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Research Article

Medication Related Problems and Its Predictors Among Heart Failure Patients at A Tertiary Care Hospital in Ethiopia: A Prospective Interventional Study

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Abstract

Background: Medication related problems in cardiovascular disease patients, especially among heart failure patients were found to be high. Medication related problem is a critical problem to provide high quality health care service for the patient which is associated with high mortality, complication, prolonged hospital stays, compromised quality of life and increase health care cost.

Objective: To determine medication related problems and its predictors in hospitalized heart failure patients at Jimma Medical Center, from May 30, 2019 to November 28, 2020.

Methods: A prospective interventional study was conducted among heart failure patients from May 30, 2020 to November 28, 2021 at Jimma Medical Center. Medication related problems were sorted based on pharmaceutical care network Europe drug classification tool version 9.0. Patient's specific data was collected using questionnaire. The data were coded, cleaned, and entered into Epidata version 4.6 and exported to SPSS version 25.0 for analysis. Binary Logistic regression was used to identify independent predictors of medication related problems occurrence. Variables having P-values < 0.05 were considered statistically significant.

Results: A total of 384 heart failure patients were included in the study. The mean (SD) age was 49.06+17.79. Two third of study participants had at least one medication related problem. A total of 483 MRPs were identified among 231(60.15%) patients. Treatment effectiveness related problem (55.48%) was the most common observed medication related problems. Alcoholism (AOR; 3.25, 95% CI (1.46-7.23), prolonged hospital stays [AOR=3.67, 95%CI= (1.85-7.27)]; comorbidity [AOR=2.88, 95%CI= (1.47-5.66)] and polypharmacy [AOR=3.07, 95%CI= (1.57-5.99) were the independent predictors of medication related problems.

Conclusion: The prevalence of medication related problem was high among heart failure patients. Alcoholism, prolonged hospital stay, comorbidity and polypharmacy were the predictors of medication related problems. Hence, to overcome these problems, clinical pharmacists, physicians and other health care professionals have to work in collaboration.

Keywords: medication related problems; heart failure; Jimma medical center; interventions

Introduction

Heart failure (HF) is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling [1]. It has emerged as dominant form of cardiovascular disease in Africa and places great stresses on patients, caregivers and healthcare system [2-3]. Hence, the development of effective treatment regimens targeted reducing morbidity and mortality of HF patients and this led to a large number of drugs with which HF patients are treated on a regular basis. However, this causes acceptance problems from the side of the patient and the treating physician. Increasing expenses for HF medication might prevent physicians from prescribing all medications that are recommended in the recent guidelines. spite of the fact that, these regimens have beneficial effect in the long-term treatment, accumulation side effects might prevent the patient from receiving full treatment [4].

Medication related problems (MRPs) are a consequence of medication -related needs that have gone unmet, central to pharmaceutical care practice [5]. There are different MRP classification systems that different literatures use. According to Pharmaceutical Care Network Europe (PCNE) classification version9, MRPs is an event or circumstance involving drug therapy that interferes with desired health outcomes (6). MRPs are common in hospitalized patients and result in patient morbidity, mortality, increased costs, impact on patients' quality of life, prolong hospital stays and increase the overall burden of healthcare expenditures (7). Older ages, different co morbidities and polypharmacy may complicate management of HF, which probably put patients

at risk for MRPs (8-12). The systematic review on MRPs revealed that, need additional drug therapy was the most common MRPs, which showed that treatment of MRP is still suboptimal (13). Systematic review carried out in Ethiopia showed that MRPs among HF was higher than other medical conditions. Taking multiple medications and having comorbid condition have been linked to adverse health outcomes including drug interaction and poor adherence to treatment (14).

The clinical pharmacist, as a part of the multidisciplinary team, could reduce MRPs (15). Interventional study done in United State of America (USA) showed that the average of MRPs reduced from 2.8 to 1.95 after intervention of clinical pharmacist (16). Pharmacist-based services can empower patients with heart failure to understand and manage their complex medication regimens through medication reconciliation, identification of drug-drug interactions. In addition, pharmacist-based interventions may improve clinical outcomes, reduce hospital stay, fewer re-admissions and fewer disease events such as HF events or thromboembolism, reuce costs of readmissions and emergency room (17, 18).

MRPs contribute to a high number of morbidities and mortalities worldwide and responsible for undesirable health consequences in patients that often result in hospitalization (19). Studies revealed that one out of six patients admitted because of MRPs (20) and up to 30% of hospital admissions related to MRPs (21). MRPs are relatively common among hospitalized patients and can result in patient morbidity and mortality thus increased cost (7, 22,23). Studies done in different parts of Ethiopia showed that MRPs were high among hospitalized HF patients (24,25, 26). Thus, hospitalization is the primary contributor to the staggering medical cost of HF: $30.7 billion annually (27, 28). Little is known about the extent of MRPs and the clinical pharmacist role in the management of HF patients in Ethiopia. Knowing extent MRPs among HF patients will lead healthcare professionals to optimize drug therapy that may influence health expenses; save lives, improves health, reduces morbidity and mortality and increases quality of life (29, 30). Hence, this study aimed to identify MRPs and predictors among HF patients and evaluate the impact of clinical pharmacist intervention for treatment optimization.

