KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI

DEPARTMENT OF CLINICAL AND SOCIAL PHARMACY

COLLEGE OF HEALTH SCIENCES

FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES

MANAGEMENT OF DIABETIC AND HYPERTENSIVE PATIENTS WHO SEEK CARE AT KOMFO ANOKYE TEACHING HOSPITAL

BY

KOFI OSEI

B.PHARM (HONS)

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A THESIS SUBMITTED IN FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF A MASTER OF SCIENCE IN CLINICAL PHARMACY

AUGUST 2016

DECLARATION

I hereby declare that the work that has been submitted towards the award of Master of Science (Clinical Pharmacy) programme is my own work; it contains no material published previously by any other person for the award of any other degree in any University, except where acknowledgement has been made in the text.

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Project Supervisor Signature Date

Dr. Berko Panyin Anto …….. ……

Head of Department Signature Date

DEDICATION

This work is dedicated to my family, most especially my lovely wife Dr. Mrs Yaa Asantewaa Osei and my two boys Nhyiraba Osei and Afriyie Osei for their immense support.

ACKNOWLEGEMENT

Now thank we all our God with all hearts, hands and voices, whose wondrous things have done. I am so grateful to God for taking me through this programme successfully. I wish to express my sincere appreciation to my supervisor Dr.K. Ohene Buabeng, for his immense support through this challenging research. Your fatherly love and friendliness have churned out the best in me. I will like to express my sincere gratitude to Komfo Anokye Teaching Hospital for given me the opportunity to undertake the study, not forgetting the Head of Diabetic and hypertensive clinic, Dr. Oparebea Ansah, Dr. Sarfo Kantanka, Mr. Shadrack Osei Assibey and Salim, all of the diabetic and hypertensive clinic. My kindest appreciation goes to my classmates for being supportive.

Finally, I will like to thank my family especially my mum and dad, Prof and Mrs. Osei for their constant advice and encouragement. Lastly, I will like to thank my dearest wife Dr. Mrs. Yaa Asantewaa Osei for her support, love, understanding and care. You are simply awesome. To my little boys Stephen Alfred Nhyiraba Osei and Joshua Ivan Afriyie Osei, you kept me awake most of the time to be able to complete my work.

Thank you all for making this project a success.

Abstract

Background

Available evidence suggest a surge in the number of people suffering from type II diabetes and hypertension worldwide, particularly in developing countries. There is also some evidence that most of these patients have poor glyceamic and blood pressure control. The aim of this study was to assess the management of patients with diabetes and hypertension who seek care at KATH. The focus was on medication, knowledge about non-pharmacological approaches and how they are responding to the various interventions given at KATH for disease management.

Method

This was a cross sectional study. The design was retrospective and it involved 325 patients who sought care at diabetic/hypertension clinic of KATH from March to September 2015.Structured questionnaire was used to extract data from Patients' folder. Patients were also interviewed on their medication to fill for missing data.

Results

About Eighty nine percent (n=289) of the patients were on metformin either as monotherapy or in combination with other agents at baseline. Ninety one percent of the participants (n=296) were also on metformin as monotherapy or in combination with other antidiabetic medications on their next review as current medication. Sulfonylurea accounted for 57.8% (n=188) of prescription at baseline and 48.9% (n= 159) on the next review.

About 43% of the patients (n=140) had their fasting blood glucose (FBG) levels within target at baseline, and 36% (n=117) had their FBG within target on the next review (Target FBG is <7mmol/l-American diabetes Association (ADA) guidelines 2014, adapted for use at KATH)

ACEIs and ARBs accounted for the majority of antihypertensive prescriptions with over 97% (n=315) receiving the medication at baseline and 99.9 %(n=324) on the next review of therapy. The ACEI's or ARB's were either given as monotherapy or in combination with other antihypertensive agents. Calcium Channel Blockers also accounted for 66.8% (n=217) of

prescriptions for antihypertensive therapy at baseline and 70 %(n=226) on the next review of patient's condition and medications.

Seventy nine percent of all the females' participants (n=173) were either overweight or obese. Seventy four percent of males (n=78) were also overweight and obese. Optimal control of BP (<140/80mmHg as defined by the American Diabetes Association guidelines 2014) was evident in 48% of patients (n=156) at baseline and 44% on the next review (n=143) of their condition and medications. All (100%) of the participants were knowledgeable about simple lifestyle and dietary approaches to improve the management of diabetes and hypertension.

Forty three percent (n=140) of participants had prescription given for medication outside the hospital at all times whereas 57 %(n=185) said they were given prescriptions for medicines outside the hospital at least once a while.

Conclusion

Majority of the patients exhibited adequate knowledge about lifestyle modifications, medications and dietary approaches to improve Blood pressure and glucose control, therapeutic outcomes observed in the clients were not optimal, based on the targets recommended in the standard guidelines (i.e,ADA 2014/STG 2010).

Majority of the patients involved in the study (both males and females) were either overweight or obese, in particular the female subjects

Majority of the patients involved in the study were prescribed ACEI/ARBs (i.e. lisinopril/losartan) and a biguanide (Metformin) for the management of hypertension and diabetes respectively. Almost all the patients were given prescription for medicines outside the hospital at least once a while.

Recommendations

Further study should be carried out to assess and understand other reasons for the sub-optimal outcomes observed in the patients, despite the use of standard guidelines by the clinicians to manage the patients.

Efficient weight management strategies with input from dieticians must be adopted by both patients and the health care team to aid optimal weight control in the patients. This may contribute to improvement in glycaemic and blood pressure control for the patients.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACE	Angiotensin converting enzyme
ADA	American diabetes association
ARB	Angiotensin receptor blockers
BMI	Body mass index
BNF	British national formulary
BP	Blood pressure
CCB	Calcium channel blockers
ESC/ESH	European society of hypertension/European society of cardiology
ESRD	End-stage renal disease
FBG	Fasting blood glucose
GLP-1	Glucagon-like peptide
HBA1C	Glycosylated haemoglobin
HPT	Hypertension
IDF	International diabetes federation
JNC 7	Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure
KATH	Komfo Anokye teaching hospital
LDL	Low density lipoprotein
MI	Myocardial infarction
STG	Standard treatment guideline 2010
WHO	World health organization

CHAPTER 1

1.1 Introduction

Estimates from KATH shows weekly reported cases of hypertension and diabetes at 120 and 30 new cases respectively. More than 5% of urban dwellers in Ghana are thought to have diabetes which is now becoming a leading cause of blindness, amputations and renal failures(Kath News, 2012).

Epidemiological data is limited about Ghanaians who have diabetes mellitus and hypertension together. Individuals with both coexisting diabetes and hypertension are at increased risk of cardiovascular disease(Epstein et al 1995). Hypertension affects about 70% of patients who have diabetes and individuals with diabetes have twice the increased risk of hypertension than individuals without diabetes (Chung & Won 2011).

Several factors including lifestyle and genetic factors contribute to hypertension and diabetes. Hypertension contribute to 35% to 75% of cardiovascular and renal complication, sexual dysfunction in the diabetic patients and also leads to diabetic retinopathy (Chung & Won 2011; Sowers & Epstein 1995). The effective management and control of diabetes and hypertension is key to the prevention of these microvascular and mascrovascular complication of diabetes.

Several drug classes are used in the management of diabetes and hypertension which includes biguanide, sulphonylureas, thiazolidinediones, dipeptidylpeptidase inhibitors, insulins for diabetes (Fowler 2007) and diuretics, ACE inhibitors , calcium channel blockers, Angiotensin II receptor blockers, beta- blockers , alpha blockers and centrally-acting agents for hypertension (WHO Guidelines Sub-Committee, 1999; Ministry of Health, 2010).

Observations made whiles dispensing hypertensive diabetic patient's prescription seem to show a constant update of drugs with an increase in the number of drugs prescribed. Therefore, this study seeks to assess the management of diabetes and hypertension among clients who seek care at the hospital's diabetic and hypertensive clinic. Assessments would be done on the various medication prescribed, levels of control of blood pressure and blood glucose, and on factors that contribute to patient compliance.

Since currently the hospital does not have their own protocol for the management of these patients (Have adapted ADA guidelines and STG 2010), this study will help management of the clinic to develop and make their protocols in the hospital to conform to national and international standards. Any shortfall identified in the management would be included in recommendation for management to act on it to improve care and management of diabetes and hypertensive clients.

1.2 Problem Statement

People with diabetes co-morbid with hypertension have a high risk of adverse events due to the complexity of events in the pathogenesis and progression of hypertension in diabetes patients. These could be due to environmental, biological and genetic factors(Campbell et al. 2011)

Major modifiable risk factors that contribute to the development of cardiovascular disease like heart failure, peripheral vascular disease and myocardial infarction is hypertension. Therefore optimal management of hypertension in diabetic patients needs special attention as it is a major determinant of morbidity and mortality.

Proper management goals and targets in diabetes mellitus management also prevents the development of macrovascular (coronary heart disease, stroke, hypertension) and microvascular complication (retinopathy, nephropathy, neuropathy, erectile dysfunctions) (Grundy et al. 1999; Walker and Whittlesea 2007).

Studies that seek to answer questions relating to how well hypertensive diabetic patients condition are being controlled is lacking in Ghana. Previous studies focused more on the general management of hypertension without much emphasis on co-morbid diabetes mellitus. Therefore this study seeks to access the management of hypertension (pharmacological and non pharmacological) and diabetes among diabetes mellitus patients who visits the Komfo Anokye Teaching Hospital diabetic clinic.

This study would be compared with international management protocols (American diabetes Association guidelines 2014 and standard treatment guidelines 2010). The study would also seek to address the effects of drug accessibility, affordability and availability on treatment outcomes.

