EVALUATION OF THE STEPPED CARE THERAPY AMONG PATIENTS WITH SEVERE HYPERTENSION (BP ≥ 180/110 mmHg) AT MUHIMBILI OUTPATIENT CLINICS AND THE COSTS OF TREATMENT

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SIGNED .....

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ABSTRACT

Objectives: To evaluate the practical adequacy, of the recommended hypertension treatment guidelines for Tanzania, estimate the direct medical cost of treatment when the guidelines are adhered to and establish factors affecting its implementation in Dar es Salaam.

Design: Prospective registration of all hypertensive patients attending medical outpatient clinics from 1st January to 3rd July 1995. One hundred patients with severe hypertension were selected and given supervised antihypertensive drugs for a period of six months. Study drugs used were bendrofluazide, propranolol and hydrallazine. A cross sectional survey was carried out among prescribers in Dar es Salaam city hospitals.

Setting: Muhimbili Medical Centre and Dar es Salaam City hospitals, Tanzania.

Subjects: Hypertensives attending Muhimbili medical outpatient clinics. Doctors in Dar es Salaam city hospitals.

Results: Sixteen percent of newly referred patients were hypertensive while 58% of all hypertensive patients had severe hypertension. Of the 100 patients on supervised treatment, 63% attained the target blood pressure, 18% did not complete follow up and 19% did not reach the target blood pressure with the three study drugs.

The average annual cost of supplying the proposed drugs to an estimated number of patients with severe hypertension in Tanzania was (TShs.4,572,453,039.00) 34% and (TShs. 13,882,523,770.00) 104% of the entire Ministry of Health budget for the year 1995/96 by whole sale government and retail prices respectively.

The cost of investigations ranged from 37.3% to 53.7% of the total treatment cost per new patient per year.

From a prescribers survey, 94.2% knew how to diagnose hypertension. But differed widely about when to initiated drug therapy. Traditional antihypertensive, e.g. methyldopa, bendrofluazide, propranolol and brinerdine were favoured when it came to drug preference.

Conclusion:

The magnitude of hypertension among our hospital medical outpatients is a large one. On treatment with the proposed drugs we can control majority of our patients. But the cost of treating even those with severe hypertension alone is so enormous that the government cannot afford. The guidelines should therefore be adapted as they seem workable but with modification to enable both the patient and the government share the costs of treatment.

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DECLARATION

I declare that the whole of this work has not been submitted for a degree in any other University.

Date 18/10/1996

Signature .....

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INTRODUCTION AND LITERATURE REVIEW

DEFINITION

Hypertension is defined by WHO as a Systolic Blood Pressure (SBP) equal to or over 160mmHg and/or a Diastolic Blood Pressure (DPB) equal to or over 95mmHg for an average adult.[1]

Individuals with SBP < 140mmHg and diastolic < 90mmHg are considered to have normal blood pressure. Borderline hypertension refers to SBP between 140 and 160 mmHg and/or a DBP of between 90 and 95 mmHg.

On the other hand, the U.S. Joint National Committee for detection, evaluation and treatment of high blood pressure (JNC)[2] has recently revised the categorization of blood pressure at an age above 18 years. Normal blood pressure is defined as SBP < 130 mmHg and DBP < 85 mmHg. A systolic reading between 130 and 139 mmHg or diastolic reading between 85 and 89 mmHg is designated as high normal blood pressure. Hypertension is diagnosed when a systolic blood pressure $\geq$ 140 mmHg or diastolic $\geq$ 90 mmHg is detected. Except for a few situations, a diagnosis of high blood pressure should be made only if high blood pressure is noticed on three readings taken in a state of rest (one which has lasted at least some minutes) and over several consultations (at least 3) a few weeks apart.[2]

In a population, there is no clear dividing line between normal and high blood pressure. The cut-off levels have been established abitralily to define those who have increased risk of developing a morbid cardiovascular event and/or will clearly benefit from medical therapy.[3]

HYPERTENSION RISK FACTORS

Some factors have been closely associated with increased prevalence rates of hypertension. Several studies have shown an association between increased body mass index (BMI), Physical inactivity, high dietary sodium intake and excessive consumption of alcohol and increased prevalence rates of hypertension.[4-8]

Smoking is a known additional risk factor for cardiovascular diseases. However, there is no direct cause effect for smoking and hypertension which has been established.[8-9]

Blood pressure elevation (both systolic and diastolic) is known to occur at least for 15 minutes, following cigarette smoking. Also cigarette smoking has been found to interfere with the pharmacological treatment of hypertension especially in black patients using propranolol.[9-10]

INCREASING PREVALENCE

Hypertension, once thought to be non-existent in African communities a few decades ago, is now a public health problem with several studies showing evidence of rising prevalence rates.[11-14]

Dannison[15] while practising in South Kavirondo district in Kenya in 1929, screened African labour recruits as well as elderly males in the villages. He also managed over 1800 inpatients. He was unable to detect a case of hypertension. He did however, detect a few cases of young men with transient elevation of BP due to anxiety. He also noted a fall in BP with increasing age. Hypertrophied hearts and strokes were rare and the few strokes he saw were not associated with any cardiovascular abnormalities.

A study conducted in the same country in 1982 revealed a point prevalence (hypertension) of 16%.[14] Also a study among Kenyan Luo urban migrants - showed a rise in blood pressure in urban migrants as compared to their rural counterparts, pointing to factors associated with a modern environment posing a risk for development of hypertension.[16]

Similar observations have been documented by various studies elsewhere in Africa. A study among urbanized Zulus in South Africa found a prevalence of 25% (F 27%, M 23%) with the mean arterial pressure according to age and sex higher than in most Caucasians.[13] 90% of the subjects with hypertension were undiagnosed, undetected or inadequately treated. Jean-

Rene in Zaire documented a prevalence of 14.2% and 9.9% in urban and rural areas respectively.[12]

In Tanzania, literature on the prevalence of hypertension is scanty. A 1970 WHO report estimated that in Tanzania the prevalence of hypertension (considering only those requiring treatment) was 2-3%. While the prevalence rate of 4.9% was reported for Zanzibar in 1969.[17]

In one of its 1988 quarterly reports[11], the World Health statistics quotes a similar hypertension prevalence rates of 2-3%. This being for subjects aged 40 - 45 years from selected surveys in Tanzania.

The most recent study by Swai et al, showed a tendency to increased prevalence rates of hypertension as one moves from rural to urban areas of Tanzania.[18] This was a non-communicable disease baseline epidemiological survey. It covered people over 14 years of age in six randomly selected villages in Morogoro, Kilimanjaro and Mara regions and two urban areas in Dar es Salaam. Number surveyed were 1457 (43% males), 3008 (38% males), 3038 (47% males) and 1062 (45% males) in Dar es Salaam, Kilimanjaro, Morogoro and Mara respectively. In Mara region which is representative of a typical underdeveloped rural Tanzania - the prevalence was 3.0%, Morogoro an Intermediate rural area 4.0%. In Kilimanjaro which is one of the most developed rural part of Tanzania the prevalence was 6.8%. Dar es Salaam, the capital city of the country had the highest prevalence of hypertension of 12.8%.[19] Prevalence rates of 25% and 39% have been reported among African nuns and executives in Dar es Salaam respectively.[20]

The emerging picture for Tanzania is indicating that hypertension is likely to be a major health problem.

MORBIDITY AND MORTALITY ASSOCIATED WITH HYPERTENSION

It is a well established fact that hypertension is associated with significant nonfatal and fatal cardiovascular events - including; premature deaths, development of ischaemic and haemorrhagic cerebrovascular accidents, myocardial infarction and heart failure. It also predisposes to other complications like renal insufficiency, peripheral vascular disease, aortic dissection and ocular vascular accident.[2,21]

All these complications increase progressively with higher levels of both systolic and diastolic blood pressure. This relationship is strong, continuous, graded, consistent, independent, predictive and aetiologically significant.[2]

There is also evidence that hypertension related morbidity and mortality tends to be higher among blacks than white, especially for renal and cerebrovascular events.[22-27]

Hence it is expected that an increase in hypertension prevalence in Tanzania will be associated with increased morbidity and mortality. From preliminary results of on going morbidity and mortality study[19], in Hai - Kilimanjaro region and Dar es Salaam in Tanzania for the year June, 1992 to May, 1995, the following are noted: That stroke is number one cause of disability in Hai district accounting for 15.9% of all causes of disability. It is number 7 among top ten causes of mortality in the same area, accounting for over 5% of total deaths among males between 15 - 59 years. For all ages stroke is number 8 major cause of mortality in the same district.

In Dar es Salaam stroke ranks number 5 (among top ten causes of mortality) accounting for 4% of total deaths among males and number 6 accounting for 3% among females aged 15 - 59 years. It ranks number one cause of mortality for those aged 60 years and above accounting for 16% of total deaths in this age group.

HYPERTENSION TREATMENT BENEFIT

There is a possibility that hypertension might have existed in some communities since ancient times. In the ancient Hindu Ayurvedie writings, there is a description of a plant resembling Rauwolfia (Reserpine). It was used to treat among other conditions, hypertension. However, it was not till 1931 when Sen and Bose described its therapeutic application for hypertension in an Indian Medical Journal.[28]

By late 1950s several antihypertensives had been studied and were in clinical use.[28-30] Methyldopa and Hydrallazine are the oldest in clinical Western medicine dating back to early 1940s or before. Ganglionic blockers followed in late 1940s (esp. Hexamethonium). Late in mid to late 1950s came the use of Reserpine, beta-blockers (propranolol) and thiazide diuretics - (Chlorothiazides). The obsolete mercurial diuretics were long in clinical use before all the rest but were replaced by Thiazides in late 1950s.

Malignant hypertension

The benefit of treating hypertension was first noted with malignant hypertension. Objective diagnosis and assessment of patients with malignant hypertension was made possible by Keith, Wagener and Barker in 1939.[31] This followed their classification of hypertensive retinopathy and their observations that patient with papilloedema (i.e. Grade IV retinopathy) had poor prognosis. That 79% of them were dead by one year of diagnosis and survival at 5 years was 1%.

In a series of observation by Smith et al[32] among patient with malignant hypertension, only one survived at 5 years out of 105 untreated patients. Mortality at one year was 90%.

Then Emile[29] decided to study 64 patients with papilloedema not associated with either cerebral haemorrhage or brain tumours. Drugs available at that time were used, the patient receiving the drug which was available. At 5 years 17 patients with papilloedema out of 64 survived, demonstrating the benefit of treatment in this group.

Sokolow et al[33] used hexamethonium chloride and decided to evaluate survival for a longer duration. Out of 26 patients with papilloedema, 4 survived longer than 5 years. Harington et al[34] used hexamethonium initially (subcutaneously), later Pentolinium (parenterally), later still Mecamylamine orally, supplemented with Reserpine and Hydrallazine. Despite side effects (paralytic ileus, Tremors-limb and trunk, slurred speech, increased muscular tone, brisk tendon reflexes, confusion, hallucinations and delirium), survival rate - overall in treated groups at one year was 50%, 2 years = 33%, 4 years = 25% compared with mortality of 90% in the first year in the untreated cases.

Yet, in another study - Harriet[30] et al reported 84 patients who had malignant hypertension; 32 were still alive at 7 years following antihypertensive treatment.

These studies involving malignant hypertension, have indicated that it is easy to evaluate the outcome of treatment. This is because the course in malignant hypertension is well characterized, predictable and relatively brief.

Severe hypertension

Evaluation of antihypertensives in terms of prolongation of life or prevention of complications was not easy. Despite, being stated in 1940 by Dublin that "Hypertension, even of mild degree shortens life span and mortality rises steadily and markedly with increasing elevations of both the systolic and diastolic pressures.

Perera[35], attempted to study patients with accelerated hypertension. There were 58 patients with primary hypertension for at least 5 years. He randomly used hexamethonium, pentolinium, mecamylamine, reserpine and hydrallazine. He compared it with symptomatic treatment, where, sedatives, analgesics, digitalis and diuretics were freely used in both groups. His target blood pressure was $\leq$ 160/104 mmHg. Mortality at 7 years was 16/29 in antihypertensive group and 16/29 in symptomatic group. Average survival was 42 months in treatment group and 45 months in the symptomatic group. He concluded that drug

treatment of primary hypertension (excluding accelerated and malignant hypertension) has no benefit. However, we realise that this study had gross methodological errors; like-thiazide used for symptomatic patients, small number of patients, not being sure if target blood pressure was maintained full time and use of mortality as the only outcome.

In 1953, Perry et al[36] compared oral hexamethonium hydrochloride and hydrallazine and surgical sympathectomy against no treatment group. Mortality was lower in patients treated with a combination of ganglion blockade and hydrallazine.

By 1963, it was the value of antihypertensive drug treatment in malignant hypertension that had been amply demonstrated.[30,32-34] There were still disputes regarding its benefit in less severe forms of hypertension.

It was the Veterans Administrations Cooperative Study group which set out to study and try to demonstrate the value of anti hypertensives in less severe forms of hypertension. In a controlled prospective study 143 male hypertensives with diastolic blood pressures at the clinic averaging between 115 and 129 mmHg. Drugs used were hydrochlorothiazide, reserpine, hydrallazine and placebo. Study period was between 1963 and 1967.

It was stopped during the fourth year as there was obvious benefit in the treatment group while the morbidity was quite significant in the placebo group. Up to 27 complicating events occurred in the placebo as compared to 2 in the active group. Deaths were 4 in the placebo against none in active treatment group. Complications in the untreated group included development of grade III - IV retinopathy, congestive heart failure, increased azotemia, cerebrovascular thrombosis, transient ischaemic attacks, cerebral haemorrhage, myocardial infarction and increase in severity of hypertension. In the active treatment group there was only one case of cerebrovascular thrombosis and one of multiple drug toxicity.

However, the Veterans administration cooperative group study had its own flows. It involved a selected group of patients, i.e. male Veterans - middle aged with sustained elevated blood

pressure. So its results could not be generalized to the general population i.e. to all races. sexes and young age group.

In 1973, began the "Hypertension detection and follow-up program cooperative group (USA)[38] study. This was a community-based, randomized controlled trial involving 10,940 persons with high blood pressure. Screening was in 14 communities, age ranging from 30 to 69 years. It compared the effects on five-year mortality of a systematic antihypertensive treatment program (i.e. stepped care) and referral to a community medical therapy. Entry blood pressure was diastolic of at least 90 mmHg. Five-year mortality from all causes was 17% significantly lower in stepped care than in referred care group (6.4 vs 7.7% $p<0.01$) and 20% also significantly lower for the stepped care group with entry DBP of 90-104 compared to the corresponding referred care subgroup (5.9 vs 7.4% $p<0.01$).

Hence this study, not only proved the benefit of active antihypertensive therapy on patients with severe hypertension, but it also gave extra evidence of the value of treating mild hypertension.

Meta-analysis of randomized trials on severe hypertension has indicated a reduction of 35-42% in stroke and 14-25% of coronary heart disease events by mere lowering of diastolic blood pressure by 5 to 6 mmHg or systolic blood pressure by 10 mmHg.[39]

If drug treatment in this category is combined with life style modification, it can reduce the number and doses of antihypertensive medications needed.

Mild hypertension

The Oslo study[40] of 1972 and 1973 recruited symptom free men aged 40 - 49 years, with no target organ damage. The study group had SBP between 150 - 179 mmHg and DBP < 110 mmHg. Drugs used were hydrochlorothiazide with alfa-methyldopa or propranolol. No placebo was given to control group. After mean follow up time of 66 months it was found that:-

1) There was significant preventive effect on pressure-related complications such as stroke, dissecting aneurysms, congestive heart failure, and ECG changes of left ventricular hypertrophy.
2) No preventive effect on coronary heart disease.
3) No effect on morbidity from cardiovascular events comparing the groups as established by randomization.
4) Due to a small sample size and short duration of follow up no effect on mortality was expected.

Much as no effect on mortality was expected, also no effect on coronary heart disease was expected in such a short duration as atheroclerosis also takes time to develop or regress.

In 1977 began the Medical Research Council (MRC) trial of drug treatment of mild hypertension.[10] The main objective of this study was to determine whether drug treatment of mild hypertension (phase V diastolic pressure 90 - 109 mmHg) reduced the rates of stroke, of death due to hypertension and of coronary events in men and women aged 35 - 64 years. The study had subsidiary aims of comparing the course of blood pressure and incidence of suspected adverse reactions to two groups - one on bendrofluazide and another on propranolol.

The results of this study was that: there was clear evidence that active treatment was associated with a reduction in stroke rates. The absolute difference was 1.2 strokes per 1000 patients years - meaning that, if 850 mildly hypertensive patients are given active antihypertensive drugs for one year about one stroke will be prevented. Treatment did not appear to save lives or substantially alter the overall risk of coronary heart disease. More than 95% of the control patients remained free of any cardiovascular event during the trial.

On the drugs used, neither had any overall clear advantage over the other. The diuretic appeared better than the beta-blocker in preventing stroke, but the beta-blocker may have prevented coronary events in non-smokers.

Patrick et al[41] did clinical epidemiological analysis of data from six studies on benefit of treating mild hypertension. These were studies done in a period between 1964 to 1979. their conclusion was that, the current evidence does not justify a uniform policy of treating all asymptomatic patients with mild hypertension.

