TREATMENT OF HYPERTENSION IN ADULT PATIENTS AT RUIRU SUB-COUNTY HOSPITAL IN KENYA

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I dedicate this thesis to my beloved family for their love and unwavering support during my studies.

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ABBREVIATIONS

ACEI	Angiotensin Converting Enzyme Inhibitor
ARB	Angiotensin 2 Receptor Blocker
ASH	American Society of Hypertension
BP	Blood Pressure
CCB	Calcium Channel Blocker
CKD	Chronic Kidney Disease
CV	Cardiovascular
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
ESC	European Society of Cardiology
ESH	European Society of Hypertension
ESRD	End Stage Renal Disease
HBP	High Blood Pressure
ISH	Isolated Systolic Hypertension
JNC	Joint National Committee
KNH	Kenyatta National Hospital
MOPC	Medical Outpatient Clinic
PAD	Periphery Artery Disease
SAHS	South Africa Hypertension Society
SBP	Systolic Blood Pressure
WHO	World Health Organisation

DEFINITION OF TERMS

Compelling indications	Certain high-risk clinical conditions that require selection of certain drug classes based on favorable outcome data from clinical trials.
Blood pressure	Force exerted by blood against the walls of arteries as a result of the pumping action of the heart.
Systolic blood pressure	The maximum arterial pressure during contraction of the left ventricle of the heart.
Diastolic blood pressure	The minimum arterial pressure during relaxation and dilatation of the ventricles of the heart when the ventricles fill with blood.
Hypertension	Repeatedly elevated blood pressure with a systolic pressure above 140 mmHg or a diastolic pressure above 90 mmHg.
Adequate blood pressure control	Maintaining blood pressure levels below those considered for diagnosis of hypertension (140/90 mmHg).

ABSTRACT

Background

Hypertension or high blood pressure has been on the rise globally. It has emerged as a major global public health issue and one of the leading causes of cardiovascular disease. Use of blood pressure lowering medications in treatment of hypertension has been shown to reduce the risk of occurrence of cardiovascular and renal events. Proper and judicious use of such medications is always recommended to ensure adequate control of blood pressure levels in hypertensive patients. Poor control of blood pressure has been reported worldwide and use of international treatment guidelines in making decisions about treatment of hypertension would result in better blood pressure control.

Study Objective

The main aim of this study was to assess the treatment of hypertension in adult hypertensive patients attending the Medical Outpatient Clinic at Ruiru Sub-county Hospital, Kenya.

Methodology

The study was a descriptive cross-sectional study involving review of records of active adult hypertensive patients on antihypertensive therapy enrolled at Ruiru Sub-county Hospital's Medical Outpatient Clinic. Qualitative data was also obtained from prescribers through interviews. Ethical approval was granted by the Kenyatta National Hospital and University of Nairobi Ethical and Research Committee. Patient files were systematically sampled and retrieved from the hospital's records department. A customized, pre-tested data collection tool was used to collect socio-demographic, clinical and treatment data from patient files. Descriptive and exploratory data analysis was carried out using STATA Version 10. Deductive analysis was also carried out on qualitative data from interviews.

Results

In this study, 247 patients' files were reviewed and of these, 87% were female. The most commonly prescribed classes of antihypertensives were angiotensin converting enzyme inhibitors (ACEIs) at 48% of all prescriptions followed by thiazide diuretics at 40%. Among the individual drugs, Enalapril was the most frequently prescribed at 48% of all prescriptions

followed by Hydrochlorthiazide at 40%. Two-drug regimens were the most popular at 44% of all prescriptions followed by monotherapies at 40%. Adherence rate of 82% to JNC-8 treatment guidelines was observed with most deviations occurring in treatment of Stage 1 hypertension where an adherence rate of only 45% was observed.

The blood pressure (BP) control rate in this study was found to be at 46% among the hypertensive patients. The independent predictor variables influencing control of blood pressure were found to be sex of the patient, number of antihypertensives prescribed and being on a beta blocker. On a multiple logistic regression model, only the sex of the patient was found to statistically influence blood pressure control.

The average monthly acquisition cost of drugs per hypertensive patient for the hospital was found to be Ksh. 87. A dose of carvedilol was found to be the most expensive at an average acquisition cost of Ksh.308 per month per prescription. The least expensive drugs were hydrochlorothiazide, furosemide, nifedipine retard and enalapril 5mg at Ksh.8, Ksh.15, Ksh.17 and Ksh.24 respectively per monthly dose per prescription.

Conclusion and recommendations

Prescribing patterns of antihypertensive drugs in this study were generally consistent with treatment guidelines where most patients were on ACEIs and thiazide diuretics. Adherence to latest treatment guidelines was found to be at 82%. This high level of adherence may have been responsible for the higher than usual level of BP control observed. Training and constant evaluation of prescribing practices in hospitals is still required to reduce deviations that cannot be justified.

CHAPTER 1: INTRODUCTION

1.0 Background information

1.1 Hypertension: Definition and description

Hypertension is defined as Systolic Blood Pressure (SBP) ≥140 mmHg or Diastolic Blood Pressure (DBP) ≥90 mmHg or both when measured on more than two occasions in all adults (1). The SBP is particularly important and is the basis for diagnosis in most patients. This definition has been accepted worldwide both to simplify the diagnostic approach and to facilitate the decision about treatment. There is evidence showing that lowering blood pressure to below these levels is associated with reduced risk of occurrence of cardiovascular and renal events such as stroke, myocardial infarction, heart failure and kidney damage (2). The relationship between blood pressure (BP) and risk of some cardiovascular events is continuous and independent of other risk factors for all ages and ethnic groups (3). For individuals aged 40 to 70 years, each increment of 20mmHg in systolic BP or 10 mm Hg in diastolic BP doubles the risk of Cardiovascular Disease (CVD) across the entire BP range from 115/75 to 185/115 mm Hg.

1.2 Hypertension: Prevalence

The prevalence of hypertension has been increasing at a rapid rate globally. According to the World Health Statistics 2012 report, one in three adults worldwide have raised blood pressure (4). There are at least 970 million people worldwide who have elevated blood pressure (hypertension). In the developed world, about 330 million people have hypertension, as do around 640 million in the developing world. The World Health Organization (WHO) rates hypertension as one of the most important causes of premature death worldwide and the problem is growing. In 2025, it is estimated there will be 1.56 billion adults living with high blood pressure (5).

Studies have shown that blood pressure levels have been reducing in almost all high income countries (6,7,8). In contrast, the prevalence of hypertension has been increasing drastically in most African countries (9). The increasing prevalence of hypertension is due to population growth, ageing and changing lifestyle habits as a result of urbanization such as unhealthy diet,

harmful use of alcohol, low levels of physical activity, excess weight and exposure to persistent stress.

Several studies in the African region have found high prevalence levels but low levels of awareness, treatment and control especially in urban areas (10,11). One of these studies, carried out in Cameroon in 2012, found a prevalence rate as high as 47.5% (10). A systematic analysis carried out to estimate prevalence and awareness rates of hypertension reported a pooled prevalence rate of 30.8% among African countries and very low awareness rates (9). Prevalence rates of hypertension in Kenya have not been extensively studied. According to a World Health Statistics report, it was estimated that by 2008, the prevalence rate of hypertension in Kenya was at 35% (4). A cross-sectional household survey carried out in rural Kenya in Nandi District between 2009 and 2011 showed a prevalence rate of 21.4% (12).

1.3 Burden of hypertension

Hypertension has emerged as a major global public health issue. It is well recognised as a key independent risk factor for cardiovascular disease and mortality worldwide. In 2010, hypertension was the leading risk factor for global disease burden accounting for 7% of all disability-adjusted life years (13). It is a major risk factor for coronary heart disease and the single most important risk factor for stroke. Of note is 13% of all attributable global deaths have been attributed to hypertension while being a direct cause of 51% of stroke deaths and 45% of coronary heart disease deaths (14). The lifetime burden of hypertension is substantial. It has been shown that the lifetime risk of a cardiovascular event is 63.3% in a hypertensive patient compared to 46.1% in a normotensive individual (15).

Hypertension burden in Africa, especially in the sub-Saharan Africa, has been heavy due to the double impact of managing both infectious and non-communicable diseases which are highly prevalent in this region (12). Age-specific mortality rates from chronic diseases have been found to be higher in the sub-Saharan region than in any other part of the world (16).

There is an enormous financial burden associated with hypertension since the disease is a lifetime condition that requires management over long periods. Most of the costs of hypertension management and its resultant complications including medications, lifestyle changes and monitoring are borne by the individuals through out of pocket payments. This economic burden

puts a strain on individual's resources and a country's health care system especially in resource limited settings (17). The cost of drugs is an important discriminating factor in making choices about initiation and maintenance of therapy. It is important that clinicians ensure that the drugs they prescribe are affordable and cost effective while still upholding the principle of rational drug use. Economic burden also incorporates lost productivity due to disability and required assistance in daily living.

1.4 Hypertension: Prognosis and outcomes

The level of BP is positively associated with the incidence of several CV events [stroke, myocardial infarction, sudden death, heart failure and peripheral artery disease (PAD)] as well as of end-stage renal disease (ESRD) (3). Clear benefits of pharmacological treatment have been demonstrated in hypertensive patients. In a meta-analysis of randomized placebo-controlled trials, antihypertensive therapy was found to reduce the risk of developing adverse health outcomes (18). The effectiveness of hypertension treatment is determined by the patient's age, sex, presence of co-morbidities and other cardiovascular risk factors, hypertension staging and choice of treatment and level of compliance to treatment. Pharmacological treatment should always be accompanied by lifestyle modifications which have been shown to prevent or delay development of complications and enhance the efficacy of antihypertensive therapy.

CHAPTER 2: LITERATURE REVIEW

2.1 Hypertension definition and classification.

Most of the major guidelines define hypertension as Systolic BP ≥ 140 mmHg and/or Diastolic BP ≥ 90 mmHg on repeated examination based on evidence from randomized control trials which show that treatment-induced BP lowering to below these levels is beneficial (2).

There has been contention in classification of hypertension by the various international and local hypertension treatment guidelines. The seventh report of the Joint National Committee of the USA (JNC-7) published in 2003, classified BP levels in adults into 4 main classes that included normal (SBP<120 mmHg and DBP<80 mmHg), prehypertension (SBP between 120 mmHg and 139 mmHg or DBP between 80 mmHg and 89 mmHg), stage 1 (SBP between 140 mmHg and 159 mmHg or DBP between 90 mmHg and 99 mmHg) and stage 2 hypertension (SBP ≥160 mmHg or DBP ≥100 mmHg) (1). Their latest eighth report published in 2013 did not change this classification.

The 2013 joint European Society of Hypertension (ESH) and European Society of Cardiology (ESC) guidelines for the management of arterial hypertension have classified blood pressure levels as shown in Table 2.1 below (19).

Table 2.1: Definitions and classification of BP levels (mmHg)

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

The BP category is defined by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension (ISH) should be graded 1, 2, or 3 according to systolic BP values in the ranges indicated.

