ASSESSMENT OF THE LEVEL OF ADHERENCE TO THE ACC/AHA 2017 GUIDELINES IN THE MANAGEMENT OF HYPERTENSIVE CRISIS AT THE KENYATTA NATIONAL HOSPITAL.

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University of Nairobi.

DECLARATION

I declare that this dissertation entitled **"ASSESSMENT OF THE LEVEL OF ADHERENCE TO THE ACC/AHA 2017 GUIDELINES IN THE MANAGEMENT OF HYPERTENSIVE CRISIS AT THE KENYATTA NATIONAL HOSPITAL"** is my original work and that to the best of my knowledge it had not been presented either wholly or in part to this or any other university for the award of any degree or diploma.

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LIST OF ABBREVIATIONS

ABPM	Ambulatory blood pressure measurement
ACC	American College of Cardiology
ACE Inhibitor	Angiotensin Converting Enzyme Inhibitor
ACS	Acute Coronary syndrome
AHA	American Heart Association
ARB	Angiotensin Receptor Blocker
CCB	Calcium Channel Blockers
CDC	Centre for disease control and prevention
COMMIT/CCS2	Clopidogrel and Metoprolol in Myocardial Infarction trial/ Second Chinese Cardiac Study
DBP	Diastolic Blood Pressure
ER	Emergency room
GDMT	Guideline Directed Medication in the treatment of heart failure
HBPM	Home blood pressure measurement
HDU	High dependency unit
ICP	Intracranial pressure
ICU	Intensive care unit
INTERRACT 2	Intensive blood pressure reduction in acute cerebral hemorrhage trial 2
JNC7	Seventh report of the joint National committee on prevention detection, evaluation and treatment of high blood pressure
MAP	Mean arterial pressure
mmHg	millimeters of Mercury
rtPA	recombinant Tissue Plasminogen activator
SBP	Systolic Blood Pressure
STAT	Studying the management of acute hypertension.

ABSTRACT

Background

Hypertensive crisis is a medical emergency that requires prompt diagnosis and management. It encompasses both hypertensive urgency and emergency. Hypertensive urgency is defined as a systolic blood pressure of ≥180 mmHg and/or diastolic blood pressure of ≥120mmHg with no evidence of acute end organ damage. Hypertensive emergency on the other hand is characterized by the same level of blood pressure and evidence of acute end organ damage.
The American Heart Association hypertensive crisis management guidelines were then recently updated in 2017 and had been adopted by different countries to assist in appropriate management of hypertensive crisis.
This study hoped to audit the adherence to the AHA/ACC 2017 hypertensive crisis management guidelines at the Kenyatta National Hospital.

Methodology

The objective was to assess the level of adherence to the ACC/AHA 2017 hypertensive crisis management guidelines at the Kenyatta National Hospital. The study was a descriptive cross-sectional study done at the accident and emergency, medical intensive care unit, renal unit and the medical wards. The study population comprised all hypertensive patients presenting in hypertensive crisis. The sample size calculation was for finite population and gave a sample size of 214. Consecutive sampling was used as the sampling technique. The lead researcher and research assistants reviewed files of patients presenting with hypertension at the different departments at the end of each day and identified those in crisis. A questionnaire based on the AHA/ACC standard hypertensive crisis guideline was used to document the practice in management and conformity to the guidelines. The frequencies of different sought symptoms, signs and investigations were calculated and represented in tables while the management was analyzed against the standard of care and represented in charts.

Results

Out of 420 files of hypertensive patients screened, 229 were found to fit into the hypertensive crisis criteria with 102 (45%) as urgencies and 127 (55%) as emergencies. The mean age was found to be 51 years with the youngest being 15 years and the oldest at 89 years. The commonest emergency was ischemic stroke at 41 (32.2%) followed by acute kidney injury at 34 (26.7%). None of the patients with a diagnosis of hypertensive emergency were admitted in ICU during the acute phase of management as expected from the AHA/ACC guideline. Challenges in evaluation of the patients by examination and investigations were evident with fundoscopy and electrocardiography being poorly done at 2.6% and 18% respectively. Management did not adhere to the AHA/ACC guidelines with oral calcium channel blockers being predominantly prescribed instead of guideline directed medication in both emergencies and urgencies. These did not achieve the desired outcome in lowering the blood pressure.

Conclusion

The audit highlighted the challenges in adequacy of diagnostic work up as well as the inappropriateness and ineffectiveness of management of hypertensive crisis as observed at the Kenyatta National Hospital. Patients in hypertensive urgency were poorly evaluated while those in emergencies were neither admitted in ICU/HDU nor managed acutely by parenteral antihypertensive therapy. This shows poor adherence to the 2017 ACC/AHA hypertensive crisis management guidelines.

1.0 CHAPTER ONE: INTRODUCTION

Hypertension is a modifiable risk factor for multiple organ damage if poorly controlled. The disease initially thought to have a high prevalence in the elderly population has now morphed to involve even the younger population. The culprits in these circumstances include a diet rich in saturated fats and carbohydrates as well as a sedentary lifestyle among other risk factors. (1). Hypertensive crisis entails both emergency and urgency. Hypertensive emergency is defined by the 2017 American College of Cardiology guidelines as systolic blood pressure ≥ 180 mmHg, a diastolic blood pressure ≥ 120 mmHg or a combination of both, with associated acute end organ damage. Hypertensive urgency on the other hand has similar blood pressures but without end organ damage (2).

1.1 Prevalence

Worldwide the prevalence of hypertension is 26% and of these 1-2% suffer a hypertensive crisis in their lifetime. Men are more likely to suffer from hypertensive emergencies than women. The probability is also higher in the elderly (3). The prevalence of hypertensive crisis in Uganda's Mulago national referral hospital based on a cross-sectional study found a prevalence of 5.1% of patients presenting on the medical side of the accident and emergency (4). A descriptive cohort study in Tanzania's Muhimbili national hospital found the prevalence of hypertensive crisis at the accident and emergency at 2.5% (5). Currently we have no data on hypertensive crisis within the country.

1.2 Burden of Disease

It has been shown that the lifetime risk of a cardiovascular event is 63.3% in a hypertensive patient compared to 46.1% in normotensive patients (6). Patients in hypertensive urgency require optimizing of their antihypertensive medication with close follow up as well as guidance in order to adhere to the treatment. The regular visits and investigations as well as management bears heavily on the financial front as well as increasing their psychological stress.

The patients in emergency on the other hand, depending on the organ involved will have the following cost implications:

1. Regular purchase of medication.
2. Physiotherapy sessions.
3. Hemodialysis.
4. Frequent physician reviews and hospital admissions
5. Renal transplant and immunosuppressive cost
6. Surgical cost for aortic dissection
7. Additional cost to manage comorbidities such as bed sores post stroke
8. Counselling session cost

Psychological burden on the patient include:

1. Depressive mood from debilitating disease
2. Stigma of being immobile with bed sores
3. Anxiety of impending doom since they are worried the event (stroke) might happen again.
4. They feel they are a burden to their family and relatives
5. Suicidal ideology as a result of all the psychological burden

1.3 Outcome and Prognosis

Hypertensive crisis over time leads to poor quality of life and a shortened lifespan (7). Reliance on medication and/or medical equipment, reduces the patient's hours of productivity and puts pressure on their finances. Multidisciplinary approach required in the management of these patients further weighs heavily on them financially. In addition, lack of adequate information and unavailability of specialized services in most parts of the country have led to poor outcomes.

In this prospective study we evaluated the management of hypertensive crisis at the Kenyatta National Hospital against the standard level of management worldwide. This was based on the American Heart Association/ American College of Cardiology 2017 guidelines on the management of different hypertensive crisis.

2.0 CHAPTER TWO: LITERATURE REVIEW

2.1 Pathophysiology of Hypertensive Crisis

The pathophysiology of hypertensive crisis is poorly understood. Two theories thought to precipitate hypertensive crisis are (8);

1. Sudden increase in peripheral vascular resistance.
2. Failed cerebral auto regulation in neurological conditions.

Vascular endothelial injury resulting from repeated instances of acute hypertension is associated with elevated systemic vascular resistance. As the pressure rises, vascular endothelium is subjected to tensile stress leading to release of vasoconstrictors that further worsen endothelial damage.

If not promptly treated, then the following occurs:

1. Progressive activation of the coagulation cascade
2. Accumulation of necrotic endothelial tissues
3. Up regulation of the systemic neurohormonal cascade
4. Oxidative stress induction
5. Accumulation of pro-inflammatory cytokines.

Deposition of platelets, fibrin, vasoconstriction and thrombosis as a result of vascular injury results in a decrease in blood supply to and from different organs. This leads to concurrent hypo-perfusion and ischemia. If this process is not terminated, then auto regulation dysfunction occurs.

Cerebral auto regulation has been well studied over the years with evidence showing that when blood pressure is severely elevated there is a right shift in the auto regulation curve. This results in the cerebral flow at a higher mean arterial pressure (9). At mean arterial pressures of between 60 - 140 mmHg, cerebral blood flow is auto regulated extremely well.

However, in hypertensive patients, the auto regulation occurs with a systolic blood pressure of up to 180 mmHg although the blood flow remains constant. During hypertensive crisis, the shift in the auto regulatory curve fails to occur leading to cerebral edema and ultimately cerebral vascular spasms and ischemia. Continuation of this vicious cycle leads to acute elevation of blood pressure through activation of different neurohormonal cascades.

Hypertensive crisis guidelines have been established globally to assist in management. The Kenya National guidelines for cardiovascular disease management published in 2018 highlighted the different hypertensive emergencies and the corresponding management. However, no clear cut steps are put in place on management of the emergencies. The guideline lists the different emergencies and the corresponding medication that should be used in the management. On the other hand, the AHA guidelines gives a step by step approach to identify and manage the different emergencies. In addition, the medication to be used, correct dosage and how to monitor the patient after administration of the medication is clearly highlighted in the guidelines.

The European society of cardiology on the management of hypertension 2018 is also quite elaborate with details on diagnosing and appropriate management of different hypertensive emergencies. In comparison to the 2017 AHA guidelines, they are similar in most areas. The only additional information present in the American guidelines is how to monitor the patient after administration of the medication.

By the time the study was being conducted the European guidelines 2018 on management of hypertensive crisis as well as the Kenyan guidelines on hypertensive crisis management were yet to be published. This is the reason why the study is based on the 2017 American Heart Association guidelines.

2.2 Hypertensive Urgency

This is also known as severe asymptomatic hypertension and normally presents with blood pressures ≥ 180/120 mmHg without concurrent acute end organ damage. This is commonly observed in hypertensive patients' non-adherent to their medication. It can also occur in patients who are adherent to their medication but triggered either due to high salt diet or sudden physical or emotional stressful situations. It's also noted in newly diagnosed hypertensive patients or in secondary hypertension (10). In known hypertensive patients in urgency, reinstituting their current antihypertensive medication immediately in case they had defaulted and monitoring the response would be effective. (11).

There has been no added benefit noted with rapid reduction of blood pressure in severe asymptomatic hypertension (12). Therefore, gradual reduction over several hours to days is recommended. This is necessary to ensure the blood pressure is not lowered too fast and reduce chances of adverse effects like acute renal failure, myocardial infarction or cerebrovascular compromise due to an imbalance in auto regulation.

Older patients are more prone to the adverse effects associated with rapid reduction of blood pressure especially since most of them have wide pulse pressures. Therefore, their blood pressure reduction plan should be over a week or more (13).

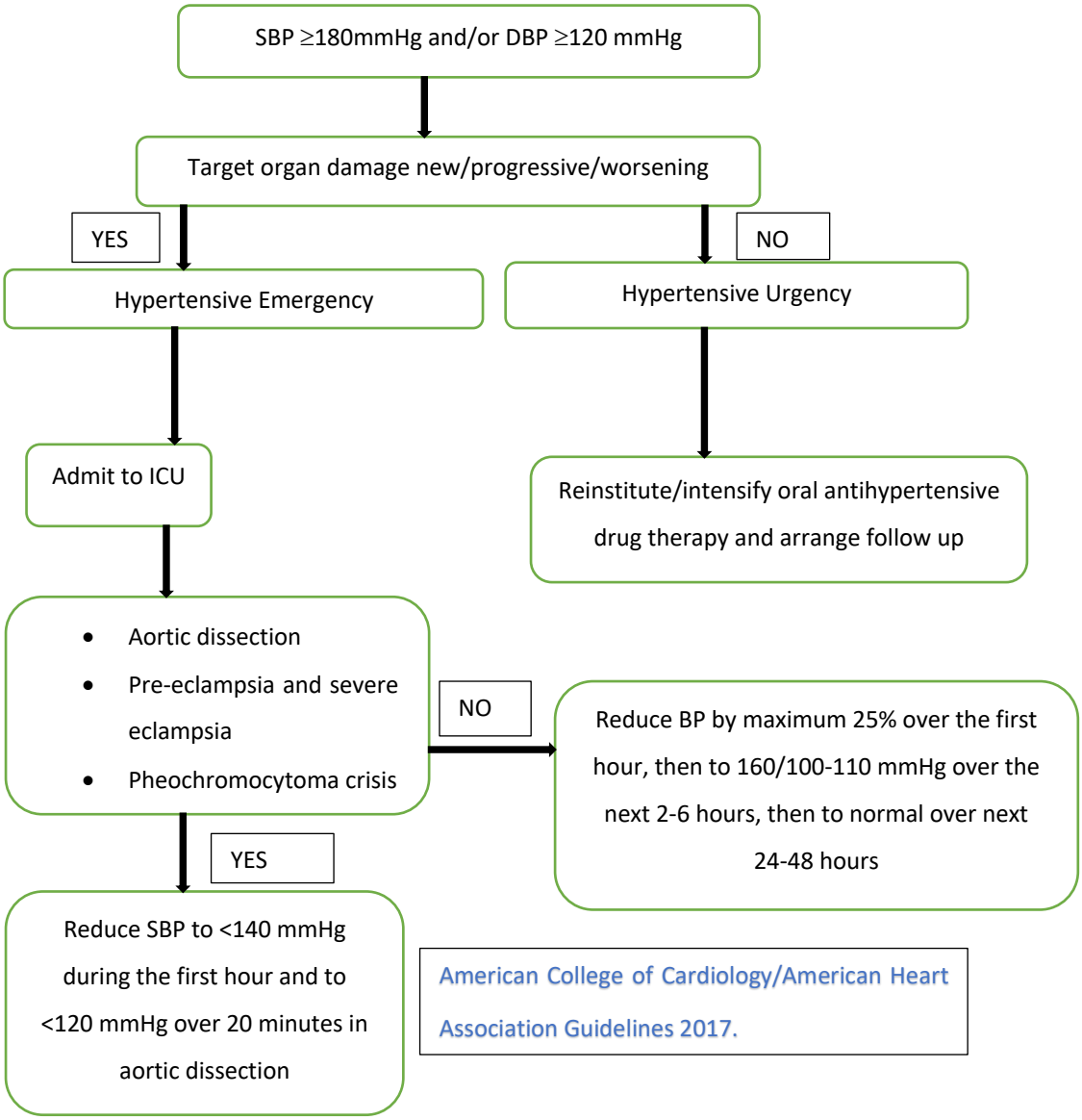
Monitoring of this high blood pressure should be done at the clinician's office. This is necessary while the clinician evaluates the patient both clinically and through laboratory as well as radiological investigations to ensure no end organ damage is involved. After a few hours of monitoring and establishing the pressure is decreasing and seems to be stabilizing, then the patient may be discharged and followed up through the outpatient clinic. Thorough follow up may be needed for these patients especially during the first two weeks. Emphasis on adherence counselling and strict blood pressure monitoring either at home using their own blood pressure device or at a nearby clinic. Advised on diet that is low in sodium and exercise should also be emphasized.

2.3 Hypertensive Emergencies

This involves elevated blood pressures with systolic ≥ 180 mmHg and/or diastolic ≥ 120 mmHg with signs and symptoms pointing towards evidence of ongoing end organ damage. The signs and symptoms are almost always of sudden onset and get worse over time. Most of these patients require time sensitive targeted clinical and laboratory investigations to ensure prompt salvaging of the affected organ. Admission in the acute phase to the intensive care unit or high dependence unit may be necessary until adequate evaluation and stabilization of the blood pressure is achieved.

Generally, it is important to slowly lower the blood pressure as ischemic damage can occur within the vascular bed now accustomed to the high level of blood pressure (auto regulation) (14), In most cases, the mean arterial pressure should be gradually reduced by approximately 10-20% in the first hour and by a further 5-15% over the next 23 hours (15). This results in target blood pressures of ≤ 180/120 mmHg over the first hour and ≤ 160/110 mmHg for the next 23 hours.