It can be summarized from existing evidence so far, that drug treatment of mild to moderate hypertension is not cost effective in developing countries. Controlled studies have shown that if 1000 mildly hypertensive patients are given active drug treatment for one year, about 1-3 cerebrovascular accidents, or 0 - 1 attacks of heart failure and 25 cases of the development of severe hypertension may be prevented without any significant effects on the mortality rate.[40-42]

This is why life style modification is the intervention of choice for the community in this category. This includes reduction in salt intake, avoidance of excessive alcohol intake, weight control and adequate physical activity. If this is properly adhered to it can offer multiple benefits at little cost with minimum risks.

Potential harms of treating hypertension

"The lower the blood pressure the better the survival was our traditional view." This does not seem to be always correct. Cruickshank et al[43] between 1972 and 1982 followed up 939 patients with moderate to severe hypertension. Thirty percent were newly diagnosed hypertensives. After a mean follow up period of 6.1 years, analysis revealed that lowering DBP to below about 85mmHg in both young and older patients, is likely to increase the incidence of death from myocardial infarction. Only those patients with evidence of ischaemic heart disease displayed the J-curve relationship between death from myocardial

infarction and treated DBP. Fannett et al[44], evaluated data from thirteen studies to find out if there is such a point beyond which blood pressure reduction in hypertensive subjects is no longer beneficial and possibly even deterious. Studies did not show a consistent J-shaped relationship between treated blood pressure and stroke. But they did demonstrate a consistent J-shaped relationship for cardiac event and diastolic blood pressure. The beneficial therapeutic threshold point was 85 mmHg. The explanation for this phenomenon may be suggested that, myocardial perfusion (which occurs mainly during diastole) will become critical at a DBP of about 85 mmHg or lower in some patients with atheromatous narrowing of the coronary arteries.

Stewart[45] concludes from his study that it would seem that, in severe middle aged hypertensives, attempts at normalization of high blood pressure may precipitate as many infarctions as it prevents!.

Hypertension in the elderly:

Up to 1975, there was no evidence shown if treatment of hypertension in the elderly patients reduced the incidence of stroke or coronary heart disease or affected cardiovascular or overall mortality.[46]

The veterans administration studies demonstrated benefit in young patients.[37,42]

Coope et al[46] in 1975 designed a randomized trial which involved 884 patients aged 60 - 79 years. Over a mean follow up period of 4.4 years it showed a reduction of 18/11 mmHg in blood pressure. There was a reduction in the rate of fatal stroke in the treatment group to 30% of that in the control group ($p < 0.025$). The rate of all strokes (fatal and non-fatal) in the treatment group was 58% of that in the control group ($p < 0.03$). The incidence of myocardial infarction and total mortality was not affected by treatment. There were no difference in symptoms experience between the two groups which were likely to be due to

treatment. Absence of difference in total mortality was attributed to increase in deaths from cancer, in the treatment group.

In this study among the elderly (60 - 79 years) patients, even those who had diastolic Blood Pressure <90 mmHg but systolic blood pressure $\geq$ 160 mmHg also benefitted. This being an important finding as it showed the benefit of treating isolated systolic hypertension in the elderly.[46-48]

Hypertension in black people

Hypertension in black people differs from the non-black population.[22-27] In blacks it is characterized by earlier onset, increased severity, and different haemodynamic and biochemical factors compared with the non-black population.

In terms of severity, hypertension in black tends to start at an early age and takes an accelerated course. Black patients are at greater risk for hypertensive complications at a young age. They are likely to present with evidence of end organ disease on first presentation.[49] Blacks are 2 to 4 times more likely to have strokes than whites and they still die from strokes at much higher rates than whites. Black hypertensives are more susceptible to the renal complications of hypertension. They are 4 to 5 times more likely to be on dialysis and in the hypertension Detection and follow-up program, serum creatinine levels were significantly higher in blacks than in whites.[38] Evidence of renal vascular damage was noted to occur more often in black hypertensives.[50]

Left ventricular hypertrophy (LVH) has been demonstrated to occur more frequently in black hypertensives.[51]

Whether the black hypertensives are protected from coronary artery disease (CAD) is still controversial. CAD was the leading cause of mortality among blacks in the United States - accounting for almost 58,000 or 25% of the deaths in the black community in 1977.[49,52] In 1980s, CAD mortality reported among blacks in the United States ranks among the highest

in the world. Recent surveys suggest similar prevalence of CAD in blacks and whites in the United States; however, case mortality appears higher in blacks, especially in black women.[49] Although most of the data on CAD have been based on mortality statistics and case series, frequently of dubious quality and frequently confounded by geographic and temporal factors, old concepts about the relative frequency of CAD in various races and countries are in need of revision.[49,52] For Tanzania, however, recent evidences still indicate lower both risk factors and prevalence of CAD among the blacks.[18,53]

Haemodynamically - blacks even the young ones tend to have increased salt sensitivity with a tendency towards expanded plasma value. There is low-renin production and low cardiac output with increased peripheral and renovascular resistance.[2,22,24,27]

Black hypertensives also tend to have increased sodium potassium ratios in their urine, reduced natriuretic vasodilatory prostaglandins and kinins. Blacks have diminished sympathetic nervous system function to explain their tendency towards renal salt retention and plasma expansion.[23]

The difference in hypertension between blacks and non-blacks appear to be more environmental than genetic. No genetic basis for these differences has been identified so far.[23] Environmental factors which are thought to contribute to severity and complications in black hypertensives include, poor access to health care, low socio-economic status, high prevalence of obesity and cigarette smoking.[2,23,26]

The therapeutic implications of these differences have been demonstrated in controlled trials. Blacks are found to respond better to diuretics than non-blacks due to their salt-sensitivity. However, they are unlikely to respond to monotherapy with beta-blockers or ACE inhibitors due to their low renin and diminished sympathetic nervous system function.[2,23,24,26,27] Addition of small doses of diuretics on beta-blockers or ACE inhibitors brings the response of blacks

to that of non-blacks.[26,37] In the Veteran Administration trial[37,42] only about 50% of black patients achieved adequate blood pressure control during propranolol monotherapy.

There is no difference in response between blacks and non-blacks regarding calcium antagonists and alfa-blockers.[2]

Life style modification may be even more effective in lowering the blood pressure of blacks than non-blacks.[26] Moderate salt intake, control of weight (since obesity is more common among black women), exercises and moderation in alcohol intake should be advised.

COST OF TREATMENT

Hypertension is a life long disease mostly requiring medications for life.[2] Despite the well established benefits of drug treatment, its implementation may be very costly. Drug costs alone can amount to 70-80% of the total costs of treatment.[2,54] Other costs are for travelling, investigations, costs during admissions and cost of time lost due to morbidity or mortality related to hypertension and its complications.

Health related costs are currently a topical issue for rich and poor nations. No data is available in Tanzania on costs of treating hypertension. In the U.S. it is estimated that the direct cost of treating hypertension per year is between 8 - 10 billion dollars.[55] This has been attributed to physicians preference for newly available antihypertensives like calcium channel blockers, ACE inhibitors and alfa-adrenergic antagonists.[55]

Kawachi and Malcolm[56] made calculations based on special surveys conducted in New Zealand in 1988. They found that the total cost of treating hypertension per patient in the first year of diagnosis was Pounds 151, and Pounds 135 for each subsequent year. Investigations accounted for 8% of the first year cost and 3% of costs in subsequent years. Drug costs represented 85% of the first year cost and 96% of the costs in each subsequent year.

In Spain the Drug's cost for treating hypertension alone amounts to 4.6% of the cost for treating all diseases.[57]

By 1992, if drug cost was related to basic needs in Tanzania an individual's monthly requirement of thiazides was equivalent to the cost of 5 litres of milk, 36 litres for beta-blocker and 300 litres for ACE inhibitors. On the other hand, if drug cost was related to income (in Tanzania), an individual's monthly treatment with thiazide was equivalent to a two days primary school teacher's salary, 14.4 days salary for beta-Blockers and 120 days salary for ACE inhibitors.[58]

This implies that with liberal prescription, this primary school teacher with severe hypertension - his monthly cost of treatment would range from half to four times his monthly income.

TREATMENT GUIDELINES

In clinical work several terms have been used meaning the same as guidelines. These include practice policies, clinical policies, practice parameters, protocols and algorithms.[59] Though the chambers' English Dictionary defines a guideline as "an indicator of a course that should be followed, or of what future policy will be[60], the institute of Medicine, Washington DC, gives the clearest definition. Guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstance.[61]

Currently, there is an explosion of interest in guidelines.[59,62,63] Though the aims differ from country to country, but broadly they intend to improve the quality and cost effectiveness of care.[62,64,65] Some use them to reduce variations in care.[64] Despite such explosion of interest in guidelines, there is equally a lot of debate about their aim, how they are made, who makes them and how best can we make them work?. Those who are against them think that guidelines are likely to be insensitive to the needs of individual patients[65], they constrain the

clinical freedom by introducing "cookbook medicine", will reduce doctor's self respect and could reduce patients confidence in them.[59,66] There is also a feeling that developing them is costly.[65]

Experience from the United States has however shown that guidelines can work, provided some basic issues are addressed to. Those guidelines should be based on the best known scientific knowledge, and designing them should include those who will use them, i.e. they should not be imposed by senior doctors.[62-64,66] Nationally set standards and consensus statements seem to have limited impact.[62] So to make sure that guidelines will be effective we have to address properly to each step from its clinical context, methods of developing, dissemination, implementation and evaluation.[59,65] Recent studies in the U.K. indicate that treatment guidelines are useless if published in a journal and only of real use if the prescribers have participated in composing them.[47]

However, guidelines should not be seen as rigid constraints on a practising doctor's decisions. Guidelines should provide extensive, critical, and well balanced information on benefits and limitations of the various diagnostic and therapeutic interventions so that the physician may exert the most careful judgement in individual cases.[67]

Decision making on Blood pressure level, where one should initiate therapy, mode of therapy (pharmacological or non-pharmacological), investigations to do, choice of drugs from a diverse list of antihypertensives and cost-effectiveness of therapy make guidelines for treating hypertension quite indispensable.

Several guidelines are in use in various countries with similarities and some differences. Reviews are frequently made as more evidence come in sight. However, two main issues are still uncertain. These are the blood pressure below which hypertension does not warrant treatment and the type of drugs to use initially when treatment is justified.[2,68]

Guidelines on blood pressure measurements:

Diagnosis and subsequent decision on the treatment of high blood pressure depends on its accurate measurement. The blood pressure reading so obtained may be affected by a variety of factors including the posture and anxiety state of patient, the machine being used, and the individual doing the measurements.[2,67-70] Standing and sitting values are likely to be different especially in elderly hypertensive on drugs. Also measurements taken with the arm hanging will be higher by 5-10 mmHg compared when the arm is at the level of the heart.[71]

Measurements taken in presence of a doctor may be raised in absence of hypertension, the effect called "White coat hypertension".[2,52,71-72] To avoid this effect, some have advised ambulatory blood pressure measurements. Ambulatory blood pressure measurements values are several mmHg lower than clinic readings.[69] Measurement by nurses or trained non-medical staff may reduce the white coat effect.

The cuff size is critical. A standard cuff on a large arm will overestimate the reading.[2,69,71-72] Also uncalibrated machines are a potential source of errors. A great caution should be exercised with electronic sphygmomanometers as many of then are inaccurate.[71] They act as a guide for one to use standard methods on finding a raised Blood pressure.

A mercury sphygmomanometer is a recommended reliable machine for measuring blood pressure. Raise pressure rapidly to 20 mmHg above level of extinction of radial pulse (this excludes the possibility of auscultatory gap). Using a bell placed gently over brachial artery, record phase I Korotkoff (i.e. first appearance of clear tapping) as systolic level. Record diastolic level at phase V Korotkoff (i.e. disappearance of sounds). If the sounds persist to near 0 mmHg, then the point of muffling of sound is used (phase IV) to indicate diastolic pressure.

To discipline the observer to deflate slowly in the critical range, measure pressures to the nearest 2 mmHg.[2,52,71-72]

To diagnose hypertension, the elevated blood pressure should persist (or be detected) on at least three different occasions (visits) several days or weeks apart.[2,67,69,71-73] For severe elevated levels SBP $\geq$ 210 or DBP $\geq$ 120 mmHg, or elevated blood pressure in presence of evidence for target organ damage a reading on a single visit is adequate for prompt action.[2]

Guidelines on drug treatment

The British hypertension society principal recommendations is that all patients below the age of 90 years who have sustained BP $\geq$ 160 mmHg systolic or $\geq$ 100 mmHg diastolic should receive anti-hypertensive drugs.[68] In addition the large cohort of the population with a diastolic BP between 90-99 mmHg should receive drugs in the presence of other cardiovascular risk factors i.e. smoking, diabetes mellitus, male sex, hypercholesterolemia, obesity, positive family history and previous evidence of atheromatous disease or if there is evidence of end organ damage or if they are older than 60 years.[68] However, the strategy of targeting anti-hypertensive therapy to those whom hypertension is not the only cardiovascular risk factor has not been tested experimentally.[46] But there is evidence that elderly patients have more to gain than the young.[46,47,74]

Smoking reduced the benefit from propranolol on stroke reduction in the MRC mild hypertension trial.[10] From this study it would appear to make more sense to encourage men to stop smoking rather than drug therapy with antihypertensive drugs when their diastolic BP crept above 90 mmHg. The multiple risk trial which was supposed to confirm this, did not do so because the placebo group enjoyed healthier diet and had stopped smoking on self drive.[75]

The New Zealand guidelines for treatment of hypertension for individuals aged 40 to 70 years old, considers a complex interplay of factors.[75] Based on the fact that BP is not a disease but rather a risk factor for cardiovascular diseases these guidelines combine age, sex, risk estimation and BP level to make decisions on when to treat. While an individual with BP

170/100 mmHg at any age, with or without any risk factor deserves treatment, one with BP 150/90 mmHg aged 40 years will deserve treatment only if he is a male with at least 3 risk factors. A female with the same score will not be treated. In general terms the New Zealand hypertension treatment guidelines recommends treatment for people with estimated risk of $\geq$ 20% in 10 years and a sustained blood pressure > 150/90 mmHg. Lowering the pressure of these patients by an average of 5-6 mmHg diastolic (and 10 mmHg systolic) would reduce the risk of cardiovascular disease by about one third. Absolute risk of 20% in 10 years would be reduced to 13% in 10 years, meaning that one event would be prevented for every 150 patients treated a year.[75] At this level of risk adverse effects of treatment are unlikely to outweigh the benefits and treatment is likely to be cost effective. The absolute benefits and cost effectiveness of treatment would be greater if larger reductions of blood pressure could be achieved.

The WHO/ISH 1993 [67] guidelines on the other hand includes management of mild hypertension. This is so because mild hypertension often presents a diagnostic and therapeutic problem. In this review emphasis is also placed on systolic blood pressure as a criterion for decision making, hypertension in elderly people, and cardiovascular risk considerations when deciding when to treat.

There was a tendency for most of the randomised therapeutic trials on hypertension, including those on mild hypertension to define and treat patients on the basis of diastolic blood pressure values. Hence diastolic blood pressure has generally been used to define mild hypertension. There is however, mounting evidence that systolic values should also be taken into account in defining and managing hypertension.[67,75-77] Indeed, cardiovascular risk is as strongly associated with systolic as with diastolic values, with no evidence of threshold below which a decrease in pressure does not reduce risk.

According to WHO/ISH 1993, mild hypertension is diagnosed when diastolic blood pressure values of 90 - 105 mmHg or systolic values between 140 - 180 mmHg or both are repeatedly measured over at least four weeks. Drug treatment should be instituted if after three additional months of observation (on non-pharmacological treatment) diastolic blood pressure is at least 100 mmHg (irrespective of systolic values), or if systolic blood pressure is between 160-180 mmHg with diastolic values of at least 95 mmHg or with diastolic values below 95 mmHg if other cardiovascular risk factors are present. After a second period of three months persistent diastolic pressures between 95-100 mmHg or persistent systolic pressures between 160 - 180 mmHg or both may justify drug treatment. At this time even diastolic values between 90 and 95 mmHg or systolic values between 140 and 160 mmHg or both, may deserve drug treatment if other substantial risk factors are present.

Isolated systolic hypertension in the elderly people (often beyond the mild range) not only carries addition risk but has recently been shown to benefit considerably from pharmacological reduction of raised blood pressure.[2,48,75,78]

In its report, the American Joint National Committee (A.J.N.C.) on detection evaluation and treatment of high blood pressure, also insists on the consideration of several factors before initiation of pharmacological treatment.[2] Apart from blood pressure elevation, target organ damage and presence of other conditions and risk factors are taken into account. Evidence for target organ damage are considered as follows:-

1. Cardiac
   - Clinical, electrocardiographic, or radiological evidence of coronary artery disease.
   - Left ventricular hypertrophy or "strain" by electrocardiograph or left ventricular hypertrophy by echocardiography.
   - Left ventricular dysfunction or cardiac failure.
2. Cerebrovascular - Transient ischaemic attack or stroke.

3. Peripheral vascular- Absence of one or more major pulses in the extremities (except for dorsalis pedis) with or without intermittent claudication; aneurysm.