The causes of hypertension can either be primary or secondary. About 95% of adults with high blood pressure have primary hypertension (sometimes called essential hypertension). The cause of primary hypertension is not known, although genetic and environmental factors that affect blood pressure regulation are now being studied. Environmental factors include excessive intake of salt, excess weight and physical inactivity. Genetic factors include inappropriately high activity of the renin-angiotensin-aldosterone system and the sympathetic nervous system and susceptibility to the effects of dietary salt on blood pressure. A small number of patients have secondary hypertension where there are identifiable causes such as chronic kidney disease, renal artery stenosis, excessive aldosterone secretion, pheochromocytoma, and sleep apnea (20).

2.2 Control of hypertension

Adequate control of BP level is an important element in prevention of mortality and cardiovascular complications resulting from hypertension. It refers to maintaining of BP levels below 140/90 mmHg for most patients. Control of hypertension with antihypertensive therapy is associated with reduction in adverse health outcomes (18). It has been shown to result in 50% reduction in heart failure, 40% reduction in stroke and 20-25% reduction in myocardial infarctions (21).

Poor rates of BP control have been reported worldwide and this should be a cause for concern especially in high risk groups including blacks, those with cardiovascular disease including stroke and those with multiple risk factors. Jenson et.al (2010) study on assessment of levels of hypertension control in antihypertensives in Mombasa, Kenya found very low levels of BP control (7.4%) among hypertensive patients on treatment (22). Various other studies in the country have found same levels of low BP control among antihypertensives (22,23). These low levels of BP control are also present in other parts of Africa and the world even in developed countries (7,13,24,25). A study by Chow et. al (2013) on prevalence, awareness, treatment and control of hypertension in rural and urban communities in high, middle and low income countries found levels of BP control less than 20% in all countries (26).

2.3 Hypertension management guidelines

Hypertension guidelines are widely available internationally. In Kenya, treatment guidelines for hypertension have been incorporated in the treatment guidelines for diagnosis and treatment of common diseases publication from the Ministry of Health (27). No Kenyan national guidelines exist specifically for management of hypertension.

The Joint National Committee (JNC) on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (HBP) of the USA have published various reports through panel members appointed to the various JNC committees with the latest report being from the JNC-8 on evidence-based guidelines for management of HBP in adults that was published in 2013 (1,29). The JNC-8 report being the latest evidence-based guidelines was used for comparison in this study. Furthermore, this report gives specific recommendations for management of black patients.

The Joint Task Force for the management of arterial hypertension of the ESH and ESC have published guidelines for management of hypertension with several updates in 2003, 2007 and the latest report being published in 2013 (21,30). The World Health Organisation (WHO) in collaboration with the International Society of Hypertension (ISH) also issued guidelines on management of hypertension in 1999 and 2003 (30). In Africa, only South Africa has developed country-specific hypertension management guidelines with the latest version published in 2011 by the South African Hypertension Society (SAHS) (31).

The various guidelines available are written based on latest evidence from various randomized control trials and their meta-analyses, high quality observational studies and clinical observations of high scientific caliber. If no evidence is available, or if weak, then recommendations are based on expert opinion. The guidelines do not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patients, in consultation with that patient, or their caregiver.

The guidelines give recommendations on definition and classification of hypertension, diagnostic evaluation (correct BP measurement, Total CV risk assessment), when to initiate treatment, BP treatment targets, treatment strategies (lifestyle changes, choice of drugs, treatment in special conditions), treatment of associated risk factors and follow up.

2.4 Treatment of hypertension.

Hypertension can be easily diagnosed using readily available diagnostic equipment and its control achieved using simple and well tolerated medication regimens to lower related morbidity and mortality even in resource-limited settings. The management of hypertension should always be comprehensive by focusing on reducing overall CV risk. It should include lifestyle modifications, BP lowering antihypertensive drug therapy and treatment for other modifiable CV risk factors as required. Appropriate and adequate lifestyle changes (healthy diet, weight control and regular physical exercise) have been recommended in all hypertension management guidelines. These have potential to improve control of BP according to recommendations of 2013 Lifestyle Working Group (32). Appropriate changes in lifestyle may prevent or delay onset of hypertension, prevent or delay the need for pharmacotherapy in those with normal high BP or grade1 hypertensive patients at low to moderate CV risk. Lifestyle changes also reduce medication needs in those already on antihypertensives and contribute in controlling other CV risk factors like high cholesterol levels. These modifications should, however, be regarded as a complement rather than an alternative to drug therapy and pharmacological management should commence if they are proved not to be effective or if other CV risk factors appear.

The 2013 joint ESH/ESC guidelines for the management of arterial hypertension give a lot of emphasis on combination of BP levels, presence of cardiovascular disease risk factors, asymptomatic organ damage and clinical complications in assessing total (global) cardiovascular (CV) risk (19). This is based on the fact that most hypertensive patients rarely have high BP levels alone and presence of other CV risk factors leads to increased total CV risk. Some of the CVD risk factors include age (≥55 years in men, ≥65 years in women), smoking, dyslipidemia, abnormal glucose tolerance, overweight, truncal obesity and family history of premature CVD. The treatment strategy, including choice of drug, use of combination therapy, when to initiate therapy, to be applied in management of each individual patient is based on the level of total CV risk.

Hypertension management guidelines give recommendations on when to initiate treatment, BP treatment targets to be achieved and treatment strategies to employ in management of hypertensive patients with different clinical characteristics. Initial treatment is based on the level of BP and total CV risk with appropriate lifestyle changes being recommended in

prehypertension and stage 1 hypertensive patients in whom there is no history of cardiovascular disease, stroke, or renal events or evidence of abnormal findings and who do not have diabetes or other major risk factors. Monitoring should then be carried out and drug treatment initiated if the BP level increases or there is evidence of increasing CV risk. In all other patients (including those with stage 2 Hypertension), it is recommended that drug therapy be started when the diagnosis of hypertension is made (20). There is evidence showing that most hypertensive patients require two or more antihypertensives to reduce their BP and maintain it within reasonable ranges as stated in the 2013 ESH/ESC guidelines (19). The JNC-8 report recommends initiating treatment in the black community with a thiazide- diuretic or calcium channel blocker alone or in combination (28). It also recommends use of an angiotensin converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) alone or in combination with another drug class as initiation therapy in patients with Chronic Kidney Disease (CKD) irrespective of age or race.

When initiating with monotherapy or with a two-drug combination, doses can be stepped up if necessary to achieve the BP target. If the target is not achieved within a month by a two-drug combination at full doses, switching to another two-drug combination can be considered or a third drug added with dose being titrated. The common algorithm used in treatment of hypertension as adapted from the 2013 ASH/ISH statement on clinical practice guidelines for the management of hypertension in the community is shown in the Figure 2.1 (20). Use of an ACEI in combination with an ARB is discouraged in all patients due to the risk of hyperkalemia. If a drug is not tolerated or is contraindicated in a patient, then another class of drug can be used. Therapeutic duplication where there is use of more than one drug from the same therapeutic class is also strongly discouraged. Follow-up visits can be scheduled at monthly intervals to review BP levels and adjust medications until goal BP is achieved. Hypertensive patients with stage 2 hypertension or complicating comorbid conditions require more frequent visits. Once goal BP level is reached, 3-6 months visit intervals can be considered. Unsuccessful BP control after this strategy should be referred to a hypertension specialist.

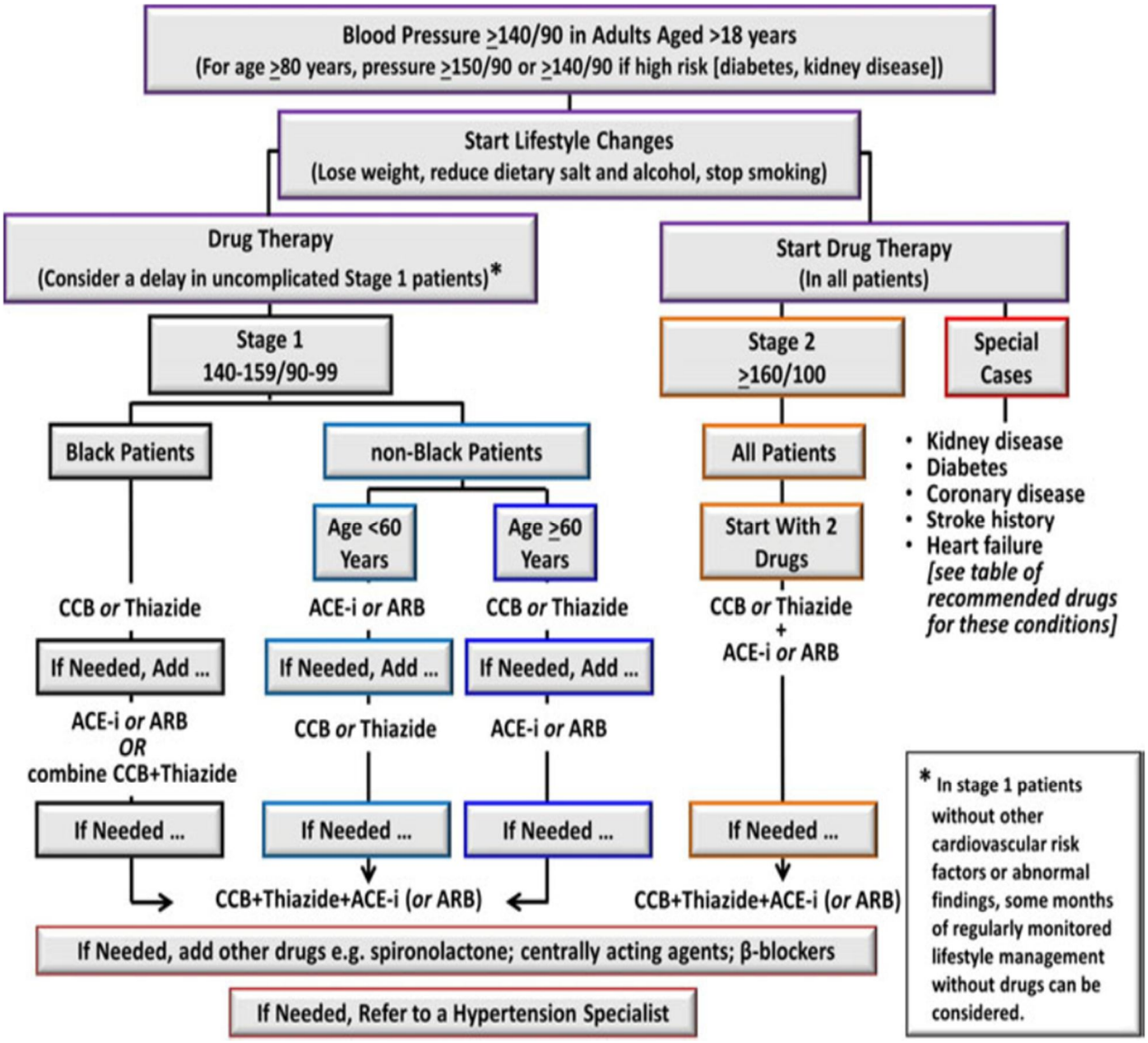

Figure 2.1: Hypertension treatment algorithm as adapted from the 2013 ASH/ISH statement on clinical practice guidelines for the management of hypertension in the community (20).