Methods and Participants

Study area and Period

This study was conducted from May 30, 2020 to November 28, 2021 at JMC, which is located in Jimma town; 345 km Southwest of Addis Ababa, the capital. JMC is the only teaching and medical center hospital in the south western part of the country with bed capacity of 600. It provides service for approximately 9000 inpatient and 80,000 outpatient clients per year with a catchment population of about 15 million people. The medical services provided by the JMC include internal medicine, surgery, orthopedics, ophthalmology, pediatrics, gynecology and obstetrics, dermatology, Oncology, psychiatric service, pathology, pharmacy, medical laboratory, intensive care unit, radiology, and others as both inpatient and outpatient services. Medical ward is among the ward which has different unit such as: cardiac unit, renal unit, Stroke unit, Intensive care unit (ICU), pulmonary unit and TB unit. Annually, about 637 HF patients were admitted to JMC.

Study Design and variable

A prospective interventional study design was conducted. All HF patients who admitted to internal medicine ward of JMC were Source Population. Study Population was All HF patients who were admitted to internal medicine ward of JMC during study period and fulfill the inclusion criteria. Heart failure patients' age ≥15 years and willing to give written consent were included. Heart failure patients died or were discharged before initiation of treatment and with incomplete chart information was excluded. Dependent variable was medication related problems. Independent Variables include Socio demographic characteristics (age, sex, marital status, educational status, residence, medication belief, Cost coverage, occupation, and social drug use), Clinical characteristics (Co morbidity, etiology of HF, LVEF, class and number of drugs, number of drugs per patient, duration of hospital stay, clinical pharmacist interventions).

Sample size determination and sampling technique

The sample size was determined by using the single population proportion formula. By considering the proportion (P) of MRP among HF patients 50 % (45), 95% confidence interval (CI) and 5% marginal error the final minimum sample size was 384. Consecutive sampling technique was used until the required sample size was achieved.

Data collection instrument

Pharmaceutical care network Europe (PCNE) version 9.00 MRP classification was used to classify and document MRPs. It has three primary domains for problems (P1-treatment effectiveness, P2-Treatment Safety and P3-others). There are nine primary domains for causes (C1-drug selection, C2-drug form, C3-dose selection, C4-treatment duration, C5-dispensing, C6-Drug use process, C7-patient related, C8- patient transfer related and C9-Others). Structured collection tool was used to extract relevant information regarding patient demographics and clinical data. Medication belief was measured by belief about medication questionnaire (BMQ), in which the patient's belief was considered as positive when the average sum of 5-item patient's medication necessity scale score exceeded the average 5-item medication concerns scale otherwise it was considered as negative (57). ADR was assessed by Naranjo drug reaction probability scale which has also been standardized and validated (58). Lexi comb, Medscape drug interaction checker accessed to check drug-drug, and drug-disease interaction. MRPs were identified by comparing patient's treatment with guidelines (60-62).

Data collection procedure

Data were collected by two pharmacists and two medical interns. The data collectors were trained for three days before starting data collection. Data were collected through medical record review of patients using a prepared standard checklist and structured questionnaire. Content of checklist include patient details, investigations, current and past medications and medical condition. The structured questionnaire content includes socio-demographic characteristics, drug and disease related questions. Provisional diagnosis was confirmed by physicians after patient stayed at least 24hours and Medication related problems were identified by evaluating the appropriateness of prescription regarding indication, dosage, and safety and by assessing patients. Interventions were done by the principal investigator and two senior clinical pharmacists. After data were collected, clinical pharmacist reviewed patient's therapy to assess MRPs. For the identified MRPs, interventions were provided through discussion with individual prescriber immediately. Additionally, recommendation was delivered during round and the prescriber acceptance documented. MRPs which are not accepted were further discussed with senior physicians or residents for further interventions.

Data Quality assurance

The questionnaires were prepared in English and translated into Amharic and local language Afan Oromo, and back-translated into English by an independent person to assure its consistency. A pre-test was conducted on 19(5%) study participants by randomly selected patients before the actual data collection to check the consistency and validity of the structured data collection format. Data were compiled, cleared, coded, and checked for consistency. All steps in data collection and recording were closely monitored by the supervisor and any gaps identified were immediately communicated with the data collectors.

