PREVALENCE OF HYPERTENSION AND ADEQUACY OF ITS CONTROL IN CHRONIC KIDNEY DISEASE PATIENTS AT THE RENAL CLINIC AT KENYATTA NATIONAL HOSPITAL.

A dissertation for the award of MMed internal medicine

DECLARATION

I certify that this is my original work and has not been presented for a degree at any other university.

Signature ..... Date 17/07/08

Dr Rajula Allan, MBCHB, University of Nairobi.

DEDICATION

I dedicate this study to my parents and the rest of my family who have been instrumental and provided moral support to ensure its completion. Special thanks go out to my supervisors Dr. Kayima, Professor Ogola and Dr Maritim who have guided me from the beginning and throughout the study. This study would also not have been possible without my statistician Dr. Mutai, the able staff at the renal clinic, and the lab technicians at the Renal Laboratory.

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1. ABBREVIATIONS

ARB- angiotensin II receptor blockers

ACEI- angiotensin converting enzyme inhibitors

BP- blood pressure

CKD – chronic kidney disease

CR CLR- creatinine clearance

CRF – chronic renal failure

CVD- cardiovascular disease

JNC - The Joint National Committee (JNC) for Prevention, Detection, Evaluation and Treatment of High Blood Pressure

KDOQI- kidney disease outcome and quality initiative

KNH- Kenyatta National Hospital

NKF- national kidney foundation

RAAS- Renin Angiotensin Aldosterone system

RCT- randomized controlled trials

2. ABSTRACT

BACKGROUND

Chronic kidney disease (CKD) is a growing problem worldwide. The prevalence in developing world remains largely unknown, but is estimated at about 150 to 200 per million population. It is much higher in developed countries. Sequel of its progression includes end stage renal failure and markedly increased cardiovascular risk.

Control of one of the major risk factors i.e. hypertension has been shown to be feasible in several studies with marked reduction in cardiovascular risk. The adequacy of blood pressure control in CKD patients in our local set up is unknown.

OBJECTIVES

The broad objective was to determine the prevalence of hypertension and the adequacy of its control in patients with chronic kidney disease in our local set up. Specifically sought to determine the prevalence of hypertension in CKD (chronic kidney disease) patients and the percentage of hypertensive CKD patients who are adequately controlled.,

Secondary objectives included comparing patients with normal blood pressure vs. those with hypertension by stage of CKD, to determine whether socio demographic factors and patients understanding of their disease had an impact on blood pressure control .The study also sought to determine use of rennin angiotensin aldosterone sympathetic (RAAS) axis modifiers

METHODOLOGY

Patients were recruited over a 3 month period from January to March 2009. A maximum of 10 patients per clinic visit were seen, every alternate patient was selected. Previous urinalysis and creatinine clearance were assessed and potential CKD cases identified. Repeat urinalysis and creatinine was taken on the morning of the clinic. Once CKD criteria was satisfied informed consent was then obtained. Inclusion and exclusion criteria were then applied, patients satisfying inclusion criteria were then recruited. Blood pressures was recorded twice and the average taken. A study questionnaire was then filled. Results were recorded and interpreted using MS EXCEL and SPSS version 11.

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RESULTS

The overall prevalence of hypertension amongst patients with CKD was 76%. 16.6% of the patients had achieved target blood pressure. Majority of patients with normal blood pressure were in stage 1 to 3 of CKD while hypertensive patients were in stage 3 to 5. Socio demographic factors were not found to have a significant impact on blood pressure control. 86.5% of the patients were using RAAS axis modifiers.

CONCLUSIONS

The vast majority of patients with CKD are hypertensive. Very few achieve target control of their blood pressures.

3. LITERATURE REVIEW

3.1 CHRONIC KIDNEY DISEASE

Chronic Kidney Disease (CKD) is an increasingly recognized global health problem. This is despite the fact that there are simple tests that can be done to detect it and treatment can retard and even reverse the disease progression and ultimately reduce cardiovascular risk. One factor that has been a deterrent to detection is the definition of CKD

In 2006 March the world Kidney Day was to send a clear message to the public, government health officials, physicians, patients and families that 'CKD is common, harmful and treatable [1] In 2004 the Kidney Disease Improving Global Outcomes (KDIGO) endorsed the Kidney Disease Outcome Quality initiative (KDOQI) on the definition of CKD. This was re emphasized in 2006.[2-4]

In the United States 9.6% of non institutionalized adults are estimated to have CKD. [5,6] and studies from Europe, Asia and Australia confirm the high prevalence rates [7-10].Local and regional studies on the magnitude are not available but the prevalence is estimated to be about 150 to 200 per million population.

3.2 CHRONIC KIDNEY DISEASE AND CARDIOVASCULAR RISK

Patients with CKD are far more likely to die from CVD (cardiovascular disease) than to develop end stage renal disease. Their cardiovascular risk is increased up to 500 times that of the normal population. Hypertension is the single most important modifiable risk factor for CVD in these patients. [11]

The KDIGO group acknowledges this risk. The concept of a 'clinical intersection' between CKD and CVD was then proposed as a 'high risk state' for poor health outcomes.[12]

The inter- relationship of CKD and CVD include; common risk factors (e.g. older age, diabetes, hypertension). Bidirectional effects of one disease process on the progression of the other (e.g. renal artery stenosis, heart failure caused by CKD). Adverse effects on one disease process when investigating another (e.g. contrast nephropathy in a patient following angiography). Treatment biases potentially influenced by both diseases (e.g. ACEI) may also contribute.

Complicating issues is the fact that some of the cardiovascular risk factors such as hypertension, diabetes may be involved in the initiation, susceptibility and progression of CKD

It is estimated that 80 to 85 per cent of all chronic renal failure patients will be hypertensive [3]
A study done by Nadeem Sheikh et al at KNH 2002 renal clinic showed 51.8% were hypertensive [13].
A study done by Dr M. Maritim in 2007 on peripheral artery disease in chronic renal failure patients came up with a figure of 74% as being hypertensive [14]

3.3 SECONDARY FACTORS AND THE PROGRESSION OF CHRONIC KIDNEY DISEASE

A multivariate analysis of the Modification of Diet in Renal Disease Study (MDRD) database of 840 patients with diverse renal diseases found that the following clinical characteristics were independent predictors of a faster decline in glomerular filtration rate [15]: proteinuria, high blood pressure, black race, lower serum HDL cholesterol and lower levels of serum transferrin
Higher levels of proteinuria and significant hypertension as independent predictors of accelerated progression of renal dysfunction was also found in a study of approximately 350 patients with nondiabetic chronic nephropathies [16].
Many other risk factors have been identified including environmental exposures such as lead, smoking, diabetes, glucose concentration, metabolic syndrome, possibly some analgesic agents, obesity, and other factors [17 – 20].
Some data, however, suggest that alcohol use may not be associated with an increased risk [21].

