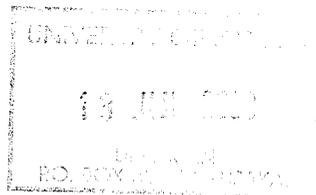




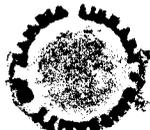
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**COMPLICATIONS OF HYPERTENSION SEEN AT THE
UNIVERSITY TEACHING HOSPITAL**

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A DISSERTATION SUBMITTED AS PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR MASTERS OF MEDICINE IN INTERNAL MEDICINE

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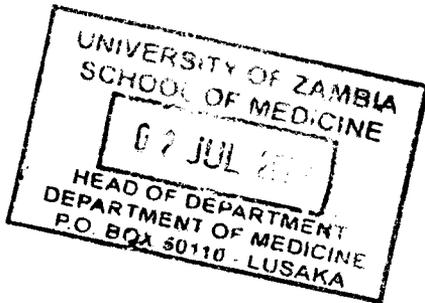
APPROVAL PAGE

The dissertation of Dr Margret C Chibowa is approved in partial fulfillment of the requirements for the award of the Masters degree in Internal Medicine.

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COPYRIGHT DECLARATION

I, hereby declare that this dissertation herein presented for the Degree of Masters of Medicine (Internal Medicine) has not been previously submitted wholly or in part for any other degree.

Signed: *[Signature]* candidate

ACKNOWLEDGEMENT

I thank all the people who helped me carry out this study, with whose help it has been possible to complete.

DEDICATION

dedicate this study to my family whose undying support has made it possible for me to achieve many things. My Lord, in whom I place all my trust.

LIST OF ABBREVIATIONS

BP - Blood Pressure
CV - Cardiovascular
CVD - Cardiovascular disease
BMI - Body mass index
SBP - Systolic Blood Pressure
DBP - Diastolic Blood Pressure
TOD - Target organ damage
ACE - Angiotensin converting enzyme
WHO - World Health Organization
ISH - isolated systolic hypertension
EDRF - endothelium derived relaxant factor
MRC - Medical research council
UTH - University Teaching Hospital
ECG - Electrocardiogram
ECHO - Echocardiogram
LVH - Left Ventricular hypertrophy
HHD - Hypertensive heart disease
HIV - Human Immunodeficiency Virus
LMNL - Lower motor neuron lesion
UMNL - upper motor neuron lesion
Hdl - High-density lipoprotein
Ldl - low density lipoprotein

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ABSTRACT

This descriptive study aimed at determining the common complications among hypertensive patients at the University teaching Hospital was conducted over a period of six months.

Two hundred and fifty patients were prospectively evaluated for complications of hypertension clinically and by laboratory methods. Target organ damage of the brain, heart and kidneys were evaluated while all patients had electrocardiogram, urinalysis, blood sugar, urea and electrolytes and echocardiogram.

The study has demonstrated that:

- a. More women are seen with hypertension than males.
- b. Hypertension tends to peak between 40 to 49 years of age for both sexes.
- c. Most of the patients seen had both systolic and diastolic hypertension
- d. The blood pressures at interview were high in most patients with a mean systolic pressure of 160 and diastolic of 103 mmHg.
- e. More than half of the patients had hypertensive retinopathy with 13% having severe retinopathy.
- f. More than half the patients (64%) had left ventricular hypertrophy
- g. One hundred and thirty-two patients (52.8%) had proteinuria in this study.
- h. Neurological deficits were seen in eighty-four patients (33.6%) at time of interview.

This study has demonstrated that most patients seen at the University Teaching Hospital have hypertensive complications.

1.1 BACKGROUND INFORMATION AND REVIEW OF LITERATURE

Hypertension is defined by the World Health Organization as systolic blood pressure greater than 140mmHg and diastolic blood pressure of above 90mmHg. Hypertension is a very common disease worldwide though the disease burden varies substantially between demographic regions and within the same economic bracket. As infectious diseases come under control in many parts of the developing world, the non-communicable diseases of which hypertension is a major component become important. In Africa hypertension is more prevalent in the urban communities, which have adopted a more Western lifestyle than in the rural population.

Non-communicable disease accounts for 10 million deaths globally with more than 5 million due to cardiovascular diseases. These cardiovascular diseases were perceived as belonging to the developed countries. 44% of deaths from non-communicable diseases occur in the developing world. Hypertension affects approximately one billion people world wide and is the commonest treatable risk factor for cardiovascular disease in patients over 50 years old. In the past four decades Africa has witnessed increasing urbanization and changing lifestyles, factors which in turn, raised incidence of cardiovascular diseases. At the same time social inequality compounded with dwindling economy in many countries in Sub-Saharan Africa (Kadiri et al 2005).

World Health report 2002, showed that cardiovascular disease accounted for 9.2% deaths in African region 2001 and hypertension, stroke, cardiomyopathies and rheumatic heart disease were the most prevalent cause of death.

The WHO reported adjusted life years lost to cardiovascular disease in Sub Saharan Africa rose from 5.3 million males and 6.3 million females in 2000 and is expected to rise to 8.1 million and 7.9 million females in 2010 (Reddy KS et al 1998).

Cardiovascular diseases have a higher mortality in developing countries than developed countries. Extrapolation of studies from Nigeria and elsewhere indicate 5% deaths maybe due to hypertension (Cooper RS et al. 2005)

The usual risk factors of obesity, smoking, heavy drinking, physical inactivity and inappropriate diet are also relevant in Africa.

People have multiple risk factors as shown in a study which looked at the prevalence of cardiovascular diseases and associated risk factors in rural black South Africans. This study reported that 32.1% of males and 18.9% females over 30years old had a 20% chance or higher likelihood of developing cardiovascular disease in the next 10years (Alberts et al 2005).