Treatment of other cardiovascular risk factors to respective goals should be included in the management strategy of the patient. Low dose aspirin may be considered only when the BP has been controlled because of increased risk of hemorrhagic stroke when aspirin is used in uncontrolled hypertension.

Table 2.2: Common antihypertensive drug classes and their characteristics (BNF 68) (33).

Class	Mode of action	Adverse effects	Contra-indications
Angiotensin Converting Enzyme Inhibitors e.g. Enalapril	Blocking the conversion of angiotensin-I to angiotensin- II, a potent vasoconstrictor hence reducing vascular resistance	Persistent cough, angioedema	Pregnancy, angioneurotic edema, hyperkalemia
Angiotensin-II receptor blockers e.g. losartan	Blocking angiotensin-II Receptors	Anemia, neutropenia, cough, headache	Pregnancy, hyperkalemia, bilateral renal artery stenosis
Thiazides e.g. hydrochlorthiazide Thiazide-like diuretics eg chlorthalidone.	Increasing fluid loss from the body. Inhibiting sodium reabsorption at the distal convoluted tubules.	Hypokalemia, hyperglycemia, hyperuricemia	Gout, metabolic syndrome, pregnancy, hypercalcemia, hypokalemia
Calcium channel blockers: Dihydropyridines e.g. nifedipine, amlodipine Non-dihydropyridines Phenylalkylamines e.g. Verapamil Benzothiazepines e.g. diltiazem	Blocking the inward flow of Ca+ ions through active cell membranes	Peripheral edema , bradycardia, A-V block, hypotension, sleep disturbances	Tachyarrythmias, heart failure,A-V block, severe Left-ventricular dysfunction.
Beta-blockers e.g. atenolol	Blocking beta-adrenoceptors in the heart, peripheral vasculature, pancreas, liver, bronchi	Decreased sexual function, Fatigue, Reduced exercise tolerance	Asthma, A-V block, chronic obstructive pulmonary disease.
Mineralocorticoid receptor antagonists e.g. spironolactone	Antagonising aldosterone	Gynecomastia, sexual dysfunction	Acute or severe renal failure, hyperkalemia

2.5 Choice of drugs

Various classes of antihypertensive medications are available for the treatment of hypertension as shown in Table 2.2 (33). The main benefits of antihypertensive drugs use are due to lowering of BP and are independent of the drugs used. Diuretics, beta-blockers, calcium channel blockers, ACEIs and ARBs are all suitable for initiation and maintenance of antihypertensive treatment either as monotherapy or combination therapy. However, certain contraindications and compelling indications may determine the type of drug to be used in a patient (1). Compelling indications are certain high-risk clinical conditions that require selection of certain drug classes based on favorable outcome data from clinical trials as shown in Table 2.3 below.

Table 2.3: Some compelling indications and recommended drugs for initiation and maintenance of therapy (1).

Compelling indication	**Recommended drugs**
Heart failure	Diuretics, beta blockers, ACEIs, ARBs, aldosterone antagonists
Post myocardial infarction	Beta blockers (BB), ACEIs, aldosterone antagonists
High coronary heart disease risk	Diuretics, beta blockers, ACEIs, CCBs
Diabetes	Diuretics, BB, ACEIs, ARBs, CCBs
CKD	ARBs, ACEIs
Recurrent stroke prevention	Diuretics, ACEIs

2.6 Antihypertensives prescribing practices

Studies on prescribing practices are an important element especially for chronic diseases such as hypertension. This is because the patients have to be on lifelong medication and control of BP levels is important in prevention of adverse complications. Hence rational prescribing in these patients is important in enhancing optimal care, ensuring cost effectiveness and improving quality of life. Often, developing countries find it hard to keep up with international standards due to poor health systems. A study by Mwangi in 2007 at Kenyatta National Hospital (KNH) on prescription patterns in management of hypertension showed that thiazide diuretics were the most commonly prescribed among the antihypertensive drug classes (34). He also found out that

most of the drugs were prescribed rationally and in accordance with local and international guidelines.

In other African countries, similar studies have been carried out. Ukwe and Ubaka (2012) carried out a study on antihypertensives prescribing in a Nigerian hospital and found that most (90%) of the hypertensive patients used two-drug combinations as recommended in the hypertension management guidelines with ACEIs and diuretics being the most commonly prescribed (35). A study in Tanzania on hypertension management in district hospitals showed that the most commonly prescribed drugs were diuretics and beta blockers. Irrational prescribing habits were identified in this study (36). A study by Gu et. al (2012) among US adults with hypertension showed a trend of increased use of multiple antihypertensives in treatment in the 10 year study period between 2001 and 2010 (37).

2.7 Cost implications

The cost of drug therapy especially in resource-poor settings is a major determinant of adherence to long term medications for chronic conditions such as hypertension. The 2013 WHO/ISH statement on clinical practice guidelines for the treatment of hypertension in the community recommend use of cheap but effective brands of drugs in these resource-limited settings (20). This increases the cost effectiveness of drug therapy while reducing adverse outcomes from hypertension. A Nigerian study carried out among rural hypertensive patients to assess the financial implication and cost effectiveness of hypertension treatment by Ilesanmi et al. (2012) showed that use of diuretics either as monotherapy or in combination therapy was the most cost-effective treatment strategy (17). This study also revealed substantial financial burden of long term antihypertensive therapy with the higher costs for patients with comorbidities, stage 2 hypertension and those on 3 or 4 drug regimens.

The major classes of antihypertensives are largely equivalent in efficacy and safety. Diuretics are the cheapest and should be used as first-line treatment if the patient has no compelling indication or risk factor for increased CV risk. Other classes such as the ACEIs and ARBs, though they may be more expensive, are cost effective in high CV risk hypertensive patients as they provide additional benefits.

The choice of antihypertensive therapy should, ideally, be evidence-based and comply with internationally acceptable guidelines. Nevertheless, an important consideration in the selection of drug therapy is the acquisition cost. This factor is even weightier in developing economies where the dual dilemmas of low per capita income and lack of medical insurance dampen the ideals of pharmacologic control of BP.

2.8 Problem statement

Prevalence of hypertension has been steadily on the rise in most African countries including Kenya. Prevalence rates as high as 40% have been reported in some countries (26). Hypertension is a key independent risk factor for cardiovascular disease and mortality worldwide. A rise in prevalence has been accompanied by low awareness, treatment and control rates (38). Adequate blood pressure control may be achieved through proper knowledge and application of management approaches in line with international standards.

With scarce resources for the health care system in Sub-Saharan African countries including Kenya, most patients find cost of medications being generally high, with the payments mostly being made out-of-pocket. Health care needs of hypertensive patients, therefore, remain largely unmet due to suboptimal services, inadequately trained staff, high cost of care and difficulties in maintaining follow-up. Currently, the Kenyan treatment guidelines available for diagnosis and treatment of hypertension are inadequate and health providers have to rely on international guidelines that are not always applicable to poor-resources settings. Plans or policies to address hypertension as a chronic disease burden in the country have not always been prioritized. The standards of care for hypertensive patients have, therefore, remained poor. This study aimed at identifying some of the gaps in care for hypertensive patients so that appropriate changes can be made to improve on standards of care.

2.9 Justification

Hypertension prevalence has been on the rise globally with about 1 billion hypertensive patients worldwide. This high prevalence is always accompanied by low rates of awareness, treatment and control of hypertension especially in developing countries. The use of blood pressure lowering medications has been shown to decrease the risk of adverse cardiovascular outcomes in hypertensive patients. Clinician practices of prescribing antihypertensives have rarely been studied in Kenya with only a few studies being confined to Kenyatta National Hospital (KNH), a

national referral hospital. Therefore, there was need for more prescribing practices studies in other parts of the country since most of the county and sub-county hospitals are not run by specialists.

This study was aimed at evaluating prescribing patterns of antihypertensives, to identify deviations from international guidelines and some barriers to compliance to these guidelines, assessing blood pressure control level and its determinants and determining the average monthly acquisition cost of antihypertensives prescribed. Knowledge of these aspects of drug utilization and outcomes would enable identification of irrational prescribing practices by prescribers and would also inform if clinical practices being employed were effective and identify areas of improvement.

2.10 Research questions

1. What are the prescribing patterns of antihypertensives among adult hypertensive patients?
2. What is the proportion of hypertensive cases treated according to the 2013 eighth report of The Joint National committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-8)?
3. What is the influence of prognostic factors such as age, sex, treatment regimen and comorbidities on adequacy of blood pressure control?
4. What is the hospital's average monthly acquisition cost of antihypertensives prescribed?
5. What are some of the barriers to adherence to hypertension treatment guidelines?

2.11 Study objectives

Main objective

To assess the treatment of hypertension in adult hypertensive patients attending the Medical outpatient clinic at Ruiru sub-county hospital

Specific objectives

1. To identify prescribing patterns of antihypertensives among adult hypertensive patients.
2. To determine the proportion of hypertensive cases treated according to the 2013 eighth report of The Joint National committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-8).

3. To explore the influence of prognostic factors such as age, sex, treatment regimen and comorbidities on adequacy of blood pressure control.
4. To determine the average monthly acquisition cost of antihypertensives by the hospital.
5. To determine some of the barriers to adherence to hypertension treatment guidelines.

CHAPTER 3: METHODOLOGY

This chapter details the methods of data collection, analysis and presentation that were used in this study. It outlines on the methodology and steps that were taken to enhance validity and reliability of the data.

3.1 Study design

The study was a descriptive cross-sectional study. Treatment records of adult hypertensive patients on antihypertensive therapy and who met the eligibility criteria were assessed and necessary information extracted using a customized data collection tool. An interview guide was also used for collecting qualitative data from prescribers working at the clinic who included 1 clinical officer, 3 medical officers and 1 consultant.

3.2 Study site

The study was carried out at Ruiru Sub-county Hospital which is one of the county referral hospitals of Kiambu County. The hospital is located in Ruiru subcounty, a semi-urban area about 30 km from Nairobi city center along the Thika Superhighway, where it is the main referral hospital for several government health centers and dispensaries. It serves a catchment population of 241,007 according to the 2009 Kenya Population and Housing Census report (39). The hospital has both inpatient department (general adult, maternity and paediatric wards) with a bed capacity of 32 and outpatient department that serve approximately 6,000 patients monthly. Part of the outpatient department is the medical outpatient clinic (MOPC) that is open three days a week and serves approximately 800 active hypertensive patients from both urban and rural areas. The patients attending the clinic are assessed and treated by the consultants, medical officers and clinical officers working there. Patients' records are then kept at the hospital's records department. A high burden of hypertension in Central Kenya has been reported in a study carried out in Nyeri in 2013 (23).

3.3 Study population

The study involved registered and active hypertensive patients on treatment at Ruiru sub-county hospital MOPC who had attended the MOPC for at least one year by the time of data collection and had complete treatment records.

3.4 Inclusion and exclusion criteria

The inclusion criteria was adults 18 years and older, diagnosed as hypertensive, registered at the MOPC for at least one year, were on at least 1 hypertensive agent and had visited the clinic at least 3 times in the last one year from the time of data collection.

Those to be excluded were those who had either visited the clinic less than 3 times a year, were pregnant or had incomplete records.