Information obtained from this study will help to provide evidence to support the hospital to in developing appropriate guidelines for hypertension and diabetes care and management and also

adopt best practices in the management of these patients. This will help improve care and reduce complications in diabetic hypertensive patients.

1.3 AIMS AND OBJECTIVES

1.3.1 MAIN OBJECTIVE

To assess the management of patients with diabetes and hypertension who seek care at KATH; their medication, non-pharmacological therapy and how they respond to the various interventions given.

1.3.2 SPECIFIC OBJECTIVES

1. To identify the most common anti-diabetics and antihypertensive medicines prescribed and used in the management of diabetic-hypertensive patients.

2. To determine the proportion of diabetic-hypertensive patients achieving the level of control expected; regarding blood glucose and blood pressure control.

3. To assess whether diabetic hypertensive patients are aware of non-pharmacological measures, including lifestyle modifications that can be used to optimize treatment outcomes.
4. To determine whether the drugs for the above mentioned conditions are readily available, accessible and affordable.

CHAPTER 2

LITERATURE REVIEW

2.1 Overview of Diabetes

Diabetes mellitus refers to a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia if left untreated is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels (ADA 2012, Paneni et al. 2013).

2.1.1 Epidemiology and Global estimates of diabetes mellitus.

Diabetes is increasing at an alarming rate due to aging, urbanization, increased level of inactivity and increasing prevalence of obesity. Global estimates show that, 347 million people in the world have diabetes and 3.4 million people are estimated to have died from consequences of high fasting blood sugar in 2004 alone. Over 80% of deaths due to diabetes occur in low- and middle-income countries (WHO, 2013). The incidence of diabetes mellitus is increasing dramatically in the developed countries and industrialized communities. In the United States alone, there are currently 20 million persons with diabetes, of whom more than 5 million remain undiagnosed.

According to the International diabetic federation, the total number of Ghanaian adults between the ages of 20-79 with diabetes as at 2013 was 440,000 with 8529 death occurring, so this implies that the burden of diabetes is increasing. (Ghana | International Diabetes Federation, 2013). In Ghana type 2 diabetes is associated with age and obesity and it affects at least 6% of adults (Amoah et al. 2002). It is also the major cause of new-onset blindness, end-stage renal disease, and non traumatic amputation in Ghana (Kath News, 2012).

2.1.2 Diagnosis of diabetes

A fasting venous plasma glucose (FPG) of ≥ 7.0 mmol/ or a venous plasma glucose ≥11.1 mmol/l at two hours after a 75 g oral glucose load which is the oral glucose tolerance test (OGTT) is the range of blood glucose set for diagnosing diabetes mellitus according to WHO.

HbA1c is recommended by WHO to be used as a diagnostic test for diabetes, to use the parameter strict quality assurance tests must be in place and the assays must be standardised to a criteria aligned to international reference values. Also, there should be no conditions present that will affect its accurate measurement. An HbA1c of 6.5% is the recommended cut-off point for the diagnosis of diabetes(George 2014)

2.1.3 Classification of diabetes mellitus

2.1.3.1 Type 1 diabetes mellitus

This is also known to as insulin dependent diabetes mellitus and occurs when there is insulin deficiency as a result of destruction of the beta cell destruction of the pancreas. It tends to develop in childhood and adolescent. Approximately 50-60% of type 1 diabetes patients will present before the age of 20. This type of diabetes has a strong genetic link and symptoms has a faster onset (Walker & Whittlesea 2007). Islet cell antibodies are present in about 70-90% of patients with type 1 diabetes at diagnosis (Kitagawa et al. 1998). If left untreated high hyperglycaemia can cause diabetic ketoacidosis and patients are at a higher risk of microvascular and macrovascular complication. For now no cure exists for type 1 diabetes and the mainstay of management is the administration of insulin (Walker & Whittlesea 2007).

2.1.3.2 Type II diabetes mellitus

This is also referred to as non-insulin dependent diabetes mellitus and it is the most encountered form of diabetes occurring in about 80-85% of diabetes patients. Both decreased insulin secretion and decreased insulin sensitivity (insulin resistance) are involved in its pathogenesis and the relative role of these two factors varies between patients. With regard to insulin secretion, the acute insulin response to a glucose load is characteristically defective. It tends to increase with

age and often results from excess body weight (obesity) due to increase insulin resistance and physical inactivity. The symptoms are slower on onset and in most cases diet control and oral hypoglycaemic agents are sufficient to control the disease. If left untreated extreme hyperglycaemia can cause hyperosmolar non-ketotic hyperglycaemia (Walker & Whittlesea 2007), also patients are at a higher risk of severe complication.

2.1.3.3 Gestational diabetes mellitus(G.D.M)

This is hyperglycaemia noticed during pregnancy which almost always resolves at least 6 weeks after delivery and it carries the high risk of a mother developing diabetes in future (Kim et al. 2002) . Thus, pregnancy is regarded as a diabetogenic factor, GDM carries the following risk on the baby; congenital defect, high birth weight, increased risk of perinatal death (WHO, 2011)

2.1.4 Common symptoms of diabetes mellitus

The most common symptoms of diabetes are increased urinary frequency (polyuria), thirst (polydipsia), hunger (polyphagia), unexplained weight loss, numbness in extremities, pain in feet (disesthesias), fatigue and blurred vision, recurrent or severe infections, loss of consciousness or severe nausea/vomiting (ketoacidosis) or coma.

2.1.5 Complications of diabetes mellitus

Several complications can arise as a result of poor glycaemic control in diabetic patients and these are basically due to the metabolic derangement the body is exposed to as a result of the persistent hyperglycaemia. These can be grouped into microvascular and macrovascular complications. Microvascular complications could lead to retinopathy, nephropathy, neuropathy and that of macrovascular could cause coronary artery disease, hypertension, cerebrovascular and peripheral vascular disease (Grundy et al. 1999;UKPDS,1998).

2.1.6 Management of diabetes

Management of type 1 diabetes mellitus is by multiple daily administration of Insulin regimens coupled with lifestyle changes by the patients and management of type 2 diabetic patients is mulftifaceted which includes lifestyle modification inculding weight reduction, calorie restriction and patient education especially on foot care. Many patients are unable to achieve adeqaute glycaemic control with these measure and would require pharmacological intervention. Adequate self-management remains the cornerstone of management of type II diabetes. However, many patients are unable to sustain satisfactory long-term glycaemic control after achieving a temporary response , as a result of the different varieties of pharmacological agents available in managing hyperglycarmia in type 2 diabetes mellitus, its management has become complex and controversial (Bolen et al. 2007; Nyenwe et al. 2011;Blonde 2010).

Different classes of pharmacological agents are used in the management of the condition. Choice of pharmacological agents is dependent on the individual patient characteristics, such as their degree of hyperglycaemia, weight and renal function (Walker & Whittlesea 2007). The classes of drugs usually include the biguanides, sulphonylureas, glucose oxidase inhibitors, metiglinides and the thiazolidines. Insulin is subsequently added, depending on the severity and the stage of the disease (Guthrie 1997; Balfour and McTavish 1993; Bailey 1993; Saltiel and Horikashi 1995). A new breed of antidiabetic drug called the SGLT-2 inhibitors (dapagliflozin, canagliflozin) are under study and not yet approved by the FDA, studies have shown that, these can used in conjunction with other oral hypoglycaemics (Shah et al. 2012).

2.1.6.1 Insulins

Insulin is a hormone secreted by the ß cells of the islets of Langerhans of the pancreas; it has molecular weight of 5808 Dalton. It regulates the energy and glucose metabolism in the body and causes cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle. It prevents the usage of fat as an energy source. (Richter and Neises 2003).

Subcutaneously injected Insulin is the main stream therapy for Type I diabetes and sometimes for uncontrolled Type II diabetes mellitus. The dosage normally depends on the type of insulin being used and the extent of the condition. Insulin may be classified as rapid-acting, very rapid-

acting, intermediate-acting, and long-acting, based on the number of hours until "peak" therapeutic effect.

Rapid and very rapid acting insulin are taken before eating to control the large rise of blood glucose that often occurs after a meal. Ideally, short-acting insulin is taken approximately 30-45 minutes before the meal. Their duration of action is about 2 hours. Example is Humulin® and Insulin Lispro® by Eli Lilly.

Intermediate-acting insulins have an absorption time of about 3-4 hours after injection and reaches their peak at about 7-9 hours. One of the best uses of this type of insulin is its injection at bedtime to control the morning glucose of the next day. An example is the Neutral Protamine Hagedorn® (NPH) insulin (also known as Humulin N, and Isophane insulin) produced by Novo Nordisk.

Long-acting insulin has a peak effect occurring after 10-12 hours and its duration of action may be 16-18 hours. Examples are Ultra Lente insulin, Human Ultra Lente (DiPiro et al. 2005).

2.1.6.2 Biguanides

Metformin which is a biguanide is the drug of choice for first line therapy in type 2 diabetes mellitus. Presence of endogenous insulin is required for metformin to exert its effect; it acts by decreasing gluconeogenesis and increase uptake of glucose by the peripheral tissues (BNF, 2009). It does not cause weight gain with chronic use and the risk of hypoglycaemia is minimal.

It is generally recommended in patients whose BMI > 25. Gastrointestinal side effects are common especially in patients put on very high doses of 3g daily. Caution is advised when Metformin is being used in patients prone to lactic acidosis especially those with advanced renal insufficiency and alcoholics (BNF 2009).

There were significant improvements in hemoglobin A1c and lipid profile in people whose baseline levels were elevated when they were obese and put on metformin. Metformin has also been found to reduce macrovascular disease endpoints in obese patients with type 2 diabetes (Turner et al. 1999)

A study also demonstrated improvement in body weight, glucose control and insulin requirement when type 2 diabetic patients on insulin were also prescribed metformin and this reduced the risk of macrovascular events. This supports the use of metformin even in patients already on insulin therapy (Kooy et al. 2009). Anderson et al (1991) also showed that metformin carried a lower risk on mortality in diabetes patients who also had heart failure compared with other treatment.

