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ORIGINAL RESEARCH

Medication Related-Problems and Associated Factors Among Patients with Hypertension at a Tertiary Care Hospital in Ethiopia: A Prospective Interventional Study

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Background: Hypertension affects more than 1.4 billion people worldwide currently, with that number anticipated to climb to 1.6 billion by 2025 with high mortality and morbidity effects. Medication related problems in cardiovascular disease patients, especially among hypertension patients were found to be high and a critical problem which is associated with high mortality, complication, prolonged hospital stay, compromised quality of life and increase health care cost.

Objective: To determine medication related problems and its predictors among hypertension patients on chronic follow-up at Jimma Medical Center.

Methods: A prospective interventional study was conducted among hypertension patients from November 28, 2021 to June 30, 2022 at Jimma Medical Center. Medication related problems were classified and identified based on Pharmaceutical care network Europe drug classification tool version 9.0. Interventions were done through discussion with individual prescriber and patients. Consecutive sampling technique was used. Binary Logistic regression was used to identify independent predictors of medication related problems. Variables having P-values < 0.05 were considered statistically significant.

Results: Among 384 hypertension patients included in the study, 219 (57.1%) were male. The mean (SD) age was 49.06+17.79. Two thirds 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; 3.15, 95% CI [1.46–7.23]), stage II hypertension (AOR=2.77, 95% CI= [3.53–4.66]); 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 problems was high among hypertensive patients. Alcoholism, stage II hypertension, comorbidity and poly-pharmacy were the predictors of medication related problems. Therefore, to overcome the problems, clinical pharmacists, physicians and other health care professionals have to work in collaboration.

Keywords: medication related problems, interventions, hypertension, Jimma

Background

Hypertension (HTN) is a condition in which the blood pressure (BP) in arteries or veins is abnormally high and defined as a systolic blood pressure (SBP) ≥140 mm Hg and/ or diastolic blood pressure (DBP) ≥90 mm Hg.[1] Worldwide, prevalence of hypertension is 31% which is almost similar with in the US adult population 31.9% (72.2 million people), defined at the SBP/DBP cutoff of >140/90 mm Hg.[2] Hypertension affects more than 1.4 billion people worldwide currently, with that number anticipated to climb to 1.6 billion by 2025.[3]

Medication related problems (MRPs) are a consequence of medication related needs that were not met, central to pharmaceutical care practice. According to Pharmaceutical Care Network Europe (PCNE) classification version 9, MRPs is an event or circumstance involving drug therapy that interferes with desired health outcomes.[4] MRPs are common in HTN

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patients and result in patient morbidity, mortality, increased costs, impact on patients quality of life, prolonged hospital stays and increase the overall burden of healthcare expenditures.[3,5] Older age, different co-morbidities and polypharmacy may complicate management of HTN, which probably puts patients at risk for MRPs.[6] Need for additional drug therapy was the most common MRP, which showed that treatment of HTN patients is still suboptimal.[7] Systematic review carried out in Ethiopia showed that MRPs among HTN was higher than other medical conditions which is due to multiple medications and having a comorbid condition has been linked to adverse health outcomes including drug interaction and poor adherence to treatment.[8]

The clinical pharmacist, as a part of the multidisciplinary team, could reduce MRPs.[9] 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.[10] Pharmacist-based services can empower patients with HTN to understand and manage their complex medication regimens through medication reconciliation, identification of MRPs and implementation of interventions on identified MRPs.[11] In addition, pharmacist-based interventions can improve clinical outcomes of HTN patients, reduce hospital stay, fewer re-admissions and fewer complications, reduce costs of readmissions and emergency room visits.[12]

MRPs contribute to a high number of morbidities and mortalities worldwide and are responsible for undesirable health consequences in HTN patients.[13] Studies revealed that one out of six patients with chronic conditions visit health facilities because of MRPs[14] and up to 30% of hospital admissions are related to MRPs.[15] MRPs are relatively common among HTN patients and can result in patient morbidity and mortality, thus the increased cost.[16–18] Little is known about the extent of MRPs and the clinical pharmacist role in the management of HTN patients in Ethiopia. Knowing the extent of MRPs among HTN patients will lead healthcare professionals to optimize drug therapy that may influence health expenses, save lives, improves health, reduce morbidity and mortality and increase quality of life.[19,20] Hence, this study aimed to identify MRPs and associated factors among HTN patients at Jimma University Medical Center (JUMC).