3.4 DEFINITION OF HYPERTENSION IN CHRONIC KIDNEY DISEASE

In the normal population hypertension is defined as a blood pressure above 140/90 as per the JNC 7 guidelines. No large scale studies are available to make a definition for hypertension in CKD so the same guidelines are adopted.
However it is clearly demonstrated that more stringent treatment targets result in better outcomes for cardiovascular risk as well as to retard progression.
The JNC 7 as well as the KDOQI guidelines suggests hypertension treatment targets as less than 130/80 [22, 23].

The MDRD (modification of diet in kidney disease) and a meta-analysis from the ACE inhibition and Progressive Renal Disease (AIPRD) study group suggest that an even lower systolic pressure may be more effective in slowing progressive renal disease in patients with a protein excretion of greater than 1000 mg/day.

They suggest a target BP of <125/75 [22,24]

3. 5 RISK FACTORS FOR HYPERTENSION IN CHRONIC KIDNEY DISEASE

The prevalence of hypertension increases linearly as the glomerular filtration rate falls and, as in patients without renal disease, is increased in patients with higher body weight and in African Americans.

Data from the Modification of Diet in Renal Disease Study, for example, showed that the prevalence of hypertension rose progressively from 65 to 95 percent as the glomerular filtration rate fell from 85 to 15 mL/min per 1.73 m2 [25].

One or more of the following factors may contribute in the individual patient:

- Sodium retention is generally of primary importance, even though the degree of extracellular volume expansion may be insufficient to induce edema.
- Increased activity of the renin-angiotensin system (probably due to regional ischemia induced by scarring) is often responsible for at least part of the hypertension that persists after the restoration of normovolemia.
- Enhanced activity of the sympathetic nervous system has been demonstrated in patients with CKD and end-stage renal disease [26, 27]. The afferent signal may arise in part within the failing kidneys, since it is not seen in patients who have undergone bilateral nephrectomy.
- Secondary hyperparathyroidism raises the intracellular calcium concentration, which can lead to vasoconstriction and hypertension [28]. Lowering parathyroid hormone secretion by the chronic administration of an active vitamin D analog can reduce both intracellular calcium and the systemic blood pressure.
- Hypertension may occur or be exacerbated in patients with advanced CKD treated with erythropoietin; this effect is in part related to the degree of elevation in the hematocrit.

Approximately 20 to 30 percent of patients who receive erythropoietin (EPO) intravenously for the anemia of chronic kidney disease may develop an elevation in diastolic pressure of 10 mmHg or more [29, 30].

In comparison, the blood pressure (BP) is less likely to rise after subcutaneous administration [31].

How EPO therapy may raise the blood pressure is not well understood.

Several factors have been identified that may contribute to the hypertensive response. These include the following [32- 42]: High dose of EPO, rapid increase in hemoglobin/hematocrit, direct vasoconstrictive effect, large absolute elevation in hemoglobin/hematocrit, diminished response to nitric oxide, marked increase in intracytosolic calcium levels, enhanced responsiveness to norepinephrine, increased plasma endothelin levels, (although some studies have not replicated this observation) arterial remodeling through simulation of vascular cell growth, increase in whole blood viscosity, prior personal or family history of hypertension.

- Impaired nitric oxide synthesis and endothelium-mediated vasodilatation has been demonstrated in patients with uremia [43].
- Although the mechanisms are unclear, potential explanations include reduced nitric oxide availability due to a state of increased oxidative stress, or cofactor deficiency-induced uncoupling of nitric oxide synthase.
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- Patients with CKD may not demonstrate the normal nocturnal decline in blood pressure (called "nondippers"), a possible risk factor for hypertensive complications [44].

3.6 MECHANISMS OF RENAL DETERIORATION DUE TO HYPERTENSION

Mechanisms by which hypertension causes further glomerular damage is a subject of much contention.

What seems to stand out most is transmission of systemic pressure to the glomerulus ie intraglomerular hypertension and glomerular hypertrophy [45].

The mechanisms by which glomerular hypertension and hypertrophy induce glomerular injury are incompletely understood, as multiple factors may be involved [46]:

Direct endothelial cell damage, similar to that induced by systemic hypertension.

The increased wall stress and increased glomerular diameter may cause detachment of the glomerular epithelial cells from the glomerular capillary wall .

These focal areas of denudation permit increased flux of water and solutes; however, very large circulating macromolecules (such as IgM and fibrinogen and complement metabolites) cannot cross the glomerular basement membrane and are trapped in the subendothelial space .

The characteristic accumulation of these "hyaline" deposits can progressively narrow the capillary lumens, thereby decreasing glomerular perfusion and filtration.

Increased strain on the mesangial cells can stimulate them to produce cytokines and more extracellular matrix [47].

The ensuing mesangial expansion can further encroach on the capillary surface area.

The release of cytokines, such as transforming growth factor-beta (TGF-beta) and platelet-derived growth factor, may also contribute to the glomerular injury, in part by mediating the rise in matrix synthesis

3.7 TREATMENT OF HYPERTENSION IN CHRONIC KIDNEY DISEASE

The following recommendations are adopted from the JNC 7 and KDOQI work group.

There are no large studies available that actually address the effect of BP lowering in CKD patients.

Many recommendations are thus adapted from the control in general population in which nearly all studies excluded patients with elevated creatinine.

As per the JNC 7, individuals at highest risk should receive most intensive treatment, including prompt pharmacological therapy, a lower blood pressure goal, and use of specific antihypertensive agents for "compelling indications," including CKD [48,49]

The goals of antihypertensive therapy in CKD are to lower blood pressure, reduce the risk of CVD, and slow progression of CKD.

As per the KDOQI group CKD patients are considered as the 'highest-risk group' for cardiovascular events.

All antihypertensive agents can be used to lower blood pressure in CKD.

Multidrug regimens will be necessary in most patients with CKD to achieve therapeutic goals.