2.1.6.3 Sulphonylureas

This class of medications are insulin secretagogues. They act by stimulating the release of insulin from the beta cells of the pancreas and enhance the effectiveness and utilization of insulin by the body which lowers blood sugar levels in patients with type 2 diabetes(Rendell 2004) Patients who do not tolerate metformin or in whom it is contraindicated and not overweight should be considered for a sulphonylurea. A sulfonylurea can also be added as a second-line therapy when blood glucose control remains or becomes inadequate with metformin(McIntosh et al. 2011)

2.1.6.4 Meglitinide derivatives

These agents are also insulin secretagogoues which are shorter acting than the sulphonylureas. These agent achieve more physiologic insulin release and the risk of hypoglycaemia is lower if taking before meals (Bellomo Damato et al. 2011). These agents are very expensive compared to sulphonylureas but similar glycaemic efficacy.

2.1.6.5 Thiazolidinediones (glitazones) pioglitazone

This group of drugs improves insulin sensitivity by decreasing insulin resistance. This allows the insulin that the body produces to work more effectively. It also helps to protect the cells in the pancreas, allowing them to carry on producing insulin for longer(Kahn et al. 2000) They can be used alone or in combination with either a sulphonylurea or metformin or in combination with both. It can also be used in combination with insulin, if intolerant to metformin. The early

addition of pioglitazone in patients unresponsive to combination therapy has been shown to be beneficial by decreasing HbA1c, as well as improving FBG levels (Charpentier & Halimi 2009).

2.1.6.6 Dipeptidylpeptidase -4 inhibitors

These agents tends to increase insulin secretion and decrease glucagon secretions by inhibiting dipeptidylpeptidase-4 (BNF, 2009). These agents are considered second line agents to first line metformin or sulphonylureas in patient in whom glucose control is not adequate. In those at risk of hypoglycaemia or in whom sulphonylurea is contraindicated or not tolerated, it should be added to metformin as second line. In those whom metformin is contraindicated or not tolerated, it should be added to sulphonylureas as a second line agent. Sixagliptin should be added to both metformin and suphonlyureas if insulin is not tolerated or contraindicated (NICE, 2009).

2.1.6.7 GLP-1 mimetic (exenatide)

These agents are added as third line agents to first line metformin and second line sulphonylureas when glycaemic control is not achieved or becomes inadequate. These agents are beneficial in overweight patients as it is associated with prevention of weight gain.

2.2 Overview of Hypertension

Hypertension is elevated blood pressure and is caused by raised pressure of the blood in the arteries and this result from two major factors that is the heart pumping with extra force or the body's smaller vessels narrowing, so that the flow of blood exerts extra pressure on the vessels wall (Sinny Delacroix 2015). These factors may present independently or together. Blood pressure is measured as systolic and diastolic pressures. "Systolic" refers to blood pressure when the heart beats while pumping blood and "Diastolic" refers to blood pressure when the heart is at rest between beats. The mmHg, is millimeters of mercury—the units used to measure blood pressure (Kannel 1996; Makridakis & DiNicolantonio 2014).

Hypertension (HTN), is a common medical condition, estimated to occur in about one in three young adults, increasing to about 60% for those over 60 and affects more than three of four people older than 70 (Makridakis S. 2014). Hypertension is a major cause of morbidity and mortality in people because it is known to be associated with cerebrovascular disease, coronary heart disease and kidney disease. The extent to which the target organ involved or compromised determines the outcome (Foex 2004).

2.2.1 Classification of Hypertension

Hypertension can be categorized based on how the condition comes about and also by BP readings of the patients. They are classified as either essential or secondary hypertension.

- Essential or idiopathic hypertension as is commonly called accounts for over 90% of high blood pressure presentations. The cause of essential or idiopathic is not known but are base on a cascade of events involving various organs and systems namely the cardiovascular, certain hormones, nerves and blood vessels and the renal system(Akpunonu et al. 1996). Essential hypertension usually occurs closely together with major cardiovascular risk factors such as increasing age, overweight, diabetes mellitus, and dyslipidaemia(Messerli et al. 2007) It is generally asymptomatic but has a high risk of mortality and morbidity.

- Secondary Hypertension is high blood pressure caused by another medical condition and is seen in less than 10% of hypertensive cases. The secondary cause of hypertension may be due to disorders of the adrenals glands, renal disorders, coarctation of the aorta or caused by certain drugs namely corticosteroids, oral contraceptive, antidepressants (Akpunonu et al. 1996).

Classification by BP readings

Table 1: JNC 7 classification of BP for adults (Tran & Giang 2014)

Blood pressure classification	**SBP (mm Hg)**		**DBP (mm Hg)**
Normal	< 120	and	< 80
Prehypertension	120–139	Or	80–89
Stage 1	140–159	Or	90–99
Stage 2	≥ 160	Or	≥ 100

Table 2: ESC/ESH classification of BP levels (Tran & Giang 2014)

Blood pressure classification	**SBP (mm Hg)**	**DBP (mm Hg)**
Optimal	< 120	< 80
Normal	120–129	80–84
High normal	130–139	85–89
Grade 1 hypertension (mild)	140–159	90–99
Grade 2 hypertension (moderate)	160–179	100–109
Grade 3 hypertension (severe)	≥ 180	≥ 110
Isolated systolic hypertension	≥ 140	< 90

2.2.2 Complications of Hypertension

Hypertension that is uncontrolled can lead to different types of complications, the presentation of the complication is dependent on the target organ or system affected by the rise in blood pressure. The stress that Hypertension places on these organs causes them to deteriorate over time (figure 1). The existence of several other risk factors such as increasing age, smoking, abnormal cholesterol, obesity and diabetes risk complications or rapid progression of the

hypertension. The complications that can affect the heart include coronary artery disease, heart failure, cardiac arrhythmias and strokes.

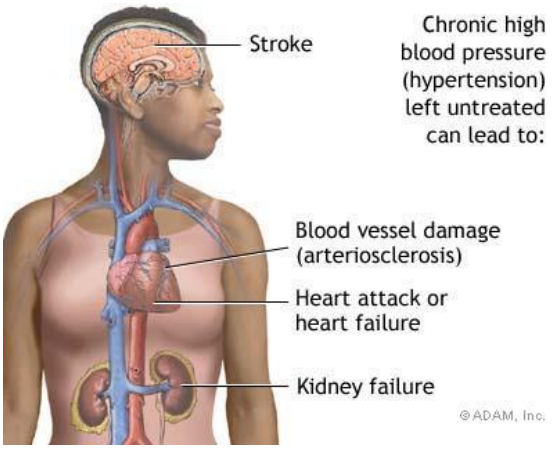

Figure 1: Target organs involved in complications of Hypertension (adapted from A.D.A.M. medical encyclopedia 2015)

The presence of hypertension and the drugs used in its management can predispose one to the development of diabetes. A significant association exist between hypertension and insulin resistance either with diabetes or without diabetes) and hypertension. It is not clear which of the two conditions causes the other. Three-quarter of all problems relating to the cardiovascular system in those with diabetes could be as a result of hypertension (Tran & Giang 2014; Chobanian et al. 2003).

End-stage kidney disease (ESRD) is also a complication and can result from HPT. Over one-third of all medically referred ESRD are usually caused by HPT. Patients with Diabetes have greater risk of developing kidney failure, therefore regular monitoring is needed in these patients to slow or prevent this occurrence (Lea & Nicholas 2002; Keane et al. 2003) . HPT is known to pose a risk for the development of dementia. It can also cause retinopathy and sexual dysfunction (Henis et al. 2011).

2.2.3 Management of Hypertension

The management of HPT is multifaceted and patients' needs to work closely with physicians in setting realistic blood pressure targets. Lifestyle modifications are important for all patients and drug therapy needs to rigorously planned for each patient. One-third of patients with hypertension are not treated at all and among treated hypertensive patients, only about one-fourth seems to have their BP under control (Foex 2004).

Starting drug therapy for pre hypertensive patients has always been debatable. In this regard, initiation of therapy is guided by guidelines set by the U.S. National Heart, Lung, and Blood Institute. Patients have been categorized into group A, B and C based on their risk factors for heart disease. The application of these categories to the severity of hypertension helps in the determination whether lifestyle changes alone can affect the needed change or medications are needed.

Table 3: Recommended treatment by Stage of disease classification and risk groups

Risk Groups	Blood Pressure Stages (Systolic/Diastolic)		
Risk Group A Have no risk factors for heart disease.	Lifestyle changes only. (Exercise and dietary program with regular monitoring.)	Year trial of lifestyle changes only. If blood pressure is not lower at 1 year, add drug treatments.	Lifestyle changes and medications.
Risk Group B Have at least one risk factor for heart disease* (excluding diabetes) but have no target organ damage (such as in the kidneys, eyes, or heart, or existing heart disease).	Lifestyle changes only.	6-month trial of lifestyle changes only. If blood pressure is not lower at 6 months, add drug treatments. Medications considered for patients with multiple risk factors.	Lifestyle changes and medications.

Risk Group C Have diabetes with or without target organ damage and existing heart disease (with or without risk factors for heart disease).	Lifestyle changes and medications.	Lifestyle changes and medications.	Lifestyle changes and medications.

*Risk factors for heart disease include the following: family history of heart disease, smoking, unhealthy cholesterol and lipid levels, diabetes, being over 60 years old.