Data processing, analysis and presentation

Data were entered into Epidata version 4.6.0.4 and exported to the SPSS version 25 for analysis. First, data were edited and checked for completeness and consistency, then exported into SPSS for descriptive statistical analysis. Categorical variables were described by frequencies and percentages. Continuous variables were presented by means and standard deviations. A bivariate analysis was performed with binary logistic regression to assess association between the MRPs and independent variables. Those variables with a p value<0.25 in bivariate analysis were introduced into multivariate analysis and those variables with a p value<0.05 were considered as significant.

Ethical Consideration

The study was conducted in accordance with the principles of the Declaration of Helsinki and the International Council on Harmonization Guidelines for Good Clinical Practice. The Jimma University institution review board (IRB) granted ethical clearance and approval, and the JMC clinical director office was given a letter of authorization. The internal medical ward unit received a letter from the JUMC clinical director office. By employing identification numbers rather than patient names, confidentiality was guaranteed. Written informed consent was obtained from patients, parent or legal guardian.

Operational definition and definition of terms

Medication related problem: event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.

Hospitalized heart failure patients: those patients who have been diagnosed with heart failure and stayed at least 24hours in medical ward

Adverse drug reaction: is a noxious and unintended response to a drug which occurs at doses normally used for the prophylaxis, diagnosis, or treatment of disease that reducing the study period (58).

Poly-pharmacy: defined as concomitant use of five or more prescription medications (4).

Clinical pharmacist interventions: Is any action by a clinical pharmacist that directly results in a change in patient management or therapy.

Comorbidity: presence of other medical condition other than heart failure

Duration of hospital stay: length of days from admission to discharge

Non-compliance: the patient doesn't understand instruction, cannot afford drug product, prefers not to take medication, and forgets to take medication timely and drug product not available

Insurance: cost coverage of available medication provided by health institution

Results

Socio-Demographic characteristics of the study participants

Among 384 study participants included in this study,219(57.1%) were male. The mean ± SD age of the patients was 49.06 +17.79 years. Most156(40.63%) of them were in the age range of 17-47 years. About 268(69.79%) of patients were residing in the rural area. More than half of patients were farmers, married, while 222(57.81%) of participants had no formal education and 133(56.1%) of patients have positive belief (Table1).

variables	Frequency (%)
Sex (male)	219(57.1)
Age, years (Mean ± SD)	49.06 ±17.79
17- 47	156(40.63)
48-63	121(31.51)
≥64	107(27.86)
Educational level	
no formal education	222(57.81)
primary education	51(26.3)
secondary education and above	61(15.89)
Occupational status	
Unemployed	70(18.23)
Farmer	202(52.6)
Merchant	69(17.97)
government employee	43(11.2)
Marital status	
Single	79(20.57)
Married	171(57.55)
widowed or divorced	84(21.88)
Residence	
Urban	116(30.21)
Rural	268(69.79)
Cost coverage method	
Insurance	121(31.51)
out of pocket	263(68.49)
Social drug users	
Khat chewers	112(29.17)
Alcohol consumers	78(20.31)
Smokers	88(22.92)
Medication belief	
Positive belief	210(54.68)
Negative belief	173(45.32)

Table 1: Baseline socio-demographic characteristics among heart failure patients at JMC, from May 30, 2020 to November 28, 2021

Clinical Characteristics of study participants

Of 384 patients included in the study, more than half of the patients had 246(64.1%) comorbid condition. The most common causes of HF were IHD134(34.89%) followed by CRVHD96(25%) and CMP 91(23.69%) and most of them 234(60.94%) are newly diagnosed HF patients. About 210(54.69%) of patients had stayed less than eighteen days in hospital with the mean duration of 18.25 + 7.82 (Table2).

Variables	Frequency (%)
Patient type	
Newly diagnosed HF patients	234(60.94)
Known HF patients	150(39.06)
NYHA Class	
II	43(11.2)
III	108(28.12)
IV	233(60.68)
Etiology	
IHD	134(34.89)
CRVHD	96(25)
CMP	91(23.69)
HHD	40(10.42)
Corpulmonale	23(5.99)
Comorbid condition	246(64.1)
Anemia	51(20.73)
AF	41(16.67)
HTN	36(14.63)
CKD	25(10.16)
AKI	24(9.76)
DM	21(8.54)
Thrombosis	18(7.32)
thyrocardiac disease	16(6.5)
chronic pulmonary disease	14(5.69)
Number of comorbidities	
<2	90(61.6)
≥2	56(38.4)
length of hospital stays	
<7	210(54.69)
≥7	174(45.31)
Mean ±SD	18.3 ± 7.8
Laboratory investigation	
Serum electrolyte, N=195	
Potassium	4.2± 0.7
Sodium	136.2± 3.9
RFT, N=233	
Creatinine	0.9(0.68-1.28)
Vital sign	
Systolic BP	116.4 ± 16.9
Diastolic BP	72.9 ± 10.3
HR	92.5 ± 14.7
LVEF (%) N=191	
≤40	104(54.5)
41-49	23(12)
≥50	64(33.5)
Coagulation profile, N=57	
INR	1.3(1.1-1.7)
PT	17.2 ± 7.4
LFT, N=207	
AST	29.1(21-41.2)
ALT	22.8(15.7-37.4)
CBC, N=231	
WBC	7.7 ±3.4
HGB	12.1 ± 2.7
PLT	250.5 ± 100.8