Target blood pressure for CVD risk reduction in CKD should be <130/80 mm Hg

Antihypertensive agents should be prescribed by giving preferred agents for CKD first. Diuretics should be included in the antihypertensive regimen in most patients. Any additional agents should be based on cardiovascular disease-specific indications to achieve therapeutic and preventive targets and to avoid side-effects and interactions

The antihypertensive regimen should be simplified as much as possible and long-acting (once-daily agents) should be used when possible.Two agents, either as separate prescriptions or as a fixed-dose combination containing preferred agents, may be considered as initial therapy for SBP >20 mm Hg above goal according to the stage of CKD and CVD risk. Fixed-dose combinations may be used for maintenance therapy after the antihypertensive regimen has been established

Classes of antihypertensive agents.

ACE inhibitors and ARBs

ACE inhibitors and ARBs have many potential advantages for patients with CKD and associated comorbid medical conditions. They slow down the progression of CKD in diabetic kidney disease and nondiabetic kidney disease with proteinuria, and in addition, they reduce proteinuria, irrespective of the type of kidney disease.

In the benazepril trial, benazepril produced a greater reduction in blood pressure than placebo (3.5 to5.0 vs 0.2 mmHg diastolic reduction) and a 25% reduction in proteinuria. The risk reduction of progression of CKD was 53% overall. [50]

The REIN trial (ramipril efficacy in nephropathy) was terminated prematurely amongst patients excreting more than 3 grams of protein per day due to a significant benefit in ameliorating the rate of decline of renal function (0.53 vs 0.88ml/min/month for placebo. [51]

In the AASK trial, hypertensive african americans were generally considered to respond better to monotherapy with a calcium channel blocker than an ACE inhibitor. Despite this, an interim analysis of the African American Study of Kidney Disease and Hypertension (AASK) suggested that an ACE inhibitor (ramipril) was more effective in slowing progression of benign hypertensive nephrosclerosis in blacks than either amlodipine or metoprolol. [52] The final results of the AASK trial showed no difference among the drug groups in reducing the rate of decline of GFR ; however, the ramipril group had a 22 percent reduction in risk of the composite outcome (reduction in GFR by 50 percent or more from baseline, ESRD or death)

There is limited data on combined use of ACEI,s and ARB,s. The best data comes from th COOPERATE trial where groups were taken either lorsatan, trandolapril or both. [53]. The incidence of the combined primary end point of time to doubling of the serum creatinine concentration or end-stage renal disease was significantly less common with combined therapy and the largest decrease in proteinuria was observed with combination therapy.

Diuretics

In the CKD subset of patients from ALLHAT it was shown that use of thhiazide diuretics was associated with lower rates of CVD outcomes and Heart failure compared with CCB's and ACEI's

Loop diuretics have not been studied in large hypertension trials in the general population; thus, their effectiveness in reducing CVD risk is not known.

However, they are effective in reducing ECF volume and have been used in combination with other antihypertensive agents in many studies in CKD.

Loop diuretics have a shorter duration of action than thiazide diuretics; hence, they are less effective in patients with normal kidney function, unless they are given in multiple daily doses.

However, since thiazide diuretics are of minimal effectiveness for ECF volume reduction at low levels of GFR, a loop diuretic is preferred for this purpose in patients with GFR less than 30 mL/min/1.73 m^2.

Patients with resistance to loop diuretics may benefit from a combination of a loop diuretic with metolazone, which has a mechanism of action at several sites in the renal tubule. As in patients without CKD, volume depletion may occur from the use of diuretics.

Other medications.

The below named antihypertensive agents may be additionally used to the above to control hypertension, though they don't directly act on the kidney to retard disease.

Beta-adrenergic blockers

They can be classified into selective and non selective beta blockers

Some may have added alpha blocking effects eg labetolol and carvedilol

Other beta-blockers have intrinsic sympathomimetic activity (ISA), causing activation of the beta-receptor, while also preventing catecholamines from binding to the receptor site. Acebutolol and pindolol have ISA.

Second, beta-blockers can be classified by their solubility properties and routes of metabolism. Lipid soluble beta-blockers are eliminated by hepatic metabolism, have a short half-life, and do not require dose adjustment in CKD.

However, their metabolism is slowed in heart failure and in the elderly, and they can accumulate causing an increased incidence of side-effects.

In addition, they can enter the central nervous system in high concentrations, and are associated with a higher incidence of insomnia, hallucinations, nightmares and depression. Propranolol and metoprolol are examples of lipid soluble beta-blockers.

Water-soluble beta-blockers are excreted by the kidney, have a longer half-life, and may accumulate in CKD. They do not readily enter the CNS. Atenolol and sotalol are water soluble. Esmolol has a half life of less than 10 minutes due to rapid metabolism by both hepatic esterases and blood tissue.

Carvedilol, extended release metoprolol, and bisprolol are effective agents for the treatment of both essential hypertension and congestive heart failure.

Beta-blockers are beneficial in patients with a prior history of angina, myocardial infarction, congestive heart failure (due to diastolic dysfunction and for certain agents also for systolic dysfunction), resting tachycardia, migraine headaches, and glaucoma.

Conversely, beta-blockers should in general not be used in patients with bradycardia, second- or third-degree heart block, asthma, chronic obstructive pulmonary disease, severe peripheral vascular disease, or depression, as ß-adrenergic tone is beneficial in these circumstances.

Calcium-channel blockers The calcium-channel blockers can be subdivided into dihydropyridine and nondihydropyridine agents.

The dihydropyridines preferentially block L-type calcium channels. They are potent vasodilators with little or no effect on cardiac contractility or cardiac conduction.

The nondihydropyridines include verapamil, a cardiac depressant, and diltiazem, which has both mild vasodilator and cardiac depressant activity.

In general, calcium-channel blockers are of particular benefit in patients with angina pectoris, recurrent supraventricular tachycardia (verapamil only), Raynaud's phenomenon (dihydropyridines only), congestive heart failure, migraine headaches, and esophageal spasm.

The nondihydropyridine calcium-channel blockers have beneficial effects on CKD and CVD. Diltiazem and verapamil are effective in decreasing proteinuria in diabetic kidney disease [54].

In addition, the combination of lisinopril and verapamil resulted in a greater reduction in proteinuria than using either drug at twice the dose used in combination therapy [55] Similar findings were seen with a combination of trandolapril and verapamil [56].

