




BMJ Open Impact of medication therapy management interventions on drug therapy problems, medication adherence and treatment satisfaction among ambulatory heart failure patients at Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia: a one-group pre-post quasi-experimental study

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ABSTRACT

Objective To determine the impact of medication therapy management interventions on drug therapy problems (DTPs), medication adherence and treatment satisfaction among ambulatory heart failure (HF) patients.

Study design, setting and participants A one-group pre-post quasi-experimental study was conducted on 423 ambulatory HF patients at Tikur Anbessa Specialised Hospital (TASH), Addis Ababa, Ethiopia. All ambulatory HF patients ≥18 years old attending the adult cardiac clinic of TASH and having a complete medical record and fully met the inclusion criteria were taken as study participants.

Interventions Educational interventions along with a brochure with information on the nature of HF disease and its treatment were provided to study participants. DTPs encountered were resolved by a team of pharmacists and physicians.

Results In the preintervention 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 postintervention phase compared with the preintervention phase. At the postintervention phase, 36.4%, 61.9% and 1.7% of HF patients were highly, medium and low adherent to their treatment regimens, respectively. The total composite score for treatment satisfaction of the study participants was 80.35%.

Conclusions The findings of this study demonstrated that by teaming up clinical pharmacists with cardiologists and cardiology fellows, it was possible to reduce the occurrence of DTPs, improve medication adherence and increase treatment satisfaction of HF patients attending at the outpatient cardiac clinic.

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome resulting from structural or

Strengths and limitations of this study

- 'To the best of our knowledge, this is the first study in Ethiopia that assessed how the teaming up of clinical pharmacists with physicians reduces drug therapy problems, improves medication adherence, and increases treatment satisfaction in heart failure patients'.
- This study provided heart failure patients with a better understanding of their medication and lifestyle improvement, and switching to safer and more effective alternatives was possible for those with drug therapy problems through communication among patients, clinical pharmacists and physicians.
- Electronic medical record data were used to review patients' current drug regimens, updated laboratory results and comorbid conditions.
- The study was carried out among selected heart failure patients with a short duration of intervention and contact.
- Medication adherence was measured by self-reported adherence assessment method, which could have caused an overestimation of the study participants adherence.

functional impairment of ventricular filling or ejection of blood.¹ It is this impairment that leads to activation of compensatory responses to maintain circulation, which results in the cardinal symptoms (fluid retention, fatigue and dyspnoea) and signs (limit exercise tolerance, peripheral oedema and rales) of HF.^{1 2}

Worldwide, HF is affecting greater than 20 million people. HF prevalence rising with

age follows an exponential pattern and affects 6%–10% of people aged >65 years. In developed countries, HF prevalence in the adult population is 2%.¹ In sub-Saharan African countries, HF affects young-aged and middle-aged adults unlike in developed countries, which is considered as a disease of the elderly.³

Medical therapy of HF, in contrast to too many other diseases, has been largely an add-on phenomenon. Optimal HF therapy has therefore become increasingly complex.^{4–7} As a result, many patient factors should also be considered when selecting HF medications.⁸

Medication therapy management (MTM) is used to achieve better treatment outcomes in HF patients through lifestyle modification and pharmacotherapy.^{9,10} It is effective for patients with multiple chronic conditions, high prescription costs, take at least two or more medications, on complex drug therapies, and multiple prescribers.^{11,12} MTM is a distinct service or group of services that optimises therapeutic outcome for individual patients.¹³

Most HF patients have comorbid problems^{7,14} and take polypharmacy. As a result, HF patients are at high risk for developing drug therapy problems (DTPs). 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.¹⁵ Different research groups classify DTPs into different classification systems. According to Cipolle's textbook of pharmaceutical care practice, there are seven categories of DTPs that fall into indication, effectiveness, safety and compliance.¹⁶ Published reports indicate that there is a high prevalence of DTPs in HF patients, ranging from 29.8%¹⁷ to 88.66%.¹⁸ DTPs cause worsening of HF and augment the risk of mortality and morbidity.¹⁹ Furthermore, DTPs are a major cause for emergency department (ED) visits and hospital admission of HF patients.^{20–22}

Clinical pharmacists play a vital role in HF clinics, ranging from patient education and support to involvement in treatment plans. Numerous studies showed that clinical pharmacists' interventions have a positive impact on reducing DTPs among ambulatory HF patients.^{23–27} Various studies also suggested that HF patients who adhere to their medications are associated with improved survival, fewer ED visits, fewer HF exacerbations and use of lower healthcare expenditure.^{28–30} HF patients can avoid frequent hospital stays if they take care of themselves at home and take their medication properly.³¹

Treatment satisfaction is a patient-reported outcome that provides useful insights into patients' perspectives on willingness to continue treatment.^{32,33} It helps to show the consistent and correct use of drug therapy over time.^{34–36} HF patients must be satisfied with their treatment to remain a member of the healthcare organisation and to apply the prescribed treatment options.³⁷

In resource-limited countries, particularly in Ethiopia, clinical pharmacists are still underutilised in contrast to developed countries.³⁸ There are no studies regarding pharmacists' interventions among HF patients at an

outpatient adult cardiac clinic in Ethiopia. This study was, therefore, conducted to assess the impact of pharmacist-led MTM in improving outcomes in HF patients.