The study population for the interviews was all prescribers working at the MOPC by the time of data collection.

3.5 Sample size determination

The Cochran (1977) formula for sample size calculation of categorical variables was used since the study was a cross-sectional study with a population size of more than 120 patients (40). In a study on prescription patterns of antihypertensives carried out at KNH's MOPC in 2007, a rate of compliance to treatment guidelines of 80% was reported (34). This was used as the expected estimated proportion (compliance to treatment guidelines is one of the objectives for this study) in calculating the sample size. Hence the following formula was used:

$n= z^2 (p)(q)/d^2$ where:

n= sample size

z= z statistic for 95% level of confidence which conventionally is 1.96

p= estimated prevalence or proportion in the population

q=1-p

d= level of precision used in the study set at 5%

The above formula gave a sample size of 246. Adjusting for proportion of files with incomplete data estimated at 10% yielded a final target sample size of 271.

Purposive sampling was used to determine the number of prescribers to participate in the study, as described in section 3.5.

3.6 Sampling procedure

A total of 300 patient files were retrieved from the hospital's records department. Systematic sampling method was employed where lists of patients obtained from the patients' attendance register for the last 3 months from date of commencement of data collection were used as the sampling frames. A total of 36 clinic days in this period gave a sample of 8 patients per clinic day. This figure was adjusted to 12 patients to cater for revisits and missing files. For each clinic day, a sampling interval was obtained by dividing the total number of patients attending that day by 12. Files belonging to patients selected using these sampling intervals were obtained from the records department until the sample size was achieved.

Purposive sampling was used to select the prescribers who were to participate in the study. All prescribers working at the clinic were eligible. Consent from the prescribers was sought before enrollment and interview. Since only 5 prescribers were working at the clinic by the time of data collection, all were interviewed after obtaining informed consent.

3.7 Data collection techniques

3.7.1 Quantitative data collection

A data collection form was designed, pre-tested and modified for collecting patient information from the medical records (Appendix 1). Details abstracted from the patient files included: demographic information (age, sex, weight and height), comorbidities present, BP levels at initial visit and most current visit, antihypertensives and other medications prescribed at the last visit, their dosage and frequency of administration. The monthly acquisition cost of each antihypertensive drug prescribed per patient was then calculated as a function of the dosage prescribed and the drug price. The prices of medications used were those from Mission for Essential Drugs & Supplies (MEDS), one of the leading drugs suppliers to public hospitals and which supplies the bulk of hypertension medicines to the hospital.

A team of 2 data collectors based at the hospital were recruited and trained for the data collection process prior to commencement of the study.

3.7.2 Qualitative data collection

Prescribers working at the study site were presented with the consent form and the purpose, methods and benefits of the study explained to them. They were made to understand why they

had been chosen, the expected duration of the interview and that it was voluntary and information provided was confidential and that they could opt out at any point (Appendix 3). Prescribers' bio-data and data on aspects of hypertension treatment concerning use of treatment guidelines were collected from them. The data collected was used to explore some of the barriers to adherence to treatment guidelines. They then signed the consent form (Appendix 4). Questions were then administered to them using an interview guide (Appendix 2) and notes taken by the interviewer who was the principal investigator.

3.8 Data analysis

Quantitative data were analyzed using STATA 10 (StataCorp, Inc, Texas, USA). Data extracted from the patient files was keyed into MicroSoft Office Excel (2010). It was then cleaned for abnormal figures, missing information and inconsistency.

Description of the study population was carried out by subjecting each of the demographic variables to a summary descriptive analysis. Continuous variables were presented as mean (standard deviation) if variable was normally distributed and as median (range) if variable was not normally distributed. Categorical variables were presented as number and percentages.

Exploratory data analysis to establish patterns within the data was performed and results were presented as numbers and percentages (proportions) for categorical variables and means and standard deviation for continuous variables. Prescribing patterns of antihypertensives were identified by categorizing the drugs into therapeutic classes, identifying the most commonly prescribed drug and class of drugs.

Patients with controlled BP levels were identified as those with latest BP reading of less than 140/90 mmHg in accordance with current JNC-8 hypertension management guidelines (28). Bivariate analysis comparing traits of subjects with controlled and uncontrolled BP levels was carried out using inferential statistical tests. Pearson's chi-square test or Fischer's exact test were used to compare distribution across arms of categorical variables and unpaired t-test for continuous normally distributed variables. Kruskal-wallis and sign rank tests were used to compare continuous variables that were not normally distributed.

Multivariable logistic regression analysis was also carried out using key variables influencing BP control identified using the bivariate analysis. P-values of 0.05 or less were considered statistically significant.

The JNC-8 management guidelines were used to compare the management of hypertensive patients at the study site with internationally set guidelines based on prescription data. A pre-determined explicit criterion was used for comparison purposes. The criteria focused on choice of prescribed drugs, appropriate drug therapy for compelling indications, appropriate concurrent drugs and appropriate combination therapy and dosing.

The monthly acquisition cost of each antihypertensive drug prescribed was calculated as a function of the dosage prescribed and drug price from MEDS price list as at July 2015 (Appendix 5). The average monthly acquisition cost of each prescription was then computed by adding up the costs of all antihypertensive drugs prescribed for all patients and then dividing this figure by the total number of patients.

In this study, p-values of 0.05 or less were considered as statistically significant. The results of the quantitative analysis were then presented as graphs, tables or pie-charts.

Qualitative review of interview responses was carried out through a descriptive analysis of a summary of key data from each participant. Analysis was done by looking for patterns or themes among responses from participants and performing meaningful groupings of the themes observed.

3.9 Quality assurance and data management

The selected data collectors were trained on the objectives and relevant procedures and tested to ensure they were properly conversant with the methods. Pre-testing of the data collection tool was carried out before the study commenced at Kenyatta National Hospital Pharmacy 15 using a sample of 20 patient files and any errors noted were appropriately modified.

Data was collected and entered into the Microsoft Excel database on the same day, cleaned and stored safely with a password. A backup was performed every 3 days and a copy stored separately from the main database. Archived data and data collection forms and notes were to be destroyed within a stipulated time of 1 year after the study had been completed.

3.10 Ethical considerations

Approval to carry out the study was granted by the Kenyatta National Hospital/University of Nairobi Ethical Review Committee (KNH/UoN ERC) approval number KNH-ERC/A/163 (Appendix 6). Exception from obtaining informed consent from patients was also granted by the KNH/UON ERC since patients would not be directly involved in the study. Informed consent was sought and granted by all prescribers from whom qualitative data was collected. At the hospital level, approval was granted by the hospital management before the study commenced.

Patients were identified using patient record numbers instead of their names to maintain privacy and confidentiality of their medical information. Prescribers interviewed were also not identified by names. Patients did not benefit directly from this study but the results of the study and feedback to the health providers and policy makers would help in improving their medical care in the future. Only details relevant to the study were obtained from the patients' files and the files were promptly returned to the hospital's records department for safe keeping.

CHAPTER 4: RESULTS

A total of 300 patient files were sampled from MOPC clinic's attendance lists covering the period January 2015 to April 2015 of which 247 met the inclusion criteria. The target sample size of 246 for the study was achieved. Demographic characteristics (age and sex), comorbidities, duration of treatment for hypertension, hypertensive drugs prescribed and other drugs prescribed at the last visit were recorded and analyzed. The BP readings at diagnosis and at the last visit were also recorded and analyzed.

4.1 Demographic characteristics of patients

Most (87.4%) of the patients sampled were female with 12.6% being male. The mean age of hypertensive patients was 55.8 years with a range of between 21 and 82 years. The mean age for males was 55.2 years while that of females was 55.9 years. Most of the study population was in the age group 40-59 years at 44.1% with those in the age group 60-79 being 43.3%. Table 4.1 below shows age and sex distribution among the study population.

Table 4.1: Age and sex distribution of hypertensive patients (N=247)

Characteristic	n (%)	Mean (SD)	Median (Range)
Sex			
Male	31 (12.6)		
Female	216 (87.4)		
Age (years)		55.8 (12.5)	58 (21,82)
Female		55.9 (12.4)	
Male		55.2 (13.5)	
Age group (years)			
20-39	28 (11.3)		
40-59	109 (44.1)		
60-79	107(43.3)		
≥80	3(1.2)		

4.2 Comorbidities present

Diabetes was the most common comorbidity present in 36.8% of the patients. Five (2%) of the patients had cardiovascular disease. Over half (56.2%) of the patients did not have any comorbidity present as shown in Table 4.2 below.

Table 4.2: Comorbidities present in hypertensive patients

Comorbidity	n	%
Diabetes	91	36.8
Cardiovascular disease	5	2.0
Peripheral neuropathy	6	2.4
Asthma	4	1.6
HIV/AIDS	1	0.4
Arthritis	1	0.4
None	139	56.2

4.3 Treatment duration

The Figure 4.1 below illustrates treatment duration in years observed among the patients. Most (72.1%) of the patients had been in treatment for 1 to 5 years.

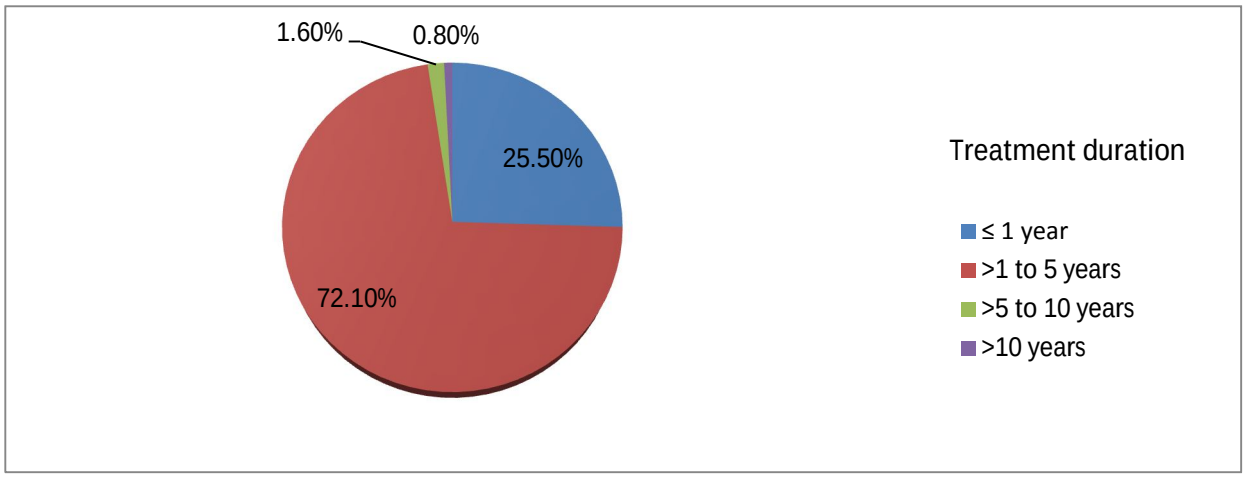

Figure 4.1: Treatment duration of hypertensive patients.