2.2.3.1 Diuretics

Diuretics work by helping the kidneys eliminate excess salt and water. These agents are normally first to be selected when treating HPT patients. diuretic treatment in low doses has proven effective in reducing the risk of stroke, coronary heart disease, congestive heart failure, and overall mortality (Shah 2004; Shchekochikhin et al. 2013). They are helpful in the management of HPT in diabetes patients. Diuretics are often used in combination with other antihypertensive drugs because even in small doses they potentiate other anti hypertensive drugs (James et al. 2014). Long term studies have suggested that diuretics work as well as newer drugs in bringing blood pressure down and they help in the prevention of stroke, heart failure and heart attack (Felker et al. 2009), common side effects associated with the use of diuretics include depression, fatigue, urinary incontinence, irritability, reduced sexual drive and problems with obtaining and maintaining an erection.

2.2.3.1.1 Thiazide diuretics

Thiazide diuretics work by inhibiting the tubules from reabsorbing sodium and chloride and this results in duiresis and natriuresis. Some of the drugs in this group are indapamide, hydrochlorothiazide, bendroflumethiazide, and metolazone. These agents are usually preferred to other diruetics for treatment of hypertension (Grossman et al. 2011). Thiazide diuretics must be

used at appropriate and/or optimal doses to achieve the optimal antihypertensive effect with the smallest occurrence of side effects, including alterations in glucose and lipid profiles and hypokalemia. Moreover, because thiazide diuretics can increase blood sugar levels especially when combined with β blockers, new cases of diabetes may increase (Lindholm et al. 2003). It is therefore advised that, when using these drugs in patients who are at high risk for developing diabetes, in whom thiazide diuretics should be used, the lowest active dose and possibly in combination with drugs that block the renin-angiotensin system should be considered (Salvetti & Ghiadoni 2006). Erectile dysfunction (impotence), hypokalaemia and elevated uric acid levels, and possibly gout, are possible side effects of thiazide diuretics (Ernst & Marvin Moser 2009).

2.2.3.1.2 Potassium-sparing diuretics

Their value is in their ability to reduce the loss of potassium when they are used with thiazides and also prevents the urinary loss of magnesium. Magenesium restoration is important for optimal correction of diuretic-induced hypokalemia (Ernst & Marvin Moser 2009). Potassium-sparing agents causes only minimal natriuresis and are relatively ineffective in lowering blood pressure (Saha et al. 2005).

These include spironolactone, amiloride, triamterene and Eplerenone. In patients with impaired renal function, spironolactone is preferred, but the effective monitoring of hyperkalaemia must be pursued. Agents such as eplerenone that are more selective for aldosterone than for androgen and progesterone receptors are preferred. Non receptor selective agents are associated with gynecomastia and breast tenderness. However, direct comparisons of their efficacies in patients with treatment-resistant hypertension are lacking (Ernst & Marvin Moser 2009).

Potassium and magnesium losses due to the use of thiazide diuretics can be corrected by the use of spironolactone, when used in low doses 12.5 to 50 mg per day, they provides additive hypotensive effects in patients who are resistant to treatment (Nishizaka et al. 2003).

2.2.3.1.3 Loop diuretics

These diuretics acts in the loop of Henle to lower blood pressure but their use in the long term has proved ineffective compared to thiazides (Finnerty et al. 1977). The duration of action of loop diuretics is shorter (around 6 hours). These agents are mostly preferred in the treatment of hypertension that is complicated by impaired renal function, in congestive heart failure or nephrotic syndrome. Avoidance of dehydration and potassium loss is important in the use of these diuretics. Examples of loop diuretics include furosemide and bumetanide (Ernst & Marvin Moser 2009).

2.2.3.2 Beta Blockers

Beta blockers lower blood pressure by acting on the β1 and β2 receptors of the sympathetic nervous system in different organs producing a variety of effects depending on the organ affected. Beta blockade results in reduced cardiac output, reduction in rennin release which reflects in reduced angiotensin II and aldosterone release and also reduces peripheral resistance. They are used in combination with ACE inhibitors and calcium channel blockers. These can be used to treat people with history of arrhythmias with fast heart rate and heart attack. These can also be used in heart failure patients with caution. Common side effects reported with the use of beta blockers are depression, fatigue and sexual dysfunction. These side effects needs to be given the necessary consideration in the assessment of the benefits of treatment. Examples are Propranolol, acebutolol, atenolol, metoprolol, carvedilol, timolol (DiNicolantonio et al. 2015)

Notwithstanding, the usage of beta blockers present their own setbacks, their sudden withdrawal can precipitate angina or heart attack. If it becomes necessary for the usage of beta blockers to be stopped, the dose must be slowly decreased before stopping completely. Non-selective or selective beta blockers, may sometimes narrow bronchial airways hence may have limited use in patients with asthma, emphysema, or chronic bronchitis. The warning of hypoglycemia in diabetic patients can be masked by these agents. When beta blockers are used in combination with diuretics, the risk of the development of diabetes may increase (Wiysonge et al. 2012).

2.2.3.3 Calcium channel blockers

Calcium channels are responsible for regulating the inflow of calcium into the cells of the muscles which causes smooth muscles of the vasculature and myocardium to contract. CCBs will block this entry of calcium into the cells leading to smooth muscle relaxation and decrease peripheral vascular resistance and ultimately a reduction in Blood pressure(Elliott & Ram 2011).

Table 4: Class and examples of Calcium channel blockers

Class	Example
Dihydropyridine	Nifedipine, amlodipine etc.
Benzothiazipines	Diltiazem
Phenylakylamine	Verapamil

Some side effects of CCBs are palpitation, ankle oedema, severe headache and flushing prominent with dihydropyridines constipation especially when verapamil given at a high dosage (Elliott & Ram 2011).

2.2.3.4 ACE Inhibitors

ACE inhibitors are another group of antihypertensive that act by blocking the rennin-angiotensin aldosterone system to cause vasodilation which helps reduce blood pressure. ACE inhibitors are the preferred agents in the management of blood pressure in patients with diabetes, kidney disease, heart failure and left ventricular hypertrophy. ACE inhibitors should not be used during pregnancy as they can harm the foetus. Several types are available which include captopril, enalapril, ramipril, perindopril, and lisinopril. Some of the main side effects of ACE inhibitors are hyptotension, rare case of angio-oedema, irritating dry cough due to the ACEIs preventing the breakdown of kinins leading to kinin buidup. The cough may be intolerable for some patients in which case an ARB is preferred, ACE inhibitors can also increase potassium levels (Sweitzer 2003).

2.2.3.5 Angiotensin-Receptor Blockers (ARBs)

These agents inhibit the action of angiotensin II which leads to the blockage of the vasocontrictive effects of angiotensin II. The end result of the blockage is decreased peripheral resistance and vasodilation leading to reduced blood pressure. Side effects such as coughing associated with ACEI are often not seen in the use of ARBs due to the fact ARBs do not Inhibit ACE avoiding the buildup of bradykinins which causes the dry cough. This makes ARBs the preferred choice in patients who do not tolerate ACEIs due to persistent cough.

Hypotension, giddiness, hyperkalaemia, lethargic and sinus congestions are common side effects associated with the usage of ARB's. Its use is contraindicated in pregnancy. Examples are Losartan, candesartan and valsartan (Barreras & Gurk-Turner 2003; Israili 2000)

ARBs have vasodilating and hypotensive effects just as the ACE inhibitors and they are also known as s angiotensin II receptor antagonists. Side effects such as coughing associated with ACEI are often not seen in the use of ARBs and they are usually prescribed as an alternative to ACE inhibitors. They are usually prescribed to patients who do not respond to or tolerate ACE inhibitors.

In a study, about 9000 patients were randomly selected to receive either the ARB losartan or a β-blocker (atenolol). A better reduction of mortality and morbidity was seen in patients treated with losartan, because of reduction in strokes. Losartan also proved more effective in reducing left ventricular hypertrophy, an independent powerful risk factor for adverse outcome., the superiority of losartan over atenolol has been demonstrated in the management of isolated systolic hypertension isolated and it is more pronounced than in those with established systolic and diastolic hypertension (Cuspidi et al. 2002).

Hypotension, giddiness, hyperkalaemia, lethargic and sinus congestions are common side effects associated with the usage of ARB's. Its use is contraindicated in pregnancy. Examples are Losartan, candesartan and valsartan (Barreras & Gurk-Turner 2003; Israili 2000)

2.2.3.6 Alpha Blockers

They are normally not the first line drug for high BP, their prescription usually serves as an adjunct to other therapy. They help widen small vessels hence reducing peripheral resistance and they are free from metabolic side-effect. They are known to reduce blood cholesterol. Doxazosin, indoramin and terazosin are longer acting than prazosin. They have an unprecedented selectivity for α_1-adrenoceptors and some of its potential side effects include drowsiness, postural hypotension, and sometimes tachycardia.

2.2.3.7 Vasodilators

Vasodilatores are normally combined with other agents such as diuretics or beta blockers. These agents are seldomly used alone. They work by helping the opening up of the blood vessels by relaxation of the muscles walls. Vasodilators include such as hydralazine, clonidine, and minoxidil. The likelihood of these agents causing significant adverse effects has led to its limited use in patients.People who have angina or have had a heart attack should exercise caution when using these agents. (Foex 2004; Cohn et al. 2011)

2.2.3.8 Central adrenergic agents

Central acting anti hypertensive block and supresses the secretion of catecholamines. They act by inhibiting the stimulation alpha-adrenergic receptors of the central nervous system leading to reduce sympathetic activity of blood vessels and the cardiovascular system specifically the heart. This tends to slow the beat of the heart and cause vasodilatation(Foex 2004). Methyldopa is the most common central adrenergic agent.

2.2.3.9 Other Drugs

The Food and drugs authority in the USA approved aliskiren in 2007 for management of hypertension and this drug can be used as monotherapy or in combination with other blood pressure medication. It is contraindicated in pregnant women, because of potential death risk and injury to the unborn child. Aliskiren is an inhibitor of rennin in the Kidneys.