METHODS

Study design and setting

A one-group pre–post quasi-experimental study was conducted from 1 July 2019 to 30 December 2019 in Tikur Anbessa Specialised Hospital (TASH). TASH is the largest tertiary care specialised hospital in Ethiopia. The hospital was established in 1972 with a bed capacity of 700 and is located in Lideta Sub-City, Addis Ababa, Ethiopia. It serves as a teaching specialised hospital, with several subspecialty clinics. Adult Cardiac clinic is one of the subspecialty clinics that provide cardiac service 4 days per week (except Thursday). On average, 105 patients are served per day and 10080 patients had visited the clinic within the study period.

Patient and public involvement

Patients did not participate in the initial conception and design of the study. However, based on the comments provided by participating patients during the pretest (5% of the sample size), we had made a correction on the patient approach and timing for an interview during data collection. Patients played the central role in this study in determining the level of medication adherence and treatment satisfaction.

Study population

All ambulatory HF patients attending at the adult cardiac clinic of TASH in the study time frame formed the study population and those who fully met the criteria of the study were taken as study participants. HF patient ≥ 18 years old, with a complete medical record and who had taken two or more medications were included. Patients who could not stand the interview (eg, too sick to be interviewed); with cognitive impairment, lost appointment date and changed follow-up site were excluded.

Sample size determination and sampling technique

Sample size determination

A single population proportion formula was used to estimate sample size.³⁹

$$n = (Z/[2])^2 p \frac{(1-p)}{d^2}$$

Where: n is sample size required for a large population ≥ 10000 .

Z $\alpha/2$ value is 1.96 from Z-table.

P is proportion of MTM related interventional studies in HF. As there were no previous studies in Ethiopia, P was taken as 50% (0.5); d, degree of accuracy desired (5%=0.05). Hence; the estimated minimum sample size was 384.

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

Taking 10% contingency for incomplete medical records and refusal of participation, provided a final sample size of 423.

Sampling technique

Participants were recruited by systematic random sampling technique. The actual sampling fraction (k) varied in the different days due to variations of the total number of patients attending at the cardiac clinic during the time of data collection. It was calculated by dividing the number of patients 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 and every k th patient (ranging from 4 to 6) was then selected.

Study variables

DTPs, medication adherence and treatment satisfaction were considered as dependent variables. The independent variables included demographic features (age, sex, marital status, educational status and economic factors), social habits, clinical characteristics and drug-related factors.

Data collection and management

Data collection instruments

Clinical characteristics of study participants were collected using data abstraction tools. Adequacy of medical therapy of HF was evaluated using the European Society of Cardiology^{40 41} and American Heart Association (AHA)/American College of Cardiology HF guidelines.⁴² Micromedex healthcare series software drug–drug interaction (DDI) checker was used to identify DDIs and only absolute and major DDIs were selected. DTPs were identified from the collected data using the above guidelines.

DTPs were categorised as adverse drug reactions, unnecessary drug therapy, need for additional drug therapy, dosage too low, ineffective drug, dosage too high and non-adherence as described by Cipolle *et al* classification system. The identified DTPs were recorded and classified using the DTP registration format, which was adapted from Cipolle *et al*.

Morisky Green Levin Medication Adherence Scale (MGL) was used to collect information necessary to assess medication adherence and reasons contributing to non-adherence. It consists of four items focusing on past medication use patterns with closed dichotomies (yes/no). Each 'no' response was rated as one and each 'yes' response was rated as 0. The total summed score ranges from 0 to 4 and is grouped into high adherence (0 score), medium adherence (1–2 score) and low adherence (≥ 3 score).⁴³

Treatment satisfaction was assessed using the Treatment Satisfaction with Medicines Questionnaire, which is composed of 17 items with 6 dimensions (treatment effectiveness, convenience to use, undesirable side effects, medical care, impact on daily activity and global

satisfaction). Each of the specific domains gives 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 point. Summing up the direct scores yields a total composite score ranging from 0 to 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 equation: $Y' = [(Y_{obs} - Y_{min}) / (Y_{max} - Y_{min})] \times 100 = Y_{obs} \times 1.471$, where $Y_{max}=68$ (maximum total score); $Y_{min}=0$ (minimum total score); Y_{obs} =total score obtained by the patient; and Y' =transformed score. A similar expression was used for each dimension.