Nondihydropyridine calcium-channel blockers can diminish cardiac contractility and slow cardiac conduction, thus they should be avoided in patients with severe left ventricular dysfunction, sick sinus syndrome, or second- or third-degree heart block.

There are a number of dihydropyridine agents. Some have cardiac depressant activity, such as short-acting nifedipine, and longer-acting felodipine, isradipine, nicardipine, nisoldipine, and long-acting nifedipine. Long-acting agents that do not have cardiac depressant effects include amlodipine and lacidipine. In general, longer acting agents without cardiac depressant effects are preferred.

Alpha-adrenergic agents

Both centrally acting sympatholytic agents (methyldopa, clonidine, guanfacine and guanabenz) and selective a-1 blockers have beneficial effects on lipid metabolism (increase HDL cholesterol levels and decrease LDL cholesterol levels) and improve insulin sensitivity.

In general, these agents should not be used as a first-line therapy for hypertension due to the relatively high incidence of side-effects.

Side-effects of the centrally acting agents include dry mouth, sedation, and sexual dysfunction and for clonidine, side-effects are rebound hypertension after sudden discontinuation of therapy and sometimes even with gradual withdrawal of therapy.

Side-effects of the selective a-1 blockers include headache, weakness, dizziness, and—on rare occasions—syncope. Dizziness and syncope can be minimized by starting with a low dose of a long-acting agent such as doxazosin and administering the initial dose at bedtime.

The selective a-1 blockers may be of benefit in men with symptomatic benign prostatic hyperplasia. This benefit is balanced by the observation in ALLHAT that the use of doxazosin increased the risk of developing congestive heart failure compared to patients treated with the diuretic chlorthalidone.

Peripheral vasodilators Minoxidil is a powerful vasodilator that can cause lower extremity edema, tachycardia, hirsutism, and—in rare cases—pleural or pericardial effusions, at therapeutic doses.

The incidence of pericardial effusion in CKD patients is higher than that seen in the general population. This agent is almost always used in combination with a beta-blocker and loop diuretic in order to minimize reflex tachycardia and lower extremity edema.

Minoxidil should be reserved for those patients who cannot obtain blood pressure control with the preferred agent and at least two of the other recommended agents.

Aldosterone antagonists Aldosterone plays a role in numerous cardiovascular effects, such as LVH, CHF, and vascular fibrosis, necrosis, and inflammation.

Aldosterone receptor antagonists can be classified as "selective" (blocking the mineralocorticoid receptor) or "nonselective" (blocking the glucocorticoid, progesterone, and androgen receptors as well as mineralocorticoid receptors).

Recently, aldosterone receptor antagonists have been identified as a treatment for congestive heart failure.

In the Randomized Aldactone Evaluation Study (RALES), patients receiving the nonselective agent spironolactone compared to those receiving placebo had a reduction in mortality of 30%.

Small doses of spironolactone resulted in an improvement in ventricular function and enhanced exercise tolerance.

In the Eplerenone Post–Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS), patients with a left ventricular ejection fraction of 40% or lower and symptoms of heart failure were randomly assigned to receive the selective agent eplerenone an average of 7 days after they had had a myocardial infarction or placebo.

During a mean follow-up of 16 months, the relative risk of death was reduced by 15% among patients receiving eplerenone and the risk of hospitalization for heart failure was reduced by 15% with eplerenone.

There was a significantly greater increase in the serum creatinine concentration in the eplerenone group than in the placebo group, however, and hyperkalemia occurred in 5.5% of patients in the eplerenone group, as compared with 3.9% of patients in the placebo group. However, the study included only patients with CKD Stages 1-2. Side-effects are likely to be more frequent in CKD Stages 3-5.

Its only now that studies have been initiated to specifically target patients with CKD stage 3 or more, till date the AHA considers they be used with caution in renal disease.

4.STUDY JUSTIFICATION

In view of the above evidence it is clear that uncontrolled hypertension has adverse consequences on an already damaged kidney and that when well controlled it results in halting and in some cases improvement of the kidney damage.

It is the single most important factor in cardiovascular risk reduction amongst CKD patients.

Management of end stage renal disease with dialysis is not only very expensive but facilities in our local set up are not readily available.

The cost of maintaining an adequate quality of life in end stage renal failure i.e. regular dialysis appropriate medication and clinic visits costs more per month than the yearly earning of most Kenyans.

The cost of a kidney transplant in most centers is more than 10 years earning of the ordinary Kenyan, not including the lifelong graft suppressive medication .

It is then abundantly clear that modifiable risk factors in CKD, if adequately addressed will be of benefit not just to the individual patient in retarding disease progression but reducing the overall economic burden of disease.

Hypertension can be easily diagnosed with simple tools that can easily be availed all over the country.Chronic kidney disease can also be diagnosed with very simple and readily available and affordable lab parameters.Therefore looking at aspects of hypertension with a view of improving their control will go a long way in slowing progression of CKD.

This study will define the magnitude of the problem at the renal clinic based at KNH.

1. OBJECTIVES

5.1 BROAD OBJECTIVE

To determine the prevalence of hypertension and the adequacy of its control in patients with chronic kidney disease at the renal clinic based at KNH..

5.2 SPECIFIC OBJECTIVES

1. To determine the prevalence of hypertension in CKD patients
2. To determine the percentage of hypertensive CKD patients who are adequately controlled

5.3SECONDARY OBJECTIVES

1 To compare patients with normal blood pressure vs. those with hypertension by stage of CKD

2 To determine the association of socio demographic factors and adequacy of blood pressure control.

3 To determine the association of the patients knowledge of their disease and adequacy of blood pressure control.

4 To determine use of RAAS axis modifiers

6.METHODOLOGY

6.1 Study design

A cross sectional survey

6.2 Study site

The renal clinic based at the Kenyatta national hospital, held once weekly. On average 40 to 60 adult patients visit the clinic on any given clinic day.

6.3 Study population

Patients with CKD aged above 13 years of age

6.4 Case definition

Chronic kidney disease-

The K/DOQI working group defined chronic kidney disease in adults as: Evidence of structural or functional kidney abnormalities (abnormal urinalysis, imaging studies, or histology) that persist for at least three months, with or without a decreased GFR (as defined by a GFR of less than 60 mL/min per 1.73 m2).

OR

Decreased GFR, with or without evidence of kidney damage.

staging as per the National Health and Nutrition Examination Survey (NHANES) performed in 1999 to 2004.

