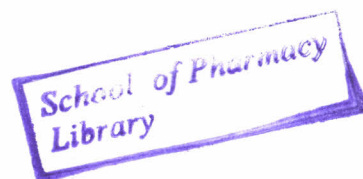


PRESCRIPTION AUDIT OF
ANTIHYPERTENSIVE MEDICATION AT THE
OUTPATIENT PHARMACY IN
KENYATTA NATIONAL HOSPITAL



By

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A dissertation submitted in partial fulfilment of the requirements of the bachelor of pharmacy degree of the University of Nairobi.

OCTOBER 2012

DECLARATION

I hereby declare that this project is my original work and has never been presented for an award of degree in any other institution.

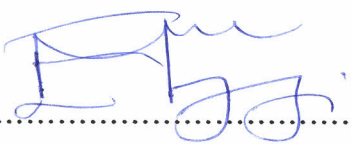
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This research project has been submitted with my approval as the supervisor.

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DEDICATION

I dedicate this project to my family who have always supported me throughout my life.

ACKNOWLEDGEMENT

Special thanks to my supervisor Dr. L. E. M. Mwangangi for his continuous guidance and advice. To all the staff of Pharmacy 15 and Records Department (no.19) in KNH for their assistance and co-operation.

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LIST OF ABBREVIATIONS.

ACEI	Angiotensin converting enzyme inhibitors
ARB	Angiotensin ii receptor blockers
BP	Blood Pressure
CCBs	Calcium channel blockers
CVA	Cerebral vascular accidents
GFR	Glomerular filtration rate
HTN, HT, HPN	Hypertension
IM	Intramuscular
IV	Intravenous
JNC	Joint National Committee
KNH	Kenyatta National Hospital
MAOI	Monoamine oxidase inhibitors
NHANES	National Health and Examination Survey
NSAIDs	Non-steroidal anti-inflammatory drugs
PO	Per oral
UON	University of Nairobi
USA	United States of America
WHO	World Health Organisation

ABSTRACT.

Background: Providing the right medication to the right patient at the right time is a central priority of healthcare. This is done through effective implementation of the World Health Organisation recommendations on rational drug policies. Prescription audits may be useful in generating data on morbidity, which forms the basis for preparing a list of essential medicines and proposing mechanisms necessary for improving prescription practice. It can also minimise overuse and misuse of drugs and plan essential drug selection.

Knowledge of the existing prescription patterns in treatment of essential hypertension can provide useful information for improving clinical practice in this field.

Aim: The aim of this study was to examine the current prescribing patterns of antihypertensive agents in outpatients with hypertension in Kenyatta National Hospital and compare this with the current national and international guidelines.

METHODOLOGY: This was a cross sectional-retrospective study which involved the review of medical records, the collection of statistical data from the records department (no. 19) and a review of prescriptions from outpatient pharmacy (no.15.) at Kenyatta National Hospital. Records were selected by random sampling technique till a sample size of 280 was achieved. The data was then recorded in a data collection form for analysis which was done by SPSS Statistics 17.0.

RESULTS:

Most (79.3%) of the patients were on combination therapy where 43.2% received 2 drugs, 25.7% three drugs and 9.6% received four drugs. A two-drug combination consisting of calcium channel blocker and angiotensin converting enzyme inhibitor was used in 9.6% of patients.

Among the drugs used as monotherapy were angiotensin converting enzyme inhibitors which were used in 30% of patients and represented the majority followed by calcium channel blockers in 28.5%, of the studied population. Vasodilators were the least prescribed in this group of patients.

The most co-morbidity seen in this group of patients was diabetes in about 36.8% of patients followed by renal diseases seen in 5.7% of patients. Angiotensin converting enzyme inhibitors were commonly preferred in these co-morbidities.

CONCLUSION:

This study showed that angiotensin converting enzyme inhibitors are the most preferred first line treatment therapy for hypertension in both monotherapy and combined therapy. The most prescribed antihypertensive agent in this category was enalapril most probably due to its relative affordability and efficacy in a diverse range of patients.

Compliance with the use of international non-proprietary name in prescriptions was poor as some physicians seemed to prefer prescribing using brand names.

CHAPTER ONE

1.1: INTRODUCTION.

A prescription is a healthcare document implemented by a physician and other health care workers in form of instructions that govern the plan of care for an individual patient¹. It may include orders to be performed by a patient, caretaker, nurse, pharmacist or other therapists.

The term prescription is however most commonly used to mean an order to take certain medications. It is designated R_x, an abbreviation of the Latin verb recipe the imperative form of 'recipere' which means 'to take' or 'take thus'. The word prescription from 'pre-' (before) and 'script' (writing, written) refers to the fact that the prescription is an order and should be written before a drug can be prepared or dispensed.

Prescriptions are handwritten or pre-printed forms that are assembled. Pre-printed on the forms is a text that identifies the document as a prescription, the name and address of the prescribing doctor and any other legal requirements such as a registration number. Unique for each prescription is the name of the patient. Each prescription is dated and some legal jurisdictions place a time limit on it. It has legal implications as it may indicate that the prescriber takes responsibility for the clinical care of the patient and in particular for monitoring efficacy and safety. As a legal document, some jurisdictions will mandate the archiving of the original paper prescriptions in the pharmacy, and some jurisdictions may entitle patients to a copy. Retention times vary and can be as long as ten years. After the retention period has passed, privacy legislation may dictate what can be done with the original prescription^[2]. There are strict legislations that have been put in place to regulate writing and use of prescriptions to promote rational drug use.

Rational drug use

Rational use of drugs is an activity that ensures patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community. It ensures therapeutically sound and cost effective drugs are used by the health professionals and consumers^[3].