Figure 1: AHA/ACC guidelines in Diagnosis and management of Hypertensive Crisis



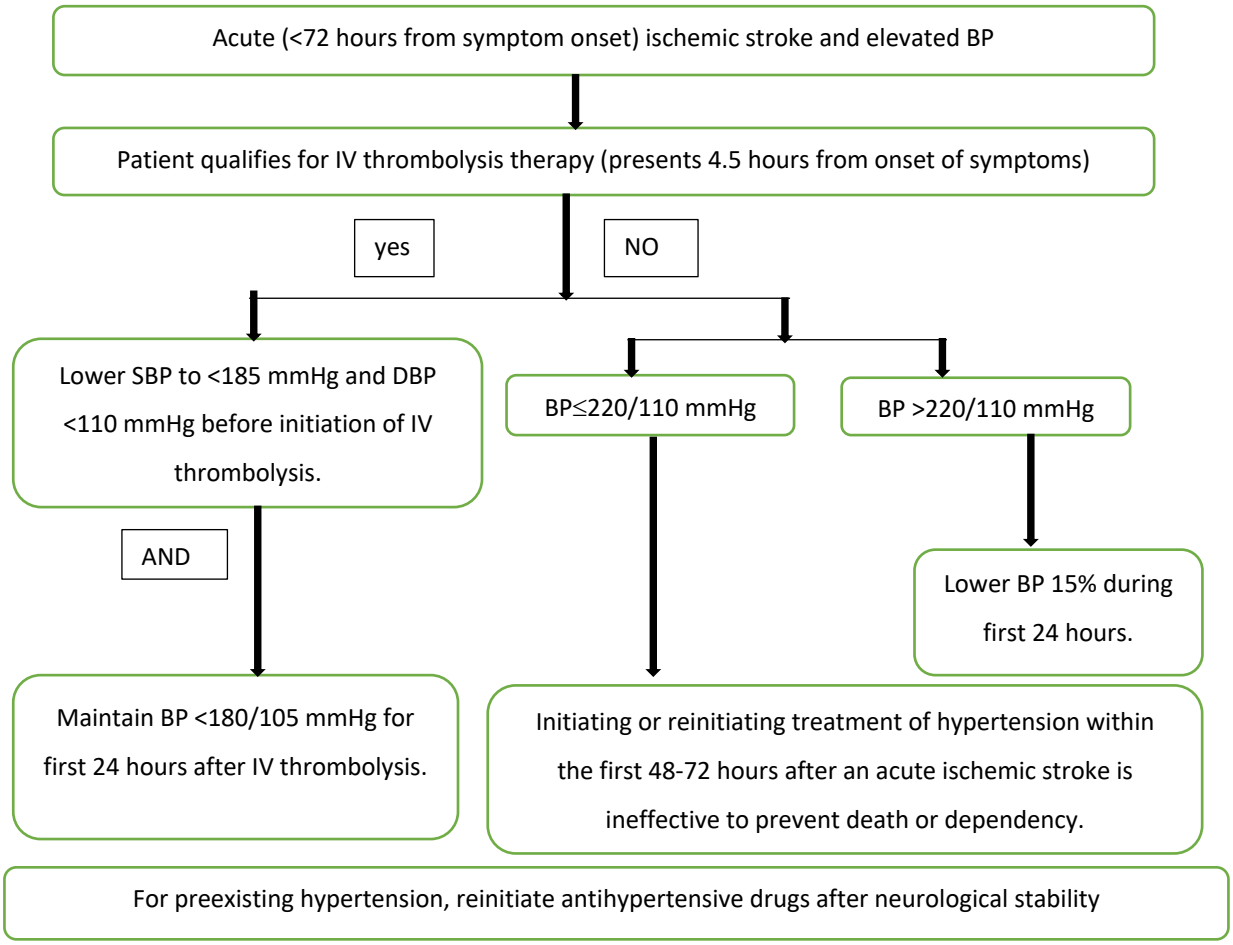
The flow chart shows the current guidelines in the identification and management of hypertensive crisis. Emergencies proceed to ICU where appropriate blood pressure management will be instituted to reduce the blood pressure by a maximum of 25% over the first hour, then to 160/100-110 mmHg over the next 2-6 hours, then to normal over the next 24-48 hours. In pheochromocytoma crisis, the systolic blood pressure is lowered to less than 140 mmHg over the first hour while in aortic dissection the systolic blood pressure is lowered to less than 120 mmHg over 20 minutes.

2.4 Neurological Emergency

2.4.1 Acute Ischemic Stroke

It's considered that the perfusion pressure distal to the obstructed vessel is low and the distal vessels dilated. This leads to impaired cerebral auto regulation and the distal vessels perfusion depends on the individual's blood pressure. The elevated pressure is necessary to maintain circulation in the borderline ischemic areas. This theory has shown that aggressive decrease of blood pressure in acute ischemic stroke leads to deterioration of clinical symptoms with accumulation of pro-inflammatory markers. Patients who require thrombolysis have to achieve a blood pressure lower than 185/110mmHg. The blood pressure must be stabilized and maintained at 180/105mmHg after thrombolytic therapy (16). Patients who do not qualify for thrombolysis, do not require blood pressure management unless found to be more than 220/120 mmHg or have other concomitant end organ damage. If indicated, the blood pressure should be lowered by 15% during the first 24 hours from the onset of the stroke.

Figure 1: AHA/ACC guidelines in Management of hypertension in patients with Acute Ischemic Stroke.



AHA/ACC guidelines in management of hypertension in patients with acute ischemic stroke above show identification of patients <72 hours after a stroke and qualify for thrombolysis will require blood pressure lowered to <185/110 mmHg, then, maintained at 180/105 mmHg after thrombolysis. If not for thrombolysis, reinstitute therapy 48-72 hours after the stroke if blood pressure <220/110 mmHg. However, if blood pressure is >220/110 mmHg then lower by 15% over the first 24 hours.

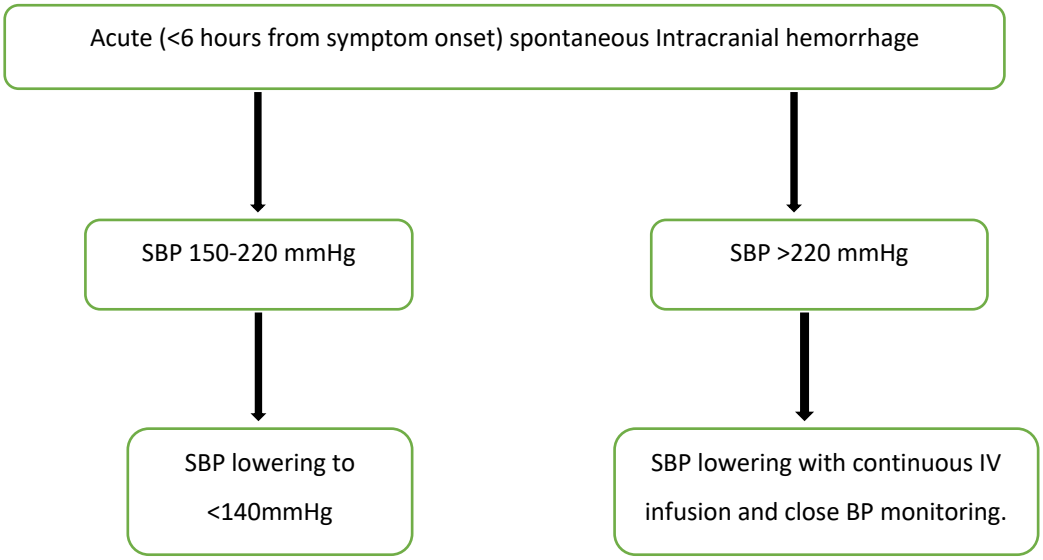
2.4.2 Acute Hemorrhagic Stroke

In intracerebral hemorrhage and subarachnoid bleed, the benefit (reducing further bleeding) of lowering the blood pressure needs to be weighed against the risks (reducing cerebral perfusion) (17). Current Guidelines entail:

1. Systolic blood pressure of more than 200 mmHg or MAP more than 150 mmHg consider aggressive reduction in blood pressure with continuous infusion of medication and monitoring the blood pressure every 5 minutes.
2. Systolic blood pressures of more than 180 mmHg or MAP more than 130 mmHg and evidence or suspicion of elevated ICP, consider monitoring the intracranial pressures and reducing the blood pressure by intravenous antihypertensive as you ensure the cerebral perfusion pressure is in the range of 61-80 mmHg.
3. Systolic blood pressures of more than 180 mmHg or MAP more than 130 mmHg with no evidence or suspicion of elevated ICP, consider lowering the blood pressure slowly with a target MAP of 110 mmHg and a target blood pressure of 160/90 mmHg using slow intravenous or oral medication with checks every 15 minutes.

The INTERACT2 study also concluded that with systolic blood pressures of 150-200 mmHg, acute lowering of systolic blood pressure to 140 mmHg is probably safe (18).

Figure 3: AHA/ACC guidelines in Management of Hypertension in Acute Intracranial Hemorrhage.



American College of Cardiology/American Heart Association 2017 guidelines 2017.

2.5 Cardiac Emergency

2.5.1 Acute Heart Failure

This is characterized by acute dysfunction of the left ventricle and pulmonary edema. This is associated with fluid overload within the lung interstitium and also within the alveoli. This makes getting rid of the fluid the prerequisite in this condition and intravenous diuretics are used for immediate relief in fluid overloaded patients. Sodium nitroprusside or nitroglycerine can be used to effectively lower the blood pressure. However, intravenous labetalol, nicardipine and other oral calcium channel blockers are contraindicated in systolic dysfunction due to their negative inotropic effect. The aim is to ameliorate excess volume and hence pulmonary edema which is achieved by 10% – 15% reduction in blood pressure within the first hour and back to normal over the next 6 hours (19). Once the patient is out of heart failure, then reintroducing the antihypertensive medication systematically with regular follow ups would be essential.

2.5.2 Acute Coronary Syndrome

The aim of treatment is to reduce myocardial oxygen consumption and hence reduce underlying coronary ischemia and improve prognosis. This is achieved in the acute phase by nicardipine, metoprolol or esmolol. Oral or sublingual nitroglycerine also can help lower the blood pressure while at the same time ameliorate retrosternal chest pain. Caution must be taken to ensure there is no evidence of an inferior myocardial infarct before administering nitroglycerin (19).

2.6 Vascular Emergency

2.6.1 Aortic Dissection

Acute medical management among others entail anti impulse therapy by lowering blood pressure and decreasing left ventricular contractility. This entails rapid lowering of blood pressure to a goal of systolic range of 100 – 120 mmHg within 20 minutes of diagnosis. Intravenous beta blockers are given first (esmolol, labetalol, metoprolol, propranolol) to reduce the heart rate below 60 beats per minute. In the process this reduces the shear stress on the aortic wall. Vasodilators like sodium nitroprusside can also be used. Hydralazine is contraindicated in aortic dissection and myocardial infarction because of its reflex increase in sympathetic nervous system tone and myocardial inotropic activity (20).

2.7 Renal Emergencies

Severe hypertension occasionally causes acute hypertensive nephrosclerosis formerly known as malignant nephrosclerosis. It's characterized by microscopic hematuria and elevated serum creatinine.

Pathological finding includes fibrinoid necrosis of small arterioles and onion skinning of small renal arterioles. The renal vascular disease leads to glomerular ischemia and activation of the renin angiotensin system culminating in worsened hypertension.

Acute hemodialysis will correct the acute renal injury, but the reduction of the renal function will require long term blood pressure control for reversal. Fenoldapam, an antihypertensive dopamine agonist, has been shown to lower elevated blood pressure and temporarily improve renal function (21).

2.8 Obstetric Hypertensive Emergency

Pre – eclampsia and Eclampsia

Pre-eclampsia is a multi-organ disease process characterized by blood pressures above 140/90 mmHg and proteinuria. Severe pre-eclampsia encompasses blood pressure ≥ 160/110 mmHg with associated proteinuria. Eclampsia on the other hand will have the patient presenting with convulsions in addition to elevated blood pressure. All above have to be in the presence of pregnancy.

Definitive treatment in eclampsia is delivery of the fetus regardless of the gestational age. However, in pre – eclampsia, the blood pressure has to be managed until the pregnancy is old enough to survive out of utero. This brings into context the management of the acute severe hypertensive phase before long-term blood pressure maintained by oral antihypertensive (22).In the acute setting with severe hypertension, labetalol and hydralazine are the first line agents. The fetal heart rate is monitored during this treatment.

2.9 Studies Assessing Hypertensive Crisis Management

Table 1: Summary of Studies on Assessment of Hypertensive Crisis Management.

Study (n)	Location	Variables assessed	Results
Aysha Almas et. al n = 1336	Karachi - Pakistan	Poorly controlled hypertensive patients > 18 years. Assessment of prevalence of hypertensive crisis, management and outcomes.	Prevalence of hypertensive crisis of 56.3% of the poorly controlled hypertension. Oral calcium channel blockers and intravenous nitrates used in management. Commonest complication acute renal failure at 11.5%.

Pinna et. al n = 1546	Multi centered Italian Study	Hypertensive crisis defined as systolic Bp >220 and/or diastolic Bp > 120mmHg. The proportion of emergencies and gender variation in confirmed crisis.	Prevalence of hypertensive emergency was 25.3%. Commonest emergency being acute pulmonary edema at 30.9%. Compared to women of the same age, men had a higher likelihood of hypertensive emergencies than urgencies.
Nakalema et. al n = 203	Mulago National Referral and Teaching Hospital	Patients ≥18 years old with blood pressures in crisis range defined as ≥180/110 mmHg.	Prevalence of hypertensive crisis was 5.1%. Hypertensive Urgency was 32.5% and emergencies at 67.5%. Acute stroke was the commonest emergencies.
Shao et. al n = 203	Muhimbili National Hospital – Tanzania	Patients in hypertensive crisis presenting at the emergency department over 4 months. Assessment of their clinical presentation, management and outcomes.	Prevalence of crisis was 2.5% with 68% emergencies and 32% urgencies. The commonest symptom was altered mental status at 53.2% and the commonest sign being a low GCS at 44.2%.
Salkic et. al n = 180	Bosnia and Herzegovina	Case control study with patients between 30 -80 years. Those in crisis being the cases and those without being the control.	Incidence of hypertensive crisis was 47.22%. Incidence of urgency being 83.53% and emergency 16.47%.

Aysha Almas et. al performed a cross - sectional study at Aga Khan Hospital in Karachi, Pakistan. The study objective was to determine the prevalence of hypertensive crisis, its management and outcomes at a tertiary centre in the region.

The sample included all poorly controlled hypertensive patients who were >18 years old presenting at the ER. Out of the uncontrolled hypertensive patients, there was a 56.3% prevalence of hypertensive crisis. The predominant class of drugs used to manage the patients in crisis were oral calcium channel blockers and intravenous nitrates. The commonest complication/emergency was found to be acute kidney injury(23).

A multi-centered trial by Pinna et. al to assess hospital admission for hypertensive crisis at the emergency department identified 1,546 patients in hypertensive crisis out of the total number 333,407 patients admitted from the emergency department over one year (2009). The prevalence of hypertensive emergencies was 25.3% with the commonest emergency being acute pulmonary edema at 30.9% followed by strokes at 22% and acute myocardial infarction at 17%. Compared to women of the same age, men were found to have a higher likelihood of developing hypertensive emergencies than urgencies (OR = 1.34, 95% CI 1.06–1.70)(24).

A study done at Mulago national referral hospital by Nakalema et. al over November 2015 to February 2016 to assess the prevalence, pattern and factors associated with hypertensive urgencies and emergencies in Uganda used a sample size of 4000. The prevalence of hypertensive crisis was 5.1% (203/4000) with urgencies constituting 32.5% and emergencies at 67.5%. Acute stroke was the commonest emergency while compliance to medication as the dominant reason for known hypertensive patients being in crisis.

A study done at Muhimbili National hospital by Shao et. al from 1st September 2015 to 31st December 2015 to identify the profile of patients of presenting at the emergency department at the facility showed that of the 8002 patients screened, 2.5% (203) were in hypertensive crisis. Hypertensive emergencies were at 68% and 32% were urgencies. Assessment of clinical presentation showed the commonest symptom was altered mental status at 53.2% and the commonest sign was low Glasgow coma scale at 44.2%. The commonest diagnosis cerebrovascular accident at 31%. 81.2% of the hypertensive emergencies and 36.9% of the urgencies were admitted. The in-hospital mortality rate for hypertensive emergencies and urgencies were 26.8 and 3.1 respectively(5).

A case control study done during November in Bosnia and Herzegovina by Salkic et. al to assess the clinical presentation of hypertensive crisis in the emergency medical department sampled 95 patients between 30-80 years not in crisis (control) and 85 in crisis (cases). 47.22% were diagnosed in crisis with 83.53% being hypertensive urgency and 16.47% being emergencies. The commonest symptom was headache at 75% and chest pain at 48%(25).