2.2.4.0 Lifestyle measures in the management of diabetes mellitus and hypertension

In the lowering and controlling of blood pressure, healthier lifestyle measures are of prime importance in lowering blood pressure and controlling blood sugar. Physical activity (exercise) helps to bring down the blood pressure and improves cardiovascular outcomes(Boman et al. 2009) Systolic blood pressure has been reduced by 3.84mmHg and diastolic blood pressure by 2.58mmHg by simple aerobic exercises which was demonstrated in a in an analysis from 54 randomized controlled trials (Whelton et al. 2002)

The role of frequent exercise plus dietary adjustment has also proven to significantly lower both systolic blood pressure and diastolic blood pressure by 4.5mmhg and 2.4mmhg respectively when compared to dietary modification alone (Blumenthal et al. 2010)

Reduction in weight has also proven to be associated with a decrease in stiffness of artery (Dengo et al. 2010) .

Exercise as part of lifestyle interventions results in significant better blood pressure control among hypertensive patients taking medications and this has been proven by the diet, exercise, and weight loss intervention trial (dew-it) (Miller et al. 2002).

Insulin resistance is one of the major causes of diabetes and exercise has been shown to reduce insulin resistance and hence improves glycaemic control (Goodpaster et al. 2010;Coker et al. 2013) and exercise decrease glucose production in the liver and help insulin-mediated suppression of hepatic glucose output (Kirwan et al. 2009;Haus et al. 2010).

Dietary management has also proved beneficial in managing hypertension and diabetes. Several trials has shown that, a diet rich in fruits, vegetables and low-fat dairy products in tandem with

reduced saturated and total fat helped in the lowering of systolic blood pressure by 5.5mm Hg and diastolic blood pressure by 3.0mm Hg(Moore et al. 2001)

An important component of the of the management of any patient with hypertension requires A dietary sodium restriction (to <100mmol i.e. 6g of sodium chloride or 2.4g elemental sodium per day) (Walker & Whittlesea 2007). Eating of regular meals and starchy food like bread, rice, potatoes and cereals and trying as much as possible to eat foods with lower glycaemic index like wholemeal bread, wholemeal cereals, beans. Trying to cut on consumption of saturated fats and instead use monosaturated fats like olive oils, cut down on the use of butter, margarine and cheese. Eating grilled, steamed or oven baked foods in preference to cooking with oils and fats. (Walker & Whittlesea 2007). Daily calories of carbohydrates must be restricted to below fifty five percent and that of cholesterol to at most 150 mg. High daily fiber diet must be encouraged (Sacks et al. 2001). A systematic review showed that long term weight loss through dietary modifications has proven to reduce blood pressure to a greater extent than pharmacological treatment.

Blood pressure is raised by excess alcohol consumption, however it is recommended by the European Society of Hypertension and Cardiology that, alcohol consumption in hypertensive subjects should not be more than 20 to 30 gm of ethanol a day for men and not more than 10 to 20 gm for Women (Mancia et al. 2007)

Lifestyle modification through dietary adjustment and frequent exercise at least 30 minutes per day on most days helps patients with hypertension to obtain better Blood Pressure control and helps to reduce complications associated with uncontrolled hypertension.

2.3 Management of Diabetes and Hypertensive patients

Patients with type II diabetes mellitus have a higher prevalence of hypertension as compared with the normal population. About 40% of type 2 diabetic patients will become hypertensive by age 45 and 60% of people with type 2 diabetes mellitus become hypertensive by age 75(Hypertension in diabetes study, 1993).

Twenty percent of non diabetic patients with hypertension matched 40 to 50% of diabetics with hypertension. There is a twofold excess risk of developing type 2 diabetes mellitus if a patient is already hypertensive within his or her lifetime. In patients with diabetes mellitus and

hypertension the risk of cardiovascular disease is about four times higher than the cardiovascular risk of non-diabetic non-hypertensive patients(Sarwar et al. 2010; Hu et al. 2007). The major complications of diabetes mellitus results from both macrovascular (nephropathy, retinopathy or neuropathy) and microsvascular complications (coronary artery disease, cerebrovascular and peripheral vascular disease) (Grundy et al., 1999;UKPDS,1998). Patients with coexisting hypertension and diabetes mellitus have cardiovascular events more as compared with patients with either diabetes mellitus or hypertension alone (Stamler et al. 1993). To lessen and slow down the vascular complications among diabetic hypertensive patients, a strict control of blood pressure (BP) and glucose levels must be pursued (Hypertension in diabetes study, 1993).

The number of hypertensive's who achieve goals set by various international guidelines is still on the low side even though some benefit exists (WHO, 1999). It is estimated that about 30% of hypertensive diabetic patients in the USA achieve the blood pressure target of <130/80 mmHg (Suh et al. 2009).

Some health care professionals have neglected various recommendations set out about the importance of treatment. The medical community fails to rigorously control blood pressure and associated risk factors (Berlowitz et al. 1998). There is still increased morbidity even in individuals with controlled risk factors and blood pressure (Arauz-Pacheco et al. 2002). These go to attest the need for rigorous management of high blood pressure and associated risk factors.

It is evidenced that, major vascular complications of patients with diabetes mellitus and hypertension can be delayed when a tight control of the blood pressure and sugar is pursued.

In the management of hypertension in diabetics different classes of drugs may be used and the classes of drugs prescribed usually falls within the standards prescribed by the STG and international protocols. Factors affecting selection and choices are influenced by cost, affordability, availability and accessibility. Prescribers may prescribe based on what is available and not necessarily what can be used effectively to control hyperglycaemia and hypertension. Patients may also not comply with therapy because of the cost of the drugs. This increases the complications associated with the condition.

With the current operation of the National Health Insurance Scheme (NHIS), not all drugs are covered and prescribers are forced to prescribe what falls within the content of the scheme, not

really focusing on tailoring therapy to suit patient needs. Patients are usually not willing to buy any drug that is not covered by the scheme due to lack of funds. In this regard patients may make do with what is covered in the scheme and ignore the rest. This leads to non compliance and poor control of the conditions.

2.3.1 Blood glucose Management for Diabetes mellitus patients with hypertension

Goals for glycaemic targets must be individualized for each patient and this should be based on age, disease duration, severe hypoglycaemia risk and the presence or absence of cardiovascular risk and life expectancy. Several studies recommended treatment target levels in people with type 1 and type 2 to levels of HbA1c less or equal 7% to minimize risk of microvascular or macrovascular complications (Nathan et al., 2003;Holman et al. 2008).

In order to reduces the nephropathy and retinopathy, HbA1c levels less of equal to 6.5% may be targeted in certain type 2 diabetic patients but the overall benefits must be balanced against the risk of hypoglycaemia developing (Patel et al. 2008;Chew et al. 2010).

In type 2 diabetes mellitus patients, the target for pre-prandial is 4.0-7.0mmol/L and for a 2-hour postprandial plasma glucose the target is 5.0-10.0mmol/L.

Aiming for this target helps to achieve the Hb1Ac to levels less than 7.0 % (Ohkubo et al. 1995;UKPDS, 1998).

The standard treatment guideline of Ghana recommends a glycaemic target of fasting blood sugar to be between 4-6mmmol/l, 2 hour post-meal blood glucose to be between 4-8mmol/l and a glycated haemoglobin of 6.5% or less (STG 2010).

The recent guideline of the American diabetes association 2014 recommends a glycaemic target of fasting blood glucose to between 3.9-7.2 mmol/l, post meal blood glucose of <10 mmol/l and glycated haemoglobin of <7%.

2.3.2 Blood Pressure Management for Diabetes mellitus patients with hypertension

The recommendation set by the eighth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 8) in 2013 indicated that, treatment should be initiated for patients who are 18 years and older with diabetes mellitus and

systolic blood pressure (BP) reading of 140 mmHg or greater or at diastolic BP reading of 90 mmHg or greater. The treatment goal of a B.P below 140/90 mm Hg was to be set (James et al. 2014) which is in line with the current guideline of the American diabetic association 2014 recommend a less stringent blood pressure target of <140/90mmHg for most individuals with diabetes and hypertension.

The earlier version of the JNC 7 and the 2011 American Diabetes Association (ADA) also recommended that target blood pressure control in diabetic individuals should be to values less than 130/80mmHg or lower to lessen the risk of developing end-stage renal failure from diabetic nephropathy (American diabetes association, 2011;Chobanian et al. 2003). This recommendation was in tandem with that of the standard treatment guideline of Ghana 2010

As a result of the higher risk of cardiovascular endpoints in diabetic patients, several antihypertensive guidelines have recommended treatment goals to lower levels in diabetic patients aiming at levels lower than <130/80mmHg (Chobanian et al. 2003;Mancia et al. 2009)
Efficient blood pressure control among diabetic hypertensive's is very difficult to achieve (Mancia et al. 2011) and so most patients are put on combination therapy to achieve BP control (Pool 2003). Even though lifestyle modification such as lowering of salt in the diet, reduction of weight, exercise and alcohol restriction, lowered Blood pressure in meta-analysis (Cutler et al. 1997;Whelton et al. 2002). Diabetic hypertensive patients almost always require pharmacotherapy to reach target Blood pressure levels with minimal complication.
Recommend guidelines set the use of thiazide diuretics, beta blockers, calcium channel blockers, Angiotensin converting enzyme inhibitors (ACEis) and Angiotensin II receptor blockers (ARBs) either as monotherapy or appropriate combinations when initiating and maintaining of antihypertensive treatment (Mancia et al. 2007).
ACE inhibitors and ARBs are the preferred agents in the management of hypertension in diabetes due to their proven reno-protective abilities. Calcium channel blockers may be used as add on in patients who do not have sufficient control with these agents alone (Wu et al. 2013; Aksnes et al. 2012).
These agents have shown to prevent or slow the course of complications in patients with diabetes (ADA 2014). ACE inhibitors have proven to improve survival in diabetes patients who present with coronary disease, microalbuminuria and nephropathy (Chobanian et al. 2003).