Rational drug use should fulfil a certain criteria outlined below:

- **Appropriate drug:** The selection of drug should be based on efficacy, safety, suitability, and cost.
- **Appropriate indication:** The decision to prescribe drugs should entirely be based on medical rationale and that drug therapy is an effective and safe treatment.
- **Appropriate patient:** No contraindications exist and the likelihood of adverse reaction is minimal and the drug is acceptable to the patient.
- **Appropriate information:** Patients should be provided with relevant, accurate, important and clear information regarding their conditions and medications that are prescribed.
- **Appropriate monitoring:** The anticipated and unexpected effects of medications should be appropriately monitored.

Irrational drug use can have various consequences to the patient, public, health system and economy. They include reduction in quality of drug therapy that can lead to increased morbidity and mortality, increased risks of unwanted effects, adverse drug reactions and emergence of resistance. Effective intervention for improving rational drug use is essential for all healthcare delivery team^[3].

1.2: LITERATURE REVIEW.

1.2.1 Definition

Hypertension is a cardiovascular disease characterized by elevated blood pressure above arbitrary values considered “normal” for people of similar racial and environmental background. It is also referred to as high blood pressure or shortened to HTN, HT or HPN. Its diagnosis involves at least two measurements; systolic and diastolic, which depends on whether the heart is contracting (systole) or relaxed between beats (diastole). It is normally reported as Systolic Blood Pressure/ Diastolic Blood Pressure mmHg. Normal blood pressure at rest is within the range of 100-140mmHg systolic and 60-90mmHg diastolic. High blood pressure is said to be present if it is persistently at or above 140/90mmHg ^[4].

1.2.2 Epidemiology

According to National Health and Examination survey (NHANES) study, it is estimated that nearly 1 billion people are hypertensive worldwide. In USA it is estimated that 43 million people are taking antihypertensive agents which is nearly 24% of the adult population ^[5]. Susceptibility varies with race (being higher in blacks and lower in whites), age, geographical patterns, gender (more prevalent in males than females), and socioeconomic status ^[4].

1.2.3 Classification

It can be classified as either primary (essential) or secondary hypertension. About 90-95% of cases are primary which means high blood pressure with no obvious underlying medical cause ^[3]. The remaining 5-10% cases are caused by other conditions that affect the kidneys, arteries, heart or endocrine system and are referred to as secondary HTN. Hypertension is a major risk factor for stroke, myocardial infarction, heart failure, arterial aneurysm and chronic renal failure.

Dietary and lifestyle changes can improve blood pressure control and decrease the risks of associated health complications. However, drug treatment is often necessary in people for whom lifestyle changes prove ineffective or insufficient.

Recent classification (JNC7) has grouped hypertension as normal, prehypertension, stage 1 hypertension, stage2 hypertension and isolated systolic hypertension. Isolated systolic hypertension refers to elevated systolic pressure with normal diastolic pressure and is common in the elderly.

Table 1: Classification (JNC7) ^[6] according to American Heart Association (2003).

CLASSIFICATION	Systolic BP(mmHg)	Diastolic BP(mmHg)
Normal	90-119	60-79
Pre-hypertension	120-139	80-89
Stage1 HTN	140-149	90-99
Stage 2 HTN	≥160	≥100
Isolated systolic HTN	≥140	<90

Hypertensive crisis

This is a sudden or sustained diastolic blood pressure of more than 120mmHg. The presence of acute or ongoing end-organ damage characterized by papilloedema, progressive decrease in renal function and evidence of neurological dysfunction constitutes a hypertensive emergency, whereas the absence of such complications is constitutes hypertensive urgency

[7]

1.2.4 Signs and symptoms

There is usually no acute clinical presentation of essential hypertension and hence the disease is usually referred to as a “silent killer”. Most patients are diagnosed as a routine check up during clinic visits. However one could have:-

- Paroxysmal headaches
- Palpitations
- Sweating
- Dizziness
- Weakness
- Polyuria
- Polydipsia
- Intermittent paralysis
- Intermittent claudication of the extremities
- Dysuria
- Nocturia
- Edema
- Nervousness
- Tremors
- Tachycardia ^[8, 9].

1.2.5 Complications

Cardiovascular system: It increases the risks of ischaemic heart disease, heart failure, aortic aneurysm, diffuse atherosclerosis, left ventricular hypertrophy and pulmonary embolism ^[6].

Brain: Predisposes one to atherothrombotic brain infarction which is the most common variety of stroke, brain tissue destruction if there are long standing multiple infarcts or hemorrhages, encephalopathy, cerebral oedema, cerebral vascular accidents-CVAs-(stroke) ^[10].

Kidney: HTN causes decreasing GFR leading to renal impairment, accelerated atherosclerosis of the renal arteries and nephrosclerosis, and eventually chronic renal failure.

Eye: Eye involvement occurs due to haemorrhage in retina and vitreous humour. Retinal lesions produce scotomas (i.e. blind spots in visual fields), blurred vision and papilloedema which may result in blindness ^[10].

1.2.6 Causes of secondary hypertension

- Renal diseases: -Renoparenchymal disease
- Reno vascular disease
- Coarctation of the Aorta
- Hyper and hypothyroidism
- Acromegaly
- Conn's syndrome ^[11, 12].
- Primary hyperaldosteronism
- Cushing's syndrome
- Pheochromocytoma^[4]
- Drugs -adrenocorticosteroids
-alcohol
-anorexics (e.g.phenylpropanolamine)

- Appetite suppressants (e.g. Sibutramine),
 - Cyclosporins
 - Decongestants
 - Licorice
 - MAOI
 - NSAIDs
 - Oral contraceptives ^[13]
- Pregnancy- Most women with hypertension in pregnancy have pre-existing primary hypertension, but high blood pressure in pregnancy may be the first signs of pre-eclampsia a serious condition of the second half of pregnancy and puerperium. It occurs in approximately 8-10% of pregnancies ^[14].