6.5 Definition of case variables

Stage 1 disease is defined by a normal GFR (greater than 90 mL/min per 1.73 m2) and persistent albuminuria

Stage 2 disease is a GFR between 60 to 89 mL/min per 1.73 m2 and persistent albuminuria

Stage 3 disease is a GFR between 30 and 59 mL/min per 1.73 m2

Stage 4 disease is a GFR between 15 and 29 mL/min per 1.73 m2

Stage 5 disease is a GFR of less than 15 mL/min per 1.73 m2 or end-stage renal disease

Hypertension will be defined as a blood pressure above 130/80 or any patient on antihypertensive medication.

6.6 Sampling technique

INCLUSION CRITERIA

1. Patients with CKD as defined by Creatinine clearance < 60mls/min/1.73m2 persisting over 3 months or persistent proteinuria over the same period of time.

2. Age above 13 years
3. Patients should have at least attended the clinic twice

EXCLUSION CRITERIA

1. Refusal to participate
2. Patients who have had kidney transplant
3. Patients on dialysis

6.7 Sample size

The minimum sample size (n) required to determine the prevalence of hypertension was calculated using the formula below[57]. Prevalence of hypertension in CKD as per study done by Nadeem Sheikh et al is 51.8 %.

$$n = \frac{Z2\pi(1-\pi)}{d2}$$

- Whereby z value is the upper $\alpha/2$ point of the normal distribution
- n. 1.96
- II is the assumed prevalence
- d is the precision, 0.1, with which to determine the prevalence
- this gives a sample size of 96 patients

6.8 Study period

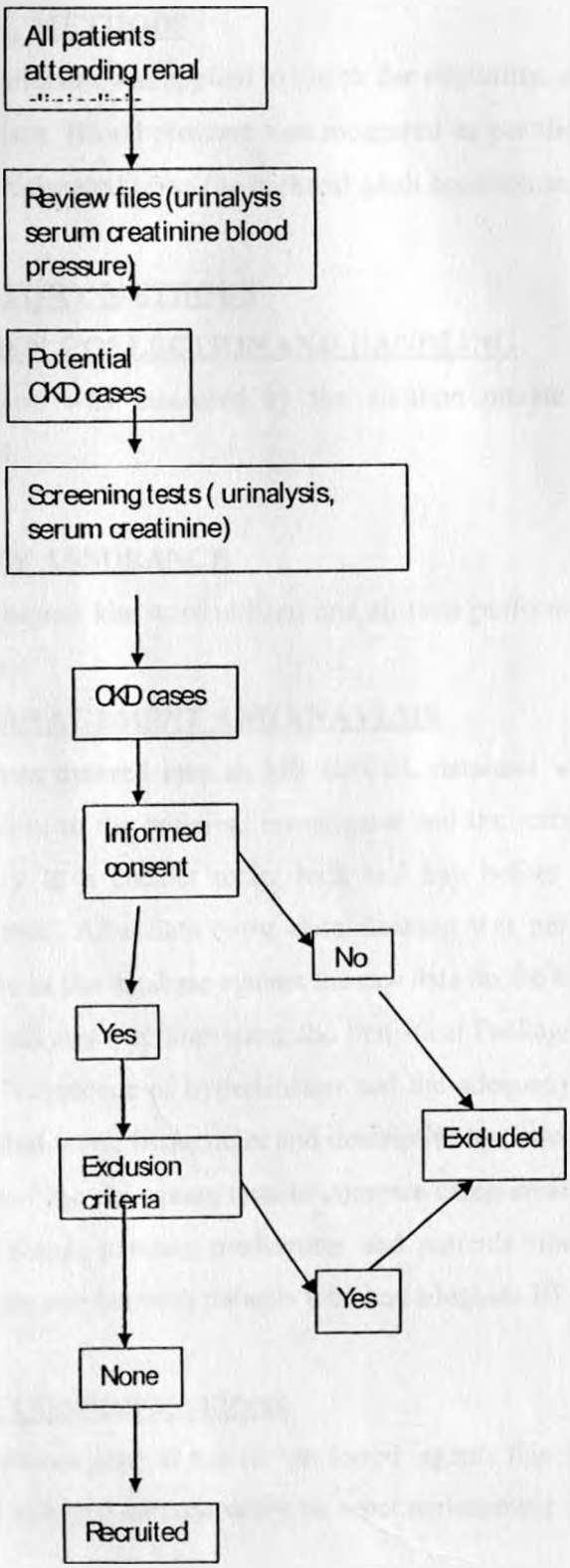
Patients were recruited over a 3 month period from January to March 2009

6.9Screening and recruitment

- A maximum of 10 patients per clinic visit were seen, every alternate patient was selected
- Previous urinalysis and creatinine clearance were assessed and potential CKD cases identified
- Repeat urinalysis and creatinine was taken on the morning of the clinic.
- Once CKD criteria was satisfied informed consent was then obtained
- Inclusion and exclusion criteria were then applied

- Their blood pressures was recorded twice and the average taken as per the WHO recommendation

Flow chart of screening and recruitment



7 DATA COLLECTION

7.1 CLINICAL METHODS

A screening proforma was applied to check for eligibility. A study proforma was used to record demographic data. Blood pressure was measured as per the WHO recommendation. Creatinine clearance was estimated using the cockroft gault equation and corrected to body surface area.

7.2 LABARATORY METHODS

7.2.1SPECIMEN COLLECTION AND HANDLING

Serum creatinine was measured by the alkaline picrate methord and dipstick analysis by multistix 10SG

7.2.2QUALITY ASSURANCE

Commercial reagent kits were utilized and all tests performed by competent technologists at the renal laboratory.

7.3 DATA MANAGEMENT AND ANAYLSIS

- Data was entered into an MS EXCEL database which was under password and only accessible to the principal investigator and the statistician. Patient data forms were kept securely in a cabinet under lock and key before during and after data analysis was completed. After data entry, data cleaning was performed and involved cross-checking the data in the database against the raw data on the forms.
- Data analysis was done using the Statistical Package for Social Scientists (SPSS) version 11.5. Prevalence of hypertension and the adequacy of its control in CKD patients was estimated using frequencies and descriptive statistics.
- We used the chi-square tests to compare categorical socio demographic characteristics , CKD stage, patients medication and patients understanding of disease and t-test to compare age between patients who had adequate BP control versus those who did not.