Because of the adverse metabolic effects and the risk of developing new onset diabetes mellitus in exposed patients especially with beta blockers and diuretics, the current European Society of Hypertension (ESH) guidelines therefore is against the use of the combination of diuretics and beta blockers as initial method for prevention in patients greater risk of developing diabetes mellitus (Mancia et al. 2007)

2.4 Aspirin use in diabetes and hypertensive patients

An important goal in the management of patients with type 2 diabetes is the prevention of cardiovascular complication, because diabetes can enhance the development of coronary heart disease by two to four fold (Sarwar et al. 2010) especially in the presence of hypertension. In diabetes, there is an increased release of thromboxane as a result of increased platelet aggregation and adhesiveness and these vascular changes are further enhanced with the presence of hypertension(Epstein et al 1992; Ferreiro et al 2011). These changes that occur in diabetic hypertensive warrant the need for the use of appropriate cardio-preventive agents. Aspirin in low doses has been shown to irreversibly inhibit the process thereby inhibiting thrombus formation. It is also cheap and also readily available.

The hypertension optimal treatment study showed the beneficial effect of low dose aspirin 75mg in reducing cardiovascular event by 15%(p=0.03) and MIs by 36%(P=0.002) in a randomized study involving 19000 patients(Hansson et al. 1998).

2.5 Statin use in diabetes and hypertensive patients

Statin use has proved beneficial in the reduction of overall morbidity and mortality in patients at high risk aside its lipid lowering effects. Statins has been shown to have pleiotropic properties (Wang et al. 2008) namely anti inflammatory effects, inhibition of thrombus formation, plaque stabilization, reduced plasma viscosity and antioxidant activity, increase in endothelial nitric oxide release which cause the endothelium to vasodilate which can prove beneficial in hypertensive's (Wang et al. 2008; Ramasubbu et al. 2008)

Type 2 diabetes patients usually have higher incidence of abnormal lipid profiles leading to a greater cardiovascular disease risk (Laakso 2010). ADA and IDF guideline recommend statins use in almost all individuals with diabetes regardless of baseline cholesterol levels due to their cardiovascular disease risk. This means statin use in diabetes shouldn't be based on LDL cholesterol level but the overall risk profile of the patients. Also several trials has shown the beneficial impact of statins for primary prevention and improvement in cardiovascular outcomes of people with coronary heart disease (Baigent et al. 2005)

CHAPTER 3

MATERIALS AND METHODS

3.1 STUDY METHODS

3.1.1 Study design

The design of the study was cross sectional and it involved retrospective evaluation of patient data including medical records of diabetic and hypertensive patients who seek care at the hospital. Folders of Patients that fell in the inclusion criteria were picked and the patients tracked during review visit and interviewed using a developed structured questionnaire. The study was piloted before full scaled.

3.1.2 Study site

The study was conducted at the diabetic and hypertension clinics of Komfo Anokye Teaching Hospital. Komfo Anokye Teaching Hospital (KATH) is located in Kumasi, Ashanti Region which is the second largest region in Ghana. The projected population of the region is around 4,780,380. It is a 1200 bed tertiary hospital which is situated at the heart of the regional capital.

Cases from the Northern, Upper East and Upper West Regions, Brong Ahafo, Central, Western, Eastern and parts of the Volta Regions which requires specialized care are mostly referred to the hospital for attention. The hospital has a special clinic dedicated solely for diabetic and hypertensive clients and that's where the study was conducted.

3.1.3 Study population

The study subjects were hypertensive diabetic patients who have had the disease for six months and beyond. Patients must have been on treatment for diabetes and hypertension for the past six months and have also reported for review of their condition and medication.

3.1.4 Sampling size estimation

Data on prevalence of hypertension among diabetic patients is limited. The EPIDIAM Study in Morocco reported a prevalence of 70.4% Hypertensive among diabetic patients (Berraho et al. 2012). Using this prevalence as a reference and a confidence interval of 95% and a margin of error of 5% .Using the WHO sample size calculator, a sample size of approximately 320 patients were arrived at.

$$n = \frac{t^2 \times p(1-p)}{m^2}$$

Description:

n = required sample size
t = confidence level at 95% (standard value of 1.96)
p = estimated prevalence
m = margin of error at 5% (standard value of 0.05)

$$n = \frac{1.96^2 \times 0.704(1-0.704)}{0.05^2} = \frac{3.8416 \times 0.208384}{0.0025}$$

n= 320.2 approx. =320

3.1.5 Sampling technique

Systematic random sampling was used to select folders of the patients recruited for the study

Inclusion criteria

- Diabetic Hypertensive patients who have had the disease for six months and over
- Patients who are reviewed at least every 4 months
- Patients who give consent

Exclusion criteria

- Patients who do not consent to the study
- Pregnant women

3.1.6 Data collection method

A structured questionnaire was used to capture data. The questionnaire was directed at hypertensive patients with diabetes mellitus. Respondents were taken through the questionnaire which was either administered in English or local language depending on the literacy level of the respondent. The needed responses were obtained from answers provided to each question posed. Respondents were assured that information obtained was confidential and data obtained would be used to better the management of their condition as well as for academic purposes. The awareness of the study participants about non-pharmacological measures, including lifestyle modifications and whether the drugs for the said conditions were readily available, accessible and affordable was sought. Data was collected through face to face interactive interview with the study participants and extraction of relevant questions on the questionnaire from patient's folders or case notes.

3.1.7 Data

The data collected included the types of antihypertensive and antidiabetics medication used before the last hospital visit which served as the baseline therapy and the current therapy of these participants, level of education of study participants, smoking status, physical activity blood pressure (measured in millimeters of mercury), age, height and weight. The weight and height were used to calculate the BMI (body mass index), Duration of diabetes, duration of hypertension, and levels of glycaemia.

3.2 DATA ANLYSIS AND HANDLING

Each patient was given a unique ID for easy identification. Data was coded and stored on a computer and backed up on a pen drive. Data was analyzed using the current version of SPSS software (Statistical Package for the Social Sciences)

3.2.1 Ethical consideration

Institutional consent

Institutional consent was sought from the diabetic and hypertension clinic of Komfo Anokye Teaching Hospital and approved after aims and objectives of study had been explained to them.

Patients consent

Participant's informed consent was taken after careful explanation of the study to them.

Ethical approval was given by the Committee on Human Research Publication and Ethics (CHPRE), KNUST.

3.2.4 Relevant information for literature review

Information was sourced from relevant journals e.g. Hindawi, Pubmed, doaj and other articles, bulletins and research papers.

CHAPTER 4

RESULTS

Table 5 Demographic characteristics of the Study Population

Variables	Male N=106	Female N=219	N= 325 All patients
Age group			
30-39	2(1.9)	6(2.7)	8(2.5)
40-49	13(12.3)	32(14.6)	45(13.8)
50-59	34(32.1)	81(37.0)	115(35.4)
60-69	45(42.5)	79(36.1)	124(38.2)
70-79	12(11.3)	15(6.8)	27(8.3)
80-89	0(0.0)	6(2.7)	6(1.8)
BMI Class (kg/m2)			
Normal (18.5 - 24.9)	28(26.4)	45(20.5)	73(22.5)
Overweight (25 - 29.9)	71(67.0)	166(75.8)	237(72.9)
Obese(BMI > or = 30)	7(6.6)	8(3.7)	15(4.6)
Religion			
Christian	105(99.1)	200(91.3)	305(93.8)
Islam	1(0.90	15(6.8)	16(4.9)
Traditional	0(0.0)	4(1.8)	4(1.2)
Educational status			
None	9(8.5)	64(29.2)	73(22.5)
Primary	22(20.8)	42(19.2)	64(19.7)
JHS	46(43.4)	74(33.8)	120(36.9)
SHS	17(16.0)	14(6.54)	31(9.5)
Tertiary	12(11.3)	25(11.4)	37(11.4)
Marital status			
Single	6(5.7)	18(8.2)	24(7.4)
Married	91(85.8)	133(60.7)	224(68.9)
Divorced	0(0.0)	37(16.9)	37(11.4)
Widow/Widower	9(8.5)	31(14.2)	40(12.3)

Occupation			
Business man/woman	33(31.1)	91(41.6)	124(38.2)
Teaching	5(4.7)	10(4.6)	15(4.6)
Farming	8(7.5)	8(3.7)	16(4.9)
Healthcare professional	0(0.0)	8(3.7)	8(2.5)
Artisans	7(6.6)	2(0.9)	9(2.8)
Driving	6(5.7)	1(0.5)	7(2.2)
Clergy	1(0.9)	1(0.5)	2(0.6)
Security services	5(4.7)	2(0.9)	7(2.2)
Unemployed	41(38.7	96(43.8)	137(42.2)

Majority of the study participants, 284 (87.4%) were between the ages of 40-69 years. The mean age was 58.2 ± 9.4 years, with 83.7% of the study participants being more than 50 years. Sixty seven percent (67%) of the study participants were females and 32.6%, who were males.