1.2.7 Diagnosis

HTN is diagnosed on the basis of a persistently high blood pressure. Initial assessment involves a complete history and physical examination. A sphygmomanometer with aneroid manometer and stethoscope are used for measurement of blood pressure. Home monitoring is useful for continuous management and diagnosis of white coat hypertension ^[15]. This is a phenomenon in which patient's exhibit elevated blood pressure in a clinical setting but not in other setting. It can also be referred to as white coat syndrome. It could be due to anxiety some people experience during a clinic visit ^[16].

1.2.8 Management

Non pharmacological management;

This usually includes; lifestyle modifications which include dietary changes, physical exercise, weight loss, stress relief, reduced alcohol intake, quitting smoking and control of other factors leading to arteriosclerosis.

Table 2: Classes of antihypertensive drugs.

Class of drugs	Examples	Side effects
Diuretics	<p>Thiazide diuretics Hydrochlorothiazide Bendrofluazide Cyclopentiazide</p> <p>Loop diuretics Furosemide</p> <p>Potassium Sparing Diuretics Spironolactone Amiloride Triamterene</p>	<p>Hyperuricemia – precipitates gout Impaired glucose tolerance Hypokalemia Hyperlipidemias</p> <p>Hypochloremia, hypokalaemia, dehydration, electrolyte imbalance.</p> <p>Hyperkalaemia, hyperchloremic metabolic acidosis, gynecomastia, acute renal failure kidney stones</p>
Beta blockers	<p>Propranolol Atenolol Bisoprolol Metoprolol Pindolol Sotalol Timolol Oxprenolol Nadolol</p>	<p>Bradycardia cold extremities fatigue unusual dreams may precipitate congestive cardiac failure may precipitate asthma (β_2 blockade) inhibit usual hypoglycemic response in Diabetics</p>
Alpha blockers	<p>Phentolamine Phenoxybenzamine Prazocin Doxazocin</p>	<p>Non selective α_1 and α_2 blockers tend to cause tachycardia. Failure of ejaculation Nasal stuffiness Incontinence especially in women Orthostatic hypotension Heart failure</p>
ACEI	<p>Captopril Enalapril Lisinopril Ramipril Quinapril</p>	<p>skin rash Taste disturbance Chronic dry cough Hyperkalemia Teratogenic effect</p>

	Fosinopril	Renal impairment Fatigue, dizziness, hypotension, headache
Angiotensin II Receptor blockers	Losartan Valsartan Candesartan Irbesartan Telmisartan	Hyperkalemia Renal insufficiency Orthostatic hypotension Dyspepsia rash dizziness
Vasodilators	Hydrallazine Minoxidil	Increase hair growth on the face, arm, back and chest. Pericardium effusion
Calcium Channel Blockers (CCBs)	Verapamil Amlodipine Nifedipine Isradipine Nicardipine Diltiazem	Reflex stimulation of sympathetic nervous system Headache Flushing Edema constipation profound negative inotropic effect
Rennin inhibitors	Aliskiren	Angioedema hypotension gout renal stones hyperkalaemia.

1.2.9 National guidelines ^[7]

According to clinical guidelines;

- For stage 1 hypertension, the initial treatment is non-pharmacological. If no response after 4-6 months monotherapy is used preferably Hydrochlorothiazide but bendroflumethiazide, furosemide or other appropriate diuretics may be substituted. For diabetics enalapril is preferred.
- For stage 2 hypertension, initiate non- pharmacological treatment and in addition give hydrochlorothiazide 25-50mg PO once daily. If no response within 4-6 weeks, add atenolol 50mg PO gradually increasing the dose up to 100mg daily, depending on patient's response and since BP response is always delayed with atenolol at least 6 weeks should elapse before changing the therapeutic regime. If no response, consider other combinations of hydrochlorothiazide with either a beta blocker or ACEI.
- In management of hypertensive crisis there are two approaches:
 - A. Furosemide is administered IV + Hydralazine 10mg IV every 15 minutes until desired effect or 50mg has been administered. The total dose may be repeated IM or IV after 6 hours or sodium nitropruside 0.25-10ug /kg/minute IV infusion.
 - B. Nifedipine 20mg PO repeated after 1 hour.

Following initial control of BP, switch to multiple oral therapy (hydrochlorothiazide + atenolol + hydralazine or nifedipine or methyldopa or captopril).

Table 3: Indications for the various classes of antihypertensive agents ^[22]

Class of drug	Indications	contraindications
ACE inhibitors	Type 1 diabetic nephropathy, non-diabetic nephropathy, Left ventricular dysfunction	Pregnancy, Bilateral renal artery stenosis Hyperkalaemia
ARBs	Type 2 diabetic nephropathy Left ventricular hypertrophy Heart failure in ACE-inhibitor intolerance	Pregnancy, Bilateral renal artery stenosis, Hyperkalaemia
CCBs (dihydropyridine)	Elderly with isolated systolic hypertension Black patients	Congestive heart Failure
Diuretics	Elderly with isolated systolic hypertension, Black patients	Gout
Beta-blockers	Following myocardial Infarction	High-degree heart block, Severe bradycardia ($< 50/\text{min}$), Obstructive airways disease, Raynaud
Alpha-blockers	Benign prostatic hypertrophy	Urinary incontinence
Central alpha-agonist	Pregnancy(methyldopa)	
Peripheral alpha-agonist	When other medicines are ineffective or not available or affordable	

CHAPTER TWO

2.1: JUSTIFICATION OF THE STUDY.

