KNOWLEDGE OF THE HYPERTENSIVE-ONLY AND THE HYPERTENSIVE-HIV PATIENTS ON HYPERTENSION AND THE ROLE OF PHARMACISTS IN THE PHARMACEUTICAL CARE OF THESE PATIENTS IN DAR-ES-SALAAM CITY

By

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A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Pharmacy (Hospital and Clinical Pharmacy) of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that she has read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled ***Knowledge of the hypertensive-only and the hypertensive-HIV patients on hypertension and the role of pharmacists in the pharmaceutical care of these patients in Dar-es-Salaam City***, in fulfillment of the requirements for the degree of Master of Pharmacy (Hospital and Clinical Pharmacy) of Muhimbili University of Health and Allied Sciences.

Dr. Kagashe G. A. B
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Date: 20th November, 2008

DECLARATION

AND

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I, **Sameera Abdulrazak Fazal**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature ..... Date..20th November, 2008

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ABSTRACT

SETTINGS

The study was conducted in public hypertension and HIV clinics, hospital and community pharmacies in Dar es Salaam.

OBJECTIVE

To assess the knowledge of the hypertensive-only and the hypertensive-HIV patients on hypertension; and the role of pharmacists in the pharmaceutical care of these patients in Dar-es-Salaam city.

DESIGN

Cross sectional descriptive study.

METHODOLOGY

Face to face interviews were conducted with the hypertensive-only, hypertensive-HIV patients and pharmacists working in hospital and community pharmacies. Convenience sampling method was used to select the patients and pharmacists. Sample sizes were chosen depending on the available time and resources. Hypertensive-only patients on anti-hypertensive medicines and hypertensive-HIV patients on both anti-hypertensive medicines and ARVs attending the clinics during the period of the study who consented to participate in the study were recruited. Pharmacists in hospital pharmacies where the clinics were situated and pharmacists in community pharmacies who consented to participate in the study were recruited.

RESULTS

A total of 200 hypertensive-only and 200 hypertensive-HIV patients were interviewed at the three district hospitals Temeke, Mwananyamala, Amana and one referral hospital Muhimbili. All of the hypertensive patients in both the groups knew the name of the disease they were suffering from. The hypertensive-only group knew more about symptoms of hypertension

than the hypertensive-HIV group. More than a half of the patients in both groups were not aware of the consequences of uncontrolled hypertension. Neither of the hypertensive-only nor the hypertensive-HIV patients knew the names of the anti-hypertensive medicines taken by them. However, they both reported to know about the types of lifestyle changes. CAM users were found to be a minority who did not know the types of CAM they were using.

Majority of the hypertensive-HIV patients reported missing out several doses of anti-hypertensive medicines in comparison to ARVs. Adverse drug reactions were reported significantly more when a combination of both ARVs and anti-hypertensive medicines were used together in comparison to when they were used alone. Fatigue and headache were reported significantly more in the hypertensive-HIV patients in comparison to the hypertensive-only patients. Fatigue and GIT disturbances were reported significantly more in the hypertensive-HIV patients who were using anti-hypertensive medicines before and now are using both ARVs and anti-hypertensive medicines in comparison to those who had been using ARVs before. Drowsiness, rash and nightmares were reported significantly more in patients who were on ARVs before and now are using a combination of both. Majority (86.5%) of the nifedipine users were using nevirapine as one of the ARVs combination therapy. About three quarters (78.13%) of these nifedipine and nevirapine combination users had their blood pressure readings not controlled.

Majority of the pharmacists (85%) could not correctly define hypertension nor classify the types of hypertension (91%) and they could also not mention more than three symptoms of hypertension. Around 90% of the pharmacists were not aware of the anti-hypertensive medicines contraindicated and useful in heart failure. 65% of the pharmacists were not aware of any drug interactions between anti-hypertensive medicines and other medicines. However, they were well versed with the goals of hypertension treatment (95%), complications of untreated hypertension (98%), causes of secondary hypertension (67%), risk factors of hypertension (90%), drugs which induce hypertension (73%) and anti-hypertensive medicines contraindicated in diabetes (59%) and asthma (75%). Most of them (90%) were not aware of

any HIV associated hypertensive problems due to ARVs and of any drug interactions with the ARVs and anti-hypertensive medicines (81%). It was also observed that pharmacists did not practice what they reported i.e they did not give any advice to the patients regarding the drug drug interactions or food drug interactions. They also did not give precautions on the side effects of the medicines.

No pharmacist was found to work in any of the hypertension clinics that were visited. Most of the counseling was done by the doctors and nurses. The pharmacist was not involved except in the HIV clinic where the pharmacist was involved in explaining the use and storage of the medicines to the HIV patients and very few of the patients found the pharmacists to be of any help to them.

CONCLUSION

There is a need to improve the patients' knowledge and awareness of hypertension so as to reduce the morbidity and mortality. An opportunity exists to focus patient education programs and interventions on the cardiovascular risks associated with uncontrolled hypertension. Monitoring of adverse drug reactions especially in the hypertensive-HIV patients is a matter of importance since these patients are usually using a lot of medications. The pharmacy profession is moving from purely product supply to a clinical and information supply role. At present, pharmacists are not fully integrated into the primary health care team. This is in part the fault of the profession and general practices for not making the most of the pharmacist's potential. Pharmacists' skills could be better used to help patients with their long term medicines. Thus, it is essential that pharmacists' knowledge should be updated regularly as they can play a major role in the society to improve the quality of life of the patients and thus reduce the morbidity and mortality of the disease.

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LIST OF ABBREVIATIONS

ACE	- Angiotensin Converting Enzyme
ADRs	- Adverse Drug Reactions
AIDS	- Acquired Immunodeficiency Syndrome
ARVs	- Antiretroviral's
CAM	- Complementary and Alternative Medicine
CDC	- Centres for disease Control and Prevention
CVD	- Cardio Vascular Disease
DASH	- Dietary Approaches to Stop Hypertension
GFR	- Glomerular Filtration Rate
GIT	- Gastro Intestinal Tract
HAART	- Highly Active Anti Retroviral Therapy
HIV	- Human Immunodeficiency Virus
HIVAN	- HIV-associated nephropathy
ISH	- International Society of Hypertension
JNC	- Joint National Committee
MNH	- Muhimbili National Hospital
MUHAS	- Muhimbili University of Health and Allied Sciences
NNRTI	- Non Nucleoside Reverse Transcriptase Inhibitor
NRTI	- Nucleoside Reverse Transcriptase Inhibitor
NHANES	- National Health and Nutrition Examination Survey
NSAIDs	- Non Steroidal Anti Inflammatory Drugs
PI	- Protease Inhibitors
SPSS	- Statistical Package for Social Sciences
WHO	- World Health Organisation

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1 Hypertension

Hypertension is a chronic health problem. The disease is usually symptomless but if left untreated it can cause heart attack, strokes, heart failure, renal failure and peripheral vascular diseases (these are diseases of blood vessels outside the heart and brain i.e narrowing of vessels that carry blood to the legs, arms, stomach or kidneys) and is thus called the "silent killer". The degree of hypertension is based on blood pressure measurement, a continuous variable, which fluctuates from minute to minute depending on the patient's mental and physical state and environmental factors [1].

The "Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure" classifies hypertension based on the average of two or more properly measured seated blood pressure readings on each of two or more office visits. A new category designated prehypertension has been added, and stages 2 and 3 hypertension have been combined as shown in the table below which provides a classification of blood pressure for adults ages 18 and older. Patients with prehypertension are at increased risk for progression to hypertension; those in the 130–139/80–89 mmHg blood pressure range are at twice the risk to develop hypertension as those with lower values. [2] High blood pressure is systolic blood pressure (SBP) $\geq$ 140 mmHg or diastolic blood pressure (DBP) $\geq$ 90 mmHg or taking anti-hypertensive medication. [3]

Hypertension is characterized by increased total peripheral resistance due to arteriolar vasoconstriction and wall thickening leading to raised systemic blood pressure.

Table 1: Classification of blood pressure for adults

Blood Pressure classification	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)
Normal	< 120	And < 80
Prehypertension	120-139	Or 80-89
Stage 1 hypertension	140-159	Or 90-99
Stage 2 hypertension	≥160	or ≥100

1.1.1 Epidemiology

Hypertension occurs in 10-20% of middle aged adults in developed countries and the prevalence tends to increase with increasing age. [1] Primary or essential hypertension accounts for approximately 95% of the hypertensive population, the remainder consisting of patients with secondary hypertension [1].

A review of recent community-based studies on the prevalence of hypertension in different regions of the world has concluded that the true global prevalence of hypertension is approximately 30% [4].

The latest estimate of the World Health Organization (WHO) is that more than 30 million people in Africa have hypertension. WHO predicts that if nothing is done about it, by 2020 three quarters of all deaths in Africa will be attributable to hypertension. It has been documented that the African Union has called hypertension "one of the continent's greatest health challenges after AIDS."[5, 6]

In Tanzania, studies conducted in rural areas showed the prevalence of hypertension to range between 3.0-12.8% [7].

The overall prevalence of hypertension was found to be 41.1% in 1998, for men and 38.7% for women in a survey carried out in Dar es Salaam (urban), Handeni (rural) and Monduli (semi-nomadic area) [8]. A cross sectional survey by others, in Temeke, revealed that in spite of a relatively high rate of hypertension in the area over 80% of the hypertensive subjects were not aware that they had high blood pressure [8].

Untreated hypertension can cause a variety of problems. One of the organs affected is the heart predisposing to heart attacks and heart failure. It also predisposes to occlusion or rupture of blood vessels in the brain leading to stroke. Stroke mortality was found to be several times more frequent in Dar-es-Salaam than in England. [9] Urban women are particularly at risk from stroke. High rate of stroke mortality was postulated to relate to high levels of blood pressure, under detection of high blood pressure and poor management and control of those diagnosed with the disease [9].

1.1.2 Types Of Hypertension

There are three types of hypertension and these include:

1) Primary hypertension
2) Secondary hypertension
3) Malignant or accelerated phase hypertension

1) Primary Hypertension

Primary hypertension also known as essential hypertension has no single identifiable cause but may be caused by a number of factors:

Age- Blood pressure tends to increase with increasing age. This is probably due to decreased compliance of the blood vessels, which leads to an alteration in peripheral resistance and hence an increase in blood pressure [1].

Genetics- There is a tendency for hypertension to run in families. The link between genetics and hypertension is quite well established e.g greater expression of enzymes such as angiotensin converting enzyme in black people compared to Caucasians or salt sensitivity. [1]

Environment

Stress- mental and physical stress causes transient increases in blood pressure. This effect is not generally sustained, and taking the hypertensive individual out of the stressful environment does not always result in a decreased blood pressure.

Diet - sodium intake and its effect on blood pressure is an area that remains controversial. Severe dietary sodium restriction in patients who usually have a high salt intake, does lead to a beneficial drop in blood pressure. However, reducing salt intake in patients whose consumption is not high does not have the same effect [1].

Alcohol- patients who drink large amounts of alcohol have a raised blood pressure, which will fall if alcohol consumption is reduced. Patients who drink no alcohol at all tend to have slightly higher blood pressures than those who drink in moderation [1].

Weight- obese patients have higher blood pressures than non obese patients, and weight reduction can lead to a decrease.

2) Secondary Hypertension

"Secondary hypertension" refers to high blood pressure with recognizable causes. The resulting high blood pressure can often be cured or controlled by eliminating the underlying problem.

Some of the more common causes of secondary hypertension include:

a) Renal disease such as glomerulonephritis, diabetic nephrosclerosis, polycystic kidneys, renal artery stenosis, chronic pyelonephritis, and renin secreting tumours

b) Drug induced hypertension - Drugs such as: corticosteroids, non steroidal anti-inflammatory drugs (NSAIDs), cold medicines, and birth control pills can cause temporary high blood pressure. [10]

c) Endocrine disorders - There are also several disorders of the adrenal glands and other glands that can cause high blood pressure such as: Hyperaldosteronism or Conn's syndrome, Cushing's syndrome, and phaeochromocytoma

3) Malignant or accelerated phase hypertension

This can occur in patients with primary or secondary hypertension and is often associated with renovascular disease. It is characterized by a rapid rise in blood pressure with associated damage to small blood vessels that is seen most markedly in the eye and appears as retinal exudates. The kidney is also damaged leading to haematuria and proteinuria.

The condition is usually seen in younger patients and is closely associated with smoking. If left untreated, 90% of patients will die within 1 year. The long term prognosis depends on the success of treatment in limiting end organ damage, particularly in the kidney [1].

1.1.3 Pathophysiology

Blood pressure is the product of cardiac output and peripheral resistance. If the output from the heart rises but the resistance from the small blood vessels remains the same then the blood pressure will rise. However, in most patients with essential hypertension the peripheral resistance increases whilst cardiac output remains the same. Peripheral resistance comprises several components that include the viscosity of the blood and the diameter and compliance of the blood vessels. High-viscosity blood will require a higher blood pressure in order to force it through the vascular bed. A high pressure is also needed to push blood through constricted and non-compliant blood vessels.

A variety of mechanisms exist to maintain normal blood pressure control, two of which are susceptible to drug therapy. Blood pressure mainly falls under the control of the sympathetic nervous system. Peripheral baroreceptors detect changes in the blood pressure and send appropriate messages to the cardiovascular centre in the medulla of the brain. This, in turn, triggers nerves, leading to a change in circulating blood pressure. Stimulation of β_1 adrenoreceptors increases the heart rate. In the blood vessels stimulation of β_2 adrenoreceptors will cause dilatation, whilst stimulation of α adrenoreceptors causes vasoconstriction.

The kidney also plays a major role in blood pressure regulation, through the renin-angiotensin system. Renin is released from the juxtaglomerular apparatus in the kidney, when a reduction in serum sodium concentration or blood volume is detected. Renin acts on angiotensinogen to release angiotensin I, which is converted by angiotensin converting enzyme (ACE) to angiotensin II. Angiotensin II produces a potent rise in blood pressure through several routes, including vasoconstriction, stimulation of the noradrenergic sympathetic nervous system and stimulation of the adrenals to release aldosterone. A similar renin-angiotensin system has been detected in the blood vessel walls, where it is probably mainly responsible for local vasoconstriction [1].