Table 2: Clinical characteristics and laboratory investigation among heart failure patients at JMC, from May 30, 2020 to November 28, 2021

NB: IHD=ischemic heart disease, CRVHD=chronic rheumatic valvular heart disease .HHD=hypertensive heart disease, CMP=cardiomyopathy, NYHA=New York Heart Association, AF= Atrial fibrillation, HTN=hypertension, CKD= chronic kidney disease, AKI= acute kidney injury, DM=diabetes mellitus, BP=blood pressure, HR=heart rate, INR=internationalized normal ratio, PT=prothrombin time, LFT=liver function test, AST=aspartate transaminase, ALT=alanine transaminase, RFT=renal function test, CBC=complete blood count, WBC=white blood cell, HGB=hemoglobin, PLT=platelet

Past medications and Medications during hospital stay

Of the study participants 210(54.69%) patients do have past medication history. The most common drugs were loop diuretics (34.2%), proven BBs (23.6%) ACEIs (16%), antiplatelet (13.1%) (figure1).

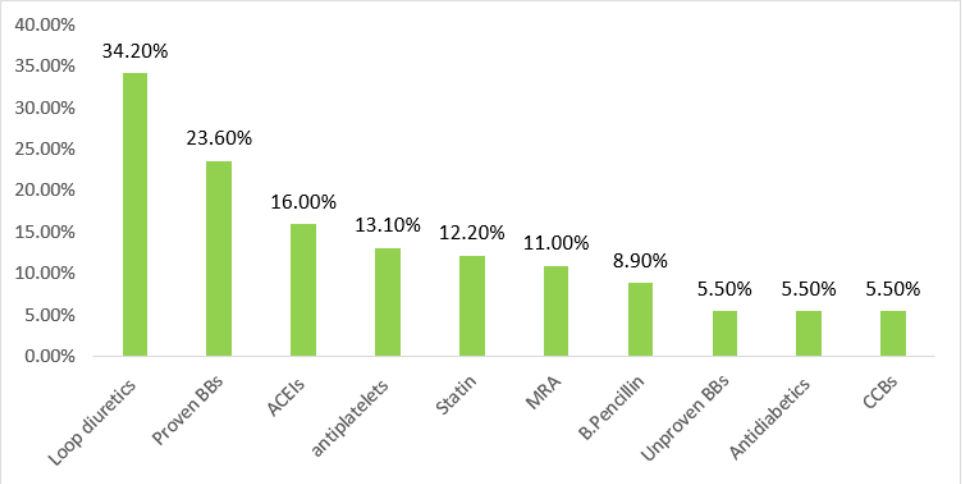

Figure 1: Top ten drug classes taken before hospitalization among heart failure patients at JMC, from May 30, 2020 to November 28, 2021

Total of 1442 drugs were prescribed for384 patients during study period. The mean number of drugperpatientwas3.75±1.82. The most commonly prescribed drugs were furosemide384 (100%) followed by enalapril 153(64.6%), antiplatelet 114(48.1%) and proven BBs 109(46%) Among study participants, 146(61.6%) of them had polypharmacy. (figure2).

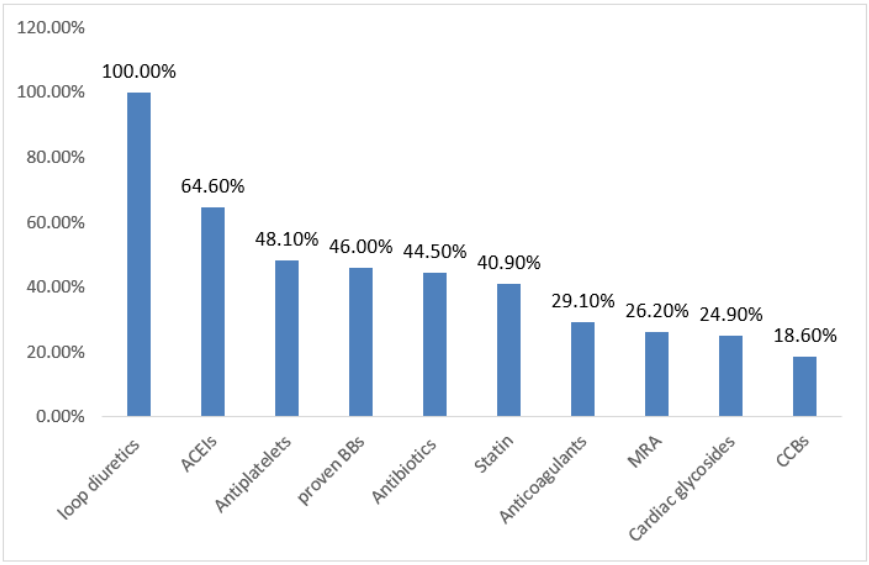

Figure 2: Top ten prescribed drug classes during hospital stay among heart failure patients at JMC, from May 30, 2020 to November 28, 2021

