribute to poor medication adherence both in the pre and in the post-intervention phases. This finding is in line with similar studies done in Carolina, USA (Shah et al., 2015) and New York, USA (Aggarwal et al., 2015). Medication adherence is adversely affected by various factors such as patient-centered, therapy-related, social and economic, disease, and health care system factors. Hence, the identification of specific barriers for each patient and designing appropriate preventing strategies are indispensable to mitigate medication adherence(Jimmy and Jose, 2011).

In multivariable linear regression analysis the number of drugs, the number of co-morbidities, drug-drug interaction, presence of co-morbidities, presence of ADR, patients had agreed on a dietary plan with a physician, and income were significant predictors of medication adherence. However, a similar study done in Iran demonstrated that medication adherence is affected by different factors such as education level, number of children, comorbidities, disease severity, and the number of tablets used per day (Amininasab et al., 2018).

As the number of prescribed drugs increased by one drug, the medication adherence was reduced by 17% (B=-0.17, 95% CI (-0.24,-0.11), $p < 0.001$). This finding is similar to previous studies done in New York, United States (Aggarwal et al., 2015), Carolina, USA(Shah et al., 2015), and Philadelphia, USA(Knafl, 2014).

As the number of co-morbidities increased by one disease, the medication adherence was reduced by 12% (B= -0.12, 95% CI (-0.19, -0.05), p=0.001). This finding is in line with similar studies done in Philadelphia, USA(Knafl, 2014).

The age of study participants is not a significant predictor of medication adherence. However, a previous study done in Philadelphia, USA showed that age was a significant predictor of medication adherence(Knafl, 2014). Furthermore, study participants who had ADR were 0.86 times lower medication adherence than those who had no ADR (B=-0.86, 95%CI (-1.54,-0.17), p=0.014). Similarly, a study done by Shah et al in Carolina, USA reported that ADR was a significant predictor of medication adherence(Shah et al., 2015).

The presence of co-morbidity was another significant predictor of medication adherence. HF patients who had co-morbidity were 0.69 times lower medication adherence than those who did not have (B=-0.69, 95% CI [-1.00,-0.38], p<0.001). This finding is similar to a study done in Iran reported that co-morbidity was a significant predictor of medication adherence in HF patients (Amininasab et al., 2018).

Income was also a significant factor in medication adherence. Study participants who had incomes equal to and greater than 5000 birrs were 95% higher medication adherence(B= 0.95, 95% CI[-1.54,-0.17), p= 0.014) than those who had very low income. However, studies done in Iran showed that income, age, gender, and place of residence was no significant association with medication adherence(Amininasab et al., 2018).

The acceptance rates of pharmacist intervention accounted for 52.42%. This finding is lower than studies done in the United Arab Emirates (70%) (El-Refae and Abuhamdah, 2017), India (96.21%) (Shareef, 2015), USA(85.3%) (Hutchison et al., 2014), Belgaum (78.37%) (Ganachari et al., 2010), China (98%) (Kucukarslan et al., 2003), and India (78.1%) (Mangasuli and Rao, 2006). Of the 52.42% of physician-accepted interventions, 35.92% of interventions made changes in drug therapy. This finding is higher than studies done in Karnataka: India (11.2%)(Mangasuli and Rao, 2006) and lower than the study done in India (41.5%)(Shareef, 2015). Although clinical evidence and treatment guidelines mandate the use of evidence-based therapies such as ACEI and BB in HF patients, these therapies are well known to be suboptimal

prescribed in actual clinical settings(Cheng and Cooke-Ariel, 2014). This finding indicated that a clinical pharmacist could contribute to better patient care when they involved in the HF health care teams.

From July to December 2019, 412 HF patients responded to the SATMED-Q questionnaire. The study participants' total composite score of treatment satisfaction was 80.35% with the pharmacist interventions. This finding is similar to studies done by Moczygemba et al (2010) (80%). Treatment satisfaction effectiveness was improved to 90%, because of interventions. However, this finding is higher than studies done in Nigeria (66.8%) (Iloh et al., 2012). This discrepancy might be explained by variation in, the assessment tool, characteristics of the study participants, and study design used. For example, the study done by Iloh et al treatment satisfaction was measured by using the following domains: patient waiting time, hospital bureaucracy, accessibility, patient-provider communication, patient-provider relationship, and hospital environment.

Study participants responded (93.3%) that, the physician told detailed information about their disease condition and their treatment. This finding is higher than studies done by Al-Windi et al (68%)(Al-Windi, 2005). Accessibility of medical care, organization of health-care services, treatment length, perceived competence of physicians, clinic size, general practitioner's (GP's) health services and the possibility of choosing one's family physician are important factors influencing patient treatment satisfaction (Lochman, 1983, Al-Windi, 2005). The variations may be treatment satisfaction measurement tools used.

The overall findings from our study, MTM interventions could identify some drug therapy problems and the reasons for medication non-adherent. The proper pharmacist interventions helped to achieve better patient care by solving drug therapy problems and reducing medication non-adherent in HF patients.

7. Limitation

This study has the following limitations.