1.1.4 Treatment of Hypertension

Goals of Therapy

The aim of treatment is to reduce the blood pressure to a normal level, thereby reducing the risk of suffering a cerebrovascular accident or a cardiovascular event, and to prevent organ damage. [11].

Therapeutic Choices

a) Non Pharmacological choices

Adoption of healthy lifestyles by all persons is critical for the prevention of high blood pressure and is an indispensable part of the management of those with hypertension.

Treatment of mild hypertension is usually started with non pharmacological measures which comprise of the following [11]:

- Weight reduction/diet.
- Decreased alcohol intake (for those who consume > 21 unit per week for men; > 14 unit per week for women).
- Decreased salt intake to < 6 mg per day.
- Increased regular physical activity: brisk walk or swim for 30-45 mins; 3-4 times a week. Strenuous exercises and isometric exercises eg. Weight lifting should be avoided.
- Smoking cessation and reduced dietary saturated fat and cholesterol intake.
- Stress reduction (relaxation).
- Increased dietary potassium, calcium, and magnesium intake should be maintained adequately. Adoption of the Dietary Approaches to Stop Hypertension (DASH) eating plan which is rich in calcium and potassium.
- A diet with increased fresh fruit, vegetables, and fish intake.
- Reduction in caffeine intake.

b) Pharmacologic choices

The JNC (Joint National Committee) in USA, the WHO/ISH (World Health Organisation / International Society of Hypertension) guidelines and the Tanzanian guidelines for the management of hypertension recommend that pharmacologic interventions should be instituted 3-6 months after the attempt of lifestyle modifications has not proven satisfactory, or sooner if the blood pressure is at a level not normally responsive to lifestyle modifications alone.

If general measures are not sufficient to control blood pressure, a stepwise approach by the physician to the treatment of essential hypertension is recommended starting with a diuretic, then a β-adrenoceptor blocker, then a combination of the two, with the addition of a vasodilator if the combination is not effective. A minimum of 8 weeks is needed at each step to evaluate the effect of the chosen treatment [11, 12].

Classes of anti-hypertensive medicines

1. Diuretics
2. Beta blockers
3. Angiotensin Converting Enzyme Inhibitors
4. Angiotensin II Receptor blockers
5. Calcium channel blockers
6. Alpha blockers
7. Centrally acting agents
8. Vasodilators

Choice of anti-hypertensive medicines

All medicine classes are suitable for the initiation and maintenance of hypertension therapy, but the choice of medicines will be influenced by [13]:-

- Socio-economic factors that determine medicine availability to the patient
  -available funding from government, employers and individuals.

-cost of medicines.
-efficiency in distribution of medicines to pharmacies.

- The cardiovascular risk factor profile of the individual patient ie. Cigarette smoking, hypertension, obesity, physical inactivity, dyslipidemia, diabetes mellitus, microalbuminuria or estimated GFR < 60 ml/min.

- The presence of target organ damage, clinical cardiovascular disease.

Major consequences of untreated Hypertension

- Accelerated atherosclerosis: peripheral and coronary artery disease, ischemic stroke, ischemic nephropathy and retinopathy.
- Haemodynamic complications: heart failure, haemorrhagic stroke, aortic dissection and encephalopathy.
- Death

1.2 Hypertension in HIV patients

Human Immunodeficiency Virus (HIV) is a retrovirus that causes *Acquired Immunodeficiency Syndrome* (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections.

HIV infection in humans is now pandemic. As of January 2006, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimate that AIDS has killed more than 25 million people since it was first recognized on December 1, 1981 by the United States Centre for Disease Control and Prevention, making it one of the most destructive pandemics in recorded history [14]. According to current estimates, HIV is set to infect 90 million people in Africa, resulting in a minimum estimate of 18 million orphans [14]. In 2005, around 1.3 million Tanzanians between the ages of 15-49 were living with HIV/AIDS.

The introduction of a Highly Active Anti Retroviral Therapy (HAART) in the treatment of HIV disease has provided gratifying results, like long-term viral suppression, decrease of opportunistic infections, repair of the immune system and increased CD4 cell counts. As a result, morbidity and mortality of HIV-infected patients continue to decline [15]. Several studies have shown that the use of HAART is frequently associated with metabolic disorders, such as hyperlipidaemia, impaired glucose tolerance and body shape changes, like visceral fat accumulation (lipodystrophy syndrome) [16,17]. As these metabolic complications may lead to premature and accelerated atherosclerosis, there is growing concern that cardiovascular disease is becoming more prevalent in this population [17]. Specific treatment of these problems will become increasingly important to further decrease long-term morbidity and premature mortality in HIV infected patients. Hypertension is one of the major risk factors for premature cardiovascular disease. While systemic hypertension was quite uncommon in HIV infected subjects prior to HAART [18], newer data suggest that younger HIV infected patients are at a higher risk for developing hypertension compared with the general population, especially if a protease inhibitor was included in the HAART regimen [17].

The prevalence of hypertension in the HIV-infected population is estimated to be around 13.1%. [19] Estimates suggest that the prevalence of hypertension in the HIV-infected population before the introduction of HAART was similar to that of the general population (between 20% and 25%) [20]. The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) study evaluated baseline data from 17,852 subjects in the HAART era and observed that more than 8% of the study population had hypertension [17]. Other results from this cross-sectional, multicenter study revealed that traditional cardiovascular risk factors, such as tobacco use, dyslipidemia, and family history of coronary heart disease, are prevalent among patients on HAART. The presence of these powerful cardiac risk factors further emphasizes the importance of treating hypertension in HIV-infected patients.

The relationship between HAART and blood pressure has not been carefully studied, and existing data do not consistently demonstrate that HAART routinely raises blood pressure.

However several studies have shown that the drugs used to treat HIV may exacerbate cardiac risk factors such as hyperlipidemia, insulin resistance, and increased visceral fat [17].

Fortunately, treatment of hypertension can reduce its associated risks eg. anti-hypertensive therapy reduces the risk of stroke by approximately 35%, congestive heart failure by 42%, and coronary heart disease by 28%. [21-24] Since renal diseases such as HIV-associated nephropathy (HIVAN) are prevalent in the HIV-infected population, it is noted that adequate control of high blood pressure can delay progression of kidney dysfunction. Therefore, an important key to reducing the burden of hypertension-related CVD and chronic kidney disease is to increase the proportion of HIV-infected patients who achieve adequate control of their blood pressure, an important goal for HIV-infected patients, who are now living much longer than ever before.

1.2.1 Management of hypertension in the HIV-infected patients

The medical literature gives no indication that HIV-infected patients with hypertension or pre-hypertension should be managed in a way other than that recommended in the standard treatment guidelines. [3] For patients with stage 1 or 2 uncomplicated hypertension, the target blood pressure level is < 140/90 mm Hg. In HIV patients with comorbidities such as diabetes or chronic kidney disease, a target blood pressure level of < 130/80 mm Hg is recommended. [25] More aggressive management is also advised for persons with "end organ" damaging diseases. It has been reported that one could consider HIV/AIDS to be a potential "end organ" disease with its propensity for nephropathy, neuropathy and retinopathy.

Lifestyle modification, initially for the treatment of hypertension, an indispensable part of hypertension management that is recommended for all hypertensive patients, is the only intervention recommended for pre-hypertension. This includes sodium restriction, decreased alcohol consumption, and other lifestyle changes including diet and exercise. It has been documented that often a weight reduction of as little as 5 or 10 pounds can reduce blood pressure to an acceptable range. Though HIV makes a person to loose weight, it has been

documented that weight reduction in persons with HIV infection, only if judged safe, must be accomplised in a reasonably paced manner with adequate nutrition and realistic exercise according to the severity of the HIV condition. Even with lifestyle changes a majority of patients will still require anti-hypertensive drug therapy.

If a patient continues to be hypertensive after a trial of lifestyle modification, anti-hypertensive drugs may be used.

1.2.2 Anti-hypertensive agents with Anti-retroviral agents

Drug drug interactions with anti-hypertensive medicines and anti-retroviral agents are of importance to the HIV provider. Anti-retroviral medications may accelerate or retard the metabolism of anti-hypertensive medicines that share the same metabolic pathways of the cytochrome P450 system. P450 cytochromes that are of particular offense are CYP2D6 and CYP3A. [26] It has been recommended specifically, that clinical effects of anti-hypertensives, especially calcium channel blockers, should be closely monitored in the person on anti-retroviral medication. [26] Calcium channel blockers should be avoided because they have been reported to interact with protease inhibitors (PI's). For example, the potential increase in serum concentrations of a calcium channel blocker during concomitant use of ritonavir or atazanavir could lead to hypotension and bradycardia [27]. On the other hand, serum concentrations of a calcium channel blocker can be decreased by non nucleoside reverse transcriptase inhibitors (NNRTI's) like nevirapine and effavirenz, leading to high blood pressure and tachycardia. [28]

Beta-blocker serum levels have also been known to be altered in patients receiving PI's. For example, atenolol levels are increased in patients taking atazanavir, and the beta blocker effects of metoprolol may be enhanced in those receiving ritonavir [27-29]. Carvedilol with NNRTI's such as effavirenz and nevirapine show potential drug interaction that requires close monitoring, alteration of drug dosage or timing of administration. There is not much

documentation on the potential drug-drug interaction between the nucleoside reverse transcriptase inhibitors (NRTI's) and the anti-hypertensive drugs.

Nephrolithiasis is a well-established complication of indinavir therapy. Since volume depletion is a known risk factor for the development of kidney stones, diuretics should be used with extreme caution in patients receiving indinavir. [30]

One final challenge to the HIV care provider whose patient also has hypertension is intermittent close monitoring for blood pressure readings, laboratory monitoring, and adverse reaction monitoring related to anti-hypertensive medications.

1.3 Use Of Complementary and Alternative Medicine (CAM)

There has been very little research on interactions between herbal products and anti-HIV medications. Recent studies have shown that St. John's Wort and garlic can both reduce blood levels of anti-retrovirals. [31-33] Many people with HIV are taking other medications in addition to HAART. These can include antibiotics, medications for high blood pressure, heart conditions, depression and diabetes to name a few, thus there is a potential for significant interactions. HIV care providers have to be aware of interactions between HAART and herbal remedies some of which even have the potential to elevate blood pressure. Ginseng which offers increased vitality and is often suggested to persons with HIV has been associated with episodes of hypertension as has Ma-Huang for "energy". [34] Ma-Huang is often the herbal of choice for truck drivers as it is the natural source of ephedra. [34] *Glycyrrhiza glabra* (liquorice) is an herbal expectorant and treatment for gastritis and gastric ulcer. It is also a treatment for viral liver inflammation. Its juice may work as an antiviral agent by means of interferon induction. Glycyrrhiza can increase potassium loss with thiazide diuretics. It also increases the half-life of cortisol which can lead to symptoms of high blood pressure, low serum potassium and edema. [35-38]

It has been documented that some people have been hurt or killed directly from the various practices or indirectly by failed diagnoses or the subsequent avoidance of conventional medicine which they believe is truly inefficacious. [39] A study conducted on the use of alternative medicine revealed death rates to be 30% higher in those who were using alternative medicine [40]. A report in Australia showed that a patient almost bled to death on the operating table due to failure to mention that she was using alternative medicine for building up her strength- the herb turned out to be a powerful anticoagulant which nearly caused her death. [41] Conventional treatments are thoroughly checked for adverse drug reactions, whereas alternative treatments are normally not. Any alternative treatment that has a biological or psychological impact may also have potentially dangerous biological or psychological side-effects. Many natural products such as ginkgo extracts, lobelia, and St. John's Wort can have serious side effects or interactions with other drugs. Some supposedly herbal products have been found to contain potent Western medicines. Others have been contaminated with poisons such as lead [41].

Alternative medicine may instantly make problems better, but actually worsen problems in the long run. The result may be addiction and deteriorating health [41].

1.4 Pharmacist and Hypertension care

Over the past four decades there has been a trend for pharmacy practice to move away from its original focus on medicine supply towards a more inclusive focus on patient care. The role of the pharmacist has evolved from that of a compounder and supplier of pharmaceutical products towards that of a provider of services and information and ultimately that of a provider of patient care. Increasingly, the pharmacist's task is to ensure that a patient's drug therapy is appropriately indicated, the most effective available, the safest possible, and convenient for the patient. By taking direct responsibility for individual patient's medicine-related needs, pharmacists can make a unique contribution to the outcome of drug therapy and to their patients' quality of life. The new approach has been given the name pharmaceutical care. Pharmaceutical care is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve or maintain a patient's quality of life. [42]

At present, pharmacists are not fully integrated into the primary health care team - this is in part the fault of the profession and in part the fault of primary care trusts and general practices for not making the most of the pharmacist's potential. Pharmacists' skills could be better used to help patients with their long term medicines.

As the experts in medicines, pharmacists have always been known as an accessible and trusted source of advice and treatment. Today, their contribution to health care is developing in new ways to support patients in their use of medicines and as a part of clinical decision-making across the range of specialities. They are the key point of contact in the pharmaceutical delivery chain; therefore they play an active role in providing information and advice on medications or potential drug interactions. They are also one of the most accessible health professionals and work closely with patients to assist them with managing their medicines and disease states as well as improving the quality of life.

Many people with hypertension are unaware that they have the disease. The pharmacist can play an important role by increasing public awareness of the risk factors of hypertension. For

those who are aware that they have the disease, the pharmacist can counsel them on the best use of their medications and providing advice on the symptoms and other life style modifications for a healthy life. Pharmacists are also able to identify drug related problems. For example, drugs used to treat HIV may exacerbate cardiac risk factors such as hypertension, and also the clinician must be aware of some pitfalls when treating hypertension in HIV-infected patients. This important information can be provided by a collaborative relationship with the pharmacist. They therefore become the basis for teamwork in resolving these problems. The pharmacist also reinforces the knowledge about medication and diseases given to patients by other healthcare staff each time a prescription is dispensed. Therefore, by assuming the role of patient educator, counselor, and drug information specialist to patients and physicians, the pharmacist, creates a niche in the health care delivery system in the management of patients with hypertension.