Hypertension cases have been rapidly increasing in Kenya in the past few years. This is partly associated with the rise of the middle class population and the drastic changes in lifestyle^[19].

This has led to a lot of spending on antihypertensive agents and the demand is rising by about 5.5% annually^[21]. This bears heavily on the national health budget hence there is need to strengthen the health care system to prevent and manage this condition. One of the main ways of doing this is by promoting rational drug use. Irrational drug use has major consequences to the patient, public in general, the health system and even economy of the country. It may lead to increased morbidity and mortality due to reduction in the quality of drug therapy. Few studies have been done on the rational use of antihypertensive agents in Kenyatta National Hospital. Prescription audit is an important measure of rational drug use. This study aims at contributing to this important area of patient management.

2.2: OBJECTIVES.

General objectives

To evaluate the prescribing patterns of antihypertensive agents at Kenyatta National Hospital outpatient clinic and to assess the adherence to the national guidelines for treatment of hypertension.

Specific objectives

- i. To find out the most prescribed antihypertensive drugs at Kenyatta National Hospital outpatient clinic.
- ii. To evaluate the use of international non-proprietary names in prescriptions of antihypertensive agents at Kenyatta National Hospital outpatient clinic.
- iii. To compare the drug regimen, dosages and dosing schedule of the antihypertensive agents prescribed at Kenyatta National Hospital outpatient clinic with the national guidelines for treatment of hypertension.

CHAPTER THREE

3.1: METHODOLOGY.

Study area

The Outpatient Pharmacy (Pharmacy no.15) of Kenyatta National Hospital(KNH), a national referral and teaching hospital in the country as well as a medical research centre established in 1901. KNH has 50 wards, 22 outpatient clinics, 24 theatres (16 specialised), Accident & Emergency Department and 10 pharmacies. It has a total bed capacity of 1800 but 209 beds are of the Private Wing. Sometimes the bed occupancy rate may go up 300%. At any given day, the hospital hosts in its wards between 2500 and 3000 patients. On average the hospital caters for over 80,000 in-patients and over 500, 000 out-patients annually. Pharmacy no. 15 serves a total of 9 clinics namely: medical outpatient clinic, surgical outpatient clinic, dental clinic, ENT, paediatric outpatient clinic, eye clinic, gaenecology outpatient clinic orthopaedic clinic and renal clinic. ^[23]

Study design

This was a cross sectional-retrospective study which involved review of medical records and statistical data collection from the records department (no.19) and review of prescriptions from outpatient pharmacy (no.15).

Study population

Files and prescriptions of hypertensive patients who had been attended at the outpatient clinic and received their medication at the outpatient pharmacy number 15 over the period January to December 2011. Another criterion for inclusion in the study was hypertensive patients above 18 years of age. Exclusion criteria were prescriptions whose files were missing and could not be traced from the records department, incomplete files and patients who had newly diagnosed hypertension and had attended the clinic only once.

Sample size.

The following formula was used to calculate the size of the sample to be taken:

$$n = [t^2 * p (1-p)] / m^2$$

Where

n=required sample size

t=confidence level at 95% (standard value of 1.96)

p=estimated prevalence of HTN in the projected area (e.g. 0.24 for 24% prevalence in adult population^[5]).

m=margin of error at 5% (standard value of 0.05)

Solving for the sample size equation:

$$n = 1.96^2 * 0.24(1-0.24) * 0.05^{-2}$$

$$= 280$$

Hence 280 patient files and their corresponding prescriptions were examined during a five weeks period.

Data collection

Collection and analysis of prescriptions was done during working hours in the pharmacy and the records department. The files and prescriptions were not taken out of the respective departments. Patients' names were not recorded to maintain the patient's confidentiality.

A pre-designed data collection form was used to capture the relevant data from patients' files and prescriptions. The data collection form contained parameters like patient's record number, age, gender, diagnosis, year of diagnosis, blood pressure at the time of the first clinic attendance and subsequent visits and the antihypertensive agents that the patient is currently on including the dosages and dosing schedule. Therapy history and any co-administered medication and adverse drug effects were also recorded. Data analysis was done using SPSS Statistics 17.0.

3.2 ETHICAL ISSUES

Official clearance was granted by KNH/UON Ethics and Research Committee which enabled access to patient information from their files and prescriptions. Patient confidentiality was maintained throughout the study by strictly examining the files personally in the records department and the outpatient clinic and none of them was carried from these areas to be examined elsewhere. The pre-designed data collection form bearing the in-patient number (IP no.) rather than the name of the patient was used.

CHAPTER FOUR

4.0 RESULTS

A total of 280 prescriptions were audited in the study. 53.9% of the studied prescriptions were for male patients as shown in table 4 below