Sixty nine percent (n=224) were married, 12% (n=40) were widowed, 11% (n=37) divorced and 8 (n=24) were single. Ninety four percent (n=305) of the participants were Christians, 5% (n=16) were Muslims and just about 1% (n=4) being traditionalist. Over seventy eight percent had either Basic education or no formal education. About 77.5 % (n=252) of our patients were either overweight or obese (Table 5)

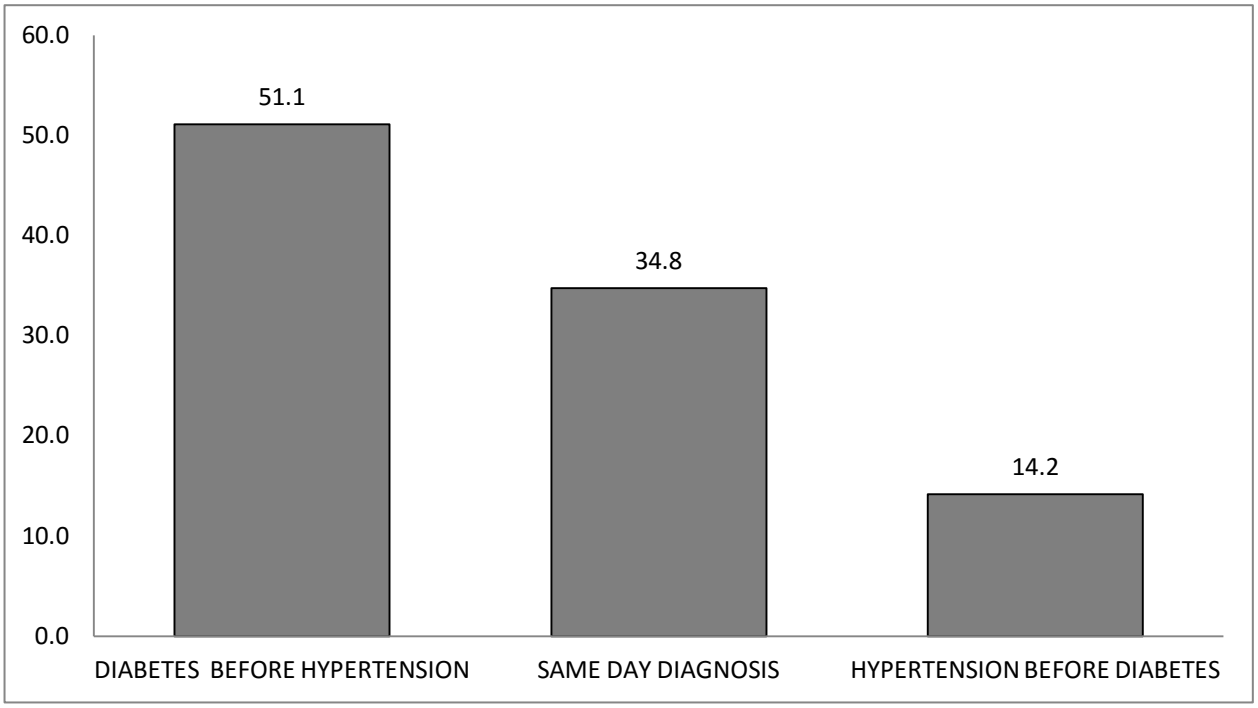

Figure 2: Diagnosis of hypertension or diabetes or both.

51.1% of the patients had diabetes before hypertension, 34.8% had the diagnosis confirmed on the same day whereas 14.2% had hypertension before diagnosis of diabetes (figure 2)

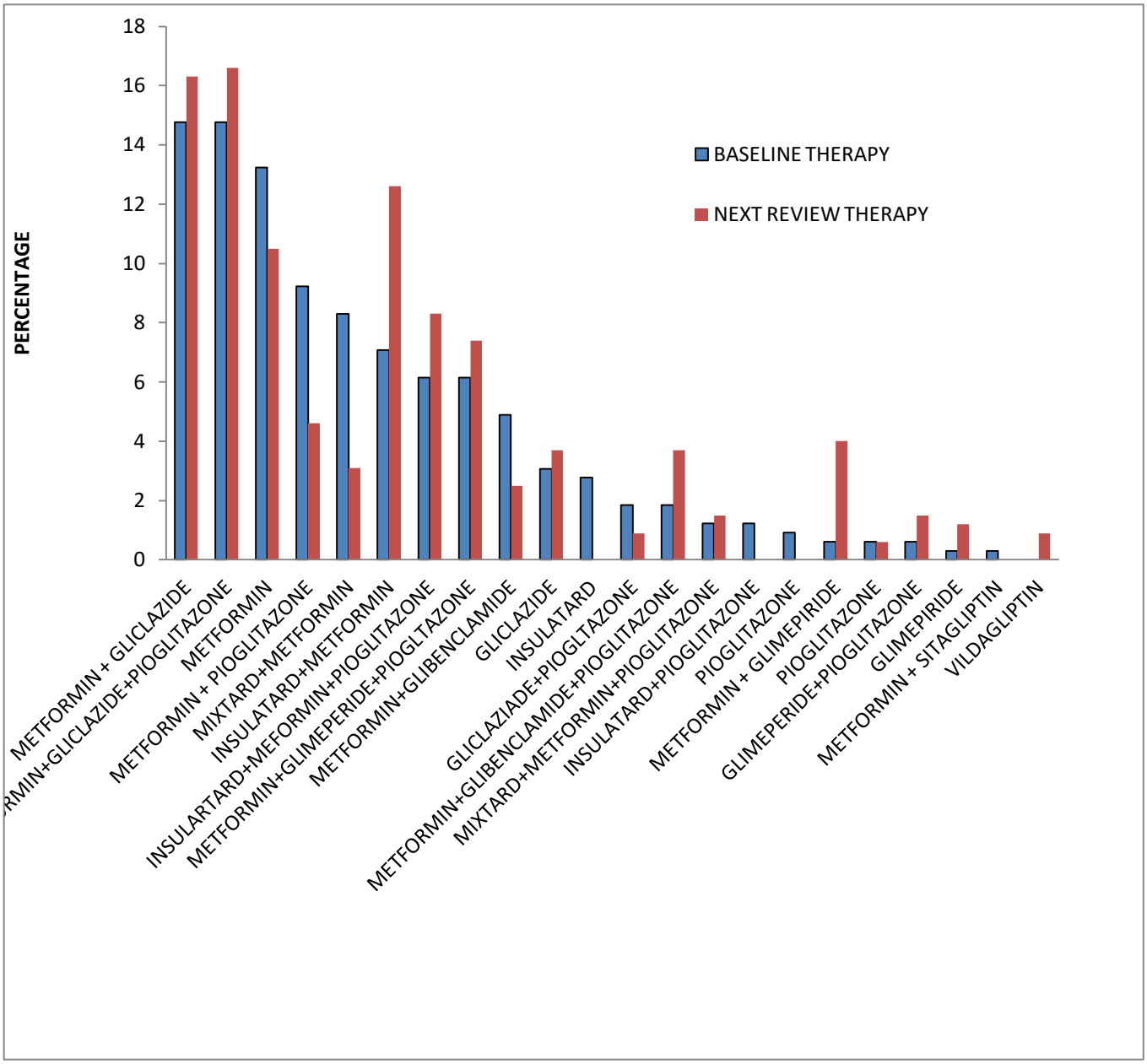

Figure 3: Patients antidiabetic medication at baseline and after next visit

4.1 Baseline anti-diabetic medication of the patients before the next visit:

Dual therapy, triple therapy and monotherapy accounted for 49%, 30.1%, and 20.9% of medications given to the patients for the management of their diabetes respectively. For dual therapy the most common prescribed combinations were Metformin+Gliclazide, Metformin+Pioglitazone, Mixtard+Metformin, Insulatard+Metformin accounting for 14.8%, 9.2%, 8.3% and 7.1% of patients respectively (Fig 3).

For triple therapy, the most common prescribed combination were metformin+gliclazide+pioglitazone, insulatard+metformin+pioglitazone and metformin+glimeperide+pioglitazone accounting for 14.8%,6.2% and 6.1% in participants respectively (fig 3).

4.2 Next visit anti-diabetic medication of the patients

Dual therapy, triple therapy and monotherapy accounted for 45.5%, 37.5%, and 17% of participants in the study respectively. For dual therapy the most common prescribed combinations were Metformin+Gliclazide and Insulatard+Metformin accounting for 16.3%, and 12.6% in participants respectively. For triple therapy, the most common prescribed combination were metformin+gliclazide+pioglitazone, insulatard+metformin+pioglitazone and metformin+glimeperide+pioglitazone accounting for 16.6%,8.3% and 7.4% in participants respectively.(fig. 3)