Another area in which pharmacists can help patients is in encouraging compliance. Issues can arise with both intentional non-compliance and non-intentional non-compliance. In intentional non-compliance, the patient has made a decision not to take a treatment. This may be an informed decision or it may be that the patient is misinformed or does not have the correct information. With education and advice, the pharmacist might be able to change the patient's behaviour. Non-intentional non-compliance is a major problem and arises when, for example, the patient forgets to take their medicine or becomes confused by their polypharmacy. Advice can be offered on making the medication regime simple for patients. Some non-compliance relates to such basic issues as the patient not being able to open the medicine container.

Several studies conducted on the involvement of pharmacists in the management of hypertension have shown that blood pressure control could be improved when pharmacists assisted with patient education, blood pressure monitoring, drug therapy management, and compliance assessment. [43, 44] It has also been shown that when pharmacists are closely involved in the co-management of patients with hypertension, greater reductions in blood

pressure are recorded, goal blood pressures are reached and maintained more frequently, patient quality of life is improved, and more patients remain adherent to their medication regimens. [45] In addition, when pharmacists become an integrated part of the primary care team, overall costs of therapy are better contained without sacrificing the quality of care [45]. Studies have also demonstrated that clinical pharmacy services are highly beneficial and enhance long term care given to hypertensive patients [45].

2.0 STATEMENT OF THE PROBLEM

Until relatively recently hypertension was considered to be a disease of the industrialised world. However, several studies conducted in Tanzania have shown that hypertension is a major problem particularly amongst urban dwellers. [46] In fact for blue collar office workers epidemiological surveys have given prevalence of 30-40% in Dar-es-Salaam. [47] With urbanisation Tanzania is increasingly being subjected to changes in lifestyle; shifts from a subsistence rural life to non farming occupations in the cities are unfortunately leading to changes in dietary habits and a reduction in physical activity that seem to increase the risk of hypertension and other cardiovascular diseases. [48]

Tanzania also has a high population of HIV infected individuals. The United Nations in 2005 estimated that 6.5% of adults around 1.3 million Tanzanians between the ages of 15–49 were living with HIV/AIDS. [49] The great strides made in developing effective anti-retroviral therapy have substantially reduced the burden of HIV disease; consequently, HIV – infected patients are living longer, and their clinicians have to focus on diseases and conditions that typically affect the middle aged, non-HIV-infected population, such as hypertension, the risk factor for cardiovascular disease [16].

The prevalence of hypertension in the HIV-infected population is around 13.1% [19] and those on HAART is around 21%. [20] Longer term assessments by health care providers have revealed patterns of elevated blood pressure in people with HIV. [26] There is concern as to whether the incidence of hypertension may become increased as compared to that of the general population in persons with HIV on anti-retroviral therapy. Metabolic complications such as hyperlipidemia and elevated blood glucose (including decreased control of existing diabetes mellitus as well as new onset diabetes mellitus) in HIV-infected patients have been associated with anti-retroviral therapy. Hyperlipidemia and diabetes have been associated with vascular changes and hypertension in those separate disease states. Theoretically, there could be an association between the metabolic complications of anti-retroviral therapy and the decreased control of existing hypertension or the onset of newly diagnosed hypertension.

This further emphasizes the importance of treating hypertension in HIV-infected patients. Renal diseases such as HIV-associated nephropathy are prevalent in the HIV-infected population, it is important to note that adequate control of high blood pressure can delay progression of kidney dysfunction [24].

Patients who are hypertensive-only and those with both hypertension and HIV are likely to be receiving multiple drug therapy for several medical problems from complications associated with the disease. Thus, these patients strongly need intervention by a pharmacist.

It has been observed especially in Tanzania in public health facilities or clinics, that a pharmacist is not part of the health worker team who provide comprehensive care to hypertensive patients. [50] Thus, the patients are deprived of the useful information regarding their dietary habits, necessary lifestyle modifications, proper use of their medication, and knowledge about their disease. Patients are losing out on the necessary information which would have improved their adherence to medicines and enabled the patient to live a much more comfortable, normal and healthy life. A gap is observed between the patient and the pharmacist. [50]

The various complications which result due to multiple drug therapy in these patients have not been determined. In addition, the involvement of the pharmacist in the management of these patients in Tanzania has not been assessed.

This study therefore focused on the assessment of the knowledge of the hypertensive-only and hypertensive-HIV patients on hypertension. The involvement of pharmacists in the counselling of these patients was assessed as well. The study also tried to find out if these patients use CAM and the types used. In addition, it also assessed problems which were encountered by both groups of patients when using anti-hypertensive and ARV medicines alone or in combination and when both groups were using conventional and CAM together. Assessment of the knowledge of pharmacists on hypertension and cardiovascular effects due

to ARVs was done as well. This cross sectional descriptive study was carried out for a period of three months beginning from 1st July to 30th September, 2007.

3.0 STUDY OBJECTIVES AND RESEARCH QUESTIONS

3.1 Broad objective:

To assess the knowledge of the hypertensive-only and the hypertensive-HIV patients on hypertension; and the role of pharmacists in the pharmaceutical care of these patients in Dar-es-Salaam city.

3.2 Specific objectives:

- ✓ To assess the knowledge of the hypertensive-only and the hypertensive-HIV patients on hypertension.
- ✓ To find out the problems faced by the hypertensive-HIV patients taking anti-hypertensive drugs and ARVs.
- ✓ To find out the problems faced by the hypertensive-only patients on anti-hypertensive drugs.
- ✓ To find out if the hypertensive-only and hypertensive-HIV patients use CAM.
- ✓ To assess the knowledge of pharmacists on hypertension and anti-hypertensive agents.
- ✓ To find out if the pharmacists are involved in the counselling of the hypertensive-only and hypertensive-HIV patients on their disease and medication.
- ✓ To find out if the pharmacists are knowledgeable on HIV-associated hypertensive problems.

3.3 Research questions:

- ✓ Do the hypertensive-only and hypertensive-HIV patients know about their disease and medication?
- ✓ What problems are faced by the hypertensive-HIV patients when on anti-hypertensive medicines and ARVs alone and in combination?
- ✓ What problems are faced by the hypertensive-only patients on anti-hypertensive medicines?
- ✓ Is CAM being used by the hypertensive-only and the hypertensive-HIV patients?
- ✓ How much knowledge do pharmacists have about hypertension and the anti-hypertensive medicines?
- ✓ Are the pharmacists involved in the counselling of both groups of these patients on their disease and medication?
- ✓ Are pharmacists knowledgeable on HIV-associated hypertensive problems?

4.0 METHODOLOGY:

This study was conducted at the hypertension and the HIV clinics in Dar-es-Salaam at the government hospitals and community pharmacies. Both the hypertensive-only and the hypertensive-HIV patients were interviewed using questionnaires after consultation with the doctor. Pharmacists were also interviewed using a self filled questionnaire in both the hospital and community pharmacies. The way the pharmacist performs his/her duties which include the counselling sessions and the dispensing of medicines was observed in hospitals using a checklist which is shown in Appendix E.

4.1 Study area:

This study was conducted in the city of Dar-es-Salaam in both hypertension and HIV clinics at government hospitals. These clinics include one at each district hospital (Amana, Temeke, and Mwananyamala) and at Muhimbili National Hospital which is also a referral hospital. The study was conducted in 4 hospitals, and in community pharmacies.

4.2 Study design:

A cross sectional descriptive study was carried out for a period of three months beginning from 1st July to 30th September 2007. Convenience sampling method was used to select the patients and pharmacists. Sample sizes were chosen depending on the available time and resources. Hypertensive-only patients on anti-hypertensive medicines and hypertensive-HIV patients on both anti-hypertensive medicines and ARVs attending the clinics during the period of the study who consented to participate in the study were recruited. Pharmacists in hospital pharmacies where the clinics were situated and pharmacists in community pharmacies who consented to participate in the study were recruited.

4.3 Study population:

The following subjects were studied:

- Pharmacists in community pharmacies and pharmacists in hospital pharmacies where the clinics were situated.

- Hypertensive-only patients on anti-hypertensive medicines and hypertensive-HIV patients on both anti-hypertensive medicines and ARVs at the clinics.

4.4 Sampling procedure:

Convenience sampling method was used.

4.5 Sample size:

Sample sizes were chosen depending on the available time and resources. The face to face interviews using questionnaires with all subjects was conducted in Dar-es-Salaam city in the four government hospitals.

The formula; $n = \frac{4p(100-p)}{\varepsilon^2}$ was used

Where,

n = minimum number of patients to be interviewed

ε = margin of error

p = proportion of hypertensive patients who know about their medication

a) Patient's sample size

The proportion of hypertensive patients who know about their disease or about their medication in Dar-es-Salaam is not known, therefore it was assumed that 50% of patients know about their disease and medication and therefore p was set at 50% (that is p = 50%)

n = minimum number of patients to be interviewed

ε = margin of error = 0.05 = 5%

p = proportion of hypertensive patients who know about their medication

Therefore; $n = \frac{4 \times 50(100-50)}{5^2}$

= 400 Patients

ie. 200 hypertensive-only patients and 200 hypertensive-HIV patients

b) Pharmacists sample size

n = minimum number of pharmacists to be studied

ε = margin of error = 0.10 = 10 %

p = proportion of pharmacists who know about hypertension and anti-hypertensive drugs is not known and therefore was assumed that 50% of pharmacists know about hypertension and anti-hypertensive drugs.

Therefore; $n = \frac{4 \times 50\ (100-50)}{10^2}$

= 100 Pharmacists

4.6 Inclusion criteria:

- ✓ Hypertensive-only and hypertensive-HIV patients attending clinics during the period of the study.
- ✓ Hypertensive-only patients on anti-hypertensive medicines.
- ✓ Hypertensive-HIV patients on both ARVs and anti-hypertensive medicines.

4.7 Exclusion criteria

All those who were not willing to participate, children, pregnant women and those not using medications were excluded from the study.

4.8 Study instrument

Three questionnaires were used and a different questionnaire was used for each group.

Hypertensive-only patient questionnaire → shown in Appendix A

Hypertensive-HIV patient questionnaire → shown in Appendix B

Pharmacist questionnaire → shown in Appendix C

Questionnaires consisted mostly of close-ended questions so as to enable getting specific responses.

A checklist was used for observational study → shown in Appendix E

4.9 Data handling

The computer was used for the immediate transfer of data from the questionnaire form to computer file Epi Info version 2002, a soft ware package developed by the WHO and Centres for disease Control and Prevention (CDC). The Statistical Package for Social Sciences (SPSS) version 11.5 for Windows was then used for data analysis.

4.10 Ethical aspects

Ethical clearance was obtained from the ethical committee of the Muhimbili University of Health and Allied Sciences (MUHAS).

- Verbal consent was obtained from all the respondents refer → Appendix D.
- Details of the research were explained and sufficient time of around 20 minutes was allocated to the subjects to decide whether or not to participate in the study.

5.0 RESULTS

A total of 400 patients were interviewed 200 of which were the hypertensive-only patients and the other 200 were the hypertensive-HIV patients at the three district hospitals Temeke, Amana, Mwananyamala and one referral hospital Muhimbili.

5.1 i) Demographic Characteristics

Table 2: Social demographic characteristics of the 200 hypertensive-only and the 200 hypertensive-HIV patients

	Hypertensive-only Patients		Hypertensive-HIV patients	
Variable	**Frequency**	**Percentage(%)**	**Frequency**	**Percentage(%)**
Age group(yrs)				
<40	12	6	52	26
40-59	93	46.5	122	61
60+	95	47.5	26	13
Sex				
Male	69	35.5	62	31
Female	131	65.5	138	69
Education level				
Non formal	74	37	44	22
Primary	98	49	116	58
Secondary	21	10.5	36	18
Post secondary	7	3.5	4	2
Occupation				
Employed	58	29	84	42
Unemployed	142	71	116	58

The majority of the hypertensive-only patients were found in the age group 40-59 and 60+ though 60+ were higher by a percent. Whereas, the majority of hypertensive-HIV patients (61%) were mainly found in the middle aged (40-59) group. The mean age for the hypertensive-only patients was 57.78 years (range of 27 to 102 years) and for the

hypertensive-HIV patients was 47.06 years (range of 21 to 80 years). The male / female ratio was lower in each group with females being twice as many as males. This finding was comparable in both groups. The majority in respective groups of the subjects had primary level education and more than a half of the subjects in both groups (71% and 58%) were unemployed. (Table 2)

5.2 ii) Knowledge and awareness of Hypertension

Patients were asked several questions about hypertension, manifestation of acute and chronic complications, consequences of uncontrolled hypertension and the type of treatment used. Their responses are shown in Table 3.