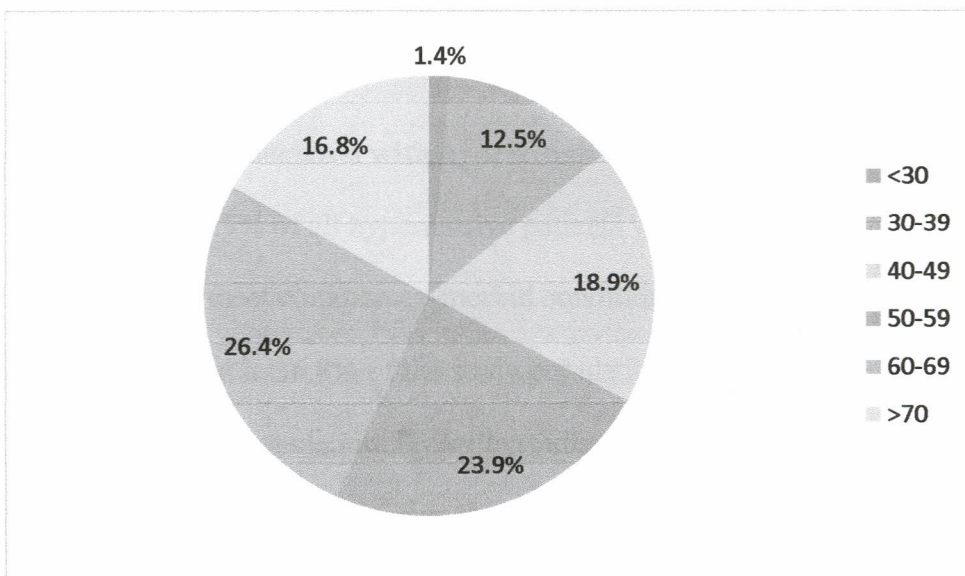
Table 4: A table showing gender distribution of hypertension.

Sex	Number of Patients	Percentage (%)
Male	151	53.9
Female	129	46.1
Total	280	100.0

Age group distribution of hypertension

From this study hypertension was seen to be most prevalent among patients aged between 60-69 years with 26.4% of the total. Those less than 30 years were 1.4% of the total and constituted the minority. Details are shown in chart 1 below.

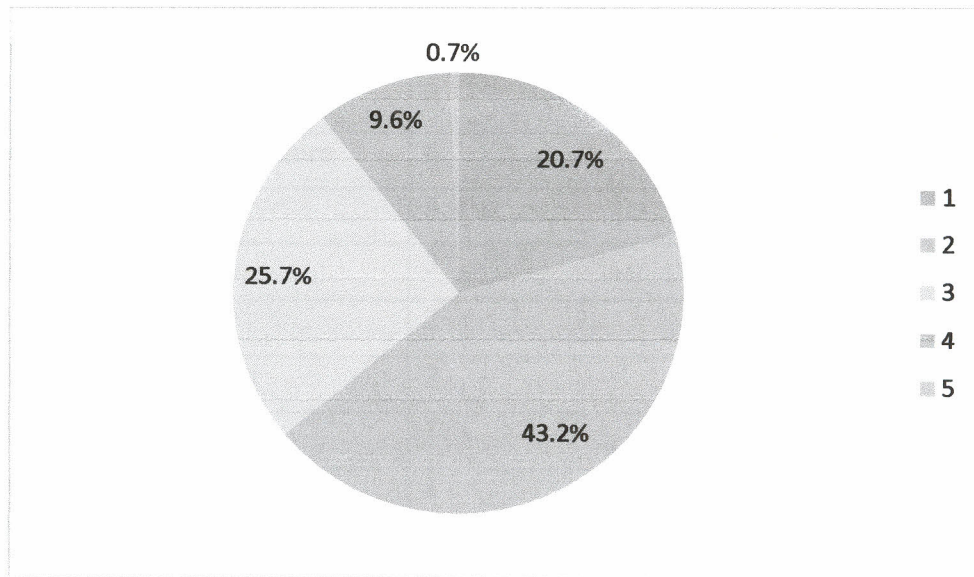
Chart 1: Chart showing age group distribution of hypertension



Number of antihypertensive drugs per prescription

The number of drugs per prescription ranged between 1 and 5. Those that contained 2 drugs constituted the majority with 43.2% of the total. Prescriptions containing 5 drugs were the least with only 0.7% as illustrated in chart 2 below.

Chart 2: chart showing the number of drugs per prescription



Adherence to international non-proprietary names in prescriptions

Majority (74.3%) of these agents were prescribed in generic names while the rest were in brand names. Generic prescribing varied between various classes of antihypertensive drugs. Larger proportions were seen with the ACEIs and CCBs.

Co-morbidities associated with hypertension

In this study, 42.9% of all hypertensive patients were not associated with any other co-morbidity. The most common co-morbid condition seen in this group of patients was diabetes mellitus observed in 36.8% of the study population. It was followed by renal diseases seen in 5.7% of the study population. Hyperthyroidism was the least common co-morbidity associated with hypertension seen at a prevalence of 1.1% as shown in table 6 below.

Other co-morbidities seen but not associated with hypertension included asthma in 2.9% of patients, rheumatic arthritis, scleroderma, peptic ulcer disease, osteoarthritis, stroke and peptic ulcer disease.

Table 5: Table showing co-morbidities associated with hypertension

Co-morbidity	number of patients	Percentage (%)
Diabetes	103	36.8
Renal diseases	16	5.7
cardiovascular disorders	14	5.0
Asthma	8	2.9
Congestive Heart Failure	6	2.1
Osteoarthritis	3	1.1
Hyperthyroidism	3	1.1
Scleroderma	2	0.7
Rheumatic arthritis	2	0.7
peptic ulcer disease	1	0.4
Osteogenic sarcoma	1	0.4
Stroke	1	0.4
Total	160	57.1

Prescribed drugs

From this study out of the 280 patients files reviewed, 20.7% were on monotherapy while 79.3% were on combination therapy. In the monotherapy category ACEI were the most prescribed with 11.4%, followed by angiotensin II receptor blockers with 4.3%. Only 0.7% of the total patients received β blockers.

Table 6: Table showing the classes of drugs used in monotherapy

Class of drug	No of patients	% total
ACEIs	32	11.4%
ARBs	12	4.3%
CCBs	7	2.5%
Diuretics	5	1.8%
β blockers	2	0.7%
Total	58	20.7

Combination therapy.