Recruitment of data collectors and training

Two clinical pharmacists and three nurses were recruited. The clinical pharmacists were involved in chart review to identify DTPs and the nurses in patient interviews. They received a 3-day training on how to collect data from patient charts, conduct a patient interview and make interventions. Besides, they were trained on strict use of study criteria, explanation of study objective, obtaining verbal consents from study participants, uniform interpretation of questionnaire and patient education materials (brochure) as well as maintaining anonymity and confidentiality.

Data collection processes

Patients' medication and medical profile was reviewed from the charts before their appointment date at the TASH MTM centre. Eligible patients were then approached and asked for their consent to participate in the study. Pretest medication adherence and patient demographic data were then collected. Pharmacists provided interventions to patients, including cautions regarding over-the-counter product use, basic diet suggestions (including sodium restriction), physical activity, self-monitoring, the benefit of proper medication use, and the advantage of medication adherence. Additionally, a brochure containing specific information about HF disease and its treatment was distributed to study participants.

In the preintervention phase, DTPs were identified, prioritised, and planned for resolution. Interventions to the identified DTPs were presented to treating physicians, who could fully accept, partially accept or decline the suggested recommendations. Accepted interventions were applied to the clinical management of patients when they came for their appointment. During this time postintervention medication adherence and treatment satisfaction data were collected.

Postintervention DTPs were identified from study participants who had undergone the previous two stages of the data collection process.

Data quality assurance

The team assessed the filled-out data collection tools (data abstraction format and questionnaire) for completeness and clarity of their contents. A pretest was performed

on 5% of the study population and all the necessary adjustments and modifications were incorporated before carrying out the main study. The data collection process was checked daily and feedback and corrections were provided on the same day.

Data analysis and interpretations

Collected data were sorted, cleaned, coded and entered into EpiData software V.4.2.0 and then exported to SPSS V.25. Descriptive statistics were used to summarise frequencies, means and percentages. Linear regression analysis was performed to see the relationship between the occurrence of DTPs and medication adherence with predictor variables. Variables that had a p value of less than 0.25 in the univariable linear regression analysis were included in the multivariable linear regression analysis to control potential confounders. Finally, the results were summarised and described using tables and figures. Paired-t-test was used to compare mean difference between the preintervention and postintervention data sets. A $p < 0.05$ was considered statistically significant.

Each study participant was informed about the objective of the study, benefits and risks of the study, procedures for selection and their rights to withdraw at any stage of the study without jeopardising the care they receive from the hospital. No identifiers were used to minimise social desirability bias and enhance anonymity. The privacy of study participants was ensured by interviewing patients in different rooms. All information obtained from the participants was kept confidential and the data were used only for research purpose.

RESULTS

Sociodemographic characteristics

Of the 423 study participants enrolled in the study, 11 of them were excluded due to a lack of complete data. As a result, data of 412 study participants were used for analysis.

Sociodemographic characteristics of the study participants are depicted in [table 1](#). The mean (SD) age of the study participants was 44.57 years (± 17.4), with a range of 18–93 years. Almost one-third (33%) were within the age range of 18–33 years and about 31% of 50–65 years of age. 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%) pay out-of-pocket for their medications.

Clinical characteristics

Among the study participants, 34.3% of them were diagnosed with HF for greater than ten years, and 33.5% had been taking HF treatments for 5–10 years. While 56.8% took 2–4 drugs, 43.2% were taking ≥ 5 drugs. Only sixteen study participants (3.9%) reported that they did experience drug allergies ([table 2](#)).

The most commonly identified aetiology of HF was chronic rheumatic valvular heart disease (56%). This was

followed by ischaemic heart disease (17%) and hypertensive heart disease (11%) ([figure 1](#)).

About 31% of the study participants did not have coexisting comorbidities. Close to 50% had, however, ≥ 2 comorbidities, while a fifth of them had a single comorbidity. Atrial fibrillation (28%) and hypertension (22%) were the commonly observed comorbidities ([figure 2](#)).

Management approaches

Although a larger proportion (73.1%) of the study participants had an agreed-upon dietary plan, a majority (63.6%) of them had no agreed plan on exercise with their physicians ([table 3](#)).

The total number of prescribed medications for HF management was 1662. The mean (SD) number of drug use per day was 4.2 ± 1.71 per patient. Commonly prescribed drug classes were diuretics (26%) and β -blockers (16%). The most frequently prescribed drug was furosemide (15%), followed by benzathine penicillin (11%) and warfarin (10%) ([table 4](#)).