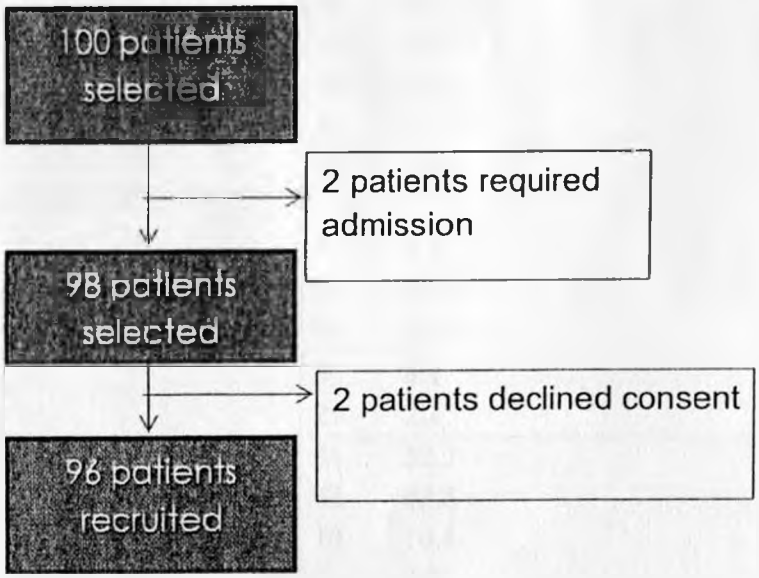
8.ETHICAL CONSIDERATIONS

For all the patients seen, if not on 'preferred' agents this was rectified. Patients in ESRD were appropriately referred for counseling on renal replacement therapy. All patients had the nature of

their disease, its course and prognosis explained. All patients not counseled on lifestyle modification were then counseled and referred to the renal team for further counseling. The study was passed through the department of medicine and the medical ethics board and approved. Parental consent for patients < 18 years was obtained after patients themselves agreed to be recruited.

9. RESULTS

Figure 2. FLOW CHART REPRESENTING PATIENTS RECRUITED



9.1 Baseline characteristics of the patients

A total of 96 patients were recruited into the study between January 2009 and March 2009. Baseline characteristics are as shown on the table below. Of interest is that the majority of the

patients had a primary school education or lower (71.9%), and majority were unemployed (58.3%)

Table 1. Socio-demographic characteristics

Variable	Frequency (%), N=96	
Age in years (SD)	48.2 years (±19.9 years)	
Sex		
Male	50	52.1
Female	46	47.9
Marital status		
Never married	22	22.9
Married	65	67.7
Separated	1	1.0
Widowed	8	8.3
Occupation		
Student	4	4.2
Housewife	9	9.4
Unemployed	43	44.8
Formally employed	17	17.7
Self-employed	23	24.0
Education		
None	7	7.3
Primary	62	64.6
Secondary	22	22.9
PSC	3	3.1
College/University	2	2.1
Nairobi	31	32.3
Central	42	43.8
Rift valley	10	10.4
Nyanza	3	3.1
Western	1	1.0
Eastern	8	8.3
North Eastern	1	1.0

9.2 Prevalence and adequacy of control of hypertension amongst patients with CKD

The overall prevalence of hypertension amongst patients with CKD was 76% . 16.6% had adequate blood pressure control.

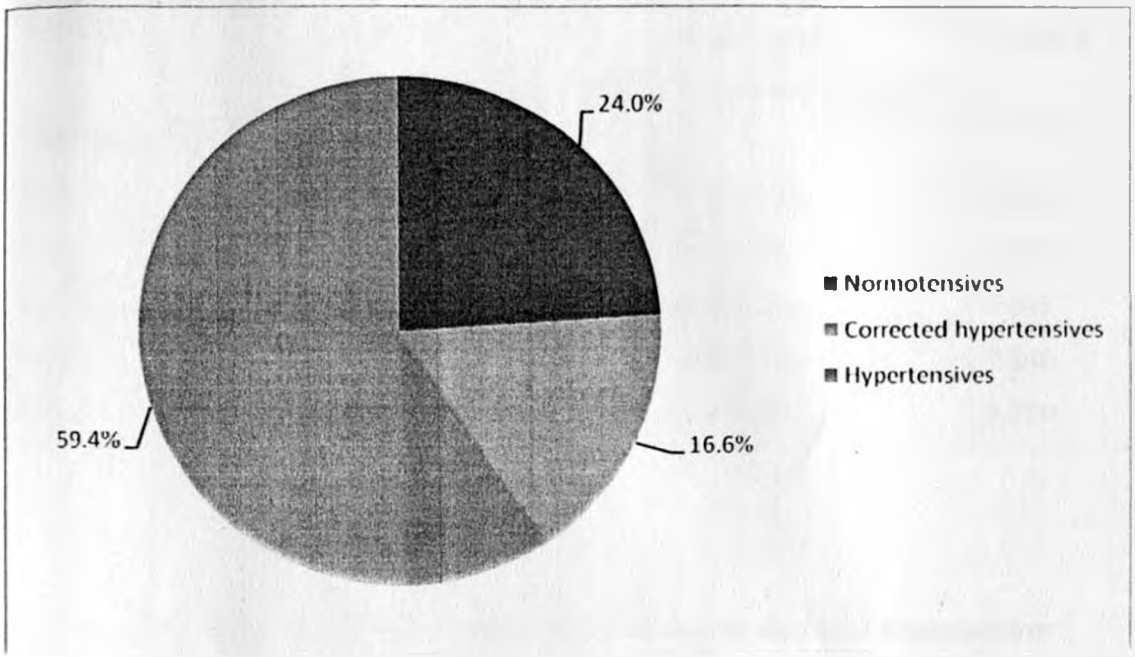


Figure 1: Percentage of adequately controlled hypertensive CKD patients

9.3 CKD stage and prevalence of hypertension

It was noted that 71.9% of the patients had a creatinine clearance of less than 60mls/kg/min

Table 2: CKD stage and prevalence of hypertension

Variable	Frequency (%), N=96	
CKD stage		
Stage 1	13	13.5
Stage 2	14	14.6
Stage 3	37	38.5
Stage 4	21	21.9
Stage 5	11	11.5

9.4 Patients with normal BP versus patients with hypertension compared to stage of CKD

Comparing patients with normal BP versus patients with hypertension compared to stage of CKD, it is clear that there is a higher incidence of hypertension amongst patients with CKD and this trend stays true through all the stages. There was no statistical difference however except for stage 2 disease.