- The study was done at the ambulatory cardiac clinic of TASH among selected HF patients with short duration of intervention and short contact time to study participants; this may not be able to generalize to all hospitals because it was a single centered study conducted in a tertiary referral hospital that serves patients having severe illnesses and multiple comorbidities.
- Medication adherence was measured by the self-reported measure of adherence, which could have caused an overestimation of adherence.

8. Conclusions

In conclusion, MTM interventions used to achieve HF treatment outcome by decreasing DTPs, and by improving medication adherence and treatment satisfaction in HF patients.

There were 27.8% of DTPs reduced following interventions. The rates of medication adherence were increase from 73% in the pre-intervention phase to 89% in the post-intervention phase.

9. Recommendation

Based on the findings of the current study the following recommendations are suggested.

Ministry of Health:

- To promote and advocate medication therapy management services in the hospitals.

Pharmaceutical Fund Supply Agency: To ensures medication availability within the hospitals.

Tikure Anbessa Specialized Hospital:

- Policies should be made to facilitate the implementation of pharmaceutical care in the hospital.
- There should be a regular patient education program to increase patients' medication adherence and patient attitude towards the disease and its treatment.

Physicians:

- Potential drug-drug interactions should be checked especially for those drugs whose interaction leads to clinically significant unwanted outcomes before starting a new drug.

Researchers: Do further studies on large samples size with interventions for a longer duration.

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11. Annexes

Annex I: Data Abstraction Format

Part I. Patients Socio-Demographic Characteristics

(Use "X" in the Boxes)

Card no /I.care	Age ---------	Gender ☐ Male	☐ Female
Weight Height	BMI…….		
Marital status	☐ Single ☐ widowed	☐ Married	☐ Divorced
Educational level	☐ No formal education	Primary ☐ Secondary ☐	College diploma and above ☐
Religion	Orthodox ☐ Catholic ☐	Islam ☐	Protestant ☐ Other----
Place of residence	☐ Urban	☐ Rural	
Income	Verylow(≤860) ☐ low(861-150) ☐	Average(1502-300) ☐	Above average(3001-5000) ☐ High(≥5001) ☐
Occupation	Governmental ☐ Private ☐	Umemploied ☐	Student ☐ Other…
Social drug use	Ever smoke yes ☐ No ☐ Cigarette smoking know ☐ Yes ☐ No	Alcohol use Yes ☐ No ☐	Khat chewing ☐ Yes ☐ No
Exercising regularly	Presence of agreed exercise plan with physicians Yes ☐ No ☐	Dietary approach Presence of agreed dietary plan with phycisians ☐ Yes ☐ No	

Part II: Clinical Characteristics

(Supplementary to the information obtained from medical chart)

No		
1	Duration of heart failure treatment	
2	Frequency of follow up	
3	Presence of Comorbidity Yes ☐ No ☐	
4	Total number of drug take	
5	How do you get your medications	☐ Free ☐ Payment ☐ Insurance ☐ Covered by Family

Part III: Data Abstraction Format from HF Patients Medical Record

Name ---------- Phone number----------

Card Number/ i-care ---------- Data extracted date----------

Present compliant (DX):

No	**Clinical characteristics**		
1	NYHA class and stage	Class 1 ☐ Class 2 ☐ Class 3 ☐ Class 4 ☐	Stage of HF (A , B ,C ,D) ----------
2	Is there co morbidity? No ☐ Yes ☐ Number of co-morbidities_____	Type of comorbidity Specify HTN ☐ DM ☐ AF ☐ Arrhythmia ☐	Etiology of HF PMI ☐ HHD ☐ MI ☐ DVT ☐ Stroke ☐ PAD ☐ Other---------- CRVHD ☐ IHD ☐ Cardiomyopathy ☐

3. Past medical conditions and medications

Indication	Drug product (Generic Name)	Dosage regimen (dose, route,	Date (dd/mm/yy)		Effectiveness/ safety
			Started	Stopped	

4. Physical Examination (PE)/vital signs: Consecutive record of visits

P/E	**Date**												
PR													
BP													

5. Physical Examination (PE)/**vital** signs: Consecutive record of visits

Parameters	Date(dd/mm/yy										
Lipid profiles	LDL: mg/dl										
	TG: mg/dl										
	HDL: mg/dl										
	Total cholesterol										
LFT	Date										
	SGPT (ALT										
	SGOT(AST)										
	ALP										
RFT	Date										
	BUN										
	SrCr										
	GFR										
Blood glucose	Date										
	FBS										
	RBS										
	HbA1C										
Electrolytes	Date										
	Na										
	K										
	Mg										
	Ca										
	Cl										
	Date										
CBC	WBC										
	RBC										
	Hgb										
	Hct										
	MCV										
	MCH										
	PLT										
	PT										

	PTT				
	aPTT				
	INR				
Other	Echo ECG				

6. **Assessment of adverse drug reaction**

Was there any experienced adverse effect of the drugs? □ Yes □ No

If yes which of the following manifestation occur?

Bleeding Penicillin allergy	Dry cough	Ankle edema Bronchospasm	UGIB
Headache Unsafe drug	Hyperkalemia Bradycardia	angioedema GI	Gynecomastia
Other(specify…….)			

