Assessment of the management of hypertension among hypertensive patients on follow-up at cardiac clinic of Zewditu Memorial Hospital, Addis Ababa, Ethiopia

By: **Degarege Yazie Liyew**

A Thesis Submitted to Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfillment of the Requirements for the Degree of Master of Pharmacy in Pharmacy Practice

June, 2017

Addis Ababa, Ethiopia

Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Degarege Yazie, entitled: Assessment of the management of hypertension among hypertensive patients on follow-up at cardiac clinic of Zewditu Memorial Hospital and submitted in partial fulfillment for the requirements of the Degree of Master of Pharmacy in Pharmacy Practice complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee:

Internal Examiner: Teshome Nedi   Signature_____ Date_____

        (PhD, Assistant Professor)

External Examiner: Desalew Mekonnen   Signature_____ Date_____

        (MD, Internist)

Advisors: Workineh Shibeshi   Signature_____ Date_____

        (PhD, Associate Professor)

        Minyahil Alebachew   Signature_____ Date_____

        (MSc in clinical pharmacy)

Abstract

Assessment of the management of hypertension among hypertensive patients on follow-up at cardiac clinic of Zewditu Memorial Hospital

Degarege Yazie

Addis Ababa University, 2017

Hypertension is a major global concern and public health problem affecting more than one billion individuals worldwide. It is the number one risk factor for cardiovascular diseases (CVDs). The main objective of this study was to determine the prescription pattern of antihypertensive medications among patients on follow-up at cardiac clinic of Zewditu Memorial Hospital. The study was based on a cross sectional retrospective study design. Data was collected from the patient chart. Out of the 356 patients studied 204 (57.3%) were females with the mean age of 56.2 ± 12.4 years. Among total study participants, 124 (34.8%) had co-morbid conditions. Majority of the patients were on combination therapy 252(70.8%). Angiotensin converting enzyme inhibitor (ACEI), 215 (60.4%) was the most prescribed drug. BP was controlled in 107(30.1%) of patients. About 140(39.3%) and 134 (37.6%) hypertensive patients were appropriately prescribed according to national guideline 2014 and JNC 8 national guideline respectively. The result of the multivariate analysis showed that there was a positive statistical significant association between inappropriate prescription pattern of antihypertensive medications and age ≥ 60 years (P=0.01) and uncontrolled BP (P=0.001). In conclusion the general use of antihypertensive medications seemed not to be in accordance with the national guideline.

Acknowledgement

Table of Contents

List of Figures

List of Tables

List of Abbreviations and Acronyms

ACEI	Angiotensin Converting Enzyme Inhibitor
AOR	Adjusted Odds Ratio
ARB	Angiotensin Receptor Blocker
BB	Beta Blocker
BP	Blood Pressure
CA$_2$	Central Alfa-2 Agonist
CCB	Calcium Channel Blocker
CHD	Coronary Heart Disease
CHF	Congestive Heart Failure
CI	Confidence Interval
CKD	Chronic Kidney Disease
COR	Crude Odds Ratio
CNCD	Chronic Non Communicable Disease
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
FMHACA	Food, Medicine and Healthcare Administration and Control Authority

HTN/HT	Hypertension
JNC	Joint National Committee
LD	Loop Diuretics
LVH	Left Ventricular Hypertrophy
NSAIDs	Non Steroidal Anti-inflammatory Drugs
OPD	Outpatient Department
PVD	Peripheral Vascular Disease
SBP	Systolic Blood Pressure
STG	Standard Treatment Guideline
SD	Standard Deviation
TD	Thiazide Diuretics
DM	Diabetes Mellitus
WHO	World Health Organization

1. Introduction

1.1 Background

Hypertension is a major global concern and public health problem affecting more than one billion individuals worldwide (Shukrala and Gabriel, 2015; Woldu *et al.,* 2014) and is one of the key preventable risk factors for cardiovascular events (Shukrala and Gabriel, 2015). Hypertension is a condition that occurs as a result of repeatedly elevated blood pressure of a systolic blood pressure (SBP) and a diastolic blood pressure (DBP) above 140/90mmHg. Hypertension is grouped into two main categories. These include primary (essential) and secondary hypertension. Primary hypertension accounts for 95% hypertension case. Secondary hypertension occurring as a result to a consequence of another disorder or a side effect of medications and it accounts for 5% cases (Janet, 2011).

There are several published guidelines on classification of hypertension which help physicians in reaching to proper control of hypertension (Al-Drabah *et al.,* 2013). Blood pressure (BP) for adults age ≥18 can be categorized based on stage: pre-hypertension SBP 120-139 mm Hg or DBP 80-89 mm Hg, stage 1 hypertension SBP 140-159 mm Hg or DBP 90-99 mm Hg and stage 2 hypertension for SBP ≥160 mm Hg or DBP ≥100 mmHg (Weber *et al.,* 2013; Ministry of Health Malaysia, 2008; FMHACA, 2014).

According to American Society of Hypertension and the International Society of Hypertension treatment with drugs should be started in patients with blood pressures >140/90 mm Hg in whom non-pharmacology treatments have not been effective. In patients with stage 2 hypertension drug treatment should be started immediately after diagnosis, usually with a 2 drug combination. (Weber *et al.,* 2013). There is a wide range of variation in the type of antihypertensive drug class prescription by physicians in different parts of the world (Sepehri *et al.,* 2008). High BP can be treated medically using several classes of drugs such as angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor antagonists (ARBs), beta-blockers (BBs), diuretics and calcium channel blockers (CCBs) are the primary drugs used in treatment (Cheng, 2011; Cidda *et al.,* 2014). Many new effective antihypertensive drugs became available for physicians, which give

hypertensive patients more opportunities to have their blood pressure controlled with fewer side effects (Al-Drabah *et al.,* 2013).

Hypertension has been shown as a major risk factor not only for the development of diabetes but also for the development of micro-vascular complications like nephropathy, retinopathy and macro-vascular complications like coronary artery disease, stroke, peripheral vascular disease (PVD) in diabetic patients (Khrime *et al.,* 2015). HTN and diabetes mellitus (DM) frequently coexist which increases with age (Kousalya *et al.,* 2012).

The choice of anti-hypertensive drug class is influenced by many factors such as age, race, stage of hypertension (Shah *et al.,* 2013) and the presence of concomitant disease (Shah *et al.,* 2013; Rimoy *et al.,* 2008). The Joint National Committee (JNC) seventh report recommended that the BP in diabetics should be controlled to levels of 130/80 mmHg or lower (Chobanian *et al.,* 2003). In adults without compelling indications initial therapy should include thiazide diuretics, ACEIs, CCBs, ARBs or BBs (in those younger than 60 years of age) (Sepehri *et al.,* 2008). But in the presence of high risk conditions and starting therapy with ACE inhibitors, ARB's, beta blockers or calcium channel blockers alone or in combination with thiazides (Chobanian *et al.,* 2003).

Several guidelines for hypertension management recommended rational combination of drugs of different mechanisms of action for effective control of BP because mono-therapy will not achieve the optimal BP goal in the majority of patients (Ukwe and Ubaka*, 2012*; Olanrewaju *et al.,* 2010; Oke and Adedapo, 2015; Rimoy *et al.,* 2008), particularly in patient with severe hypertension (Khurshid *et al.,* 2012; Oke and Adedapo, 2015). Compliance will also increase due to fewer side effects (Olanrewaju *et al.,* 2010; Rimoy *et al.,* 2008). Low dose combinations can doubly benefit the patients by being more efficacious and more safe thereby has the potential to improve the quality of life of the patient (Kaur *et al.,* 2012).

Most guidelines recommended that thiazide type diuretics or CCBs or ACEIs could be the first-choice for initial therapy and BBs are not a preferred initial therapy for hypertension (Cheng, 2011). The benefits of ACEI in preventing cardiovascular events in patients with diabetes mellitus, heart failure, hypertensive renal insufficiency and diabetic nephropathy have been documented (Etuk *et al.,* 2008).

1.2 Statement of the problem

Hypertension is the number one risk factor for cardiovascular diseases (CVDs) such as myocardial infarctions, strokes and renal failures among others in Africa (Van de Vijver *et al.,* 2013). Patients with high blood pressure often have no clinical symptoms until organ damage begins, giving the disease its reputation as a "silent killer" (Karaeren *et al.,* 2009). Because of these consequences it is the leading cause of morbidity and mortality among non-communicable diseases, which ranks third as a means of reduction in disability-adjusted life-years (Nagarkar *et al.,* 2013).

The global prevalence of hypertension in adults aged 18 years and over was around 22% in 2014. Across the WHO regions, the prevalence of hypertension was highest in Africa, at 30% for all adults combined (WHO, 2014). Hypertension is estimated to cause 7.5 million deaths annually (WHO 2009). Hypertension in Sub-Saharan Africa, less than 40% of people with BP above the normal range are diagnosed as hypertensive; less than 30% of diagnosed cases are on treatment and only less than 20% of them had BP within the defined normal range (Addo *et al.,* 2007). The overall prevalence of hypertension in Ethiopian population was 19.1% (Nshisso *et al.,* 2012). Approximately 30% of adults in Addis Ababa have BP above 140/90mmHg or reported use of antihypertensive medications (Tesfaye *et al.,* 2009).

More than 80% of deaths from hypertension and associated cardiovascular diseases occur in low and middle income countries and this is particularly common among people of low socio-economic status (Kearney *et al.,* 2005). As in any other developing countries, Ethiopia is challenged by the growing magnitude of chronic non-communicable diseases (CNCDs) which created a double burden on the population and the health system which is already hard hit by communicable diseases. Available population based studies indicated high prevalence of CNCDs including hypertension, other cardiovascular diseases, diabetes etc, in both rural and urban parts of the country. On the other hand, the Ethiopian health system is designed primarily for the prevention and control of communicable diseases, giving very little emphasis on CNCDs (Yibeltal *et al.,* 2011).