In America hypertension affects one in four adults; prevalence is higher among blacks and older person's especially older women (JNC VI 1998). In Nigeria no less than 4.33 million Nigerians (9.22%) over the age of 15 years of age have hypertension as defined by a Bp of 160/90 mmHg and above (Oladipo O akinkugbe 1996). In a review of studies published on hypertensive target organ damage in Africa, Mensah GA et al in 1994 found that atherosclerotic complications, especially those affecting the heart, is lower in Africa than in developed countries. However stroke, renal failure and heart failure appear to be the principal outcomes and are likely to be associated with high case fatality in

which looked at hypertension and target organ damage in 203 patients found that the prevalent target organ damage were LVH, chronic kidney disease, diabetic nephropathy, heart failure, cerebrovascular disease .their conclusion was a high prevalence of TOD in treated hypertensives seen in the medical outpatient department of a Nigerian state hospital(Ayodele et al 2005).At the University Teaching Hospital in Lusaka, Zambia hypertension accounted for 1343 of the 86335 admissions in the year 2000.

All stages of hypertension are associated with increased risk of non-fatal and fatal CVD events, stroke and renal disease. The higher the blood pressure, the greater is the risk. Stage 1 Hypertension is the commonest form of high blood pressure in the adult population and is responsible for a large proportion of the morbidity and mortality associated with hypertension. All stages of hypertension warrant effective long-term therapy.

The new classification of adult blood pressure is based on impact on risk. Traditional terms of mild, moderate and severe hypertension failed to convey the major impact of high blood pressure on cardiovascular disease.

CATEGORY (mmHg)	SYSTOLIC (mmHg)	DIASTOLIC
Normal	<130	<85
High normal	130-139	85-89
Hypertension		
Stage 1 (mild)	140-159	90-99
Stage 2 (moderate)	160-179	100-109
Stage 3 (severe)	180-209	110-119
Stage 4 (very severe)	>210	>120

The high normal is included as a category because persons in these ranges are at increased risk of developing definite high blood pressure and of experiencing fatal and non-fatal cardiovascular events compared with otherwise similar persons with lower blood pressures. These individuals need to be monitored yearly and counseled with regards to lifestyle modification

Hypertension is the most common disease-specific reason many patients visit a physician. Despite the risks associated with an elevated blood pressure (BP), there is still woefully low achievement of recommended BP goals. From 1991 to 1994, only 27.4% of hypertensive Americans aged 18 to 74 years had a BP <140/90 mm Hg, the current stated goal for most people with hypertension, and in those with diabetes, less than half that number (11%) were controlled to the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure VI (JNC VI 1996) recommended goal of <130/85 mm Hg.

Hypertension is also known as the "silent killer" because of its relative lack of symptoms before target organ damage has occurred.

Initial evaluation of the hypertensive patient focuses on the presence or absence of target organ damage (TOD) and includes a physical examination, blood urea nitrogen/creatinine evaluation, and measurement of electrolytes, urinalysis, and an ECG. Further, an assessment of cardiovascular (CV) risk factors with a thorough history and chemistry panel (glucose, cholesterol, and triglycerides) is

routinely administered. In every hypertensive patient the possibility of a secondary cause should always be entertained.

PATHOGENESIS

In hypertension, remodeling of large and small arteries contributes to the development and complications of hypertension.

The resistance arteries undergo eutrophic and or hypertrophic remodeling (Mulvany MJ et al 1996) In inward eutrophic remodeling, outer and lumen diameters are reduced, media cross sectional area is unaltered, and media/lumen ratio is increased, without stiffening.

When media growth encroaches on the lumen to increase the media /lumen ratio, the change has been called hypertrophic remodeling. (Mulvany MJ et al 1996).

Growth, apoptosis, inflammation, and fibrosis are all mechanisms that have been invoked to contribute to arterial remodeling in hypertension. Increased growth has been classically implicated in arterial remodeling in hypertension. (Lee RMKW et al 1995). Chronic vasoconstriction associated with mild inflammation and activation of deposition of collagen, fibronectin, and other components of the extra cellular matrix may result in a remodeled structure with a smaller lumen and increased media/lumen ratio, i.e the inward eutrophic remodeled vessel (Rizzoni D et al 1996)

Vascular remodeling contributes to end organ damage in hypertension providing a rationale for regression of blood vessels as a therapeutic aim.

Large conductance calcium channel blockers stimulate apoptosis, as shown by studies with nifedipine (Stead S et al 2000) and amlodipine (Sharifi AM et al 1998).

The actions of Angiogenesis II are mediated by stimulation of production of super oxide anion and activation of redox sensitive genes (Griendling KK et al 1999). In the heart and kidney the inflammatory regulators play a role in the progression of atherosclerosis in large conduit vessels (Weiss D et al 2001; Luft FC et al 1999)

The vessel wall includes structural proteins (collagen and elastin) and adhesive proteins (e.g. laminin and fibronectin). In hypertension there is deposition of extra cellular matrix, particularly collagen, in the arterial wall. Normal arteries fibrillar collagens I and III are the major constituents of the intima, media, and adventitia, whereas I, III, IV and V are in the endothelial and basement membranes. (Thybo NK et al 1996)

Collagen is the extracellular fibrillar component that may alter the passive pressure/diameter relation of arteries at high pressures and induce a progressive stiffening of the vascular wall. It is not only the amount of collagen in the wall but rather the recruitment of collagen fibers at higher pressures which lead to stiffness of the vessel wall. (Intengan HD et al 1999).

Arterial wall thickening increases peripheral resistance and blood pressure, in part by physically encroaching on the lumen and, where collagen is invoked, by increasing wall stiffness to reduce the lumen diameter at a given pressure. (Intengan HD et al 2000)

HYPERTENSIVE RETINOPATHY

Hypertensive retinopathy is a condition characterized by a spectrum of retinal vascular signs in people with elevated blood pressure. This is considered part of standard evaluation of hypertensive patient. This is supported by the report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) which list retinopathy as one of the markers of target organ damage in hypertension. On the basis of the JNC criteria, the presence of retinopathy may be an indication for initiating antihypertensive therapy, even in people with stage 1 hypertension (blood pressure, 140 to 159/90 to 99 mmHg) who have no other evidence of target organ damage. (JNC 7 2003)

However the clinical implications of hypertensive retinopathy remain unclear. Many physicians do not regularly perform an ophthalmoscopic examination as part of the care they provide to hypertensive patients.

The evidence in support of the JNC guidelines may not have relevance in current clinical practice because of the following important limitations.