Please specify the drug product and time of event

Drug regimen	Adverse drug event	Date the event occurred

11. Is there any drug interaction? □ Yes Specify ——————□ No

Annex II: Assessment of Medication Adherence (MMAS-8)

No	Items	No	Yes
1	Do you sometimes forget to take your pills?	□1	□0
2	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medicine?	□1	□0
3	Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it?	□1	□0
4	When you travel or leave home, do you sometimes forget to bring along your medicine?	□1	□0
5	Did you take all your medicine yesterday?	□1	□0
6	When you feel like your symptoms are under control, do you sometimes stop taking your medicine?	□1	□0
7	Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	□1	□0
8	How often do you have difficulty remembering to take all your medicine? (0. Never or Rarely (=4), 2. Once in a while (=3), 3. Sometimes (= 2), 4. Usually (=1), 5. Always (=0)). The item result ÷ 4=—(1.00, 0.75, 0.50, 0.25, 0.00, respectively).	+	
	Total score	/8	

Reasons for poor medication Adherence

Mark × No √ Yes

□ Cost of medication too expensive

□ Inadequate availability of medication

- Fear of medication adverse events
- Regimen complexity
- Difficulty of administration
- Inadequate instruction
- Simply Forgetfulness
- Disbelief in drug effectiveness
- Patient prefers not to take
- Feeling better or worse
- Due to work load/busy

Annex III. Modified DTPs Registration Format

Domains	**DTPs Categories**	**Common Cause(s) of Drug therapy**
i. Indication	1.Unnecessary drug therapy	☐ No medical condition at that time ☐ No need of drug for that condition ☐ Duplicate drug therapy ☐ Others ,specify ———
	2. Needs additional drug therapy	☐ Untreated medical condition ☐ Preventive/ prophylactic therapy ☐ Synergistic/ potentiating therapy ☐ Others, specify ———
ii. Ineffectiveness	3. Ineffective drug product	☐ More effective alternative is available ☐ Condition refractory to drug ☐ Contraindication present ☐ Not effective for condition ☐ Others, specify ———
	4. Dose too low	☐ Wrong dose(sub-therapeutic dose) ☐ Frequency inappropriate ☐ Duration inappropriate Others, specify ———

iii. Safety	5.Adverse drug reaction	□ Undesirable effect not dose related □ Unsafe drug for patient □ Drug interaction not dose related □ Dosage administered or changed too rapidly □ Allergic reactions □ Contraindications present □ Others, specify
	6. Dose too high	□ Wrong dose(over therapeutic dose) □ Frequency inappropriate □ Duration inappropriate □ Drug interaction
iv. Adherence	7. Non-adherence	□ No willingness to take the drug □ Patient forget to take the drug □ Direction is not understood □ Patient cannot swallow/administer □ Cost of medication too expensive □ Unavailability of medication □ Disbelieves on the drug effectiveness □ Patient felt better or worse □ Fear of adverse events □ Regimen complexity

Annex IV. Assessment of Treatment Satisfaction with Medicine (SATMED-Q)

For each question, **check** the number that best represents your opinion. There is no right or wrong answers. If you are not sure of any of the answers, check the one you consider most appropriate.

0 Not at all 1 A little bit 2 Somewhat 3 Quite a bit

4 Much

		0	1	2	3	4
1	The side effects of the medicine interfere with my physical activities.					
2	The side effects of the medicine interfere with my Leisure and free time activities.					
3	The side effects of the medicine interfere with my daily activities.					

4	The medicine I am taking relieves my symptoms.					
5	I am satisfied with the time it takes for the medicine to start to work					
6	I feel better now than I did before starting the treatment.					
7	I find that taking my medicine is practical for me.					
8	I find it easy to use/take the medicine in its present form (taste, size, etc.).					
9	The timetable for taking the medicine suits me.					
10	Thanks to the medicine I am taking, it is easier for me to do my leisure and free time activities.					
11	Thanks to my medicine, it is easier for me to take care of my personal hygiene					
12	Thanks to my medicine, it is easier for me to perform my daily activities.					
13	My doctor has informed me in detail about my medical condition					
14	My doctor has informed me about the right way to treat my medical condition.					
15	I intend to continue using this treatment.					
16	I feel comfortable with my treatment.					
17	In general, I feel satisfied with the treatment					
Total score						

Annex V. English Version of Information Sheet

Dear participant,

Good morning/good afternoon

Introduction

My name is Abate Wondesen, I am a member of the study that is carried out at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia entitled on " Impact of medication therapy management intervention on drug therapy problems and medication adherence among ambulatory heart failure patients at cardiac clinic of TASH''. The study is being conducted by Mr. Abate Wondesen from Addis Ababa University, school of pharmacy, department of clinical pharmacy and pharmacology, post graduate program.

Objective

The main purpose of this study is to assess impact of medication therapy management intervention on drug therapy problems and medication adherence among heart failure patients at cardiac clinic of TASH, Addis Ababa, Ethiopia. Your input will be extremely valuable, as the information will be used to identify and intervene drug therapy problem and medication adherence.