Drug therapy problems

The number of identified DTPs was 288 in the preintervention phase and 174 in the postintervention phase, providing a prevalence of 70% and 42.2% and a mean (SD) of 1.3 ± 1.1 and 0.63 ± 0.87 per patient, respectively. The number of DTPs identified vary with the phase. The occurrence of single DTPs seemed to increase in the post than the preintervention phases (27.7% vs 23.1%), whereas that of multiple DTPs decreased with the interventions. For example, the occurrence of 2 DTPs decreased from 35% in the preintervention to 8.7% in the postintervention phase. Likewise, the occurrence of ≥ 3 DTPs decreased from 11.9% to 5.8% ([figure 3](#)).

In the preintervention phase, DDIs (47.6%), non-adherence to medications (37.3%), and need additional preventive or prophylactic therapy (18.6%) were the most prevalent DTPs. Following the intervention, the corresponding values were 19%, 31.7% and 3.3%, respectively. Paired t-test analysis revealed a significant decrease in the number of DTPs in the postintervention compared with the preintervention 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](#)).

There were 290 identified DDIs in the preintervention phase and 130 in the postintervention phase. Warfarin and benzathine penicillin were the most common interacting drugs, accounting for 33% of the total DDIs, followed by spironolactone and digoxin (16%) and aspirin and furosemide (12%) in the preintervention phase. Benzathine penicillin and warfarin (67%) were the most common DDIs from the total identified DDIs in the postintervention phase ([figure 4](#)).

Multivariable linear regression analysis revealed that age, number of drugs, presence of comorbidity, number of comorbidities, income and DDIs were predictors of DTPs. However, educational level, gender, presence of

Table 1 Sociodemographic characteristics of study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, July to December 2019

Variables	Categories	No (%)	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)		
	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	96 (23.3)		

BMI, body mass index.

ADR, current smokers and other factors were not predictors of occurrence of DTPs.

For example, study participants who had DDIs had a 92% higher chance to experience DTPs than those who did not have (AOR 0.92, 95% CI 0.68 to 0.9, $p < 0.001$) (table 6).

In instances where DTPs were detected, 254 interventions were made by the clinical pharmacists. From those proposed interventions, 148 (58.2%) and 68 (26.8%) were fully and partially accepted, respectively. However, 38 (15%) interventions were not accepted (figure 5).

Medication adherence

According to the four-item MGL Medication Adherence Scale, 6.3% of the study participants had high adherence, 54.6% had medium adherence, and 39.1% had low adherence in the preintervention phase. In the postintervention phase, however, the proportion of study participants with high and medium adherence increased to 38.4% and 61.9%, respectively, while that of low adherence decreased to 1.7% (table 7). Paired t-test analysis demonstrated that the overall medication adherence was significantly higher in the postintervention (89%)

Table 2 Clinical characteristics of study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, July to December 2019

Clinical characteristics	Category	No (%)	Mean±SD	Range
Duration of HF diagnosis	<5 years	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)		
No 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)		

HF, heart failure; MTM, medication therapy management.

than the preintervention (73%) phase (mean difference (SD) 1.14±1.5, 95% CI 0.99 to 1.28), $t=15.68$, $p<0.001$). Forgetfulness (40%), inadequate availability (29%) and cost of medicines (22%) were cited as the major reasons for non-adherence in the preintervention phase. The

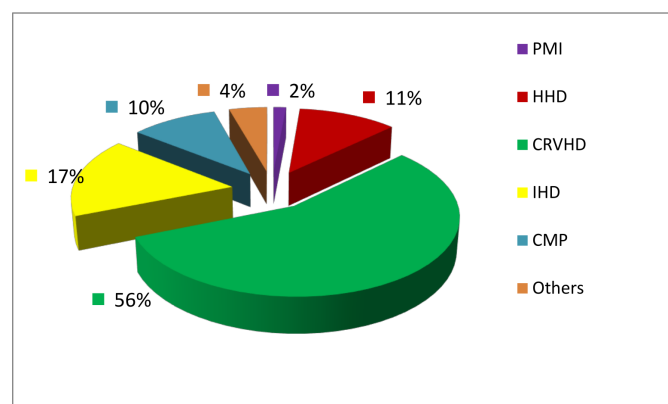


Figure 1 Aetiology of heart failure among the study participants attending cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, from July to December 2019. *Others include; degenerative valvular heart disease, cor pulmonale, congenital heart disease, constrictive pericarditis, left ventricular hypertrophy, third degree AV block. AV, atrioventricular; CMP, cardiomyopathy; CRVHD, chronic rheumatic valvular heart disease; HHD, hypertensive heart disease; IHD, ischaemic heart disease; PMI, previous myocardial infarction.