4. Renal - Serum creatinine $\geq$ 130Umol/L (1.5mg/dl)
   - Proteinuria (1+ or greater)
   - Microalbuminuria.

5. Retinopathy - Haemorrhages or exudates, with or without papilloedema.

The American Joint National Committee on detection evaluation and treatment of high blood pressure[2] classifies hypertension for adults age 18 years and older as follows:

Category:	Systolic (mmHg)	Diastolic (mmHg)
Normal	< 130	< 85
High normal	130 - 139	85 - 89
Hypertension:		
Stage I (mild)	140 - 159	90 - 99
Stage 2 (moderate)	160 - 179	100 - 109
Stage 3 (severe)	180 - 209	110 - 119
Stage 4 (very severe)	$\geq$ 210	$\geq$ 120

For stage 1 and stage 2 hypertension, this committee recommends drug treatment if blood pressure remains at or above 140/90 mmHg during a 3 to 6 months period despite vigorous encouragement of life style modification. This is especially so in those with target organ damage or additional major risk factors. In the absence of target organ damage or other major risk factors, some physicians may withhold antihypertensives from patients with DBP 90-94 mmHg range or SBP in the range 140-149 mmHg. However, careful follow up 3-6 monthly is indicated in such patients as blood pressure may rise too high and cardiac and vascular changes may occur.[2]

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It is advised, for patients with stages 1 and 2 hypertension who require drug therapy to initiate it with monotherapy using a diuretic or a beta blocker.

Patients with DBP of 110 mmHg or higher and/or SBP 180 mmHg or higher, although some may responde to one drug, it is often necessary to add a second or third agent after a short interval if control is not achieved. The interval between changes in the regimen should be decreased, and the maximum dose of some drugs may be increased. In some patients it may be necessary to start treatment with more than one agent. Patients with average DBP of 120 mmHg or greater require more immediate therapy and if significant target organ damage is present, may require hospitalization and consultation.[2]

The treatment guidelines for Tanzania recommends that only those with blood pressure persistently above 180/110 mmHg should be started on drug therapy.[70] This is based mostly on cost-effective considerations for such a poor country. However, not much is mentioned about those in moderate range who will persist on subsequent follow up despite aggressive life-style modification. It also does not address itself with the contribution of other cardiovascular risk factors on treatment decision making. This may be based on the fact that hypercholesterolemia, a necessary factor for coronary heart diseases is still rare among Tanzanian Africans.[53,73]

Drugs are recommended to be initiated in a step up care manner, starting with Bendrofluazide, then propranolol and finally hydrallazine in those where control has not been achieved.

Guidelines on withdrawal of therapy

The teaching is, once hypertensive on drug treatment it is for life and that those who stop antihypertensive medication and stay normotensive for many years were misdiagnosed in the past. Now we have some evidence that for some patients antihypertensives may be stepped down or even stopped.[79-80]

Aylett et al[79] in a multicentre trial recruited 225 out of a total of 3003 (7.5%) hypertensive patients aged 40-69 years. Their blood pressures systolic averaged <160 and mean DBP <90 mmHg. They stopped medication and were introduced to non-drug strategies. After one year 185 patients were still available, of whom 86 (38%) were still off medication and 51 of these 86 had been on more than one drug.

Van den Bosch[80] in the Nijmegen hypertension monitoring program followed up 2143 patients who were diagnosed using a standard British criteria. They stopped antihypertensive drugs if patients were on only a single drug, if DBP was lower than 85 mmHg on three or more readings, and if there were no other reasons to continue with the drugs such as co-morbidity. A total of 25 patients matched the criteria and were followed up for 5 years after discontinuation of medications. Blood pressure was checked at least annually. None died or moved during the 5 years. After 5 years 14 of 25 patients still had blood pressure lower than 100 mmHg. Their mean age 58.2 years and their mean duration of hypertension since diagnosis and withdrawal of medication was 7.8 years (range 3-13).[80]

Both Aylett and Van den Bosch suggest that it may be worthwhile to withdraw antihypertensive in some patients - especially those who are well controlled. But longterm monitoring of blood pressure (i.e. for life) after withdrawal of drugs is mandatory. Even after several years there are patients who relapse.

The recommendations of American Joint National committee is that if blood pressure has been effectively controlled for one year and at least four visits, it may be possible to reduce antihypertensive drug therapy in a deliberate, slow and progressive manner. Such patients should have regular follow up because blood pressure usually rises again to hypertensive levels, months or years after discontinuation, especially in absence of sustained improvements in lifestyles.[2]

Guidelines on investigations

In hypertension investigations are done for various reasons. There are those needed to determine the severity of cardiovascular disease and possible causes of hypertension. Others relate to cardiovascular risk factors or provide baseline values for judging biochemical effects of therapy.

The report of the second working party of the British hypertension society[68], recommends the following as essential tests needed on all patients with hypertension: urine analysis (Dipstix), measurement of serum electrolytes and urea or creatinine concentration. Electrocardiogram (for evidence of myocardial ischaemia or left ventricular hypertrophy); blood glucose and serum lipid values. Also a full blood count is recommended as polycythaemia is a risk factor for stroke and a raised mean corpuscular volume suggests a high alcohol intake. In borderline hypertension with an abnormal electrocardiogram, an echocardiogram is to determine the left ventricular hypertrophy as an indicator of target organ damage. A chest radiograph is helpful in older patients (large heart, heart failure) or when clinically indicated. In selected cases, the American joint national committee on detection, evaluation and treatment of high blood pressure[2], recommends urinary microalbumin and plasma renin/urinary sodium determination.

For Tanzania[73] investigations are considered not cost-effective in the routine management of hypertension. It is recommended that they should be reserved for secondary and severe hypertension where - urine analysis, blood urea, creatinine, electrolytes, chest radiograph, electrocardiogram and echocardiogram may be done.

STUDY RATIONALE

For Tanzania, hypertension is already a public health problem though more so in urban than in rural areas.[11,18,19,20,81] It is a problem affecting both rich and poor. Worse still, evidence from Kilimanjaro region suggests that as we struggle to develop our underdeveloped rural areas, we should at the same time, expect an increase in hypertension prevalence plus its associated morbidity and mortality.[18,19] This is probably due to the higher prevalence of risk factors like high salt intake, obesity, excessive alcohol intake, hypercholesteremia (diet) and smoking for which Kilimanjaro either ranked second to Dar es Salaam or first. The most underdeveloped area had the lowest prevalence of hypertension as well as its associated risk factors. Therefore hypertension will increase with modernization and affluence.

Though data is lacking on what part of our health budget is spent on treating hypertension alone, the total budget is already constrained. The Tanzanian health budget is based on primary health care control of infectious diseases with little allocation for non-communicable diseases. The government itself can no longer afford to provide essential health care for its people, a fact which forced it to introduce a cost sharing policy.[82]

The health budget is relatively decreasing instead of increasing. In 1994/95 the health ministry was allocated a total of Tshs. 15,185,3000,000 where by 687,539,000 was for drugs. In 1995/96 the allocation is 13,389,734,000 where Tshs. 500,000,000 is for drugs.[83]

When cost sharing policy is accompanied by trade liberalization (i.e. no drug price control) and aggressive drug advertisements, the individual patient - particularly here the hypertensive is forced to bear a greater burden of the treatment costs. This can be made worse by doctors unguided investigations and prescriptions.

Having realized this, in 1994 the department of Internal Medicine - Muhimbili University College of Health Sciences proposed some guidelines for treatment of hypertension in Tanzania.

Those guidelines aimed at assisting the government to be able to provide effective treatment to hypertensives who real require it, at affordable costs.

There are three key issues in the guidelines:-

1. That drug therapy should be instituted only in those with severe hypertension (i.e. BP $\geq$ 180/110). These are likely to benefit most.
2. That Bendrofluazide, propranolol and Hydrallazine be the basic drugs which should be available at all times at district level. As they are effective, cheap and with known range of side effects. The other drugs may be available on private practice for individual needs.
3. That investigations should be limited to minimum when needed as they are not cost effective.

From these guidelines however, there are certain issues which need to be established including:-

1. What proportion of our hypertensives will fall in this category which requires drug therapy?
2. What proportion of those requiring drug therapy will be adequately controlled by the proposed drugs and who will need extra drugs?
3. What will it cost to offer such treatment?
4. What factors are likely to influence prescribers (Doctors) to adhere to the proposed guidelines?

It's at this juncture that I was inspired to evaluate these recommendations among hypertensive patients attending our medical outpatient clinics at Muhimbili Medical Centre.

OBJECTIVES

BROAD OBJECTIVE

To evaluate the practical adequacy of the recommended hypertension treatment guidelines for Tanzania, estimate the cost of treatment when the guidelines are adhered to and establish factors affecting its implementation in Dar es Salaam.

SPECIFIC OBJECTIVES

1. To find out the proportion of outpatient hypertensives - attending Muhimbili Medical outpatient clinics who requires drug therapy according to the guidelines.
2. To assess the efficacy of the proposed drugs in controlling hypertension in those requiring drug therapy.
3. To establish predictors of response and non-response among the group requiring drug therapy under supervised drug compliance.
4. To estimate the direct medical costs of controlling hypertension with 3 drugs suggested by the guidelines.
5. To study the current prescribing habits in Dar es Salaam, in view of establishing factors which are likely to affect the implementation of the guidelines.

SUBJECTS AND METHODS

This study was conducted at Muhimbili Medical Centre between 1st January, and 31st December, 1995.

Muhimbili Medical Centre is situated in Dar es Salaam, the largest and the most populated city in the country with the population estimated at 2 million. Muhimbili is the National referral hospital and so receives patients referred from all over the country. It also receives patients from all three of the city's district hospitals, more than six private hospitals and other private health facilities in the city. It has a bed capacity of 1338 patients.

The centre runs inpatient services and various outpatient clinics which includes medical as well as specialty clinics like the cardiac clinic.

There is no special hypertension clinic at the centre; instead, hypertensive patients are attended and followed up at general medical outpatient clinics of the hospital under three medical firms and at a cardiac clinic. These clinics are conducted in the afternoons, on Monday, Tuesday, Thursday and Fridays.

A. RECRUITMENT:

Patients were recruited from all the general medical outpatient clinics and the cardiac clinic. For a period 1st January to 3rd July, 1995, I attended all the medical clinics registering all the hypertensive patients.

All the doctors running the Medical outpatient clinics had been informed about this study - and invited to refer all their hypertensives to my attention.

It is a normal practice that hypertensive patients from other speciality clinics are referred to general medical clinics or the cardiac clinic for investigations and control of their blood pressure. These were included among the newly referred patients.

Recruitment of patients from the diabetic clinic was practically difficult, as at the time of this study that clinic was being decentralized. Patients were being transferred to be attended at

their respective district hospitals. However, diabetic patients who presented at our clinics were included in the study.

At each outpatient clinic, I screened the files for patients primarily referred for hypertension. Patients referred for other medical reasons were promptly referred to me on detection of elevated blood pressure.

At the end of the clinic, the files were re-visited to see if any patient with elevated blood pressure had been missed on initial screening.

Eligibility for the Study

The following was the inclusion criteria for those found to be hypertensive:-

1. Hypertensive patients with diastolic blood pressure equal or above 110 mmHg or systolic blood pressure equal or above 180 mmHg.
2. Age at least 15 years.
3. Newly diagnosed hypertensive not on any antihypertensive or an old hypertensive patient who had not been on drugs for at least 4 weeks.
4. Patient consented for the study.
5. Patient living nearby or guaranteed of attending our clinics as advised.

Exclusion criteria:

1. History of bronchial asthma
2. Presence of heart failure (severe orthopnoea, oedema and basal crepts).
3. Evidence for peripheral vascular disease
4. History of ischaemic heart disease.

Clinical Evaluation:

(i) History - A questionnaire was used to establish the following:

a) Demographic data: i.e. age, sex, race, religion, marital status, occupation, estimated income and educational status.

b) Duration of the disease and hypertensive medications used before.

c) Risk profile - i.e. alcohol intake, use of steroids, smoking habit, salt intake, and physical activity. A family history of hypertension, diabetes mellitus, obesity and stroke were sought.

d) Profile of presenting symptoms.

(ii) **Physical Examination:**

Parameters recorded at recruitment include: weight, height, blood pressure, pulse rate, hypertensive fundoscopic findings and general cardiovascular evaluation. Evidence of renal masses/tenderness/bruit and stroke were also sought and recorded.

Blood Pressure Measurement:

A standard sphygmomanometer (ACCOSON BS 2744 Made in England) was used to record the patient's blood pressure. Calibration of the BP machine was done every week in collaboration with the cardiologist. Each patient had the blood pressure checked on the first day of the visit. The blood pressure was recorded on the right arm after at least 10 minutes of rest on a bench at the clinic. Two readings were taken at each clinic visit. One at the beginning of an interview and another at the end. Both sitting and standing BP readings to the nearest 2 mmHg were recorded, taking Korotkov phase one (for systolic) and phase V (for diastolic) blood pressure.

All the patients whose initial readings fitted the recruitment criteria were seen one week later to recheck the pressure. If found to fulfil inclusion criteria for the study, investigations were taken and they were started on treatment. Treatment was delayed till a third visit only in those patients whose blood pressure were $<$ 210/120 mmHg, with normal fundoscopic findings and with no clinical evidence of left ventricular hypertrophy or stroke.

Fundoscopy:

This was done on all patients on the first visit. In difficult situations an ophthalmologist was consulted.

Classification was done according to Keith-Wegner-Barker classification of hypertensive retinopathy. (Classification attached in the appendix).

Others: Height - was taken in centimeters (cm.) without shoes, using a "Detecto-Medic scale (Jacobs and Bros. Co. Inc. Cap 300 Labs New York U.S.A.).

Weight - was taken in kilograms without shoes and in light wear, using the Detecto-Medic Scale (Jacobs and Bros. Co. Inc. Cap 300 Labs. New York U.S.A.).

INVESTIGATIONS

Investigations were done only on those who fulfilled the inclusion criteria for the study. They included - urinalysis, fasting blood glucose, serum creatinine, cholesterol, uric acid, serum electrolytes, chest X-rays and Electrocardiography.

Echocardiography was done randomly on every second patient. More tests e.g. midstream urine for culture and sensitivity, abdominal/renal ultrasound scanning and intravenous pyelography were done on some patients if had abnormal urinalysis and/or a significantly elevated serum creatinine.

(i) **Urinalysis**

A fresh urine specimen was analysed on the spot for protein glucose and red blood cells using Multistix (Bayer Diagnostics - U.K.).

(ii) **Chest X-rays:**

Each patient had a PA chest X-ray. Cardiothorax ratios were measured and evidence for left ventricular failure and coarctation of the aorta were sought and recorded.

(iii) **Electrocardiograms:**

Each patient had a standard 12 lead electrocardiogram recorded by the same technician using a single channel ECG machine (Type XDN-3, model ECG 6511 - Shanghai Kohden Medical electronic instruments).

(iv) **Serum Biochemistry:**

Patients had been on their regular diets. They were instructed to come for a blood test after an overnight fast and without breakfast on the day of the test. Ten millilitres of venous blood was drawn and sent for specific biochemical tests.

Two millilitres of venous blood was sent immediately to the laboratory for glucose estimation. Analysis was made by a glucose analyser. (YSI model 23 AM - by Scientific Division Yellow Spring Instrument Company Inc. Ohio - U.S.A.). Five millilitres of serum was frozen then sent to New Castle upon Tyne University Laboratory for estimation of serum creatinine, cholesterol, uric acid and electrolytes. Quality control was done.

(v) **Echocardiography:**

This was done randomly on every second patient using HP Sonos 500.

Standard M-Mode and 2D-Echocardiography and colour flow mapping were recorded. Standard measurement were done as recommended by the Association of Echocardiography. Calculations of the left ventricular mass is included in the appendix.

B. **TREATMENT AND FOLLOW UP:**

Drug therapy and life style modification were instituted simultaneously. Appropriate counselling regarding their weight, salt intake, alcohol consumption, physical activity and smoking was given at the beginning and subsequently at follow up visits.

The drugs used in this study were bendrofluazide, propranolol and hydrallazine. Patients were started on bendrofluazide starting with 2.5mg once daily till a maximum dose of 5 mg once daily was reached. The target blood pressure being equal to or just below 140/90mmHg. Propranolol starting with a dose of 40 mg twice daily was added in case of failure to achieve a target blood pressure with bendrofluazide. The maximum dose of propranolol used was 320 mg/day. Hydrallazine was used as a third drug when control could not be achieved with bendrofluazide and propranolol. Initial doses were 25 mg thrice daily to a maximum dose of 75 mg thrice daily.

Where maximum doses of a particular drug could not be tolerated, only tolerable dosages were used while the next drug was added. Also when one drug was contraindicated in a particular patient, one or a combination of the other two would be substituted. In patients with blood pressure $\geq$ 210/120 mmHg or with above grade II-K-W retinopathy, therapy was initiated with more than one drug and doses required to maintain the blood pressure between 140/90 - 130/80 mmHg were instituted accordingly.

Patients were evaluated initially at least every two weeks and doses of drugs were reviewed at a four weekly interval to achieve the target blood pressure. Doses were increased or the next drug added if target blood pressure had not been attained after four weeks on a previous dose or on a maximum dose of a previous drug(s). When a combination of these three drugs could not attain the target blood pressure, substitution or addition of another anti-hypertensive was considered. Patients were followed up at the outpatient clinics where blood pressure, pulse rate and weight were recorded at each visit. Patients were asked to report any adverse effects and subjective benefit from the treatment. In case of any hospital admission or death of the study patient, relatives were instructed to inform me.

Patients who missed their appointments were followed up at home guided by a detailed home address taken at recruitment.