The status of hypertension management is far from being satisfactory (Maziak *et al.,* 2003). Many studies have demonstrated that lifestyle modifications and adherence to appropriate drug

treatments are sufficient to maintain blood pressure at optimal levels. However, available evidence has also shown that about 75% of hypertensive patients do not have optimal blood pressure control (Bakare *et al,* 2016).

Hypertension is an important risk factor for cardiovascular disease and has become a major global burden on public health. Therefore, blood pressure control needs to be considered in conjunction with the control of other concomitant cardiovascular risk factors. The prevalence of hypertension is high and the prescription containing antihypertensive drug is increasing day by day associated with other diseases such as diabetes and cardiovascular disease (Kousalya *et al.,* 2012). Clinical trials have shown that antihypertensive therapy was associated with reductions in incidence of stroke by about 35-40%, myocardial infarction 20-25% and heart failure > 50% (Olanrewaju *et al.,* 2010; Maghrabi, 2013). If hypertension left untreated about 50% of the patients will die of coronary heart disease, 33% of cerebrovascular stroke, 20% of diabetes and 10-15% chronic renal failure (Cidda *et al.*, 2014).

Despite of the availability of a wide range of medications, and increasing awareness of the dramatic impact of BP treatment on reduction of cardiovascular morbidity and mortality, hypertension is still under uncontrolled condition (Gimpel *et al.,* 2006). Control may remain poor as a result of limited resources, poor adherence to medication as well as inappropriate choice of medication. Published evidence has shown that only 50% of physicians complied with guideline recommendations (Ramli *et al.,* 2010).

The goals for management of hypertension are well defined, effective therapies are widely available, and practice guidelines for hypertension have been disseminated extensively. Even with such advances, hypertension control rates are still low. Hence determining the prescription pattern of the antihypertensive medications and identifying whether such prescription pattern of antihypertensive medications is appropriate in accordance with national guideline could lead to an improvement in the management of hypertension. To reflect back what the overall prescribing patterns are regarding the antihypertensive drugs with the various co-morbidity, would offer a valid indication and also to see the BP control status is regarding the nature of therapy, would aid in promoting an intervention to reduce blood pressure more proficiently.

The study conducted in Zewditu Memorial Hospital Ethiopia showed that the most prescribed drug was ACEI (70.2%) and 83.1% hypertensive patients were treated with combination of antihypertensive drugs. Moreover, the most frequently used two drug combination was ACEI + BB (14.2%) and 26.2% patients had controlled BP (Adugna, 2015). Another study conducted in diabetics clinic in Zewditu Memorial Hospital showed that ACEI was the most commonly prescribed drug (84%) and 15% of diabetics hypertensive patients had controlled BP. Among patients who were treated with mono-therapy 26.3% had Controlled BP while among patients who were treated with combination therapy10.6% had controlled BP. Among patients who were treated with two drugs therapy 9.4% and three drugs therapy 14.3% had controlled BP (Abera and Woldemichael, 2016).

The present study gave more emphases on the appropriateness of the use of antihypertensive medications in accordance with national guideline for management of hypertension. This study might help the prescribers to give more attention for the national guideline and for appropriate management of hypertension and also it enables to practice uniform prescribing pattern. Another point the present study showed which drug class to be used in which co-morbidity condition. This study tried to show the association between the appropriateness of the use of antihypertensive medications and BP control. The data gave a descriptive detail about whether the combination therapy or mono-therapy was effective in controlling BP. It also considered the BP control according to the national guideline.

1.3 Literature review

1.3.1 Pharmacologic treatment of hypertension

There are a growing number of pharmacological treatment options for patients with hypertension. However, the choice of anti-hypertensive drug class is influenced by many factors such as age, severity of hypertension and the presence of co-morbid conditions (Shah *et al.,* 2013). According to Ethiopian STG guideline; diuretics, ACEIs, ARBs and CCBs are now the initial therapy of choice but BBs are second line (FMHACA, 2014).

A Study performed in a general hospital in China the most prescribed antihypertensive were CCB (58.0%), ARB (34.2%), ACEI (17.5%), BB (16.9%) and diuretic (16.7%) (Cheng, 2011). On the other hand, the study conducted in Nigeria the most prescribed antihypertensive were diuretic (84.4%), ACEI (66.0%), CCB (65.8%), BB (12.7%) and methyldopa (28.5%) (Olanrewaju *et al.,* 2010). Similarly, the studies conducted in India showed that ACEI (44.3%) followed by CCB (27.8%), diuretic (16.0%), BB (10.3%), ARB (6.8%) (Arief *et al.,* 2011) and ARB (42.2%) followed by CCB (22.0%) (Cidda *et al.,* 2014). The study also conducted in general hospitals, Malaysia showed that BB (85.9%), ACEI (69.6 %), CCB (18.8 %), diuretic (10.2 %) and ARB (7.9 %) (Abdulameer *et al.,* 2012). On the other hand, a health center based study was done in Ethiopia, the most commonly used antihypertensive drug was thiazide diuretic (36.5%) followed by ACEI (29.2%), CCB (25.8%), Ca2 (23.8%) and BB (7.3%)(Amare, 2016).

According to the studies conducted in Togo (81.4%) and Nigeria (80%) majority of hypertensive patients were treated with combination of antihypertensive drugs (Potchoo *et al.,* 2012; Etuk *et al.,* 2008). On the other hand, the studies reported from China (62.9%), Bangladesh (61.6%) and Ethiopia (65.5%) the majority of the hypertensive patients were on mono-therapy (Cheng, 2011; Hasan, 2016; Shukrala and Gabriel, 2015). Moreover, according to the health center based study which was conducted in Ethiopia majority of the patients were on mono-therapy (78.9%) (Amare, 2016).

In a survey conducted in India showed that the most commonly prescribed hypertensive drug class as mono-therapy was ACEI (38.25%) followed by CCB (19.25%) and diuretic (13.25%) (Arief *et al.,* 2011). On the other hand, the study was conducted in Bangladesh by Hassan (2016)

has shown that the most commonly used drugs were ARB (37.3%), CCB (32.8%), ACEI (17.9%), BB (6%), thiazide and non-thiazide diuretic (1.5%) each and health center based study in Ethiopia the most common mono-therapy used were alpha 2 agonist (methyldopa) (20.8 %), ACEI (20.0%), CCB (17.7%) and diuretic (17.5%) (Amare, 2016).

A study which was conducted in India by Arief *et al* (2011) has shown that the most common prescribed two antihypertensive drugs combination was ACEI + CCB (5%) followed by BB+ CCB (3.5%). On the other hand, the study conducted in Nigeria the most frequently used two drug combinations were CCB + diuretic (36.6%), CCB+ ACEI (19.5%) and CCB + BB (11.4%) (Odili *et al.,* 2008).

Patients who were on three antihypertensive therapy the most frequently used drug combinations regards to the study conducted in Nigeria were CCB + diuretic + BB (32.9%) and CCB + diuretic + ACEI (31.43%) (Odili *et al.,* 2008). On contrary, the survey conducted in India ACEI + BB + CCB (52.5%) and ACEI + BB + diuretic (36.4%) were the most commonly prescribed among the three drug combinations (Khurshid *et al.,* 2012). Patients who were on the four antihypertensive therapies the most frequently used drug combinations were ACEI + CCB + diuretic + methyldopa (9.9%) and ACEI + BB + CCB + diuretic (2.5%) (Olanrewaju *et al.,* 2010).

Hypertension has been shown as a major risk factor for the development of chronic co-morbidities. The prevalence of hypertensive patients with co-morbid disease in different studies across the world have reported. The most prevalence co-morbid disease was diabetes mellitus regards to many studies report (Shukrala and Gabriel, 2015; Woldu *et al.,* 2014; Murti *et al.,* 2015; Ukwe and Ubaka*, 2012*; Kalamdani *et al.,* 2014).

The presence of concomitant disease also influences selection of antihypertensive drugs because two diseases may be treated with a single drug (Rimoy *et al.,* 2008). The survey conducted in tertiary care hospital in Nigeria among the study participants with co-morbid diseases diuretic was the most frequently used drug in these groups of patients (100% heart failure, 91.7% renal disease and 61.5% diabetes mellitus of hypertensive patients) followed by ACEI (69.2% in heart failure, 54.5% in renal disease and 53.8% in diabetes mellitus (Etuk *et al.,* 2008). On contrary,

the study conducted in China general hospital CCB was used most frequently in hypertensive patients in all co-morbidities.

The commonest prescribed class of drugs in hypertensive with DM were CCB (61.7%), ARB (36.8%), ACEI (17.4%), BB(15.4%) and diuretic(9.5%), in CKD hypertension patients CCB (60.7%), ACEI and diuretic (57.1%) each and BB (25.0%), in case of CHF CCB (61.7%) followed by ARB (36.8%), ACEI (17.4%), BB (15.4%) and diuretic (9.5%). But in case of hypertension patients without compelling conditions the most prescribed class of drug was CCB (56.4%) followed by ARB (33.5%), BB (28.9%), ACEI (26.3%) and diuretic (23.1%) (Cheng, 2011). Moreover, a prospective study conducted in the western region of Saudi Arabia showed that the commonest prescribed class of drug in CKD hypertension patients was CCB (about 40%) followed by ACEI (the exact data not available) and diuretic (about 7%), in DM ACEI (about 75.0%) followed by CCB (about 5.0%), diuretic (about 4%) and BB is almost negligible (Maghrabi, 2013).