The result of the study will provide valuable insights for the healthcare professionals and policy makers and can also be used as base line information for further similar studies.

Therefore, the study will identify and investigate the main gaps and challenges associated with drug use adherence and will propose possible recommendations that may benefit you directly or indirectly by improving heart failure treatment

If you have any questions concerning the study, please call

Abate Wondesen (+251 921126837.

Thank you for your time

Annex VI: English version of informed consent form

The study is being conducted by Mr Abate Wondesen from Addis Ababa University, College of Health Sciences, school of pharmacy, department of clinical pharmacy and pharmacology in postgraduate program. The study will be conducted by providing information to your medications that used to treat HF, interviewing, and reviewing your medical record. Therefore, I am kindly requesting you to take part in this study by allowing your medical data to be included in the study. The interview will take 10-15 minutes. Your name will not be written in the data collection form and will never be used in connection with any information you tell us. There is no risk associated with participating in this study. All information regarding your medical condition will be kept strictly confidential. Your participation is voluntary and you are not obligated to participate in the study. If you feel discomfort with study, it is your right to drop at any time you want. If you have questions regarding this study, please feel free to contact the principal investigator via his address.

Abate Wondesen, Tell:+251- 921126837,
e-mail: wondesenabate2007@gmail.com

Signature of respondent ------- Signature of interviewer ---

Thanks for your time.

Annex VII. Personal Medication Record Form

My Medication Record

Name: ———————————————————————

You can include all of your medications on this record: prescription medications, non-prescription medications, and other dietary supplements.

Always carry your medication record with you during your appointment date and show it to your clinical pharmacists.

Drug			When do I take it				Start date	Stop date	Dr.	Special Instruction
Name	dose	Take for	Morning	Noon	Evening	Bedtime				

Annex VIII. Medication Related Action Plan for the Patient

Pharmacy Care Plan

Data: Subjective information provided by the patient and/or objective data that you have collected.

Assessment: State the drug therapy problem.

Plan: For each alternative, consider treatment efficacy, safety and drug interactions, adherence, cost, drug coverage, and non-pharmacological interventions.

Alternative 1

Alternative 2

Monitoring

Planned date of follow-up: _____

Pharmacist signature Date of Review

Annex IX. Health Care Practitioner Communication Form

Date _____

Health care practitioner	Patient's Name
Address	I.care/C.No.
Phone number	Age Phone number

Dear Dr. _____

Your patient had a comprehensive medication review completed on ————————. Listed below are my assessments(s) and recommendation(s). Please provide a response below. If you like to discuss any of the information contained do not hesitate to contact me.

Drug Therapy Problems	Pharmacist Recommendation		Acceptance of Recommendation	Prescriber Comments
	Information only	Action required	Fully ☐ Partially ☐ Not accepted(rejected) ☐	
Pharmacist name:————————			Prescriber signature:———————— Date: ————————	

Annex X : Heart Failure Brochure

- የሚያፈስ የልብ ቫልቭ፣ ሲጋራ ማጨስና በከፍተኛ መጠን አልኮል መጠጣት፡፡

የልብ ድካም ህመም ምልክቶች

- በሳንባና በተለያዩ የሰውነት ክፍሎች ውስጥ ፈሳሽ መጠራቀሙ
- የትንፋሽ ማጠር በተለይ በእንቅስቃሴ ወቅትና ጋደም በሚሉበት ወቅት
- በቁርጭምጭሚት፣ እግሮች እና ሆድ አካባቢ እብጠት መኖር
- ድካምና አቅም ማነስ
- የሰውነት ክብደት መጨመር
- የረሀብ ስሜት፣ ትንሽ ከተመገቡ በኋላ የመጥገብ ስሜት ወይም የመመገብ ፍላጎት መቀነስ
- ለረዥም ጊዜ የሚቆይ ሳል
- ነጭ አራፋ ያለው ንፍጥ በሳል ወቅት ማውጣት
- በእንቅልፍ ወቅት ከሁለት በላይ ትራስ ማስፈለግ

የልብ ድካም ህመም ህክምና

በአጠቃላይ የልብ ድካም ቀድሞውኑ በምርምራ ከታወቀና ህክምናቸውን በአግባቡ ከተከታተሉ የልብ ድካም ያለባቸው ህሙማን ደስተኛ እና ምቾት ያለው ሕይወት መኖር ይችላሉ፡፡ የልብ ድካም ህመም ያላባቸው ሰዎች በሽታውን ለመቆጣጠርና

ይህ ሕመም የልብ የቀኝ አሊያም የግራ ክፍል ሊያጠቃ ይችላል፡፡ አብዛኞቹ ታማሚዎችም ሁለቱ ዓይነት የልብ ክፍሎች ላይ ህመሙ ይከሰትባቸዋል፡፡

የቀኝ ክፍል የልብ ድካም ሲከሰት ልብ በሚፈለገው መጠን የተጣራ ንጹሕ አየር ለማግኘት ደም ወደ ሳንባ መርጨት የሚያቅተው ሲሆን፤ የግራ ክፍል የልብ ድካም ደግሞ ልብ የተጣራ ንጹህ አየር የተሸከመውን ደም ወደ ሰውነት ማስተላለፍ ሲያቅተው የሚከሰት ነው፡፡