There were 10 different two-antihypertensive drug combinations prescribed for each category, 9 different three-drug combinations, 3 different four- drug combinations and 1 five-drug regimen combination. ACEI + CCB was the most frequently prescribed combination with 10.0% of the total prescriptions. Details of the other combinations are shown in table 7 below.

Table 7: Table showing classes of drugs used in combination therapy

<u>Combination</u>	<u>No of patients</u>	<u>Percentage</u>
ACEI+CCB	28	10.0%
ACEI+diuretic	27	9.6%
CCB+ACEI+diuretic	27	9.6%
CCB+ARB	21	7.5%
CCB+ACEI+B blocker	17	6.1%
ARBs+diuretic	13	4.6%
b blocker+ACEI	12	4.3%
Diuretic+CCB	9	3.2%
ACEI+B blocker+2diuretic	9	3.2%
CCB+ACEI+diuretic +B blocker	8	2.9%
b blockers+CCB	7	2.5%
B blockers+ARB	7	2.5%
CCB+ARB+b blocker	7	2.5%
diuretic+CCB+ARB	7	2.5%
Diuretic+b blocker+CCB	5	1.8%
ACEI+B blocker+diuretic	4	1.4%
ACEI+ARB	3	1.1%
ACEI+2 B blocker+ Diuretic	3	1.1%
b blocker+diuretic	2	0.7%
ACEI+2CCB	2	0.7%
CCB+ARB+ACEI	2	0.7%
CCB+B blocker+diuretic+vasodilator	1	0.4%
ACEI+CCB+B blocker+diuretic+ ARB	1	0.4%
Total	222	79.3

Table 8: Table showing the classes of drugs prescribed used in both monotherapy and combined therapy

Class	No. of prescriptions	% out of 280
ACEIs	163	58.2%
CCBs	155	55.4%
Diuretics	132	47.1%
Beta blockers	93	33.2%
ARBs	75	26.8%
vasodilators	1	0.4%
Total	280	

This indicates that out of the prescriptions analysed, most (58.2%) contained an ACEI, while only 0.4% of the prescriptions had a vasodilator prescribed.

Types of antihypertensive agents prescribed

The most prescribed antihypertensive agent was enalapril with 49.6% of the total. The dose ranged between 5-20mg taken once daily or twice daily orally either alone or in a combination. It was mainly prescribed to patients with diabetes mellitus.

Nifedipine was the second most prescribed agent with a total 4.6%. It was taken as 20-40mg orally as a twice daily and in some few cases as a once daily dose either in a combination with other antihypertensive agents or alone.

Hydrochlorthiazide was the third most prescribed antihypertensive agent with a total 28.2% prescribed as a 50mg once daily dose orally.

The least prescribed drugs were hydralazine, amiodarone, lisinopril, nebivolol, felodipine and irbesartan with less than 1% of the total prescriptions. This has been illustrated in table 9 below.

Atortastatin was prescribed in combination with antihypertensive agents in 34.3% of patients in supportive management of hypertension.

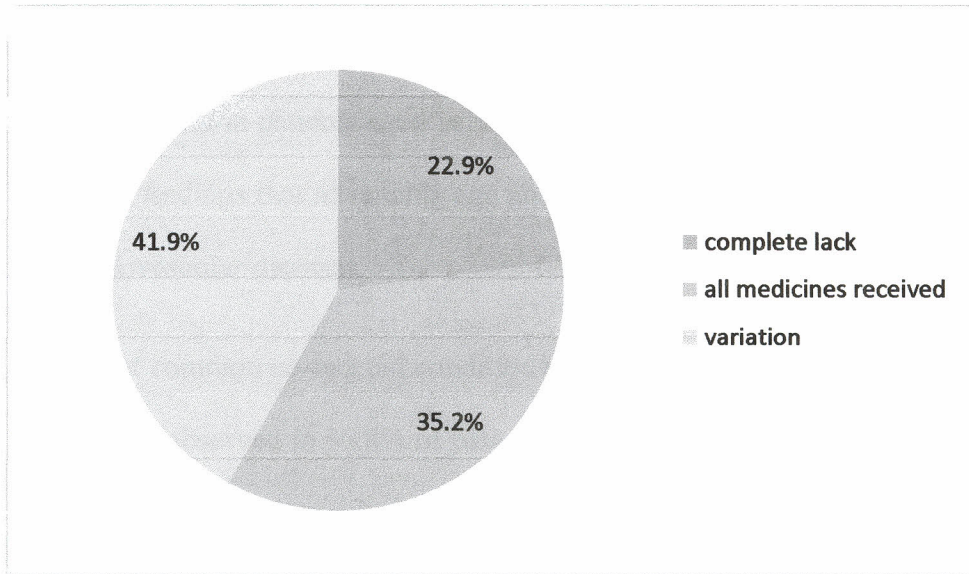
Table 9: Type of antihypertensive agents prescribed.

TYPE	NO. OF PRESCRIPTIONS	% TOTAL
Enalapril	139	49.6%
Nifedipine	97	34.6%
Atorvastatin	96	34.3%
Hydrochlorothiazide	79	28.2%
Losartan	73	26.1%
Atenolol	59	21.1%
Amlodipine	56	20.0%
Furosemide	37	13.2%
Carvedilol	30	10.7%
Captopril	20	7.1%
Spirolactone	15	5.4%
Bendroflumethiazide	14	5.0%
Propranolol	4	1.4%
Irbesartan	2	0.7%
Verapamol	1	0.4%
Amiodarone	1	0.4%
Felodipine	1	0.4%
Nebivolol	1	0.4%
Lisinopril	1	0.4%
Hydralazine	2	0.7
Total	280	100

Availability of antihypertensive agents in pharmacy 15.