Methods and Participants

Study Area and Period

This study was conducted from November 28, 2021 to June 30, 2022 at JMC, which is located in Jimma town; 345 km Southwest of Addis Ababa, the capital. JUMC 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 JUMC include internal medicine, surgery, orthopedics, ophthalmology, pediatrics, gynecology and obstetrics, dermatology, oncology, psychiatric services, pathology, pharmacy, medical laboratory, intensive care unit, radiology, and others as both inpatient and outpatient service. Chronic follow-up clinic provides different services such as: DM, TB, HTN, neurology and AIDS. Annually, about 937 HTN patients come to HTN clinic of JUMC for follow up.

Study Design and Variable

A prospective interventional study design was conducted among HTN patients at JUMC. All HTN patients who had follow-up at chronic follow up clinic of JUMC were Source Population. Study Population was all HTN patients who had follow-up at chronic follow up clinic of JUMC during study period and fulfill the inclusion criteria. HTN patients' age ≥18 years and willing to give written consent were included. HTN patients who died or were lossed to follow-up and with incomplete medical charts were 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, stage of HTN, etiology of HTN, class and number of drug, duration of HTN diagnosis [years], and laboratory investigation).

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 HTN patients 50%, 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 obtained.

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 data 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 the 5-item patient's medication necessity scale score exceeded the average 5-item medication concerns scale, otherwise it was considered as negative.[21] ADR was assessed by Naranjo drug reaction probability scale which has also been standardized and validated.[22] 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.[23–25]

Data Collection Procedure

Data were collected by two pharmacists and two nurses. The data collectors were trained for five 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, laboratory investigations, current and past medications and medical condition. The structured questionnaire content includes socio-demographic characteristics and clinical characteristics. After data were collected, clinical pharmacist reviewed patient's therapy to assess MRPs. Medication related problems were identified by evaluating the appropriateness of prescription regarding indication, dosage, and safety and by assessing patients for adherence. Interventions were done by the principal investigator and three senior clinical pharmacists through discussion with individual prescriber and patients immediately. 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 Vernacular 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 analysis. 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 logistic regression analysis and those variables with a p value<0.05 were considered as spastically 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) (Ref.No IRB 000238 /2021/2022) granted ethical clearance and approval, and the JUMC clinical director office was given a letter of authorization. By employing identification numbers rather than patient names, confidentiality was guaranteed. Written informed consent was obtained from HTN patients.

Operational Definition and Definition of Terms

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

Hypertension: Is an increase in arterial BP measured at least twice and the result in SBP and/or DBP readings are ≥ 140 and/ or ≥ 90 mm HG, respectively.[2]

Clinical inertia: Physicians' failure to introduce and/or enhance drugs.

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.[26]

Poly-pharmacy: defined as concomitant use of five or more prescription medications.[27]

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 hypertension.

Non-compliance: the patient does not understand instruction, cannot afford drug product, prefers not to take medication, forgets to take medication timely or 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. Most 156 (40.63%) of them were in the age range of 19–47 years. Most, 268 (69.79%), of patients were residing in the rural area. More than half (202, 52.6%)of patients were farmers, while 222 (57.81%) of participants had no formal education and 133 (56.1%) patients have positive belief. Almost nearly one third of participants 211 (55.0) had family history of hypertension (Table 1).

Table 1 Baseline Socio-Demographic Characteristics Among Hypertension Patients at JMC, from November 28, 2021 to June 2022

Variables		Frequency (%)
Sex (male)		219(57.1)
Age, years	(Mean ± SD)	49.06 ±17.79
	19–47	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)
Family history of hypertension	Yes	211(55)
	No	173(45.1)
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)

(*Continued*)

Table 1 (Continued).

Variables		Frequency (%)
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)

Clinical Characteristics of Study Participants

Of 384 HTN patients included in the study, most of patients (246, 64.1%)had comorbid condition. The most common causes of HTN were CKD 134 (34.89%) followed by CVD 96 (25%) and CMP 91 (23.69%). Majority of participants 221 (57.55%) were with less than five years of duration of diagnosis of hypertension. The overall proportion of controlled BP (SBP and/or DBP) in the last 7 months of follow-up period was 124 (50.8). The mean SBP and DBP readings of the participants were 143.25 (± 8.75 SD) and 88.75 (± 5.5 SD) mm HG, respectively. Slightly more than half (127, 52.0%)of the participants had comorbidity, DM 246 (64.1%) was the most encountered, followed by CKD 96 (25%) (Table 2).