1.3.2 The prescription pattern of antihypertensive medications according to recommended guidelines

Practice guidelines serve as useful tools for clinical decision making. They also help to reduce the variation in practice, guide appropriateness and measure quality of care (Odili *et al.,* 2008). Studies have shown that the application of guidelines to clinical practice improve the treatment outcomes (Jarari *et al.,* 2016). Report of different hospital based studies was in accordant to the recommended guidelines. The appropriate use of antihypertensive medications of hypertensive patients showed 60% in Saudi Arabia (Maghrabi, 2013), 97.0% in Ethiopia (Shukrala and Gabriel, 2015), 85.3% in Malaysia (Abdulameer *et al.,* 2012) and published evidence has shown that 50% of physicians complied with guideline recommendations (Gupta *et al.,* 2015; Ramli *et al.,* 2010). According to the study conducted in India 62.7% of patients in stage 1 hypertension and 68.4% of patients in stage 2 hypertension were prescribed according to the guideline (Kousalya *et al.,* 2012).

1.3.3 Blood pressure control

Studies conducted at different level (tertiary and general hospitals) have reported different BP control levels. Similarly, health center based study in Ethiopia showed that the overall control of BP was achieved in one third of the study participants (31%) (Amare, 2016). The report of different studies conducted on BP control level of hypertensive patients includes 72% in Saudi Arabian (Maghrabi, 2013), 54.4% in Togo (Potchoo *et al.,* 2012), 43.2% in Italian (Filippi *et al.,* 2009) and 30.5% in Nigeria (Etuk *et al.,* 2008).

2. Objective

2.1 General objective

- To assess the management of hypertension among patients on follow-up at cardiac clinic of Zewditu Memorial Hospital.

2.2 Specific objectives

- To describe the commonly used antihypertensive drugs in the management of hypertension.
- To determine the prevalence of the overall prescribing pattern of antihypertensive therapy and in patients with various co-morbidities.
- To assess the use of antihypertensive medications in accordance with national guideline for management of hypertension (Ethiopian STG 2014).

3. Methods

3.1 Study setting and period

The study was conducted at Zewditu Memorial Hospital located in center of Addis Ababa. It is a teaching and general referral hospital under the administration of Addis Ababa city health bureau. The area was selected because it is a teaching and referral hospital that provides organized hypertension follow up care. There were around 274 hypertension patients on treatment receiving services per month in ambulatory cardiac clinic. Around 112,172 patients were served per year in the hospital. The hospital has 872 clinical and non-clinical staff members. The services given in the hospital include hospital pharmacy, cardiac clinic, diabetic clinic, internal medicine, surgery, pediatrics, gynecology/obstetrics, psychiatry, neurology, dermatology, HIV clinic, dental clinic and dialysis center. The study was conducted during the period from July 24-August 23, 2016 G.C.

3.2 Study design

A retrospective cross-sectional study was employed to conduct the study. Simple random sampling technique was used in the data collection. Data was collected from the patient chart by reviewing the patient's medical record of hypertension patients.

3.3 Population

3.3.1 Source population

All hypertensive patients who visited ambulatory cardiac clinic

3.3.2 Study population

All randomly selected adult patients with a documented diagnosis of hypertension who fulfill the inclusion criteria

3.4 Eligibility criteria

Inclusion criteria:

- All hypertension patients with a documented diagnosis
- All ambulatory cardiac clinic hypertension patients who have taken antihypertensive medications at least for 6 months
- Age 18 years and above
- Patients having with or without the following co-morbidities along with hypertension: diabetes mellitus, cardiovascular disease and chronic kidney disease.

Exclusion criteria:

- Patients with pre-eclampesia
- Patients with incomplete information or records

3.5 Sample size and sampling methods

Sample size was calculated by assuming 0.3 of proportions (p) of hypertension since the prevalence of hypertension in Addis Ababa is estimated to 30% of total population(Tesfaye *et al*., 2009), 5% marginal error (d) and confidence interval of 95%. Based on this assumption, the sample size was calculated by single population proportion formula n= $((Z\alpha/2)2 \times p \ (1-p))/ d2$.This yield sample size of 323. Since the source population was less than 10,000 the sample size was adjusted with correction formula and with the assumption of 10% incomplete data, the final sample size was 356 hypertension patients' card.

3.6 Study variables

3.6.1 Dependent variable

- Appropriate prescription pattern of antihypertensive medications

3.6.2 Independent variables

- age
- sex
- Co-morbid disease
- BP readings

3.7 Data collection and management

Four nurses were recruited and trained for one day to give standardized instruction and clarify data abstraction format. One nurse was assigned to supervise the data collection process. The supervisor and principal investigator were closely followed the data collection process at the spot.

Data was collected by using a data abstraction format. Although supervision was carried out, daily checking of the collected data was made during data collection by principal investigator. Quantitative data collection techniques were used to gather information. Data collected include sex, age, systolic and diastolic BP readings, duration of antihypertensive therapy, stage of hypertension, co-morbid conditions (diabetes mellitus, cardiovascular disease and chronic kidney disease), nature of therapy and the antihypertensive medications prescribed.

3.8 Data quality assurance

The completeness of the data collected from the survey was checked by the principal investigator in order to maintain consistency. The data abstraction format for the study was prepared in the English language. The data collectors as well as the supervisor were given one day training on the overall data collection procedure. Five percent of the sample was pre-tested to check acceptability and consistency two weeks before the actual data collection.

3.9 Data analysis

The data was entered in to computer using EPI-info 3.5.4 software. Data checking and cleaning was done by principal investigator on daily basis during collection before actual analysis. Analysis was done using statistical software for social sciences (SPSS) 20.0. Descriptive data

was generated and placed in terms of frequency and percentage. Results were expressed as proportions and as Means ± Standard Deviations (SD). The level of BP control was assessed by using the average of three BP records obtained from three different visits (Alexander *et al.*, 1999). Univariate and multivariate logistic regression was used to analyze the associations between dependent variable and independent variables by using crude odds ratio (COR) and adjusted odds ratio (AOR) at 95% confidence level. A p-value of less than 0.05 was considered statistically significant.

3.10 Ethical consideration

Ethical clearance was obtained from ethical review board of school of pharmacy, Addis Ababa University. The aim and objectives of the study was explained to the health facility before data collection and permission was obtained from the hospital medical director to access patients' medical record and conducts the study. Privacy and confidentiality was guaranteed by storing data in a safe place, by excluding identifiers (patients' files were coded and name was not recorded).

3.11 Operational definitions

Appropriate antihypertensive medication use: (FMHACA, 2014).

1. Hypertensive patients without co-morbidity condition and stage 1, the prescribed drugs should be one of these prescriptions protocol:- ACEI/ARB, thiazide diuretics (TD), CCB, ACEI/ARB + CCB, ACEI/ARB + TD, ACEI/ARB + CCB+TD.

2. Hypertensive patients without co-morbidity condition and stage 2, the prescribed drugs should be one of these prescriptions protocol:- ACEI + CCB, ACEI+CCB+TD, ACEI+ CCB+TD+ (BB or CA_2 or spironolactone).

3. Hypertensive patients with DM, the prescribed drugs should be one of these prescriptions protocol: - ACEI/ARB, ACEI/ARB + CCB, ACEI/ARB + TD, ACEI/ARB + CCB+TD.

4. Hypertensive patients with CKD, the prescribed drugs should be one of these prescriptions protocol: - ACEI/ARB, ACEI/ARB + CCB, ACEI/ARB +loop diuretics (LD), ACEI/ARB + CCB+LD.

5. Hypertensive patients with CHF, the prescribed drugs should be one of these prescriptions protocol: - ACEI/ARB+ metoprolol/carvedilol, ACEI/ARB+ metoprolol/carvedilol + diuretic.

6. Hypertensive patients with CHD, the prescribed drugs should be one of these prescriptions Protocol: - ACEI/ARB + BB, ACEI/ARB + BB + CCB.

7. Hypertensive patients with left ventricular hypertrophy, the prescribed drugs should be one of these prescriptions protocol: - ACEI/ARB, ACEI/ARB + TD.

Monotherapy: The prescription of one antihypertensive drug with only one active ingredient (Gupta *et al*, 2015).

Polytherapy: It was denoted when patients were prescribed more than one active ingredient, either in one combination or as two different, single pills (Gupta *et al*, 2015).

Controlled BP: Achieve target blood pressure ($< 140/90$ mmHg hypertensive patients in all age or in patients having diabetes with proteinuria and chronic kidney disease ($< 130/80$ mmHg) (FMHACA, 2014).

Uncontrolled BP: BP$\geq 140/90$ mmHg in hypertensive patients in all age, or BP $\geq 130/90$ mmHg in hypertensive patients with diabetes or chronic kidney disease (FMHACA, 2014).

Co-morbid: It is either the presence of one or more additional disorders (diseases) co-occurring with a primary disease or disorder, or the effect of such additional disorders or diseases (Woldu *et al.,* 2014).

4. Results

4.1 Demographic and clinical characteristics

A total of 356 hypertensive patients on treatment were included. Out of the 356 patients studied, 204(57.3%) and 152(42.7%) were females and males, respectively and gender ratio of study group was 1.34:1(females: males). The mean age of patients was 56.2 ± 12.4 years (range 23 to 92 years) .The mean duration of antihypertensive therapy was 11.27 ± 8.34 years (range of 1-51years). Among hypertensive patients 151(42.4%) have been taking antihypertensive therapy for more than 10 years while 114 (32%) have been taking antihypertensive drugs for 5 to10 years and 91(25.6%) have been taking antihypertensive drugs for less than 5 years. Age groups were divided into different categories namely, 20-29 years 8 (2.2%), 30-39 years 22 (6.2%), 40-49years 70 (19.7%), 50-59 years 118 (33.1%) and $\geq$60 years 138 (38.8%). Out of the total study participants, 124 (34.8%) hypertensive patients had co-morbid conditions. Among the co-morbid conditions 78 (21.9%) patients were with diabetic, 17 (4.8%) patients had CKD, 8 (2.2%) had CHF, 4(1.1%) had CHD and 1 (0.3%) had LVH, 10 (2.8%) had DM and CKD (Table1). But most of the study participants were without co-morbid condition i.e. 232 (65.2%) hypertension only.