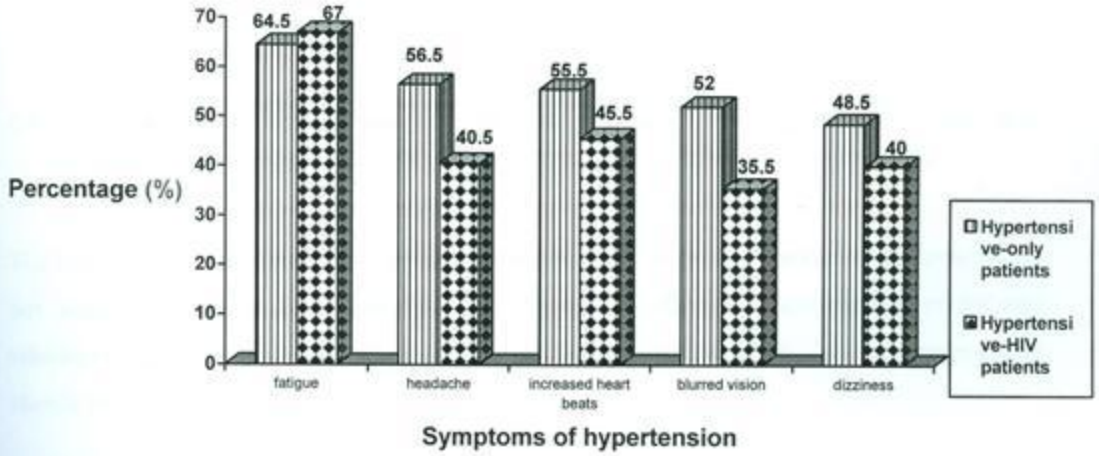
Table 3: Knowledge and awareness of hypertension in the hypertensive-only (n=200) and hypertensive-HIV subjects (n=200)

	Hypertensive-only subjects		Hypertensive-HIV subjects	
Knowledge on:	**Freq.**	**%**	**Freq.**	**%**
Name of disease	200	100	200	100
Symptoms of hypertension	120	60	96	48
Consequences of untreated hypertension	81	40.5	58	29
Names of anti-hypertensive medicines	48	24	26	13
Source of Information on hypertension				
Peer	142	71	152	76
Media	13	6.5	45	22.5
Formal education	1	0.5	-	-

All of the hypertensive patients in both the groups knew the name of the disease they were suffering from. Only a few knew the names of the medicines they were using. The biggest source of information on hypertension was from the peer groups. All these are shown in Table 3.

The level of knowledge on the symptoms of hypertension was significantly higher in the hypertensive-only group (60%) in comparison to the hypertensive-HIV group (48%) (chi square = 5.79; $p < 0.05$; df = 1). The most mentioned symptoms by both groups are indicated in Figure 1.

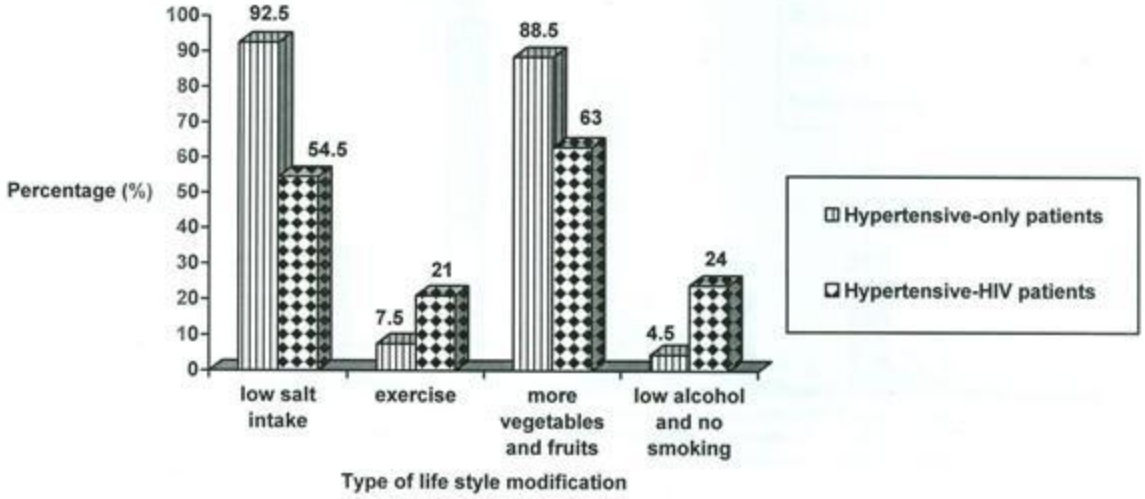
Figure 1: Common symptoms as mentioned by the hypertensive-only and hypertensive-HIV patients



More than a half of the subjects in both groups (hypertensive-only 59.5% and hypertensive-HIV 71%) were not aware of the consequences of uncontrolled / untreated hypertension. (Table 3)

Both groups reported to be informed on the types of lifestyle modification. The most prevalent reported lifestyle changes were as shown in Figure 2.

Figure 2: Advice on the type of lifestyle modification



5.3 Involvement of pharmacists in the counselling of the hypertensive-only and hypertensive-HIV patients

The hypertensive-only and the hypertensive-HIV patients were asked several questions to find out whether the pharmacists were involved in the counselling of these patients or not and whether the patients were counselled properly by the pharmacist or not. The responses are as shown in Figure 3 and 4.

Figure 3: Involvement of pharmacists in the counselling of the hypertensive-only patients as reported by the hypertensive-only patients

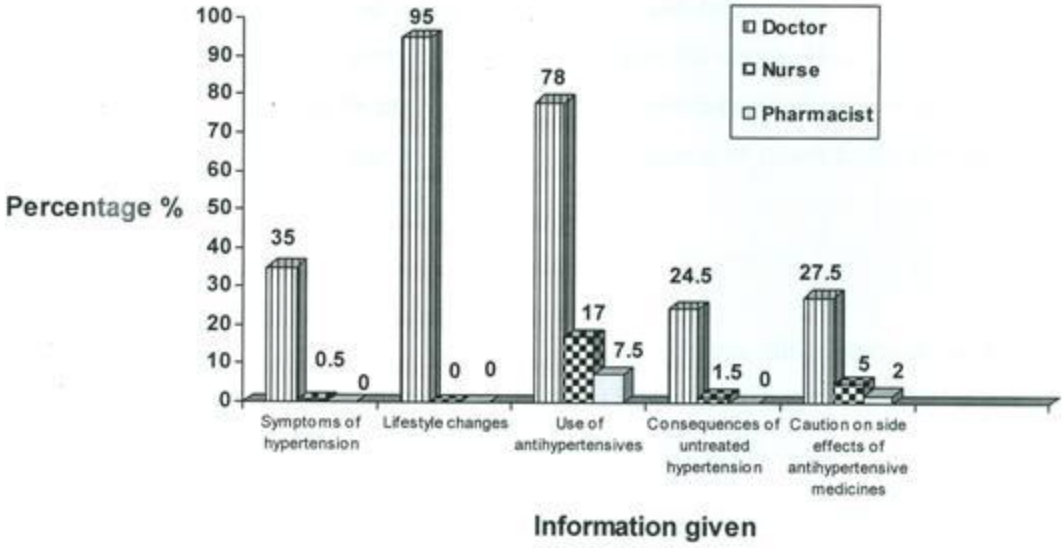
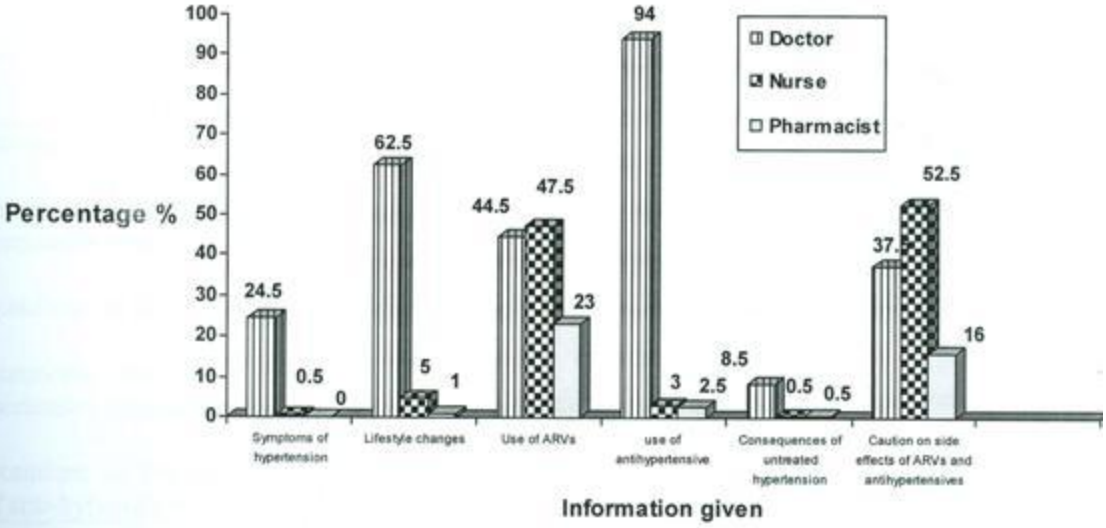


Figure 4: Involvement of pharmacists in the counseling of the hypertensive-HIV patients as reported by the hypertensive-HIV patients



It was reported by both the hypertensive-only and hypertensive-HIV patients that they got the information on symptoms of hypertension, lifestyle modification, use of anti-hypertensive medicines, cautions on side effects and precautions on use of anti-hypertensive medicines and use of ARVs, and consequences of untreated hypertension from the doctor. Information on the use of ARVs was mostly provided by nurses. Doctors were reported to be the major source of information regarding both the disease and medication use instead of pharmacists who were found to be the least involved. (Figure 3 & 4)

Information to the dispenser

Only 20% of the hypertensive-HIV patients reported to inform the dispenser at the hypertensive clinic that they were using ARVs as well. On the other hand only 36% of the hypertensive-HIV patients informed the dispenser at the HIV clinic that they were using anti-hypertensive medicines.

Table 4: Cautions given by doctors and nurses to the hypertensive-HIV and the hypertensive-only patients

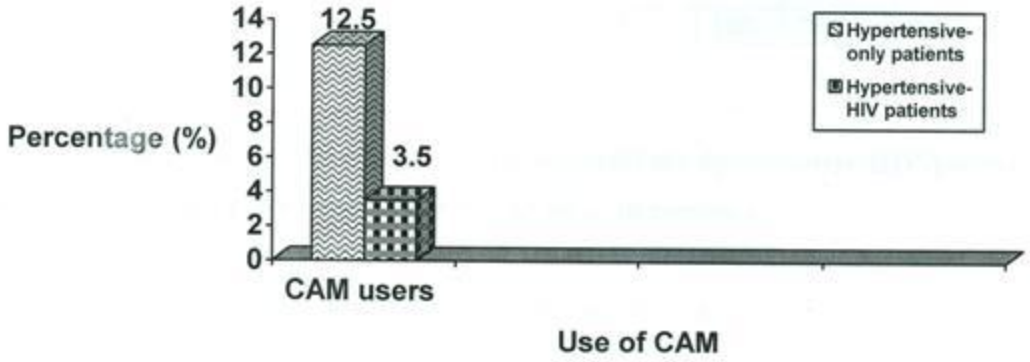
	Hypertensive-only patients		**Hypertensive-HIV patients**	
	Freq.	**%**	**Freq.**	**%**
Cautions on side effects of ARVs	-	-	174	87
Cautions on side effects of anti-hypertensive medicines	33	16.5	8	4
Precautions on the use of ARVs	-	-	180	90
Precautions on the use of anti-hypertensive medicines	144	72	71	35.5
Precautions on the use of both ARVs and anti-hypertensive medicines	-	-	1	0.5

The number of hypertensive-HIV and hypertensive-only patients who were given cautions on the side effects and the use of ARVs and anti-hypertensive medicines either alone or in combination is shown in Table 4.

5.4 iii) Use of CAM by the hypertensive patients and the type used

The number of hypertensive-only and hypertensive-HIV patients who reported using CAM for hypertension was a minority. Only 12.5% and 3.5% of the hypertensive-only and hypertensive-HIV patients respectively reported using CAM for hypertension. (Figure 5)

Figure 5: Use of CAM by the hypertensive-only and hypertensive-HIV patients



Among the CAM users in both groups, most reported not knowing the types of CAM they were using. The peers were found to be the most influential group in advising the use of CAM in both groups.

The most frequent reported reasons for using CAM in both the groups are as shown in Table 5.

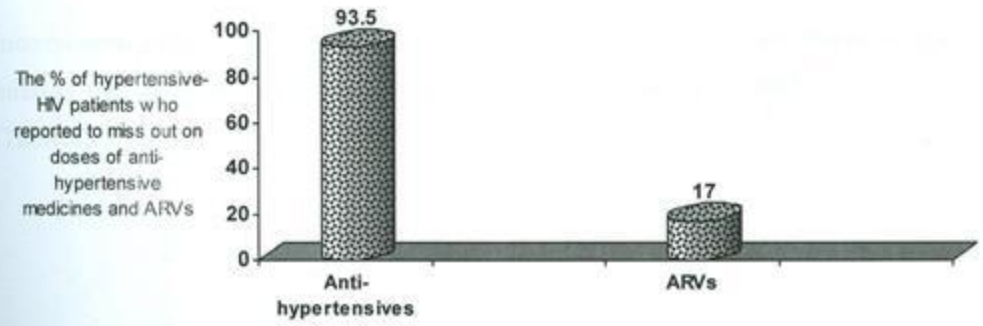
Table 5: Reported reasons by both groups of patients for using CAM

	Hypertensive -only patients		Hypertensive-HIV patients	
Reasons for using CAM	**Freq.**	**%**	**Freq.**	**%**
Peer's influence	12	48	3	42.86
Blood pressure not controlled by conventional medicines	9	36	3	42.86
Cheap	4	16	-	-
Conventional medicines have side effects and so they are avoided	-	-	1	14.3
Total	**25**	**100**	**7**	**100**

5.5 Problems faced by both the hypertensive-only and the hypertensive-HIV patients taking anti-hypertensive medicines and ARVs alone or in combination

1. a) Missing out doses of anti-hypertensive medicines and ARVs

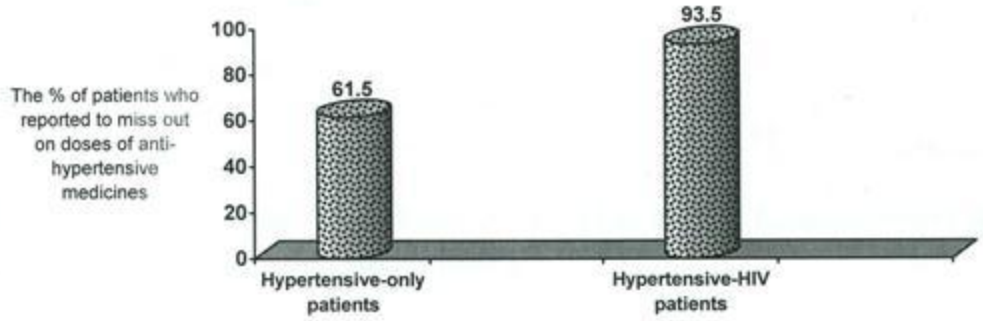
Figure 6: Hypertensive-HIV patients (n =200) missing out doses of anti-hypertensive medicines and ARVs