First, they involved patients with uncontrolled and untreated hypertension, generalization to contemporary populations of patients with lower hypertension may be problematic. Second, retinopathy was based on direct ophthalmoscopic examination. This technique showed to be unreliable due to high rates of interobserver variability (20-42 percent) and intraobserver variability (10 to 33 percent) when used in persons with mild hypertension (Dimmitt SB et al 1989; Kagan A et al 1996). Third, although many earlier studies cite increased mortality among patients with hypertensive retinopathy few studies have demonstrated associations between hypertensive retinopathy and specific cardiovascular outcomes, whether hypertensive retinopathy predicts the risk of cardiovascular independently of other risk indicators has not been studied till recently.

Marcus Gunn was the first to describe retinal signs in the 19th century. These included generalized and focal retinal narrowing, arteriovenous nicking, flame shaped and blot shaped retinal haemorrhages, cotton-wool spots, and swelling of optic disc. In 1939, Keith et al showed these retinal changes were predictive of death in patients with hypertension.

Sheie modified the classification but in both major criticisms are that it is difficult to distinguish low grades (grade 1 from grade 2 signs) and retinopathy grades not correlated with severity of hypertension.

PATHOPHYSIOLOGY

The raised blood pressure leads to changes in the retinal vessels. Initially; there is vasoconstriction stage, vasospasm and increased retinal arteriolar tone owing to local auto regulatory mechanisms. This is seen clinically as generalized narrowing of retinal arteioles. Persistently elevated blood pressure leads to intimal thickening, hyperplasia of the medial wall, hyaline degeneration in the subsequent sclerotic, stage. This is seen as arteriovenous nicking or nipping and alterations in the arteriolar light reflex (i.e. widening and accentuation of central light reflex, or "copper wiring")

The disruption of the blood-retina barrier, necrosis of the smooth muscles and endothelial cells, exudation of blood and lipids, retinal ischemia leads to the exudative stage.

These changes manifest in the retina as microaneurysms, haemorrhages, hard exudates and cotton wool spots. Swelling of the optic disc may occur at this time and usually indicates severely elevated blood pressure (malignant hypertension). Retinal vascular complications of hypertension such as macro aneurysms and branch -vein occlusions are not uncommon in patients with chronically elevated hypertension (Fuchs FD et al 1995; Pache M et al 2002)

EPIDEMIOLOGY

Seven population based studies have been done between 1990-2004 involving total 26,477 participants in communities with or without history of hypertension, looking at hypertensive retinopathy. In all retinal photographs were used to standardize examination (Klein R et al 1994; Sharp PS et al 1995; Stolk RP et al 1995; Yu T et al 1998; Klein R et al 2000; Wong TY et al 2003; Klein R et al 1997; van Leiden HA 2003)

Signs of hypertensive retinopathy are common in people 40 years of age or older with or without history of hypertension, prevalence rates ranged from 2-15 percent (Klein R 1994, Sharp PS et al 1995, Stolk RP et al 1995, Wong et al 2003). In contrast the Framingham Eye Study found a prevalence of 1 percent among participants who underwent ophthalmoscopic examination with dilatation (Leibowitz HM et al 1980). This may be due to the greater sensitivity of photography over clinical ophthalmoscopy though no study has been done to compare the sensitivity or reliability of the two.

Higher prevalence in blacks than whites explained due to higher levels of blood pressure among blacks. (McDonough JR et al 1994).

A higher prevalence of retinopathy among blacks suggests that retinal examination may be particularly useful for risk stratification.

Two studies have evaluated the effect of a history of elevated blood pressure on the occurrence of specific retinal signs. In both generalized retinal arteriolar narrowing and arteriovenous nicking are markers of vascular markers from chronic hypertension.

In contrast, the focal arteriolar narrowing, retinal haemorrhages, microaneurysms, cotton wool spots were related to current but not previous hypertension.(Sharrett AR et al 1999,Wong TY et al 2002).

Signs of hypertensive retinopathy in people with no previous history may be markers of pre hypertensive state.(Wong TY et al 2004)

Hypertensive retinopathy has been useful in the risk stratification of stroke. Retinal circulation shares anatomical, physiological, embryonic features with cerebral circulation. An autopsy study showed a strong correlation between retinal and cerebral arteriolar findings (Goto I et al 1975).

The Atherosclerosis Risk in Communities Study which was a multisite cohort study showed that some retinopathy was seen in strokes, reduced cognitive functions (Wong TY et al 2002).

The National Health Examination Survey showed that persons with retinal arteriolar narrowing were two to six times as likely to have pre existing coronary artery disease as those without these changes, after analysis controlled for presence or absence of hypertension and diabetes and serum cholesterol levels (Gillum RF et al 1991).In a study involving 560 men with hypertension and hyperlipidemia, the presence of hypertensive retinopathy predicted the doubling of the risk of coronary artery disease (relative risk 2.1;95 percent confidence interval,1.0 to 4.2),and the presence of generalized or focal narrowing of arterioles predicted almost a tripling of this risk(relative risk 2.9;95 percent confidence interval 1.3 to 6.2)

Some clinical trials have shown that signs of hypertensive retinopathy regress with the control of blood pressure(Bild DE et al 2002).A small study of 28 patients with mild hypertension showed that after 26weeks those randomized to enalapril(ACE inhibitor)had a reduction in retinopathy while no changes on hydrochlorothiazide(thiazide diuretic).

Signs of hypertensive retinopathy are common and are correlated to elevated blood pressure and some changes have been shown to predict stroke and death from stroke independently of elevated blood pressure and other risk factors.

CARDIOVASCULAR COMPLICATIONS

Hypertension is an important contributor to morbidity and mortality from cardiovascular disease. Men and women with hypertension are at increased risk for cardiovascular disease especially when left ventricular hypertrophy is present. (JNC1997, JNC 1993, Stamler J et al 1993).Multiple clinical trials have shown that the treatment of hypertension reduces the risk of cardiovascular disorders (Collins R et al 1990)

The risk of cardiovascular disease at any level of high blood pressure increases markedly for patients with damage to heart kidneys, brain, or large arteries (JNC VI 1997).

Persons with left ventricular hypertrophy are at an increased risk for a variety of cardiovascular sequelae, including angina pectoris, myocardial infarction, stroke, heart failure and sudden death (MacMahon S et al 1986, Levy D et al 1994, Sullivan JM et al 1993, Knutsen SF et al 1988)

The Framingham Heart Study since its inception in 1948 has obtained information on blood pressure measurement, treatment and changes in left ventricular hypertrophy. The Framingham Heart Study 5209 men and women free of cardiovascular disease aged 24 to 64 years were followed up every two years and thorough physical examination including ECG and other physiologic variables.