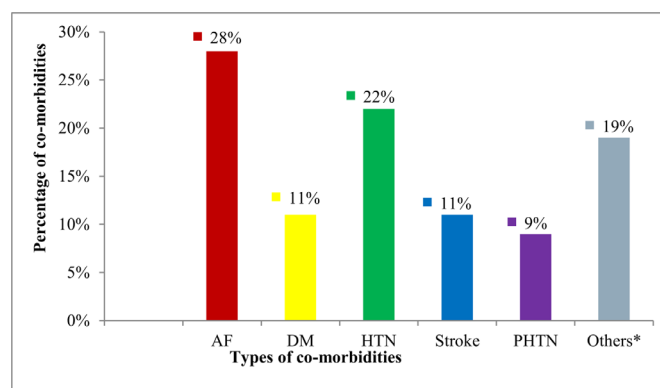


Figure 2 Percentages of comorbidities among study participants attending the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, from July to December 2019. *Others: chronic kidney disease, dyslipidaemia, benign prostate hyperplasia, bronchial asthma, gouty arthritis, osteoarthritis, peripheral arterial disease, retroviral infection, erectile dysfunction, schizophrenia, chronic myeloid leukaemia, depression, aortic Aneurism, hypothyroidism, left atrial thrombus, severe anaemia, cardiac cirrhosis, chronic hepatitis B-virus, and atria-ventricular-block, bradycardia. AF, atrial fibrillation; DM, diabetic; HTN, hypertension; PHTN, pulmonary hypertension.

Table 3 Non-pharmacological management approaches of study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, 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 chewing	
Yes	14 (3.4)
No	398 (96.6)

intervention brought down the proportion of study participants who cited forgetfulness as a reason for non-adherence to 13%, although unavailability (31%) and cost (50%) still remained to be a challenge.

In the multivariable linear regression analysis, number of drugs, number of comorbidities, presence of comorbidity, DDIs, presence of ADR, having agreed on dietary plan and income level of study participants were found to be predictors of medication adherence. For example, study participants who experienced DDIs had a 29% lower chance to be adherent than those who did not (AOR -0.29, 95% CI -0.52 to -0.07, $p=0.01$) (table 8).

Treatment satisfaction

The total composite score of treatment satisfaction of the study participants was 80.35%. For medical care services, 93.3% of the study participants were satisfied regarding detailed information on drug treatment and disease. Undesirable effects that interfere with daily physical activity and leisure were experienced by 9% of the participants (table 9).

Discussion

Clinical pharmacists provided a variety of services in the outpatient cardiac clinic that improved the therapeutic outcome of HF patients. This study revealed that the total

Table 4 Profile of prescribed medications for study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, July to December 2019

Variables	Frequency	Per cent
Diuretics		
Furosemide	243	15
Spironolactone	149	9
Hydrochlorothiazide	27	2
Beta-blockers		
Atenolol	132	8
Metoprolol	120	7
Carvedilol	14	1
Anticoagulants		
Warfarin	164	10
Rivaroxaban	3	0.1
ACE Inhibitor		
Enalapril	150	9
Angiotensin receptor blocker		
Losartan	10	1
Cardiac glycoside		
Digoxin	95	6
Antidiabetic medications		
NPH insulin	25	2
Metformin	20	1
Glibenclamide	3	0.1
Calcium channel blockers		
Amlodipine	53	3
Antiplatelets		
Aspirin	119	7
Clopidogrel	12	1
Statins		
Benzathine penicillin	182	11
Others*		
	19	1
Total no of medications	1662	

*alfuzosin, captopril, amitriptyline, allopurinol, isosorbide dinitrate, amlodipine/valsartan, telmsartan. NPH, neutral protamine hagedorn.

number of prescribed medications used for HF management was 1662 with a mean (SD) of 4.2 ± 1.71 drugs per day per patient. This finding was lower than that reported from China⁴⁴, Australia²⁰ and Taiwan.⁴⁵ The possible reasons for this difference could be related to differences in the study area and the study setting (outpatient vs inpatients).

Diuretics (26%) were the most widely used drug class in the management of HF, followed by B-blockers (16%) and ACE Inhibitors (ACEIs) (9%). This finding is lower than reported by Niriayo *et al* (B-blocker (59.1%) and

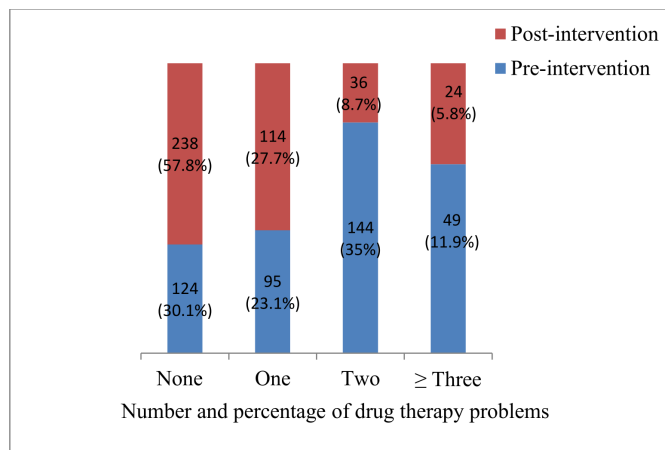


Figure 3 Number of identified drug therapy problems per patient during preintervention and postintervention phases among study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, from July to December 2019.