2.10 Problem Statement

The burden of hypertensive crisis in our country had yet to be clearly defined despite most patients being on follow up with hypertensive crisis related complications. Lack of published data on the gaps in the diagnosis and management of patients in our country has left most patient in hypertensive crisis to be partially managed. Recommended medication and emergency set up needed for management of patients presenting in hypertensive crisis needed to be evaluated on availability and affordability.

2.11 Justification for the Study

Early identification of patients in hypertensive crisis is key in controlling related complications. Key to this is the establishment of a diagnosis by thorough history taking, astute examination and investigations. This is in order to avoid missing target organ damage that might be subtle. The availability and affordability of the diagnostic investigation in our set up had not been assessed and this study provided an opportunity to address this gap.

The Kenyan 2018 guidelines on hypertensive crisis management that came out during the study, provides different medication to be used for different hypertensive emergencies. However, the recently updated 2017 AHA guidelines on the management of hypertensive crisis offered the best elaborate approach to asses our management of hypertensive crisis. No published data had been collected to establish our diagnostic and management capabilities against any guidelines. This study helped provide information in establishing policy in terms of accurate and affordable diagnostic and treatment guidelines.

Therefore, auditing the clinical practice at the Kenyatta National Hospital against known treatment guidelines was to help interrogate the system.

2.12 Research Questions

Does the current management of patients presenting in hypertensive crisis at the Kenyatta National Hospital adhere to the 2017 AHA/ACC guidelines on blood pressure management?

2.13 Broad Objectives

To evaluate the management of hypertensive crisis against the American Heart Association/American College of Cardiology 2017 blood pressure management guidelines at the Kenyatta National Hospital.

2.14 Specific Objectives

2.14.1 Primary Objective

1. To assess adequacy of diagnostic work up in patients presenting in hypertensive crisis.
2. To assess the appropriateness of treatment in patients presenting in hypertensive crisis.
3. To assess effectiveness of treatment in patients presenting in hypertensive crisis.

2.14.2 Secondary Objectives

1. To determine the proportions of different hypertensive emergencies.

3.0 CHAPTER THREE: METHODOLOGY

3.1 Study Site

The study was conducted at the Kenyatta National Hospital. This is Kenya's main referral hospital located in Nairobi. It has a high influx of patients from all over the country and the main study areas were the accident and emergency department, renal unit, medical wards and medical ICU.

3.2 Study Design

This was a descriptive cross-sectional study.

3.3 Study Population

The records of all hypertensive patients presenting at the Kenyatta National Hospital in hypertensive crisis.

3.4 Inclusion Criteria

Records of all patients offering informed consent presenting with hypertensive crisis range blood pressure.

3.5 Exclusion Criteria

Records of patients presenting with preeclampsia and eclampsia.

3.6 Definition of End Organ Damage

3.6.1 Acute Renal Failure

Kidney Disease Improving Global Outcome (KDIGO) classification of acute kidney disease involve:

1. Increase in serum creatine by ≥ 0.3 mg/dl (≥ 26.5 micro mol/l) within 48 hours.
2. Increase in serum creatinine to ≥ 1.5 times baseline which is known or presumed to have occurred within the previous 7 days.
3. Urine volume < 0.5 ml/kg/h for 6 hours (26).

Examination findings include;

- Edema/anasarca/periorbital edema.
- Pulmonary edema characterized by respiratory distress and bilateral course crackles on auscultation of the chest.
- Uremia characterized by uremic frost, uremic encephalopathy by altered Glasgow coma scale.

Investigation findings would require;

- Urinalysis to asses proteinuria ≥ 300mg/dl, leukocytes or hematuria on dipstick done by the bed side.
- Blood gas analysis to give the pH whether in acidosis or alkalosis with bicarbonate levels and anion gap.
- Abnormal blood urea, electrolyte and creatinine.
- Imaging showing the kidneys and its collecting system to eliminate structural damage by either an ultrasound or Ct scan.

To be included into the study one needed to have documented increase in serum creatinine as defined by the Kidney Disease Improving Global Outcome (KDIGO) classification of acute kidney disease and history and examination finding suggestive of kidney disease above. The above criteria have to be in the presence of hypertensive crisis range blood pressure.

3.6.2 Retinopathy

This was based on fundoscopy finding done at the bed side or ophthalmologist review documented on the file to determine the stage of retinopathy based on the 1939 staging by Keith-Wagener-Barker. Qualification for the study required group 3 or 4 below in the presence on hypertensive crisis range blood pressure.

1. Group 3 – cotton wool patches, arteriosclerosis and retinal hemorrhages
2. Group 4 – Neuro-retinal edema and papilloedema.

3.6.3 Acute Myocardial Infarction/Acute Coronary Syndrome

The American College of Cardiology defines acute myocardial infarction as acute myocardial injury with clinical evidence of acute myocardial ischemia. Additional detection of a rise and fall of cardiac troponin levels with at least 1 value above the 99th percentile of the upper limit and least one of the following (27):

- Symptoms of myocardial ischemia.
- New ischemic ECG changes.
- Development of pathological Q waves.

Symptoms of myocardial ischemia were characterized by acute onset squeezing chest pain and/or associated sweating, dry mouth, difficulty breathing, and dizziness.

ECG showed elevated ST segment for STEMI or an absence of ST segment elevation in NSTEMI. New onset Left bundle branch blocks and axis deviation. Serum troponin levels elevated above the 99th percentile of the upper limit to confirm myocardial injury.

To qualify for the study one had to have at least one symptom and a new elevation of troponin I above the normal levels. Availability of ECG was a welcomed addition. All these had to be in the presence of hypertensive crisis range blood pressure.

3.6.4 Ischemic and Hemorrhagic Cerebrovascular Disease

The American Heart Association defines a stroke as a neurological deficit attributed to an acute focal injury of the central nervous system by a vascular cause, including cerebral infarction, intracerebral hemorrhage and subarachnoid hemorrhage (28).

Clinical symptoms included headache, dizziness, confusion, convulsions, blurry vision or sudden onset blindness, diplopia and dysarthria.

Clinical signs included pupils dilated on one or both eyes or and not responding to light (direct or consensual reflex). Lateral gaze, mouth deviation, para/hemi/quadriplegia, weakness or paresthesia of one side or both, facial droop, ataxia, aphasia and coma. Papilledema on fundoscopy.

Radiological imaging either CT scan brain or MRI can be done if available to confirm diagnosis.

Qualification for the study entailed presence of at least one symptom and one sign with radiological imaging by CT scan or MRI confirming the diagnosis in the presence of hypertensive crisis range blood pressure.

3.6.5 Aortic Dissection

Description of tearing or ripping mild to severe chest, neck, jaw or infra-scapular pain with or without syncope.

Signs included inter-arm blood pressure differential greater than 20mmHg. Chronic Aortic regurgitation signs that include;

a) Becker sign – retinal arterioles visible systolic pulsation on dilatational fundoscopy.
b) Corrigan pulse (water hammer pulse) – peripheral pulse abrupt distension and quick collapse on palpation.
c) De Musset sign – Head bobbing motion with each heartbeat.
d) Hill sign – popliteal cuff systolic blood pressure is 40 mmHg above the brachial cuff systolic blood pressure.
e) Duroziez sign – Systolic murmur over the femoral artery on proximal compression of the artery and diastolic murmur over the femoral artery on distal compression of the artery.
f) Muller sign – Visible systolic pulsations of the uvula
g) Quincke sign – Visible pulsation of the fingernail beds on slight compression of the fingernails.
h) Traube sign (pistol-shot pulse) – Booming systolic and diastolic sounds auscultated over the femoral artery.

Chest x Ray showed a widened mediastinum with a hemothorax in case of raptured aortic aneurysm. If patient was hemodynamically stable and test was available, a CT scan with contrast of the aorta (CT Aortogram) or echocardiogram either trans-thoracic or trans-esophageal was done.

Qualification entailed presence of new onset chest pain with at least 1 sign above and imaging either ultrasound or CT scan confirming the diagnosis in the presence of hypertensive crisis range blood pressure at presentation.

3.6.6 Acute Heart Failure

The American Heart Association defines heart failure as a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood (29). The Framingham criteria has a major and minor criteria as shown below:

Major criteria:

- Paroxysmal nocturnal dyspnea/ orthopnea
- Neck veins distension
- Rales
- Cardiomegaly
- S3 gallop
- Acute pulmonary edema
- Increased venous pressure >16 cmH2O

Minor criteria:

- Ankle edema
- Night cough
- Dyspnea on exertion
- Hepatomegaly
- Pleural effusion
- Tachycardia >120 beats per minute

Chest x ray showed cardiomegaly with widened mediastinum and pulmonary edema. ECG showed tachycardia or bradycardia with left or right axis deviation with bundle branch or fascicular blocks. If available a proBNP level was elevated.

Qualification of patient to be included in the study was based on the Framingham diagnostic criteria of heart failure. 2 major criteria or 1 major and 2 minor criteria in the presence of hypertensive crisis range blood pressure.

3.7 Sampling Technique

Consecutive sampling

3.8 Sample Size

This was determined after pre-screening done over 1 month at the different locations where the study was to be done. During this period, a total of 160 study participants were identified. An extrapolation of this number over 2 months gave a sample size of 320. A sample size calculated using the formula for finite population gave a sample size of 214 and based on the extrapolation from the pre-screening done, this sample size could effectively be obtained over 2 months. This determined the duration of the study.

$$n = \frac{Nz^2pq}{E^2(N-1) + z^2pq}$$

n = Desired sample size

N = population size (number of hypertensive crisis patients reviewed per month at casualty, medical intensive care unit, medical wards and renal unit in Kenyatta National Hospital is approximately 160, and for the 2 months of the study duration the total will be approximately 320).

Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

p = expected true proportion (estimated at 56.3%, from a study conducted by Aysha Almas. et al (2014) looking at patients with hypertensive crisis burden, management and outcomes found 56.3% of them were in hypertensive crisis.)

$q = 1 - p$

E = desired precision (0.05)

$$n = \frac{320\ x\ 1.96^2\ x\ 0.563\ x\ 0.747}{0.05^2(320-1) + (1.96^2\ x\ 0.563\ x\ 0.747)} = 214$$

A Sample size of 214 patients was required for the study.

3.9 The Sampling Procedure

The medical records of all hypertensive patients in the medical wards, accident and emergency, medical intensive care unit and renal unit were reviewed on weekends by the principle investigator and any other day of the week by the two research assistants. The principle investigator would collect data on Saturday and Sunday from 8 am to 4 pm. Each weekend had a site visited and thus in total visited the 4 sites twice over the study period. The two assistants would each alternate days to visit the different sites during the week days from Monday to Friday from 9 am to 2pm. Those with hypertensive crisis range blood pressure identified and their permission sought to participate in the study and if one agreed they would give consent. Those admitted had their files reviewed again after 24 and 48 hours to assess how management was instituted over that period and the outcome.

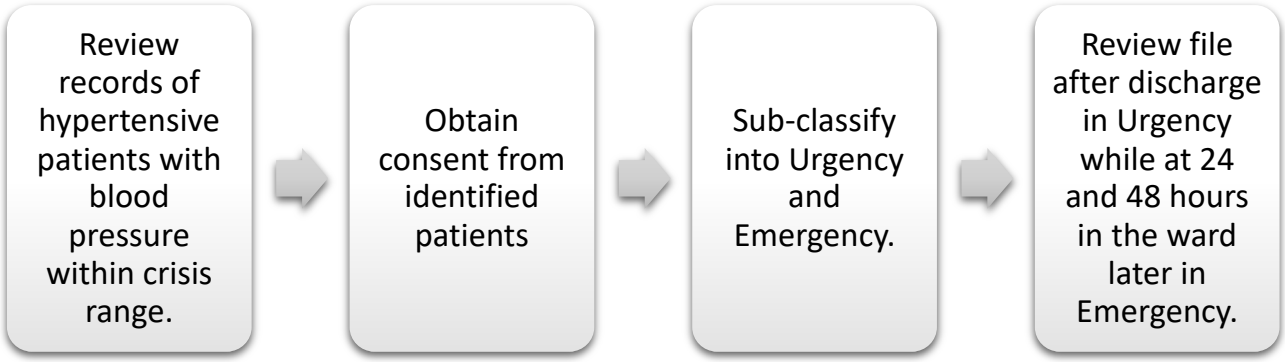
The patients managed at the accident and emergency as urgency had their files reviewed again after discharge to assess the management prior to discharge.

Research Assistant recruitment

The two research assistant was selected and recruited from the university of Nairobi medical school group of third years who had just completed their course work and were on holiday. They were introduced to clinical medical practice that include history taking and examination that include blood pressure measurement.

A week prior to collection of data was used to introduce them to each other and inform them on what the study entailed. This included the definition of hypertensive crisis and what to look for in the file in terms of signs, symptoms and management. Thereafter, they were oriented to the different study sites.

Figure 4: Summary of participants recruitment.



3.10 Study Execution

3.10.1 Adequacy of diagnostic work up.

A clear diagnostic formulation was necessary in order to corroborate the history, examination and investigations in determining the diagnosis. Thus, a preempted guide on the documented history, examination and investigations was formulated. This was to ensure thorough systemic evaluation of the patients presenting in hypertensive crisis.

Once the documented history had been taken, the initial criteria was to determine baseline examination and investigation to help in making the diagnosis and at the same time give evidence of certain target organ damage that can be subtle but critical.

The documented baseline examination included:

1. Blood pressure measurement
2. Pulse rate, rhythm and character
3. Glasgow coma scale
4. Fundoscopy

The documented baseline investigations on the other hand included:

1. Urea, creatinine and electrolytes
2. Urinalysis
3. Electrocardiogram

Upon establishment of the above, then more targeted evaluation was sought after keeping in mind the different target organs damage expected. The evaluation was targeted according to the definition criteria of end organ damage described earlier.

3.10.2. Appropriateness of treatment.

The treatment administered by the health practitioners at the hospital was compared to the AHA/ACC guideline recommended therapy for hypertensive crisis. In hypertensive urgency, known hypertensive patients had their medication prescribed and administered to them for acute management. The newly diagnosed hypertensive patients on the other hand were initiated on appropriate medication as per the Kenyan Hypertensive Management guideline 2018. Patients in emergency on the other hand had the medications listed as the standard.

Table 2: AHA/ACC Management of different Hypertensive Emergencies.

Morbidity	**Medication**
Ischemic Stroke	Labetalol
Hemorrhagic Stroke	Labetalol
Acute Renal Failure	Clevidipine, Fenoldopam, Nicardipine
Acute Coronary syndrome	Esmolol, Labetalol, Nicardipine, Nitroglycerine
Acute Heart Failure	Clevidipine, Nitroglycerine, Nitroprusside
Acute Aortic Dissection	Esmolol, Labetalol

3.10.3. Effectiveness of treatment.

The medication administered was expected to achieve desired blood pressure reduction as per the AHA/ACC guidelines. In hypertensive urgency, no target blood pressure was expected, and the patient was discharged through a medical outpatient clinic for follow up. In case of confirmed end organ damage, following the guideline in the different sequences of therapy were expected to be adhered to while aiming to achieve the desired result.

3.11 Data Variables

3.11.1 Exposure Variables

1. Age – determined from records
2. Sex – determined from records
3. Antihypertensive administered - from records

3.11.2 Outcome Variables

1. Clinical signs and symptoms as documented.
2. Documented investigations
3. Blood pressure outcome after 24 and 48 hours.

3.12 Data Collection

The tool used to collect the data (questionnaire) was designed and modified to collect information from the patients' files. The details included the biodata (age and sex), documented clinical signs, symptoms, investigations and medication given. The information on the blood pressure at presentation and after medication was given at 24 and 48 hours for the emergency group as well as the pressure at presentation and before discharge for the urgency group.

3.13 Data Management

The data collected by questionnaires was coded and entered in a Microsoft Access 2013 database at the end of each day. The data was encrypted to ensure safety and confidentiality. Validation was ensured to minimize errors during entry with regular cleaning in the course of entry. All the hard data collecting tools were kept safe in the principle investigators office under lock while the soft copy data was secured in a hard drive that was password protected and only available to him.

3.14 Data Analysis

Data collection in line with the objectives using the questionnaire was then upon completion transferred to the Statistical Package for social Science version 21. This data was cleaned and stored safely by password protection. The continuous variables (age) was analyzed and expressed as means and median. The categorical variables including signs, symptoms, investigations and medication given were presented as frequencies. The prevalence of hypertensive emergency and urgency was calculated separately against the total number of patients in crisis.

3.16 Ethical Considerations

The project commenced after approval by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (P840/12/2018). All procedures were carried out after elaborate explanation to the study participant and relative/guardian then ensuring verbal confirmation from the participant, guardian or relative before the participants consented in writing or by finger print. The participants in this study were not involved in any other study.