The candidates were followed up for four decades. 1829 of the 5209 of the original subjects during follow up through 1989. In the Offspring study whose enrollment started in 1971, 152 of the 5124 participants developed left ventricular hypertrophy, so between 1950-1989, 1265 participants developed Left ventricular hypertrophy. (Ashizawa N et al 1989, Schmieder RE et al 1996, Dawber TR et al 1951)

Their analysis agreed with the hypothesis that widespread use of antihypertensive have resulted in the decline in severe blood pressure as well as left ventricular hypertrophy.

Hypertrophy increases the myocardial oxygen requirements, which when supply is decreased because of atherosclerosis and decreased coronary reserve, imposes a risk of ischemia. Left ventricular hypertrophy is associated with increased risk of arrhythmias and sudden death (Ghali JK et al 1991, McLenachan JM et al 1987, Lanti M et al 1990)

Blood pressure is a major determinant of ventricular hypertrophy, in terms of both voltage criteria and depolarization abnormalities. (MacMahon S et al 1989, Levy D et al 1994).

Regression of LVH has been observed in hypertensive patients in response to treatment with anti hypertensive drugs and it apparently reduces the risk of cardiovascular. (Van Hoof R et al 1991, National Heart, Lung and Blood institute 1998, MacMahon S et al 1989).

In a study involving 1 2,031 initially middle aged men observed relative risk of death from coronary heart disease was observed to rise continuously with increasing levels of systolic and diastolic blood pressure.

Sustained differences of 10 mmHg in systolic blood pressure and of 5mmHg in diastolic blood pressure were each associated with a 28 percent difference in the risk of death from coronary artery disease. (van den Hoogen et al 2000).

The risk of death from coronary heart disease among patients with sustained elevations in blood pressure (SBP>160mmHg, DBP>95mmHg) was about two times as high as that among patients with lower blood pressure levels.

RENAL COMPLICATIONS

The recognition that essential hypertension is a primary renal disease was recognized as early as 1836 by Richard Bright. He had observed that "the kidney is the chief promoter of the other derangements ... including hypertrophy of the heart." This was during an era where blood pressure was not measured and so some of the findings would have been due to chronic glomerulonephritis. Goldbatt et al in the 1930s noted that ischaemia limited to the kidneys may be the initial condition in the pathogenesis of hypertension associated with nephrosclerosis. Guyton et al theorized that hypertension does not occur in the presence of a normal kidney. Provided that sensing by the kidney of systemic

hypertension was unimpaired, and sodium reabsorption not enhanced, natriureisis and diuresis would reduce plasma volume and restore normotension. Essential hypertension results from an inherited renal tendency towards excessive vasoconstriction or an inability to appropriately increase renal blood flow (Robert G Luke et al 1993).

Supportive evidence includes studies on transplantation of hypertension or normotension with the kidney, prehypertensive evidence of abnormal renal vascular responses, epidemiological association of a high sodium chloride with hypertension, cyclosporine induced hypertension as a model for essential hypertension, and the lack of prevention to date of end-stage renal disease due to hypertensive nephrosclerosis despite widespread availability of antihypertensive therapy.

An imbalance of endocrine, paracrine, and autocrine regulators of renal blood flow may lead to exaggerated renal vasoconstriction (Dahl et al 1993)

Nitrogen oxide functions as a regulator of basal vasomotor tone and also inhibits smooth muscle and mesangial cell mitogenesis. Thus nitrogen oxide in excess can lead to defective vasodilatation and inhibit smooth muscle proliferation (Dahl et al 1993).

Normotensive relatives of patient with essential hypertension have shown increased renal vasoconstriction in response to mental stress and postural changes. Studies have also shown interactions between stress, renal blood flow and sodium chloride retention. (Burt V L et al 1995)

Essential hypertension is usually associated with a normal cardiac output and enhanced peripheral resistance. Arteriosclerotic changes in hypertensive are most severe in the kidneys. (Ault et al 1985)

Renal vasoconstriction may lead to both hypertension and nephrosclerosis on high sodium intake leading to a vicious circle (Milne FJ et al 1989)

The kidneys in hypertensive patients are subjected to raised blood pressure and this leads to damage as evidenced by proteinuria and raised creatinine.

The chronically elevated pressure if not controlled can eventually lead to chronic kidney disease. This can compound blood pressure control as the kidney function deteriorates the damage to the kidneys will progress.

CEREBROVASCULAR COMPLICATIONS

Hypertension occurs in acute stroke in up to 75% of cases. Subsequently BP settles over a period of one week, but about 40% remain hypertensive (Wallace et al 1981, Britton M et al 1986 et al).

Pathophysiological response are multifactorial and are related to preexisting high BP, activation of the neuroendocrine systems (sympathetic nervous system, renin-angiotensin axis, glucocorticoid system), increased cardiac output, and white coat hypertension (Carlberg B et al 1994, Treib J et al 1996).

Data from the International Stroke Trial confirmed that the risk of early and late death or dependency was dependent associated with increasing systolic BP (SBP) in 17398 patients (Leonardi-Bee J et al 2002).

Patients with primary intracerebral hemorrhage showed increased odds of death and death or disability or deterioration in patients with high BP. It was also found

that mean arterial blood pressure was higher in patients who died after primary intracerebral hemorrhage. The odds of hematoma expansion were increased for patients with high systolic blood pressure (Wilmot et al 2004).

Patients with ischaemic stroke were found to have higher SBP/DBP by 12/6 mmHg died or became dependent. Ischaemic stroke patients had a 2-fold increase in the risk of stroke recurrence when their DBP was elevated (Willmot et al 2004).