Table 1: The demographic and clinical characteristics of ambulatory hypertensive patients attending Zewditu Memorial Hospital, Ethiopia, 2016.

Variables	Mean ±Std.Deviation	Frequency (%)
Sex		
Male		152(42.7)
Female		204(57.3)
Age categories	56.2± 12.4	
20-29		8(2.2)
30-39		22(6.2)
40-49		70(19.7)
50-59		118(33.1)
≥60		138(38.8)
Duration of therapy(year)	11.27±8.34	
<5		91(25.6)
5-10		114(32.0)
>10		151(42.4)
Co-morbidity		
DM		78(21.9)
CKD		17(4.8)
CHF		8(2.2)
CHD		4(1.1)
LVH		1(0.3)
DM and CKD		10(2.8)
DM and CHF		3(0.8)
DM and CHD		1(0.3)
DM and LVH		1(0.3)
DM, CKD and CHF		1(0.3)

HTN=Hypertension DM=Diabetes mellitus CKD=Chronic kidney diseases CHF=Congestive heart failure

CHD=Coronary heart disease LVH=Left ventricular hypertrophy

4.2 Appropriateness of the prescription pattern of antihypertensive medications

Out of the total study subjects, 140(39.3%) hypertensive patients appropriately prescribed antihypertensive medications according to Ethiopian STG 2014 and 134 (37.6%) hypertensive patients appropriately used according to JNC8 guideline (figure 1).
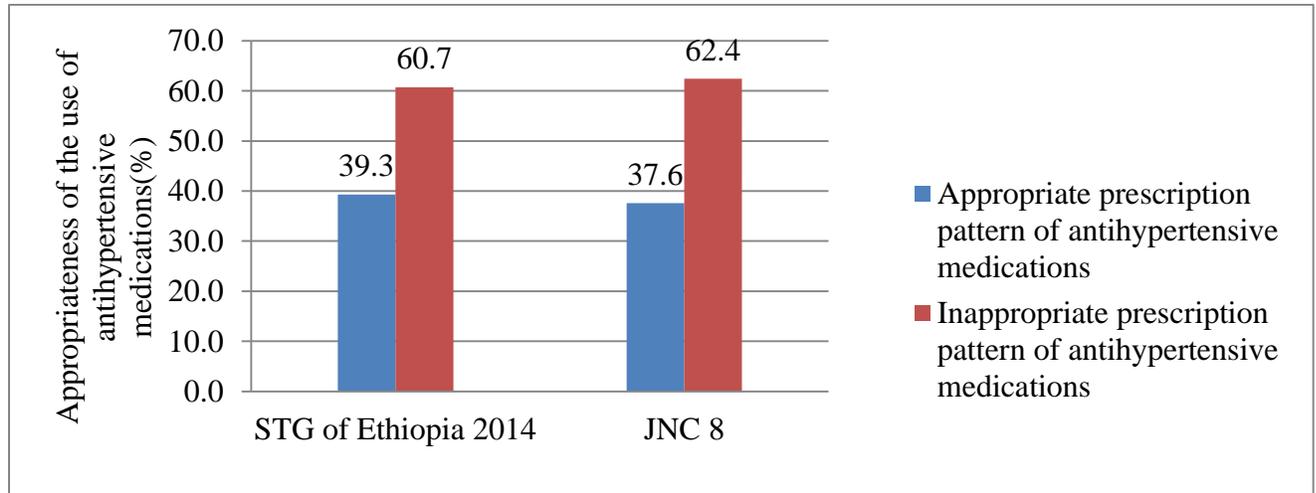
Figure 1: Appropriateness of the prescription pattern of antihypertensive medications according to Ethiopian STG 2014 and JNC 8 guideline among hypertensive patients attending Zewditu Memorial Hospital, Ethiopia, 2016.

4.3 Frequency of administration of individual antihypertensive medications

The overall utilization pattern of antihypertensive agents showed that ACEI was the most frequently prescribed class of drugs 215 (60.4%) followed by CCB 211 (59.3%), BB 167 (46.9%), diuretic 114 (32.0%), Central alpha-2 agonist 9 (2.5%) and ARB 8 (2.3%)(Table 2).

Table 2: Frequency of administration of individual antihypertensive medications among hypertensive patients attending Zewditu Memorial Hospital, Ethiopia, 2016.

Antihypertensive group	Frequency (%)
ACEI	215(60.4)
Enalapril	215(60.4)
CCB	211(59.3)
Nifedipine	195(54.8)
Amlodipine	16(4.5)
BB	167(46.9)
Atenolol	166(46.6)
Metoprolol	1(0.3)
Diuretic	114(32.0)
Hydrochlorothiazide	82(23.0)
Furosemide	32(9.0)
ARB	8(2.3)
Losartan	7(2.0)
Candesartan	1(0.3)
Central alpha-2 agonist	9(2.5)
Methyldopa	9(2.5)

ACEI=Angiotensin converting enzyme inhibitor   BB= Beta blocker   ARB=Angiotensin receptor blocker

CCB=Calcium channel blocker

4.4 Antihypertensive therapy

Among the study participants, 104 (29.2%) were on mono-therapy and 252 (70.8%) were on combination therapy. Among the study participants who received mono-therapy the most prescribed drugs were ACEI 46 (12.9%), CCB 38 (10.67%), diuretic 9 (2.5%), BB 4 (1.1%), CA_2 4 (1.1%) and ARB 3 (0.84%) (Table 3).

Concerning patients who were on combination antihypertensive drugs therapy 149 (41.9%) of patients were on two antihypertensive drugs. The most frequently used combinations were ACEI + CCB 35 (9.8%), CCB + BB 33 (9.3%), ACEI + BB 31(8.7%) of the total patients (Table 3).

Ninety two (25.8%) patients were on three drugs and among these 46 (12.9%) were on ACEI + CCB + BB and the rest of the triple therapy combinations are shown in Table 4. Eleven (3.1%) patients were received four antihypertensive drugs and among these the most prescribed combinations were diuretic + ACEI + BB + CCB, 10 (2.8%) (Table 3).

Table 3: Antihypertensive therapy among hypertensive patients attending Zewditu Memorial
Hospital, Ethiopia, 2016.

Nature of therapy	Frequency (%)
Mono-therapy	104 (29.2)
ACEI	46 (12.9)
CCB	38(10.7)
Diuretic	9(2.5)
LD	5(1.4)
TD	4(1.1)
BB	4(1.1)
Ca2	4(1.1)
ARB	3(0.56)
Dual therapy	149(41.9)
ACEI + CCB	35(9.8)
ACEI + BB	31(8.7)
CCB +BB	33(9.3)
ACEI + diuretic	23(6.5)
CCB + diuretic	15(4.2)
BB + diuretic	8(2.2)
diuretics + CA2	2(0.84)
ARB + diuretic	1(0.3)
ARB + CCB	1(0.3)
Triple therapy	92(25.8)
ACEI + BB + CCB	46(12.9)
BB + CCB + diuretic	20(5.6)
ACEI + BB + diuretic	12(3.4)
ACEI + CCB + diuretic	9(2.5)
ACEI+ diuretic + CA2	3 (0.8)
ARB + BB + CCB	1(0.3)
ARB + BB + diuretic	1(0.3)
Four drugs therapy	11(3.1)
ACEI + BB + CCB + diuretic	10(2.8)
ARB + BB + CCB + diuretic	1(0.3)

ACEI=Angiotensin converting enzyme inhibitor   BB= Beta blocker   ARB=Angiotensin receptor blocker
CCB=Calcium channel blocker   CA2=Central alpha-2 agonist TD= Loop diuretic   LD=Thiazide diuretic

4.5 Prescription pattern of antihypertensive medications in patients with various co-morbidities

Among the hypertensive cases with diabetes mellitus the most prescribed class of drug was ACEI 64 (68.1%) followed by CCB 54 (57.45%), BB 34 (36.2%), diuretic 20 (21.3%) and ARB and central alpha-2 agonist 1 (1.1%)each. In CKD hypertension patients the most prescribed class of drug was CCB 17 (60.7%) followed by ACEI 16 (57.1%), diuretic 16 (57.1%) and BB 7 (25.0%). The most prescribed class of drugs in CHF hypertension patients was diuretic 9 (75.0%) followed by ACEI 6 (50.0%), BB 5 (41.7%), CCB 4 (33.3%) and ARB and central alpha-2 agonist 1 (8.3%) each. The most prescribed class of drug in CHD was ACEI 5 (100.0%) followed by CCB 4 (80.0%), BB 3 (60.0%) and diuretic 1 (20.0%). The commonest prescribed class of drug in LVH hypertension patients was CCB 2 (100.0%) followed by ACEI 1 (50.0%) (Table 4). But in case of hypertension patients without compelling conditions the most prescribed class of drug was CCB 141 (60.8%) followed by ACEI 131 (56.5%), BB 126 (54.3%), diuretic 76 (32.8%), CA_2 7 (3.0%) and ARB 6 (2.6%).

Table 4: Prescription pattern of antihypertensive medications among hypertensive patients with various co-morbidities attending Zewditu Memorial Hospital, Ethiopia, 2016.