The prevalence, type and causes of Medication Related Problems

From a total of 384 patients, 231(6 0.15%) patients experienced Medication related problems. A total of 483 MRPs were identified, out of this 40 MRPs were in non-heart failure. The average number of MRP per patient was 1.25+ 1.18. Among Patients experienced MRPs, 130 (61.93%) had 1 MRP, 56(26.67%) 2 MRPs and 45(21.42%) > 3 DRPs. The most commonly found DRPs were treatment effectiveness related (no effect of drug treatment, untreated indication, effect of drug not optimal) 55.46% followed by others (unnecessary drug treatment, compliance and cost effectiveness related) 22.97% and safety related (ADE occur or may occur) 21.57% (figure3).

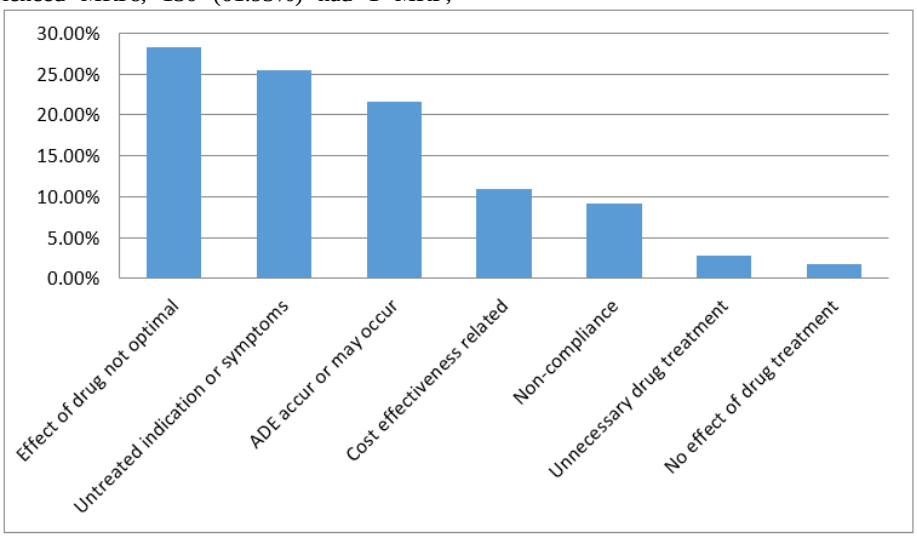

Figure 3: Medication related problems among heart failure patients at JMC, May 30, 2020 to November 28, 2021

Three hundred twenty-seven causes of MRPs were identified. Drug selection (33.33%), dose selection (20.49%) and patient related were the most common causes (table 3).

Cause domain, total= 327	Frequency (%)
C1: Drug selection causes	109(33.33)
New indication for drug treatment	67(61.47)
Inappropriate drug according to guidelines	19(17.43)
Contra-indicated	7(6.42)
No indication for drug	6(5.50)
In appropriate combination of drugs, drugs and foods	6(5.50)
In appropriate duplication of therapeutic agents	4(3.68)
C2: Drug form causes	33(10.09)
Inappropriate drug form	33(100)
C3: Dose selection causes	67(20.49)
Dosage regimen not too frequent	32(47.76)
Drug dose too high	17(25.37)
Drug dose too low	10(14.93)
Dosage regimen too frequent	8 (11.94)
C4: treatment duration causes	1(0.31)
Duration of treatment too long	1(100)
C5: Dispensing causes	7(2.14)
Prescribed drug not available	5(71.43)
Necessary information not available	2(28.57)
C6: Drug use process causes	17(5.20)
Drug under administered	11(64.70)
Inappropriate timing of administration	3(17.65)
Drug not administered at all	3(17.65)
C7: Patient related causes	63(19.27)
Patient unable to understand instructions	33(52.38)
Patient takes less drug than prescribed	17(26.98)
Patient takes more drug than prescribed	7(11.11)
Inappropriate timing or dosing intervals	5(7.94)
Patient uses unnecessary drug	1(1.59)
C8: Other causes	30(9.17)
not safe or drug-drug interaction	17(56.67)
No or inappropriate outcome monitoring	13(43.33)

Table 3: Causes of Medication related problems among heart failure patients at JMC from May 30, 2020 to November 28, 2021

Drugs involved in Medication Related Problems

There were different classes of drugs involved among HF patients with Medication related problems. The most frequently encountered drug classes were beta-blockers (34%), of which 11% was unproven BBs. Angiotensin converting enzyme inhibitors and antithrombotic were about 24 % and 22% respectively. From the antithrombotic, anticoagulant was about six percent (Figure 4).