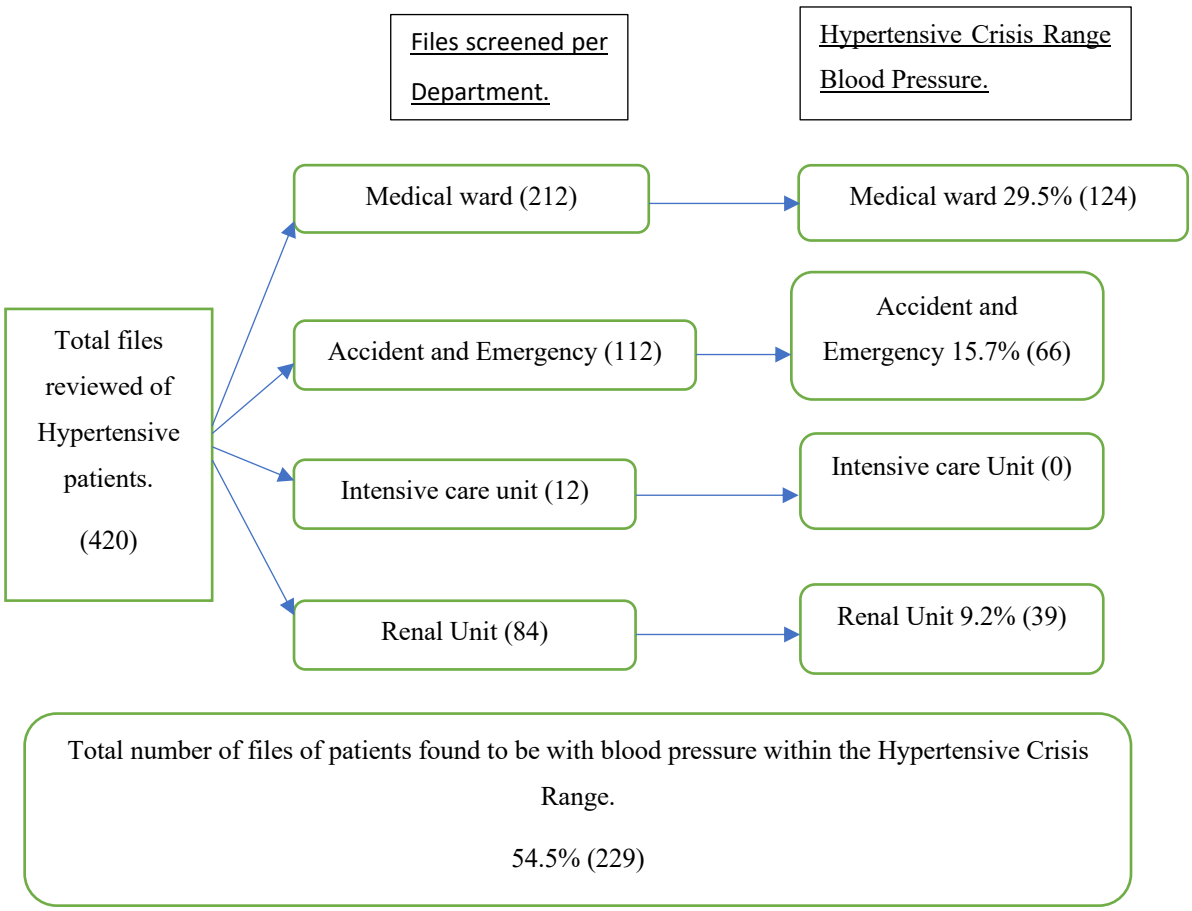
The study was an audit of care given to the patient. There were no invasive procedures involved during execution of the study. The study also did not interfere with patients care. Absolute confidentiality was observed, and the results obtained from the survey was only released into the public domain after permission was obtained from the Kenyatta National Hospital.

4.0 CHAPTER FOUR: RESULTS

4.2 Patient Selection and Distribution

The data was collected between April 4th and May 31st, 2019 and a total of 420 files of hypertensive patients were found and evaluated. 212 files of hypertensive patients in the medical wards were reviewed and out of these 124 were identified to have blood pressure within the hypertensive crisis range. At the accident and emergency, 112 files of hypertensive patients were reviewed, and 66 files were found in hypertensive crisis. 84 files were reviewed at the renal unit and 39 were found to have blood pressures within the crisis range. In the medical ICU, 12 files of patients in hypertension were reviewed but none was found to be within the hypertensive crisis range.

Figure 5: Participants file screening and selection.



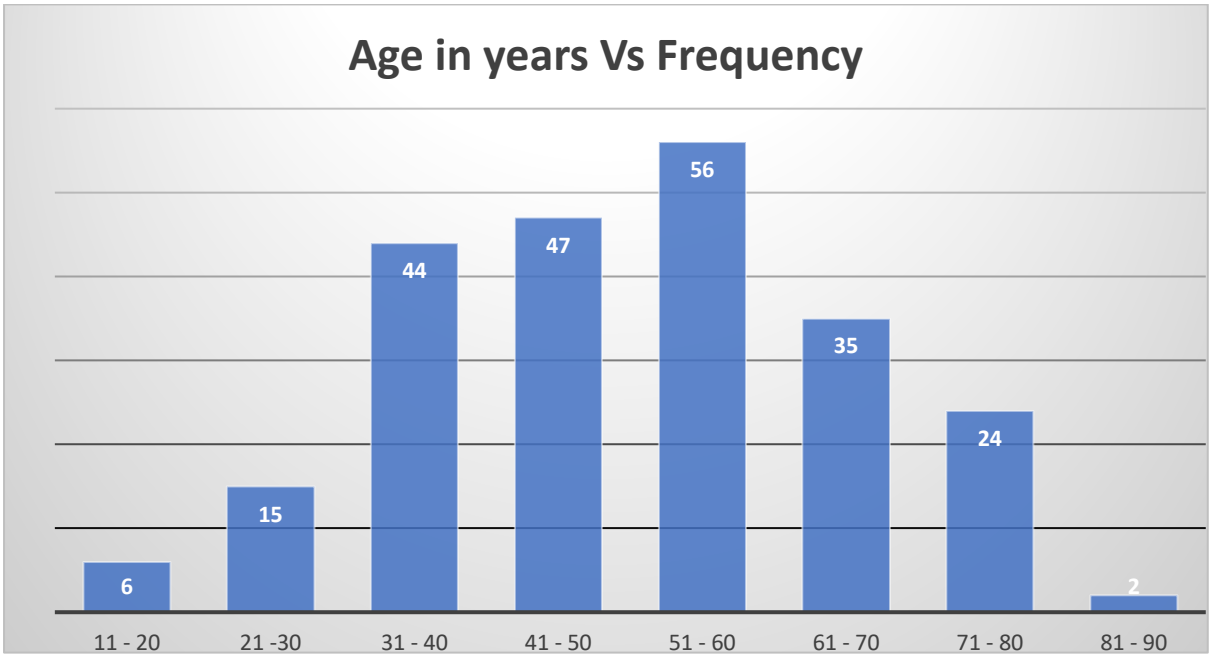
Patient Demographics

The mean age of patients presenting in hypertensive crisis was 51.06 (SD 16.35) with the youngest participant being 15 years and the oldest 89 years. Majority, (52%), of the patients were between 46 – 55 years followed closely by those between 56 – 65 years at 47%. The gender distribution had 109 (47.6%) males and 120 (52.4%) females.

Table 3: Demographic characteristics of study population.

Age Variables	**Frequency n = 229**
Mean (SD)	51.06 (1.081)
Median (IQR)	52.00 (25)
Gender	**Frequency n = 229 (%)**
Male	109 (47.6)
Female	120 (52.4)

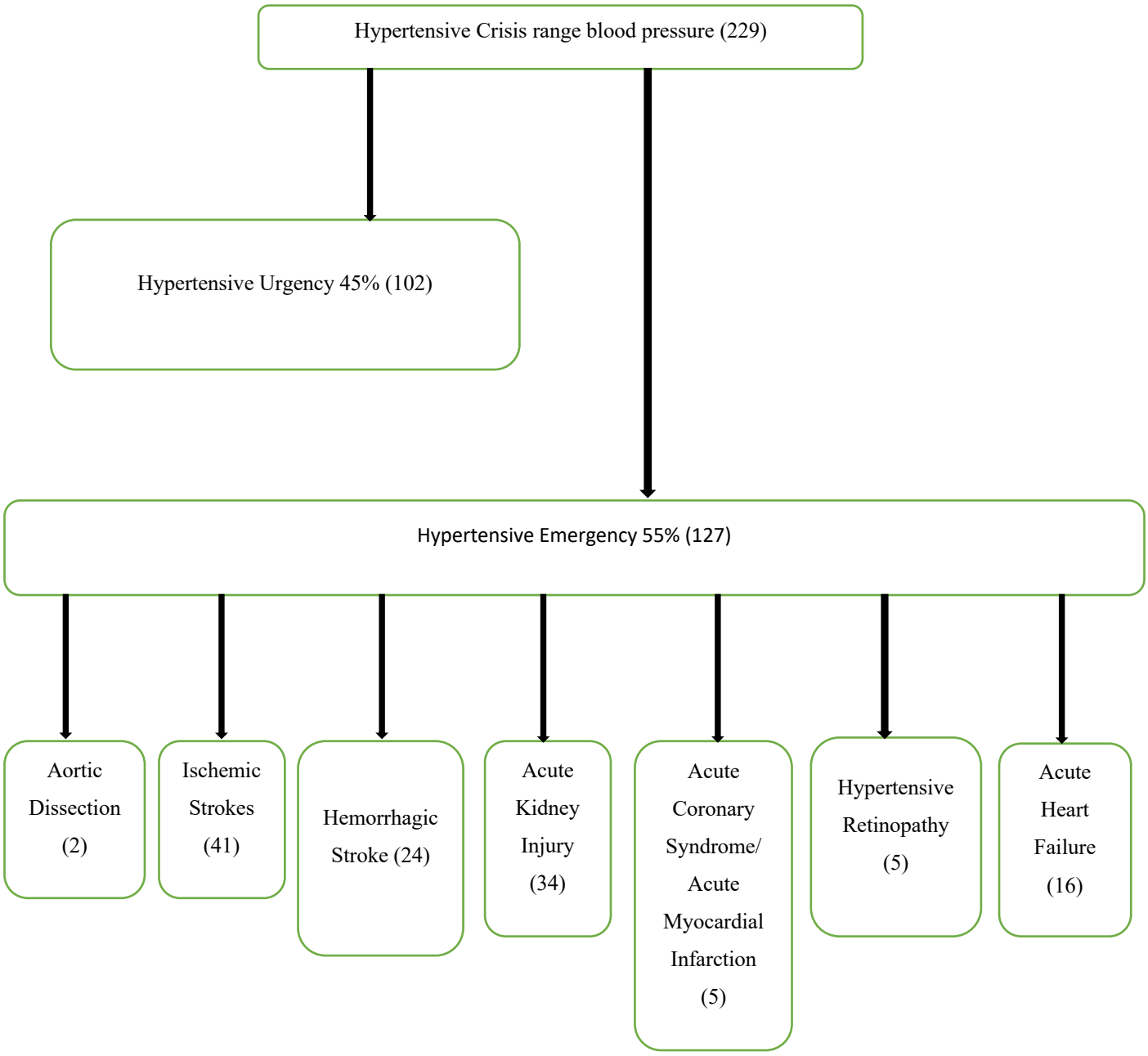
Figure 5: Age in years vs Frequency



4.3 Distribution of Hypertensive Crisis

The files diagnosed as hypertensive crisis were further classified as hypertensive urgency or emergency based on documented absence or evidence of target organ damage respectively. The patients identified as emergencies had the organ involved highlighted and the frequencies of the different emergencies documented as shown below.

Figure 7: Distribution of different hypertensive crisis.



Hypertensive emergencies were dominant at 127 patients (55%) while urgencies were found in 102 patients (45%).

Table 4: Distribution of Sampled Hypertensive Emergencies.

Hypertensive Emergency	Frequency (n=127)	Percentage of Emergency
Ischemic Stroke	41	32.2%
Hemorrhagic Stroke	24	18.8%
Acute Kidney Injury	34	26.7%
Acute Heart Failure	16	12.6%
Acute Coronary Syndrome/Acute Myocardial Infarction	5	3.9%
Aortic Dissection	2	1.6%
Hypertensive Retinopathy	5	3.9%

Stroke was the dominant emergency (combining both ischemic at 41 patients and hemorrhagic at 24 patients) followed by acute kidney injury with 34 patients. Cardiac involvement was also dominant with acute heart failure at 16 patients, acute coronary syndrome at 5 patients and aortic dissection at 2 patients. Hypertensive retinopathy was at 5 patients.

Adequacy of Evaluation

4.4 Evaluation of Hypertensive Crisis

Table 5: Evaluation of symptoms assessed in Hypertensive Crisis.

Brain	% Done	Cardiac	% Done	Renal	% Done	Retina	% Done
Headache	92% (210)	Dyspnea	89% (203)	Urine frequency or amount	52% (119)	Change in vision	21% (50)
Focal Weakness	85% (194)	Fatigue	61% (139)	Urine colour change	37% (84)		
Confusion	88% (201)	Chest pain	62% (141)	Abdominal Pain	81% (185)		
Convulsion	84% (192)	Cough	85% (194)	Body swelling	94% (215)		
Altered level of consciousness	80% (183)	Syncope	66% (151)				
		Dizziness	90% (206)				

The symptoms assessed showed good neurological assessment with headaches being assessed in 92% (210) followed by confusion in 88% (201). The frequencies of assessment for focal neurological deficit, convulsion and altered level of consciousness were at 85% (194), 84% (192) and 80% (183) respectively. Cardiac symptoms were also well evaluated with 90% (206) having been evaluated for dizziness followed by 89% (203) evaluated for dyspnea. Other symptoms assessed were syncope at 66% (151), chest pain at 62% (141) and fatigue 61% (139).

The assessment of the renal system had body swelling assessed in 94% (215) and abdominal pain assessed in 81% (185). However, urine frequency and character were poorly assessed with change in the frequency or amount of urine at 52% (119) and change in urine colour assessed in 37% (84). Visual change was poorly assessed in only 21% (50).

The baseline examination done showed all files had blood pressure measurement while pulse examination was documented on 78% (178) of the study population. The Glasgow Coma Scale was also documented in 71% (162) but fundoscopy was poorly done at 2.6% (6). The baseline investigations had urea electrolytes and creatinine done at 80% (184), urinalysis at 36% (82) and electrocardiography done at 18% (41). This showed poor baseline screening examination and investigations.

4.5 Evaluation of Hypertensive Emergencies

Table 6: Evaluation of the examination and investigation done in hypertensive emergency involving the central nervous system (n = 65).

Examination	Frequency (n)	Investigations	Frequency (n)
Cranial Nerve Examination	58	Brain Imaging CT scan or MRI	65
Focal Neurological Deficit examination	65		
Fundoscopy	4		

These were patients identified to have ischemic or hemorrhagic stroke. Their assessment was well done clinically with cranial nerve examination in 58 patients. All patients had examination to look for focal neurological deficit. However, only 4 had fundoscopy done.

Imaging of the brain as a confirmatory investigation was done on all the patients with hemorrhagic or ischemic stroke.

Table 7: Evaluation of examination and investigation finding in acute heart failure as a hypertensive emergency (n = 16).

Examination	Frequency (n)	Investigation	Frequency (n)
Bilateral Chest Crackles	16	Chest X ray	16
Edema	16	Echocardiograph	14
Oxygen Saturation	16	ECG	14
Fundoscopy	1		

The examination of patients in acute heart failure was excellently done with all of them having auscultation of the chest to assess bilateral crackles. All the patients also had documentation on oxygen saturation and edema. Fundoscopy was documented on 1 patient.

All the patients had a chest x ray done and 14 had an electrocardiogram and echocardiogram done.

Table 8: Evaluation of examination and investigation finding in Acute Coronary Arterial Disease as a hypertensive emergency (n = 5).

Examination	Frequency (n)	Investigations	Frequency (n)
Oxygen Saturation	5	Troponin	5
Fundoscopy	1	Chest X ray	2

All the patients with acute ischemic heart disease had comments on their oxygen saturation by pulse oximetry with subsequent intervention upon noticing an abnormality.

Troponin levels were done on all the patients while a chest x ray was done in 2 of the patients.

Table 9: Evaluation of signs and investigations in Aortic Dissection (n = 2).

Examination	Frequency (n)	Investigations	Frequency (n)
Chronic Aortic Regurgitation signs	2	Echocardiograph	2
Pulsatile Abdominal Aorta	2	CT Aortogram	2

All the patients had at least 1 documented examination finding suggestive of aortic regurgitation signs and a pulpable abdominal aorta.