Co-morbid condition	N	ACEI N (%)	CCB N (%)	BB N (%)	Diuretic N (%)	ARB N (%)	CA2 N (%)
DM	94	64(68.1)	54(57.45)	34(36.2)	20(21.3)	1(1.1)	1(1.1)
CKD	28	16(57.1)	17(60.7)	7(25.0)	16(57.1)	0	0
CHF	12	6(50.0)	4(33.3)	5(41.7)	9(75.0)	1(8.3)	1(8.3)
CHD	5	5(100.0)	4(80.0)	3(60.0)	1(20.0)	0	0
LVH	2	1(50.0)	2(100)	0	0	0	0

DM=Diabetes mellitus CKD=Chronic kidney diseases CHF=Congestive heart failure   CHD=Coronary heart disease LVH=Left ventricular hypertrophy ACEI=Angiotensin converting   inhibitor BB= Beta blocker ARB=Angiotensin receptor blocker CCB=Calcium channel blocker   CA2=Central alpha-2 agonist   N=Frequency

4.6 Blood pressure control

Among the study participants 137 (38.5%) had a controlled SBP while 174 (48.9%) had a controlled DBP. The overall control of BP was achieved 107 (30.1%) of the study participants according to national guideline (STG2014) (figure 2).
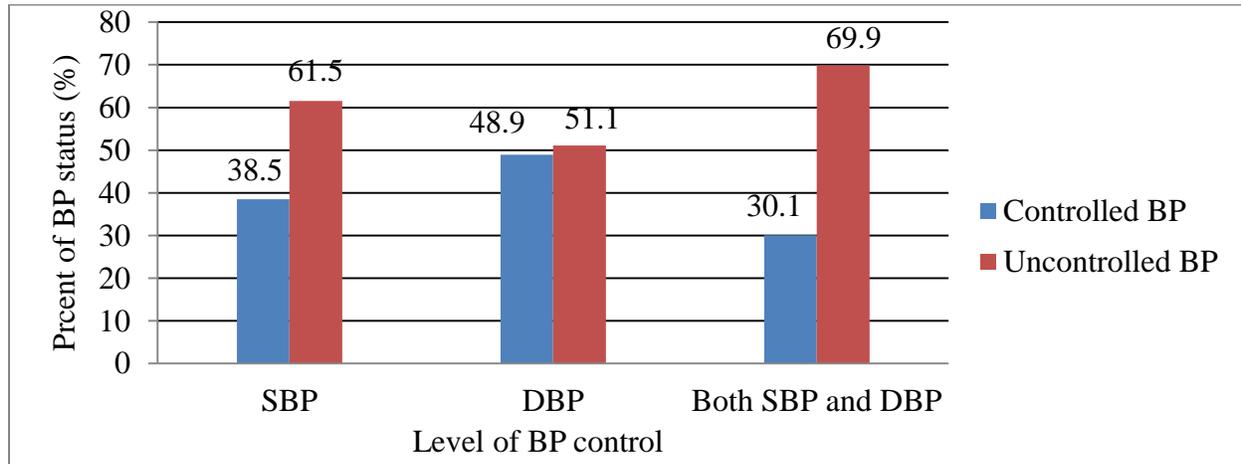
Figure 2. Blood pressure control among hypertensive patients attending Zewditu Memorial Hospital, Ethiopia, 2016.

4.7 Determinants of the appropriate prescription pattern of antihypertensive medications

The association of independent variables with the dependent variable was investigated using both univariate and multivariate logistic regression. Only two variables were shown to have significant association with the appropriateness of the prescription pattern of antihypertensive medications.

The result of the multivariate analysis showed that there was a positive statistical significant association between inappropriate prescription pattern of antihypertensive medications and age ≥60 years (P=0.01) and uncontrolled BP (P=0.001) (Table 5).

Table 5: Determinants of the appropriate use of antihypertensive medications among
hypertensive patients attending Zewditu Memorial Hospital, Ethiopia, 2016.

Variables	Appropriate prescription pattern of antihypertensive medications		COR(95% CI)	AOR(95% CI)	P-value
	Yes (%)	No (%)			
Sex					
Female	79(22.2)	125(35.1)	1.00	1.00	
Male	61(17.1)	91(25.6)	0.94(0.62, 1.45)	1.14(0.71, 1.82)	0.58
Age category					
< 60 years	72(20.2)	146(41.0)	1.00	1.00	
$\geq$ 60 years	68(19.1)	70 (19.7)	0.51(0.33, 0.79)	0.54(0.34,0.87))	0.01
Co-morbid condition					
HTN alone	92(25.84)	140(39.33)	1.00	1.00	
DM	36(10.1)	42(11.8)	0.77(.46, 1.29)	0.83(0.48,1.43)	0.50
CKD	7(1.97)	10(2.8)	0.94(.35, 2.56)	0.89(0.32,2.50)	0.82
DM and CKD	4(1.12)	6(1.69)	0.99(.27, 3.59)	0.90(0.24,3.36)	0.88
CHD	1(0.3)	4 (1.1)	2.63(0.39, 23.90)	3.14(0.33,30.02)	0.32
BP status					
Controlled	57(16.0)	50(14.0)	1.00	1.00	
Uncontrolled	83(23.3)	166(46.7)	2.28(1.44, 3.62)	0.45(0.27, 0.73)	0.001

Others[*]**:** BB, ARB, ARB + Diuretic, CA_2, ARB + CCB, CCB + BB, CA_2 + Diuretic, CCB + BB + Diuretic,
ARB + CCB + BB + Diuretic, ARB + BB + CCB, ARB + BB + Diuretic and ACEI + Diuretic + CA_2.

ACEI=Angiotensin converting enzyme inhibitor   BB= Beta blocker   ARB=Angiotensin receptor blocker

CCB=Calcium channel blocker   CA2=Central alpha-2 agonist HTN=Hypertension DM=Diabetes mellitus

CKD=Chronic kidney diseases   CHD=Coronary heart disease

5. Discussion

This study was a retrospective cross sectional study designed to assess the pattern of antihypertensive medications in order to obtain an insight into the current utilization of antihypertensive drugs in Zewditu Memorial Hospital. Blood control status was also found to be associated with inappropriate prescription pattern of antihypertensive medications when compared patients with controlled BP. Patients with controlled BP two fold more likely to have appropriate prescription pattern of antihypertensive medications when compared patients with uncontrolled BP (AOR= 0.45, 95% CI: 0.27-0.73, P=0.001). The result of the current study showed that only one third of hypertensive patients on pharmacologic treatment had a controlled BP 107(30.1%). The level of BP control found in this study was closely similar with the study conducted in Nigeria (30.5 %) (Etuk *et al.,* 2008). The present study revealed similar result with the health center based study (31%) (Amare, 2016). This similarity might be due to the study conducted in the same geographic area and similar inclusion criteria. But the level of BP control found in this study was lower than the studies from Saudi Arabian (72%) (Maghrabi, 2013)**,** Italian (43.23%) (Filippi *et al.,* 2009) and Togo (54.4%) (Potchoo *et al.,* 2012). This difference in the level of BP control might be due to a more aggressive therapy with two or more drug combinations. The race difference might have contributed to this inconsistency. Moreover, the level of BP control in the present study a little bit higher than the study performed two years ago (26.2%) by Adugna (2015). This difference might be due to the use of different guidelines as a standard. But the level of BP control in the present study was higher than the study performed (15%) by Abera and Woldemichael (2016).This difference might be due to patients with co-morbid conditions difficult to achieve target BP easily. In case of the study conducted by Abera and Woldemichael all hypertension patients had DM.

Some of the reasons attributed to the inadequate BP control were: poor compliance with medications which is strongly determined by poverty, excessive salt intake, use of non-steroidal anti-inflammatory drugs (NSAIDs) and inappropriate combinations with inadequate dosing of antihypertensive agents (Etuk *et al.,* 2008). The result of the current study showed that only 140 (39.3%) and 133 (37.4%) of hypertensive patients on pharmacologic treatment had appropriate use of antihypertensive medications according to Ethiopian national guideline (STG 2014) and JNC 8 guideline respectively. This small difference might be because of the prescription pattern

of antihypertensive medications in JNC 8 consider the race difference. The prevalence of appropriate use of antihypertensive medications found in this study (39.3%) was lower than the studies from Saudi Arabia (60%) (Maghrabi, 2013), Malaysia (85.3%) (Abdulameer *et al.,* 2012), Ethiopia (97.0%) (Shukrala and Gabriel, 2015) and published evidence has shown that 50% of physicians complied with guideline recommendations (Gupta *et al.,* 2015; Ramli *et al.,* 2010). In the present study appropriate use of antihypertensive medications was found to be low which might be associated with the adherence of the prescriber to the national STG.

The results of the present study indicated that the proportion of females with hypertension 204 (57.3%) was high. This study was in line with two Ethiopian studies (Shukrala and Gabriel, 2015) and (Woldu *et al.,* 2014) and Nigeria (Olanrewaju *et al.,* 2010). In contrary, the present study was inconsistence with other studies which were conducted in Bangladesh (Hasan, 2016) and India (Murti *et al.,* 2015). The result of the multivariate analysis showed that age was significantly associated with inappropriate prescription pattern of antihypertensive medications in patients age ≥ 60 years (AOR= 0.54, 95% CI: 0.34, 0.87, P=0.01). This study also revealed that 256 (71.9%) of hypertension patients were age over 50 years. The current study was in line with the study conducted in Ethiopia (Shukrala and Gabriel, 2015) and India (Romday *et al.,* 2016). These results showed that age may affect the incidence of hypertension.

The classes of antihypertensive agents prescribed in this study were ACEI 215 (60.4%), CCB 211 (59.3%), BB 167 (46.9%), diuretic 114 (32.0%), CA_2 9 (2.5%) and ARB 8 (2.3%). Results resembling such pattern in the use of antihypertensive drugs were observed in a tertiary care hospital based study from India which reported that the most frequent group of antihypertensive medication was ACEI (44.25%) (Arief *et al.,* 2013) and the study conducted in the current study area two years ago (Adugna, 2015). ACEI was the first line antihypertensive drug for hypertension patients and the result of the study was comparable with the current national guidelines of Ethiopia 2014 (STG).