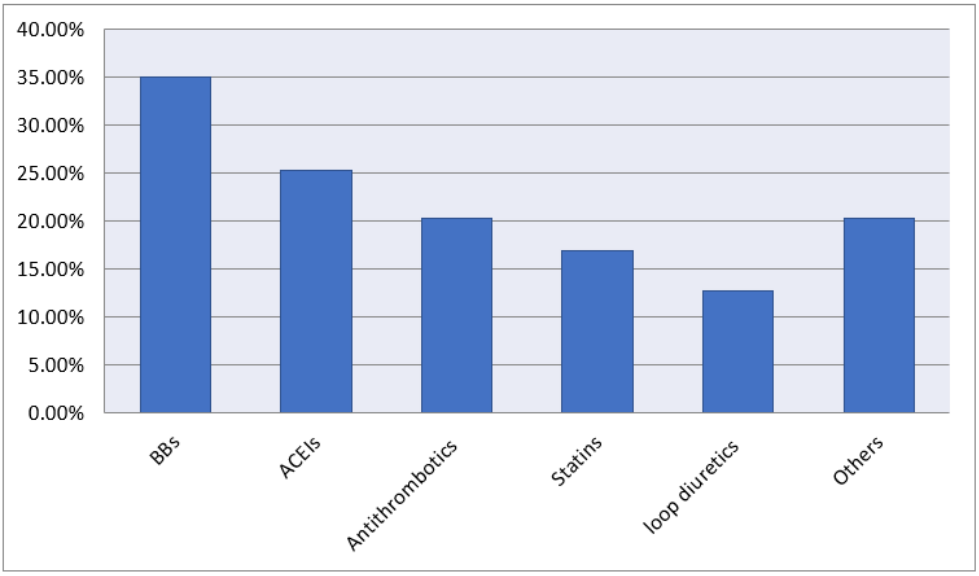

Figure 4: Common drug classes implicated in MRPs among heart failure patients at JMC, May 30, 2020 to November 28, 2021

Others: *Ferroussulphate (4.6%), Spironolactone (3.8%), digoxin (2.1%), thionamides (2.1%), antibiotics (1.7%), calcium channel blockers (1.7%), omeprazole (1.3%), cimetidine (0.8%), amiodarone (0.8%), antiTB (0.8%) and hydrochlorothiazide (0.4%)*

Intervention, acceptance rate and outcome of intervention of medication related problems

For the identified MRPs, a total of 458 intervention were delivered at different levels, out of these 198(43.23%) interventions were done at prescriber level, 421(91.92%) of them were accepted. After intervention, 401(87.55%) and 37(10.26%) of the problems were solved and not solved respectively (table 4).

Intervention domain (N=458)	Frequency (%)
I1: Intervention at prescriber level	198(43.23)
Intervention proposed and discussed with prescriber	143(72.22)
Prescriber informed only	55(27.78)
I2: intervention at patient level	150(32.76)
Patient drug counseling	80(53.33)
Spoken to family member/caregiver	70(46.67)
I3: Intervention at drug level	110(24.02)
drug stopped	38(34.54)
New drug started	27(24.54)
Formulation changed	24(21.81)
Drug changed	13(11.81)
Instruction for use changed	6(5.45)
Dosage changed	2(1.81)
Intervention acceptance domain(N=458)	
A1: Intervention accepted	421(91.92)
Intervention accepted and fully implemented	360(78.6)
Intervention accepted and partially implemented	31(7.36)
Intervention accepted but not implemented	20(4.75)
Intervention accepted, implementation unknown	10(2.37)
A2: Intervention not accepted	37(8.08)
Not accepted; unknown reason	21(56.76)
Not accepted; no agreement	16(43.24)
Problem status domain (N=458)	
O1: Problem totally solved	401(87.55)
O2: Problem not solved	37(10.26)
Lack of cooperation of prescriber	27(78.97)
No need/ possibility to solve problem	10(27.02)
O3: problem partially solved	6(1.31)
O4: Problem status unknown	4(0.8)

Table 4: Intervention, prescriber acceptance rate and outcome of intervention for MRPs among heart failure patients at JMC, May 30, 2019 to November 28, 2020

Predictors of Medication related problems

In crude analysis using binary logistic regression: Sex, age, chat chewers, alcohol drinkers, comorbidity, hospital stay and polypharmacy were found to predispose HF patients for MRPs with statistically significant association. Independent predictors for encountered MRPs were identified using multivariate logistic regression, finally alcohol drinker (AOR; 3.25, 95% CI (1.46-7.23), P=0.004), prolonged hospital stay (AOR; 2.77, 95% CI 1.93-7.37, P=0.001), presence of comorbid condition (AOR: 2.59, CI 1.35-4.96, P=0.004) and polypharmacy (AOR; 2.94, 95% CI 1.54-5.61, P=0.02) were found to be independent predictors of MRPs.