Target blood pressure was regarded as having been achieved if the blood pressures was stable on the same dose of drugs for two consecutive visits at least 2 weeks apart. The study treatment schedule was continued for a total of 6 months since recruitment. Investigations were repeated at the end of the 6 months study:

Compliance:

Drug were supplied to patients free of charge at the clinic by the investigator. A four weeks dosage was prepacked with 6 excess tablets to enable counting during the next visit. Patients were encouraged to return with the packing bags together with the remaining drugs at each visit. Our centre lacks facilities for serum drug level monitoring.

C. **DIRECT COST ESTIMATES:**

For each patient, a record was kept by a questionnaire regarding the direct costs incurred during each visit. These included Medical travelling, food and consultations. Average costs for these expenses were calculated from individual costs for each visit for all visits till the last clinic visit.

The drug costs were based on both government medical stores whole sale and average retail prices from top ten reputable pharmacies in the city, which included National Pharmaceutical Company retail shops. The drug costs are for the dosages required to maintain a target blood pressure. Costs of investigations was based on the average costs from private hospitals in Dar es Salaam city as well as subsidized government prices.

Drugs:

For calculation of drug costs, only those patients whose blood pressure were successfully lowered to a target blood pressure level (controlled) were considered.

Calculations were made for individual drug, individual dose and for a number of patients who used it. The mean, median, and range of dosages used for each drug were calculated. Then their costs were computed. Calculations of costs per day and per year were done. One year

calculations were based on a 365 days year. Conversion to United States dollars (USD) used an exchange rate of TShs. 560 - One USD - by 1995.

Costs based on government medical stores department whole sale prices and retail prices in private pharmacies are compared. Extrapolation of these costs to the entire population was also done.

Investigations

For calculation of investigation costs, eight investigations were assumed to be basic. These are urinalysis, serum creatinine, cholesterol, uric acid, fasting blood glucose, electrolytes, chest x-ray and electrocardiogram. The assumption was based on the fact that they are frequently done either to provide clues on the end organ damage (urinalysis, creatinine, chest x-ray and an electrocardiogram) or provide baseline values for judging biochemical effects of drugs (serum cholesterol, uric acid, fasting blood glucose and serum electrolytes). These basic investigations may also pertain to risk profile and even possible cause of hypertension. The other three investigations (special investigations) were done according to the actual patient indication. Every patient who had an abnormal urinalysis and/or initial serum creatinine above 150ummol per litre, a repeat test was ordered on receiving the results. On persistence of the abnormality a midstream urine culture and sensitivity, and abdominal ultrasound scan were ordered. These determined further need of other investigations like an intravenous urography.

The costing of basic investigations was analysed in three steps to assess its contribution to total cost of treatment. First it was considered when they are done twice in a year for follow up. Second when they are done once without a repeat follow up and thirdly when treatment is done without any prior investigations.

Special investigations were done only once. The cost is given as an average cost per patient per year. in TShs. or USD.

Cost of consultations

Costs of consultations are the average of the actual costs per patient for all the visits made during the study period based on cost as directed by the Ministry of Health.

D. **SURVEY:**

A mini-survey was done on all health facilities in Dar es Salaam, which held the registration status of a hospital. Doctors filled in a questionnaire which aimed to provide information on current practice regarding treatment of hypertension. The questionnaire asked what level of blood pressure practitioners felt it appropriate to start treatment, their opinion on the role of investigations in hypertension, their drug preference and awareness of any treatment guidelines for hypertension in Tanzania.

E. **DATA ANALYSIS:**

Was done using statistical package for social scientists (SPSS) and EPIINFO. Proportions were compared using the X^2, t-test for the means, paired sample t-test for the change in baseline parameters at six months of treatment. Significance is at 95% confidence interval, P-value 2 tailed.

RESULTS

HYPERTENSION AMONG MEDICAL OUTPATIENTS

During the period between 1st January to 3rd July, 1995, 2641 patients attended the medical outpatient clinics. These consisted of 1292 (48.9%) males and 1349 (51.1%) females. Of the 2641 patients, 498 (18.9%) had hypertension while 289 (10.9%) of the 2641 patients at the clinic had severe hypertension (blood pressure $\geq$ 180/110 mmHg). Thus, fifty eight percent of all hypertensive patients attending the clinic had severe hypertension. The prevalence of hypertension was significantly higher among females with a male to female ration of 1:2 (P-value $<$ 0.0001) (Table 1).

TABLE 1: PREVALENCE OF HYPERTENSION AMONG PATIENTS SEEN AT MEDICAL OUTPATIENT CLINICS BETWEEN 1ST JANUARY TO 3RD JULY, 1995

	Males	Females	Total
	n (%)	n (%)	n (%)
Total patients seen at MOPD Jan. - July, 1995	1292 (48.9)	1349 (51.1)	2641
Patients with hypertension	173 (34.7)	325 (65.3)	498
Patients with severe hypertension (BP > 180/110mmHg)	94 (32.5)	195 (67.5)	289
Overall prevalence of hypertension at MOPD	(13.4)	(24.1)	(18.9)
Prevalence of severe hypertension at MOPD Jan. - July, 1995 BP > 180/110 mmHg.	(7.3)	(14.5)	(10.9)

PREVALENCE OF HYPERTENSION AMONG NEWLY REFERRED PATIENTS

When newly referred patients were considered alone, the prevalence of hypertension among them was 15.6% and 9.6% for severe hypertension. The prevalence of hypertension was also significantly greater in females than in males (M 12.6% : 18.5% F) Table 2.

TABLE 2: PREVALENCE OF HYPERTENSION AMONG NEWLY REFERRED PATIENTS AT MEDICAL OUTPATIENT CLINICS BETWEEN 1ST JANUARY TO 3RD JULY, 1995

Patients	Males	Females	Total
	n (%)	n (%)	n (%)
New patients at MOPD Jan. - July, 1995	429 (49.5)	437 (50.5)	866
Newly referred hypertensive patients	54 (40)	81 (60)	135
Newly referred patients with severe hypertension BP $\geq$ 180/110	33 (39.8)	50 (60.2)	83
Prevalence of hypertension among new patients at MOPD Jan. - July, 1995	(12.6)	(18.6)	(15.6)
Prevalence of severe hypertension among newly referred patients at MOPD Jan. - July, 1995	(7.7)	(11.4)	(9.6)

CLASSIFICATION OF PATIENTS AT TIME OF REFERRAL

The 498 patients with hypertension were placed into two major groups "NEW" hypertensives were those who presented for the first time at the clinics, while "OLD" hypertensives were those who were known to have hypertension. There were 135 (27.1%) "NEW" and 363 (73.9%) "OLD" hypertensives giving a ratio of "NEW" to "OLD" hypertensives of 1:3 (Table 3)

TABLE 3 HYPERTENSIVE PATIENTS BY SEX AND STATUS AT REFERRAL 1ST JANUARY TO 3RD JULY, 1995

	"NEW"	"OLD"	TOTAL
	n (%)	n (%)	n (%)
M	54 (40)	119 (32.8)	173 (34.7)
F	81 (60)	244 (67.2)	325 (65.3)
Total	135 (27.1)	363 (73.9)	498 (100)

AGE AND SEX DISTRIBUTION OF HYPERTENSIVE PATIENTS

The age and sex distribution of the hypertensive patients is shown in Table 4. The mean age (sd) for males was 49.6 (12.2) years and 50.7 (10.9) years for females. 380 (76.3%) of all hypertensive patients were adults and 105 (21.1%) were elderly. For 13 (2.6%) patients age was not known.

TABLE 4: AGE AND SEX DISTRIBUTION HYPERTENSIVE PATIENTS SEEN AT THE OUTPATIENT CLINIC BETWEEN 1ST JANUARY - 3RD JULY, 1995

Age (Years)	Males	Females	Total
	n (%)	n (%)	n (%)
15-24	2 (1.2)	1 (0.3)	3 (0.6)
25-29	7 (4.1)	7 (2.2)	14 (2.9)
30-34	7 (4.1)	13 (4.1)	20 (4.1)
35-39	10 (5.9)	26 (8.2)	36 (7.4)
40-44	31 (18.3)	39 (12.3)	70 (14.4)
45-49	34 (20.1)	58 (18.4)	92 (19.0)
50-54	24 (14.2)	55 (17.4)	79 (16.3)
55-59	18 (10.7)	48 (15.2)	66 (13.6)
60-64	13 (7.7)	29 (9.2)	42 (8.7)
65-69	8 (4.7)	21 (6.6)	29 (6.0)
70-74	10 (5.9)	15 (4.7)	25 (5.2)
75+	5 (3.0)	4 (1.3)	9 (1.9)
All ages	169	316	485

Age was not known for 4 males and 9 females.

BLOOD PRESSURE LEVELS OF HYPERTENSIVE OUTPATIENTS

When they were classified according to blood pressure levels at the time of recruitment, the 498 hypertensive outpatients fell into three groups. 289 (58.0%) had blood pressure ≥ 180/110 mmHg, 174 (34.9%) had blood pressure between 140/90 and 180/110 mmHg and 35 (7.0%) had blood pressure ≤ 140/90 mmHg. The 35 (7.0% patients whose blood pressures were ≤ 140/90 mmHg, were known hypertensive patients on treatment. Therefore they were controlled hypertensives under routine clinic care. (Table 5).

TABLE 5: DISTRIBUTION OF ALL HYPERTENSIVE PATIENTS ACCORDING TO SEX AND BLOOD PRESSURE LEVEL

SEX	BP≤ 140/90	BP 140/90>180/110	BP≥180/110	TOTAL
	n (%)	n (%)	n (%)	n (%)
Males	14 (40)	65 (37.4)	94 (32.5)	173 (34.7)
Females	21 (60)	109 (62.6)	195 (67.5)	325 (65.3)
Total	35 (7.0)	174 (34.9)	289 (58.0)	498 (100)

STUDY PATIENTS

It took six months and three days to recruit the 100 patients required for the study. Of the 289 patients with severe hypertension, 189 (65.4%) were not included in the present study. Tables 6 and 7 show patients with severe hypertension not studied and how they compared with those who were studied. These two groups did not differ significantly in terms of age and sex distribution. However, the studied patients had significantly higher systolic and diastolic blood pressures at the time of recruitment.

TABLE 6: PATIENTS WITH SYSTOLIC BLOOD PRESSURE (SBP) ≥ 180 AND/OR DIASTOLIC BLOOD PRESSURE (DBP) ≥ 110 mmHg WHO WERE NOT STUDIED

SEX	"NEW"	"OLD"	TOTAL
	n (%)	n (%)	n (%)
Males	18 (38.3)	47 (33.1)	65 (34.4)
Females	29 (61.7)	95 (66.9)	124 (65.6)
Total	47 (24.9)	142 (75.1)	189 (100)

TABLE 7: CHARACTERISTICS OF PATIENTS WHO WERE STUDIED AND WHO WERE NOT STUDIED

	STUDIED (n - 100)	NOT STUDIED (n - 189)	SIGNIFICANCE
Age (years)			
Mean (SD)	50.9 (10.5)	51.3 (11.5)	(P = 0.8) NS
Range	27-77	22-80	
Sex Ratio			
M:F	29/71 (1:2.5)	62/127 (1:2)	(P = 0.5) NS
BP at Recruitment			
Mean SBP (SD)	204.8 (50.0)	187.4 (23.2)	(P<0.0001) S
Mean DBP (SD)	116.3 (14.8)	112.4 (12.9)	(P<0.02) S

REASONS FOR EXCLUDING PATIENTS FROM STUDY

The reasons for not including 189 (65.4%) patients with severe hypertension in the study are shown in table 8. The age and sex distribution of 100 patients who were studied is shown in table 9.

Of the 189 patients excluded 65 (34.4%) were males and 124 (65.6%) were females. 134 (70.9%) were excluded because they were already on antihypertensive drugs, 15 (7.9%) had features of congestive cardiac failure and 14 (7.4%) were missed during initial file screening and were not subsequently referred to me by doctors who attended them.

Other reasons for not being included were: living far from Dar es Salaam, and hence could not afford fares to attend follow up 10 (5.3%), were asthmatic 8 (4.8%), did not like to be included in the study 7 (3.7%) and one patient (0.5%) had aortic regurgitation.

Of the 100 study patients, 29 (29%) were males and 71 (71%) were females. Twelve (12.0%) were young adults, 65 (65.0%) were adults and 23 (23.0%) elderly.

This study group had predominantly older patients, 88 (88%) being over 40 years of age. The male to female ratio was 1:2.5 reflecting the higher prevalence of severe hypertension among females noted earlier. (Table 9).

TABLE 8: REASONS FOR EXCLUDING PATIENTS FROM THE STUDY

Reason for exclusion	Males	Females	Total
	n (%)	n (%)	n (%)
On antihypertensive drugs	49 (75.4)	85 (68.6)	134 (70.9)
Congestive cardiac failure	5 (7.7)	10 (8.1)	15 (7.9)
Missed	4 (6.2)	10 (8.1)	14 (7.4)
Asthmatic	3 (4.6)	5 (4.0)	8 (4.8)
Living away from Dar es Salaam	2 (3.1)	8 (6.5)	10 (5.3)
No consent	1 (1.5)	6 (4.8)	7 (3.7)
Aortic regurgitation	1 (1.5)	0 (0.0)	1 (0.5)
Total	65 (34.4)	124 (65.6)	189 (100)

TABLE 9: AGE AND SEX DISTRIBUTION OF STUDY PATIENTS

Age (Years)	Males	Females	Total
	n (%)	n (%)	n (%)
15-39	4 (13.8)	8 (11.3)	12 (12.0)
40-59	19 (65.5)	46 (64.8)	65 (65.0)
60+	6 (20.7)	17 (23.9)	23 (23.0)
All ages	29 (29.0)	71 (71.0)	100 (100)

PRESENTING SYMPTOMS AMONG STUDY PATIENTS

The presenting symptoms of 100 study patients with severe hypertension are shown in Table 10. Palpitation was a leading presenting symptom. It was present in 73 (73%) patients. The second common presenting symptom was headache (all types) in 66 (66%), general malaise was present in 38 (38%) and exertional dyspnoea in 26 (26%). Other presenting symptoms were chest pain 9 (9%), dizziness 8 (8%), cough 6 (6%), visual symptoms 5 (5%), arthralgia 4 (4%) and numbness in the limbs 3 (3%). Impotence was complained of by 2 (2%). One who complained of impotence was on antihypertensive drugs before while another was a newly diagnosed patient not on treatment. Backache was complained of by 2 (2%) patients. Epistaxis, insomnia, weight loss, and loin pain were the presenting symptoms in 1% of the patients. 4 (4%) of the patients had no symptoms. Only visual symptoms and arthralgia were significantly commoner among females than males. For other symptoms there were no significant difference between the sexes. (Table 10).

TABLE 10: PRESENTING SYMPTOMS OF 100 STUDY PATIENTS WITH SEVERE HYPERTENSION (BP ≥ 180/110) mmHg

SYMPTOM	Males	Females	Total
	n (%)	n (%)	n
Palpitations	20 (69.0)	53 (74.6)	73
Headaches	17 (58.6)	49 (69.0)	66
Malaise	9 (31.0)	29 (40.8)	38
Exertional dyspnoea	8 (27.6)	18 (25.4)	26
Chest pain	5 (17.2)	4 (5.6)	9
Dizziness	2 (6.9)	6 (8.5)	8
Cough	1 (3.4)	5 (7.0)	8
Visual symptoms	0 (0.0)	5 (7.0)	5
Arthralgia	0 (0.0)	4 (5.6)	4
Numbness in limbs	1 (3.4)	2 (2.8)	3
Impotence	2 (6.9)	0 (0.0)	2
Backache	1 (3.4)	1 (1.4)	1
Epistaxis	1 (3.4)	0 (0.0)	1
Insomnia	0 (0.0)	1 (1.4)	1
Weight loss	1 (3.4)	0 (0.0)	1
Loin pain	0(0.0)	1 (1.4)	1
No symptoms	2 (6.9)	2 (2.8	4

RESULTS OF TREATMENT

Of the 100 patients, 63 (63%) had their blood pressure successfully lowered to $\leq$ 140/90 mmHg (i.e. controlled) by use of one or a combination from the three study drugs. 19 (19%) could not be controlled by the three drugs and hence an extra drug was prescribed. 18 (18%) did not complete follow up for various reasons. (Table 11).

TABLE 11: OUTCOME OF TREATMENT AT SIX MONTHS IN STUDY PATIENTS BY SEX:

	Controlled	Not Controlled	Did not complete follow up	Total
	n (%)	n (%)	n (%)	n
M	20 (31.8)	3 (15.8)	6 (33.3)	29
F	43 (68.2)	16 (84.2)	12 (66.7)	71
Total	63 (63)	19 (19)	18 (18)	100

Table 12 shows drug combinations required to achieve control in 63 patients. Only 3 (4.8%) patients were controlled by bendrofluazide alone. 45 (71.4%) required a combination of bendrofluazide and propranolol, 2 (3.2%) needed bendrofluazide and hydrallazine while 13 (20.6%) required three drugs (i.e. bendrofluazide, propranolol and hydrallazine). In total all 63 (100%) of the controlled patients used bendrofluazide 5mg daily. 58 (92.1%) needed propranolol. The dosage of propranolol required by these 58 patients are, 14 (24%) patients used 80mg daily, 14 (24%) patients used 160mg daily, 17 (29%) patients used 240mg daily, 13 (22%) patients used 320 mg daily. So, 30 (52%) of all patients who used propranolol needed larger doses of six to eight tablets of 40 mg a day. Hydrallazine was used by only 15 (23.8%) of all the patients whose blood pressure got controlled. Dosages required were, 4 (27%) of those who used hydrallazine required 50 mg a day, 7 (47%) patients required 75 mg a day, 3 (20%) required 150 mg a day and one (7%) required 225mg a day. For hydrallazine, 14(93%) of all the patients who required it for control, needed not more than 150 mg a day. This matches the recommended safe dose for this drug.