In the present study, the overall prescription pattern of antihypertensive medication was inconsistent with a study conducted in a general hospital in China; CCB (58.0%), ARB (34.2%), ACEI (17.5%), BB (16.9%) and diuretic (16.7%) (Cheng, 2011). This difference might be due to age variation of the study participants. In the present study the majority of the patients were younger than 60 years with a mean age of 56.2± 12.4 but the study conducted in China the

majority of the patients were older than 60 years with the mean age was 61.3 ± 13.7 years. According to the study conducted in India the most common drug class involved in the study was ARB (42.24%) (Cidda *et al.,* 2014). This discrepancy might be due to cost variation across the study places. The result of cost evaluation showed that diuretics had the lowest cost and ARBs had the highest cost per day (Abdulameer *et al.,* 2012; Rachana *et al.,* 2014).The study also conducted in Malaysia the most prescribed antihypertensive medications were BBs (85.9%) (Abdulameer *et al.,* 2012). The discrepancy of the use of BB over ACEI might be associated with the prevalence of types of co-morbid condition since the majority of the patients in Abdulameer *et al* study occurred with CHD. On the contrary, the study conducted in Addis Ababa health centers showed that the most commonly used antihypertensive drugs were thiazide diuretics (36.5%) (Amare, 2016). This difference in frequent use of ACEI over diuretic might be due to the high prevalence of co-morbid conditions (i.e. DM and CKD).

In the current study, BB which was considered as a second line antihypertensive agent; it was reported to be used in 167 (46.9 %) of the hypertensive patients. This discrepancy might have resulted from lack of adherence to national guideline (STG). Since BB is a second line drug this result showed that BB was inappropriately prescribed. Beta blockers should only be prescribed when compelling conditions such as CHF and CHD are co-diagnosed regards to Ethiopian STG 2014. But in case of this study these two diseases were 17(4.8%) only.

The result of the study showed that majority of the patients were on combination therapy 252 (70.8%) which was consistent with the study conducted in Nigeria (80%) (Etuk *et al.,* 2008), Togo (81.40%) (Potchoo *et al.,* 2012) and the study conducted in Ethiopia (83.1%) (Adugna, 2015). The present result and the study conducted by Adugna showed that combination therapy practice had consistency. But higher than the study which was done in Ethiopia (34.5%) (Shukrala and Gabriel, 2015)**,** Bangladesh (38.4%) (Hassan, 2016) and China (37.1%) (Cheng, 2011). The higher prescription rate of combination therapy might be due to the longer duration of hypertension therapy and being high risk patients. Moreover, according to the study conducted in Addis Ababa health centers, Ethiopia the majority of the patients were on mono-therapy (78.9%) (Amare, 2016). The present study was inconsistent with the above study might be due to the hospital based patients presented with severe and more complicated hypertension since they are referred from the health center.

Out of 104 (29.2%) patients who received mono-therapy ACEI, 46 (44.2%) was the most prescribed drug. This study was similar to a study conducted in India which showed that ACEI (38.25%) was the most prescribed drug (Arief *et al.,* 2013). On contrary, the study conducted in Addis Ababa health centers showed that Ca_2 (methyldopa) was the most common mono-therapy used (20.8 %) (Amare, 2016). This discrepancy might be because of the difference in level of knowledge on the management of hypertension.

According to the Ethiopian guideline 2014, mono-therapy was only preferred if the target blood pressure was achieved successfully by that particular antihypertensive agent. But if the target blood pressure was not achieved with one agent, then poly-therapy should be introduced and low doses of two or more agents should be given.

Nature of therapy was also found to have association with inappropriate prescription pattern of antihypertensive medications in that when compared with mono-therapy. The most frequently used two drug combinations were ACEI + CCB, 35 (9.8%).This combination is strongly supported by the national guideline for patients without co-morbid conditions (FMHACA, 2014) hence the prescribers might be familiar with this combination. This study was similar to a study conducted in India (Arief *et al.,* 2013). On the other hand, the study conducted in Nigeria CCB + diuretic (36.6%) were the most frequently used combinations (Odili *et al.,* 2008). This difference might be due to the variations of the prevalence of the types of co-morbid condition and the recommended guidelines. Moreover, the study conducted by Adugna (2015) in Zewditu Memorial Hospital, Ethiopia the most frequently used two drug combination was ACEI + BB (14.2%). This difference might be associated that in the present study the prescriber's awareness for the national guideline was improved.

Regarding patients who were on three antihypertensive therapies ACEI + CCB + BB combinations were the most prescribed drugs. This study showed similarity with the survey conducted in India (Khurshid *et al.,* 2012**).** On contrary, a study conducted in Nigeria the most prescribed antihypertensive drugs were CCB + diuretic + BB (Odili *et al.,* 2008**).** This difference might be associated with the prevalence of the types of co-morbidity and the professional awareness of the recommended guideline.

With respect to patients receiving four antihypertensive drugs therapy the most frequently used combinations were ACEI + diuretic + BB + CCB. On the other hand, the study conducted in Nigeria the most frequently used combinations were ACEI + CCB + diuretic + methyldopa (Olanrewaju *et al.,* 2010). The observed difference of this study with the above study might be attributed to the possibility of some patients presenting with multiple co-morbid conditions.

The result of the current study showed that among the study participants on mono-therapy 41 (40.6%) had controlled blood pressure while among patients on combination therapy 68 (26.7%) had controlled BP. The current study showed similarity with a study conducted in Nigeria with mono-therapy 41.4% had BP controlled and with combination therapy 17.9% had controlled BP (Oke and Adedapo, 2015). In contrary, another study conducted in Nigeria showed that with mono-therapy 34.4% had BP controlled and with combination therapy 47.2% had controlled BP (Busari *et al.,* 2014). The higher proportion of controlled BP with mono-therapy when compared with combination therapy might be associated with the more appropriate prescribed pattern of mono-therapy.

According to the present study the most prevalent co-morbid disease was DM. Similarly, the most prevalent co-morbid disease was DM according to many studies reported (Shukrala and Gabriel, 2015; Woldu *et al.,* 2014; Murti *et al.,* 2015; Ukwe and Ubaka, 2012; Kalamdani *et al.,* 2014). The increase incidence of DM in hypertensive patients might be due to factors which have been proposed to contribute to hypertension in diabetes: hyperinsulinemia, extracellular fluid volume expansion and increased arterial stiffness (Bakris, 2013).

Among the hypertensive cases with DM, the most prescribed class of drugs was ACEI 64 (68.1%). This study showed similarity with a study conducted in Saudi Arabia; ACEI (about 75.0%) (Maghrabi, 2013) and in diabetic clinic at Zewditu Memorial Hospital, Ethiopia; ACEI (84%) (Abera and Woldemichael, 2016). ACE-inhibitors are the only class of drugs that are often prescribed to diabetic hypertensive patients, as these drugs prevent the chance of occurrence of retinopathy and other related complications (Arief *et al.,* 2013). On the other hand, the study conducted in Nigeria the most prescribed class of drug was diuretic (61.5%) (Etuk *et al.,* 2008) and in China CCB (61.7%) (Cheng, 2011). These differences in result might be due to the status of prescribers' awareness about the national and international guidelines and the presence of other compelling conditions.

The commonest prescribed class of drug in CKD hypertension patients was CCB 17 (60.7%). This study was in line with the studies conducted in China CCB (56.4%) (Cheng, 2011) and Saudi Arabia CCB (about 40%) (Maghrabi, 2013). But the study conducted in Nigeria the first choice drug was diuretic (91.7%) (Etuk *et al.,* 2008). In the current study, CCB was preferred to treat hypertensive patients with CKD in contrast to guideline that recommended ACEI/ARB. Seventh Report of the Joint National Committee guidelines advocate ACEIs as the favored drug for hypertension associated with chronic kidney disease, diabetes or congestive heart failure (Gupta *et al.,* 2015).

The most prescribed class of drug in CHF hypertension patients were diuretics 9 (75.0%). Similar study was conducted in Nigeria and the most prescribed drugs were diuretic (100%) (Etuk *et al.,* 2008). On the other hand, the study conducted in China has shown that CCB (61.7%) was the most prescribed drug (Cheng, 2011). In the current study the preferred drug was diuretic as first line to treat hypertensive patients with CHF in contrast to guideline that recommended ACEI/ARB + metoprolol/carvedilol. The present study showed that the physicians might not be paid sufficient attention to the benefits of ACE inhibitor as the first line drug in treatment of co-morbidities (CHF and CKD) associated with hypertension.

The most prescribed class of drug in CHD was ACEI 5(100.0%) followed by CCB 4 (80.0%). In the present study the preferred drug was ACEI (100.0%) to treat hypertensive patients with CHD and also it was consistent with the guideline (STG). The commonest prescribed class of drugs in hypertension patients with LVH was CCB 2 (100.0%). The result of the present study showed that 100% not in accordance with the national guideline (Ethiopian STG 2014). Since the first choice of hypertension patients with LVH was ACEI/ARB and the second line was thiazide diuretics but CCB even not an alternative choice according to Ethiopian STG 2014. But in case of hypertension patients without co-morbid conditions the most prescribed class of drugs was CCB (60.8%). This study was in line with the study conducted in China which showed that the most prescribed class of drug was CCB (56.4%) (Cheng, 2011). In the present study CCB was first choice of class of antihypertensive which might be associated with the race (since being black).