About 22.4% of the patients did not receive any of their prescribed medication while 41.9% received their full medications occasionally. Only 35.2 received all the medicines all the time.

Chart 3: chart showing availability of antihypertensive agents in Pharmacy 15



CHAPTER FIVE

DISCUSSION

The ability to lower blood pressure in common practice depends on many factors. These include; the efficacy of the drug, adherence to treatment, adverse effects, convenience, patient selection and monitoring.

From this study it was noted that hypertension was more common in men having 53.9% and more prevalent in patients aged between 60 to 69 years of age with 26.4%. This supports the common findings that advancing age and male gender are among the non-modifiable causes of cardiovascular diseases.

The most common co-morbid condition seen in this group of patients was diabetes mellitus which was observed in 36.8% of patients. This could be due to hyperlipidemia observed in diabetes mellitus that results from elevated levels of free fatty acids as there is no glycerol to conjugate them. This formed the basis of using the atorvastatin, a hypolipidemic agent in 34.3% to control hyperlipidemia not only in diabetic patients but also in patients with elevated BMI. The drug of choice for diabetic patients with hypertension was enalapril. This could be due to the fact that ACEIs and ARBs have renoprotective effects independent of the level of blood pressure or the extent of blood lowering^[19].

Patients who had renal diseases (5.7%) were on a combination therapy which included a diuretic and ACEI preferably enalapril. This could be due to the fact that ACE inhibitors have a particularly useful role in treating patients with chronic kidney disease because they diminish proteinuria and stabilize renal function (even in the absence of lowering of blood pressure). There were those on a single drug regimen mainly furosemide and hydrochlorothiazide although it was effective in lowering BP only in a small percentage of patients.

About 20.7% of all patients were on monotherapy regimen which consisted mainly of an ACEI or a diuretic mainly hydrochlorothiazide. This could have been preferred because compliance was likely to be better, cost is lower, and in some cases adverse effects may be fewer.

Most patients with hypertension require two or more drugs, preferably acting by different mechanisms (combination therapy) but some patients may respond inadequately even to two agents requiring addition of a third agent. The rationale for using more than one drug is that each of them acts on one of a set of interacting, mutually compensatory regulatory mechanisms for maintaining blood pressure. It was also noted that a small group of patients were on a combination that included drugs from the same class which have the same mechanism of action hence adding no therapeutic advantage to the patient but rather increasing the pill burden which could compromise the compliance. Carvedilol and atenolol despite being beta blockers were used together in 1.1% of patients and nifedipine and amlodipine which are CCBs were used together in 0.7% of patients. The use of 23 different combinations of antihypertensive drugs prescribed for each class indicates poor control of hypertension in the outpatient clinic of KNH. This calls for a development drug formulary in KNH outpatient to improve on the outcome of therapy.

74.3% of the prescribing doctors adhered to the use of international non-proprietary names in prescriptions of anti-hypertensive agents at Kenyatta National Hospital where generic names were used rather than the brand names. 25.7% of the prescribers are still using the brand names to prescribe drugs and this is an indication that they do not comply with the set guidelines.

Carvedilol was used in 10.7% of patients who had cardiovascular diseases because being a beta blocker it offers additional benefits in reducing mortality after myocardial infarction as

prescribed in the WHO guidelines. It lowers blood pressure by reducing systemic vascular resistance without significant alteration in heart rate or cardiac output. Because of its combined α - and β -blocking activity, it is useful in treating the hypertension of pheochromocytoma and hypertensive emergencies.

Nifedipine was the most prescribed CCB with a total of 97 prescriptions out of 280 because it is more selective as vasodilator and has less cardiac depressant effect than verapamil and diltiazem ^[19]. Amlodipine which is in the same class as nifedipine had a total of 56 prescriptions due to the same principle.

It was also noted that spironolactone was prescribed to a very small percentage of patients (5.4%) despite the increased use of high dose diuretics which are potassium losing. It is a potassium-sparing diuretic and could be useful both to avoid excessive potassium depletion and to enhance the natriuretic effects of other diuretics.

Diuretics either alone or in combination were highly prescribed in 33.2% to manage both mild to moderate and severe hypertension. Monotherapy with diuretics was observed in severe hypertension (1.8%). They are indicated for stage1 hypertension in the national guidelines.

CHAPTER SIX

CONCLUSION.

This study showed that angiotensin converting enzyme inhibitors are the most preferred first line treatment therapy for hypertension in both monotherapy and combined therapy. The most prescribed antihypertensive agent in this category was enalapril most probably due to its relative affordability and efficacy in a diverse range of patients.

Compliance with the use of international non-proprietary name in prescriptions was poor as some physicians (25.7%) seemed to prefer prescribing using brand names. Most of the outpatients in Kenyatta National Hospital are maintained on combination therapy although some combinations seemed to be non-compliant with both national and WHO guidelines. Some irrational combinations were used in some patients. Certain classes of antihypertensive combinations were used in high doses and there was poor control of blood pressure

RECOMMENDATIONS:

1. Physicians should adhere to the latest WHO guidelines for the management of hypertension and copies should be distributed to all clinics to ensure compliance.
2. All healthcare workers should be sensitized on the importance of adherence to both the national and WHO guidelines to ensure better outcomes on the management of hypertension.
3. The pharmacists should review the prescriptions regularly to ensure rational drug use and avoid dispensing of irrational combinations.