TABLE 12: DRUGS REQUIRED FOR CONTROL BY SEX

Drugs used	Males	Females	Total
	n (%)	n (%)	n (%)
B	2	1	3 (4.8)
BP	13	32	45 (71.4)
BH	1	1	2 (3.2)
BPH	4	9	13 (20.6)
TOTAL	20	43	63

B = Bendrofluazide
P = Propranolol
H = Hydrallazine.

PATIENTS WHO WERE NOT CONTROLLED BY THE STUDY DRUGS

19 (19%) of the study patients completed follow up but could not be controlled by use of the three study drugs. These either could not torelate the drugs or their blood pressures did not respond to maximum doses. Manipulation of drug combinations and doses was attempted. If this failed to achieve a target blood pressure they were considered not controlled. A fourth drug was then considered. Table 13 shows combinations used after final manipulation. Two (10.5%) patients could not use bendrofluazide, one because of excessive weakness and another one had congestive cardiac failure and was on frusemide. Three (15.8%) could not use proranolol, these are among the 4 patients who developed bronchospasm while on treatment. Eight (42.0%) could not use hydrallazine, 6 due to palpitations not controlled by propranolol. One is a patient who presented in congestive cardiac failure following loss to follow up. She was already on nifedipine and frusemide. Hence she did not use any of the study drugs. The last one developed syncope attacks on addition of hydrallazine.

TABLE 13: DRUG COMBINATIONS IN PATIENTS WHO WERE NOT CONTROLLED BEFORE ADDITION OF AN ALTERNATIVE DRUG

Drugs used	Males	Females	Total
	n (%)	n (%)	n (%)
B	-	1	1 (5.3)
BP	2	4	6 (31.6)
BH	-	1	1 (5.3)
PH	-	1	1 (5.3)
BPH	1	8	9 (47.4)
No drugs	-	1	1 (5.3)
TOTAL	3	16	19

COMPLIANCE AND SIDE EFFECTS OF THE DRUGS:

Compliance was studied at by checking tablet counts at each visit and by records of attendance. Of the 63 controlled patients, 14 (22.2%) had regular attendance record and no discrepancy in tablet count. 31 (49.2%) showed discrepancies in tablet counts despite a regular attendance record and 18 (28.6%) had irregular attendance records. For those 19 patients who were not controlled, only 3 (15%) had regular attendance records with no discrepancies in tablet counts, 5 (26.3%) had regular attendance records but showed discrepancies in tablet count and 11 had irregular attendance. 18 patients (18%) did not complete follow up. There was no statistical association between compliance and control. This, is however, in view of the small number of patients who were not controlled. Eighteen patients who did not complete follow up were not included in statistical analysis. (Table 14).

TABLE 14: COMPLIANCE OF STUDY PATIENTS

	Controlled	Not controlled	Total
	n (%)	n (%)	n (%)
No discrepancy in tabs count or any missed appointment	14 (22.2)	3 (15)	17 (20.7)
Discrepancy in tablet count at least once	31 (49.2)	5 (26.3)	39 (43.9)
Irregular attendance or default from clinic till home follow up	18 (28.6)	11 (27.9)	29 (35.4)
Total	63 (76.8)	19 (23.20)	82 (100)

18 did not complete follow up.

P = 0.06 overall.

The commonest side effects were burning epigastric pain 13 (13%), excessive weakness 11 (11%), dizziness 10 (10%) and impotence 7 (7%), bradycardia 6 (6%), palpitations 6 (6%) and bronchospasm 4 (4%). Antiacids gave good relief of the epigastric pain. For bronchospasm propranolol was substituted with hydrallazine. Sometimes diazepam at night was prescribed for insomnia. Palpitations led to stop hydrallazine in 6 patients. The pulse rate was not allowed to drop below 50 per minute. One patient could not use bendrofluazide because of excessive weakness. Impotence persisted. (Table 15).

TABLE 15 FREQUENCY OF SIDE EFFECTS AMONG STUDIED PATIENTS

SIDE EFFECT	PATIENTS n (%)
Epigastric pain	13 (13%)
Excessive weakness	11 (11%)
Dizziness	10 (10%)
Impotence	7 (7%)
Bradycardia	6 (6%)
Palpitations	6 (6%)
Bronchospasm	4 (4%)
Diabetes mellitus	3 (3%)
Insomnia	3 (3%)
Headache	2 (2%)
Drowsiness	2 (2%)
Excessive hunger	2 (2%)
Weight loss	2 (2%)
Syncope	1 (1%)
Light headiness	1 (1%)

Table 16.1 and 16.2 show blood pressure changes among 19 patients who did not reach target blood pressure.

These patients demonstrated significant reduction in both systolic and diastolic blood pressures at six months. $P < 0.0001$ in both cases.

TABLE 16.1 COMPARISON OF BLOOD PRESSURES AT RECRUITMENT AND AFTER 6 MONTHS OF TREATMENT. PATIENTS WHO DID NOT REACH TARGET BLOOD PRESSURE

CODE NUMBER	INITIAL BLOOD PRESSURE	FINAL BLOOD PRESSURE	BLOOD PRESSURE CHANGE
	Systolic/Diastolic	Systolic/Diastolic	Systolic/Diastolic
6	199/132	222/113	+23/-19
7	198/106	160/94	-38/-12
10	220/100	150/80	-70/-20
13	199/90	179/85	-20/-5
21	219/121	189/110	-30/-11
33	240/131	211/121	-29/-10
36	224/119	239/81	+15/-38
45	218/130	146/101	-72/-29
47	205/109	180/98	-25/-11
48	194/96	216/87	+22/-9
51	202/141	179/84	-23/-57
57	272/178	195/114	-77/-64
58	217/109	157/74	-60/-35
66	220/132	151/91	-69/-41
76	227/118	156/81	-71/-37
83	211/103	180/108	-31/+5
86	200/113	158/97	-42/-16
87	216/112	169/91	-47/-21
96	239/133	145/84	-94/-49

TABLE 16.2 MEAN BLOOD PRESSURE CHANGES AFTER 6 MONTHS OF TREATMENT. PATIENTS WHO DID NOT REACH TARGET BLOOD PRESSURE.

	INITIAL BLOOD PRESSURE (n=19)	FINAL BLOOD PRESSURE (n=19)	DIFFERENCE	P-VALUE
Systolic blood pressure				t=5.02
Mean (SD)	216.5 (18.9)	177.8 (27.9)	38.7 (33.7)	P<0.0001
Median	217.0	178.5		
Range	(193.5-271.5)	(145-239)		
Diastolic blood pressure				t=5.89
Mean (SD)	119 (20)	94.2 (13.5)	25.3 (18.7)	P<0.0001
Median	119.0	90.5		
Range	(90-178)	(74-121)		

ASSOCIATION BETWEEN PATIENT CHARACTERISTICS AND OUTCOME

When patients' baseline characteristics were analysed against those controlled and not controlled, no single parameter showed any significant association with blood pressure control. However, the number of patients not controlled may have been too small for its most effective analysis. (Tables 17.1, 17.2 and 17.3).

TABLE 17.1: DEMOGRAPHIC DATA

PARAMETER	CONTROLLED	NOT CONTROLLED	P - VALUE
	n (%)	n (%)	n (%)
Sex			
Male	20 (87.0)	3 (13.0)	0.175 NS
Female	43 (72.9)	16 (27.1)	
Religion			
Christian	22 (75.9)	7 (24.1)	0.914 NS
Moslem	40 (76.9)	12 (23.1)	
Marital Status			
Married	48 (81.4)	11 (18.6)	Not done
Single	3 (100)	0	
Divorced	3 (50)	3 (50)	
Widow	9 (64.3)	5 (35.7)	
Education status			
Elutriate	18 (72.0)	7 (28.0)	
Adult education	3 (75.0)	1 (25.0)	Not done
1^{o} Education	31 (77.5)	9 (22.5)	
2^{2} Education	11 (84.6)	2 (15.4)	
Referral status			
New	22 (81.5)	5 (18.5)	0.484 NS
Old	41 (74.5)	14 (25.5)	

TABLE 17.2: RISK FACTORS AND PHYSICAL FINDINGS

	CONTROLLED	NOT CONTROLLED	P-VALUE
	n (%)	n (%)	n (%)
Alcohol intake			
Yes	9 (75.0)	3 (25.0)	0.487 NS
No	54 (77.1)	16 (22.9)	
Physical activity			
Sedentary	11 (73.3)	4 (26.7)	0.817 NS
Active	41 (73.7)	15 (26.3)	
Very active	10 (100)	0	
Salt intake			
Normal	33 (76.7)	10 (23.3)	0.723 NS
Low	19 (73.1)	7 (26.9)	
Liberal	11 (84.6)	21 (5.4)	
Family history of Diabetes			
Yes	5 (83.3)	1 (16.7)	0.881 NS
No	58 (76.3)	18 (23.7)	
Obesity			
Yes	27 (75.0)	9 (25.0)	0.728 NS
No	36 (76.3)	10 (21.7)	
Hypertension			
Yes	23 (67.6)	11 (32.4)	0.097 NS
No	40 (83.3)	8 (16.7)	
Stroke			
Yes	8 (66.7)	4 (33.3)	0.494 NS
No	55 (78.6)	15 (21.4)	
Fundoscopy findings			
Normal	27 (87.1)	4 (12.9)	0.184 NS
Gd. I/II	27 (73.0)	10 (27.0)	
Difficult	9 (64.3)	5 (35.7)	
X-Ray CTR	17 (73.9)	6 (26.10)	
≤ 0.5	46 (78.0)	13 (22.1)	0.699 NS
>0.5			

TABLE 17.3: OTHER PATIENT CHARACTERISTICS

CHARACTERISTIC AT RECRUITMENT	CONTROLLED	NOT CONTROLLED	P-VALUE
	Mean (SD)	Mean (SD)	
Age (Mean SD	49.6 (10.1)	53.4 (9.7)	0.151 NS
	n = 63	n = 19	
BMI	26.8 (5.5)	25.9 (5.5)	0.534 NS
Mean duration of hypertension (months)	103.6 (84.9)	198.1 (128.1)	0.096 NS
	n = 63	n = 19	
Mean BPS	195.5 (31.3)	216.5 (18.9)	0.064 NS
	n = 63	n = 19	
Mean BPD	113.0 (12.7)	119.5 (20.0)	0.259 NS
	n = 63	n = 19	
Mean creatinine	102.2 (43.2)	118.7 (78.8)	0.360 NS
	n = 63	n = 19	
Mean Uric acid	0.36 (0.12)	0.37 (0.11)	0.747 NS
	n = 63	n = 19	
Mean Cholesterol	4.9 (1.1)	4.7)1.1)	0.487 NS
	n = 63	n = 19	
Mean fasting blood glucose	4.0 (1.6)	4.9 (2.8)	0.261 NS
	n = 63	n = 19	
Mean cardiothoracic ratio	0.57 (0.07)	0.59 (0.11)	0.410 NS
	n = 58	n = 17	

COMPARISON OF VARIABLES AT THE START OF TREATMENT AND SIX MONTHS AFTER TREATMENT

Certain variables were measured at the start and at the end of the study. This was partly to check on possible adverse effects of the drugs used. Analysis was done in subgroups.

Patients who completed follow up showed significant decrease in serum creatinine mean -7.33 (28.1) ($p = 0.02$) and voltage on electrocardiogram mean -3.0 (6.8) ($p = 0.002$). They also showed significant regression of the left ventricular mass as measured by echocardiogram mean -44.9 (97.7) ($p = 0.043$). The decrease in cardiothoracic ratio was not statistically significant. However, they also demonstrated a significant increase in body mass index mean +0.25 (1.1) ($P = 0.045$) and serum uric acid 0.18 (0.75) ($p = 0.0315$). An apparent rise in serum cholesterol was not statistically significant. There was a paradoxical statistically significant increase in serum potassium (mean difference +0.958 (1.88) P=0.0003). An increase in serum sodium was not statistically significant.

When controlled patients were analysed alone only the fall in serum creatinine and voltage on electrocardiogram were statistically significant. Echocardiographic left ventricular mass regression sub-analysis was not done in this group due to the small number of patients who had this repeat measurement ($n = 22$).

There was no statistically significant changes in variable in a group which was not controlled.

Tables 18.1, 18.2 and 18.3.

TABLE 18.1: CHANGES OF VARIABLES AT START OF TREATMENT AND AFTER SIX MONTHS TREATMENT IN ALL PATIENTS WHO COMPLETED FOLLOW UP

	INITIAL	AT 6/12	DIFFERENCE	P-VALUE
	Man (SD)	Mean (SD)	Mean (SD)	
BMI (N=82)	26.6 (5.5)	26.9 (5.5)	+0.25 (1.1)	0.045 S
S.creatinine (n=82)	106.1 (53.5)	98.7 (56.3)	7.33 (28.1)	0.020 S
S.cholesterol (n=82)	4.9 (1.1)	5.1 (3.3)	+0.22 (3.3)	0.554 NS
S.uric acid (n=82)	0.36 (0.12)	0.54 (0.72)	+0.18 (0.75)	0.0315 NS
F.B.Glucose (n=77)	4.4 (1.8)	4.4 (1.2)	+0.03 (1.4)	0.835 NS
Electrolytes Na^+ (n=66)	136.8 (5.8)	137.9 (3.7)	+1.19 (6.9)	0.129 NS
Electrolytes K^+ (n=66)	4.1 (0.7)	5.1 (1.8)	+0.958 (1.9)	0.0003 S
CXR (CTR) (n=58)	0.58 (0.08)	0.58 (0.06)	0.0 (0.05)	0.724 NS
ECG Voltage (n=56)	34.5 (8.3)	31.4 (8.9)	-3.0 (6.8)	0.002 S
LVMI (n=22)	220.9 (84.4)	176.0 (78.4)	-44.9 (97.7)	0.043 S

BMI - Body mass index

S. - Serum

FB Glucose - Fasting blood glucose

CXR (CTR) - Chest X-ray (Cardiothoracic ratio)

ECG - Electrocardiogram

LVMI - Left ventricular mass index.

Na^+ - Sodium

K^+ - Potassium

TABLE 18.2 CHANGES IN PATIENT VARIABLES AFTER SIX MONTHS OF TREATMENT (CONTROLLED PATIENTS).

	INITIAL	AT 6/12	DIFFERENCE	P-VALUE
	Means (SD)	Means (SD)	Means (SD)	
BMI (n=63	26.8 (5.5)	27.0 (5.5)	+0.2 (1.1)	0.100 NS
S.creatinine (n = 63)	102.2 (43.23)	93.8 (43.8)	-0.89 (28.4)	0.015 S
S.cholesterol (n=63)	4.9 (1.1)	4.7 (1.3)	-0.2 (1.5)	0.340 NS
S.uric acid (n=63)	0.4 (0.1)	0.5 (0.5)	+0.1 (0.5)	0.098 NS
F.B. Glucose (n=59)	4.2 (1.3)	4.4 (1.2)	+0.1 (1.1)	0.373 NS
Electrolytes Na^+ (n=63)	136.2 (6.7)	138.4 (2.7)	+2.1 (7.5)	0.051 NS
Electrolytes K^+ (n=63)	4.1 (0.7)	4.9 (1.4)	+0.8 (1.4)	0.0005 S
CXR (CTR) (n=46)	0.58 (0.07)	0.57 (0.06)	-0.01 (0.05)	0.318 NS
ECG Voltage	33.9 (7.9)	30.5 (7.7)	-3.4 (6.6)	0.002 S

TABLE 18.3 CHANGE IN VARIABLES AFTER SIX MONTHS OF TREATMENT (PATIENTS NOT CONTROLLED)

	INITIAL	AT 6/12	DIFFERENCE	P-VALUE
	Means (SD)	Means (SD)	Means (SD)	
BMI (N=19	25.9 (5.5)	26.1 (5.6)	+0.2 (1.2)	0.557 NS
S.creatinine (n = 19)	118.7 (78.8)	116.7 (54.8)	-2.1 (26.7)	0.741 NS
S.cholesterol (n=19)	4.7 (1.075)	6.3 (6.3)	+1.5 (6.3)	0.300 NS
S.uric acid (n=19)	0.37 (0.1)	0.79 (1.18)	+0.42 (1.22)	0.155 NS
F.B. Glucose (n=18)	5.0 (2.8)	4.7 (1.5)	-0.3 (2.1)	0.556 NS
Electrolytes Na^+ (n=19)	138.9 (2.9)	137.6 (4.7)	-1.4 (6.3)	0.603 NS
Electrolytes K^+ (n=19)	4.2 (0.7)	5.5 (2.5)	+1.3 (2.9)	0.0886 NS
CXR (CTR) (n=12)	0.60 (0.11)	0.62 (0.07)	+0.02 (0.06)	0.410 NS
ECG Voltage (n=13)	36.2 (9.8)	34.4 (12.0)	-1.9 (7.6)	0.400 NS

PATIENTS WHO DID NOT COMPLETE FOLLOW UP

Table 19 shows some particulars of 18 patients who did not complete follow up. Strenuous efforts were made to trace them at the end of the study through the records department, relatives and home visits. One (5.7%) had died, 9 (50%) were known to be alive and the status of the remaining 8 could not be determined. However, among those 8 patients, 5 (63%) had responded well to treatment before they were lost to follow up.