The result of chi-square test showed that the hypertensive-HIV patients significantly missed out more on doses of anti-hypertensive medicines in comparison to ARVs. (Chi- square = 236.72; $p < 0.05$; df = 1)

b) Missing out doses of anti-hypertensive medicines in both groups of patients

Figure 7: Comparison of the hypertensive-only and hypertensive-HIV patients missing out doses of anti-hypertensive medicines



The result of chi-square test for comparing the hypertensive-HIV and hypertensive-only patients missing out several doses of anti-hypertensive medicines showed that the hypertensive-HIV patients missed several doses of anti-hypertensive medicines more significantly than the hypertensive-only patients in this study. (Chi-square = 58.74; $P < 0.05$; df = 1)

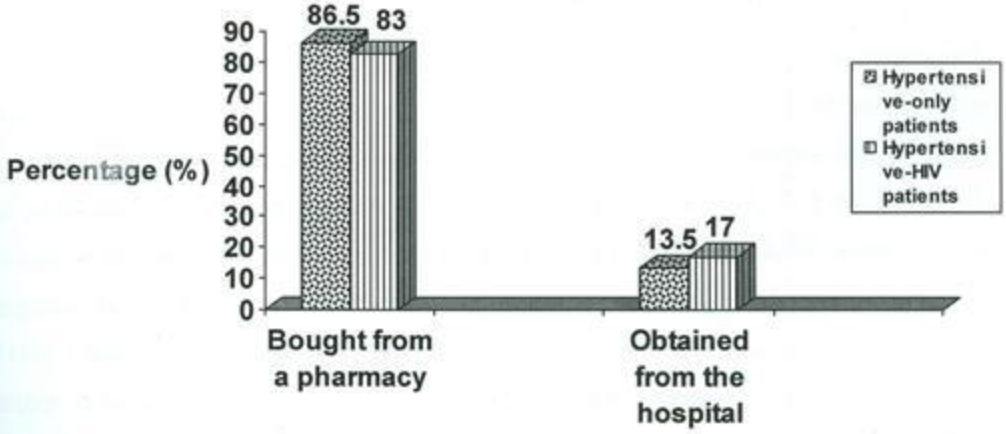
Inconvenience due to the number of medicines and affordability were the main reasons for missing out doses of anti-hypertensive medicines as reported by both groups of patients. (Table 6)

Table 6: Reasons for missing out doses of anti-hypertensive medicines

	Hypertensive-only patients		Hypertensive-HIV patients	
Reasons for missing doses	**Freq.**	**%**	**Freq.**	**%**
Inconvenience due to the number of medicines	-	-	164	88
Non-affordability	55	45	18	10
Side effects	-	-	5	2
Forgetfulness due to busy life	27	22	-	-
Felt better so skipped dose	29	23	-	-
Others	12	10	-	-

The source of anti-hypertensive medicines as reported by both the hypertensive-only and the hypertensive-HIV patients is shown in Figure 8.

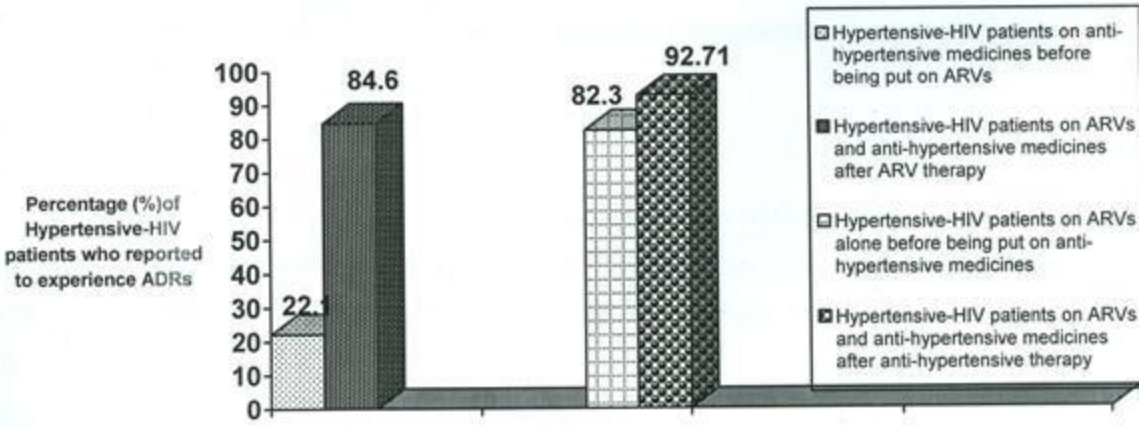
Figure 8: Source of anti-hypertensive medicines



2. Adverse Drug Reactions (ADRs)

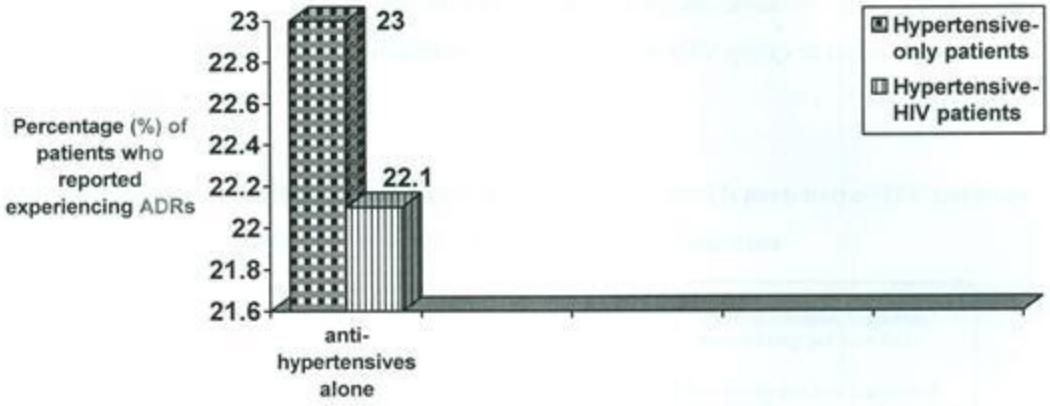
The number of hypertensive-HIV patients who developed hypertension before HIV and were on anti-hypertensive medicines before being put on ARVs was 104 (52%) and those who developed hypertension after HIV and were on ARVs before being put on anti-hypertensive medicines was 96 (48%).

Figure 9: Hypertensive-HIV patients who reported experiencing ADRs with anti-hypertensive medicines and ARVs; each class alone and in combination



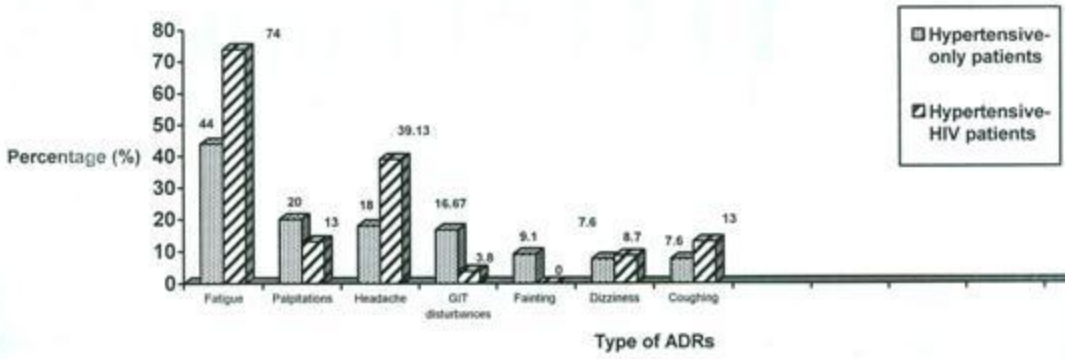
Less than a quarter (22.1%) of the hypertensive-HIV patients who were using anti-hypertensive medicines alone had reported to experience ADRs. (Figure 9) However, when these patients started to use ARVs in combination with the anti-hypertensive medicines the ADRs were reported significantly more (84.6%). (Chi-square = 81.833; $p < 0.05$; df =1) Likewise, the majority of the hypertensive-HIV patients who were using ARVs alone (82.3%) had reported to experience ADRs. However, these ADRs were reported significantly more (92.71%) when these patients used a combination of both ARVs and anti-hypertensive medicines. (Chi-square = 4.766; $p < 0.05$; df = 1) When a comparison of the hypertensive-HIV patients on both ARVs and anti-hypertensive medicines after ARV and anti-hypertensive therapy was done, no significant difference in the incidence of ADRs was observed.

Figure 10: Hypertensive-only and hypertensive-HIV patients who reported experiencing ADRs with anti-hypertensive medicines alone



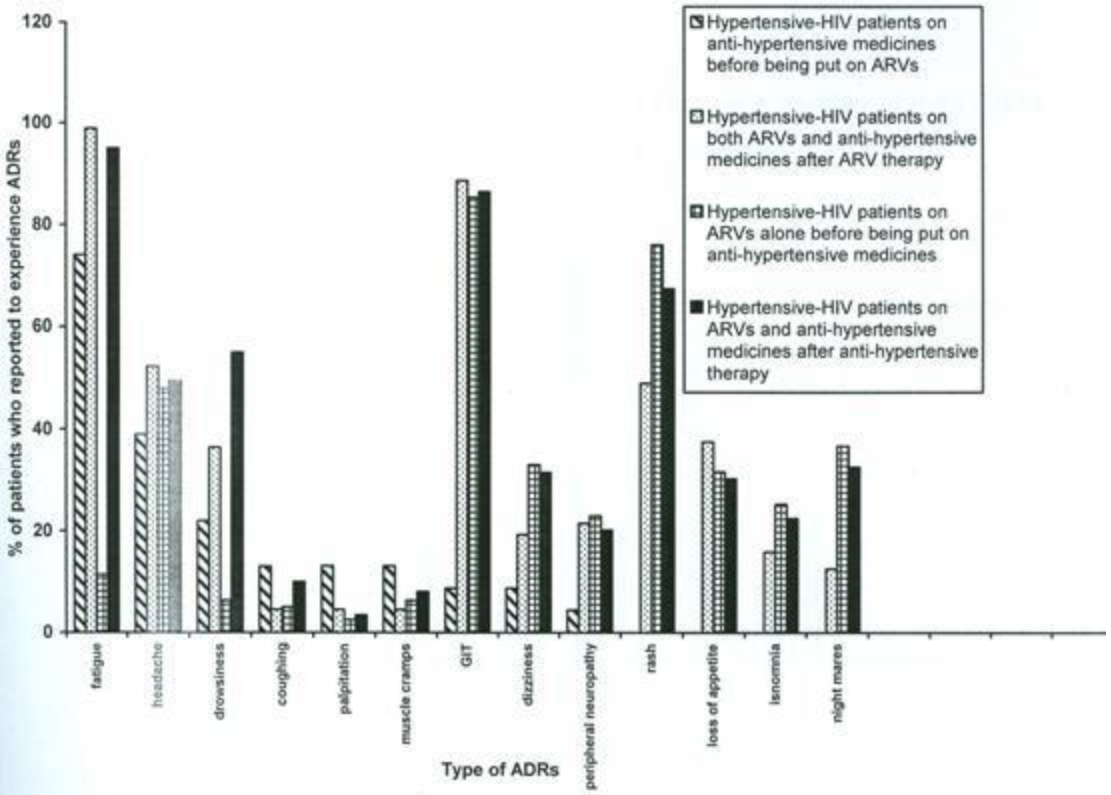
23% of the hypertensive-only and 22.1% of the hypertensive-HIV patients reported to experience ADRs when using anti-hypertensive medicines alone. However, the difference between the two groups was not significant. (Chi-square = 0.051; $p < 0.05$; df = 1). (Figure 10)

Figure 11: Comparison of the type of ADRs experienced by the hypertensive-only and the hypertensive-HIV patients on anti-hypertensive medicines alone



The type of ADRs reported to be experienced by both the Hypertensive- only and the hypertensive-HIV patients on anti-hypertensive medicines alone are shown in Figure 11. Fatigue (chi-square = 6.1523; $p < 0.05$; df = 1)) and headache (chi-square= 4.246; $p < 0.05$; df = 1) were reported to be more significant in the hypertensive-HIV group in comparison to the hypertensive-only group.