REFERENCES

1. Belknap SM, Moore H, Lanzotti SA et al(September 2008). Application of software debugging methods to an analgesia prescription reduces severe injury from medical use of opioids. *Clinical pharmacology& Therapeutics* 84(3):385-92
2. Batey MV, Holland JM(March 2001). Prescribing practices among health practitioners in adult and family health. *American Journal of Public Health* 75(3):258-62
3. WHO website (www.who.int/medicines/areas/rational_use/en/) Searched 05.05.2012 at 10.25a.m.
4. Carretero OA, Oparil S. (January 2009). Essential hypertension part1: definition and aetiology. *Circulation*101(3):329-35
5. Burt VL, Curtler JA, Higgins M et al. (July 2004). Trends in the prevalence, awareness, treatment and control of hypertension among the adult USA population. Data from the health examination surveys, 1960-1991. *Hypertension* 26(1):60-9
6. Chobanian AV ,Bakris GL, Black HR et al. (December 2003). Seventh report of the Joint National Committee on Prevention, Detection, Evaluation and treatment of High Blood Pressure. *Hypertension* 42(6): 1206-52.
7. Clinical management and referral guidelines volume (iii) pg36-38.
8. Nadar SK, Tayebjee MN(2006). Target organ damage in hypertension, pathophysiology and implications for drug therapy. *Current pharmaceutical design* 12(13):1581-1592.
9. Chiang WK, Jamshashi B(November 2008). Asymptomatic hypertension in the emergency department.*American Journal of Emergency Medicines* 16(7):701-704

10. Giacchetti G, Turchi F, Boscaro M et al (April 2009). Management of primary aldosteronism, its complications and their outcomes after treatment. *Current Vascular Pharmacology* 7(2):244-249.
11. Bailey MA, Paterson JM, Hadoke PW et al. (January 2008). A switch in the mechanism of hypertension in the syndrome of apparent mineralocorticoid excess. *J AM Soc Nephrol.* 2008 19(1):47-58
12. Robertson JI (Jan 1997). Risk factors and drugs in the treatment of hypertension. *Journal of hypertension supplement. Official journal of the international society of hypertension* 15(1); 43-46
13. Chesley LC, Annitto JE, Cosgrove RA(2002). Hypertensive disorders of pregnancy. *Williams Obstetrics* 14(2): 700-4.
14. Reeves R, Myers MG, Joyner CD et al (1995). The rational clinical examination for hypertensive patients: *JAMA* 273(15): 1211-18.
15. CG34 Hypertension quick reference guide (June 2006). National Institute for Health and Clinical Excellence pg 102
16. Pickering TG, Hall JE, Appel LJ et al(1994). Blood pressure measurement and detection of hypertension. *Lancet* 344(8914): 31-5
17. Guyton and hall (2005). *Textbook of medical physiology*_7th edition. pg 220-225
18. Robbins *Basic Pathology*_8th edition pg 353-357
19. *Basic and Clinical Pharmacology* _11th edition. Chapter 11p588-607.
20. *Katzung pharmacology*_10th edition.(2007) by Vishal chapter 11 pg468-483.
21. Frost and Sullivan (2008). Strategic analysis of the Kenyan hypertension markets. Pg134;Pub ID:MC1806128
22. WHO Website: <http://www.ish-world.com/Documents/> searched on 03/10/2012 at 1719hrs

23. Kenyatta National Hospital website: <http://knh.or.ke> searched on 19.09.2012 at 0918hours.
24. Wofford MR, Hall SE(2004). Pathophysiology and treatment of hypertension. Current Pharmaceutical Design 10(29):3681-87)
25. Ecdet T, Schrier RW (April2009).Cardiovascular abnormalities in autosomal dominant polycystic kidney disease. Nephron 81(1):117-8.
26. East African medical journal (1997). Cardiovascular disease in elderly patients at the Kenyatta national hospital, Nairobi-Kenya. Vol174;pg647-51
27. Ansel, H. Pharmaceutical Calculations. 13th edition,Philadelphia. Lippincott, Williams, and Wilkins.2010.p59-60.

APPENDICES

APPENDIX 1:

DATA COLLECTION FORM.

Patient's record no.

Age

Gender

Diagnosis

Year of diagnosis

Blood pressure at the time of the first clinic attendance

Blood pressure during last three visits

.....

.....

Generic names used for all the drugs prescribed [Y] [N]

Antihypertensive agents currently being administered

Drug name	Dosage	Frequency of taking medications	Route of administration	Common side effects

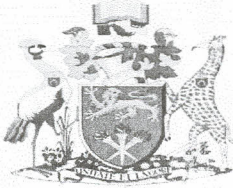
APPENDIX 2

BUDGET.

Typing and printing	4000
Miscellaneous	<u>500</u>
TOTAL	4500

APPENDIX 3

ETHICS REVIEW COMMITTEE CLEARANCE



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5th June 2012

Kamau Caroline Gathoni
U29/2963/2008
School of Pharmacy
University of Nairobi

Dear Caroline

Research Proposal – Clearance “Prescription audit of Antihypertensive Medication at the Outpatient Pharmacy in Kenyatta National Hospital” (UP274/05/2012)

Your above proposal refers.

This is to inform you that permission has been granted by the KNH/UON-Ethics & Research Committee to carry out research on study titled “Prescription audit of Antihypertensive Medication at the Outpatient Pharmacy in Kenyatta National Hospital”.

By a copy of this letter, I am requesting the relevant persons to accord you the professional support and other materials that may be useful to your research.

Yours faithfully

Handwritten signature of Prof. A N Guantai.

PROF A N GUANTAI
SECRETARY, KNH/UON-ERC

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