Table 3; normal versus hypertensive patients compared to stage of CKD

Variable	Normal Frequency (%), N=23	Hypertensive Frequency (%), N=73	P value
CKD stage			
Stage 1	4	9 (69.2%)	0.536
Stage 2	7	7 (50%)	0.014
Stage 3	8	29 (78.4%)	0.671
Stage 4	3	18 (85.7%)	0.240
Stage 5	1	10 (90.9%)	0.220

9.5. Impact of socio demographic characteristics on prevalence of hypertension

When socio demographic characteristics were compared between patients with normal blood pressure and those with hypertension, no statistical difference was found

Table 4; association of socio demographic characteristics on prevalence of hypertension

Variable	Normal (n=23)	Hypertensive (n=73)	P value
Age (mean)	42.5 years	50.0 years	0.118
Sex			
Male	12 (52.2%)	38 (52.1%)	0.992
Female	11 (47.8%)	35 (47.9%)	
Marital status			
Never married	6 (26.1%)	16 (21.9%)	0.678
Married	15 (65.2%)	50 (68.5%)	0.770
Separated	1 (4.3%)	0 (0.0%)	0.073
Widowed	1 (4.3%)	7 (9.6%)	0.428
Occupation			
Student	1 (4.3%)	3 (4.1%)	0.960
Housewife	0 (0.0%)	9 (12.3%)	0.077
Unemployed	13 (56.5%)	30 (41.1%)	0.195
Formally employed	2 (8.7%)	15 (20.5%)	0.194
Self-employed	7 (30.4%)	16 (21.9%)	0.404
Education			
None	3 (13.0%)	4 (5.5%)	0.224
Primary	15 (65.2%)	47 (64.4%)	0.942
Secondary	5 (21.7%)	17 (23.3%)	0.878
PSC	0 (0.0%)	3 (4.1%)	0.323
College/University	0 (0.0%)	2 (2.7%)	0.422
Province			
Nairobi	6 (26.1%)	25 (34.2%)	0.466
Central	12 (52.2%)	30 (41.1%)	0.350
Rift valley	1 (4.3%)	9 (12.3%)	0.275
Nyanza	0 (0.0%)	3 (4.1%)	0.323
Western	1 (4.3%)	0 (0.0%)	0.073
Eastern	3 (13.0%)	5 (6.8%)	0.349
North Eastern	0 (0.0%)	1 (1.4%)	0.573

9.6 Patients understanding of their disease

Amongst the 96 patients, only 74% knew that they had the diagnosis of CKD. Only 11.5% of the patients understood that they would be taking their medication indefinitely. The majority (71.9%) had been taught about lifestyle modification as part of the management of their disease. Majority of the patients (91.7%) took their medication on a daily basis.

Table 5: Patients' understanding of disease

Variable	Frequency (%),N=96	
Knowledge of the diagnosis of kidney disease		
Yes	71	74.0
No	25	
Knowledge of the duration of treatment of CKD		
Yes	11	11.5
No	85	
Knowledge of lifestyle modification		
Yes	69	71.9
No	27	
Daily medication		
Yes	88	91.7
No	8	

9.7 Patients understanding of their disease and the association to blood pressure control

No statistical difference was found when patients with normal pressure versus those with hypertension were compared to see if there was a correlation between their understanding of their disease (knowledge of the diagnosis and management of CKD) and blood pressure control.

Table 6; Patients understanding of their disease and its association to blood pressure control

Variable	Normal Frequency (%), n=23	Hypertensive Frequency (%), n=73	P value
Knowledge of the diagnosis of kidney disease			
Yes	14 (60.9%)	57 (78.1%)	0.101
No	9 (39.1%)	16 (21.9%)	
Knowledge of the duration of treatment of CKD			
Yes	1 (4.3%)	10 (13.7%)	0.220
No	22 (95.7%)	63 (86.3%)	
Knowledge of lifestyle modification			
Yes	15 (65.2%)	54 (74.0%)	0.415
No	8 (34.8%)	19 (26.0%)	
Daily medication			
Yes	22 (95.7%)	66 (90.4%)	0.428
No	1 (4.3%)	7 (9.6%)	

9.8 Use of RAAS axis modifiers

Amongst the 96 patients, 86.5% were using either ACEI/ARB. 59.4% of the patients were appropriately using diuretics.

Table 7; Use of RAAS axis modifiers

Variable	Frequency (%),N=96
ACEI/ARB	
Yes	83 86.5
No	13
Appropriate use of diuretics	
Yes	57 59.4
No	39

9.9 Use of RAAS axis modifiers compared to stage of CKD

When the prescription of an ACEI/ARB was compared to stage of CKD, no statistical difference was noted

Table 8; Use of RAAS axis modifiers compared to stage of CKD

Variable	ACEI/ARB		P value
	Yes	No	
CKD stage			
Stage 1	11	2 (18.2%)	0.835
Stage 2	13	1 (71.4%)	0.449
Stage 3	34	3 (8.8%)	0.218
Stage 4	17	4(19%)	0.404
Stage 5	8	3 (27.3%)	0.157

9.9b Patient management

It was noted that 62.5% of patients had been taught about lifestyle modification, and were at least on an ACEI/ARB. Only 45.8% were on the above and knew their diagnosis.

Table 9; Patient management

Variable	Frequency (%)
CKD 1,2,3	44 45.8
CKD 1,2,3,4	14 14.6
CKD 1,3	60 62.5

KEY

1 – Life style modification

2 – Knowledge of kidney disease

3 – ACEI/ARB

4 – Appropriate diuretics

10. DISCUSSION

The overall prevalence of hypertension was found to be 76%. In a study done by Nadeem Sheikh et al at Kenyatta National Hospital renal clinic in 2004, in cardiovascular risk factors in chronic kidney disease, a prevalence of 51.8% was found amongst hypertensive patients. This most likely is due to the fact that he included only patients with a blood pressure of above 140/80 and therefore excluded many patients at increased cardiovascular risk as was the definition at the time. Studies elsewhere estimate a prevalence of 80 to 85 %.(14, 3). These figures are similar to the prevalence found in this study.

Only 16 (16.6%) of the patients had achieved the target blood pressure of 130/80 (22, 23). Although no large scale trial exists to determine optimal blood pressure, it is well known that CKD markedly increases cardiovascular risk; therefore lower blood pressure should be targeted.