According to our finding HF patients stay in hospital greater than 18 days are 2.77(AOR; 2.45, 95% CI 2.32-5.34) times at risk for MRPs than those stay in hospital less than 18 days, HF patients had comorbid condition were 2.59(AOR: 2.59, CI 1.35-4.96) times likely to encounter MRPs than those without comorbid condition. HF patients who Alcohol drinker was 3.25(AOR; 3.25, 95% CI (1.46-7.23) times likely to encounter MRPs than those not chew khat (Table 5).

	MRP Status		COR (95%CI)	p-value	AOR (95%CI)	p-value
Variable	Yes	No				
Sex	88(56.1%)	34(42.5%)		0.049	1.17(0.56-2.45)	0.681
Age group						
≤ 47	72(45.9%)	34(42.5%)				
48-63	50(31.8%)	21(26.3%)	1.12(0.59-2.16)	0.725	1.06(0.49-2.29)	0.875
≥ 64	35(22.3%)	25(31.2%)	0.66(0.34-1.27)	0.216	0.52(0.24-1.12)	0.097
Residence	110(70.1%)	61(76.2%)	0.73(0.39-1.35)	0.32		
Alcohol drinker	50(31.8%)	12(15%)	2.648(1.316-5.33)	0.006	3.25(1.46-7.23)	0.004*
Khat chewing	24(15.3%)	7(8.7%)	1.88(0.77-4.58)	0.16	1.48(0.49-4.41)	0.478
Smokers	28(17.8%)	10(12.5%)	1.52(0.69-3.31)	0.29		
Payment method						
Insurance	49(31.2%)	22(27.5%)				
Out of pocket	108(68.8%)	58(72.5%)	0.84(0.461-1.52)	0.56		
Medication belief						
Positive belief	92(58.6%)	41(51.3%)				

Negative belief	65(41.4%)	39(48.7%)	0.74(0.43-1.28)	0.282		
Comorbidity	114(72.6%)	32(40%)	3.98(2.25-7.02)	<0.001	2.59(1.35-4.96)	0.004*
polypharmacy	119(75.8%)	32(40%)	4.69(2.64-8.37)	<0.001	2.94(1.54-5.61)	0.001*
Duration of hospital stay						
<7days	72(45.9%)	61(76.3%)				
≥7 days	85(54.1%)	19(23.7%)	3.79(2.07-6.93)	<0.001	2.77(1.93-7.37)	<0.001*

Table 5: Predictors of MRPs among heart failure patients at JMC, May 2020 to November 28, 2021

Discussion

Out of 231(60.15%) patients experienced MRPs, 56% of MRPs were found in males, which is similar with the result of two studies done in India. This might be due to increased medication use because of comorbid condition was higher in males and other various risk factors like smoking, alcoholism and chewing chats compared to females (34, 36). The prevalence of MRP was found to be 60.15% and average of MRPs per patient was 1.25+ 1.18, which was lower than study conducted at JUMC (83.5%) and 2.6 + 1.8, the difference could be due to setting difference where our study conducted in hospitalized patients in which senior physicians and clinical pharmacists are available more frequently than being at ambulatory(30).However, it is almost in line with study conducted at TASH (65.5%) (23) and GUH 63.4% or average 1.17 + 1.1 per patient (41). Moreover, study done on hospitalized heart failure patient at JUMC in 2014 showed that MRPs was about 91% (41). This difference from current study could be due to there were no clinical pharmacists' ward (when clinical pharmacists were not involved in the ward) in the previous study.

The most common DRPs in our study were treatment effectiveness related problem (55.46%) and the least was ADE occurrence (21.57%). Of the treatment effectiveness related problem, suboptimal drug treatment and untreated indication were about 28% and 25% respectively. This finding was in line with study conducted in Barcelona which showed that suboptimal drug therapy (31%) and probability of ADE occurrence (16%) (40). In contrary to this finding, study conducted at JUSH in 2014 showed that treatment effectiveness related was about 83%, of which suboptimal drug therapy and untreated indication were about 55% and 27% respectively (29). Whereas, study conducted at TASH treatment effectiveness related problem (39%) was lower than our findings (28). Furthermore, study done in USA on outpatient heart failure showed that treatment effectiveness related problem was about 36.8%(37). The discrepancy could be due to difference in classification of MRPs, study setting, where studies done at JUMC, TASH and USA were at ambulatory clinic at which senior physicians, residents and clinical pharmacists less frequently available than in medical wards.