Table 2 Clinical Characteristics Among Hypertension Patients at JMC, from November 28, 2021 to June 2022

Variables		Frequency (%)
Stage of HTN	Pre hypertension	43(11.2)
	Stage I	108(28.12)
	Stage II	233(60.68)
Etiology of HTN	Chronic kidney disease	134(34.89)
	Cardiovascular disease	96(25)
	CMP	91(23.69)
	HHD	53(16.41)
Comorbid condition	Diabetes mellitus,	246(64.1)
	Chronic kidney disease,	69(28.03)
	Acute kidney injury	46(18.7)
	Coronary artery disease	36(14.63)
	Heart failure	41(16.67)
	Peripheral neuropathy	31(8.07)
	Chronic pulmonary disease	23(5.98)

(*Continued*)

Table 2 (Continued).

Variables		Frequency (%)
Number of comorbidity	<3	90(61.6)
	≥3	56(38.4)
Duration of HTN diagnosis (years)	<5	221(57.55)
	6–10	100 (26)
	>10	63 (16.4)
Laboratory investigation		
Serum electrolyte, N=214	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
	RR	23±7.8
CBC, N=231	WBC	7.7 ±3.4
	HGB	12.1 ± 2.7
	Platelet	250.5 ± 100.8

Abbreviations: BP, blood pressure; CBC, complete blood count; HR, heart rate; RR, Respiratory rate; HGB, hemoglobin; WBC, white blood cell.

Past Medical and Medications History and Medication Involved in Medication Related Problems Among Study Participants

Total of 669 drugs were prescribed for 384 HTN patients during study period. The mean number of drug per patient was 1.18±0.82. Diuretics 252 (65.62%) were the most commonly prescribed antihypertensive medications, followed by ACEI 241 (62.72%) and CCB 102 (26.565%). The most commonly prescribed specific drugs were enalapril 241 (62.72%) followed by Hydrochlorothiazide 232 (60.41%). Nearly two thirds 202 (67.15) of participants were with high adherence to their medications. More than half 207 (53.9%) of participants were prescribed one antihypertensive drug regimens. The most frequently encountered drug classes involved in MRPs were diuretics 134 (34.72%), of which 126 (36.41%) was Hydrochlorothiazide, Angiotensin converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCBs) were about 141 (40.75%) and 51 (13.74%) respectively (Table 3).

Table 3 Overall Distributions of Antihypertensive Drugs Classes and Common Drug Classes Implicated in MRPs Among Study Participants at JUMC Chronic Clinic Follow Up from November 28, 2021 to June 30, 2022

Drug Class		Frequency (n), Total N =384	Percent (%)
ACEIs	Enalapril	241	62.76
ARBs	Losartan	14	3.6

(*Continued*)

Table 3 (Continued).

Drug Class		**Frequency (n), Total N =384**	**Percent (%)**
BBs	Metoprolol Atenolol Propranolol	47	12.23
		7	1.8
		4	1.06
Diuretics	Furosemide	16	4.16
	Hydrochlorothiazide	232	60.41
	Spironolactone	4	1.06
CCBs	Amlodipine	102	26.56
Other	(hydralazine)	2	0.7
Duration of therapy (years)	<2	103	26.82
	2–4	166	43.22
	≥5	115	29.94
Adherence	Low	72	18.75
	Medium	100	26.02
	High	202	52.60
Antihypertensive drug regimen	1	207	53.90
	2	104	27.08
	≥ 3	73	19.01
Common drug classes implicated in MRPs		**Frequency (n), Total N =346**	**Percent (%)**
ACEIs	Enalapril	141	40.75
ARBs	Losartan	7	2.02
BBs	Metoprolol Atenolol Propranolol	10	2.89
		1	0.29
		2	0.57
Diuretics	Furosemide	8	2.31
	Hydrochlorothiazide	126	36.41
CCBs	Amlodipine	51	13.74

The Prevalence, Type and Causes of Medication Related Problems

From a total of 384 HTN patients, 231 (60.15%) patients experienced MRPs and 483 MRPs were identified. The average number of MRP per patient was 1.25± 1.18. Among Patients who experienced MRPs, 130 (61.93%) had 1 MRP, 56 (26.67%) had 2 MRPs and 45 (21.42%) had ≥ 3 MRPs. The most commonly found MRPs were treatment effectiveness related (no effect of drug treatment, untreated indication, effect of drug not optimal) 268 (55.48%) followed by others (unnecessary drug treatment, compliance and cost effectiveness related) 111 (22.97%) and safety related (ADE occur or may occur) 104 (21.57%). Six hundred fifty-four causes of MRPs were identified. Drug selection 109 (16.67%), dose selection 67 (10.24%) and patient related 63 (9.63%) were the most common causes of MRPs (Table 4).