Regardless of the type of stroke, in the acute phase poor outcome i.e. death, or combined death and disability were associated with high SBP, mean arterial blood pressure and DBP (Bowes MP et al 1996)

1.2 TREATMENT OF HYPERTENSION

Treatment of hypertension prolongs life and prevents or delays congestive heart failure and nephrosclerosis and reduces the incidence of stroke (Sokolow M et al 1961, smirk FH 1972, Bulpitt c 1979) antihypertensive treatment has, however, been less effective in preventing coronary heart disease (Collins R et al 1990). It is not clear whether this is due to inadequate blood pressure control, inadequate intervention of other risk factors, negative effects on the risk of cardiovascular disease from antihypertensive drugs, intervention being too late to affect arterioscleroses, or inadequate effect of present drugs on arterioscleroses.

Persons with mild (Stage 1) to moderate (Stage 2) JNC VI 1997) diastolic hypertension (90-109 mm Hg) also benefit from treatment (Collins et al 1990) This was confirmed in the Hypertension Detection and Follow-up Program, a randomized controlled trial involving nearly 11,000 hypertensive men and women, of whom 40% were black (Hypertension detection and follow up programme cooperative group 1979). The intervention group received standardized pharmacological treatment ("Stepped care") while the control group was referred for community medical care. There was a statistically significant 17% reduction in 5 – year all-cause mortality in the group receiving standardized drug therapy; the subset with diastolic blood pressure 90 – 104 mm Hg experienced a 20% reduction in mortality. Deaths due to cerebrovascular disease, ischemic heart disease, and other causes were also significantly reduced in the stepped care group. (Medical research council working party 19988) similar effects on all-cause mortality and cardiovascular events have been reported in other randomized controlled trials, such as the Australian National Blood Pressure Study (initial diastolic blood pressure 95 – 109 mm Hg) (Management committee of the Australian National blood pressure society 1980) and the Medical Research Council (MRC) trial (Diastolic blood pressure 90 – 109 mm Hg). In these two trials, the relative reduction in rates of stroke or other trial endpoints with treatment was similar in those with diastolic blood pressures, although the absolute benefit was less due to smaller initial risk or stroke and other diseases at lower blood pressures. Both trials included untreated control groups and did not report a significant reduction in deaths from non-cardiovascular causes in the actively treated groups, confirming that the benefit was due to antihypertensive treatment.

Studies included persons with diastolic blood pressures of 90 – 120 mm Hg, and among them reported significant reductions in all – cause mortality, cardiovascular mortality (Amery et al 1986, Dahlof B et al 1998) cardiovascular events and strokes (Dahlof B et al 1998, MRC working party 1992). The Systolic Hypertension in the Elderly Program (SHEP 1991) trial included over 4,000 subjects ≥ 60 years of age with isolated systolic hypertension (systolic blood pressure ≥ 160 mm Hg, with diastolic blood pressure < 90 mm Hg), and reported significant reductions in the incidence of stroke, myocardial infarction, and left ventricular failure. A meta-analysis combining these and other trials that included persons aged ≥ 60 years demonstrated that antihypertensive treatment in elderly persons significantly reduced mortality from all cause (-12%), stroke (- 36%), and coronary heart disease (-25%), as well as stroke and coronary heart disease morbidity. (Insua et al 1994). This Meta – analysis suggested reduced benefits with increasing age, although differences were not statistically significant. Treatment of hypertension is associated with multiple benefits; including reduced coronary heart disease and vascular deaths, but meta-analysis suggest it produces the largest reductions in cerebrovascular morbidity and mortality. (Collins R et al 1990, Insua et al 1994), Improved treatment of high blood pressure has been credited with a substantial portion of the greater than 50% reduction in age-adjusted stroke mortality that has been observed since 1972. (Garraway WM et al 1987, Casper AJ 1992).

Although the efficacy of antihypertensive treatment for essential (also called primary) hypertension has been well established in clinical research, certain factors may influence the magnitude of benefit from hypertension screening achieved in actual practice. Compliance with drug therapy may be limited by the inconvenience, side effects, and cost of these agents (McClellan WM et al 1988) serious or life-threatening drug reactions in the clinical trials were rare, but less serious side effects were common, resulting in discontinuation of randomized treatment (almost 20% by the fifth year in the MRC trial, for example) or a substantial increase in patient discomfort. (Veterans Administration Cooperative Study Group on antihypertensive Agents 1972).

National surveys continue to reveal incomplete detection, treatment and control of hypertension. (Colhoun HM et al 1998) Furthermore, treated hypertensive patients still die prematurely from cardiovascular disease. (Andersson OK et al 1998) These guidelines aim to present the best currently available evidence on hypertension management and their implementation.

All adults should have their blood pressured measured routinely at least every five years until the age of 80 years. Those with high-normal values (135 – 139/85 – 89 mm Hg) and those who have had high readings at any time previously should have their blood pressure measured annually. Seated blood pressure recordings are generally sufficient, but standing blood pressure should be measured in elderly or diabetic patients to exclude orthostatic hypotension. All hypertensive patients should have a thorough history and physical examination, but need only a limited number of routine investigations which are urinalysis, urea and electrolytes, creatinine, blood glucose, serum total: HDL cholesterol ratio, 12 lead ECG. The purpose of the evaluation is to assess the cause of the hypertension, associated cardiovascular risk factors, evidence of

target organ damage, and co morbid diseases, all of which may influence treatment decisions.

The hypertension optimal treatment (HOT) trial was under powered but provides the best evidence to date on optimal blood pressure targets. (Hansson L et al 1998) Optimal blood pressure for reduction of major cardiovascular events (based on an analysis of patients receiving treatment) was reported to be 139/83 mm Hg and reduction of blood pressure below this level caused no harm. However, patients whose blood pressure was below 150/90 mm Hg were not apparently disadvantaged.

Three long terms, double blind studies have compared the major classes of antihypertensive drugs (thiazide, beta blocker, calcium antagonist, angiotensin converting enzyme inhibitor and alpha blocker) and overall showed no consistent or important differences as regards antihypertensive efficacy, side effects, or quality of life. (Neaton JD et al 1993) differences in average response between drug classes are, however, related to age and ethnic group. (Materson BJ 1993) Few trials have compared different classes of drugs directly as regards reduction in cardiovascular events, (Psaty BM et al 1997) and none is entirely satisfactory, but they have shown no consistent differences between regimens based on different drug classes. With the exception of the systolic hypertension – Europe and systolic hypertension – China trials and the captopril prevention project study, (Staessen JA et al 1997) most evidence from outcome trials is for treatment based on thiazide or beta-blockers. Indirect comparison between the systolic hypertension in the elderly program, (Systolic hypertension in the elderly cooperative research group 1991) based on diuretic treatment, and the systolic hypertension – Europe trial, (Staessen LJ et al 1997) based on a dihydropyridine calcium antagonist, found that the outcome with these regimens was similar.