6. Conclusion

 Overall utilization pattern of antihypertensive medications indicates that ACEI and CCB were the most frequently prescribed class of drugs in both mono-therapy and combination therapy. There was underutilization of diuretics in this study, in spite of reasonable evidences backing their prescription. Uncontrolled BP and age ≥ 60 years were positively associated with inappropriate prescription pattern of antihypertensive medications. Despite the use of different antihypertensive drugs, most of the patients did not achieve the target blood pressure and the general use of antihypertensive medications seemed not to be in accordance with the national guideline of Ethiopia for management of hypertension.

7. Recommendations

Based on the findings of the study the following recommendations can be made:

- It is recommended to arrange awareness campaigns and continued medical education activities about the national guideline (Ethiopian STG) among health care providers and prescribers.
- It is recommended to assess barriers to using the national guideline in the management of hypertension.
- Further studies focused on the rationale for choice of drugs based on demographic data, economic status, associated conditions and complications would give additional insights into prescribing patterns in hypertension.

8. Limitations of the Study

This was a single center study and therefore, the findings cannot be generalized to reflect the health care setting in Ethiopia. Adherence to the treatment was not taken because of retrospective survey. BP readings were taken from patients' medication records.

References:

Abdulameer SA, Sahib MN, Aziz NA, Hassan Y, AlRazzaq HA, Ismail O (2012). Physician adherence to hypertension treatment guidelines and drug acquisition costs of antihypertensive drugs at the cardiac clinic: a pilot study. *Patient Preference and Adherence* 6:101-108.

Abera H and Woldemichael M (2016). Pattern of antihypertensive therapy among diabetic hypertensive patients in Zewditu Memorial Hospital, Addis Ababa. *Ethiopian Medical Journal* 54(2): 77-82.

Addo J, Smeeth L, Leon DA (2007). Hypertension in Sub-Saharan Africa: A Systematic Review. *Hypertension* 50:1012-1018.

Adugna B (2015). Assessment of hypertension control and factors associated with the control among hypertensive patients attending at Zewditu Memorial Hospital, Ethiopia. MSc Thesis, Addis Ababa University.

Al-Drabah E, Irshaid Y, Yasein N, Zmeili S (2013). Prescription pattern of antihypertensive drugs in Family Practice Clinics at Jordan University Hospital. *Medicine Science* 2(1):469-488.

Alxander M, Tekawa I, Hunkeler E, Fireman B, Rowell R, Selby JV, et al (1999). Evaluating hypertension control in a managed care setting. *Archives of internal medicine*159:2673-2677.

Amare F (2016). Blood pressure control and associated factors among hypertensive patients attending health centers of Addis Ababa, Ethiopia. MSc Thesis, Addis Ababa University.

Arief M, Harika B, Satyanarayana B, Pasha SW, Paladugu ND, Pasha SI, et al (2013).Evaluation of prescribing pattern of antihypertensive drugs in a tertiary care hospital. *Acta Chimica and Pharmaceutica Indica* 3(2): 172-181.

Bakare OQ, Akinyinka MR, Goodman O, Kuyinu YA, Wright OK, Adeniran A, et al (2016).

Antihypertensive use, prescription patterns, and cost of medications in a teaching hospital in Lagos, Nigeria. *Nigerian Journal of Clinical Practice* 19(5): 668-672.

Bakris GL (2013). Treatment of hypertension in patients with diabetes mellitus. *Topic 3829 Version 17.0*. Up-to-date 21.1 versions.

Cheng H (2011). Prescribing pattern of antihypertensive drugs in a general hospital in central China. *International Journal of Clinical Pharmacy* 33(2): 215-220.

Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al (2003). Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Journal of the American Medical Association* 289: 2560-2571.

Cidda C, Mateti UV, Batchu MK, Martha S (2014).Study of prescribing patterns of antihypertensive in South Indian population. *International Journal of Basic and Clinical Pharmacology* 3 (2): 303-307.

Etuk E, Isezuo S A, Chika A, Akuche J, Ali M (2008). Prescription pattern of antihypertensive drugs in a tertiary health institution in Nigeria. *Annals of African Medicine* 7(3): 128 – 132.

Filippi A, Paolini I, Innocenti F, Mazzaglia G, Battaggia A, Brignoli O (2009). Blood pressure control and drug therapy in patients with diagnosed hypertension: a survey in Italian general practice. *Journal of Human Hypertension* 23:758-763.

FMHACA (2014). Standard treatment guidelines for general hospital. 3rd Edition. Addis Ababa, Ethiopia.

Gimpel N, Schoj V, Rubinstein A (2006).Quality management of hypertension in primary care: do physicians treat patients' blood pressure level or cardiovascular risk? *Quality in Primary Care* 14: 211-217.

Gupta SK, Nayak RP, Rahavi R, Kumar A (2015). A cross-sectional retrospective study to assess the pattern of prescribing for inpatient hypertensive cases in a tertiary hospital and to find out the possible avenues for betterment of hypertension management. *Archives of Medicine and Health Sciences* 3(1): 1.60-165.

Hasan J (2016). Pattern of drugs prescribed for treatment of hypertensive patients: Bangladesh. *African Journal of Pharmacy and Pharmacology* 10(25): 521-525.

James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al (2014). 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the eighth joint national committee (JNC 8). *Journal of the American Medical Association* 311(5):507-520.

Janet K (2011). Prevention and management of hypertension: A study on knowledge and attitudes of women of child bearing age. *Central Ostrobothnia University of Applied Sciences Degree Programme in Nursing*.1-53.

Jarari N, Rao N , Peela JR, Ellafi KA, Shakila S, et al(2016). A review on prescribing patterns of antihypertensive drugs. *Clinical Hypertension* 22(7):1-8.

Kalamdani AR, Bhandare B, Hemamalini MB, Krishna MV (2014).A prospective study of prescribing pattern of antihypertensive drugs in tertiary care hospital, Bangalore. *Journal of Evolution of Medical and Dental Sciences* 2(52):10339-10344.

Karthikeyan G and Ranganayakulu D (2015). Prescription pattern and therapeutic response of various anti hypertensive drugs for the hypertensive patients at private hospitals in Tamilnadu, India. *International Journal of Pharmaceutical Sciences and Drug Research* 7(3): 270-274.

Karaeren H, Yokuşoğlu M, Uzun S, Baysan O, Koz C, Kara B, et al (2009). The effect of the content of the knowledge on adherence to medication in hypertensive patients. *Anadolu Kardiyol Derg* 9: 183-188.

Kaur S, Gupta S, Kumar D, Lal M, Gilani Z (2012). Prescribing pattern of antihypertensive drugs in a tertiary care hospital in Jammu-a descriptive study. *JK-Practitioner* 17(4): 38-41.

Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J (2005). Global burden of hypertension: analysis of worldwide data. *Lancet* 365(9455):217-23.

Khrime D, Kumar A, Pandey AN, Bansal N, Sharma U, Varma A (2015). Antihypertensive drug utilization pattern and awareness in diabetic hypertensive patients at tertiary care centre. *International Journal of Research in Medical Sciences* 3(2): 461-465.

Khurshid F, Aqil M, AlamMS, Kapur P, Pillai KK (2012). Antihypertensive medication prescribing patterns in a University teaching hospital in South Delhi, India. *International Journal of Pharmaceutical Sciences and Research* 3(7): 2057-2063.

Kousalya K, Chirumamilla S, Manjunath S, Ramalakshmi S, Saranya P, Chamundeeswari D (2012). Prescribing trend of antihypertensive drugs in hypertensive and diabetic hypertensive patients. *Asian Journal of Pharmaceutical and Clinical Research* 5(4): 22-23.

Maghrabi IA (2013). Evaluation of antihypertensive prescribing patterns in the western region of Saudi Arabia and its compliance with national guidelines. *Saudi Journal for Health Sciences* 2(2): 118-126.

Maziak W, Keil U, Do¨raing A, Hense HW (2003). Determinants of poor hypertension management in the community. *Journal of Human Hypertension* 17: 215-217.

Ministry of Health, Malaysia (2008). Clinical practice guideline on management of hypertensionn. 3rd Edition. 1-44.   www.moh.gov.my, www.acadmed.org.my or www.msh.org.my

Murti K, Khan MA, Dey A, Sethi MK,Das P, Pandey K (2015). Prescription pattern of anti-hypertensive drugs in adherence to JNC-7 guidelines. *American Journal of Pharmacology and Toxicology* 10 (1): 27-31.

Nagarkar A, Gadhave S, Sharma I, Choure A, Morisky D (2013). Factors influencing medication adherence among hypertensive patients in a tertiary care hospital, Pune, Maharash, India. *National Journal of Community Medicine* 4(4): 559-563.

Nshisso LD, Reese A, Gelaye B, Lemma S, Berhane Y, Williams MA (2012).Prevalence of hypertension and diabetes among Ethiopian adults. *Diabetes Metabolic Syndrome* 6(1): 36-41.

Odili VU, Oghagbon EK, Ugwa NA, Ochei UM, Aghomo OE (2008). Adherence to
international guidelines in the management of hypertension in a tertiary hospital in
Nigeria. *Tropical Journal of Pharmaceutical Research* 7 (2): 945-952.

Oke O and Adedapo A (2015). Antihypertensive drug utilization and blood pressure control
in a Nigerian hypertensive population. *General Medicine* 3(2):1-5.

Olanrewaju TO, Aderibigbe A, Busari OA, Sanya EO (2010). Antihypertensive drug utilization
and conformity to guidelines in a sub-Saharan African hypertensive population.
International Journal of Clinical Pharmacology and Therapeutics 48(1): 68-75.

Potchoo Y, Goe-Akue E, Damorou F, Massoka B, Redah D, Guissou IP (2012). Effect of
antihypertensive drug therapy on the blood pressure control among hypertensive
patients attending campus' teaching hospital of Lome, Togo, West Africa.
Pharmacology and Pharmacy 3: 214-223.