An echocardiogram suggestive of aortic aneurysm and a subsequent CT aortogram was done on all the patients.

Table 10: Evaluation of signs and investigations in Acute Kidney Injury (n = 34).

Examination	Frequency (n)	Investigations	Frequency (n)
Fluid overload signs	34	Urinalysis	17
		Renal Imaging	29

Different signs of fluid overload were documented in all the patients in acute kidney injury. Renal imaging was done in 29 of the patients to assess any structural pathology of the kidney while urinalysis was documented in only half the number of patients in acute kidney injury.

Appropriateness and Effectiveness of Treatment

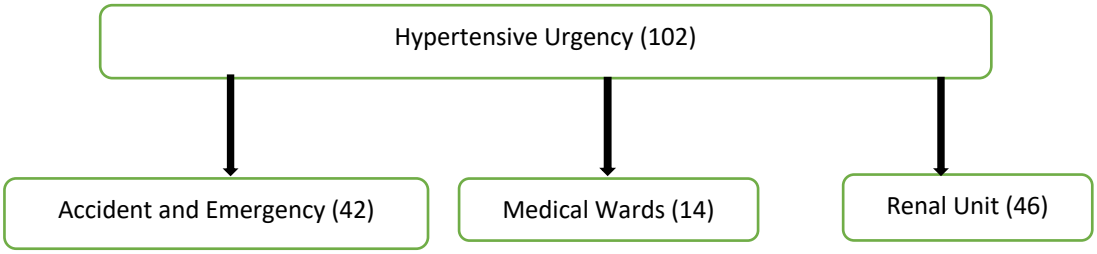
4.6 Management of Hypertensive Urgency (n = 102).

The files of patients identified to be in hypertensive urgency were distributed between the renal unit, medical ward and accident and emergency. Those in the renal unit (46 patients) were chronic kidney disease patients with hypertensive crisis range blood pressure and underwent twice weekly dialysis.

The files of patients identified at the accident and emergency were either newly diagnosed or known hypertensive patients with acute symptoms and hypertensive crisis range blood pressures. They presented to casualty for evaluation of any underlying condition and were a total of 42.

In the medical wards, a total of 14 hypertensive patients were identified. They were admitted to either manage the blood pressure and investigate for end organ damage or admitted for ailments unrelated to the hypertension. However, during the hospital stay they developed hypertensive crisis range blood pressures that required treatment.

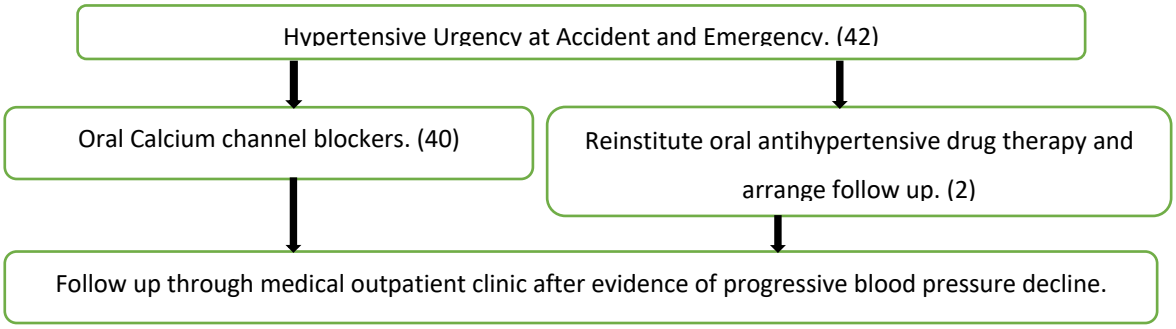
Figure 8: Distribution of Hypertensive Urgency managed in different departments.



At the accident and emergency, the newly diagnosed hypertensive patients in crisis were 16 while those known to be hypertensive and in crisis were 26. All newly diagnosed hypertensive patients had a calcium channel blocker prescribed after identification of the elevated blood pressure. Blood pressure was later measured prior to discharge through the medical outpatient clinics.

The known hypertensive patients also had similar treatment with 24 patients receiving calcium channel blockers. However, 2 patients had their own antihypertensive medication prescribed. Their blood pressures were measured prior to discharge through the medical outpatient clinic.

Figure 9: Management of Hypertensive Urgency at the Accident and Emergency.

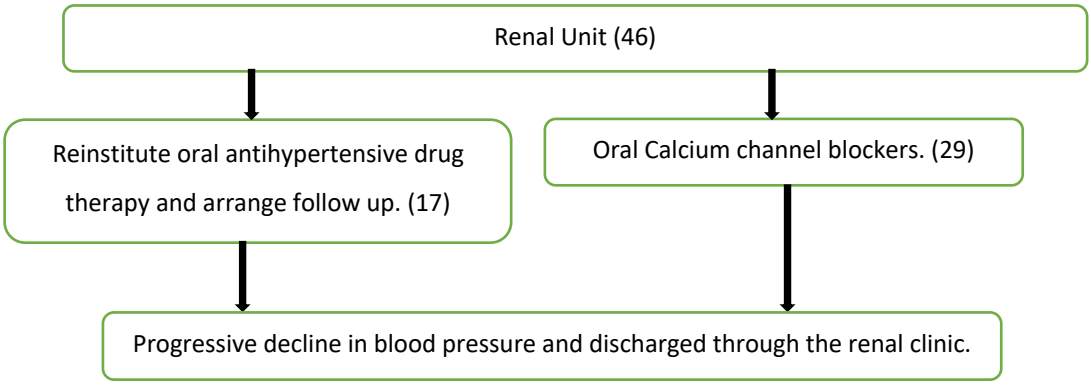


The files identified at the medical ward had 14 patients in urgency. However, unlike the accident and emergency, all the patients were known hypertensive. They all had their already prescribed medication given to them. The blood pressure measurement was done in the morning and evening with no documented monitoring in between to assess progress. The patients once stable and evaluation showing no end organ damage were discharged through the medical outpatient clinic.

The files identified at the renal unit had 46 patients identified as hypertensive urgency who either had the elevated blood pressure before, during or few minutes after dialysis. All these patients were known hypertensive patients either due to renal parenchymal disease or had renal disease as a consequence of hypertension.

17 patients were able to take their own antihypertensive medication while the rest of the patients received calcium channel blockers at different doses. Nifedipine was given to 20 patients and 9 patients received amlodipine. Both groups of patients had progressive decline in blood pressure and were discharged through the renal clinic.

Figure 10: Management of Hypertensive Urgency at the Renal Unit.



4.7 Management of Hypertensive Emergency (n=127).

The files in this group of patients had evidence of end organ damage. The AHA/ACC recommends that these patients should be managed in the intensive care unit or high dependence unit. However, all the patients identified with end organ damage were managed within the medical ward.

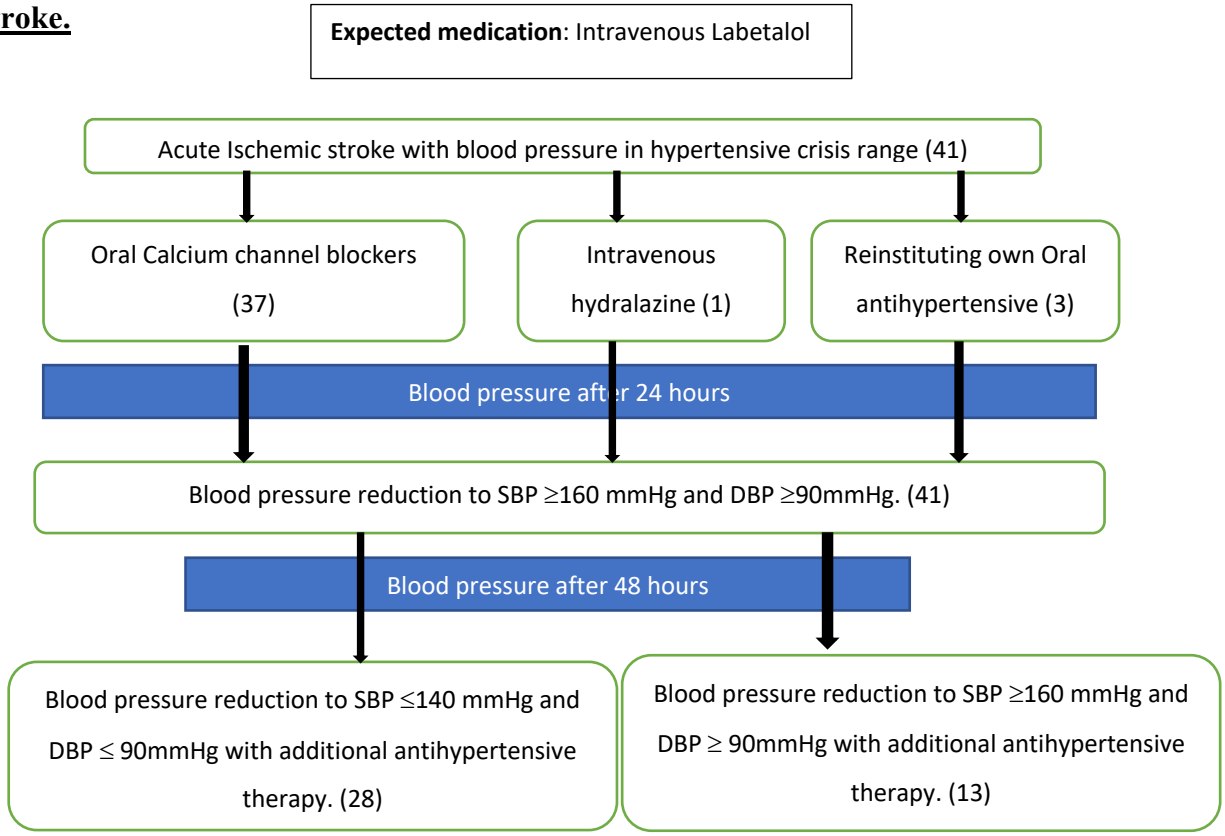
4.7.1 Acute ischemic Stroke (n = 41)

The AHA/ACC has guidelines for the management of blood pressure in ischemic stroke during the acute phase in case thrombolysis is indicated or not (31). The recommended medication is intravenous labetalol to lower the blood pressure with close monitoring in an ICU setting. Thrombolysis is indicated within 4.5 hours of onset of symptoms and absence of contraindication of thrombolysis such as bleeding dyscrasias, intracranial hemorrhage and head trauma in the previous 3 months (32). All the patients managed within the medical ward presented at the accident and emergency within 48 – 120 hours (2 – 5 days) from onset of symptoms. None of the patients underwent thrombolysis and were all admitted to the medical ward.

At the accident and emergency, the patients were started on different antihypertensives to lower the blood pressure. 37 patients were started on calcium channel blockers with 33 patients on nifedipine and 4 patients on amlodipine. 1 patient was started on intravenous hydralazine and 3 patients had reintroduction of their own antihypertensive medication. The patients were then admitted but no clear monitoring was done after the initial reading until once in the ward. Therefore; no clear decline in blood pressure was documented.

The guidelines also instruct the initiation of therapy should be at least 48 – 72 hours after the initial symptoms; however, the patients were started on the antihypertensive medication at presentation once identified at the accident and emergency. 24 hours from admission, the blood pressure in all the patients was ≥160/90 mmHg regardless of the therapy administered.

Figure 11: Management of Hypertensive Crisis range blood pressure in Acute Ischemic Stroke.

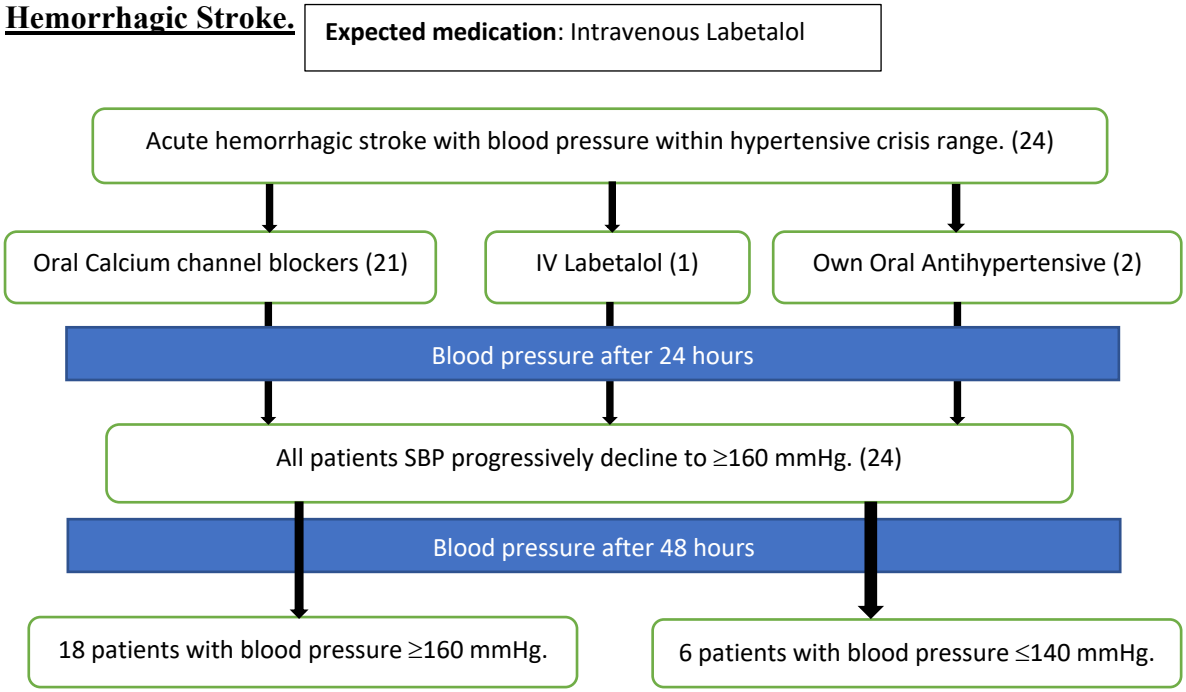


After 48 hours, the blood pressure in 28 patients had been reduced to ≤140/90 mmHg upon additional antihypertensive therapy. Once stable the patients were discharged through the medical outpatient clinic and the neurology clinic.

4.7.2 Acute Hemorrhagic Stroke (n = 24).

The recommended medication in the management of hypertensive crisis blood pressure range in the presence of hemorrhagic stroke is labetalol. However, only 1 patient had the drug used to manage the blood pressure while at the accident and emergency. 21 patients were started on calcium channel blockers with 16 started on nifedipine and 5 on amlodipine. 2 patients were reinitiated on their own antihypertensives. The guidelines advised management to be based on maintaining the systolic blood pressure range between 150-220 mmHg. However, all the patients were managed without following this management criteria. No documentation of mean arterial pressure was noted during the treatment process.

Figure 12: Management of Hypertensive crisis range blood pressure in Acute Hemorrhagic Stroke.



The patient initiated on intravenous labetalol, the guideline prescribed medication for management of elevated blood pressure in crisis, was given the initial stat dose and the repeat measurement had the systolic blood pressure lowered and still ≥160 mmHg.

The treatment was hence stopped, and patient transferred to the medical ward after review by the neurosurgical and ICU team. Two patients reinitiated on their prescribed antihypertensives and 17 patients started on oral calcium channel blockers had their systolic blood pressure reduced to ≥160 mmHg and transferred to the ward. After 48 hours, 6 patients had their systolic blood pressure ≤140 mmHg on additional antihypertensive medication. The rest required titration of the different antihypertensives to lower the blood pressure further.

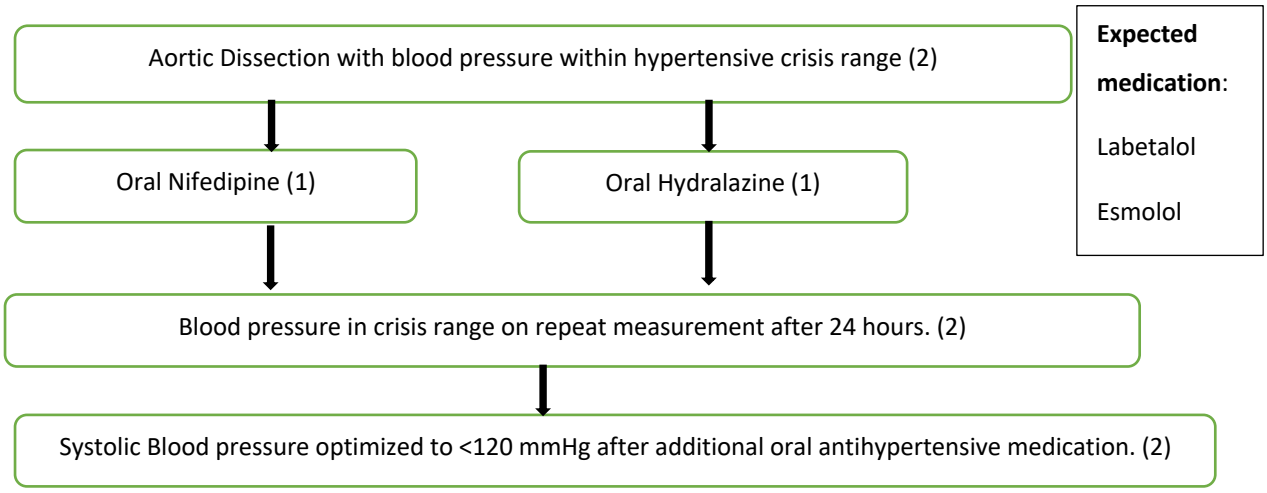
The patients were then discharged through the medical outpatient clinic and the neurology clinic once stable.