Controlled trials of dihydropyridine calcium antagonists have not supported earlier concerns about the safety of these drugs, (Staessen JA 1997)

The drug or formulation used should ideally be effective when taken as a single daily dose. An interval of at least four weeks to observe the full response should be allowed, unless it is necessary to lower blood pressure more urgently. The dose of drug (except thiazide diuretics) should be increased according to manufacturers' instructions. If the first drug is well tolerated but the response is small and insufficient, substitution of an alternative drug is appropriate when hypertension is mild and uncomplicated. In more severe or complicated hypertension it is safer to add drugs stepwise until blood pressure is attained. Treatment can be stepped down later if blood pressure falls substantially below the optimal level.

Most hypertensive people will require combinations of antihypertensive therapy to achieve optimal control. (Hansson L et al 1998). Drugs from different classes generally have additive effects on blood pressure when they are prescribed together. Sub maximal doses of two drugs result in larger responses of blood pressure and fewer side effects than maximal doses of a single drug. Rational drug combinations combine drugs with different modes of action that are additive or example, diuretic with beta blocker, diuretic with angiotensin converting enzyme inhibitor, beta blocker with calcium antagonist, calcium antagonist with angiotensin converting enzyme inhibitor. Fixed dose combinations may be convenient for patients and are acceptable when monotherapy is ineffective.

individual drug components are appropriate, and there are no major cost implications.

When hypertension is first diagnosed in people over 80, there is limited evidence to guide policy but treatment decisions should probably be based on biological rather than chronological age. Low dose thiazides are the accepted first line treatment for elderly people. Beta Blockers are less effective than thiazides as first line treatment; in a Meta – analysis they were shown to reduce only stroke events (Messerli FHA 1998). Dihydropyridine Calcium antagonists are suitable alternatives for elderly patients when thiazides are ineffective, contraindicated, or not tolerated (Staessen JA et al 1997).

In the hypertension optimal treatment trial, 75 mg aspirin daily reduced major cardiovascular events in hypertensive patients by 15%, but not fatal events (Hansson L et al 1998). Similar effects were observed in the hypertensive cohort within the thrombosis prevention trial of aspirin. (Medical Research Council General Practice research Framework 1998) In both trials, however, the number of major bleeding episodes due to aspirin was similar to the number of cardiovascular events saved.

Several trials have shown that statin treatment reduces coronary events and all cause mortality and is safe, simple, and well tolerated in both secondary and primary prevention. (Joint British recommendations on prevention of coronary heart disease in clinical practice 1998) Statin treatment also reduces stroke risk substantially in patients who have coronary heart disease. In subgroup analyses, benefits were similar in hypertensive patients. Given the persistent high cardiovascular risk in treated hypertensive patients, and the relation of this risk to serum cholesterol, (Andersson OK et al 1998) these trials have large implications for hypertension management. Statin treatment could not be justified at a 10 year coronary heart disease risk of 6%, (Downs JR et al 1998) but this would entail treating over half of all hypertensive patients. The main constraint on strain treatment at present is its cost.

The frequencies of follow up for treated patients with adequate blood pressure control depends on factors including severity and variability of blood pressured, complexity of the treatment regimen, compliance, and the need for non-pharmacological advice. Three monthly reviews are sufficient when treatment and blood pressured are stable; the interval should not generally exceed six months. The routine for follow up visits, at which trained nurses have an important role, should be simple: measure blood pressure and weight; inquire about general health and side effects; reinforce non-pharmacological advice; and test urine for proteinuria annually.

1.3 JUSTIFICATION FOR THE STUDY

Clinical observations at the University Teaching Hospital show that hypertension is a very common disease among the Zambian population. Its prevalence in the general population still remains unknown though most patients with the disease end up with a high morbidity and mortality as evidenced by the increasing number of hypertensive strokes and heart failure.

Apart from one study done by Levitt et al in the early 70s, which looked at the etiology and incidence of complications in 65 in patients, no other study has evaluated the prevalence of hypertensive complications in the Zambian set-up. In the absence of such a study, it is impossible to evaluate the efficacy of the current treatment regimens as is offered to out patients at the university Teaching Hospital out patients. It is equally difficult to implement primary care for our hypertensive patients.

This study was able to determine the prevalence of hypertensive complications in the study group.

1.4 OBJECTIVES OF THE STUDY

A. GENERAL OBJECTIVES

To determine the common complications associated with hypertensive patients seen in clinic five at the university teaching hospital

B. SPECIFIC OBJECTIVES

- I. To determine the common complications associated with hypertension and their prevalence in the outpatient clinic at the University Teaching Hospital
- II. To determine factors associated with complications
- III. To determine the standard of care of hypertensive patients in the clinic
- IV. To make recommendations on the improving of care of hypertensive patients

1.5 RESEARCH METHODOLOGY

a. Study site

The study was conducted at the University Teaching Hospital out patient clinic in Lusaka, Zambia. The outpatient clinic is situated in the specialist block and usually an estimated 70 patients a day are seen with 15% estimated to be hypertensive.

b. Study design

This was a cross sectional descriptive study involving 250 patients attending the medical out patient clinic and involved the review of medical records, detailed history, physical examination and investigations. Hypertensive patients were randomly selected and educated about the study

c. Inclusion criteria

- i. adults older than 16 years
- ii. Hypertensive already on treatment or found hypertensive on more than 3 occasions (Systolic Bp>140 and diastolic >90)
- iii. Willing to participate in the study and undergo clinic on at least two occasions

d. Exclusion criteria

- i. Under 16 years
- ii. Pregnant woman
- iii. Diabetes mellitus or patients with abnormal fasting blood sugar
- iv. Unwilling to consent to the study

e. Clinical methods

All patients in the study underwent a thorough clinical examination. A medical history was obtained and physical examination as well as a review of the medical records.