Table 4 Medication Related Problems and Causes of Medication Related Problems Among Patients with Hypertension at JMC from November 28, 2021 to June 30, 2022

Primary Domain	Code V9.1	Problem	Frequency (%), N=483
P1.Treatment effectiveness	P1.1 P1.2 P1.3	No effect of drug treatment despite correct use Effect of drug treatment not optimal Untreated symptoms or indication	98(20.29) 44(9.1) 26(26.1)
P2. Treatment safety	P2.1	Adverse drug event (possibly) occurring	111(22.98)
P3. Other	P3.1 P3.2	Unnecessary drug-treatment Unclear problem/complaint	72(14.9) 31(6.42)
Cause domain, total= 654			Frequency (%)
C1: Drug selection causes New indication for drug treatment Inappropriate drug according to guidelines Contra-indicated No indication for drug In appropriate combination of drugs, drugs and foods In appropriate duplication of therapeutic agents			109(16.67) 67(10.24) 19(2.9) 7(1.07) 6(0.92) 6(0.92) 4(.61)
C2: Drug form causes Inappropriate drug form			33(5.04) 33(5.04)
C3: Dose selection causes Dosage regimen not too frequent Drug dose too high Drug dose too low Dosage regimen too frequent			67(10.24) 32(6.62) 17(2.59) 10(1.52) 8 (1.65)
C4: treatment duration causes Duration of treatment too long			1(0.51) 1(0.15)
C5: Dispensing causes Prescribed drug not available Necessary information not available			7(1.07) 5(0.76) 2(0.41)
C6: Drug use process causes Drug under administered Inappropriate timing of administration Drug not administered at all			17(2.59) 11(1.68) 3(0.45) 3(0.45)
C7: Patient related causes Patient unable to understand instructions Patient takes less drug than prescribed Patient takes more drug than prescribed Inappropriate timing or dosing intervals Patient uses unnecessary drug			63(9.63) 33(5.04) 17(2.59) 7(1.07) 5(0.76) 1(0.15)
C8: Other causes not safe or drug-drug interaction No or inappropriate outcome monitoring			30(4.68) 17(2.59) 13(1.98)

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 this 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 5).

Predictor's of Medication Related Problems

In crude analysis using binary logistic regression: Sex, age, chat chewers, alcohol drinkers, comorbidity, stage of hypertension 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), stage II HTN (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 polyp-harmacy (AOR; 2.94, 95% CI 1.54–5.61, P=0.02) were found to be independent predictors of MRPs.

Table 5 Intervention, Prescriber Acceptance Rate and Outcome of Intervention for MRPs Among Hypertension Patients at JMC, November 28, 2021 to June 2022

Intervention Domain (N=483)	**Frequency (%)**
I1: Intervention at prescriber level	198(40.99)
Intervention proposed and discussed with prescriber	143(29.6)
Prescriber informed only	55(11.38)
I2: intervention at patient level	150(30.05)
Patient drug counseling	80(16.56)
Spoken to family member/caregiver	70(14.42)
I3: Intervention at drug level	110(22.77)
Drug stopped	38(7.86)
New drug started	27(5.59)
Formulation changed	24(4.96)
Drug changed	13(2.69)
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 unknowns	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 6 Predictors of MRPs Among Hypertension Patients at JMC, November 28, 2021 to June 2022

Variable	MRP Status		COR(95% CI)	p-value	AOR(95% CI)	p-value
	Yes	No				
Sex						
Male	143(37.24)	76		0.049	1.17(0.56–2.45)	0.681
Female	88(56.1%)	77(42.5%)	1		1	
Age group						
≤ 47	72(45.9%)	34(42.5%)	1		1	
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		1	
Payment method					1	
Insurance	49(31.2%)	22(27.5%)	1			
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%)	1		1	
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
<5days	72(45.9%)	61(76.3%)	1		1	
≥5days	85(54.1%)	19(23.7%)	3.79(2.07–6.93)	<0.001	2.77(1.93–7.37)	<0.001
Stage of HTN Pre HTN	30(7.8%)	13(3.39%)	1		1	
Stage I HTN	58(15.1%)	50(13%)	8.78(2.53–3.66)	0.28	1.77(2.35–4.52)	0.076
Stage II HTN	123(32.0%)	110(28.6%)	2.77(3.53–4.66)	<0.001	1.87(2.4–3.53)	<0.000

According to our finding HTN patients with stage II HTN are 2.77 (AOR; 2.45, 95% CI 2.32–5.34) times more at risk for MRP than those pre-HTN, HTN patients who had comorbid condition were 2.59 (AOR: 2.59, CI 1.35–4.96) times more likely to encounter MRP than those without comorbid condition. HTN patients who are Alcohol drinkers were 3.25 (AOR; 3.25, 95% CI (1.46–7.23) times more likely to encounter MRPs than those not khat chewers, with smokers (Table 6).