TABLE 19 PARTICULARS OF THE 18 PATIENTS WHO DID NOT COMPLETE FOLLOW UP

CODE NO.	AGE (YEARS) (SEX)	BLOOD PRESSURE (INITIAL) mmHg	BLOOD PRESSURE (AT TIME OF LOSS) mmHg	NO. OF VISITS BEFORE LOSS	REASON FOR LOSS	CURRENT STATE
3	43 (F)	212/130	190/112	3	Travelled	A
5	49 (F)	182/106	-	1	K	K
8	45 (F)	22/130	-	1	Can't afford Travel cost	A
28	41 (M)	210/138	-	1	Migrated-Bukoba	K
30	61 (F)	220/128	210/125	3	Migrated-Tabora	A
37	70 (F)	228/148	212/141	4	Alternative Therapy	A
44	37 (M)	170/111	150/89	3	Transfer-Arusha	K
46	55 (F)	190/110	130/78	3	Travelled	A
50	59 (F)	212/134	209/137	2	K	K
64	51 (F)	192/105	160/88	4	K	K
65	66 (F)	163/112	150/95	2	Alternative therapy	A
67	50 (M)	200/134	156/108	3	K	K
68	77 (M)	240/132	-	1	Travelled	A
73	48 (M)	210/150	200/110	2	Poorly motivated	A
75	73 (M)	181/119	-	1	+	+
77	38 (M)	220/132	156/118	4	Transfer-Tabora	K
79	40 (M)	180/119	-	1	Busy - Travelling	A
93	50 (F)	178/121	166/81	3	K	K

NB: A - Alive + - Died K - Not known

MORBIDITY AMONG STUDY PATIENTS

During 6 months of follow up, the following morbid events were observed among the study patients. One (1%) patient had a transient ischaemic attack during the first two months of therapy. Her blood pressure was successfully controlled. Two (2%) patients developed renal failure. One died, the second one is still on treatment. She needed addition of nifedipine to control her blood pressure. One (1%) had an abdominal ultrasound scan and intravenous pyelogram suggesting renal stones. She was taken over by urologists. Her blood pressure was however, controlled with bendrofluazide and propranolol. Another patient, was lost to follow up early during the study, she later appeared at the clinic in congestive cardiac failure. She is on nifedipine and frusemide.

It is difficult to ascertain if there were no any morbid event among some patients who were lost to follow up and whose status were not determined at the end of the study. (Table 20).

TABLE 20: OBSERVED MORBIDITY AMONG STUDY PATIENTS

Morbid event	Patients n (%)	Remarks
Transient ischaemic attack	1 (1)	Was well controlled with study drugs
Chronic renal failure	2 (2)	One died before the 2nd visit. One could not be controlled - still under follow up.
Renal stone	1 (1)	Was well controlled with study drugs. Taken over by urologist.
Congestive cardiac failure	1 (1)	Followed loss to follow up.
Total	5 (5%)	4 (4%) alive 1 (1%) died

DIRECT MEDICAL COSTS OF TREATMENT

Direct medical costs estimation includes cost of drugs, investigations and consultations. Table 21 shows the average drug cost for one hypertensive patient per year. (By whole sale government medical stores prices). The average drug cost of controlling one patient with severe hypertension per year is Tshs 19,199.00 or U.S.$ 34.28.

TABLE 21: AVERAGE COST OF DRUGS FOR PATIENTS WHOSE BLOOD PRESSURE WAS SUCCESSFULLY CONTROLLED: (PRICES ACCORDING TO WHOLE SALE GOVERNMENT MEDICAL STORES DEPARTMENT JULY-DECEMBER 1995

	Daily dosage requirements (mg)	Cost per person per day (Tshs)	Cost per person per year (Tshs)
Bendrofluazide (5 mg)			
(n = 63)			
Mean	5	4.30	1,569.50
Median	5	4.30	1,569.50
Range	5-5	4.30-4.30	1,569.50-1,569.50
Propranolol (40 mg)			
(n = 58)			
Mean	200	37.00	13,505.00
Median	240	44.40	16,206.00
Range	80-320	14.80-59.20	5,402.00-21,608.00
Hydrallazine (25 mg)			
(n = 15)			
Mean	93	64.20	23,433.00
Median	75	51.60	18,834.00
Range	50-225	34.40-154.80	12,556.00-56,502.00
Total (drug combinations)			
(n = 63)			
Mean		52.60	19,199.00
Median		48.70	17,775.50
Range		4.30-166.70	1,569.50-60,845.50

Table 22 shows the average drug cost for controlling one hypertensive patients per year (prices are the average from Dar es Salaam retail pharmacies). The average drug cost of controlling one patient with severe hypertension per year is Tshs. 58,290.50 or US $ 104.10.

TABLE 22: AVERAGE COST OF DRUGS FOR PATIENTS WHOSE BLOOD PRESSURE WAS SUCCESSFULLY CONTROLLED (PRICES ARE AVERAGE FROM DAR ES SALAAM RETAIL PHARMACIES)

	Daily dosage requirements (mg)	Cost per person per day (Tshs)	Cost per person per year (Tshs)
Bendrofluazide (5 mg)			
(n = 63)			
Mean	5	9.00	3,285.00
Median	5	9.00	3,285.00
Range	5-5	9.00-9.00	3,285.00-3,285.00
Propranolol (40 mg)			
(n = 58)			
Mean	200	122.50	44,712.50
Median	240	147.00	53,655.00
Range	80-320	49.00-196.00	17,885.00-71,540.00
Hydrallazine (25 mg)			
(n = 15)			
Mean	93	173.60	63,364.00
Median	75	139.50	50,917.50
Range	50-225	93.00-418.50	33,945.00-152,752.50
Total (drug combinations)			
(n = 63)			
Mean		159.70	58,290.50
Median		148.50	54,202.50
Range		9.00-484.00	3,285.00-176,660.00

Table 23.1 shows estimates for investigation costs. In this estimates eight investigations were assumed to be basic and so were done on every study patient. These were urinalysis, serum creatinine, cholesterol, uric acid and electrolytes. Others were fasting blood glucose, chest x-ray and an electrocardiogram. In the table it is shown that they were done twice in six months.

Three other investigations were considered to be special. These were renal ultrasound scan, intravenous urogram and urine culture and sensitivity. These were done only in special circumstances. The cost estimate for these special investigations were based on actual number done among 100 study patients. If basic investigations are done twice within one year and special investigations are done as the need arises; the annual cost of investigations per single new patient is estimated to be Tshs 69,377.60 or US$ 123.89 by using actual market prices. Further sub-analysis of the cost of investigations is shown in tables 23.2.

TABLE 23.1: COST OF INVESTIGATIONS (PRICES AS PER AVERAGE COSTS IN DAR ES SALAAM PRIVATE HOSPITALS)

INVESTIGATION	AVERAGE COST PER SINGLE INVEST.	NUMBER OF PATIENTS	AVERAGE COST FOR INITIAL INVEST.	AVERAGE REPEAT COST	TOTAL COST
	(Tshs)	n	(Tshs)	(Tshs)	(Tshs)
Urinalysis	1050.00	100	105000.00	105000.00	210000.00
Creatinine	3633.00	100	363300.00	363300.00	726600.00
Cholesterol	3633.00	100	363300.00	363300.00	726600.00
Uric acid	3633.00	100	363300.00	363300.00	726600.00
Fasting blood glucose	3166.00	100	316600.00	316600.00	633200.00
Electrolytes	5450.00	100	545000.00	545000.00	1090000.00
Chest X-ray	6500.00	100	650000.00	650000.00	1300200.00
Electrocardiogram	6800.00	100	680000.00	680000.00	1360000.00
Renal USS	17566.00	*6	105396.00	-	105396.00
Renal IVU	27166.00	*1	27166.00	-	27166.00
MSU - C/S	5366.00	*6	32196.00	-	32196.00
Total (All invest.) Tshs.			3551258.00	3386500.00	6937758.00
US $			6341.50	6047.30	12388.90

*The patients 6, 1 and 6 are those who received special tests apart from the basic 7 tests. (They are the same 6 patients)
Average investigation cost per new patient per year is Tshs. 69,377.60 or US $ 123.89.
Exchange rate Tshs. 560 = US $ 1 1995.

Table 23.2 shows average cost of investigations per new patient per year according to government prices of investigations. The average cost of investigations per patient per year is Tshs. 8,495.00 or US $ 15.20.

NB: (These prices are not real. They are meant for cost sharing, with a greater proportion being subsidised by the government).

TABLE 23.2: COST OF INVESTIGATIONS (BASED ON SUBSIDIZED PRICES FOR GOVERNMENT GRADE 4 PATIENTS)

INVESTIGATION	AVERAGE COST PER SINGLE INVEST.	NUMBER OF PATIENTS	AVERAGE COST FOR INITIAL INVEST.	AVERAGE REPEAT COST	TOTAL COST
	(Tshs)	n	(Tshs)	(Tshs)	(Tshs)
Urinalysis	200.00	100	20000.00	20000.00	40000.00
Creatinine	600.00	100	60000.00	60000.00	120000.00
Cholesterol	600.00	100	60000.00	60000.00	120000.00
Uric acid	600.00	100	60000.00	60000.00	120000.00
Fasting Blood Glucose	600.00	100	60000.00	60000.00	120000.00
Electrolytes	600.00	100	60000.00	60000.00	120000.00
Chest X-ray	500.00	100	50000.00	50000.00	100000.00
Electrocardiogram	500.00	100	50000.00	50000.00	100000.00
Renal USS	500.00	*6	3000.00	-	3000.00
Renal IVU	500.00	*1	500.00	-	500.00
MSU - C/S	1000.00	*6	6000.00	-	6000.00
Total (All invest.) Tshs.			429500.00		849500.00
US $			767.00	750.00	1517.00

*The patients 6, 1 and 6 are those who received special tests apart from the basic 8 tests. (They are the same 6 patients)
Exchange rate Tshs. 560 = US $ 1 1995.

Tables 24 and 25 show the average annual cost of one hypertensive patient when investigations are repeated for follow up. Table 24 shows costs based on charges for investigations in Dar es Salaam city private hospitals and drugs as per retail pharmacy prices. In such a situation the total cost for treating one patient for one year is Tshs 129,168.10 or US$ 230.69. The cost of drugs being Tshs 58,290.40 (45.1%) while the cost of investigations is Tshs 69,377.60 (53.7%) of the total cost.

TABLE 24: AVERAGE COST PER NEW PATIENT PER YEAR (BASIC INVESTIGATION REPEATED WITHIN ONE YEAR: PRICES AS PER DAR ES SALAAM CITY PRIVATE PHARMACIES AND HOSPITALS)

	Average cost Tshs. (%)	Average cost US $
1. Drugs	58290.40 (45.1)	104.10
2. Investigations		
Initial	35512.60 (27.5)	63.42
Repeat	33865.00 (26.2)	60.47
3. Consultation	1500.00 (1.2)	2.70
Average total cost/patient/year	129168.10	230.69

Table 25 shows costs based on whole sale government medical stores department prices for drugs. For the investigations the charges are subsidized, meant for cost sharing policy for grade 4 patients.

The average annual cost of treatment per patient is Tshs. 29,194.00 or US $ 52.20. Drugs costing Tshs. 19,199.00 (65.8%) of the total costs, costs for investigations being Tshs. 8,495.00 (29.1%) of the total costs and consultations costs being Tshs. 1,500.00 (5.1%) of the total costs.

TABLE 25: AVERAGE COST PER NEW PATIENT PER YEAR (BASIC INVESTIGATIONS REPEATED WITHIN ONE YEAR): PRICES ARE AS PER GOVERNMENT CHARGES

	Average cost	Average costs
	Tshs. (%)	US $
1. Drugs	19199.00 (65.8)	34.30
2. Investigations		
- Initial	4295.00 (14.7)	7.7
- Repeat	4200.00 (14.4)	7.5
3. Consultation	1500.00 (5.1)	2.70
Average cost per patient per year	29194.00	52.20

Figures 1.1, 1.2 and 1.3. Demonstrate how investigations can exaggerate the treatment costs. In this demonstration, retail drug prices and prices of investigations as charged by private hospitals in Dar es Salaam city have been used.

Government prices for investigations have not been used to avoid extreme under estimation because they are subsidized and therefore unrealistic.

Figure 1.1 Demonstrates contribution of drug and other costs to total treatment costs when no investigations are done

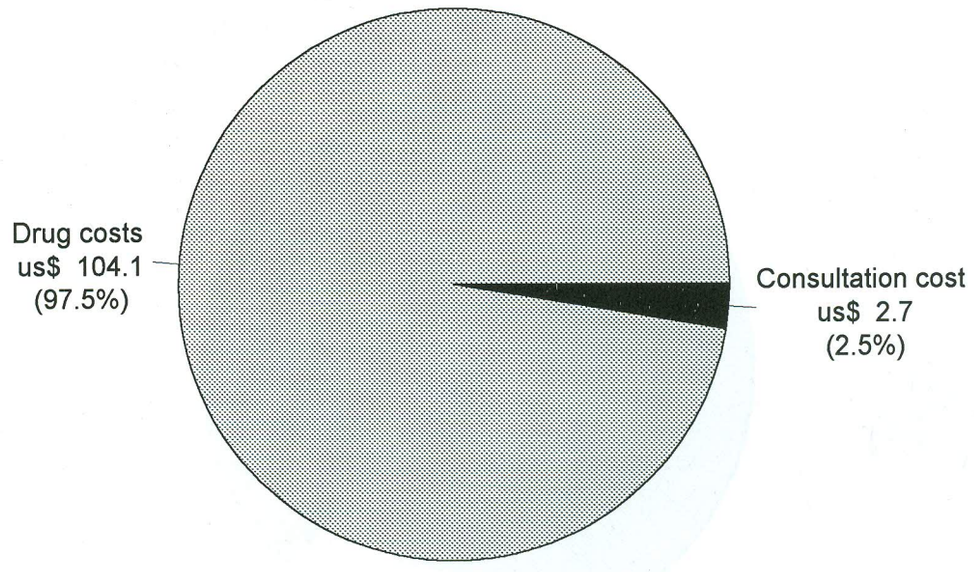


Figure 1.2: When basic investigations are done once in a year total costs of treatment raises by US $ 63.4 (59.4%) compared to when no investigations are done. Total costs become US $ 170.2 per new patient per year. Where by US $ 104.10 (61.16%) is for drugs, US $ 63.4 (37.25%) for investigations and US $ 2.7 (1.59%) for consultations.

Figure 1.2 Demonstrates contribution of investigations to the total treatment costs when investigations are done once

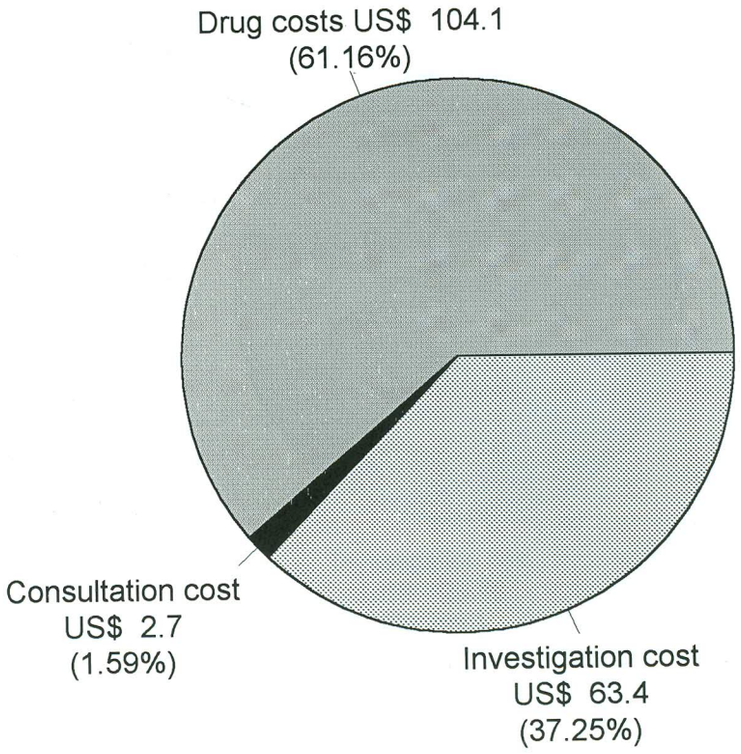


Figure 1.3: When basic investigations are repeated within the same year, total costs of treatment raises by US $ 123.89 (116%) compared to when no investigations are done. Total costs becomes US $ 230.7 per new patient per year. Where 104.1 (45.13%) for drug costs, 2.7 (1.17%) for consultations and 123.89 (53.70%) for investigations.