- i. Anthropometric measurements height and weight from which the body mass index was calculated using the formula:

BMI = Weight (kg)/ (height in meters)

- ii. Blood pressured measured in sitting and standing position
Hypertension was defined as BP equal to or greater than 140/90 on three occasions or those already on treatment.
- iii. Full physical examination with emphasis on the cardiovascular, respiratory, abdomen and neurological examination
- iv. Fundoscopy

f. Laboratory

- i. fasting blood sugar
- ii. Urea and electrolytes
- iii. Urinalysis
- iv. Lipid profile
- v. Chest x rays
- vi. Electrocardiogram
- vii. Echocardiogram

g. Data Collection

Data collection sheets were used and the analysis was done with the help of the biostatistician using Epi-Info. See appendix

h. Consent form

The study was explained to all participants and a verbal or written consent was obtained as attached in the appendix.

i. Ethical Considerations

The study was presented to the University of Zambia Ethics committee and was approved before commencing.

j. Budget

See appendix

1.6 RESULTS

Two hundred and fifty patients were enrolled in the study and results analyzed.

Table 1 Sex distribution

Males	124
Females	126

There were more women than men seen in the study. This is usually because more women than men tend to seek medical help.

Table 2 Residential areas of patients

	Number	Percentage
Low density	32	12.8
Medium density	90	36.0
High density	128	51.2
Total	250	100

The majority of patients in high density areas where people are of a lower income bracket. The patients in low density areas come from higher income market and most people in these areas tend to go private rather than public health institutes.

* **Table 3 Age distribution**

	Male		Female	
	Number	Percentage	Number	Percentage
30-34	15	12.1	13	10.5
40-49	42	33.9	46	36.8
50-54	31	25	35	27.9
60-69	28	22.6	25	19.8
70-74	8	6.4	6	4.9
80-89			1	

The majority of patients with hypertension were in the age group 40-49 for

both sexes the mode being 46years. This is age where most people are in management and tend to have a higher income and tend to lead a more sedentary lifestyle.

Table 4 Body mass index

	Number	Percentage
Above 25	160	64
Below 25	90	36
Total	250	100

The majority of patients had a BMI > 25.84. The normal BMI is 19-24.5. Thus the majority of patients were overweight.

Table 5 Blood pressure readings at time of interview

	Mean	Mode
SBP	160	105
DBP	103	100

The majority of blood pressures were elevated at time of interview. This might have been due to the fact that most of the patients blood pressures were not well controlled or might have been affected by the white coat syndrome.

Table 6 Hypertensive retinopathy

	Number	Percentage
No retinopathy	90	36.0
Grade 1	82	32.8
Grade 2	56	22.4
Grade 3	22	8.8
Total	250	100

Most of the patients had some degree of hypertensive retinopathy. This showed that most of the patients seen had microvascular complications. These tend to be associated with poor control or late detection of hypertension.

Table 7 Patients with neurological deficits at time of interview

	Number	Percentage
No deficits	166	66.4
Neurological deficits	84	33.6
Total	250	100

There were 33.6 %with neurological deficits at time of interview. This may appear a small percentage but may be due to the high mortality associated with cerebrovascular accidents.

Table 8 Left ventricular hypertrophy

	Number	Percentage
No LVH	90	36
Hypertensive changes	160	64
Total	250	100

The significant numbers of patients have some hypertensive changes on ECG.This occur as the heart muscle modifies itself as it pumps against a higher resistance.

Table 9 Urinalysis for proteinuria

	Number	Percentage
No proteinuria	118	47.2
Proteinuria	132	52.8
Total	250	100

Proteinuria was found more than 50% of patients indicating renal complications associated with hypertension.

Table 10 Adherence to drugs

Irregular	147
Regular	113

Adherence to drugs was not 100% as there were many factors including availability and side effects which were not well tolerated. Adherence is a major setback in managing all forms of chronic diseases.

1.7 DISCUSSION AND CONCLUSION

This study evaluated the common complications associated with hypertension at the University Teaching Hospital and two hundred and fifty patients were analyzed.

The study demonstrated that a large number of patients seen at the UTH have hypertensive related complications.

The study showed that in our hospital, there are slightly more females being seen in the hypertensive clinic than males. There were a total of 126 females and 124 males seen. In many clinical studies elsewhere, the pattern of disease tends to be the same across the different sexes though observations are that more females tend to access health care facilities than males in our setting. The USA hypertensive figures have demonstrated that more blacks and elderly women are more prone to hypertension than other groups. If this study was to be reproduced and this find confirmed, there could be a role on focusing on women older than forty in the prevention of hypertensive complications.

The Age distribution ranged from 24 to 88 with a mean of 53 and a mode of 46. This suggests that hypertension is commonest in our setting in the mid forties and therefore any preventive measures must target this age group. This is critical as many Zambians are usually breaking into managerial positions just at about this age. This age group would have a marked increase in income and changes in lifestyle that predisposes them to hypertension. The number of complications seen in this cohort of patients does seem to reemphasize the importance of non-communicable disease in our society. As the HIV/AIDS epidemic ravages across the country, the temptation to focus on it at the expense of other diseases is great and therefore we ought to adopt a more lateral approach.

Providers of primary and secondary health care in Nigeria reported barriers to managing cardiovascular risks which included inadequate funding; low competence among health workers and poor laboratory support (Mendis S et al 2004). Though similar studies have not been done here the lack of laboratories in our primary and secondary health institutions was noted as the files were being reviewed as patients had no baseline investigations done at first presentation.

A Gambia study found poor recording of demographic data hindered smooth execution of project for people with cardiovascular disease. There is no standard format in obtaining history from patient with hypertension in the clinics and so vital information is not always obtained. The more experienced clinicians were more likely get history which would find out if there was target organ damage.

Furthermore and surprisingly Africa has the lowest output in the world of cardiovascular research. (Rosmaakis ES et al 2005)

More than 50% of the patients had hypertensive retinopathy despite regular reviews at the clinic. One hundred and twenty-eight patients had moderate to severe retinopathy with forty-eight patients having exudates and some hemorrhages. This has a lot of implications on the quality of care in our clinic including availability of drugs, diagnostic work out and indeed follows up of these patients. Many of the patients were having a Fundoscopy done for the very first time despite having been on medications for longer than five years. There was also a tendency to prescribe whatever medication was available in the UTH pharmacy at the time. This study showed that of the 250 patients in the study 147 patients took their medications irregularly reasons given where due to cost if prescribed drugs were not available in the pharmacy or misconstrued idea that medication was to be taken only when they felt blood pressure was high. The importance of compliance to medication was reemphasized during the study and some misconceptions corrected. A study to find the most effective drugs which would improve compliance would need to be carried out.