4.4 Blood pressure levels

Mean systolic blood pressure at diagnosis was found to be 155mmHg among the hypertensive patients while that at the last visit was 141 mmHg showing a reduction. At diagnosis, mean diastolic blood pressure was 91 mmHg and 83 mmHg at the last visit. Patients were categorized depending on their blood pressure levels both at diagnosis and at the last visit as shown in the Table 4.3 below and Figure 4.2 using the JNC-7 classification of hypertension (1). The classification was as follows: Normal BP (SBP less than 120 mmHg and DBP less than 80 mmHg), Prehypertension (SBP between 120 mmHg and 139 mmHg or DBP between 80 mmHg and 89 mmHg), stage 1 hypertension (SBP between 140 mmHg and 159 mmHg or DBP between 90 mmHg and 99 mmHg) and stage 2 hypertension (SBP ≥ 160 mmHg or DBP ≥ 100 mmHg). Isolated Systolic Hypertension was considered as SBP ≥ 140 mmHg and DBP < 90 mmHg.

Table 4.3: Distribution of blood pressure levels among hypertensive patients

Description	At Diagnosis	At the last visit	P-value
Systolic blood pressure (mmHg)			
Mean (SD)	155 (20.4)	141 (20.5)	**<0.001***
Median (Range)	151 (101,230)	138 (97,210)	
Diastolic blood pressure (mmHg)			
Mean (SD)	91 (10.7)	83 (10.5)	**<0.001***
Median (Range)	90 (62,123)	83 (52,111)	
Staging n (%)			
Normal BP	0 (0.0)	18 (7.3)	**<0.001***
Prehypertension	27 (11.0)	96 (38.9)	
Stage 1 hypertension	115 (46.5)	86 (34.8)	
Stage 2 hypertension	105 (42.5)	47 (19.0)	
Isolated Systolic Hypertension n (%)	90 (36.4)	67 (27.1)	**<0.001***
Stage 1 ISH	58 (23.5)	43 (17.4)	**<0.001***
Stage 2 ISH	32 (13.0)	24 (9.7)	

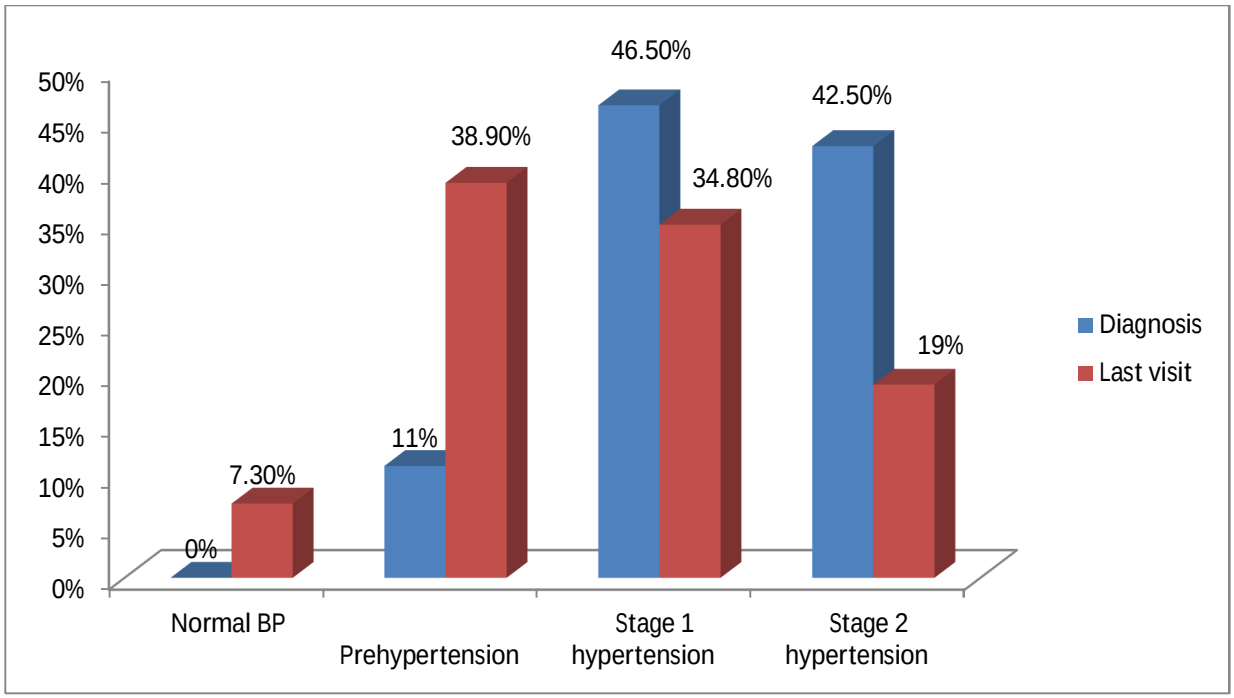

Figure 4.2: Hypertension staging at diagnosis and at the last visit.

At diagnosis, most patients were in stage 1 hypertension at 46.5% while 11% were prehypertensive. Those in stage 2 hypertension were 42.5% while 90 (36.4%) had isolated systolic hypertension. At the last visit, 18 (7.3%) were at normal blood pressure levels while 38.9% (96) were prehypertensive. Nineteen percent (47) of the hypertensive patients were still at stage 2 hypertension. It was noted that there was a statistically significant reduction in mean blood pressures (P=<0.001). The number of patients in stage 1 and stage 2 hypertension also reduced significantly from diagnosis to the last visit (P=<0.001). It was also noted that the number of patients with isolated systolic hypertension reduced significantly from diagnosis to the last visit (P=<0.001).

4.5 Prescribing patterns

The antihypertensive drugs and other concurrent drugs prescribed were classified into their pharmacological classes and medications in each class and their frequencies and percentages calculated.

4.5.1 Prescribing patterns of antihypertensives

The most frequently prescribed class of antihypertensives was ACE inhibitors at 48.2% of total prescriptions followed by thiazide diuretics at 40.5% as shown in Table 4.4. Among specific antihypertensives, Enalapril was the most commonly prescribed drug at 48.2% with Hydrochlorthiazide being the second most prescribed at 40.5%. The least prescribed drugs were Telmisartan with only 1 patient on the drug and Methyldopa and Hydralazine at 0.8%.

Table 4.4: Antihypertensive drug classes and specific medications for hypertensive patients

Class and drug	n	%
ACE inhibitors	**119**	**48.2**
Enalapril	119	48.2
ARBs	**67**	**27.1**
Losartan	66	26.7
Telmisartan	1	0.4
CCBs	**64**	**26.0**
Nifedipine	29	11.7
Amlodipine	35	14.3
BBs	**71**	**28.7**
Atenolol	64	25.9
Carvedilol	4	1.6
Propranolol	3	1.2
Thiazide diuretics	**100**	**40.5**
Hydrochlorthiazide	100	40.5
Other diuretics	**12**	**4.8**
Furosemide	7	2.8
Spironolactone	5	2.0
Miscellaneous	**4**	**1.6**
Methyldopa	2	0.8
Hydralazine	2	0.8

ACE= Angiotensin converting enzyme, ARBs= Angiotensin receptor blockers, BBs= Beta blockers, CCBs= Calcium channel blockers

4.5.2 Number of antihypertensives prescribed

Figure 4.3 below shows the number of antihypertensives prescribed per prescription where the highest percentage was a 2-drug regimen at 43.7% with almost a similar number in monotherapy at 40.5%. 4-drug regimens were the least prescribed at 0.8%.

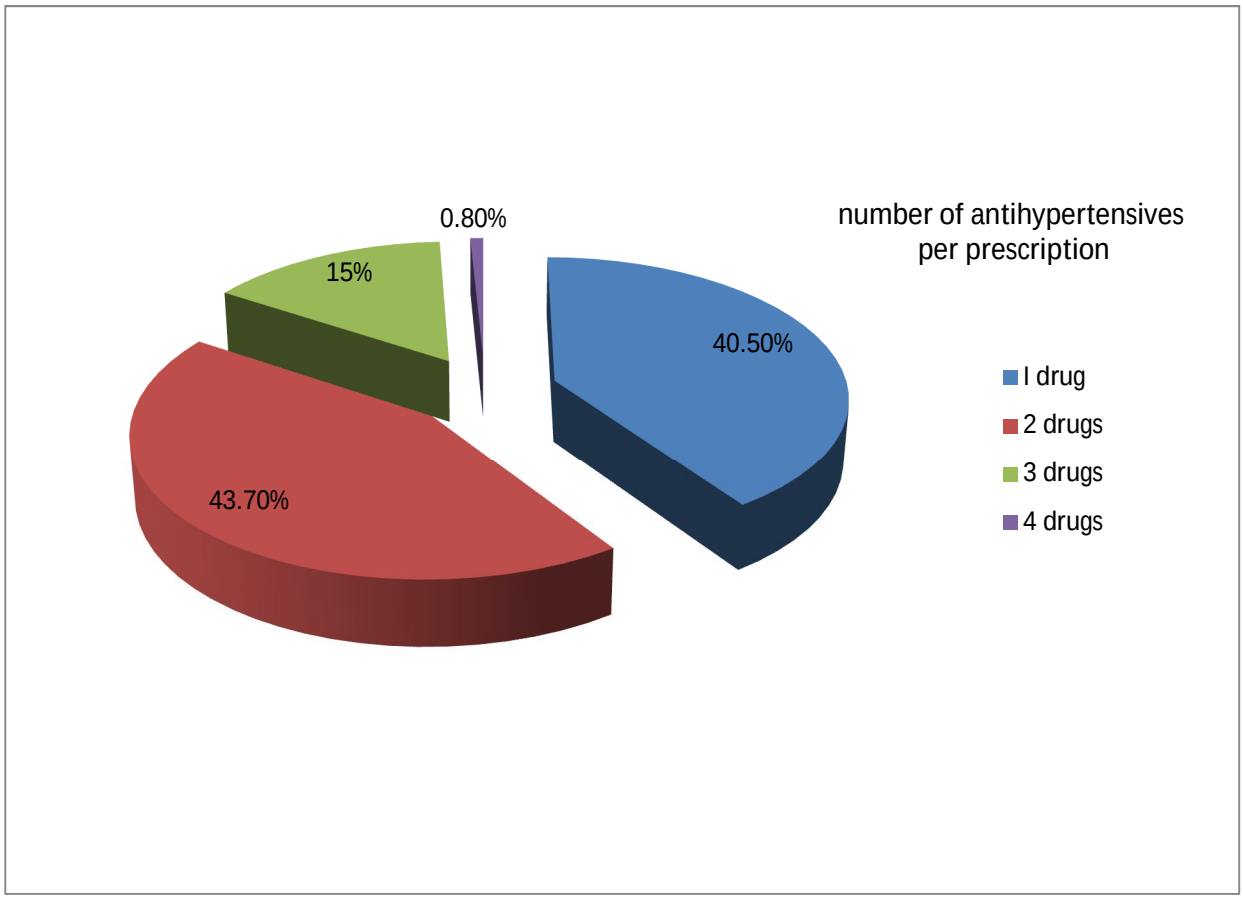

Figure 4.3: Number of antihypertensives prescribed per prescription for hypertensive patients.