Figure 1.3 Contribution of investigation costs to total costs of treatment when basic investigations are repeated within the same year

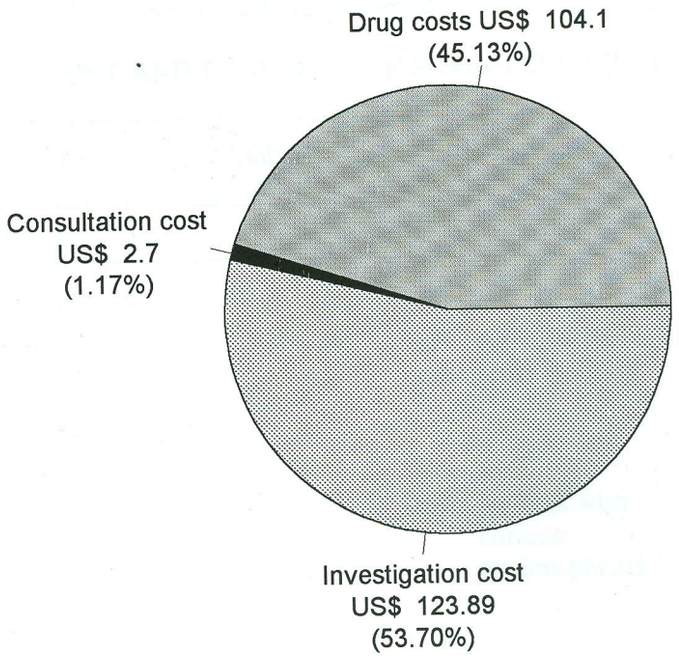


Table 26 shows the costs incurred to pick some pathologies during the study.

Out of 100 (100%) patients studied, ten (10%) had abnormal initial urinalysis and/or serum creatinine $\geq$ 150 μmol/l. Repeat tests were done on these 10 patients. Six (60%) of the 10 patients, the abnormality persisted. To these 6 patients midstream urine cultures and abdominal ultrasound scans were done. One patient (16.7%) of the six, an intravenous urogram was indicated. It costed Tshs. 680,497.10 or US $ 1,215.17 to pick one patient with renal stones and 4 with chronic pyelonephritis. Out of 84 electrocardiograms done, 48 patients were found to have features of left ventricular hypertrophy and one with an old myocardial infarct. These costed 571,200 or US $ 1,020.

Out of 79 repeat fasting blood glucose tests done at the end of the study, three patients had their blood glucose in diabetic range - this costed Tshs. 250,114.00 or US $ 447.

TABLE 26: COST AND OUTCOME OF SOME INVESTIGATIONS DONE

Investigation done	Number of tests	Pathology picked	Total costs Tshs. (US $)
	n		
Urinalysis	110		
Serum creatinine	110	1 patient with renal stones	
Urine culture and sensitivity	6		
Abdominal ultrasound scan	6	4 patients with chronic pyelonephritis	680,497.10 (1,215.17)
Intravenous pyelography	1		
Electrocardiograms	84	48 patients with left ventricular hypertrophy 1 old myocardial infarct	571,200.00 (1,020)
Repeat fasting blood glucose	79	3 patients with fasting blood glucose in diabetic range	250,114.00 (447)

Table 27 below shows cost extrapolations for Tanzania. Prevalence of severe hypertension was estimated to be 1.9% during Hai and Morogoro surveys. This gives a number of patients with severe hypertension in Tanzania to be 238,161. To supply them with the study drugs for one year will cost Tshs. 4,572,453,039 or US $ (8,165,094.71) by whole sale government prices. But it will cost 13,882,523,770.00 or US $ (24,790,221.00) by average retail private pharmacies prices of generic preparations.

TABLE 27: ANNUAL DRUG COST EXTRAPOLATIONS FOR THE ENTIRE COUNTRY

ITEM	ESTIMATE
Drug costs	
A one year supply for all patients with severe hypertension.	
(1) By government whole sale prices Tshs. (US $)	4,572,453,039.00 (8,165,094.71)
(2) By average retail private pharmacy prices (generic preparations) Tshs.(US $)	13,882,523,770.00 (24,790,221.02)
Budget: Health ministry	
1994/95 - Total Tshs. (US $)	15,185,300,000.00 (27,116,607.10)
- Drugs Tshs. (US $)	687,539,000.00 (1,227,748.20)
1995/96 - Total Tshs. (US $)	13,389,934,900.00 (23,910,598.00)
- Drugs (Tshs. (US $)	500,000,000.00 (892,857.10)

Estimated prevalence of severe hypertension in Tanzania is 1.9%.

Tanzanians aged 15 years and above are 12,534,808.

Hence estimated number of patients with severe hypertension in Tanzania 238,161.

SURVEY RESULTS

A survey was carried in October 1995 which covered a total of ten medical centres in the city. Each held the registration status of a hospital. Questionnaires were dispatched to a total of 94 practitioners. However only 69 filled them giving a response rate of 73.4%.

The prescribers consisted of 26 (37.7%) medical assistants, 5 (7.2%) assistant medical officers, 33(47.8%) medical officers and 7 consultants (7.1%)) 5 physicians, one surgeon and one gynaecologist).

39 (57.4%) of them were seeing at least 5 cases of hypertension a week, while the rest were seeing fewer.

Only 4 (5.8%) of the 69 respondents reported that they make a diagnosis of mild to moderate hypertension using a single reading. 65 (94.2%) required at least 2 visits before the diagnosis was ascertained. 53 (81.5%) of the 65 responded that they required at least three visits to confirm the diagnosis.

When it came to the level where they consider starting drug therapy, 45 different levels were given. The majority of the respondents 65 (97%) consider starting some one on drug therapy when the diastolic pressure is between 90 - 115 mmHg or systolic blood pressure between 140 - 165 mmHg. For 2 respondents (3%) one responded that they would start drug therapy when systolic blood pressure is at least 130 mmHg and another when systolic blood pressure is at least 200 mmHg. 15 (22.4%) of the responses considered diastolic blood pressure level as the sole determinant of a decision to treat.

Table 28 shows drug preference (first choice for initiation of therapy) by status of prescribers from survey responses. (One could give alternative of drugs). Traditional antihypertensive drugs scored the top five positions. Hydrallazine however scored lower than newer and expensive antihypertensive drugs like captopril. Diazepam is considered by some as an antihypertensive drug. Medical officers significantly preferred to initiate treatment in a new hypertensive patient with either bendrofluazide, propranolol or atenolol. Consultants significantly preferred to prescribe moduretic and adalat retard. All the prescribers showed a similar attitude towards hydrallazine. The preference of medical assistants and assistant medical officers were not statistically different from medical officers and consultants. This was not surprising since they had learned their practice from medical officers and consultants.

TABLE 28: DRUG PREFERENCE BY STATUS OF PRESCRIBER

Drug	Medical assistants	Assist. med. officers	Med. officers	Consultants	Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Bendrofluazide	6 (19.4)	1 (3.2)	20 (64.5)	4 (12.9)	31
Frusemide	17 (48.6)	5 (14.3)	13 (37.1)	0 (0.0)	35
Propranolol	4 (22.2)	1 (5.6)	11 (61.1)	2 (11.1)	18
Hydrallazine	2 (40.0)	1 (20.0)	2 (40.0)	0 (0.0)	5
Moduretic	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1
Brinerdine	6 (35.3)	0 (0.0)	10 (58.8)	1 (5.9)	17
Pindolol	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1
Methyldopa	14 (43.8)	2 (6.3)	14 (43.8)	2 (6.3)	32
Adalat	1 (9.1)	0 (0.0)	7 (63.6)	3 (27.3)	11
Atenolol	1 (6.3)	1 (6.3)	11 (68.8)	3 (18.8)	16
Captopril	0 (0.0)	1 (11.1)	5 (55.6)	3 (33.3)	9
Diazepam	4 (66.7)	0 (0.0)	2 (33.3)	0 (0.0)	6

*(%) are for the rows.
Med = Medical

Table 29 shows responses for what were considered to be initial basic investigations for a new hypertensive patient. Urinalysis, serum creatinine, electrocardiogram, chest x-ray and electrolytes were considered to be basic by most prescribers.

TABLE 29: CHOICE OF INITIAL INVESTIGATIONS BY STATUS OF PRESCRIBERS

Invest	Medical assistants	Assts. med. officers	Medical officers	Consultants	Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Urinalysis	20 (35.1)	3 (5.3)	29 (50.9)	5 (8.8)	57
Chest Xray	10 (21.7)	4 (8.7)	27 (58.7)	5 (10.9)	46
Electrocardiogram	16 (32.0)	2 (4.0)	27 (54.0)	5 (10.0)	50
Creatinine	16 (29.1)	4 (7.3)	30 (54.5)	5 (9.1)	55
Electrolytes	5 (18.5)	2 (7.4)	15 (55.6)	5 (18.5)	27
Echocardiogram	3 (50.0)	0 (0.0)	1 (16.7)	2 (33.3)	6
Creatinine Clearance	4 (36.4)	0 (0.0)	5 (45.5)	2 (18.2)	1
Renal ultrasound	5 (33.3)	1 (6.7)	5 (33.3)	4 (26.7)	15
Serum cholesterol	1 (20.0)	1 (20.0)	3 (60.0)	0 (0.0)	5
Urine VMA	1 (50.0)	0 (0.0)	1 (50.0)	0 (0.0)	2
Random blood sugar	0 (0.0)	0 (0.0)	3 (100.0)	0 (0.0)	3
Fundoscopy	0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	1
IV	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1

Urine VMA - urine for vanylmandelic acid

IVP - Intravenous pyelogram.

*(%) are for the rows.

Respondents were asked if they knew of the existence of guidelines on the treatment of hypertension in Tanzania. 67 doctors responded. 32(47.8%) had never heard of any such guidelines. 35(52.2%) said they had heard about one, but none was clear about which one. All responses suggested a need for such guidelines. But guidelines which take into considerations the availability, cost and effectiveness of the proposed drugs. They also need to be uniform, properly communicated to the prescribers and reviewed regularly.

DISCUSSION

Prevalence of hypertension among medical outpatients

Hypertension is on the increase in Africa and other developing communities.[11-14] Prevalence rates vary from 15 to 30% in different areas, in some places being higher among blacks than in Caucasians.[11]

This study revealed a high prevalence of hypertension of 16% among newly referred outpatients over a six month period. This is comparable to the findings by Lyimo.[84] Over two consecutive years of recruitment, he found a prevalence of 18.5% among newly referred outpatients at Muhimbili Medical Centre.

Prevalence rates for rural Tanzania are however lower. The non-communicable disease survey in Mara, Morogoro and Hai revealed prevalence rates of 3.0%, 4.0% and 6.8% respectively.[19]

The prevalence of 16% at the clinic is however comparable to community based prevalence rates of 12.8% in Dar es Salaam [84], Lyoga reported prevalence of 16% in Nyeri district Kenya[14] and Kabangu a prevalence rate of 14.3% in Zaire.[5]

For Dar es Salaam community based prevalence is comparable to hospital rate the explanation may be that this reflects an increase in risk factors for developing hypertension in Dar es Salaam as noted during recent surveys.[19] The other possibility is that this results from a breakdown of the health referral system such that Muhimbili clinics are now serving as Dar es Salaam community dispensaries. Patients being referring themselves because of the increased awareness for hypertension.

From the results of this study the prevalence of severe hypertension is also high. Fifty eight percent of all hypertensive patients at the clinic had severe hypertension. For newly referred hypertensive patients, 62% had severe hypertension.

An excess of severe hypertension among hypertensive patients at outpatient clinics is expected. The first reason being that Muhimbili Medical Centre is a referral hospital where serious or difficult conditions are referred. A second reason why there is excess of severe hypertension at the clinics, is the nature of the condition (hypertension) itself. Mild to moderate hypertension is mostly asymptomatic.[3] Severe forms are therefore more likely to be referred. Also doctors at referral hospitals prefer to deal with patients with severe conditions not manageable at peripheral hospitals.

This study also shows a high prevalence of hypertension among females with a male to female ratio of 1:1.5 among newly-referred patients. This is despite equal sex ratios in total outpatients and a similar mean age in years among the two sexes.

A high prevalence of hypertension among females has been documented by some authors[84-86], while others have reported a lack of difference between sexes.[87] In Africa Saxton (1969) reported male:female sex ratio of hypertension of 9:16.5 in a rural community outside Kampala city.[85] Akinkugbe in 1968 reported a prevalence of 9.1% among males and 11.2% among females in Nigeria.[86] In a non-communicable disease survey in Tanzania hypertension prevalence rates for both sexes ranged from 3.0% - 10.5%. For males the range was 2.6% - 10.5% and 3.4 - 14.6% for females.[19] Van Dongeu (1983) noted that blood pressures were higher for older women in Tanzania.[88]

From Western literature the prevalence of hypertension is known to increase in females after the menopause, reversing the male predominant ratio seen in young age groups.[89,90] The reasons for this is not known. Prevalence rates among sexes therefore vary with the age structure of the population in question.

In this study 85% of the female patients were above 40 years of age. In this study therefore most females were in the age group where their blood pressures were expected to be higher.

Exclusion of patients from study

As already noted earlier, the number one cause of exclusion of hypertensive patients from the study was because they were on antihypertensive drugs at the time of recruitment. No washout period was planned for ethical reasons. Fourteen (7.4%) of the patients with severe hypertension at the clinics were not included in this study because they were missed. These are the patients who might have fulfilled the study criteria. It is presumed that these were patients who preferred to be regularly seen by particular doctors and so could not be referred to me.

The consequences of excluding 8 (4.8%) patients with asthma, can be looked at from two different approaches. One is that their inclusion could exaggerate the number of patients regarded as not controlled by the study drugs. This is because an asthmatic patient would be limited not to use propranolol and hence an increased chance of not getting controlled. This is likely if considering the fact that propranolol was required in larger doses by most study patients to achieve control. On the other hand it is likely that some of these patients would have responded without the addition of propranolol. Of the 4 patients who developed bronchospasm during the study, only 2 (50%) were not controlled.

Presenting Symptoms

Mild to moderate hypertension is mostly an asymptomatic condition.[3] However, severe hypertension is mostly symptomatic, with occipital headache being characteristic. Other known symptoms include dizziness, palpitations and easy fatigability. Blurring of vision due to retinal changes, angina pectoris and dyspnoea and cough due to cardiac failure, may also occur.[3]

Other symptoms may relate either to a possible underlying secondary cause of hypertension or coexisting conditions.

The presenting symptoms of my study patients did not differ from what was expected. In 1977 Mtulia studied 172 inpatients consecutively admitted due to hypertension in Muhimbili Medical wards. The leading symptoms were dyspnoea 71 (41.3%), headaches 63 (36.6%), palpitations 56 (32.6%), dizziness/giddiness 38 (22.1%0 cough 24 (14.5%) and chest pains 21 (12.2%).[91] These presenting symptoms however, cannot be solely attributed to hypertension. In this study, it was not possible to completely rule out secondary cause of hypertension or other coexisting conditions at the time of recruitment.

Outcome of drug treatment

Sixty three (63%) of the study patients were controlled according to the study definition. Nineteen (19%) were not controlled and 18 (18%) did not complete follow up. These results cannot be properly interpreted without considering other facts, which show that the actual number controlled was higher than 63%.

First is the exclusion criteria discussed earlier. That a good number of asthmatic patients, eight (4.8%) excluded from this study could possibly have been controlled without addition of propranolol.

Second is the fact that the definition of control may have been too strict. Such strict definitions are rarely achieved in actual practice. Some patients classified as not controlled had good blood pressure response. As a group patients who were not controlled had significant fall in both systolic (mean 38.7 mmHg) and diastolic (mean 25.3 mmHg) blood pressures, (P-value < 0.0001) at 6 months of treatment.

A third possible reason why control may have been better is that some patients got lost to follow up when their blood pressures had responded well to treatment table 19. This again under-estimates the actual number controlled by these three drugs.

Considering these limitations in the assessment of control, the actual number which these drugs can potentially control is much higher than 63%.

Eighteen (18%) of all study patients did not complete the follow up. This appears to be a large number, especially so because assessment of control was supposed to be done under strictly supervised compliance. However, this loss occurred despite strenuous efforts of supervision. Without frequent home follow ups 29 (35.4%) study patients would have been lost.

Drug requirements

Of the 63 (63%) patients who were controlled, all used bendrofluazide either alone or in various combination with the other two drugs. This should indicates a high demand for this drug (bendrofluazide) in case the guidelines are put into practice.

Propranolol was used by 58 (92%) of all the patients who were controlled. Also it was the drug which was used in large quantities. Thirty (52%) of all the patients who needed it for control used 240 mg to 320mg a day. If the guidelines are put into practice, propranolol will need to be ordered in stronger preparations to avoid patients having to take many tablets a day. The strength used in this study was a 40 mg tablet.

Only one patient used 225 mg of hydrallazine a day. All the other patients who needed hydrallazine, required smaller doses for control. So from this study, there is no need to use hydrallazine in doses beyond 150mg daily. Patients who did not respond to lower doses did not do so with larger dosages. Serious side effects may also occur if the daily dose exceeds 200 mg a day.

Patients who were not controlled by the three study drugs, an extra drug was prescribed to buy from the private pharmacies. None of them managed to secure an extra drug in order to achieve control. Those who continued with the follow up, went on using only the drugs supplied free at the clinic.

Compliance and side effects of the drugs

Non compliance is a well documented problem among hypertensive patients.[84,92-94] However reasons for this are not clearly known. Efforts to look into the postulated factors have not revealed evidence for association. Factors like socioeconomic status, personality, eduction and fear of side effects of drugs did not show significant association with non-compliance in several studies.[40,84,95]

Lyimo[84] in 1991 found that hypertensive patients were still non-compliant even when treated in the community to avoid distances to travel and queues at hospital. He found that 70% of his community patients had disappeared by the end of one year. He also noted from the same study that patients who were lost from the study earlier had significantly higher levels of blood pressures during their last clinic visits, a fact showing that relief of symptoms was not the cause for non-compliance.