4.7.3 Aortic Dissection (n = 2),

The guideline prescribed medication for lowering hypertensive crisis range blood pressure in the presence of aortic dissection include labetalol or esmolol. The medication should be given with a target of lowering the systolic blood pressure to < 120 mmHg over 20 minutes. However, the medication used on the 2 patients had 1 patient receiving a calcium channel blocker (nifedipine) while the other patient received a vasodilator (hydralazine).

Repeat blood pressure monitored (time not documented) showed no significant reduction in blood pressure and patients were transferred to the ward. Over 24 hours none of the patients achieved the desired target blood pressure reduction. After 48 hours, the desired blood pressure was achieved after addition of other antihypertensive medication.

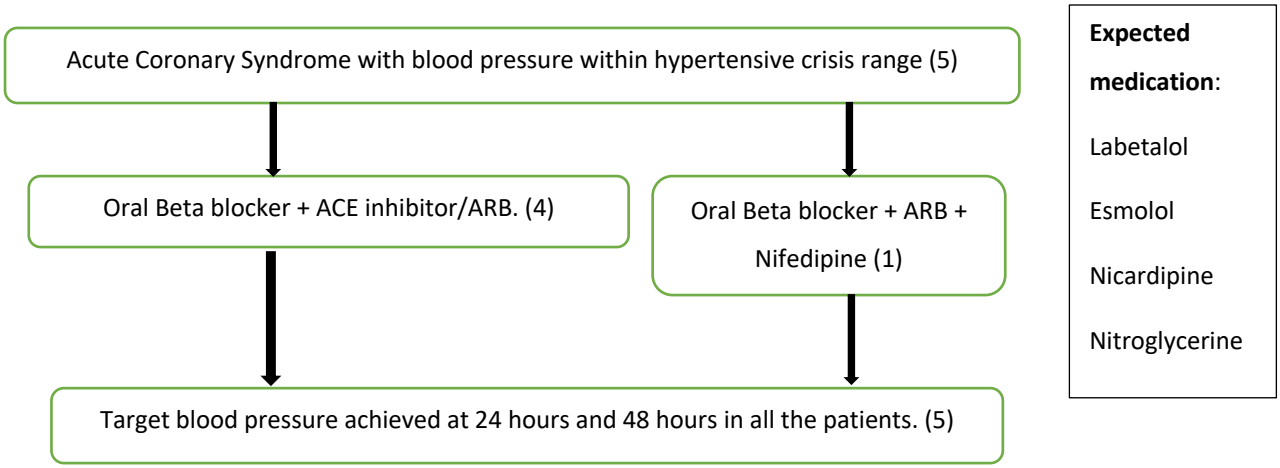
Figure 13: Management of Hypertensive Crisis range blood pressure in Aortic Dissection.



4.7.4 Acute Coronary Syndrome (n = 5).

The guideline prescribed medication used in reduction of hypertensive crisis range blood pressure in acute coronary syndrome include labetalol, esmolol, nicardipine or nitroglycerine.

Figure 14: Management of Hypertensive Crisis range blood pressure in Acute Coronary Syndrome.



However; the drugs used in management of elevated blood pressure in acute ischemic heart disease included beta blockers, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers. There was addition of a dihydropyridine calcium channel blocker in one patient who did not achieve desired target blood pressure reduction and had angina. These combination therapy, at different titrated formulation, achieved the targeted blood pressure

reduction in all the patients at 24 and 48 hours respectively. The patients once stable were discharged through the cardiology clinic.

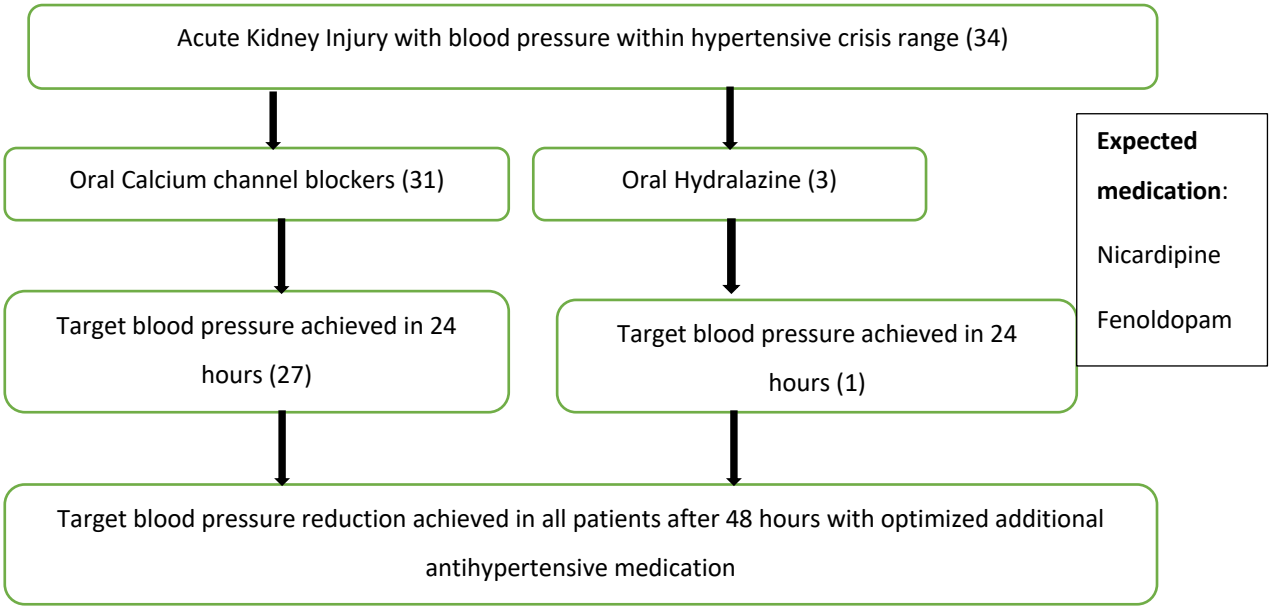
4.7.5 Acute Kidney Injury

The guideline prescribed medication expected include nicardipine and fenoldopam, however, in the study, the drugs used included nifedipine, amlodipine and hydralazine.

The aim was to lower the blood slowly targeting ≤130/80 mmHg. Of the 34 patients found in acute kidney injury 23 received nifedipine and 8 received amlodipine.

Hydralazine was administered to 3 patients.

Figure 15: Management of Hypertensive Crisis range blood pressure in Acute Kidney Injury.



The sample that received the calcium channel blockers showed great reduction in blood pressure.

Nifedipine reducing the blood pressure in 20 patients over 24 hours and all the patients achieved target blood pressure reduction after 48 hours on additional antihypertensive therapy.

Amlodipine as well had target reduction in blood pressure achieved in 7 patients after 24 hours and all achieved target blood pressure after 48 hours on additional antihypertensives.

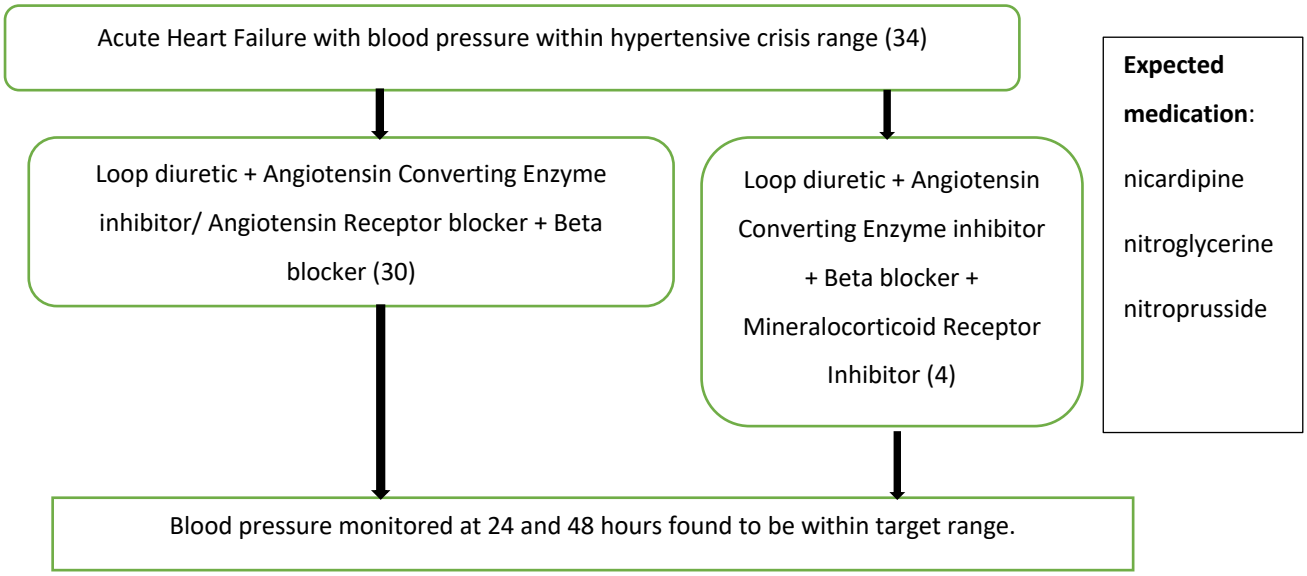
Hydralazine had only 1 patient achieving target blood pressure in 24 hours and the rest after 48 hours on introduction of additional antihypertensives.

Once stable, the patients were discharged through the renal clinic.

4.7.6 Acute Heart Failure (N = 16)

The guideline recommended drug of choice is nicardipine, nitroglycerine or nitroprusside in the management of high blood pressure in heart failure. However, in the study different medication were used in the 16 patients found to be in failure.

Figure 16: Management of Hypertensive Crisis range pressure in Acute Heart Failure.

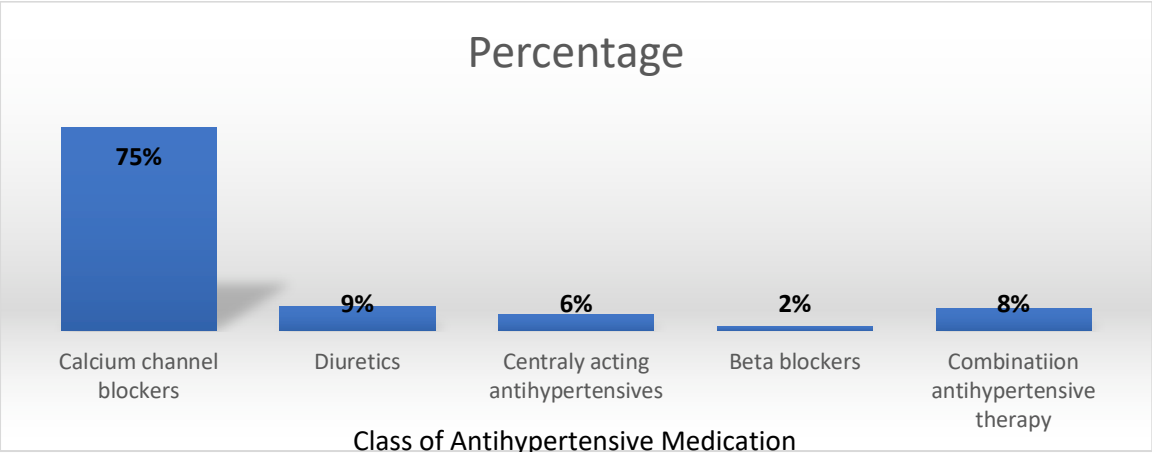


Treatment options used on 12 patients included a combination of loop diuretics, ACE inhibitor and a beta blocker. 18 patients received a loop diuretic, ARB and a beta blocker. 4 patients received a loop diuretic, ACE inhibitor, a beta blocker and a mineralocorticoid antagonist.

These medications were started at high tolerable doses and titrated down against the blood pressure. This would lead to very rapid reduction in blood pressure with documented hypotension in 8 patients after 24 hours.

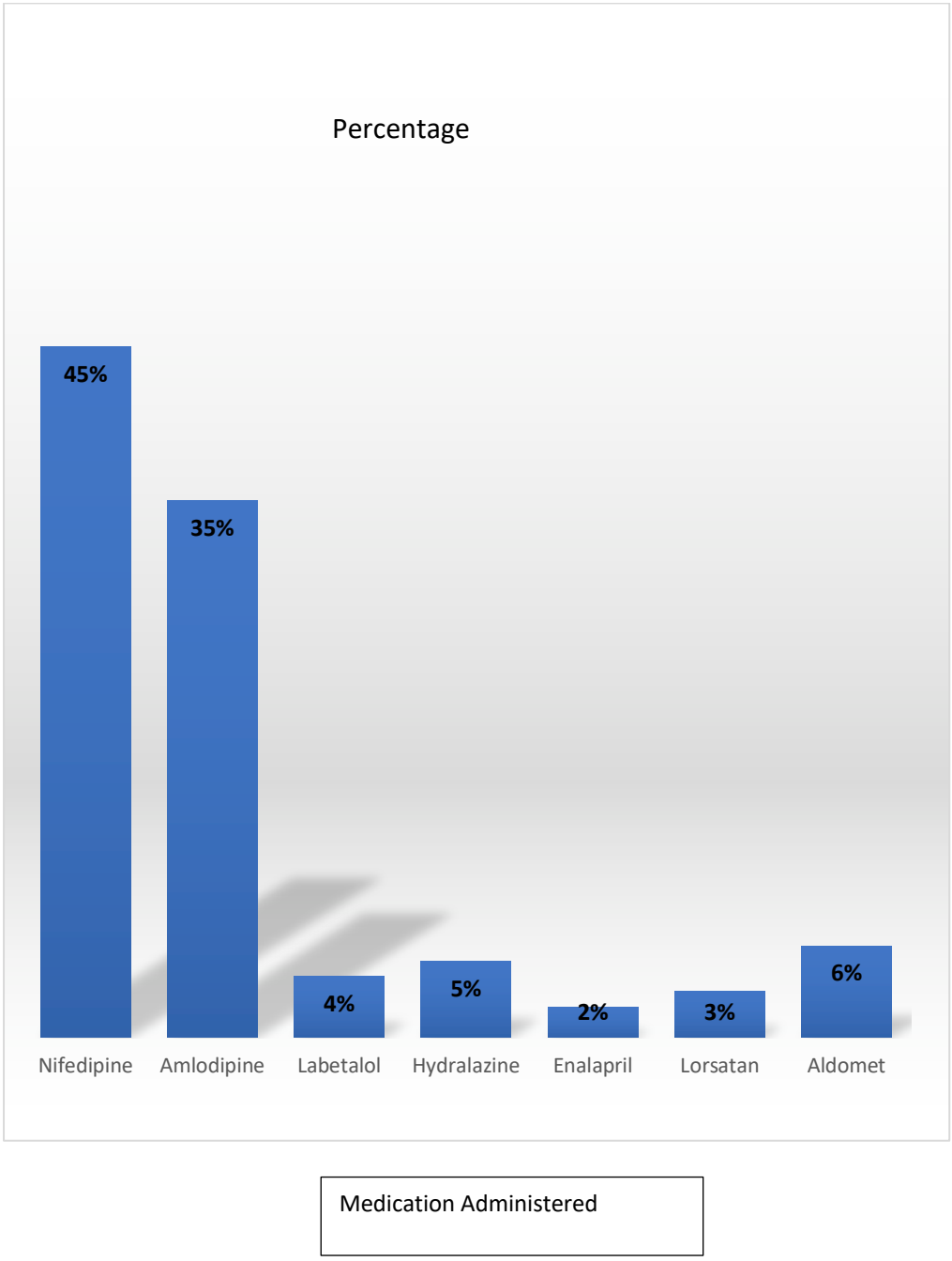
4.8 Medication Used in Hypertensive Crisis at The Kenyatta National Hospital

Figure 17: Class of drugs used on patients in Hypertensive crisis.



The commonest class of medication used were the calcium channel blockers on 173 patients (75.5%) with the commonest drugs being Nifedipine on 109 patients (47.6%) and Amlodipine on 82 patients (35.8%).