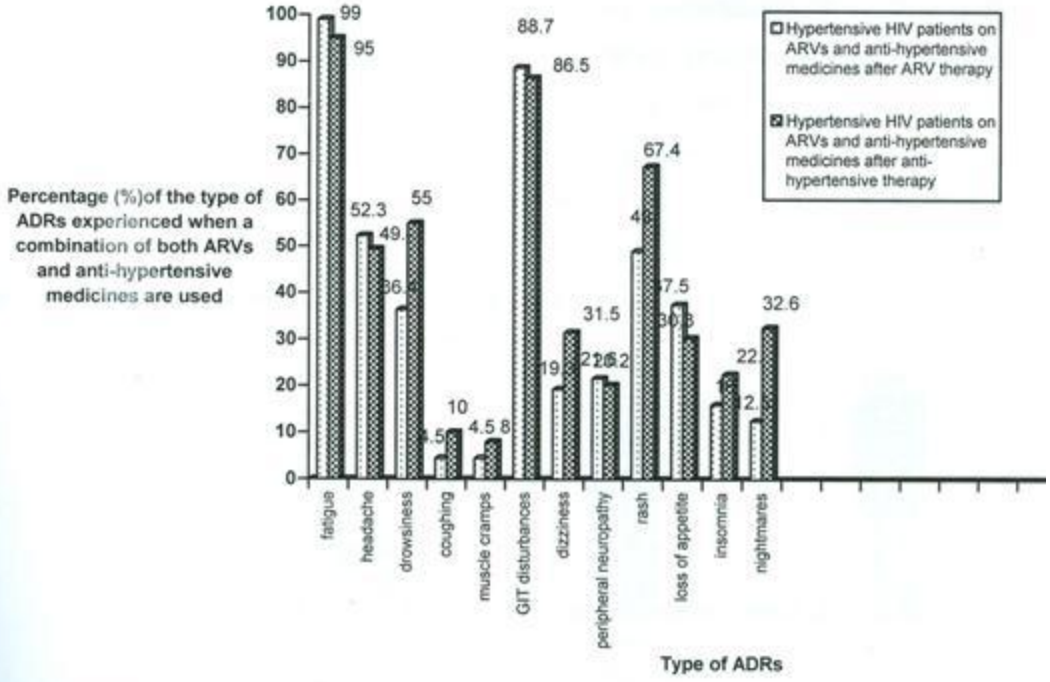
Figure 12: Type of ADRs reported to be experienced by the Hypertensive-HIV patients on anti-hypertensive medicines and ARVs alone and in combination



The type of ADRs in the hypertensive-HIV patients on anti-hypertensive medicines and ARVs alone and in combination are shown in Figure 12. In those patients who were using anti-hypertensive medicines before ARVs, fatigue and GIT disturbances were less frequently

reported but when used in combination with ARVs they were reported at a higher rate (fatigue chi-square = 19.82; $p < 0.05$; df = 1 and GIT disturbances chi-square = 57.86; $p < 0.05$; df = 1). However, in patients who were using ARVs before anti-hypertensive medicines, fatigue and drowsiness were less frequently reported but when used in combination with the anti-hypertensive medicines they were reported at a higher rate (fatigue chi-square = 118.77; $p < 0.05$; df =1 and drowsiness chi-square = 45.59; $p < 0.05$; df = 1). Fatigue was reported at a higher rate in the hypertensive-HIV patients on anti-hypertensive medicines before being put on ARVs in comparison to those who were on ARVs before (chi-square = 33.62; $p < 0.05$; df =1).

Figure 13: Comparison of the Type of ADRs when using a combination of both ARVs and anti-hypertensive medicines in the hypertensive-HIV patients



Drowsiness (Chi-square = 6.25; $p < 0.05$; df = 1), rash (Chi-square = 6.79; $p < 0.05$; df =1) and nightmares (Chi-square = 10.13; $p < 0.05$; df = 1) were reported to be more significant in

the hypertensive-HIV patients who were on ARVs before and now are using a combination of both ARVs and anti-hypertensive medicines in comparison to those who were on anti-hypertensive medicines before but now are using a combination of both medicines. (Figure 13)

The most common anti-hypertensive medicine used by the hypertensive-HIV patients on anti-hypertensive alone was frusemide (15.4%) and for the hypertensive-only patients was atenolol and nifedipine (6.5%). While the common ARVs used by the hypertensive-HIV subjects was reported to be Triomune (72%) which is a combination of stavudine, lamivudine and nevirapine. Of the Triomune users, the most common anti-hypertensive combination used was frusemide and nifedipine (15.3%).

When frusemide and nifedipine were used alone in the hypertensive-HIV subjects the incidence of adverse drug reactions was lower (33.3%). When Triomune was used alone the incidence of adverse drug reactions was high (85.94%). However, when frusemide and nifedipine were used with Triomune the incidence of adverse drug reactions increased significantly to 95.45% (chi square = 6.02; $p < 0.05$; df = 1). This is shown in Figure 14.

Figure 14: Hypertensive-HIV patients reported to experience ADRs

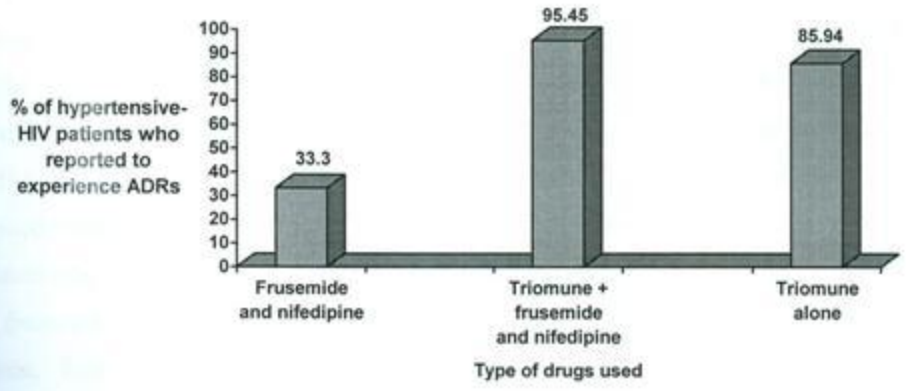
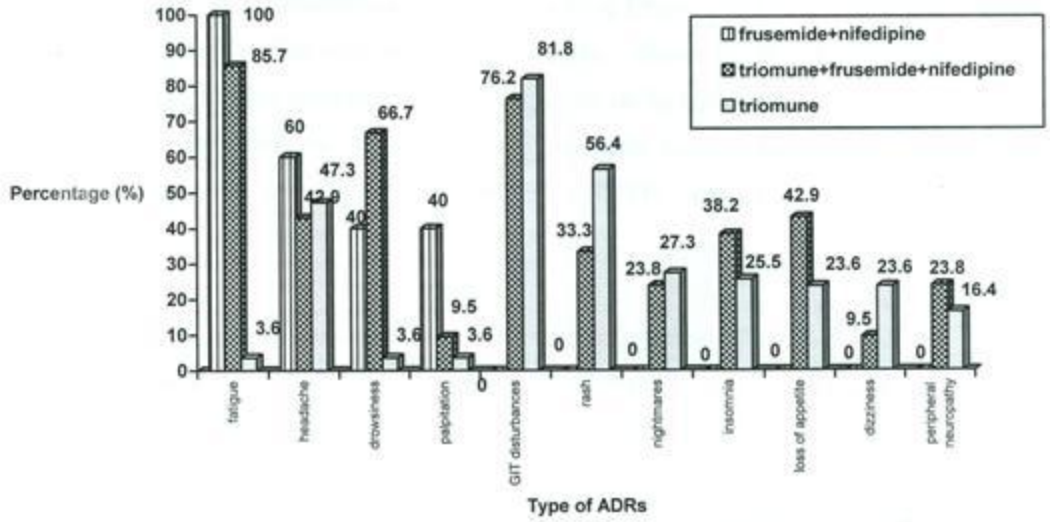


Figure 15: Frequency and type of ADRs with frusemide and nifedipine alone, triomune alone and when in combination with frusemide, nifedipine and Triomune as reported by the hypertensive-HIV patients



The types of adverse drug reactions experienced when frusemide and nifedipine and Triomune were used alone and when used in combination with Triomune are as shown in Figure 15. Drowsiness (chi-square = 5.84; $p < 0.05$; df = 1) was found to be reported more significantly when a combination of Triomune and frusemide and nifedipine were used than when the medicines were used alone. Fatigue (chi-square = 176.22; $p < 0.05$; df =1), insomnia (chi-square = 4.822; $p < 0.05$; df = 1), and loss of appetite (chi-square = 10.87; $p < 0.05$; df = 1), were found to be reported more significantly when frusemide and nifedipine were used together with Triomune in comparison to when Triomune was used alone. Palpitation (chi-square = 6.627; $p < 0.05$; df =1) was found to be reported more significantly when frusemide and nifedipine were used alone than when used in combination with Triomune. Rash (chi-square = 14.5; $p < 0.05$; df = 1) and dizziness (chi-square = 9.63; $p < 0.05$; df =1) were found to be reported more significantly when Triomune was used alone than

when used in combination. The rest of the adverse drug reactions whether used alone or in combination were found to be not significantly different.

3. DRUG INTERACTIONS

More than a half (57%) of the hypertensive-HIV patients were found to use diuretics either alone or in combination with other anti-hypertensive agents. However, the second most common (37%) anti-hypertensive medicine used either alone or in combination with other anti-hypertensive medicines were the calcium channel blockers i.e nifedipine. Calcium channel blockers interact with the ARVs especially the NNRTIs such as nevirapine and effavirenz.

In this study, majority (86.5%) of the nifedipine users were using nevirapine as one of the ARVs combination therapy. About three quarters (78.125%) of these nifedipine and nevirapine combination users had their blood pressure readings not controlled.

5.6 Pharmacists' knowledge on hypertension and anti-hypertensive agents

Several questions were asked to investigate pharmacists' level of education on hypertension.

The pharmacists' responses to questions to assess their knowledge on hypertension are as shown in Table 7.

Table 7: Knowledge of pharmacists on hypertension

Characteristic		Freq.	%
Awareness of	Definition of hypertension	15	15
	Goals of treatment of hypertension	95	95
	Types of hypertension	9	9
	Causes of secondary hypertension	67	67
	Signs and symptoms of hypertension	98	98
	Complications of untreated hypertension	98	98
	Risk factors of hypertension	90	90
	Type of life style modification in hypertension	100	100

In our study, only 15% of the pharmacists could clearly define hypertension as per the seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure and only 9% of the pharmacists replied correctly that there were 3 types of hypertension i.e. primary, secondary, and malignant hypertension. (Table 7)

The most common causes of secondary hypertension as mentioned by the pharmacists were endocrine disorders (89.55%), renal disorders (88%), and drug induced (21%).

The most common complications mentioned by the pharmacists were stroke / paralysis (91.8%), heart failure (88.77%) and renal failure (83.67). Visual defects (45.92%) and death (31.63%) were the least complications reported.

The majority of the pharmacists (90%) were able to mention the risk factors of hypertension as shown in Table 8.

Table 8: Risk factors of hypertension as mentioned by pharmacists

Risk Factors of Hypertension	Freq.	%
High salt intake	89	89
Genetic	82	82
Smoking	71	71
Stress	63	63
Weight	51	51
Alcohol	45	45
Age	11	11

Table 9: Knowledge of pharmacists on anti-hypertensive medicines

Characteristic	Freq.	%
Knowledge on drugs which induce hypertension	73	73
Knowledge on types of anti-hypertensive medicines contraindicated in:		
Diabetes	59	59
Asthma	75	75
Heart failure	10	10
Knowledge on anti-hypertensive drug of choice in heart failure and diabetes	13	13
Knowledge on drug interaction between anti-hypertensive medicines and other medicines	35	35

Seventy three percent of the pharmacists reported knowing the drugs which tend to induce hypertension. (Table 9) The most frequently reported drugs by the pharmacists which can induce hypertension included caffeine containing drugs (59%), adrenaline (56%), nor-

adrenaline (52%), corticosteroids (52%), pseudo ephedrine (37%), xylometazoline (33%), ephedrine (30%) while codeine (20.5%), oral contraceptives (20.5%), cardiac glycosides (19.2%), epinephrine (19.2%), phenylephrine (16.4%), nor epinephrine (16.4%) and NSAIDs (9.6%) were amongst the least reported.

More than a half of the pharmacists (59%) responded correctly that both the beta blockers and thiazide diuretics have to be avoided in the diabetics. Three quarters of the pharmacists knew that beta blockers have to be avoided in asthmatic patients and only 10% of the pharmacists knew that both beta blockers and calcium channel blockers have to be avoided in patients with heart failure. Whereas, 44% of the pharmacists mentioned only beta blockers and 19% mentioned only calcium channel blockers to be avoided in patients with heart failure. Only 13% of the pharmacists mentioned correctly that ACE inhibitors were useful in patients with both heart failure and diabetes. (Table 9)

5.7 Pharmacists and hypertension in HIV patients

Only 19% of the pharmacists reported to know of drug-drug interactions between the ARVs and anti-hypertensive medicines. Of those who had the knowledge, the most common interactions mentioned are shown in Table 10.

Table 10: Drug drug interactions between ARVs and anti-hypertensive medicines as mentioned by the pharmacists

Drug drug interactions	Freq.	%
Abacavir, ritonavir and saquinavir with diuretics	12	63.2
Amprenavir with amiodarone	8	42.1
Amprenavir and ritonavir with calcium channel blockers	6	31.6
Others i.e ARVs with p450 related drugs	1	5.3
NNRTIs and protease inhibitors with beta blockers and calcium channel blockers		

Majority (90%) of the pharmacists were not aware of the current HIV associated hypertensive problems due to the ARVs.

The pharmacists were asked whether they counselled their patients regarding medicines, their responses are shown in Table 11.

Table 11: Counselling by pharmacists

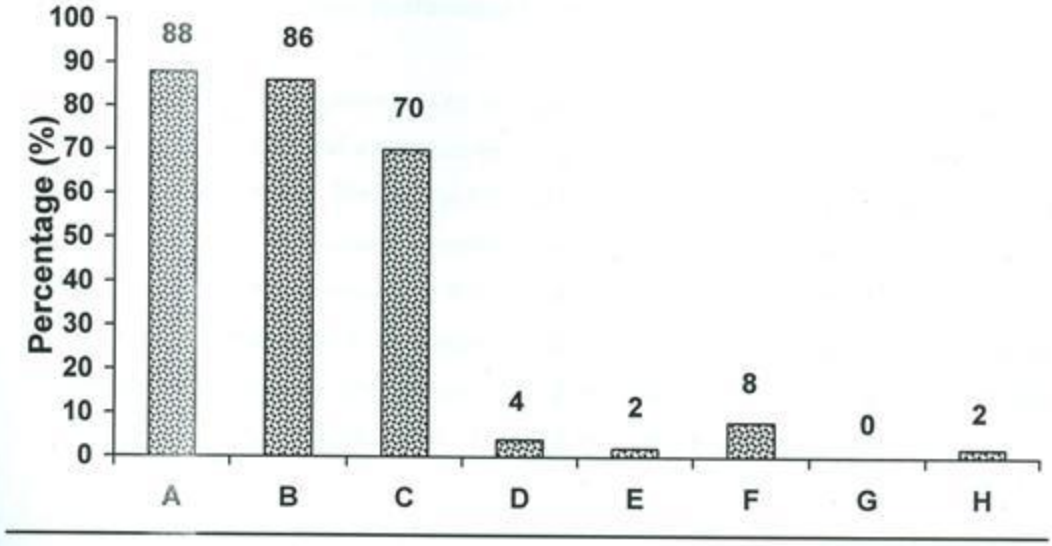
	Freq.	%
Gave advice to the hypertensive-HIV patients on the use of medicines	39	39
Counsels the hypertensive-HIV patients on every visit to the pharmacy	25	25
Gave precautions on the use of other medicines apart from the ARVs and anti-hypertensive medicines	38	38
Asked the hypertensive-HIV patients on the use of other medicines apart from the ARVs and the anti-hypertensive medicines	27	27
Reminded their patients that their refill of medicines was due	9	9
Monitored their patients with the difficulties they were facing	43	43

5.8 Observational Study:

The dispensers were observed in the HIV clinic dispensing anti-retroviral drugs to 100 hypertensive-HIV patients. The dispensers were not informed that they were being observed. They were just told that the patients will be interviewed. This was done so as to not influence the outcome. The observations are shown in Figure 16.