This study aimed at strict supervision to ensure compliance. Supervision was done by counting tablets supplied in the previous clinic, recording missed clinics and home visits for those who got lost to follow up. Yet, still compliance was not 100% and 18% of the study patients were lost to follow up. Lack of consistent symptoms even with severe hypertension may be the explanation for this tendency. Several reasons may account for the loss of 18% of my study patients. Most of them, 8 (44.4%) moved away from Dar es Salaam before completion of the study period. This followed transfers at their working places, transfer of their supporting relatives, loss of jobs in the city or business travelling. For 5 (27.8%) patients it was not possible to locate their residencies despite detailed addresses taken. Most of these were living in unsurveyed areas, some might at the same time have been sharing homes with friends, therefore not known to their neighbours. Four (22.2%) were not willing to return back to the clinic when last contacted. Two of these had changed their antihypertensive drugs following advise from their family doctors, while the other two said

could not afford to travel frequently to attend clinics. Only one patient (5.6%) died during the study. During analysis, however, compliance did not show any significant association with control. The small number of patients who were not controlled may be the explanation for this outcome which is against normal logic. Epigastric pain emerged as the most frequent side effect of drugs. This is not widely documented as a side effect of the three drugs used. However, in the Veterans Administration Cooperative Study Group on antihypertensive agents[96], ulcer symptoms, weakness and nasal stuffiness were the only symptoms occurring with greater frequency in the treated group. They were significantly higher in the treated than control group. Bronchospasm necessitated substitution of propranolol in 4 (4%) of patients. For the three (3%) patients whose fasting blood glucose crossed to the diabetic range, no drug was withdrawn. Instead they were registered at the diabetic clinic and started on dietary management. Drugs were not withdrawn in these patients because it is recommended that a hypertensive patient in whom hyperglycaemia develops during diuretic therapy should be considered as having diabetes mellitus, independent of diuretic use.[24] Bradycardia which occurred in 6 (6%) patients was reversed by reducing dosages of propranolol and increasing or adding hydrallazine. Palpitations led to withdrawal of hydrallazine in 6 (6%) of patients and 1 (1%) stopped bendrofluazide because of excessive weakness.

Predictors of response to antihypertensives

Among hypertensive patients, age and race have been the widely documented factors affecting response to antihypertensive drugs.[10,24,26,27,74,97] Young black patients are less responsive to diuretics due to their high renin levels, but respond better to beta blockers, while older hypertensive patients respond better to diuretics than beta blockers. In general, black hypertensive patients have been found to respond better to diuretics and are unlikely to

respond to monotherapy with beta blockers. However, the addition of small doses of diuretics to beta-blockers brings the response of blacks to that of non-blacks.[26,37]

Smoking was found to interfere with the response to propranolol among black patients in the MRC trial.[10]

In this study none of the studied factors was found to be statistically associated with control. Age and race were not expected to predict control in this study as a combination of a diuretic and a beta-blocker were used and all patients were Africans. The small number of patients who were not controlled may be another factor which made some other factors not to be significantly associated with control.

Safety of drugs

Assessment of the safety of drugs used in this study was made by observing the side effects as well as noting changes in some patient variables at the end of the study.

The absence of severe side effects has been discussed before. In addition, these drugs caused a significant fall in mean serum creatinine of 7.33 (28.1) μmol/l (P-value=0.020) and a significant regression of the left ventricular mass mean regression 44.9 (97.7) gm/m^2 (P-value=0.043). Out of 22 patients who had repeat echocardiogram done, 14 (64%) had regression of the left ventricular mass (LVM). Eight (36%) had showed increase in LVM of various degrees.

Renal dysfunction and left ventricular hypertrophy are known complications of hypertension. There are disputes if hypertension alone causes left ventricular hypertrophy.[98] This is because left ventricular hypertrophy has been detected even before arterial blood pressure elevation has become fixed.[99] However, left ventricular hypertrophy is found in 20% to 50% of patients in clinical studies of essential hypertension and it is associated with a higher incidence of subsequent cardiovascular morbidity and mortality.[98,100,101] So the reduction of left

ventricular mass noted in this study is a favourable outcome, especially if one considers the fact that the drugs used have variable effects on the left ventricular mass.[16]

An increase in the body mass index of 44 (44%) patients was noted during follow up. Forty seven (47%) lost weight, while for 7 (7%) there was no weight change. The explanation for weight gain may be a reflection of non compliance to non pharmacological measures. An alternative explanation for this increase may be that as blood pressure started to fall and symptoms disappeared, some patients become relaxed and gained weight.

Paradoxically, there was an increase in serum potassium at 6 months of follow up. Mean difference of 0.953 (1.880) (P=0.0003). A mean difference in serum sodium of 1.19 (6,962) was not statistically significant. An increase in serum potassium was not expected. It is difficult to explain this finding, especially if one considers that the analysis was done at a good laboratory with good quality control. The possible explanation may be a possibility of red blood cell haemolysis either during blood drawing or during centrifuging. At most minimal decrease was expected as low doses of bendrofluazide was used (5mg od).

An increase in serum uric acid was expected but no patient developed clinical symptoms of hyperuricemia. An increase in serum cholesterol was not significant. Propranolol is known to increase triglyceride levels and reduce high density lipoprotein cholesterol levels without affecting total cholesterol.[97] Triglycerides and high density lipoproteins were not measured.

Direct medical costs of treatment:

This includes the costs of drugs according to the suggested guidelines, investigations and consultations. Analysis of drug cost was done using government whole sale prices and private pharmacies retail prices. The aim is to compare and emphasize the question of high costs and a need for treatment guidelines. The average annual drug cost of controlling one patient with severe hypertension is Tshs. 58,290.00 equivalent to US$104.10 per year, when average retail pharmacy prices are used. The average annual cost for bendrofluazide alone

is Tshs. 3,285.00 or US$ 6 per person, Tshs 44,712.50 or US $ 80 and Tshs. 63,364.00 or US$ 113.15 for propranolol and hydrallazine respectively. The drug prices used here are for generic preparations.

Brandy preparations were 25% to 300% more expensive than generic ones for propranolol and 60% to 133% more expensive for hydrallazine. Hence use of generic preparations may help to reduce the treatment cost quite significantly.

According to the 1988 Census Tanzania has 12,534,808 people aged 15 years and above.[83] No actual data is available for the prevalence of severe hypertension in Tanzania. However, from surveys conducted in Hai and Morogoro the prevalence of severe hypertension was estimated to be 1.9%.[19] If this prevalence is extrapolated to the entire population it means that there are 238,161 patients with severe hypertension. To supply a one year requirement of bendrofluazide, propranolol and hydrallazine to control these patients (according to retail market drug prices) would cost the nation a total of Tshs 13,882,523,770.00 or US$ 24,790,221.02 for drugs alone. This is almost equal to the entire budget for the Ministry of Health in 1994/95 which was Tshs 15,185,300,000.00 or US$ 27,116,607.10. It is also in excess of the entire budget for the Ministry of Health for the year 1995/96 which was Tshs. 13,389,934,900.00.[83] Budgets for drugs were, 1994/95 Tshs. 687,539,000 or US $ 1,227,748.20 and for 1995/96 was Tshs. 500,000,000 or US $ 892,857.10.

However if these drugs were made available at whole sale government prices, the costs will fall to Tshs. 4,572,453,039.00 or US $ 8,165,094.71. This is equal to 33% of the retail price costs. The implication being that, the government can reduce the cost incurred by hypertensive patients by 67% by selling these study drugs to patients at whole sale prices.

The guidelines do not specify when and which investigations should be done. It however, warns that investigations are generally not cost-effective. This made analysis of investigation costs difficult. However, to bring out a clear picture of their contribution to the total costs

of treatment, analysis of costs was done in three ways. Both analysis used market price costs for investigations and drugs.

The first analysed a situation when treatment is carried out without any prior investigations. Here the total cost of treatment would include mainly the cost of drugs (US$104.1) and costs, for consultation which were US$2.70. The average annual cost of controlling one patient with severe hypertension would therefore be US$ 106.80, whereby 97.5% of total costs is the cost of drugs and 2.5% for consultation Figure 1.1.

The second analysis of cost assumed that investigations are done only once at the start of treatment. According to this analysis the average costs would be US$ 170.2 per person per year. The cost of drugs (US $ 104.10) would account for 61.16% of total costs, while the cost of investigations (US$ 63.40) would account for 37.25% of the total costs. Costs for consultation contributing US $ 2.70 (1.59%).

The third analysis of costs assumed that investigations are repeated within the same year during follow up. Now the cost of investigations would be US$ 123.89 (53.70%). The total cost would therefore be US $ 230.70. Costs for investigations would therefore be as much as 53.70% of the total costs.

Is this component of the cost necessary? To answer this question I looked at the cost and outcome of investigations done among 100 patients in this study.

A the start of the study 10(10%) of the patients had abnormal urinalysis and/or elevated serum creatinine. For these 10 patients urinalysis and estimation of serum creatinine were repeated on receiving the results. Six persisted with abnormal levels on repeat test. Urine culture and sensitivity and abdominal ultrasound scan were done to these 6 patients. Only one patient was discovered to have renal stones, and 4 had features of chronic pyelonephritis. Out of 84 electrocardiograms done 48 (57%) showed clear evidence of left ventricular hypertrophy and one (1.2%) revealed an old anterior myocardial infarction and out of 79

repeat fasting blood glucose tests only 3 patients had their blood glucose levels in the diabetic range. Table 27.

To pick one patient with renal stones and 4 patients with chronic pyelonephritis therefore, I had to do 110 urinalysis and serum sample test for serum creatinine, six urine cultures, six abdominal ultrasound scan and one intravenous pyelography. These costed Tshs. 680,497.10 or US$ 1,215.17.

For the electrocardiogram it costed Tshs. 571,200.00 or US$ 1,020 to pick up 48 patients with left ventricular hypertrophy and one with an old anterior myocardial infarct. While 79 repeat fasting blood glucose estimation had to be done to pick 3 patients with diabetes mellitus. This costed Tshs. 250,114 or US $ 447. In none of the study patients did the investigations lead to a change of antihypertensive drugs.

Though this shows that investigations are very costly, yet some patients will require investigations. There is no clear rule as to who should be investigated and when. The decision on how and when to investigate will still remain in the hands of a well informed doctor, bearing in mind the cost implications of the decision to investigate.

Studies indicate that in other countries the treatment of hypertension is not cheap either. In the U.S. the direct cost of treating hypertension per year is between 8-10 billion dollars.[55] Drug costs alone constitute 70-80% of the total costs of treatment. In New Zealand by 1988 the total cost of treating hypertension per patient in the first year of diagnosis was sterling pounds 151 and pounds 135 for each subsequent year. Drug cost represented 85% of the first year costs and 96% of the cost in each subsequent year.[56]

Can the Government therefore afford to pay for the costs of treating severe hypertension?

The answer is almost certainly no. What we thought was cheap, is in fact not so. These three drugs are relatively cheap when we compare them with other antihypertensives. They

are also relatively cheap when we consider an individual choosing between a group of drugs. But they are not cheap when it comes to the government supplying them free of charge to all patients with severe hypertension. By retail price cost it will mean that almost the entire budget of the Ministry of Health, including salaries be used to treat a single condition in the country! However by government whole sale prices the cost is reduced by 69% but it is still 9 times the total ministry drug budget for treating all diseases.

Despite such enormous costs, how does it compare with newer drugs like Lomir (Isradipine). A maintenance dose of Lomir 2.5 mg a day cost Tshs. 400.00. The annual cost per patient will be Tshs. 144,000.00 or US$ 257. A one year supply for the entire population with severe hypertension in Tanzania will cost Tshs. 34,295,184,000.00 or US $ 61,241400.00. This is 2.3 times the retail cost of the study drugs while not being sure if we can achieve the same level of control with this dose. Therefore these three study drugs are relatively cheap in comparison with other drugs, but still very expensive for a poor government like ours to supply them free of charge.

Prescribers' Survey

Most prescribers agree that the diagnosis of hypertension should never be based on a single reading. Sixty five (94.2%) required at least 2 visits before the diagnosis was ascertained. Fifty three (81.5%) of the 65 responded that they required at least 3 visits to confirm the diagnosis. Therefore diagnosis of hypertension as stipulated by the guidelines, should never be a problem. What is needed is to keep reminding and emphasizing it to the prescribers. However, there was no consistency regarding the blood pressure level when they consider to start one on drug therapy. Forty five different choices were given. This indicating lack of agreement on when drug therapy is indicated. Such a response indicates that the treatment cut off level given in the guidelines is a new message. For this to make meaning, it needs to be communicated properly to prescribers. Adequate reasons being given to make them not

only get informed but also appreciate the sense in it. Otherwise it will be difficult to be practically followed.

The question of initiating therapy in a patient with less severe form of hypertension together with other risk factors or with less severe form of hypertension persisting despite adequate non-pharmacological measures, was not adequately addressed by the Tanzanian guidelines. It is therefore necessary that it becomes clarified simultaneously with the setting of a new cut off level for treatment.

It was interesting to note that in a place like Dar es Salaam, where there is a lot of advertisements on newer antihypertensive drugs, traditional antihypertensive drugs were still favoured. Drugs which scored the first five positions were frusemide, methyldopa, bendrofluazide, propranolol and Brinerdine. For unknown reasons hydrallazine was less favoured by all prescribers. Table 23. This eliminates the worry that in Dar es Salaam doctors will be in favour of newer expensive drugs.

Most prescribers also responded that investigations were vital in management of a new hypertensive patient. Urinalysis, serum creatinine, electrocardiogram, chest x-ray, electrolytes and renal ultrasound were selected as basic for every new patient. Table 24. Having realized the cost of investigations in hypertension, there is a need to educate prescribers so as to protect patients against unnecessary costs.

Hence when disseminating the guidelines, the opinion of prescribers will be vital. Where there is common agreement, like the number of visits before to confirmation of hypertension, it will need to remind and insist on. But where there is no agreement or knowledge, like about the blood pressure level at which drug therapy is indicated, a comprehensive programme to educate the prescribers will be necessary.

CONCLUSION

This study has demonstrated that the magnitude of hypertension among over hospital medical outpatients is already a large one. The prevalence is comparable to that reported in other African countries where it has been documented to be increasing. Targeting treatment to the severe form will reduce the number requiring treatment by 40%. By using bendrofluazide, propranolol and hydrallazine either singly or in combinations we can control the majority of our patients. It is however, difficult, to predict who will and who will not respond to these drugs. The great problem is that although these drugs seem relatively cheap, the cost of providing them freely by government to those in need is quite enormous amounting to over nine times the entire drug budget for treating all diseases.

But the evils of not treating severe hypertension are also great. Costing the nation dearly in terms of premature deaths, morbidity like strokes, heart failure and chronic renal failure. We therefore need to modify the proposed guidelines, to enable both the patient and the government to share and make this burden bearable.

RECOMMENDATIONS

1. Antihypertensive therapy be given only to those patients who have severe hypertension. It is in this group that reduction of diastolic blood pressure by 5-6 mmHg or systolic blood pressure by 10mmHg has been found to reduce strokes by 35-42% and coronary heart diseases by 14-25%. At Muhimbili medical outpatient clinics, treatment of those with severe hypertension will reduce the number of patients who requires treatment to 58%. Treatment cost are expected to be reduced by the same proportion.

   It should be noted however, that drug treatment of less severe forms of hypertension may be necessary in those with other risk factors apart from hypertension. Same consideration should include cases of failure of non-pharmacological therapy or hypertension associated with evidence of any target organ damage.

2. The government on its own will not be able to supply these drugs free of charge to all districts. The cost is too enormous. A plan must be worked out where the government and the patients contribute to accommodate the costs. This can be done as follows:-

a) Removal of all taxes from these three drugs.

b) These drugs should be imported and supplied by the Central Medical Stores department.

c) Generic preparations should be imported.

d) The drugs should be made available to private pharmacies, but at a fixed price throughout the country.

e) Patients should be able to buy the drugs at such subsidized prices.

d) Heavy penalties should be imposed on those who will hike prices for profit reasons.

3. Propranolol should be ordered and supplied in tablets of 80mg strength. This will increase compliance by reducing the number of tablets to be taken each day. Many patients will require high doses.

4. Investigations are very costly while they do not contribute much to the management of the patient. Yet it is difficult to give a cleat cut guide on when and which ones should be ordered. Hence doctors should be left to make the best judgement when the need for investigation arises. Routine investigations must be abandoned.

5. Current guidelines appear to include ideas which are new to prescribers, or the reasons for certain recommendations may not be easily understood. For example, from the survey findings, setting a cut off point for the treatment of hypertension is a new message. This needs to be properly communicated to all prescribers at all levels of practice. No journal in this country can fulfil such an obligation. Such a communication can be made as follows:

a) The Ministry of Health should hold seminars with Regional Medical Officers (RMOs), discuss the guidelines with them and make sure they appreciate and understand them. In the process some changes may need to be made to accommodate contributions from both sides.

b) The RMOs should then go, and discuss the guidelines with District Medical Officers, who, in turn, should discuss them with their staff at district level. In the process changes to accommodate local circumstances can be made.

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