4.5.3 Specific regimens used

The most commonly prescribed regimen was monotherapy with an ACE inhibitor at 20.2% followed by a combination of an ACE inhibitor with a thiazide diuretic at 14.2%. Table 4.5 shows the frequency and percentage of various regimens used. Among the monotherapy, CCBs were the least prescribed at 3.2% while 2-drug combination therapies of a CCB and a Beta Blocker and a CCB and a Thiazide diuretic being the least prescribed at 2.4%.

Table 4.5: Specific regimens of antihypertensives prescribed for hypertensive patients

Regimen	n	%
Monotherapy		
CCB	8	3.2
Thiazide diuretic	9	3.6
ACE inhibitor	50	20.2
ARB	21	8.5
Beta blocker	11	4.5
2-drug combination therapy		
CCB + Thiazide diuretic	6	2.4
CCB + ACE inhibitor	12	4.9
CCB + ARB	11	4.5
CCB + BB	6	2.4
Thiazide diuretic + ACE inhibitor	35	14.2
Thiazide diuretic + ARB	12	4.9
Thiazide diuretic + BB	15	6.1
3-drug combination therapy		
CCB + ACE inhibitor + Thiazide diuretic	3	1.2
CCB + ARB + Thiazide diuretic	2	0.8
CCB + BB + Thiazide diuretic	5	2.0
CCB + BB + ACEI	3	1.2
CCB + BB + ARB	2	0.8
BB + Thiazide diuretic + ACEI	7	2.8
BB + Thiazide diuretic + ARB	7	2.8

ACE= Angiotensin converting enzyme, ARB= Angiotensin receptor blocker, BB= Beta blocker, CCB= Calcium channel blocker

4.5.4 Prescribing patterns of co-medications prescribed

Medications prescribed concurrently with antihypertensives **at the last visit** were as shown in Table 4.6. Metformin and glibenclamide were the most commonly prescribed drugs at 28.7% and

23.1% respectively. The least prescribed were glimepiride, naproxen and diclofenac at 0.4% each.

Table 4.6: Co-medications prescribed for hypertensive patients

Drug	n	%
Antidiabetics		
Metformin	71	28.7
Glibenclamide	57	23.1
Insulin	13	5.3
Glimepiride	1	0.4
Statins		
Atorvastatin	11	4.4
Antiplatelets		
Aspirin	22	8.9
NSAIDs		
Meloxicam	14	5.7
Diclofenac	1	0.4
Naproxen	1	0.4
Antiasthmatics		
Salbutamol inhaler	2	0.8
Salbutamol tablets	2	0.8
Antihistamines	6	2.4
Antibiotics	8	3.2
Supplements (vitamins)	13	5.3

NSAIDs= Non-steroidal anti-inflammatory drugs

4.5.5 Prescriber designation.

The Figure 4.4 shows distribution of the various prescribers of the prescriptions obtained. Most of the prescribing was done by medical officers at 93.1% with the least being done by clinical officers at 2.4%.

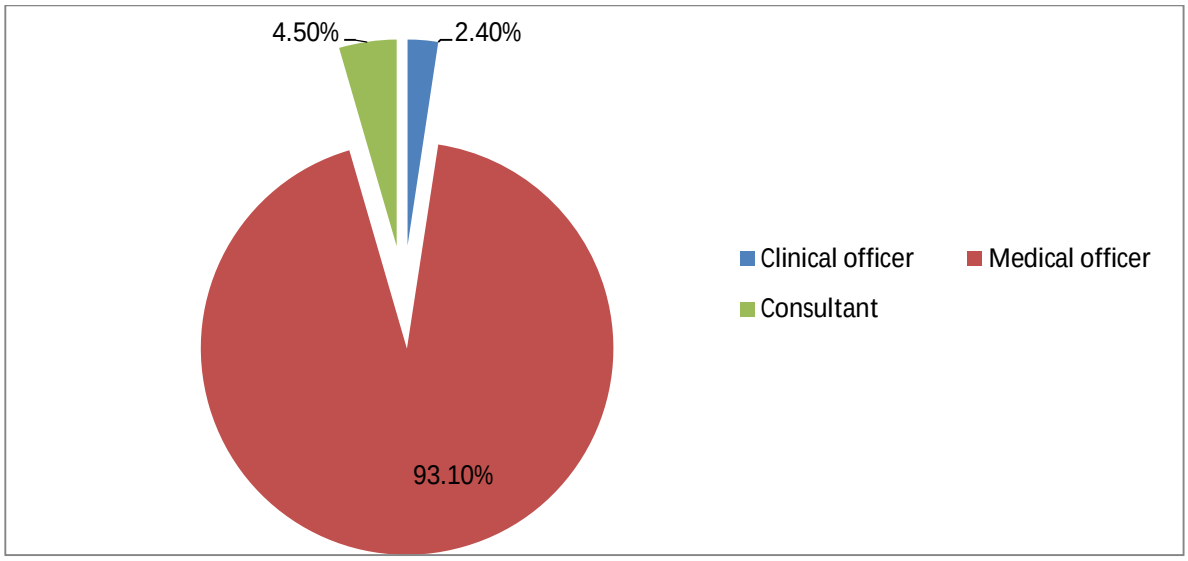

Figure 4.4 Prescriber designations

4.6 Adherence to JNC-8 guidelines

Predetermined criteria were used to compare prescribing among the hypertensives to JNC-8 guidelines as shown in Table 4.7. It was observed that only 60 (45.1%) of the study population was treated for Stage 1 hypertension according to the guidelines. However, all patients were given appropriate drugs for compelling indications while almost all at 96.4% and 95.4% were given appropriate doses and appropriate concurrent drugs respectively. Majority (75.2%) of the patients were treated appropriately for Stage 2 hypertension.

Most of the deviations from the JNC-8 recommendations were observed in management of Stage 1 hypertension where hypertensive patients who had diabetes were put on an ACEI or an ARB as first choice drug in management. Other deviations included being on more than two drugs in Stage 1 hypertension and use of regimens that did not contain the recommended classes, either a CCB or a thiazide diuretic. Deviations in treatment of Stage 2 hypertension included prescribing only one agent. Cases of use of inappropriate concurrent drugs were mostly observed in patients who had been prescribed non-steroidal anti-inflammatory drugs like meloxicam and antidepressants like amitriptyline and those on salbutamol for treatment of asthma.

Table 4.7: Adherence to JNC-8 guidelines by prescriptions

Criteria	Frequency	%
Use of 1 or 2 agents in stage 1 hypertension which include a calcium channel blocker or a thiazide diuretic	60	45.1
Use of two or more agents in stage 2 hypertension	85	75.2
Use of appropriate drugs for compelling indications	100	100
Use of appropriate dosing	238	96.4
Use of appropriate concurrent drugs	145	95.4

4.7 Blood pressure control

Of the 247 patients sampled, 114 (46.2%) had their BP controlled at the last visit while 53.8% had uncontrolled BP. Analysis of prescribing patterns by use of different drug combinations showed no statistically significant difference between those with uncontrolled BP and those with controlled BP as shown in Table 4.9 (P=0.659). The number and proportion of patients with controlled BP and uncontrolled BP were not significantly different suggesting other factors could have been responsible for poor control of BP in the latter group.

A bivariate analysis of the association between BP control and other study variables was carried out as shown in Table 4.8. Sex, number of antihypertensives prescribed and being on a beta blocker were found to have a statistically significant influence on blood pressure control. Females were found to be 2.4 times more likely to have uncontrolled blood pressure compared to males (P=0.028). The odd ratios of having uncontrolled blood pressure increased with increasing number of antihypertensives prescribed up to a 3-drug regimen where those on 3 drugs were 2.8 times more likely to have uncontrolled blood pressure compared to those on 1-drug regimen (P=0.011). This is in contrast to the expected finding that increasing the number of antihypertensives in those with poor BP on monotherapy would reduce the BP hence increase the odds of having adequate BP control. Those on a regimen containing a beta blocker were also found to be more likely to have uncontrolled blood pressure (OR 1.8, P=0.028) compared to those without a beta blocker in their regimen. Other variables like age, treatment duration, being on a thiazide diuretic, a CCB, an ACEI or an ARB or having diabetes were not found to statistically influence blood pressure control.

Table 4.8: Bivariate analysis of the association between blood pressure control and other study variables

Variable	Total	Blood pressure controlled n (%)	Blood pressure uncontrolled n (%)	OR(95% CI)	P value
Sex					
Male	31	20 (64.5)	11 (35.5)	1	
Female	216	94 (43.5)	122 (56.5)	2.4 (1.1-5.2)	**0.028***
Age					
<60 years	137	64 (46.7)	73 (53.3)	1	
≥60 years	110	50 (45.5)	60 (54.5)	1.1 (0.6-1.7)	0.843
Treatment duration					
1 year	63	30 (47.6)	33 (52.4)	1	
>1 year	184	84 (45.7)	100 (54.3)	1.1 (0.6-1.9)	0.787
Number of antihypertensives					
1	100	57 (57)	43 (43)	1	
2	108	44 (40.7)	64 (59.3)	1.9 (1.1-3.4)	**0.019***
3	37	12 (32.4)	25 (67.6)	2.8 (1.2-6.2)	**0.011***
4	2	1 (50)	1 (50)	1.3 (0.1-22.1)	0.844
On a thiazide diuretic	100	43 (43)	57 (57)	1.2 (0.7-2.1)	0.412
Yes	147	71 (48.3)	76 (51.7)	1	
No					
On a CCB					
Yes	64	27 (42.2)	37 (57.8)	1.2 (0.7-2.2)	0.460
No	183	87 (47.5)	96 (52.5)	1	
On an ACE inhibitor					
Yes	119	60 (50.4)	59 (49.6)	0.7 (0.4-1.2)	0.195
No	128	54 (42.2)	74 (57.8)	1	
On an ARB					
Yes	67	25 (37.3)	42 (62.7)	1.6 (0.9-2.9)	0.089
No	180	89 (49.4)	91 (50.6)	1	
On a Beta blocker					
Yes	71	25 (35.2)	46 (64.8)	1.8 (1.1-3.3)	**0.028***
No	176	89 (50.6)	87 (49.4)	1	
Diabetic					
Yes	91	41 (45.1)	50 (54.9)	1.1 (0.6-1.8)	0.791
No	156	73 (46.8)	83 (53.2)	1	

ACE= Angiotensin converting enzyme, ARB= Angiotensin receptor blocker, CCB= Calcium channel blocker, *p-values statistically significant.

Multivariable logistic regression analysis was then carried out to identify variables that predicted BP control using predictor variables with p-values ≤ 0.2 from the bivariate analysis. It was found that only the sex of the patient significantly influenced whether their blood pressure would be

controlled or not (P=0.046). Only 4.4% of the outcome (uncontrolled BP) was explained by a multiple logistic regression model containing those variables.