About 91% of patients were compliant to medication which was comparable with study done in Netherlands (98.6%) (39). Non-adherence was about 9%, which was in line with studies done at ambulatory care of JUSH (9%), Harar 12 % (25), Barcelona and Spain (14%) (29,37). However, study done at TASH showed that, non-compliance was about 45% (30). The difference could be due to difference in compliance assessment method and in our study, patients may be more access to information about medication from health professional and caregiver. In our study, one third of MRPs was due to inappropriate drug selection and about 21% was dose selection related problem. Indication (need additional drug therapy) was about 60% causes of inappropriate drug selection, which was comparable with studies conducted at GUH which showed inappropriate drug selection and new indication were about 36% and 59% respectively (40) and in India inappropriate drug selection 34% and dose selection 27% (34). However, study on general medical conditions of admitted geriatric patients at JUMC showed that inappropriate drug selection was about 54% and the main causes of it was about 36% (59). This discrepancy may be due to difference in study population, medical conditions and study design.

In the present study, the most common classes of drugs implicated in MRPs were BBs (35%) and ACEIs (25.3%) which was in consistent with studies conducted in JUSH, which BBs and ACEI were 34.4% and 24.8% respectively (29), in Taiwan showed that ACEI was about (21%) (32), at ambulatory clinic of TASH and in hospitalized HF patients at JUSH showed that BBs, ACEIs and antithrombotic were the most common implicated drug classes in MRPs likewise our findings (28, 41).

The result of multivariate logistic regression showed that alcoholism, comorbidity, prolonged hospital stay and polypharmacy were independent predictors of DRPs. Study conducted in southern India supports our findings which showed that patients had social history of alcoholism do have independent predictors of MRPs. The plausible argument is social drug use (alcoholism) causes patients' financial issues to be disrupted (34). Prolonged hospital stay was one of the independent predictors of MRPs among HF patients admitted to JUMC. This was supported by studies done by Fentie et al, Murtaza et al, Sharma et al, Wright et al and Urbina et al. (41, 45-48). The reason might be, the likelihood of getting the multiple drugs increases with the increased length of hospital stay which in turn will increase the likelihood of MRPs.

Comorbidity was other independent risk factors of MRPs in HF patients admitted to JUMC. This is augmented by studies carried out at ambulatory clinic of GUH and JUMC (7, 28, 29, 48, 51). This could be due to patients with comorbidity are more likely to take more drugs to treat other diseases, causing disease-disease interaction, drug-drug interaction, drug- disease interaction which in turn makes patients more vulnerable to MRPs. Moreover, polypharmacy was also independent predictors of MRPs, which was also supported by several studies (7, 30, 28, 35, 47, 48-51). This could be due to the fact that the more the more the number of medications prescribed, the more drug-drug interaction, risk for adverse events, difficulties for adherence and cost.

Clinical pharmacists' interventions in medical ward play a vital role in effectively identifying, resolving and preventing MRPs. According to our study clinical pharmacists' intervention acceptance rate was about 91.92%, of which about 87.55% interventions were fully implemented and 82% of interventions were totally solved problem. This result was comparable with studies carried out in Southern India and Karnataka, India which revealed that clinical pharmacists' acceptance was about 97% and 96% respectively (34, 54). Moreover, clinical pharmacists' intervention and acceptance rate were about two thirds of MRPs (56-58).

Conclusion

Our study showed that, the prevalence of MRPs was high among HF patients at JMC. The most common identified MRPs were treatment effectiveness related problems which mainly includes suboptimal effect of drug and untreated indication. Prolonged hospital stay, comorbidity and polypharmacy were found to be independent predictors of MRPs. Clinical intervention acceptance rate and implementation including totally solved outcome of intervention were high.

List of acronyms and abbreviations

ACEIs: Angiotensin converting enzyme inhibitors

ADR: Adverse drug reaction

AHA: American heart association

ARB: Angiotensin receptor blocker

BBs: Beta blockers

BMQ: Belief about medication questionnaire

CP: Clinical pharmacist

CVD: Cardiovascular disease

MRP: Medication related problems

ESC: European Society of Cardiology

ESTG: Ethiopian Standard treatment guideline

HF: Heart Failure

ICU: Intensive care unit

JMC: Jimma Medical Center

MRA: Mineralocorticoid receptor antagonist

NSAID: Non-steroidal anti-inflammatory drugs

PCNE: Pharmaceutical care Network Europe

TASH: UK: United Kingdom

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Competing Interests

All authors have no competing interests with the material presented in this manuscript

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Authors' contributions

W.A. and T.G wrote the main manuscript, prepared tables and figures. W.A and T.G have made substantial contributions to the conception, design of the work, the acquisition, analysis and interpretation of data. All authors also have drafted the work, substantively revised it and approved the submitted version. All authors read and approved the final manuscript.

Availability of data and materials

Readers who will require data and materials of the current study can communicate and get from the corresponding author with a reasonable request.

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