Normotensive vs hypertensive compared to stage of disease, showed no statistical difference despite worsening kidney function, the trend however showed that patients with CKD are more likely to be hypertensive. For instance patient in stage 5 disease, 90.9% were hypertensive. Exception was stage 2 disease in which the number of patients who were hypertensive and those with normal blood pressure was equal. This was likely to be because of the few numbers studied.

The reasons for poor control are myriad. In this study it was noted that only 74% of the patients realized that they were attending a renal clinic, i.e. 26% had no idea about their diagnosis. To compound this, only 11.5% of the patients knew that they would be taking their medication indefinitely, therefore several would stop when either the medications got finished, or when they felt better or if they didn't feel better, not realizing that some of the benefits from the medication may take months to work.

A large number of the patients were poorly educated (71.9%) yet interestingly enough, 91.7% claimed to be taking their medication daily. Whether they were taking their correctly prescribed medication or all their medication was not assessed in this study but could impact on their overall poor blood pressure control.

It was noted that 28.1% of all patients had not been taught about lifestyle modification, despite evidence base for its benefit in blood pressure control. (13, 14). This error could stem partly from physician negligence, but also the sheer number of patients at the renal clinic may contribute to the lack of allocation of time to study each patients file in detail.

It was noted that only 62.5% of patients had received the bare minimum of lifestyle modification and the prescription of an ACEI/ARB.

Once again this echoes strongly on the points brought out above that patients have insufficient contact time with their health care providers.

All patients with CKD unless contraindicated should be on either an ACEI/ARB, several large trials have shown support for this.(50,51,52,53). Despite this only 86.5% of the patients had these medications prescribed. Reason for this is unclear, but likely that same reasons as above apply.

When the prescription of ACEI/ARB was compared to stage of CKD no statistical difference was noted. Traditionally these medications were avoided in patients with advanced renal disease, but studies have shown their benefit, therefore the reasons why these patients were not receiving the drugs remains unknown, the fault could be with the prescriber.

More patients came from Central province and Rift Valley (54.2%). These patients perhaps contributed to the congested clinics. These patients can easily be handled out of a tertiary level institution. Reasons for why they would travel all the way to KNH were not elucidated in this study, but could stem from misinformation, or lack of confidence in their local hospitals, or inappropriate referral.

11. CONCLUSIONS

This study demonstrates that the burden of hypertension in patients with chronic kidney disease is very high. Furthermore the overall control of their hypertension is poor.

12. RECOMMENDATIONS

All patients with chronic kidney disease should be screened for hypertension and for the adequacy of its control. Studies should be carried out that would help delineate where the problems may lie and appropriate action taken where deficits are found.

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APPENDIX 1- Study participation consent form

I am Dr. Allan Rajula. I am carrying out a study on adequacy of blood pressure control in patients with chronic kidney disease. I intend to find out how many people with the above disease develop high blood pressure. And out of those who do how many are well managed.

It is well known that uncontrolled hypertension can lead to further renal deterioration which might end up with patient needing renal replacement therapy or a transplant. It also markedly increases the risk of a cardiovascular event such as heart failure or a heart attack

This information will lead to better control once we know where the problems lie.
If you agree to participate in this study, we will take your blood pressure twice, perform a few simple tests and ask a few questions relating to your disease. This information will be recorded on a questionnaire but your details and the information you give will remain confidential. If you are willing to participate in this study, please sign on the consent form.
You stand to benefit as I will give you any relevant advice as will pertain to your health care as well as submit my recommendations to the care givers at the renal clinic.
The only side effect or discomfort will be when blood is been drawn from your arm but it will just be a single needle prick. You will also be required to pass urine into a container for assessment.

I _____ patient/parent/guardian of _____ hereby consent to the inclusion into the above study the nature and effect of which have been fully explained to me.

Signature _____ Date _____

Witness (researcher) _____ Date _____

APPENDIX 2 – Study questionnaire

Study number _ _ _

Date of enrolment (day, month, year) _ _ / _ _ / _ _ _ _

File no _ _ _ _ _ _ _ _

BIO DATA

Creatinine clearance (ml/min/1.73m2) _ _ _

Stage of CRF

1) Stage 1 ☐
2) Stage 2 ☐
3) Stage 3 ☐
4) Stage 4 ☐
5) Stage 5 ☐

BP (Systolic/Diastolic)

1st reading _ _ _ / _ _ _

2nd reading _ _ _ / _ _ _

Average _ _ _ / _ _ _

SOCIAL DEMOGRAPHIC DATA

Age of patient (years) _ _

1. Sex
    (1) Male
    (2) Female

2. Marital staus
    a. Never Married
    b. Married
    c. Separated
    d. Divorced
    e. Widowed

3. Occupation status
    (1) Unemployed
    (2) Self employed
    (3) Housewife
    (4) Formally employed
    (5) Student

4. Level of education
    (1) None
    (2) Primary
    (3) Secondary
    (4) Post secondary certificate
    (5) College/university

5. Provincial residence
    (1) Nairobi
    (2) Central
    (3) Rift valley
    (4) Nyanza

(5) Western

(6) Eastern

(7) N. eastern

(8) Coast

PATIENTS UNDERSTANDING OF DISEASE

1. What you are suffering from?

   (1) Kidney disease

   (2) Hypertension

   (3) Both of the above

   (4) Other (specify) _____

   (5) I don't know

2. How long are you going to continue medication?

   (1) Until they run out

   (2) Until the next clinic visit

   (3) Until I feel better

   (4) Indefinitely

   (5) I don't know

3. Do you take your medication every day?

   (1) Yes

   (2) No

4. If no why not?

   (1) Side effects

   (2) Drugs not available

   (3) Too many drugs

   (4) Drugs too expensive

(5) I didn't know I was to take them every day

(6) The drugs don't seem to work

(7) I felt the drugs made me better

(8) Other (specify) _____

5. Have you been told about;

(1) Diet modification

(2) Alcohol consumption

(3) Cigarette smoking

(4) Body exercises

PATIENTS MEDICATION

1. Are you on medication?

a. Yes

b. No

2. If yes, which ones?

Drug	**Type**	**Dose**	**Frequency**	**Duration**
ACEI				
ARB				
Thiazide diuretics				
CCB				
Beta blocker				
Direct vasodilators	Hydrallazine			
Centrally acting	Alpha methyl dopa			