Discussion

Out of 231 (60.15%) patients who experienced MRPs, 62% of MRPs were found in males, which is similar with the result of two studies done in India.[28,29] 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 Khat compared to females. 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 chronic follow up patients in which senior physicians and clinical pharmacists are available more frequently.[20] However, it is almost in line with study conducted at TASH (65.5%)[26] and GUH 63.4% or average 1.17 ± 1.1 per patient.[30]

The most common MRPs in our study were treatment effectiveness related problems 268 (55.48%) and the least was ADE occurrence (21.57%). Of the treatment effectiveness related problems, suboptimal drug treatment and untreated indication were about 28% and 25% respectively. This finding was in line with a study conducted in Barcelona which

showed suboptimal drug therapy (31%) and probability of ADE occurrence (16%).[31] In contrary to this finding, a 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.[20] Furthermore, a study done in USA on outpatient heart failure showed that treatment effectiveness related problems was about 36.8%.[32] The discrepancy could be due to difference in methods of MRPs classification, study setting, sample size, or study design.

About 91% of patients were compliant to medication which was comparable with a study done in Netherlands (98.6%).[33] Non-adherence was about 9%, which was in line with studies done at ambulatory care of JUSH (9%), Harar 12%,[34] Barcelona and Spain (14%).[20,31] However, study done at TASH showed that non-compliance was about 45%.[19] The difference could be due to difference in compliance assessment method and in our study patients may have more access to information about medication from health professional and caregiver, a problem in patients' adherence to self-care activities or non-pharmacological therapy, and the patient was not given instruction in or did not understand non-pharmacological therapy or self-care advice in previous studies.

In our study, one third of MRPs was due to inappropriate drug selection and about 21% was a dose selection related problem. Indication (need additional drug therapy) was case of about 60% of inappropriate drug selection, which was higher than study conducted at GUH which showed inappropriate drug selection and new indication were about 36% and 59% respectively[30] and in India inappropriate drug selection 34% and dose selection 27%.[35] 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%.[36] This discrepancy may be due to difference in study population, medical conditions, sample size 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 inconsistent with studies conducted in JUSH, which BBs and ACEI were 34.4% and 24.8% respectively,[20] in Taiwan showed that ACEI was about (21%),[37] at ambulatory clinic of TASH and in chronic follow up HTN patients at JUSH showed that BBs, ACEIs and antithrombotic were the most common implicated drug classes in MRPs likewise our findings.[19,38]

The result of multivariate logistic regression showed that alcoholism, comorbidity, stage II HTN and poly-pharmacy were independent predictors of MRPs. Study conducted in southern India supports our findings which showed that having history of alcoholism put patients at high risk of MRPs. The plausible argument is social drug use (alcoholism) causes patients' financial issues to be disrupted.[35] Stage II HTN was one of the independent predictors of MRPs among HTN patients follow their treatment at JUMC. This was supported by studies conducted in Saudi and Nepal.[38–42] This might be due to the likelihood of increasing the stage of HTN increases the number the drugs the patient need, which in turn will increase the likelihood of MRPs.

Comorbidity was other independent risk factors of MRPs in HTN patients followed their care at JUMC. This is augmented by studies carried out at ambulatory clinic of GUH and JUMC.[5,19,20,43,44] This could be due to patients with comorbidity being more likely to take more drugs to treat other diseases, causing disease-disease interaction, drug-drug interaction, or drug- disease interaction which in turn makes patients more vulnerable to MRPs. Moreover, polypharmacy was also an independent predictor of MRPs, which was also supported by several studies conducted in different settings.[5,19,20,39,43,45,46,47,23] This could be due to the fact that the greater the number of medications prescribed, the more drug-drug interactions, risk for adverse events, difficulties for adherence and cost.

Clinical pharmacists' interventions among chronic patients 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 totally solved the problem. This result was comparable with studies carried out in Southern India and Karnataka, India which revealed that clinical pharmacists' acceptance were about 97% and 96% respectively.[28,24] Moreover clinical pharmacists' intervention and acceptance rate were about two thirds of MRPs.[25,48,49]

Limitation of Study

The study involved patients being admitted at a single hospital, not community-based, and thus may not reflect the real picture of the general population. Besides the study was not conducted to assess effectiveness of the intervention.

Conclusion

Our study showed that the prevalence of MRPs was high among HTN 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 and its acceptance rate were high.

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.

Data Sharing Statement

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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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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

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