Table 4.9: Blood pressure control and drug combinations

Regimen	Total	BP uncontrolled n (%)	BP controlled n (%)	P-value
Monotherapy				
CCB	8	3 (2.6)	5 (4.7)	0.659
Thiazide diuretic	9	4 (3.5)	5 (4.7)	
ACE inhibitor	50	20 (28.3)	30 (17.5)	
ARB	21	11 (9.7)	10 (9.4)	
Beta blocker	11	5 (4.4)	6 (5.7)	
2-drug combination therapy				
CCB + Thiazide diuretic	6	2 (1.8)	4 (3.8)	
CCB + ACE inhibitor	12	7 (6.1)	5 (4.7)	
CCB + ARB	11	6 (5.3)	5 (4.7)	
CCB + BB	6	4 (3.8)	2 (1.9)	
Thiazide diuretic + ACEI	35	17 (14.9)	18 (17.0)	
Thiazide diuretic + ARB	12	8 (7.0)	4 (3.8)	
Thiazide diuretic + BB	10	6 (5.3)	4 (3.8)	
3-drug combination therapy				
CCB + ACEI + Thiazide diuretic	3	2 (1.8)	1 (0.9)	
CCB + ARB + Thiazide diuretic	2	2 (1.8)	0 (0.0)	
CCB + BB + Thiazide diuretic	5	4 (3.5)	1 (0.9)	
CCB + BB + ACEI	3	1 (0.9)	2 (1.9)	
CCB + BB + ARB	2	2 (1.8)	0 (0.0)	
BB + Thiazide diuretic + ACEI	7	5 (4.4)	2 (1.9)	
BB + Thiazide diuretic + ARB	7	5 (4.4)	2 (1.9)	

ACEI= Angiotensin converting enzyme inhibitor, ARB= Angiotensin receptor blocker, BB= Beta blocker, CCB= Calcium channel blocker

4.8 Cost of drugs

The monthly acquisition cost of various antihypertensives prescribed was calculated as a function of the monthly dosage and unit drug price for all patients. The price of the drugs used was sourced from the July 2015 MEDS price list (Appendix 5). The total cost obtained for all drugs and all patients was divided by the number of patients sampled to get an average monthly acquisition cost per patient in Kenyan Shilling (Ksh). An average monthly acquisition cost per patient was calculated to be Ksh.87. The average monthly acquisition costs per prescription for individual drugs were also calculated using the number of prescriptions containing the particular drug as the denominator. The various costs obtained are outlined in Table 4.10 below.

Table 4.10 Average monthly acquisition costs per prescription for hypertensive patients

Drug	Average monthly acquisition cost per prescription of the drug (Ksh)
CCBs	**136**
Amlodipine 5mg	119
Nifedipine retard 20mg	17
Beta blockers	**378**
Atenolol 50mg	40
Carvedilol 6.25mg	303
Propranolol 40mg	35
ACE inhibitors	**78**
Enalapril 5mg	24
Enalapril 10mg	54
ARBs	**84.50**
Losartan	84.50
Diuretics	**137**
Furosemide 40mg	15
Hydrochlorthiazide 50mg	8
Spironolactone 25mg	114
Miscellaneous	
Hydralazine 25mg	297
Methyldopa 250mg	121.50

ACE= Angiotensin converting enzyme, ARB= Angiotensin receptor blocker, CCB= Calcium channel blocker

It was found that carvedilol 6.25mg was the most costly drug per prescription at an acquisition cost of Ksh. 303 per month per prescription of the drug. This was followed by hydralazine 25mg at Ksh. 297 though this is not a routine drug for hypertension. The cheapest drug to acquire was hydrochlorthiazide 50mg at Ksh. 8 per month per prescription.

4.9 Barriers to adherence to hypertension guidelines as reported by prescribers

Of the 5 prescribers interviewed, 3 were medical officers, one clinical officer and one consultant physician as shown in Table 4.11 below. The average duration of practice of the prescribers was 5.3 years. The mean age of the prescribers was 30 years. The prescribers interviewed reported that they saw 10 to 50 hypertensive patients per clinic day.

Table 4.11: Characteristics of prescribers interviewed

Interview Code	Sex	Age (Years)	Duration of practice (Years)	Patients seen per day at the MOPC (Range)
R1	**F**	**29**	**5**	**40**
R2	**M**	**26**	**2**	**30-50**
R3	**F**	**28**	**2.5**	**20-40**
R4	**F**	**28**	**2**	**20-40**
R5	**M**	**39**	**15**	**10-15**

Knowledge and application of treatment guidelines

All prescribers reported that hypertension staging is one of the bases they use for drug selection in management of hypertension. Others reported that presence of comorbidities and availability of drugs also formed a basis for drug selection.

The prescribers reported knowing of JNC-8, JNC-7 and national guidelines for management of hypertension. Three of the prescribers said that they used JNC-8 guidelines in managing patients while one still used the JNC-7 and another used the national guidelines.

All the prescribers reported that they had been trained on these guidelines with most of the prescribers (4) reporting to have been trained via a professional course. Two of them had

received continous medical education (CME) while one had been trained via a workshop. The prescribers demonstrated a degree of knowledge on what the guidelines recommended with most mentioning management according to hypertension staging and comorbidities.

They all agreed that the guidelines available were useful in their practice with positive results being seen and ease of use. They also agreed that the guidelines were applicable in their setting with medications prescribed being available.

Deviation from the treatment guidelines

Most of the prescribers (4) reported that they did not deviate from the treatment guidelines and that they were satisfied with the outcomes. They said that with good adherence to medications prescribed, good blood pressure control was achieved in most cases. Only one interviewee did not share these sentiments reporting that the outcomes were poor with poor BP control observed.

"..No. Patients are rarely well controlled."(Interviewee 5)

Challenges in management of hypertension and recommendations

The most commonly reported challenge faced by the prescribers when managing hypertension was poor adherence to medications by patients. Other challenges included poor follow up by patients and costly medications that the patients could not afford and sometimes the medicines were out of stock. They suggested counselling on adherence to medications, availability of subsidized medicines and upgrading of laboratories to handle investigations as some of the ways of overcoming these challenges.

Additional recommendations included consistent supply of medicines in the hospital pharmacy at subsidized prices, support groups for hypertensive patients, proper Non-Communicable Diseases (NCD) policy, free counselling for patients, improving laboratory and imaging services at public facilities and standardised forms for review.

CHAPTER 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

The objectives of this study were to determine prescribing patterns of antihypertensives, level of compliance to JNC-8 treatment guidelines, explore factors influencing blood pressure control, determine monthly acquisition costs of various antihypertensive agents by the hospital and explore on some of the barriers to adherence to hypertension treatment guidelines.

5.1 Characteristics of hypertensive patients

The ratio of males to females in this study was found to be 1:7 which is extremely high but similar studies in other parts of the country have found more women than men on treatment for hypertension (22–24,41). In a study carried out in Mombasa in 2010, it was found that 16% of men and 39% of women were on treatment for Hypertension (22). A similar study on hypertensive patients in a regional referral hospital in Central Kenya found that 73% of patients sampled were female (23). This gender difference can be attributed to differences in health seeking behavior among males and females with women more likely to visit health facilities compared to men (42).

The mean age was found to be 55.8 years for all patients. This is consistent with another study on hypertensive patients in a national referral hospital in Kenya where the mean age was found to be 57 years (34). The most common comorbidity among the hypertensive patients was diabetes with a prevalence of 37%. A study carried out in Central Kenya found prevalence of diabetes among hypertensive patients at 42% (23). It has been found that hypertension and diabetes frequently coexist due to similar range of risk factors (44).

5.2 Prescribing patterns and compliance to treatment guidelines.

ACEIs were the most commonly prescribed class of antihypertensives at 48% followed by thiazide diuretics at 40% specifically hydrochlorthiazide. The high use of ACEIs was also observed among the monotherapy regimens where only an ACEI was prescribed in 20% of all prescriptions reviewed. This could be due to prescribers applying recommendations by the Kenyan treatment guidelines which recommend use of an ACEI in diabetic hypertension patients either as monotherapy in Stage 1 hypertension management or in combination with other classes

of antihypertensives in Stage 2 hypertension management (27). Use of thiazide diuretics as first-line therapy has been recommended in most hypertension treatment guidelines published worldwide especially in blacks. The observed high use of thiazide diuretics in this study was therefore consistent with these recommendations.

Most patients were on monotherapy and 2-drug regimens at 40.5% and 43.7% respectively. Combination therapies accounted for approximately 60% of all prescriptions. This finding was consistent with results of a similar study carried out in India in 2012 which found a prevalence of 55% prescribing of combination therapies (45). The high rate of monotherapy prescribing may be explained by clinical inertia where prescribers are reluctant to intensify therapy due to factors like tolerance to medications and high cost of medicines.

It was found that the most commonly prescribed con-current medications were antidiabetics with metformin and glibenclamide present at 29% and 23% of all prescriptions reviewed, respectively. This can be explained by the high prevalence of diabetes among the hypertensive patients at 37%. It was also observed that low dose aspirin was prescribed at 9% of all prescriptions. Aspirin is recommended in secondary prevention of CV outcomes when BP is well controlled (19).

Compliance to treatment guidelines (JNC-8 for this study) on average was at 82%. This means that most prescribers adhered to the JNC-8 recommendations on choice of drugs for specific hypertension staging and compelling indications, correct dosing and use of appropriate concurrent drugs. A similar study carried out at Kenyatta National Hospital in Kenya that assessed rational prescribing of antihypertensives found adherence rates of 80% which is similar to the findings in this study though the comparison criteria was different (34). Deviations from the guidelines were mostly observed in treatment of Stage 1 hypertension where only 45% of patients were treated according to the recommendations of JNC-8.

5.3 Factors affecting blood pressure control

In this study, a 46% BP control rate was observed. This finding is higher than those found by other studies carried out around the country. A 2009 study at the KNH found a low rate of 26% of BP control among hypertensive patients which was replicated by a study in Mombasa which found BP control levels of 25% among hypertensive patients on treatment (22,41). A study

carried out at Nyeri Provincial General Hospital in 2013 also found low levels of BP control of 33% among hypertensive patients on follow up at the hospital (23). Poor control of BP in this 2013 study was attributed to old age, having diabetes and being on three or more drugs. The better BP control rate in the current study may be explained by the high rate of adherence to the latest hypertension treatment guidelines (JNC-8 for this study) as demonstrated by findings from the study of 82% compliance rate.

Predictors of poor blood pressure control in this study were found to be sex, number of antihypertensives and being on a beta blocker. However, on logistic regression, only the sex of the patient had a statistically significant influence on blood pressure control with females being more likely to have poor blood pressure control. This finding is in contrast to findings from a review carried out in 2013 of African studies on prevalence, awareness and control rates which showed better control rates in women than men in Africa (38). It should be noted, however, that the sample in this study included only a proportion of 13% male subjects. The finding that females were significantly more likely to have poor blood pressure control could be due to the fact that the majority of subjects were in fact female. Being on a multi-drug regimen was expected to increase the odds of having adequate blood pressure control. The result of poorer BP control in those patients on more than one drug found in this study could be due to recently prescribed multi-drug regimens that had not yet improved BP levels.

A study carried out in 2014 on predictors of poor BP control at a regional referral hospital in Kenya showed that old age, diabetes, and the use of three or more drugs were significant predictors of poor blood pressure control (23). These findings were not replicated in this study. Analysis showed that only 4.4% of the outcome (uncontrolled BP) was explained by the multiple logistic regression model used in this study. This could be due to absence of key predictor factors that may have influenced blood pressure control. These factors include adherence to prescribed medications, proper lifestyle changes, patient knowledge on drugs and their condition among others.