Figure 18: Drugs used on patients in Hypertensive crisis.



5.0. CHAPTER FIVE: DISCUSSION

In the audit, demographic characteristics that included age and gender showed similar trends with the median age in the study being 51 years while in Muhimbili and Mulago being 55 years. Hypertensive emergencies were dominant at 127 (55%) while hypertensive urgency at 102 (45%). This was comparable to the cross-sectional study in Mulago national referral hospital that found hypertensive urgency at 32.5% and emergencies at 67.5%. The sample participants in Mulago and Muhimbili were both from the accident and emergency unlike in our audit where we included both the in and outpatients' participants. A similar descriptive study at the accident and emergency department in Muhimbili national hospital found more patients 138 (68%) as emergencies and 65 (32%) as urgencies.

It was important to highlight the younger population (< 20 year old) who presented in hypertensive crisis. 2.6% (6) were under 20 years and had a diagnosis of secondary hypertension. The commonest emergency was acute kidney injury in 4 of the study participants and the other 2 had no evidence on end organ damage. However, its important to state that none of them had an eye check via fundoscopy nor slit lamp.

Table 11: Prevalence of Hypertensive Crisis in East Africa.

	KNH (KENYA)	MULAGO (UGANDA)	MUHIMBILI (TANZANIA)
Median Age (years)	51	55	55
Hypertensive Urgency (%)	45	32.5	32
Hypertensive Emergency (%)	55	67.5	68
Commonest Emergency (Acute Stroke as a %)	51	58	31
Female: Male ratio	1.1: 1	1.2: 1	1.1: 1

The ACC/AHA guidelines direct that the management of hypertensive emergency should be in an emergency setting preferably in intensive care unit or high dependence unit (33). However, from the audit, none of the patients in emergency were managed in an intensive care unit. In fact, no patient was identified during the study period to have been admitted in the medical ICU. Most of the patients admitted through the accident and emergency had documentation citing lack of bed space as the reason for not being admitted in the medical ICU. The patients within the medical wards upon review by an intensivist had similar comments on the file.

The nephrology team on the other hand would instruct that the patient be initiated on renal replacement therapy as concurrent blood pressure management continued within the medical ward.

Acute ischemic stroke was the commonest hypertensive emergency at 41 (17.9%) while both ischemic and hemorrhagic stokes constituted 51% as the dominant emergency. Similarly, both studies in Mulago and Muhimbili had acute stroke in 58% and 31% respectively as the commonest emergencies.

The baseline examination and investigations were effective screening methods for identification and classification of the different emergencies. These were well done and assisted in diagnosing different emergencies, however, fundoscopy was hardly done with the examination being done on 6 patients (2.6%). This could also be a reason as to why the diagnosis of retinopathy was scarce. Fundoscopy was not done on hypertensive urgency patients and none were referred to the ophthalmology clinic for follow up. The patients who had documented fundoscopy results were all within the medical wards and this was done by the ophthalmology residents.

A study showing the benefit of early fundoscopy in patients in hypertensive crisis showed younger patients in hypertensive urgency were at higher risk of developing stage 3 or 4 retinopathy since chronic compensatory mechanisms may not have developed (34).

The hospital had certain basic investigations that all patients had to undergo before getting into the ward as baseline investigations. These included a total blood count, liver function tests and urea creatinine and electrolytes. This would explain the result of 184 patients (80%) having urea creatinine and electrolytes test found in the study as well as more patients in acute kidney injury.

Cardiac evaluation with electrocardiographs was at 41 (18%), which was quite poor considering it should at least be a baseline investigation to help determine the next step in management (35). The electrocardiographs were all done within the medical wards and none were done at the accident and emergency nor the renal unit due to lack of the electrocardiograph machines in these departments. This also could explain the reduced diagnosis of cardiac disease especially at the accident and emergency where screening should be done on all patients with crisis range blood pressure. Delays in having an electrocardiograph could lead to delays in appropriate treatment and hence poor outcomes (36).

Urinalysis, also another investigation considered to be part of the baseline investigations was also not well done with only 82 (36%) of the patients having the investigation done. Majority of the patients who had urinalysis done were from the medical ward. None of the patients at the accident and emergency department had a urinalysis done. A bedside dipstick urinalysis at casualty could be a prompt and affordable test to perform in a resource limited area to help in the diagnosis of acute kidney injury in hypertensive crisis (37). This would give an initial assessment of renal injury and guide on the next evaluation process.

Investigations to confirm emergencies were based on the clinician's judgement after taking the history and examining the patients. These investigations were targeted to the different organs to detect injury. The study showed great precision in targeted approach to detect organ damage with both laboratory and imaging investigations. Although there are no guidelines on the appropriate investigations to perform in patients in hypertensive crisis, organizing them into the baseline investigations and examination first prior to the targeted ones would help avoid missing subtle end organ damage. Of note as well is that attempts to search for another organ damage other than the identified injured one was hardly done.

The AHA/ACC guidelines have a list of approved medication to be used in management of different hypertensive emergencies. Most of these medications however are expensive and not easily available at the institution unless one can purchase from outside the facility if financially capable.

Patients in acute ischemic stroke needed to be classified as those who need to undergo thrombolysis and those disqualified depending on the time from onset of symptoms (38). However, the patients in the study were not classified and none underwent thrombolysis. One reason could be a delay in presentation with most of the patients presenting days after the onset of symptoms hence out of the time threshold for thrombolysis.

Thrombolysis should ideally be done in an ICU setup, however, all the patients identified during the audit were admitted within the medical ward or the renal unit and therefore no close monitoring could be done in case thrombolysis was initiated. The medication of choice according to the guideline should be intravenous labetalol (39). However, none of the patients with acute ischemic stroke received the medication. No documentation explained the reason why alternative medication was prescribed.

The introduction of the antihypertensive medication, in those who don't qualify for thrombolysis, should also be started at least 48-72 hours since no benefit has been seen with early reintroduction of the medication. The patients were started on antihypertensive medication upon admission and the blood pressures were noted to have reduced quite fast. Most of the patients with acute ischemic stroke (37 patients) were started on calcium channel blockers and seem to lower the blood pressure very fast contrary to the American Ischemic Stroke management guidelines (40).

Patients with acute hemorrhagic stroke also needed blood pressure reduction within a specific range. Those with systolic blood pressure above 220 mmHg needed blood pressure reduction by slow infusion of labetalol over 24 hours. Those with systolic blood pressure below 220 mmHg needed the blood pressure maintained within 220-150 mmHg by the same medication (41). Most of the patients received oral calcium channel blockers with comparable reduction in blood pressure in the acute phase as 1 patient who received intravenous labetalol. However, the decision to choose the oral calcium channel blocker over the preferred medication was not documented. Although there was adequate reduction in the blood pressure, the reduction was fast and the dip in pressure lower than the desired level. This highlights calcium channel blockers a good alternative especially if the patient is well monitored (42).

In aortic dissection the guideline prescribed medication for lowering hypertensive crisis range blood pressure in the presence of aortic dissection include labetalol or esmolol. The medication should be given with a target of lowering the systolic blood pressure to < 120 mmHg over 20 minutes (43). However, none of the patients in the audit received neither medication. In fact, one of the patients received hydralazine, a drug that is contraindicated in aortic dissection due to its positive inotropic effect. Subsequently, none had the appropriate response in blood pressure. None had the desired decrease in blood pressure. However, additional oral antihypertensive therapy led to the desired blood pressure.

Once the pressure was stable, the patients had surgical repair of the dissection and discharged for follow up through both the cardiology and cardiothoracic clinic.

In patients with acute coronary syndrome, the medication necessary to lower the blood pressure include labetalol, esmolol, nicardipine or nitroglycerine. The decline in blood pressure after the episode should follow a J or U-shaped curve association between the decline in blood pressure and risk of subsequent cardiovascular event. Target systolic blood pressure should range 130-140 mmHg with diastolic blood pressure of 80-90 mmHg.

A decline of blood pressure <110/70 mmHg was considered dangerous (44). None of the patients received the guideline prescribed medication in the acute phase. However, they were started on a combination of therapy to manage the coronary syndrome with beta blockers, ACE inhibitors or ARB and dihydropyridine calcium channel blockers. These combination over 24 and 48 hours seem to have adequately lowered the blood pressure. This was achieved by titration of different doses of each of the medication to achieve the desired effect.

In acute renal failure, calcium channel blockers like amlodipine and nifedipine or vasodilator - hydralazine - was used. Despite the use of the above medication, the target reduction in the blood pressure was achieved slowly over 24 – 48 hours in all the admitted patients. Intensive blood pressure reduction has been noted to lead to frequent events of acute kidney injury (45). Therefore, systolic blood pressure targets should range 140-130 mmHg while diastolic blood pressure range of 90-80 mmHg. The medication was administered orally before, during or after dialysis with the desired target being achieved eventually. Calcium channel blockers also have been shown to prevent progression from acute to chronic kidney disease by acting at the vascular and tubular epithelium level (46).

The patients in acute heart failure needed guideline directed medication that included nicardipine, nitroglycerine or nitroprusside to lower the blood pressure in the acute phase. However, neither of the patients received the medication but instead received different doses of left sided heart failure therapy with subsequent progressive decline in blood pressure (47). The targeted systolic blood pressure of <120 mmHg compared to <140 has shown significant reduction of acute decompensated heart failure events (48).

5.1 CONCLUSION

The audit highlighted the challenges in the adequacy of diagnostic work up as well as the inappropriateness and ineffectiveness of management of hypertensive crisis as observed at the Kenyatta National Hospital. Patients in hypertensive urgency were poorly evaluated while those in emergencies were neither admitted in ICU/HDU nor managed acutely by parenteral antihypertensive therapies. This shows poor adherence to the 2017 ACC/AHA hypertensive crisis management guidelines.

5.2 RECOMMENDATIONS

1. A chart to provide guidance so as not to miss subtle organ damage would be essential.
2. A study to assess whether hypertensive emergencies in resource limited areas can be managed in the general ward instead of the intensive care unit or high dependency unit should be carried out.
3. Improved use of equipment such as an ECG for diagnosis would be important.
4. Bedside affordable investigations like urinalysis would be quick and efficient in diagnosis.
5. Improved eye exam on all hypertensive patient by either fundoscopy or slit lamp should be encouraged.

Table 12: Recommended Examination and Investigation in Hypertensive Crisis.

Examination		**Investigations**	
Fundoscopy	√	Urinalysis	√
Neurological	√	ECG and Echocardiograph	√
Respiratory	√	Troponin	√
Abdominal	√	Liver function	√
Cardiovascular	√	Urea electrolyte and creatinine	√

5.4 LIMITATIONS

Limitations of the study included:

1. Lack of data due to poor documentation on the charts.
2. No standardized criteria for examination and investigation to guide in further evaluation and management hence missed important information.
3. Sample size in some of the emergencies – due to their scarcity- was low to determine if the therapy used was the standard.
4. The audit since was done after the therapy was administered relied on the assumption that the documented data was the actual practice and not derivative data.
5. By the time of data collection, the 2018 Kenyan guideline on management of hypertensive crisis had been disseminated to the clinicians and this could have influenced the management.
6. The guidelines used in the study was based on a resource rich set up hence not the best guide in resource poor setting.

REFERENCES

1. Olack B, Wabwire-Mangen F, Smeeth L, Montgomery JM, Kiwanuka N, Breiman RF. Risk factors of hypertension among adults aged 35–64 years living in an urban slum Nairobi, Kenya. BMC Public Health. 2015 Dec 17;15(1):1251.

2. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. J Am Coll Cardiol. 2018 May;71(19): e127–248.

3. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-based Studies from 90 Countries. Circulation. 2016 Aug 9;134(6):441–50.

4. Nakalema I, Kaddumukasa M, Nakibuuka J, Okello E, Sajatovic M, Katabira E. Prevalence, patterns and factors associated with hypertensive crises in Mulago hospital emergency department; a cross-sectional study. Afr Health Sci. 2019 Mar;19(1):1757–67.

5. Shao PJ, Sawe HR, Murray BL, Mfinanga JA, Mwafongo V, Runyon MS. Profile of patients with hypertensive urgency and emergency presenting to an urban emergency department of a tertiary referral hospital in Tanzania. BMC Cardiovasc Disord [Internet]. 2018 Aug 2 [cited 2018 Nov 8];18. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6090910/

6. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. The Lancet. 2014 May;383(9932):1899–911.

7. Shamsi A, Dehghan Nayeri N, Esmaeili M. Living with Hypertension: A Qualitative Research. Int J Community Based Nurs Midwifery. 2017 Jul;5(3):219–30.

8. Migneco A, Ojetti V, De Lorenzo A, Silveri NG, Savi L. Hypertensive crises: diagnosis and management in the emergency room. Eur Rev Med Pharmacol Sci. 2004 Aug;8(4):143–52.

9. Shekhar S, Liu R, K Travis O, Roman R, Fan F. Cerebral Autoregulation in Hypertension and Ischemic Stroke: A Mini Review. J Pharm Sci Exp Pharmacol. 2017 Aug 14; 2017:21–7.

10. Mahfoud F, Himmel F, Ukena C, Schunkert H, Böhm M, Weil J. Treatment Strategies for Resistant Arterial Hypertension. Dtsch Ärztebl Int. 2011 Oct;108(43):725–31.

11. Miller JB, Arter A, Wilson SS, Janke AT, Brody A, Reed BP, et al. Appropriateness of Bolus Antihypertensive Therapy for Elevated Blood Pressure in the Emergency Department. West J Emerg Med. 2017 Aug;18(5):957–62.

12. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003 Dec 1;42(6):1206–52.

13. Calhoun DA, Oparil S. Treatment of Hypertensive Crisis. N Engl J Med. 1990 Oct 25;323(17):1177–83.

14. Regenhardt RW, Das AS, Stapleton CJ, Chandra RV, Rabinov JD, Patel AB, et al. Blood Pressure and Penumbral Sustenance in Stroke from Large Vessel Occlusion. Front Neurol [Internet]. 2017 Jul 3 [cited 2019 Apr 26];8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5494536/

15. Mayet J, Hughes A. Cardiac and vascular pathophysiology in hypertension. Heart. 2003 Sep;89(9):1104–9.

16. Tissue Plasminogen Activator for Acute Ischemic Stroke. N Engl J Med. 1995 Dec 14;333(24):1581–8.

17. Anderson CS, Heeley E, Huang Y, Wang J, Stapf C, Delcourt C, et al. Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage. N Engl J Med. 2013 Jun 20;368(25):2355–65.

18. Hill MD, Muir KW. INTERACT-2: Should Blood Pressure Be Aggressively Lowered Acutely After Intracerebral Hemorrhage? Stroke. 2013 Oct 1;44(10):2951–2.

19. Srikanth Penumetsa JM. Management of Hypertensive Emergencies. J Hypertens- Open Access [Internet]. 2013 [cited 2018 Aug 16];02(02). Available from: https://www.omicsgroup.org/journals/management-of-hypertensive-emergencies-2167-1095.1000117.php?aid=14875

20. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adultThe Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2014 Nov 1;35(41):2873–926.

21. Alexander S, Varughese S, George PJ, Kirubakaran R. Fenoldopam for preventing and treating acute kidney injury. Cochrane Database Syst Rev [Internet]. 2012 [cited 2019 Jul 26] ;(5). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD009838/full

22. World Health Organization. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia. [Internet]. 2011 [cited 2018 Aug 16]. Available from: http://whqlibdoc.who.int/publications/2011/9789241548335_eng.pdf

23. Almas A, Ghouse A, Iftikhar AR, Khursheed M. Hypertensive Crisis, Burden, Management, and Outcome at a Tertiary Care Center in Karachi. Int J Chronic Dis [Internet]. 2014 [cited 2018 Nov 8];2014. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4590913/

24. Pinna G, Pascale C, Fornengo P, Arras S, Piras C, Panzarasa P, et al. Hospital Admissions for Hypertensive Crisis in the Emergency Departments: A Large Multicenter Italian Study. PLoS ONE [Internet]. 2014 Apr 2 [cited 2018 Nov 8];9(4). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3973569/

25. Salkic S, Batic-Mujanovic O, Ljuca F, Brkic S. Clinical Presentation of Hypertensive Crises in Emergency Medical Services. Mater Socio-Medica. 2014 Feb;26(1):12–6.

26. Moore PK, Hsu RK, Liu KD. Management of Acute Kidney Injury: Core Curriculum 2018. Am J Kidney Dis. 2018 Jul 1;72(1):136–48.

27. Thygesen Kristian, Alpert Joseph S., Jaffe Allan S., Chaitman Bernard R., Bax Jeroen J., Morrow David A., et al. Fourth Universal Definition of Myocardial Infarction (2018). Circulation. 2018 Nov 13;138(20): e618–51.