Proper treatment of hypertension prolongs life and prevents or delays congestive heart failure, nephrosclerosis and reduces the incidence of strokes. Hypertensive patients at all stages benefit from treatment. One hundred and sixty patients which translates to 64% had ECG evidence of left ventricular hypertrophy and there is every likelihood that if this is not checked; majority of our patients may end up with congestive cardiac failure. Treatment of hypertension is associated with multiple benefits and this has been demonstrated in many randomized clinical trials where mortality and morbidity have been shown to decrease.

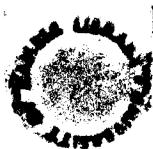
The maximum benefits have been in the reduction of cerebrovascular morbidity and mortality (Garraway et al 1987). Many national surveys conducted in different parts of the world have consistently demonstrated incomplete detection, treatment and control of hypertension (Colham 1998). It is generally felt that in order to avoid complications such as we have seen in this study, all adults should have their blood pressure measured once every five years until they are eighty. Those with high normal blood pressure should then be recommended for annual check up. Majority of the patients in this study had BMI above 25 and this may in fact suggest that they could be some element of obesity and therefore dietary measures must be critical in the control of our hypertensive. Cardiovascular disease risks are expected to systemically shift to low income and middle income countries and together with the burden of infectious diseases further increase the global health inequalities. Preventing obesity should be a priority in early stages of economic development, accompanied by population level and personal intervention (Erzzati M et al 2005). This is surprising as most of our patients came from high density areas where it is assumed that starvation is the order of the day. However it would appear that in spite of living in high density area there is a marked increase in their economic status so as to affect their dietary habits as well as physical inactivity.

There were 132 patients with proteinuria though this is difficult to determine whether it was purely due to hypertension or other causes as no detailed examination were conducted due to limited funds and laboratory backup. However, routine examination of the urine should be encouraged especially in peripheral clinics where fundoscopic examination is not possible.

In this study eighty-four patients had neurological deficits at time of interview

This is about 34% of the patients seen. Some patients had recovered completely from minor strokes and transient ischemic attacks.

Another significant observation in this study was that majority of the patients had both systolic and diastolic hypertension with the mean of 160 and 103 respectively. This may seem to suggest that despite the increased number of years on therapy, most patients have not achieved optimal control and this may explain the large number of complications seen. There is a possibility though that this may be the white coat effect as previously described in this thesis. Hypertension is one of the major reasons that a patient may visit a physician but despite many physicians recognizing the complications associated with hypertension: there is still woefully low achievement of recommended blood pressure goals. Taking a proper BP is an important first step in the diagnosis of hypertension. Using the proper cuff size and the patient resting quietly and comfortably and elevated BP demonstrated on at least two occasions is crucial. An initial evaluation should include the check on TOD and targeted investigations are important. With the current management of hypertension in our clinic, we shall continue to witness increased complications.



RECOMMENDATIONS

This study has demonstrated an increased number of complications among our hypertensive patients and there is urgent need to improve the following:

1. Structured care with protocols that detail patient evaluation at the University Teaching Hospital
2. A list of recommended drugs and ensure regular supply
3. A multidisciplinary team to regularly review the hypertensive patients at least once a year.
4. Hypertensive specialist clinic so as to provide an individualized care program without necessarily having to lump this category of patients in the general clinic.

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APPENDICES

CONSENT FORM

I have been asked to participate in a study looking at complications of hypertension in patients at the University Teaching Hospital.

The study has been explained to me very clearly and I fully understand what it is all about. I am prepared to spend more time in the clinic and I do consent to all the investigations being done as has been explained to me. This may include fundoscopy (special investigation of your eyes) looking at my urine, fat levels in my blood, checking how my kidneys are working and special investigations of my heart.

I also do understand that the blood samples taken will include checking for sugar disease, which is very common in patients with disease. The blood taken will be no more is usual for routine investigations, 5ml and will just be used for the purposes mentioned above.

It has been explained to me that I can withdraw at any time and there will be not change in the treatment or care I will receive. My participation is purely voluntary and refusal to take part will not compromise my care in anyway.

Name:.....

Signature:.....

Date:.....

Thumbprint

Witnessed by

Name:.....

Signature:.....

Date:.....

DATA COLLECTION FORM

Identification

Study number:

File number:

Age:

Marital Status:

Address:

Duration of hypertension:

History of hypertension in close relative Yes/No

Smoking Yes/No

Alcohol Yes/No

If female contraceptive use/steroid use Yes/No

Did you have the following before you were diagnosed with hypertension?

Kidney Problem Yes/no

Heart problem Yes/No

Thyroid problem Yes/No

Diabetes mellitus Yes/No

What medication are you on?

How many anti-hypertensive drugs are you taking? One Two three or more

Is your supply of drugs regular/irregular?

PHSICAL EXAMINATION:

Weight Height BMI
BP1 BP2 BP3

Pedal oedema Yes/No

Basal crepitations Yes/No

Apex

Hepatomegaly Yes/No

Palpable Kidney Yes/No

Ascites Yes/No

Able to communicate coherently

Faical palsy umnl/lmnl

Hemiplegia

Hemipareisis

Paraplegia

Parapaeisis

Fundoscopy Normal Grade 1 2 3 4

slurred speech	Aphasic
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LABORATORY

Urinalysis	blood	
	Glucose	
	Proteins	
	Granular casts	
Lipids		HDL
		LDL
		Triglycerides
Urea and electrolytes		Creatinine
		Urea
		Potassium
		Sodium
		Chloride
Fasting blood sugar		
ECG	Ivh	strain pattern
Echo	Normal	HHD

BUDGET

Laboratory investigations	K	500,000.00
IMAGING (ECHO, ECG, CHEST XRAY)	K	750,000.00
SECRETARIAL SERVICES	K	300,000.00
DATA COLLECTION STAFF	K	500,000.00
INCIDENTALS	K	<u>680,000.00</u>
	K	<u>2 730,000.00</u>