የልብ ድካም ሲባል ልብ ደም ማሰራጨቱን አቁሟል ወይም ሊያቆም ነው ማለት ሳይሆን እንደ ሚፈለገው መጠን ልብ ጠንካራ አለመሆኑና አፋጣኝ የህክምና ክትትል የሚያስፈልገው የህመም አይነት ነው፡፡የልብ ድካም በአጠቃላይ በጊዜ ሒደት ውስጥ የልብ ደም መርጨት አቅም እየተዳከመ የሚሔድበት የህመም ዓይነት ነው፡፡

የልብ ድካም ህመም መንስኤዎች

- ከፍተኛ የደም ግፊት፣ የስኳር ህመም፣ ከፍተኛ ውፍረት፣ እርግዝና የልብ ጡንቻ በሽታ፣ ከፍተኛ የልብ መጠን፣

በኢ.አ.ዩ. የፋርማሲ ትምህርት ቤት እና

ጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል

AAU-MTM Project

ልብ ድካም

ልብ ድካም ህመም ምንድን ነው?

ልብ ድካም (Heart failure) ብዙ ሰዎችን የሚያጠቃ የህመም ዓይነት ሲሆን የሚከሰተውም ልብ የሚጠበቅበትን ሥራ ማከናነወን ሲያቅተው ነው፡፡ ይህ ሲሆንም ልብ ደምን በሚፈለግበት መጠን ወደ የተለያዩ የሰውነት ክፍሎች መርጨት ያቅተዋል፤ ወይም አንዳንድ ጊዜም ልብ በሚፈለገው መጠን በደም ሳይሞላ ሲቀር ነው፡፡

ለመጠበቅ የተለያዩ ዘዴችን መጠቀም ይኖርባቸዋል። እነርሱም

1. በየወቅቱ ክብደትዎን ይመዘኑ

ድንገተኛ የክብደት መጠን መጨመር የልብ ድካም ህመም ላይ አንዱ ምልክት የሆነውን የፈሳሽ በሰውነት ውስጥ መከማቸቱን ሊጠቁም ስለሚችል ለመመዘንም ተመሳሳይ ሰዓት በይበልጥ ጠዋት ከእንቅለፍ ሲነሡ ውኃ ሽንት ከተጠቀሙና ቁርስ ሳይመገቡ ቢሆን ይመረጣል።ክብደትዎን በመቆጣጠር ጤናማ የሰውነት ክብደት እንዲኖር ማድረግ ። ይህንን ለማድረግ ከጤና ባለሞያው ጋር በመነጋገር ከህመሙ ጋር ተስማሚ የአካል እንቅስቃሴ በማድረግ እና ጤናማ አመጋገብ በመከተል የሰውነት ክብደትን መቆጣጠር ይቻላል።

2. በየወቅቱ የህኪም ክትትል ያድርጉ

የልብ ድካም ህመም ያለባቸው ህሙማን በሽታው ከፍተኛ ክትትል የሚያስፈልገው በመሆኑ፣ ለህመሙ የታዘዘው መድኃኒት በሰውነት ላይ እያደረሰ ያለው ተጽእኖ (በጎ/ያልታሰበ) ለመረዳት የህክምና ቀጠሮ ላይ በመገኘኘት ክትትል ማድረግ ይገባቸዋል።

3. የታዘዙትን መድኃኒቶችን በጊዜውና በመጠኑ ይውሰዱ።

ብዙ የልብ ድካም መድኃኒቶች ያሉ ሲሆን የጤና ባለሞያው ባዘዘው መጠንና ጊዜ መውሰድ በጣም አስፈላጊ ነው። የሚታዘዙት መድኃኒት የተለያዩ አገለግሎቶችን የሚሰጡ ሲሆኑ፤ ለምሳሌ

- **በሰውነት ውስጥ የፈሳሽ ክምችት እንዳይኖር የሚያግዙ፣**
- **በልብ ላይ ያለውን የሥራ ጫና የሚቀንሱ**
- **የልብ ቅርጽ ለውጥን (ቅርጽ ለውጥ ሲባል ልብ ጠንካራ ለመሆን በመጠን መተለቅ ነው) የሚከላከሉ፣**
- **ልብን ጠንካራ የሚያደርጉና የደም ሥር ግድግዳዎችን ዘና በማድረግ ልብ በቀላሉ ደም እንድትረጭ የሚያደርጉ ይጠቀሳሉ።** ከእነዚህ መድኃኒቶች ውጪ መውሰድ የልብ ድካም ያለበት ሰው መውሰድ የሌለባቸው መድኃኒቶች በመኖራቸው የጤና ባለሞያውን በመጠየቅ ጥንቃቄ ማድረግ ይገባል። ለምሳሌ ለህመም ማስታገሻነት ከፓራሲታሞል ውጪ ሌሎች ማስታገሻ መድኃኒቶችን አይውሰዱ።