ACEI (71.2%).⁴⁶ The reason for this lower percentage could be the inaccessibility of those medications in the study setting that has a benefit of reducing morbidity and mortality of HF.

Beta-blockers, ACEIs, diuretics, anticoagulants, cardiac glycosides and antiplatelet were common drug classes involved in the occurrence of DTPs in this study. This is in line with other study conducted elsewhere.²⁰

Pharmacists' intervention significantly reduced DTPs in the postintervention phase in this study, although the extent of reduction is lower than a study carried out in Indonesia.⁴⁷ The reason for the difference could be related to the existence of very little experience of pharmacists and doctors working together in this area.⁴⁸

DDIs were the most common identified DTPs. In the preintervention phase, DDIs accounted for 47.6%. However, the teaming up of clinical pharmacists with cardiologists and cardiology fellows brought down the rate to 19% through replacing drugs that have serious DDIs with those with mild DDIs. The rate, however, is found to be lower than reported from Nepal,⁴⁹ probably attributed to the use of a different standard drug interaction checker database, drug interaction classification or operationalisation of drug interaction. In this study, valvular heart disease was the most common cause of HF in the study participants. Due to this, higher DDIs were identified between warfarin and benzathine penicillin in both the preintervention and postintervention phase. After pharmacist interventions, for some study participants who had AF and coagulations problems, warfarin was replaced by rivaroxaban. Using warfarin together with penicillin G benzathine may increase the risk of bleeding.

Needs additional drug therapy accounted for 18.6% in the preintervention phase. The intervention enabled to initiate new safer and more effective drugs for patients (15.3%), which made it possible to prevent further disease complications and increase effectiveness of the drug. The achievement made in this study was; however, lower than

other studies done in Saudi Arabia (35%),⁵⁰ USA (38%)⁵¹ and Mexico (38.3%).⁵² This can be due to differences in the healthcare system, study area and healthcare practitioners' experience.

The use of ineffective drug therapy was the second common identified DTPs both in the preintervention (8.7%) as well as the postintervention phase (3.4%). The intervention identified the less effective drugs used by HF and allowed their replacement with the most effective drugs in 5.3% of the cases. This rate was found to be lower than studies done in Australia (45%)²⁰ and Asia (25.4%).⁵³ But it was relatively similar to the study in India (5.6%)¹⁹ and higher than that of Spain (2.23%).¹⁷ The discrepancy could emanate from several factors, including limited access to medications, socioeconomic factors and the cost of drugs.

Dose too low accounted for 4.4% in the preintervention phase and 0.9% in the postintervention phase. The intervention was able to increase the recommended dose by 3.5% for patients with HF as per guideline-recommended target doses. During the intervention, ACEIs and evidence-based β -blockers titrated up towards established ESC and AHA guidelines recommended target doses.^{40 54} The finding of this study is considerably comparable with two studies done in Taiwan (dose too low=4.1%),⁴⁵ and Spain (dose too low=0.45 %).

The number of drugs, number of comorbidities, DDIs, age and presence of comorbidities were found to be significantly associated with the number of DTPs. It is demonstrated that for every drug added, there was a 10.6% increase in the number of DTPs, suggesting the presence of a strong relationship between the number of drugs and DTPs. This finding is consistent with several studies across the literature.^{17 20 22 46 55 56}

As the number of comorbidities was increased by one unit, there was a 10.4% increase in the number of DTPs. A similar finding was reported from some local studies conducted at Jimma, Ethiopia.^{18 46} Study participants who had significant DDIs were 0.92 times more likely to experience DTPs compared with those who did not have DDIs. This is concordant with studies done in Jimma University specialised hospital, Ethiopia.⁵⁵

We found that 14 (3.4%) study participants had developed ADRs. Seven participants had dry cough while five participants had bleeding. This finding is lower than studies done in Minnesota (34%)⁵⁷ and Spain (16%).²⁰ This discrepancy may be due to differences in the clinical characteristics of study participants included in the study.