5.4 Medication cost implications

The cost of medications remains a major challenge in poor-resource settings especially in Sub-Saharan Africa since most patients rely on out-of-pocket funding for healthcare. Average monthly acquisition costs of hypertensive medications per prescription by the hospital were

calculated in this study. The lowest cost was found to be that of hydrochlorthiazide, a thiazide diuretic, at Ksh.8 per month per prescription. This price seems affordable to the hospital hence also affordable to the patients. Thiazide diuretics have been found to be the cheapest and most cost-effective drugs among the various antihypertensive drug classes in studies carried out in Nigeria (17,45). This has been supported by guidelines which also recommend use of thiazide diuretics alone or in combination for effective blood pressure control especially in blacks (20).

Among the antihypertensives, carvedilol, hydralazine, methyldopa, amlodipine and spironolactone were found to be the most costly to acquire with monthly acquisition costs per prescription of more than Ksh. 100. It should be noted that among these, hydralazine, methyldopa and spironolactone are not routine drugs for management of hypertension hence cost implications would not be as significant to the hospital and patients. Other costly drugs like carvedilol, amlodipine have cheaper alternatives in the same class which can be substituted to reduce acquisition costs to the hospital and patients.

5.5 Compliance by prescribers to treatment guidelines

The interview responses from the prescribers generally revealed that the prescribers were aware and had undergone some form of training on the latest guidelines for hypertension management. However, this awareness and knowledge did not fully translate into application of the guidelines in treatment of hypertensive patients at the hospital since results showed that the level of adherence to the JNC-8 guidelines especially in treatment of stage1 hypertension was relatively low. It is speculated that one of the reasons for non-adherence could be clinical inertia where prescribers are unwilling to intensify treatment in patients with uncontrolled hypertension and consideration of patient circumstances like other CV risk factors, concurrent disease or other medications (47).

5.6 Conclusion

Prescribing patterns of antihypertensive drugs in this study were consistent with treatment guidelines where most patients were on ACEIs and Thiazide diuretics. Adherence to latest treatment guidelines was found to be at 82% though deviations in treatment of stage 1 hypertension were found to be substantial. This high level of adherence may have been responsible for the higher than usual level of BP control observed at 46%. The number and proportion of drug combinations used in those with controlled and those with uncontrolled BP

were found to be no different suggesting other factors may have been responsible for poor control of BP.

Hydrochlorthiazide was found to be the cheapest among all antihypertensives prescribed consistent with other studies and with recommendations from the guidelines that thiazide diuretics are the most cost effective drugs in hypertension treatment. Prescribers' awareness and knowledge about the latest clinical guidelines as observed from the interviews did not fully translate into clinical practice as evident from the compliance level to treatment guidelines.

5.7 Limitations of the study

This study used in-depth interviews from prescribers in order to corroborate quantitative data on compliance to treatment guidelines. However, the retrospective data used for this study from patients' records may not always be accurate and complete. Only one study site was considered for this study due to cost and time limitations which may not be representative of other hospitals in the region or the country.

Only limited data which include prescription data and comorbidity data was used to examine adherence to treatment guidelines which may not always be reliable. Implicit criteria may be required to assess if other patient factors were considered apart from blood pressure levels and comorbidities when choosing drugs for treatment. Some factors affecting control of BP were not considered in this study including adherence to treatment, accessibility of prescribed drugs, awareness and level of understanding of the patient concerning need for proper BP control.

5.8 Recommendations

5.8.1 Policy changes

1. The Kenyan National guidelines on treatment of various conditions were last updated in 2009. There is need for an urgent update of these guidelines and if possible, a guideline specifically for management of hypertension in consideration of local settings.
2. Regular training of health workers dealing with hypertensive patients is required to ensure that they keep up to date with changing trends with emerging new evidence for management of these patients.
3. Some recommendations as reported by prescribers include consistent supply of medicines in the hospital pharmacy at subsidized prices, support groups for hypertensive patients,

proper Non-Communicable Diseases (NCD) policy, free counselling for patients, improving laboratory and imaging services at public facilities and standardised forms for review. These will enhance delivery of optimal care to hypertensive patients by the health workers.

5.8.2 Further research

1. Studies on prescribing patterns of chronic diseases such as hypertension have rarely been carried out in Kenya. There is need for more studies to ensure that prescribing is carried out according to the latest clinical guidelines.
2. Other factors that influence blood pressure control like adherence to prescribed drugs, lifestyle changes, comorbidities and other patient factors should be investigated.
3. Affordability of medicines to the patients by comparing cost of acquisition of drugs by the patients and their income levels can be investigated since affordability is a key factor in adherence to medications.
4. Studies on why there is gender differences among hypertensive patients need to be carried out by sampling larger populations.
5. A study focusing on patients' views on the condition, reasons for non-adherence, affordability of medications need to be carried out where the interviews focus on the patient.

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APPENDICES

APPENDIX 1: DATA COLLECTION FORM

Date: _____ Outpatient Number_____ Form Number_____

5.1.1 Demographic characteristics

Age (years) …….

Sex Male ☐

Female ☐

Height (cm) …….....

Weight (Kg) ……..

5.1.2 Comorbidities present and their duration in years (Tick if present)

Diabetes ☐ ……

Renal problems ☐ ……

Cardiovascular disease ☐ …….

Others (specify)

1. …….. …….
2. …….. …….
3. …….. …….
4. …….. …….
5. …….. …….

5.1.3 Hypertension management

Date of diagnosis _____

Number of years on hypertensive treatment _____

BP reading at diagnosis _____

Latest BP reading _____

Antihypertensive drugs prescribed (last visit only)

Drugs	Dosage	Frequency

Other drugs prescribed (last visit only)

Drugs	Dosage	Frequency

Designation of prescriber (Tick as appropriate)

Clinical Officer ☐ Medical officer ☐ Consultant ☐

APPENDIX 2: INTERVIEW GUIDE FOR PRESCRIBERS

SECTION I: BIODATA

Age (years) …….

Sex Male ☐

Female ☐

Current designation Clinical officer ☐

Medical officer ☐

Consultant ☐

Duration of Practice (years) ……..

SECTION II: HYPERTENSION MANAGEMENT

1. How many patients do you see per clinic day? (Give range) ……..
2. What do you base your drug selection for hypertension management on?

   Age ☐

   Comorbidities ☐

   Hypertension staging ☐

   Others (Specify)……
3. Which hypertension management guidelines do you know of? (State)

   ……

   ……

   ……

4. Which guidelines do you use? (State)

   ……

   ……

5. Have you received training on these guidelines? Yes ( ) No ( )
6. How was the training done?

   CME ☐

   Workshop ☐

   Professional course ☐

   Others (Specify) ……

7. What do the guidelines generally recommend? (Briefly explain)

   ……

   ……

   ……

8. The guidelines available are useful in my practice.

   Strongly agree ( )

   Agree ( )

   Disagree ( )

   Strongly disagree ( )

9. Briefly elaborate on your response above

   ……

   ……

10. Are they applicable in your setting? Yes ( ) No ( ) (Briefly explain)

    ……

    ……

11. Do you deviate from these guidelines? Yes ( ) No ( )
12. If yes above, briefly explain the kinds of deviations and reasons for deviation.

    ……

    ……

    ……

……

……

13. Are you satisfied with the outcomes of current hypertension management?

Yes ( ) No ( ) (Briefly explain your response)

……

……

……

14. What challenges do you face during management of hypertensive patients? (List)

……

……

……

15. How do you overcome them?

……

……

……

16. What additional recommendations to inform policy would you make?

……

……

……

……

Thank you for your time.

APPENDIX 3: CONSENT EXPLANATION FORM

Hello, my name is Dr. Jennifer Muthoni Mbui. I am a post graduate student pursuing a degree of Master of Pharmacy in Pharmacoepidemiology and Pharmacovigilance at the School of Pharmacy, University of Nairobi and the principal researcher in this study.

Permission is requested from you to enroll in a study about management of adult hypertensive patients at Ruiru sub-county hospital's Medical Outpatient Clinic. This study involves research whose purpose is to identify prescription patterns of antihypertensives, determine if the prescribing is being carried out according to international standards and the affordability of medicines prescribed. The study is also aimed at exploring some of the barriers associated with compliance to hypertension treatment guidelines. This will take about 30 minutes of your time. If you choose to be in the study, I will ask you some questions regarding use of hypertension treatment guidelines and you will be expected to give responses that are as honest as possible.

There are no foreseeable risks or benefits to you for participating in this study. There is no cost or payment to you. If you have questions while taking part, please stop me and ask. We will do our best to keep your information confidential include removing potential identifiers such as names from data.

If you have questions about this research study, you may contact Dr. Jennifer Muthoni Mbui at 0725211720. If you feel as if you were not treated well during this study, or have questions concerning your rights as a research participant call the KNH/UoN-ERC Chairperson on Tel. No. 2726300 Ext 44102.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to stop. May I continue?

I certify that I have consented the participant (code no.) …….

Researchers name …….

Signature----------Date ----------

APPENDIX 4: CONSENT FORM

PARTICIPANT AGREEMENT

I have fully understood the objectives of this study and hereby sign as a show of my willingness to participate as a volunteer.

Signature……. Date…….

Witnessed by:

Signature……. Date…….

If you have questions about this research study, you may contact Dr. Jennifer Muthoni Mbui at 0725211720. If you feel as if you were not treated well during this study, or have questions concerning your rights as a research participant call the KNH/UoN-ERC Chairperson on Tel. No. 2726300 Ext 44102 or the lead supervisor Dr. M.N. Oluka at 0722604216

APPENDIX 5: COSTS OF SELECTED DRUGS USED IN THE STUDY

Generic name	Dosage form	Price per unit(Ksh)
Amlodipine 5mg	Tablets	2.20
Atenolol 50mg	Tablets	1.00
Carvedilol 6.25mg	Tablets	2.45
Enalapril 5mg	Tablets	0.65
Enalapril 10mg	Tablets	0.90
Furosemide 40mg	Tablets	0.40
Hydralazine 25mg	Tablets	2.20
Hydrochlorthiazide 50mg	Tablets	0.30
Losartan 50mg	Tablets	2.20
Methyldopa 250mg	Tablets	2.85
Nifedipine retard 20mg	Tablets	0.35
Propranolol 40mg	Tablets	0.70
Spironolactone 25mg	Tablets	3.80

Source: MEDS Price guide July 2015

APPENDIX 6: KNH/UoN ERC APPROVAL LETTER

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Ref: KNH-ERC/A/163

9th April, 2015

Dr. Jennifer M. Mbui
Dept. of Pharmacology and Pharmacognosy
School of Pharmacy
University of Nairobi

Dear Dr. Jennifer

Research Proposal: Attributes and Cost of Pharmacotherapy of Adult Hypertensive Patients in a Rural Outpatient Setting in Kenya (P734/12/2014)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 9th April 2015 to 5th April 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director CS, KNH
The Chair, KNH/UoN-ERC
The Dean, School of Pharmacy, UoN
The Chair, Dept. of Pharmacology and Pharmacognosy
Supervisors: Dr. Margaret N. Oluka, Dr. E.M. Guantai, Dr. Kipruto A. Sinei