28. Sacco Ralph L., Kasner Scott E., Broderick Joseph P., Caplan Louis R., Connors J.J. (Buddy), Culebras Antonio, et al. An Updated Definition of Stroke for the 21st Century. Stroke. 2013 Jul 1;44(7):2064–89.

29. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 2017 Aug;70(6):776–803.

30. Bhaskar A, Oommen V. A simple model for demonstrating the factors affecting glomerular filtration rate. Adv Physiol Educ. 2018 May 15;42(2):380–2.

31. Robinson T, Zaheer Z, Mistri AK. Thrombolysis in Acute Ischaemic Stroke: An Update. Ther Adv Chronic Dis. 2011 Mar;2(2):119–31.

32. Fugate JE, Rabinstein AA. Absolute and Relative Contraindications to IV rt-PA for Acute Ischemic Stroke. The Neurohospitalist. 2015 Jul;5(3):110–21.

33. Varon J, Marik PE. Clinical review: The management of hypertensive crises. Crit Care. 2003 Jul 16;7(5):374.

34. Henderson AD, Biousse V, Newman NJ, Lamirel C, Wright DW, Bruce BB. Grade III or Grade IV Hypertensive Retinopathy with Severely Elevated Blood Pressure. West J Emerg Med. 2012 Dec;13(6):529.

35. Farha KA, van Vliet A, van Marle S, Vrijlandt P, Westenbrink D. Hypertensive crisis-induced electrocardiographic changes: a case series. J Med Case Reports. 2009 Aug 20; 3:7283.

36. Mullvain R, Saman DM, Rostvedt A, Landgren P. ECG-to-Decision Time Impact on 30-Day Mortality and Reperfusion Times for STEMI Care. Crit Pathw Cardiol. 2018 Mar;17(1):19.

37. Karras DJ, Heilpern KL, Riley LJ, Hughes L, Gaughan JP. Urine dipstick as a screening test for serum creatinine elevation in emergency department patients with severe hypertension. Acad Emerg Med Off J Soc Acad Emerg Med. 2002 Jan;9(1):27–34.

38. Robinson T, Zaheer Z, Mistri AK. Thrombolysis in Acute Ischaemic Stroke: An Update. Ther Adv Chronic Dis. 2011 Mar;2(2):119–31.

39. Lebel M, Langlois S, Belleau LJ, Grose JH. Labetalol infusion in hypertensive emergencies. Clin Pharmacol Ther. 1985 Jun;37(6):615–8.

40. Bath Philip M., Appleton Jason P., Krishnan Kailash, Sprigg Nikola. Blood Pressure in Acute Stroke. Stroke. 2018 Jul 1;49(7):1784–90.

41. Patel RV, Kertland HR, Jahns BE, Zarowitz BJ, Mlynarek ME, Fagan SC. Labetalol: response and safety in critically ill hemorrhagic stroke patients. Ann Pharmacother. 1993 Feb;27(2):180–1.

42. Blood-Pressure Lowering in Acute Intracerebral Hemorrhage | NEJM [Internet]. [cited 2019 Aug 23]. Available from: https://www.nejm.org/doi/full/10.1056/NEJMc1309586

43. Suzuki T, Eagle KA, Bossone E, Ballotta A, Froehlich JB, Isselbacher EM. Medical management in type B aortic dissection. Ann Cardiothorac Surg. 2014 Jul;3(4):413–7.

44. Bangalore S, Qin J, Sloan S, Murphy SA, Cannon CP, for the PROVE IT-TIMI 22 Trial Investigators. What Is the Optimal Blood Pressure in Patients After Acute Coronary Syndromes? Relationship of Blood Pressure and Cardiovascular Events in the Pravastatin or Atorvastatin Evaluation and Infection Therapy–Thrombolysis in Myocardial Infarction (PROVE IT-TIMI) 22 Trial. Circulation. 2010 Nov 23;122(21):2142–51.

45. Rocco MV, Sink KM, Lovato LC, Wolfgram DF, Wiegmann TB, Wall BM, et al. Effects of Intensive Blood Pressure Treatment on Acute Kidney Injury Events in the Systolic Blood Pressure Intervention Trial (SPRINT). Am J Kidney Dis Off J Natl Kidney Found. 2018;71(3):352–61.

46. Schrier RW, Burke TJ. Role of calcium-channel blockers in preventing acute and chronic renal injury. J Cardiovasc Pharmacol. 1991;18 Suppl 6: S38-43.

47. Arellano DL. Reducing blood pressure in acute decompensated heart failure. Nurse Pract. 2016 Jul 16;41(7):11.

48. Upadhya B, Rocco M, Lewis CE, Oparil S, Lovato LC, Cushman WC, et al. Effect of Intensive Blood Pressure Treatment on Heart Failure Events in the Systolic Blood Pressure Reduction Intervention Trial. :10.

TIMELINE OF STUDY PHASES

Table 13: Timeline of study at different phases.

EVENT/MONTH	NOVEMBER 2018	DECEMBER2018 – MARCH 2019	APRIL 2019 - MAY 2019	JUNE - SEPTEMBER 2019	OCTOBER 2019
PROTOCOL PRESENTATION					
ETHICAL APPROVAL					
DATA COLLECTION					
DATA ANALYSIS REPORT WRITING					
RESULTS PRESENTATION					

PROPOSED BUDGET

Table 14: Budget used during the study.

ITEM	**COST (Ksh.)**
STATIONERY AND PRINTING	15,000
STATISTICIAN	35,000
RESEARCH ASSISTANT (2 research assistants)	60,000
SUBTOTAL	110,000
10% CONTINGENCY	8,000
TOTAL	**118,000**

Appendix I: Consent Explanation:

My name is Dr. Douglas Nyandika Otondi, currently pursuing my post graduate study in Internal Medicine at the University of Nairobi. I am the lead researcher in a study to assess whether the management of hypertensive crisis at the Kenyatta National Hospital is up to standard with the current 2017 American College of Cardiology/American Heart Association. I will compare the management as recorded in the file with standard hypertensive crisis management guidelines. This will help in identifying challenges that hinder provision of standard management as recommended in the guidelines.

This statement is to inform you about the research we are performing to try and evaluate the current management of very high blood pressure with the related complications. Hypertensive crisis has become a very common disease in our population and despite being on different medications to manage the blood pressure, there are still increasing cases of very high blood pressures leading to complications that involve damage to body organs like the kidney, heart, brain and eyes. The objective of our study is to try to find out whether there are any deficiencies in our management of hypertensive urgency and emergency and in the long run improve.

You have been selected to be in this study because of one of two reasons:

a. You have been diagnosed with hypertension and during the routine check, your blood pressure was noted to be above 180/120 mmHg.

b. You might or might not have end organ damage as a result of the very high blood pressure.

Below is a summary of what to expect should you choose to participate in the study. You are encouraged to ask for clarification of any point that is not clear to you. After reading and understanding the information provided, you will be required to sign an informed consent form. Parents and guardians/next of kin will sign on behalf of participants aged less than 18 years, or participants unable to give consent due to disease severity. Participants aged less than 18 years will also be required to sign consent forms prior to their inclusion into the study.

Participation

Participation is voluntary and you have the right to withdraw at any point. You will not be victimized if you refuse to participate in this study, and you will still get management.

Procedures

A brief medical history will be taken, including your age, sex, blood pressure at presentation, treatment given and blood pressure after medication at 24 and 48 hours. I will then assess all the management procedures administered by going through your notes and charts.

Risks

There are no risks (physical or financial) in this study.

Benefit

You will participate in increasing information on hypertensive crisis management at the Kenyatta National Hospital.

Confidentiality

Data gathered will be kept locked in a secure location at all times and only those directly involved in the research will have access to them. No identifying information will be used on the data collection form or during data analysis and presentation.

Compensation

There is no compensation, either monetary or otherwise, for participation in this study.

Enquiries

Any enquiries about the study should be directed to the following contact persons

1. DR. DOUGLAS NYANDIKA OTONDI
   DEPARTMENT OF CLINICAL MEDICINE AND THERAPUTICS
   UNIVERSITY OF NAIROBI,
   Mobile: 0727 586202. ***OR***

2. PROF. J. K. KAYIMA
   SPECIALIST PHYSICIAN AND ENDOCRINOLOGIST, KNH
   DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS
   UNIVERSITY OF NAIROBI
   P.O. BOX 30197-00100, NAIROBI.
   TEL: 0733730650. ***OR***

3. PROF. E. N. OGOLA
   SPECIALIST PHYSICIAN/CARDIOLOGIST
   DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS
   UNIVERSITY OF NAIROBI
   P.O. BOX 30197-00100, NAIROBI.
   TEL: 0722737944. ***OR***

4. CHAIRPERSON, KNH/UON ETHICAL REVIEW COMMITTEE,
   TEL: 020-2726300 EXT 44355.
   P.O. Box 20723, Nairobi.

Before I involve you in my study, I request you to sign the consent/assent form below.

Appendix II: English Version of Consent Form

I, _____

_____ have read carefully and

understood the objectives and procedure of the study and agree to participate.

Signed_____ Name_____

Date_____

I, _____, have explained to

Mr./Mrs./Miss_____ the full consent of the study and

Witness that he/she has voluntarily consented to participate.

Signed _____ Date _____

Witness _____

Appendix III: Swahili Version of Consent Explanation

Maelezo Ya Idhini

Jina langu ni Douglas Nyandika Otondi na naendeleza masoma ya uzamili katika chuo kikuu cha Nairobi. Ninaongoza utafiti kuweza kuelewa kama ugonjwa wa mgogoro wa shinikizo la damu, unatibiwa kwa njia ipasayo kwa kufuatilia mwongozo kutoka Amerika mwaka wa 2017. Nitalinganisha matibabu kwenye faili na usimamizi wa kawaida.

Sehemu hii ni ya kukuelezea juu ya utafiti tunayofanya kuweza kuelewa jinsi tunavyotibu ugonjwa wa shinikizo la damu. Ugonjwa huu umepata umaarufu sana hata ingawa kuna madawa tofauti ya kuiitibu, bado kuna uongezeko wa visa vya madhara kutokana na shinikizo la damu ikiwamo figo, moyo, ubongo na macho.

Lengo la utafiti wetu ni kuweza kugundua upungufu katika matibabu ya madhara yanayotokana na ugonjwa huu ili tuweze kutafuta mbinu za kuikinga.

Umechaguliwa kuwa kwenye utafiti huu kwa sababu ya jambo moja katika hizi;

Aidha,

a) umepatikana ama umekuwa ukiugua ugonjwa wa shinikizo la damu na shinikizo lenyewe liko kiasi cha juu kuliko 180/120 mmHg;

   AU

b) Ugonjwa huu wa shinikizo la damu ya kupindukia umeleta madhara kwenye viungo muhimu mwilini kama vile ubongo, figo, macho au moyo.

Ifuatayo ni muhtasari wa yale yote utatarajia kupata kwenye utafiti. Unahimizwa kuuliza maswali kwenye eneo yoyote ambayo hauelewi. Baada ya kuisoma na kuielewa taarifs hii, unahitajika kutia sahihi fomu itakayofuatia. Wazezi na walezi wataweza kutia sahihi kwa niaba ya wale ambao wako na miaka chini ya 18 au wale wasiojiweza kwa sababu ya kulemewa na ugonjwa.

Kushiriki

Kushiriki au kujitoa kwenye utafiti ni kwa hiari yako. Hakuna dhulma utakayokumbana nayo kwa kutoshiriki kwenye utafilti huu na bado utaweza kutibiwa.

Taratibu

Nitachukua historia fupi ya kimatibabu ikiwapo miaka, jinsia, shinikizo la damu ulipofika hospitali na baada ya masaa 24 na 48. Kisha nitachunguza matibabu uliyopewa kwenye faili yako.

Hatari

Hakuna hatari yoyote ya kifedha au kimwili kwenye utafiti huu.

Faida

Utakuwa miongoni mwa wale watakaoongeza maarifa kuhusu mgogoro unaoletwa na shinikizo la damu.

Usiri

Takwimu yote itakayopatikana kwenye utafiti hii itahifadhiwa salama na wale tu wenye uhusiano na utafiti huu ndio wataoweza kuziona. Hakuna habari yoyote kwenye fomu hii ambayo itaweza kukutabulisha.

Fidia

Hakuna fidia yoyote kutokana na utafiti huu.

Maswali

Kwa maelezo yoyote kuhusu utafiti huu waweza kuwauliza watu wafuatao:

1. DR. DOUGLAS NYANDIKA OTONDI
   DEPARTMENT OF CLINICAL MEDICINE AND THERAPUTICS
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   Mobile: 0727 586202. ***OR***

2. PROF. J. K. KAYIMA
   SPECIALIST PHYSICIAN AND ENDOCRINOLOGIST, KNH
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3. PROF. E. N. OGOLA
   LECTURER AND CONSULTANT PHYSICIAN/CARDIOLOGIST
   DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS
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   TEL: 0722737944. ***OR***

4. CHAIRPERSON, KNH/UON ETHICAL REVIEW COMMITTEE,
   TEL: 020-2726300 EXT 44355.
   P.O. Box 20723, Nairobi.

Kabla kuweza kuhusishwa kwenye utafiti wangu, tafadhali tia sahihi kwenye fomu ifuatayo.

Appendix IV: Kiswahili Version of Consent Form

FOMU YA RIDHAA

Mimi, _____, nimeisoma na kuielewa lengo la utafiti huu na nakubali kujiunga kwa hiari yangu.

Sahihi _____ Jina _____

Tarehe _____

Mimi, _____, nimemwelezea, Bwana/Bi

_____, mambo yote kuhusu utafiti huu na ni shahidi kuwa amekubali kujiunga kwa hiari yake

Shahidi _____ Sahihi _____

Tarehe _____

Appendix IV: Questionnaire

1. Patient number: ……
2. Patient Initials: ……
3. Age(years): <20 ☐ 21-30 ☐ 31-40 ☐ 41-50 ☐ 51-60 ☐
   61-70 ☐ 71-80 ☐ 81-90 ☐ > 90 ☐
4. Sex: Male ☐ Female ☐
5. Triage location: Accident and emergency ☐ Medical ward ☐
   Medical ICU. ☐ Renal Unit. ☐
6. Blood pressure at triage;

Systolic: 180-190 ☐ 191-200 ☐ 201-210 ☐ 211-220 ☐ 221-230 ☐
231-240 ☐ 241-250 ☐

Diastolic. 120-130 ☐ 131- 140 ☐ > 140 ☐

7. Clinical symptoms: Headache ☐ Chest pain. ☐ Dyspnea ☐
   Blurry vision ☐ Dizziness. ☐ Anasarca ☐
   Reduced urine output. ☐ Epistaxis. ☐
   Others……
8. Clinical signs:
   a) Neurological: Lateralizing signs ☐ Lowered GCS. ☐
      Papilledema ☐
   b) Respiratory: Bilateral crackles ☐
   c) Ocular: Diminished visual acuity. ☐
      Keith Wagener class III. ☐
      Keith Wagener class IV. ☐
   d) Cardiovascular:

e) Abdomen:

Ascites. ☐

Tenderness. ☐

Pulsating Abdominal aorta. ☐

Chronic Aortic regurgitation signs ☐

9. Investigations: Urinalysis ☐

Urea Creatinine and electrolytes ☐

Kidney Urinary bladder ultrasound ☐

Electrocardiogram. ☐

Troponin ☐

NT pro BNP. ☐

Chest X ray. ☐

CT scan brain ☐

MRI brain. ☐

CT Aortogram ☐

10. Diagnosis: Hypertensive Urgency. ☐

Hypertensive Emergency. ☐

11. Types of Hypertensive Emergencies:

Ischemic stroke ☐ Dissecting Aortic Aneurysm ☐

Hemorrhagic stroke ☐ Ischemic Stroke. ☐

Hypertensive encephalopathy ☐ Acute pulmonary edema. ☐

Acute Myocardial Infarction ☐ Hypertensive retinopathy ☐

Acute Kidney Injury ☐

12. Antihypertensive administered (include the method I.e. IV labetalol)

    …….

13. Blood pressure Monitoring

    Time from initial therapy. Blood pressure.

14. Additional therapy in case initial therapy did not achieve target

    Yes ☐ No. ☐

15. If yes, the antihypertensive administered and how it was administered

    ……

16. Outcomes at 24 hours: Discharged home ☐

    Admitted to Resuscitation room B Casualty ☐

    Admitted in the medical ICU. ☐

    Admitted in the renal unit. ☐

    Admitted to the medical ward. ☐

    Dead ☐

17. Outcome at 48 hours : Discharged home ☐

    Admitted at Resuscitation room B Casualty ☐

    Admitted in the medical ICU. ☐

    Admitted in the renal unit. ☐

    Admitted to the medical ward. ☐

    Dead ☐