Our study found that greater than 39% of the study participants had poor medication adherence, and less than 7% of them had high medication adherence in the preintervention phase. With the intervention, less than 2% had low medication adherence and greater than 36% had high medication adherence. The improvement rate reported in this study is higher than studies conducted in USA^{58 59} and Mexico.⁵² This variation could be attributed to differences in the study setting, methods used to measure medication adherence, study design, level of

Table 5 Identified drug therapy problems (DTPs) of study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, July to December 2019

Type of DTPs	Specific DTPs	Prephase n (%)	Postphase 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 to 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)			
	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)			
Dose too high	Wrong dose (over therapeutic dose)	6 (1.4)	0			
	Drug interaction	0	2 (0.5)			
Non-adherence	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)			

*Paired t-test at 5% significance level

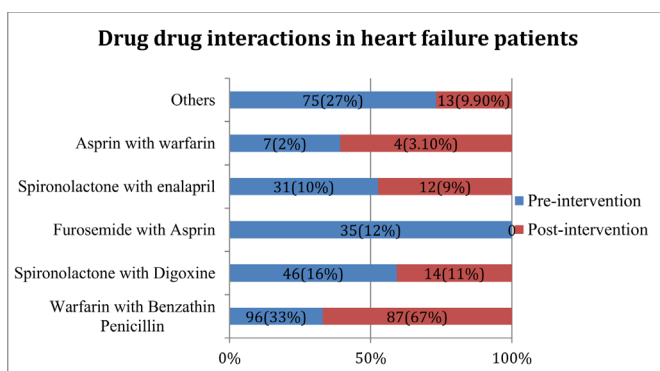


Figure 4 Frequency of major drug-drug interacting regimens among study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, from July to December 2019.

health facilities and pharmacists' approach to patients. A systematic review and meta-analysis done by Ruppap *et al*⁶⁰ reported that pharmacist intervention had significant effects to improve medication adherence among HF patients.

Forgetfulness was the main reason that contributed to poor medication adherence both in the preintervention and postintervention phase. It was also a common problem in studies performed elsewhere.^{61 62} Hence, the identification of specific barriers for each patient and designing appropriate prevention strategies are indispensable to mitigate poor medication adherence.⁶³

In this study, we found that for every drug added, there was a 17% decrease in adherence to HF medications. This finding was consistent with three studies performed in the USA.^{59 61 62} We also found that there was a negative association between the number of comorbidities

Table 6 Univariable and multivariable linear regression analysis of predictors of drug therapy problems among study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, July to December 2019

Variables	Univariable analysis unstandardised coefficient (B) (95% CI)	P value	Multivariable analysis unstandardised coefficient (B) (95% CI)	P value
Age (years)	-0.003 (-0.01 to 0.003)	0.3	-0.01 (-0.01 to 0.002)	0.014
No of drugs	0.073 (0.02 to 0.13)	0.014	0.106 (0.03 to 0.15)	0.001
No of Comorbidities	0.096 (0.03 to 0.16)	0.003	0.104 (0.03 to 0.16)	0.002
Gender				
Male	1		1	
female	0.11 (-0.11 to 0.32)	0.32	0.13 (-0.1 to 0.36)	0.28
Smoking				
No	1		1	
Yes	-0.68 (-1.77 to 0.41)	0.22	-0.62 (-1.6 to 0.43)	0.25
ADR				
No	1		1	
Yes	0.49 (-0.11 to 1)	0.1	0.34 (-0.27 to 0.9)	0.3
Drug interaction				
No	1		1	
Yes	0.76 (0.56 to 0.97)	<0.001	0.92 (0.68 to 0.91)	<0.001
Comorbid disease				
No	1		1	
Yes	0.42 (0.19 to 0.65)	<0.001	0.66 (0.41 to 0.9)	<0.001

ADR, adverse drug reaction.

and adherence to HF medications. This has also been reported in a US study,⁵⁹ implying prescribing medications is often challenging in people with multiple chronic diseases. The presence of comorbidity was another significant predictor of medication adherence. This finding is similar to a study done in Iran reported that comorbidity was a significant predictor of medication adherence in HF patients.⁶⁴

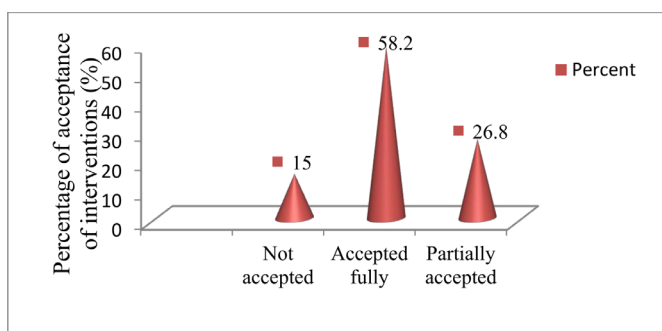


Figure 5 Percentages of acceptance of clinical pharmacist interventions on drug therapy problems among study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, from July to December 2019.