4. ጤናማ አመጋገብ ይከተሉ

ጤናማ አመጋገብ የሰውነት ክብደትን ለመቆጣጠር፣ በልብ ላይ የሚከሰተውን ጫና ከመቀንስ አንጻርና ለሌሎች ህመሞች የመጋለጥ እድልን የመቀንስ ከፍተኛ አቅም ያለው በመሆኑ የልብ ድካም ህሙማን ስለአመጋገባቸው ጥንቃቄ ማድረግ ይገባቸዋል። ለምሳሌ

- **ምግብ ላይ አነስተኛ ጨው ብቻ አድርጎ መመገብ**
- ፍራፍሬና አትክልቶችን በአዲስነታቸው ይመገቡ
- **ከሚያስፈልገው መጠን በላይ ፈሳሽ አለመውሰድ** (በቀን ውስጥ 2 ሊትር ብቻ ፈሳሽ (ውኃ፣ ሻይ፣ ጁስ፣ ቡና ወዘተ በአንድ ላይ) ይጠቀሙ)
- **ሲጋራ የሚያጨሱ ከሆነ ያቋርጡ።**
- **አልኮል (ቢራ፣ ወይን፣ አረቄ፣ ዊስኪ ወዘተ. . .) መጠጥን አይጠጡ።**
- አልኮል የልብ ሕዋሶችን ስለሚጎዳና ልብን የበለጠ ስለሚያደክም **አልኮል መጠጥ የተከለከለ ነው።**

5. ከሐኪምዎ ጋር በመነጋገር የአካል ብቃት እብቅስቃሴ ያድርጉ ።

አድራሻ፡- ጥቁር አንበሳ /ሆ/ል 3ኛ ፎቅ ከተመላላሽ መድኃኒት ቤት አጠገብ

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Annex XI: የአማርኛ መጠይቅ ቅፅ (Amharic version)

አዲስ አበባ ዩኒቨርሲቲ፣ ጤና ሳይንስ ኮሌጅ፤ ፋርማሲ ት/ቤት፤ ፋርማኮሎጅና ክሊኒካል ፋርማሲ ትምህርት ክፍል

ውድ የቃለ መጠይቅ ተሳታፊ፤ እንደምን አደሩ/ ዋሉ?

ስሜ አባተ ወንድወሰን ይባላል። ‘‘በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል በልብ በሽታ ታካሚዎች ላይ በመድሀኒት ህክምና ተያያዥ ችግሮች እና መድሀኒትን ባግባቡ በመዉሰድ ዙሪያ’’ በተሰኘ የድህረ ምረቃ ጥናት አባል ነኝ። ጥናቱ የሚካሄውም በጥናቱ ተመራማሪ አባተ ወንድወሰን እና የጥናቱ ዋና አማካሪ ፕ/ር ኤፍሬም እንግዳወርቅ ከአዲስ አበባ ዩኒቨርሲቲ፣ ጤና ሳይንስ ኮሌጅ፤ ፋርማሲ ት/ቤት የድህረ ምረቃ ፕሮግራም ነው።

የጥናቱ አላማ

የዚህ ጥናት ዋና አላማው በመድሀኒት ህክምና ተያያዥ ያላቸው ችግሮችን መለየት፣ የተለዮ ችግሮችን ከሀኪም ጋር በመነጋገር መፍትሄ እንዲያገኙ ማድረግ፣ በታዘዘው መሰረት በአግባቡ እንዴት መድኃኒትዎን እንደሚወሰዱት እና መድኃኒትዎን ሁል ጊዜ እንዳይወሰዱ የሚያደርጉ ዋና ዋና ክፍተቶችን በመለየት የመፍትሄ ሀሳቦችን ማቅረብ ነው።

ከጥናቱ የሚጠበቁ ውጤቶች/ ጥቅሞች

በዚህ ጥናት ላይ በመድኃኒት ህክምናዎ ላይ የሚከሰቱ ችግሮች፤ በታዘዘው መሰረት በአግባቡ የአወሳሰድና የአጠቃቀም ክህሎት ይጠናሉ። በተጨማሪም ከጥናቱ በሚገኙ ግኝቶች የልብ ህክምና ዉጤትን በተወሰነ መልኩ ለማሻሻል እንደሚቻል በመገመት፤ እርስዎ የጥቅሙ ተቋዳሽ ይሆናሉ ብለን እናምናለን። ጥናቱ የሚካሄደው የህክምና ካርድዎን በመከለስ ከሀኪም ጋር በመነጋገር መፍትሄ እንዲያገኙ ማድረግና በቃለ መጠይቅ ነው፡፡ ስለዚህ የእርስዎ ቅንና ሓቀኛ መረጃ ለጥናቱ እጅግ በጣም ወሳኝ ነው።