Rachana PR, Anuradha HV, Shivamurthy MC (2014). Antihypertensive prescribing patterns and
cost analysis for primary hypertension: A Retrospective Study. *Journal of Clinical and
Diagnostic Research* 8(9): 19-22.

Ramli S, Miskan M, Ambigga D, Ambigga D, Nafiza MN *,* Mazapuspavina MY et al (2010).
Prescribing of antihypertensive agents in public primary care clinics-is it in
accordance with current evidence? *Malaysian Family Physician* 5: 36 -40.

Rimoy G H, Temu MJ, Nilay C (2008). Prescribing patterns and cost of antihypertensive drugs
in private hospitals in Dares Salaam in Tanzania. *East and Central African Journal of
Pharmaceutical Sciences* 11: 69-73.

Romday R, Gupta AK, Bhambani P (2016). An assessment of antihypertensive drug prescription
patterns and adherence to JNC-8th hypertension treatment guidelines among
hypertensive patients attending a tertiary care teaching hospital. *International Journal of
Research in Medical Sciences* 4(12): 5125-5133. www.msjonline.org

Sekokotla D, Steyn K, Bradshaw D, Mbananga N. (2003). Hypertension management and
surveillance at primary care level: a situational analysis in the Limpopo Province. Cape

Town: *South African Medical Research Council*.1-76.

Sepehri G, Talebizadeh N, Mirzazadeh A, Mohsenbeigi M (2008).The patterns of
    antihypertensive drug prescription by cardiologists in Kerman province of Iran.
    Pharmacoepidemiology and Drug Safety 17: 180-185.

Shah J, Khakhkhar T, Bhirud S, Shah RB, Date S (2013). Study of utilization pattern of anti-
    hypertensive drugs in hypertensive diabetic patients with or without reduced renal
    function at tertiary care teaching hospital. *International Journal of Medical Science and
    Public Health* 2 (2):167-172.

Shukrala F and Gabriel T (2015). Assessment of prescribing, dispensing, and patient use pattern
    of antihypertensive drugs for patients attending outpatient department of HiwotFana
    Specialized University Hospital, Harar, Ethiopia. *Drug Design, Development and
    Therapy* 9: 519-523.

Tesfaye F, Byass P, Wall S (2009). Population based prevalence of high blood pressure among
    adults in Addis Ababa: uncovering a silent epidemic. *BMC Cardiovasc Disord*. 9:39.

Ukwe CV and Ubaka CM (2012). Antihypertensive drug prescribing in a tertiary hospital in
    Eastern Nigeria. *Tropical Journal of Pharmaceutical Research* 11 (2): 297-305.

Van de Vijver S, Akinyi H, Oti S, Kyobutungi C (2013).The Impact of non-communicable
    diseases (NCDs) and neglected tropical diseases (NTDs) on development in Africa.
    AU Conference of Ministers of Health (CAMH6).1-13.

Weber MA, Schiffrin ES, White WB, Mann S, Lindholm LH, Kenerson JG, et al (2013). Clinical
    practice guidelines for the management of hypertension in the community a statement
    by the American Society of Hypertension and the International Society of Hypertension.
    The Journal of Clinical Hypertension: 1-13.

WHO (2009). Global health risks: Mortality and burden of diseases attributable to selected major
    risks. Geneva.

WHO (2010). Global status report on non-communicable diseases: Description of the

global burden of NCDs, their risk factors and determinants. WHO, Geneva.

WHO (2014). Global status report on non-communicable diseases 2014. Geneva, Switzerland.

Woldu MA, Shiferaw DF, Lenjisa JL, Tegegne GT,Tesafye G, Dinsa H (2014). Antihypertensive medications pattern and their effect in blood pressure control in patients attending Bishoftu general hospital ambulatory ward, Debrezeit (Bishoftu), Ethiopia. *World Journal of Pharmaceutical* 2(10): 1198-1205.

Yibeltal K, Challi J, Dereje N (2011). The Quality of care provided to patients with chronic non-communicable diseases: A Retrospective Multi-Setup Study in Jimma Zone, Southwest Ethiopia. *Ethiopian Journal Health Science 21* (2):1-12.

Annex

Annex I- Data abstraction format

1. Registration Details

1.01 Patient initials

1.02 Age---------

1.03 Sex   male   female

1.04 Date of registration _____

1.05 ethnicity _____

1.06 Duration of therapy…………………….

2. Co morbid Condition

2.01 Hypertension alone	YES	NO
2.04 Liver disease	YES	NO
2.02 Cardiovascular disease	YES (specify)……………..	NO
2.03 DM	YES	NO
2.05 kidney diseases	YES	NO
2.06Thyroid disease	YES	NO

3. Stages of hypertension

3.1 At target BP	YES	NO
3.2 Stage 1 of hypertension	YES	NO
3.3 Stage 2 of hypertension	YES	NO

4. Blood pressure Recordings (both SBP and DBP)

4.01 visit 1 ……………..mmHG

4.02Visit 2(last previous)…………..mmHG

4.03 visit 3(current)……………………mmHG

5. Antihypertensive prescribed

5.01ACE inhibitor	YES (drug name) _____	NO
5.02 BB	YES (drug name) _____	NO
5.03 Diuretics	YES (drug name) _____	NO
5.04 ARB	YES (drug name) _____	NO
5.05 CCB	YES (drug name) _____	NO

5.06 others (specify)   YES (drug name) _____   NO
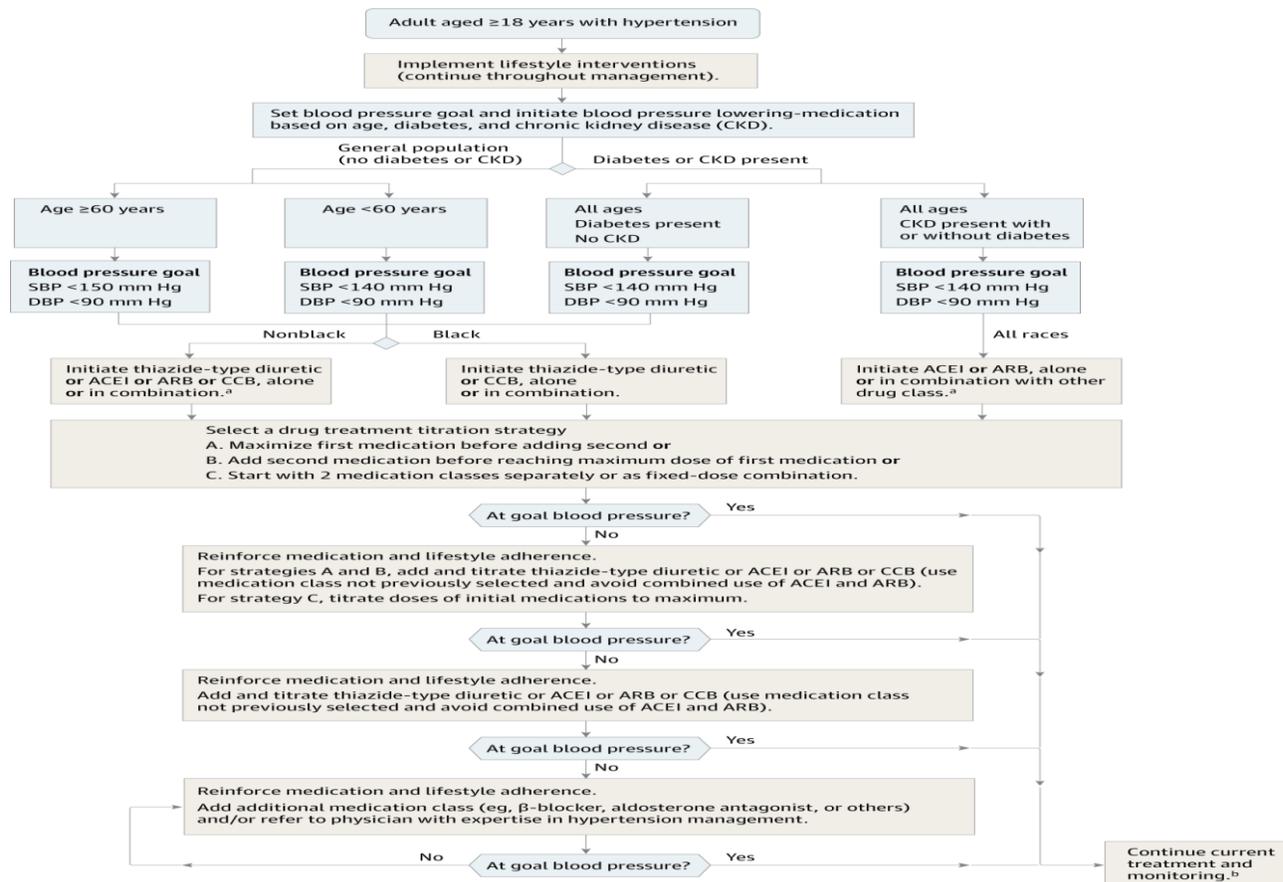
6. Nature of therapy

6.01 Mono-therapy   YES   NO

6.02 Two drug therapy   YES   NO

6.03 Three drugs therapy   YES   NO

6.04 Greater than 3 drugs therapy (specify) _____

7. BP Control Status

8.01 controls------

8.02 not control------

Annex II- JNC 8 Hypertension guideline management algorithm

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; and CCB, calcium channel blocker. a ACEIs and ARBs should not be used in combination. b If blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan.

Compelling condition	First line	Second line	Third line
Coronary artery diseases	BB plus ARB or ACEI	(add-on): CCB or thiazide	BB plus ARB or ACEI plus CCB plus thiazide
Heart failure	ACEI or ARB plus BB plus diuretic plus aldosterone antagonist. Start with ACEI, BB, diuretic. Can add BB even before ACEI optimized. Use diuretic to manage fluid.	Amlodipine can be added for additional BP control.	