Observation of the dispensing of anti-retroviral medicines in the HIV clinic by the dispenser to the hypertensive-HIV patients

Figure 16: Counselling of the hypertensive-HIV patients on the use of ARVs by the dispensers (n = 100)



KEY:

A = Name and description of the medication

B = Instruction on the use of the drug

C = Dosage form, route, frequency and duration of therapy

D = What to do if a dose is missed

E = Food drug interaction

F = Precaution on common severe side effects

G = Drug drug interaction

H = Referral to physician in case of allergies or if medication does not work

6.0 DISCUSSION

The importance of blood pressure control in preventing cardiovascular disease and stroke is well established. Patient knowledge and awareness of blood pressure play important roles in the ability to successfully control hypertension. [51] The Pharmacist's knowledge of hypertension is also essential as they are in an ideal position to assist with patient education and monitoring. This helps to improve blood pressure control and decrease morbidity and mortality by increasing patient awareness of hypertension.

We conducted this descriptive survey to understand and compare the current status of hypertension knowledge and awareness in two groups that is the hypertensive-only and the hypertensive-HIV patients. We tried to find out the problems faced by both groups of patients in terms of adherence to treatment, potential adverse events and drug interactions all of which affect the control of blood pressure. We also tried to find out whether these two groups of patients used complementary alternative medicines and the type used. In addition, we assessed the knowledge of pharmacists on hypertension and HIV associated hypertensive problems. Counselling of these patients by the pharmacist was also assessed.

6.1 Socio-demographic characteristics

The sex distribution for both the groups was found to be a male to female ratio of 1:2 which is consistent with other studies. [52] The mean age at which hypertension occurred was 57.78 for the hypertensive-only patients and 47.06 for the hypertensive-HIV patients. The results indicate that there are fewer patients below the age of 40 suffering from hypertension which is in line with other studies [53] where prevalence tends to be lowest among persons less than 45 years of age. However, in the HIV group the hypertensive patients were concentrated more in the middle age group of 40-59 years (Table 2) in comparison to the hypertensive-only group where the hypertensive patients were concentrated more in the elderly age group (Table 2). This could be due to the underlying metabolic complications of HIV such as hyperlipidemia and elevated blood glucose which have been associated with anti-retroviral therapy. [26] Hyperlipidemia and diabetes have been associated with vascular changes and hypertension in

those separate disease states. Theoretically, it has been reported that there could be an association between the metabolic complications of anti-retroviral therapy and the difficulty in controlling of existing hypertension or the onset of newly diagnosed hypertension. [26] Thus, this could explain why the hypertensive-HIV patients tended to develop hypertension at a younger age in comparison to the hypertensive-only group. However, this has yet to be proved.

6.2 Knowledge of the patients on hypertension and anti-hypertensive medicines

Our results indicate that both groups of patients are not knowledgeable when it comes to specific factors related to hypertension such as the symptoms of hypertension, consequences of uncontrolled hypertension, names of the anti-hypertensive medicines they are using, and specifically their own level of blood pressure control. (Table 3) Lack of knowledge on hypertension can result in the blood pressure of these hypertensive patients not being controlled as shown in other studies which indicate that about 50-75% of patients diagnosed with or being treated for hypertension did not have adequate control of their blood pressure due to lack of knowledge on hypertension. [45 & 54-61]. Efforts to control hypertension have included increasing public knowledge and awareness, especially about the risks associated with uncontrolled blood pressure.

The median duration of hypertension for the hypertensive-only group was 6 years and for the hypertensive-HIV group was 2 years, suggesting that even though these patients have had this condition for a long duration their knowledge is inadequate. All of the hypertensive patients in both the groups knew the name of the disease they were suffering from and were also aware that people can do things to lower their high blood pressure [Table 3]. Amongst the things they would do to control their blood pressure the least reported were regular exercises, low alcohol intake and no smoking as shown in Figure 2. However these are amongst the major life style changes in order for blood pressure to be controlled as they affect the most common risk factors of hypertension.

Considering the results of chi-square test the level of knowledge of symptoms of hypertension was significantly higher in the hypertensive-only group this could be due to the counselling done in the hypertension clinics whereby focus is on hypertension only whereas in the HIV clinics emphasis is on HIV only. Thus, the hypertensive-HIV patient tends to give more importance to HIV than to hypertension.

Both groups did not know the names and strength of the anti-hypertensive medicines they were using. [Table 3] Thus, if they experience any adverse drug reaction or any other problems they would not be able to report which drug caused it. Moreover they would not be able to inform their doctors what medicines they were using and what medicines they are currently on. This was witnessed in the hypertension clinics of Temeke, Mwananyamala and Amana district hospitals whereby when case notes are not available and the patient is newly referred from another doctor and probably the patient has lost his previous medical documents or when the patients' files get misplaced and a new file has to be opened, and so the patients' medical history is lost making it difficult for the doctor to know the medicines which the hypertensive patient is on. Despite not knowing the names of their anti-hypertensive medicines all the patients knew how many tablets they took and the frequency with which to use their medications. This is probably due to the reinforcement of the instructions by the dispenser during dispensing of the medicines in the pharmacy.

More than a half of the subjects in both the groups were not aware of the consequences of uncontrolled hypertension [Table 3]. This is very dangerous and can lead to an increase in morbidity and mortality as uncontrolled hypertension can cause death, stroke / paralysis, and end organ damage such as renal failure, cardiovascular problems like heart failure or myocardial infarction, and even blindness. A previous study has shown that patients who were aware that elevated blood pressure levels leads to reduction in life expectancy; had a greater compliance level with medication use and follow up visits than patients without this awareness. [62]

Most of the patients in both groups were not knowledgeable enough on hypertension, its complications, risk factors and their medication. Hypertension knowledge is related to blood pressure control. Thus, there is a need to improve hypertension knowledge and awareness in order to reduce morbidity and mortality.

6.3 Use of CAM by the hypertensive patients and the type used

In this study, only a minority of the hypertensive-only and hypertensive-HIV groups reported using CAM (Figure 5). This is not consistent with other studies which report a higher usage of CAM by such patients [63]. The hypertensive patients in each group also had very poor knowledge on the type of CAM they were using. This is risky as the medical practitioner is unaware of the type of CAM and its contents used by the patient and which may also be the cause of drug interaction or cause harmful adverse events.

Use of CAM for disease prevention and treatment is prevalent in patients with chronic diseases such as chronic pain, cancer, hypertension, diabetes and HIV infection. [64] In most cases, CAM is used adjunctively to conventional therapy but patients may completely stop conventional therapy in favor of CAM as well. CAM can benefit as well as harm patients, it is vital that health workers are aware of all treatments their patients are receiving. It may interact with other pharmacotherapy or cause adverse reactions. [65]. Because use of CAM can have potentially deleterious effects, it is important to determine how frequently hypertensive patients utilize alternative treatment modalities.

The common reasons for using CAM in our setup as shown in table 5 is similar to other studies. [66, 67]

Considering the goals of pharmaceutical care, perhaps the greatest cause for concern from a safety and efficacy perspective is that none of the respondents ever discussed CAM with a pharmacist. The peers were found to be the most influential group in advising the use of CAM in both groups. Self medicating with CAM presents additional risks to patients. Since

patients do not always discuss CAM therapy, causal factors of adverse events (related to CAM use) may be difficult to ascertain when no documentation of usage exists.

6.4 Problems faced by the hypertensive-only and hypertensive-HIV patients when using anti-hypertensive and anti-retroviral medicines

1. Missing of doses of anti-hypertensive medicines and ARVs

This study based on patient self reporting showed that the hypertensive-only patients were more adherent to the anti-hypertensive medicines in comparison to the hypertensive-HIV patients. (Figure 7) The reasons for this could be that the hypertensive-only patients do not use ARVs and thus the number of drugs used is reduced and so the tendency to miss doses of anti-hypertensive medicines is also reduced. On the other hand, only 17% of the hypertensive-HIV patients missed out on doses of ARVs. (Figure 6) This shows that the hypertensive-HIV patients were more adherent to ARVs than to the anti-hypertensive medications. It was observed in the HIV clinics that even the doctors were not aware whether the HIV patient was hypertensive or not. Unless if it was a very severe case like that of admission to the wards or if the patient decided to inform the doctor. The doctors in the HIV clinic do not treat hypertension. Patients have to visit the hypertension clinic for treatment. Hypertension lacks a tangible reinforcement factor to foster medication adherence i.e patients with hypertension are often asymptomatic in contrast with what may be seen in other chronic conditions such as HIV. With HIV, there is fear of the knowledge of development of resistance to the ARVs and thus uncontrolled growth of the virus which cannot be controlled by any medication. This knowledge is reinforced during their counselling sessions which remind the patient constantly about the need to take ARVs daily and makes them aware of the seriousness of missing out on a dose of ARVs. However, in the HIV clinic the counsellor is not aware of the hypertensive status of the HIV patient and thus no reinforcement is made on the use of anti-hypertensive medicines. Had they been aware maybe the reinforcement would have been more and patients would have adhered more to the anti-hypertensive medicines. Moreover, even in the hypertension clinic not much reinforcement is being made on the

regular use of anti-hypertensive medicines which if not taken regularly can lead to serious complications and even death. This makes the patient unaware of the seriousness of missing out several doses of anti-hypertensive medicines. Thus, the hypertensive-HIV patients appear not to adhere to the anti-hypertensive medicines. In our study, 86% of the hypertensive-HIV subjects purposely missed taking their anti-hypertensive medications just because they felt better i.e. when there were no tangible symptoms.

The second major reason for missing out several doses of anti-hypertensive medicines by the hypertensive-HIV and hypertensive-only patients was non-affordability. [Table 5] The fact that most of the patients were unemployed implies that these patients may not be able to afford the anti-hypertensive medicines. Majority of the hypertensive-HIV and hypertensive-only patients reported that they had to buy the anti-hypertensive medicines at community/ retail pharmacies as most of the time the hospital pharmacy was out of stock with the anti-hypertensive medicines. (Figure 8) Medicines at the government hospitals are usually sold more cheaply at a subsidized rate which can be afforded by all. However, in contrast medicines at community pharmacies are relatively expensive and cannot be afforded by many of the patients. This may explain the lower number (7%) of compliant hypertensive-HIV on anti-hypertensive medicines. There is no problem of affordability or accessibility to the ARVs due to the medicines being distributed free by the government unlike the anti-hypertensive medicines.

Both ARVs and anti-hypertensive medicines have to be taken life long. These medications bring about side effects enforcing the belief that the cure is worse than the disease. Adverse drug reactions of the anti-hypertensive medicines as a reason for missing several doses of anti-hypertensive medicines was reported by a minority (5%) of the hypertensive-HIV patients on both ARVs and anti-hypertensive medicines.

2. Adverse Drug Reactions (ADRs)

ADRs induced by both ARVs and anti-hypertensive medicines alone or in combination in the hypertensive-HIV and the hypertensive-only patients

The problem of adverse drug events with different drug therapies has been reported since 1961. [68] It has been reported that adverse drug events are considered as 4th to 6th cause of death in the US. [68] Studies show that anti-hypertensive agents are among the most common cause of adverse events in hospitalized patients. [69] Some studies report that cardiovascular drugs may cause half of all hospital admissions due to adverse drug reactions. [70] Evaluation of adverse drug reactions is particularly essential especially in people who use both anti-hypertensive medicines and HAART together posing an increased threat of experiencing severe adverse drug reactions.

In this study 22.1% of the hypertensive-HIV and 23% of the hypertensive-only patients developed at least one ADR when they were on anti-hypertensive medicines alone. This rate is higher than the rate of 15.3% previously reported in a similar study conducted in Denmark. [71] This difference may be due to the difference between the population studied, types and number of drugs used by the patients, definition used for ADR and the susceptibility of patients for developing adverse reactions induced by anti-hypertensive medicines.

Hypertensive-HIV patients on ARVs alone had a greater incidence of experiencing ADRs in comparison to those who were on anti-hypertensive medicines. Almost majority of the study group had experienced ADRs when using ARVs alone. Effective treatment of HIV infection requires three or four drug regimens which are commonly associated with adverse effects. This is consistent with other studies which report that the HAART are toxic drugs and induce several adverse drug reactions. [26]

Hypertension and HIV are both life long diseases and the use of medicines is thus life long. Considering the results of a chi-square test ADRs were reported significantly more when a

combination of both ARVs and anti-hypertensive medicines were used together in comparison to when either of these medicines was used alone. (Figure 9) Studies have shown that anti-hypertensive agents when used together with ARVs tend to increase the side effects of anti-retrovirals [26]. The incidence of adverse drug reactions was reported more in patients using ARVs before but now are using a combination of both medicines in comparison to those who were using anti-hypertensive medicines before but now are using a combination of both. However statistical analysis showed that the result was not significant.