የተከበረ ጊዜዎን ስለሰጡን እጅግ በጣም እናመሰግንዎታለን፡፡

ቅጽ2፡ በቃለ መጠይቅ ለመሳተፍ የፈቃደኝነት ቃል መቀቢያ ቅጽ

በዚህ ጥናት የእርስዎ መረጃ ሙሉ በሙሉ በሚስጥር የተጠበቀና ለምርምሩ አላማ ብቻ የሚዉል ነው። በተጨማሪም የእርስዎ ተሳታፊነት በፈቃደኝነት ላይ የተመሠረተ ነው። የጥናቱ አላማውን ተረድተውና ጊዜዎን ሰውተው፤ ከ 10-15 ደቂቃ ለሚፈጅ ቃለ-መጠይቅ መረጃ ለመስጠት ፍቃደኛ በመሆንዎ በቅድሚያ አመሰግናለሁ።

በየትኛውም ጊዜ ጥያቄ ካለዎት አባተ ወንድወሰን በ ስ.ቁ +251921126837

ወይም በ ኢ-ሜይል፡ wondesenabate2007@gmail.com ይጠይቁን

ሀ. የታካሚው ማህበረሰባዊ ባህርያቶች መረጃ በተመለከተ (መመርያ፡ ለመረጡት ምላሽ የx ምልክትን ያድርጉ)

ክፍል አንድ ፡ ማህበረሰባዊ ባህርያቶች:			
1. እድሜ፤		ከብደት	ቁመት
2. ፆታ፤	ወንድ	ሴት	
3. ሀይማኖት	ክርስትያን ☐ ካቶሊክ ☐	እስላም ☐ ፕሮቴስታንት ☐	ሌላ ☐
4. የጋብቻ ሁኔታ፤	ያላገባ/ች ☐	ያገባ/ች ☐ አግብቶ/ታ የፈታ/ች ☐	ሚስቱ/በሏየሞተችበት/ባት ☐
5. የትምህርት ሁኔታ፤	ያልተማረ/ች ☐	ከ1ኛ-8ኛ ክፍል ☐ ከ9ኛ-12ኛ ክፍል ☐	ኮሌጅ ዲፕሎማ እና ከዚ ያበላይ ☐
ሃይማኖት	ኦርቶዶክስ ካቶሊክ ☐ ☐	እስልምና ፕሮቴስታንት ☐ ☐	ሌላ ---------
ሥራ	የመንግሥት የግል ☐ ☐	ሥራ የለኝም ☐ ተማሪ ☐	ሌላ …… ..
6.አሁን የሚኖሩበት	ከተማ ☐	ገጠር ☐	
7. የወር ገቢ			
8. የማህበራዊ ሂወትዎ ሁኔታ	ሲጋራ ያጨሳሉ አዎ ☐ አላጨስም ☐	አጭሰዉ ያዉቃሉ አዎ ☐ አላጨስኩም ☐	

	ጫት ይቅማሉ አዎ ☐ አልቅምም ☐	መጠጥ (የአልኮል) በየሳምንቱ ይጠጣሉ? ☐ አዎ ☐ አልጠጣም
የአካል ብቃት እንቅስቃሴ ለማድረግ ከሐኪሞች ጋር የተስማሙት እቅድ አለ አዎ ☐ የለም ☐	ከሐኪሞች ጋር የተስማሙት የአመጋገብ እቅድ አለ አዎን ☐ የለም ☐	የጨው ገደብ አለ አዎ ☐ የለም ☐

ክፍል ሁለት ፡ የታካሚዎች በሽታ ባህርያትን በተመለከተ ተጨማሪ መረጃ

1. .የልብ በሽታ እንዳለብዎት ተመርምሮ ካወቁ ስንት ዓመት ሆኖቷል?_____

2.የልብ መድኃኒት መውሰድ ከጀመሩ ስንት ዓመት ሆኖቷል? _____

3. በልብ በሽታዎ ምክንያት ሆስፒታል ተኝተዉ ያዉቃሉ ☐ አላውቅም ☐ አዎ (ምክንቱንይ ግለጹ)

4 ተጨማሪ በሽታ አለብዎት ☐ የለብኝም ☐ አዎ (ይግለጹ) _____

5.በአሁኑ ጊዜ የሚወስዱት የልብ መድሀኒት ብዛት _____

6 .በየስንት ጊዜ ክትትል ያደርጋሉ _____

7.መድሃኒት የሚያገኙት በምን መልኩ ነዉ;☐ በግዢ ☐ በነጻ ☐ በካመፓኒ ☐ ቤተሰቦቸ ይገዙልኛ

ክፍል4: ሞሪስኪ” መድኃኒትን በታዘዘው መሰረት በአግባቡ ስለመውሰድ” መለኪያ- 8

ተ.ቁ	ጥያቄዎች	አዎ	አይደለም
1	አንዳንድ ጊዜ መድኃኒትዎን ረስተው ሳይወሰዱ ቀርተዉ ያዉቃሉ?	☐	☐
2	ሰዎች አንዳንድ ጊዜ ከመርሳት በተጨማሪ ባሉት የተለያዩ ምክንያቶች መድኃኒታቸውን ሳይወስዱ ይቀራሉ፡፡ ባለፉት ሁለት ሳምንታት፣መድኃኒትዎን ሳይወስዱ የቀሩበት ቀናቶች ነበሩ?	☐	☐
3	መድኃኒትዎን እየወሰዱ ህመምዎ ሲባባስ ሐኪምዎን ሳያማክሩ መድኃኒትዎን አቋርጠው ያዉቃሉ?	☐	☐