Clinical pharmacists made a recommendation to physicians after reviewing medical charts and records of HF patients using HF standard treatment guidelines. Close to 53% of the recommendations were accepted, however. This acceptance rate was found to be lower than rates reported from several countries, including United Arab Emirates (70%)⁵³; USA (85.3%)⁵¹; Belgium (78.37%)⁶⁵; China (98%)⁶⁶ and India (78.1%)⁶⁷. Although the cardiologists' acceptance rate of pharmacists' intervention to optimise drug therapy could vary depending on the study

Table 7 Major findings of impact of MTM interventions in HF patients attending at the cardiac clinic of TASH, Addis Ababa, Ethiopia from July to December 2019

Items	Pre-MTM (N (%))	Post-MTM (N (%))
No of DTPs	288 (70)	174 (42.2)
Medication adherence	High adherence	26 (6.3)
	Medium adherence	225 (54.6)
	Poor adherence	161 (39.1)
		150 (36.4)
		255 (61.9)
		7 (1.7)

DTPs, drug therapy problems; HF, heart failure; MTM, medication therapy management; TASH, Tikur Anbessa Specialised Hospital.

Table 8 Univariable and multivariable linear regression analysis of predictors of medication adherence among study participants attending at the cardiac clinic of Tikur Anbessa Specialised Hospital, Addis Ababa, Ethiopia, July to December 2019

Variable	Univariable analysis		Multivariable analysis	
	unstandardised coefficient (B) (95% CI)	P value	unstandardised coefficient (B) (95% CI)	P value
Age	-0.002 (-0.01 to 0.01)	0.67	-0.01 (-0.01 to 0.003)	0.24
Total no of drugs	-0.19 (-0.25 to 0.13)	<0.001	-0.17 (-0.24 to 0.11)	<0.001
No of comorbidities	-0.11 (-0.18 to 0.05)	0.001	-0.12 (-0.19 to 0.05)	0.001
Gender				
Male	1		1	
Female	0.02 (-0.24 to 0.27)	0.91	-0.12 (-0.39 to 0.17)	0.44
Agreed dietary plan				
No	1		1	
Yes	0.55 (0.27 to 0.83)	<0.001	0.48 (0.18 to 0.79)	0.002
Drug interaction				
No	1		1	
Yes	-0.30 (-0.53 to 0.08)	0.008	-0.29 (-0.52 to 0.07)	0.011
Adverse drug reaction				
No	1		1	
Yes	-1.3 (-2.0 to 0.63)	<0.001	-0.86 (-1.54 to 0.17)	0.014
Presence of comorbidities				
No	1		1	
Yes	-0.72 (-0.98 to 0.45)	<0.001	-0.69 (-1.00 to 0.38)	<0.001
Drug allergy history				
No	1		1	
Yes	0.31 (-0.34 to 0.97)	0.35	0.24 (-0.52 to 1)	0.53
Income				
Very low income	-0.47 (-0.79 to 0.15)	0.5	1	
Low income	-0.23 (-0.54 to 0.08)	0.15	0.2 (-0.24 to 0.63)	0.38
Average income	0.18 (-0.11 to 0.44)	0.19	0.38 (-0.006 to 0.77)	0.059
Above average income	0.2 (-0.12 to 0.51)	0.2	0.27 (-0.15 to 0.69)	0.2
≥5000 income	1.2 (0.47 to 1.9)	0.001	0.95 (-1.54 to 0.17)	0.014

setting, there appeared to be a general increasing trend in the acceptance rate. The possible reasons for increased physicians' acceptance rate for pharmacist's intervention

could include increased regimen complexity due to comorbid diseases and the occurrence of DTPs during patient admission and discharge. Although clinical

Table 9 Treatment satisfaction among study participants attending at the cardiac clinic of Tikur Anbessa Specialised 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

SATMED-Q, Treatment Satisfaction with Medicines Questionnaire.



evidence and treatment guidelines recommend the use of evidence-based therapies such as ACEI and BB in HF patients, these therapies are well known to be suboptimally prescribed in actual clinical practice.⁶⁸

In this study, the total composite score of study participants' treatment satisfaction rate was relatively high (80.35%) and the same rate (80%) is also reported in studies conducted elsewhere.⁶⁹ The study participant's treatment satisfaction effectiveness rate was 90%. This finding was higher than a study reported from Nigeria (66.8%).⁷⁰ This discrepancy might be explained by variation in treatment satisfaction assessment tool, characteristics of the study participants and study design.

CONCLUSIONS

The study clearly showed that teaming up of clinical pharmacists with cardiologists and cardiology fellows would help in resolving and reducing most of the DTPs as well as in improving medication adherence in HF patients (table 7).

In addition, the clinical pharmacist interventions could improve treatment satisfaction of HF patients. This calls for the scaling up of such initiatives in the study hospital as well as other hospitals where clinical pharmacists are deployed.

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Data availability statement All relevant data to the study are included in the article or uploaded as online supplemental information. Extra data which form the basis for this study are accessed upon reasonable request of the corresponding author.

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