The type of adverse drug reactions experienced when anti-hypertensive medicines were used alone in the hypertensive-HIV patients were almost similar to that experienced by the hypertensive-only patients. Considering the results of a chi-square test, fatigue and headache were found to be reported more significantly in the hypertensive-HIV patients in comparison to the hypertensive-only patients. (Figure 11) These may also be due to the infection itself as HIV tends to cause fatigue and headache. However, if we look at fatigue in the hypertensive-HIV patient on ARVs before being put on anti-hypertensive medicines it is shown to be lower in comparison to the hypertensive-HIV patient who was on anti-hypertensive medicines before. (Figure 12) Use of anti-hypertensive medicines in HIV patients before the use of ARVs seems to make fatigue worse as can be seen in Figure 12. This could be due to the combined effect of anti-hypertensive medicines which has a tendency of inducing fatigue and HIV itself which also tends to cause fatigue.

In the hypertensive-HIV patients who were using anti-hypertensive medicines before they were put on ARVs, fatigue and GIT disturbances were less reported but when used in combination with ARVs they were reported significantly more. (Figure 12) This suggests that fatigue and GIT disturbances may be attributed to the use of ARVs. In those patients who were using ARVs before being put on anti-hypertensive medicines, fatigue and drowsiness were reported less but when used in combination with anti-hypertensive medicines they were reported significantly more. This suggests that fatigue and drowsiness may be attributed to

the use of anti-hypertensive medicines. Fatigue may also be attributed due to the disease itself i.e HIV and hypertension. (Figure 12)

Drowsiness, rash and nightmares were reported significantly more by the hypertensive-HIV patients who were on ARVs before but now are using a combination of both ARVs and anti-hypertensive medicines in comparison to those who were on anti-hypertensive medicines before and now are using a combination of both. This suggests that the addition of anti-hypertensive medicines to the regimens of those who were using ARVs before resulted in more drowsiness, rash and nightmares. (Figure 13) This is consistent with other studies which have shown that anti-hypertensive medicines when used together with ARVs tend to increase the side effects of anti-retrovirals [26].

We then singled out the common medicines used by the hypertensive-HIV patients i.e a combination of frusemide, nifedipine and Triomune and compared the ADRs. Drowsiness was again reported significantly more when these patients used frusemide, nifedipine and Triomune in combination in comparison to when either of the medicines was used alone. This may be attributed to the combined effect of Triomune and nifedipine as both drugs have a tendency to cause lethargy in these patients. Fatigue, insomnia and loss of appetite were reported significantly more when the medicines were used in combination in comparison to when Triomune was used alone. This suggests that the addition of frusemide and nifedipine may be responsible for these ADRs. On the other hand palpitation was reported significantly more in patients using frusemide and nifedipine alone in comparison to when they used it in combination with Triomune showing that palpitation may be attributed to the use of frusemide and nifedipine. Rash and dizziness was reported significantly more in patients on Triomune alone suggesting that Triomune is the cause of these ADRs. (Figure 15)

The profile of adverse drug reactions for both anti-hypertensive medicines and ARVs is similar to that cited in the literature. [1] The common expected ADRs with frusemide are hypotension, nausea, gastro-intestinal disturbances, gout, photosensitivity, tinnitus, and

deafness. With nifedipine, the type of ADRs expected are headache, flushing, dizziness, lethargy, tachycardia, palpitation, gravitational edema, rash, nausea, constipation or diarrhea, increased frequency of micturition, visual disturbances and impotence. The type of ADRs reported to be experienced by patients when using frusemide and nifedipine alone are shown in Figure 15. These patients reported ADRs were somewhat similar to the expected ADRs. However, not all of the expected ADRs were reported by these patients. This could be due to the fact that this was based on the patients' observations. The patients may not have been able to express themselves clearly as most of them have primary level of education. Some ADRs cannot be observed and can only be determined via laboratory tests.

Adverse effects of anti-retroviral agents are common and an important cause of treatment discontinuation and non-adherence to therapy. Triomune is a combination of stavudine, lamivudine and nevirapine. The common expected ADRs with this drug combination includes systemic allergic reactions, peripheral neuropathy, myopathy, fatigue and weakness; GIT disturbances, tachypnoea, dyspnoea, lipodystrophy, rash, fever, and myalgia. However, this was different from the patients' reported ADRs as shown in Figure 15. This could be due to the fact that some of the ADRs require laboratory investigations inorder to be determined, physical detection by the physicians and also the patients' failure to express them. However, the patient reported ADRs such as GIT disturbances, rash, headache, nightmares, insomnia, loss of appetite; dizziness, peripheral neuropathy, palpitation, drowsiness and fatigue were similar to the expected ADRs. (Figure 15)

3. Drug Interaction

The most common anti-hypertensive combination used by the hypertensive-HIV patients in this study was frusemide and nifedipine. 86.5% of the users were using nevirapine. In this study, it was found that more than three quarters of these patients who were using a combination of nifedipine and nevirapine had their blood pressure readings not controlled. This may be attributed to drug drug interactions i.e serum concentrations of calcium channel blocker such as nifedipine are said to be decreased by NNRTIs like nevirapine and effavirenz,

leading to increased blood pressure and tachycardia. According to the literature review, use of calcium channel blockers such as nifedipine and beta blockers such as atenolol should be avoided in HIV patients using either protease inhibitors or NNRTIs. NNRTIs induce the metabolism of all calcium channel blockers hence reducing their anti-hypertensive effect. [27-29] It is recommended that use of calcium channel blockers should be avoided or be carefully monitored in HIV patients on NNRTIs. However, this can only be done when the health care providers know that the HIV patient is also using anti-hypertensive medicines and that the hypertensive patient is also using ARVs. In the hypertension clinic, it is very difficult to know the HIV status of a patient due to confidentiality of the disease unless if the patient decides to disclose his or her status. Similarly, in the HIV clinic the current system which is operating does not record if the patient is hypertensive or not unless if the patient discloses this information. In addition, the doctors do not record other medicines used by the HIV patients in the patient card. These are all setbacks in our system as now the health care providers especially the pharmacist would not be able to advise and caution the patients on the drug drug interactions between NNRTIs and calcium channel blockers. As a result, their blood pressure would continue to be uncontrolled resulting in the failure of treatment. This can be avoided only if the health care provider is aware of all the medications the patient is using.

In our setup, no special treatment guidelines for hypertension in HIV patients was available and they were treated as normal hypertensive patients. However, looking at the tendency of drug drug interactions with ARVs and anti-hypertensive medicines there is a need to have special treatment guidelines for hypertension in HIV patients so that the HIV patients can effectively benefit from the treatment and have their blood pressure under control.

6.5 Pharmacists' knowledge on hypertension

Our findings show that the pharmacists are not very knowledgeable about specific factors such as the definition and classification of hypertension, symptoms of hypertension,

contraindications, drug drug interactions relating to hypertension. (Table 6) Thus, these findings indicate the pharmacists' not being able to execute their duties as a pharmacist.

6.6 Pharmacists and hypertension in HIV patients

It was surprising to note that a majority of the pharmacists i.e 90% were not aware of any HIV related hypertensive problems. Most (81%) of them also did not have any knowledge on drug drug interactions between the ARVs and anti-hypertensive agents. This can be very serious and lead to mis-management of the hypertensive-HIV patients as the pharmacist would not be able to advise correctly.

The poor responses above show that most of the pharmacists are not aware of the recent happenings with HIV and hypertension. The HIV patient's last stop is usually at the pharmacy where the pharmacist dispenses the medicines and advises the patients on the use of the medicines. Thus, it is very important that the pharmacist be up to date in his knowledge as they are in an ideal position to manage the hypertensive-HIV patients by assisting in patient education, enabling the HIV patient to deal with hypertension and avoid problems such as drug drug interactions, non-adherence to medications and adverse drug reactions enabling the patient to live a normal healthy life. A heightened awareness and routine screening for cardiovascular involvement in HIV-infected patients leads to earlier detection and the hope for a reduction in associated morbidity and mortality.

6.7 Involvement of the pharmacists in patient education

In Dar es Salaam, all types of out patient clinics are normally conducted by doctors and nurses, and patients are directed to the pharmacy to collect their medicines. In this study, it was reported by both the hypertensive-only and hypertensive-HIV patients that patient education on their disease and medication was mostly provided by the doctors and nurses. (Figure 3 & 4) The pharmacist was not involved in patient education concerning their disease. This could be explained by the fact that the hypertension clinic does not involve a pharmacist where as the HIV clinic does and we can see some involvement of the pharmacist

in the HIV clinic especially when the patients come to collect their medications from the pharmacist are counseled on the name, description of the medicines, usage of the medicine, dosage form, route, frequency and the duration of therapy. [Figure 3, 4 and 16].

The pharmacists reported that they gave advice to the hypertensive-HIV patients on the use of medicines, counselled the patients on every visit to the pharmacy, gave precautions on the use of other medicines apart from the anti-hypertensive medicines and ARVs, and monitored their patients with the difficulties they were facing (Table 11). However, this was not observed in the observation study where by patients were just told the name and description of the medication; instruction on the use of the medicine, the dosage form, route, frequency and duration of therapy. The patients were not advised on what to do if they missed a dose, food drug interaction, drug drug interaction, and precaution on side effects. (Figure 16) Usually, what is reported by the pharmacists in questionnaires may not be the practice. This is similar to other studies conducted where by the pharmacists were interviewed using questionnaires and observation of the practice was done using simulated patients. The pharmacists reported differently in the questionnaires in comparison to what was observed happening in practice. [72]

It has been shown that when pharmacists are closely involved in the co-management of patients with hypertension, greater reductions in blood pressure are recorded, goal blood pressures are reached and maintained more frequently, patient quality of life is improved, and more patients remain adherent to their medication regimens. [73] Pharmacists can assist in reducing the morbidity and mortality associated with hypertension. Studies have also demonstrated that clinical pharmacy services are highly beneficial and enhance the long term care given to hypertensive patients. [74]

In the current system that is operating, even if the pharmacist was to involve himself he would not be able to do so due to a multitude of problems for example the current card of the HIV patient does not include the previous drug history of the patient, other chronic illnesses which

the patient is suffering from and other medications apart from the ARVs which the patient is using. Thus, the pharmacist would not be able to know whether the patient is hypertensive or not and the medication he / she is using as the patients also do not know the names of the medicines they are using and thus they are unable to tell. This leads to the patient losing out on a lot of important information regarding his disease and a high possibility of drug interactions and thus adverse drug reactions occurring.

All these problems may account for the failure of the pharmacist to discharge their duties as hypertension educators, and indeed a failure in monitoring. All members of the health care team should be trained on hypertension in HIV patients so that the HIV patient can be treated effectively.

It is important to note that though hypertension being an important risk factor for cardiovascular complications and one of the routine vital statistics it was not monitored at the HIV clinics. Only Mwananyamala HIV clinic had a BP machine, the rest of them i.e Muhimbili National Hospital, Temeke and Amana district hospital did not have one so could not record the HIV patients' blood pressure readings. This is risky as we are losing out on many HIV patients who may be hypertensive and as we know early detection can lead to prevention of further complications. All these complications and confusion in the system is leading to mis-management of the HIV patients and so the mortality and morbidity due to cardiovascular complications in the HIV patients is on the increase and will continue to increase if we do not change our system. [75]

7.0 CONCLUSION

Among the major findings of this study (in our setup), the hypertensive-only and the hypertensive-HIV patients interviewed did not have adequate knowledge on hypertension and its medication which led to negligence in the use of the anti-hypertensive medicines. This finding was also eminent in the hypertensive-HIV patients who tended to miss out more on doses of anti-hypertensive medicines in comparison to the anti-retrovirals. Knowledge and awareness of hypertension are important factors in controlling hypertension.

Another important finding reported in the present study (in our setup) was on the adverse drug reactions. Adverse drug reactions were reported significantly more in the hypertensive-HIV patients when a combination of both ARVs and anti-hypertensive medicines were used together.

CAM appeared to have been used by very few of the hypertensive-only and the hypertensive-HIV patients thus no in-depth analyses were carried out. This calls for more research to be done.

No pharmacists were found working in any of the hypertension clinics that were visited. These clinics were run mostly by the doctors and nurses who gave information to patients on hypertension and its medication. Moreover, the anti-hypertensive medicines were reported not to be available at the hospitals most of the time. None of the patients were found to have talked to pharmacists about their hypertensive problems. However in the HIV clinics, the pharmacist was found to be involved in instructing patients on how to use and store ARVs and so we see that majority of the hypertensive-HIV patients were adherent to the ARVs in comparison to the anti-hypertensive medicines.

There is a need to improve the patients' knowledge and awareness of hypertension so as to reduce the morbidity and mortality. An opportunity exists to focus patient education programs and interventions on the cardiovascular risk associated with uncontrolled hypertension.

Monitoring of adverse drug reactions especially in the hypertensive-HIV patients is a matter of importance since these patients are usually using a lot of medications. The pharmacy profession is moving from purely product supply to a clinical and information supply role. At present, pharmacists are not fully integrated into the primary health care team. This is in part the fault of the profession and general practices for not making the most of the pharmacist's potential. Pharmacists' skills could be better used to help patients with their long term medicines. Thus, it is essential that pharmacists' knowledge should be updated regularly as they can play a major role in the society to improve the quality of life of the patients and thus reduce the morbidity and mortality of the disease.

8.0 RECOMMENDATIONS

1. Patient education should be conducted as team work involving different health personnel.

2. Pharmacists in hospitals should take part in hypertension care in the clinics by visiting the clinics regularly and spending some time with patients and health care providers.

3. The system in the HIV clinic should be revised so that the HIV patient file and card should state all other chronic illnesses the HIV patient is suffering from, all the medicines that the patient is using, the past medical history and any adverse drug reactions experienced.

4. To mount continuing education to pharmacists on hypertension and other common illnesses in their work places hoping that they would then share this knowledge to hypertensive patients they are likely to meet in their work places.

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