4	በጉዞ ወይም በሌላ ምክንያት ከቤትዎ አርቀው ሲጓዙ አንዳንድ ጊዜ መድኃኒትዎን ረስተውት ሳይወስዱት ያውቃሉ	□	□
5	በትላንትናው ዕለት ሁሉንም መድኃኒትዎን ወስደዋል	□	□
6	ህመምዎ ሲሻልዎት(የህመምስሜቶችሲጠፉ) አንዳንድ ጊዜ መድኃኒትዎን አቋርጠው ያውቃሉ	□	□
7	መድሀኒቶችን በየቀኑ መውሰድ ለአንዳንድ ሰዎች ምቾት ይነሳቸዋል። እርስዎ በህክምና ክትትልዎ ወቅት በየቀኑ ወይም አንድም ጊዜ ሳያዛንፉ መድሐኒ ትበትክክል ለመዉሰድ ተሰላችተዉ ያዉቃሉ	□	□
8	ሁሉንም መድሐኒቶች መውሰድ አለመዉሰድዎን ማስታወስ የከበድዎት ጊዜ አለ በፍፁም □ አልፎአልፎ □ አንዳንድ ጊዜ □ አብዛኛው ጊዜ □ ሁል ጊዜ □	□	□
	አጠቃላይ ድምር		

መድሃኒቱን በአግበቡ ካልወሰዱ እባክዎ ምክንያቱን ይግለጹ (ከ አንድ በላይ መልስ መምረጥ ይቻላል)

ምድሃኒቱን ስወስድ ህመሜ ስለሚባባስበኝ

የምወስዳቸው መድሃኒቶች ብዙና ግራ የሚያጋቡ ስለሆኑ

መድሃኒቱን ማግኘት ስላልቻልኩ

ስለምረሳው
መድሃኒቱ ውድ ስለሆነ
ሌላ ምክንያት ——————

SATMED-Q መድሃኒት የሚሰጠው ህክምና ላይ የእርካታ መጠይቅ :

ህመሞን ለማከም የሚሰጠውን ህክምና በተመለከተ የሚከተሉትን ጥያቄዎች ይመልሱ፡፡ ከቀረቡት መልሶች መካከል በህክምናው ግኙትን እርካታ ልክ የሚያሳዩ አማራጮች ቀርበዋል፤ እያንዳንዱን መልስ እላዩ ላይ በማከበብ መልሱን መስጠት ይችላሉ፡፡

0 በጭራሽ 1 በትንሹ 2 በመጠኑ 3 በጣም 4 እጅግ በጣም

ተ.ቁ	የ ሳት ሜድ ኪው (SATMED-Q) መጠይቅ	0	1	2	3	4
1	የመድሃኒቱ የጎንዮሽ ጉዳት በአካላዊ እንቅስቃሴዎ ላይ ተጽእኖ አለዉ?					
2	የመድሃኒቱ የጎንዮሽ ጉዳት በ እረፍት እና በትርፍ ጊዜዎ ላይ ተጽእኖ አለዉ?					
3	የመድሃኒቱ የጎንዮሽ ጉዳት በ እለት ተእለት የ ህይወት እንቅስቃሴዎ ላይ ተጽእኖ አለዉ?					
4	የሚወስዱት መድሃኒት የህመም ስሜቶን አስታግሶሎታል?					
5	መድሀኒቱ ስራውን ለመስራት በሚወስደዉ ጊዜ ረክተዋል?					
6	ህክምና ከ ጀመሩ በጎላ ከ በፊቱ ጥሩ ስሜት እየተሰማዎት ነዉ?					
7	እለት ተለት መድሃኒቶን የመዉሰድ ላምድ አዳብረዋል?					
8	መድሃኒቱ አሁን ባለዉ ይዘት (ጣዕም፣መጠን፣) መዉሰድ ለእርሶ ቀላል ነዉ?					
9	እየወሰዱ ያሉት መድሃኒት የሚወስዱበት ሰዓት ና ድግግሞሽ ተስማምቶታል?					
10	እየወሰዱ ያሉት መድሃኒት የእረፍትና የትርፍ ጊዜዎን ቀላል አድርጎሎታል?					
11	እየወሰዱ ያሉት መድሃኒት የግል ንጽህናዎን ለመጠበቅ ቀላል አድርጎሎታል?					
12	እየወሰዱ ያሉት መድሃኒት የእለት ተእለት እንቅስቃሴዎን ለማከናወን ቀላል አድርጎሎታል?					
13	ሀኪሞ ስለ ህመሞ በተመለከተ ዝርዝር መረጃ ይሰጥታል?					
14	ሀኪሞ ህመሞን ለማከም ትክክለኛወን መንገድ ይነግሮታል?					
15	ይህንን መድሀኒት ለመቀጠል አስበዋል?					
16	በህክምናዎ ምቾት ይሰማዎታል?					
17	በአጠቃላይ በሚወስዱት መድሃኒት ምቾት ተሰምቶታል?					
	ጠቅላላ ድምር					