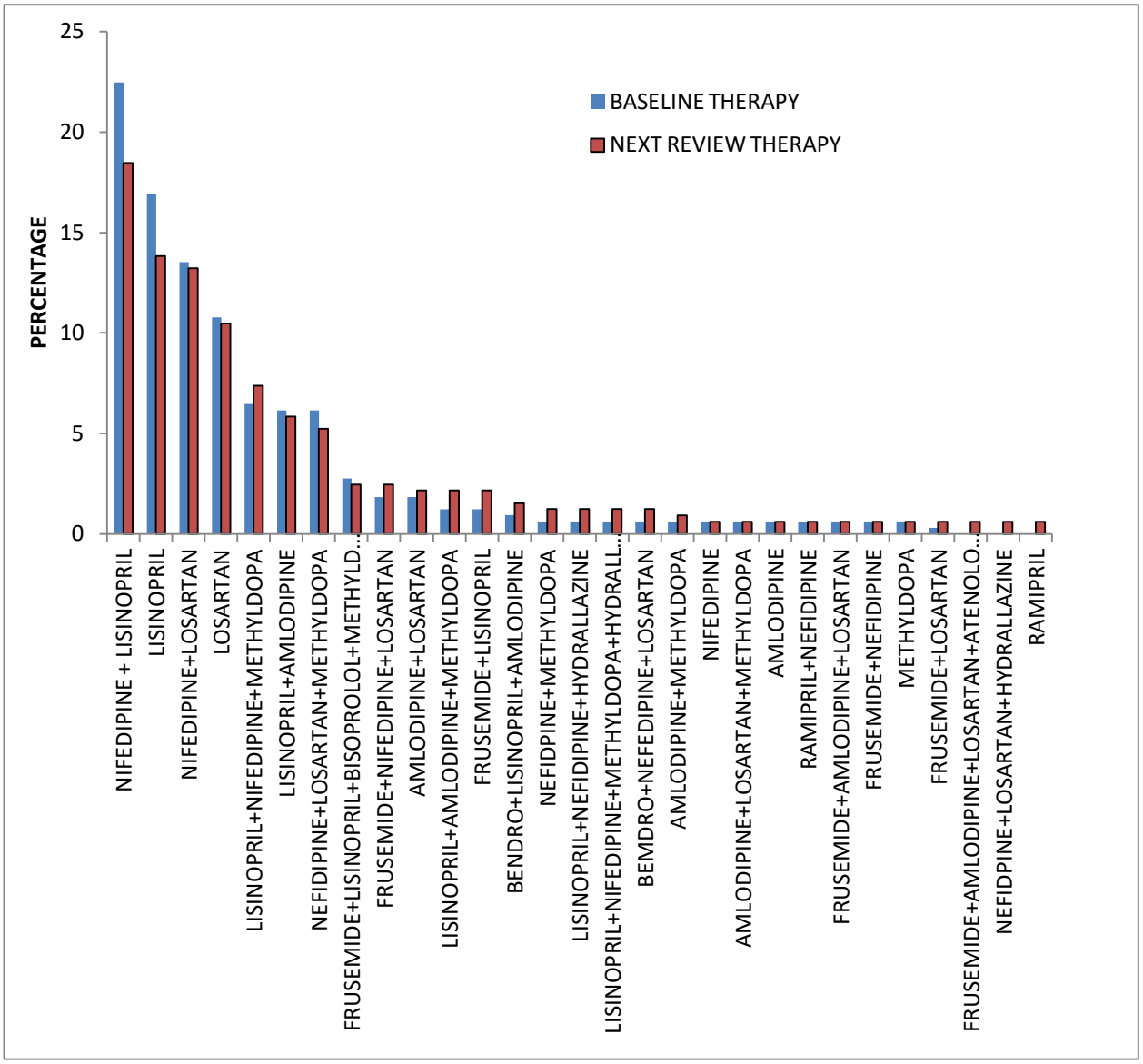

Figure 4: Patients antihypertensive medication at baseline and after next visit

4.3 Baseline anti-hypertensive medication of the patients before next visit:

Dual therapy, monotherapy, triple therapy and quadruple therapy accounted for 55%, 31%, 12.6% and 1.4. % of the drugs used in the management of hypertension respectively. For monotherapy, the predominant drug was Lisinopril and Losartan which accounted for 16.9% and 10.8% of prescriptions respectively. For the Dual therapy, the predominant combinations were Nifedipine+Lisinopril which accounted for 22.5%, Nifedipine+Losartan (13.6%), Amlodipine+Losartan and Amlodipine+Lisinopril accounting for 6.2% of prescription each. For

triple therapy combinations, the most prescribed was Lisinopril+Nifedipine+Methyldopa in 6.5% of participant. (figure 4)

4.4 Next visit anti-hypertensive medication of the patients

Dual therapy, monotherapy, triple therapy and quadruple therapy accounted for 45.8%, 26.7%, 23% and 3.7% of the drugs used in the management of hypertension respectively. Of the Dual therapy, the predominant combinations were Nifedipine+Lisinopril which accounted for 18.5%, Nifedipine+Losartan (13.2%), Amlodipine+Lisinopril accounting for 5.8% of prescription each. Of monotherapy, the predominant drugs were Lisinopril and Losartan which accounted for 13.8% and 10.5% of prescriptions respectively.

For triple therapy combinations, the most prescribed were Lisinopril+Nifedipine+Methyldopa in 7.4% of participant and nifedipine+losartan+methyldopa in 5.2% of participants. (Figure 4)

Table 6: Blood pressure and blood glucose control from Baseline and After Next visit

Parameter	Baseline levels n (%)	Next visit n (%)	P value
Fasting blood glucose mmol/L American diabetes association 2014			
≤7.2	138 (42.5)	117 (36)	
>7.2	187 (57.5)	208 (64.0)	P=0.190
Standard treatment guideline 2010			
≤6	81 (24.9)	68 (20.9)	
>6	244 (75.1)	257 (70.1)	
Systolic blood pressure mmHg			
<130	77(23.7)	80(24.6)	
≥130<140	79(24.3)	69(21.2)	
≥140<150	66(20.3)	74(22.8)	
≥150<180	91(28.0)	93(28.6)	
≥180	12(3.7)	9(2.8)	P=0.772
Diastolic blood pressure mmHg			
<80	94(28.9)	80(24.6)	
≥80<90	122(37.5)	126(38.8)	
≥90<100	88(27.1)	96(29.5)	
≥100	21(6.5)	23(7.1)	P=0.434
Blood pressure grouping mmHg			
<130/80	144(44.3)	116(35.7)	
<140/80	12(3.7)	34(10.5)	
≥140≥80	64(19.7)	65(20.0)	
<140≥80	2(0.6)	0	
≥140<80	103(31.7)	110(33.8)	

4.5 Baseline fasting blood glucose readings of the patients before the next visit

About 42.5 % (138) of the patients had a fasting blood sugar of ≤7.2mmmol/l as when using the ADA guidelines and 24.9 %(81) had their fasting blood sugar within the range of ≤6mmol/l when using the STG.(table 6)

4.6 Next review blood glucose readings of the patients.

About 36% (117) of the patients had their fasting blood sugar ≤7.2mmol/l when using the ADA guidelines and 20.9% (68) had their fasting blood sugar ≤6mmol/l when using the STG (table 6)

4.7 Baseline blood pressure readings of the patients before the Next visit

Forty eight percent of participants (n=156) had their systolic blood pressure controlled to <140mmHg, 48.3 %(n=157) had their systolic blood pressure between 140 to <180mmHg, with 3.7 %(n=12) having theirs above 180mmHg and nearly sixty six percent of the study group had their diastolic blood pressure controlled to <90mmHg, 27.1 %(n=88) had blood pressures to ≥90<100 mmHg whiles 6.5 %(n=21) had diastolic blood pressures of ≥100mmHg.

Further grouping showed one hundred and sixteen (35.7%) of the patients had their blood pressure <130/80, one hundred and fifty six (48%) had their blood pressure <140/80. One hundred and three patients (31.7%) had isolated systolic hypertension whereas two patients (0.6%) had isolated diastolic hypertension. Sixty four of the participants (19.7%) had uncontrolled hypertension with blood pressure ≥140≥80 (table 6)

4.8 Next review blood pressure readings of the patients

Forty six percent of participants (n=149) had their systolic blood pressure controlled to <140mmHg, 51.4 %(n=167) had their systolic blood pressure between 140 to <180mmHg, with 2.8 %(n=9) having theirs above 180mmHg and 63.4 %(n=206) had their diastolic blood pressure controlled to <90mmHg, 29.5 %(n=96) had blood pressures to ≥90<100 mmHg whiles 7.1 %(n=23) had diastolic blood pressures of ≥100mmHg.

Further grouping showed One hundred and forty four (44.3%) of the patients had their blood pressure <130/80, one hundred and fifty (46.2%) had their blood pressure <140/80. One hundred

and ten patients (33.8%) had isolated systolic hypertension. Sixty five of the participants (20%) had uncontrolled hypertension with blood pressure ≥140≥80 (table 6)

Table 7: Cholesterol Lowering Therapy

Parameter	N (%)
Cholesterol lowering therapy prescribed	116 (35.7)
No cholesterol lowering therapy	209 (64.3)
Total	325 (100)

One hundred and sixteen (35.7%) of the study participant were prescribed cholesterol lowering therapy (table 7)

Of the 35.7 %(n=116) who had cholesterol lowering therapy prescribed, 86.2 %(n=100) were prescribed Atorvastatin, 13 %(n=13) were prescribed Rosuvastatin and 2.6 %(n=3) were prescribed fluvastatin.

Table 8: Aspirin use among study participants

Drug	n (%)
No aspirin prescribed	227(69.8)
aspirin	98(30.2)
Total	325(100)

Low dose Aspirin therapy was prescribed in 30.2 %(n=98) of patients.

4.9 Patient's Knowledge about non pharmacological approaches in management of diabetes and hypertension

All participants 100 %(n=325) answered positively when asked about knowledge about these non pharmacological approaches that when adopted could help improve their blood glucose and blood pressure.

All participants (100%) knew the importance of Moderate exercise at least 30 minutes a day in helping to improve their blood pressure.

All participants knew about the importance of eating diet high in fruits and vegetables, high fiber diets and low cholesterol diets, cutting consumption of high levels of energy rich diets. Eg. soft drinks in improving the blood sugar and blood pressures

All participants knew they had to limit intake of salt, drinking alcohol in moderation eg. two units per day for women and three units per days for men in other to improve their blood pressure control

All respondents knew about the detrimental effects of smoking on hypertension.

Only a minority 0.6 %(n=2) had no knowledge about never adding salt to already prepared food being able to improve their blood pressure.

4.10. Availability, accessibility and affordability of drugs

All participant interviewed 100 %(n=325) were registered with National health insurance.

4.10.1 Copayment before insured drugs are given

Majority of patients 58.8% (n=191) had to do copayment before insured drugs are given at accredited facilities outside KATH.

4.10.2 How often Prescription cards are given to patients to collect drugs outside the Hospital

Of the 325 participants interviewed. 57.5 %(n=187) said prescription cards were given to them once a while.42.5% (n=138) said they way given prescription cards anytime they came to the pharmacy for medication

4.10.3 Drug accessibility

Of the 325 participants interviewed 77.5 %(n=252) said drugs were easily accessible when prescription cards are given out to them and 22.5 %(n=73) said they encounter difficulty getting drugs on prescription cards.

4.10.4 None insured medication and affordability

Eighty three patients (25.5%) had non insured medication prescribed for them and of that number (83), 66 (79.5%) were able to buy them whereas 17 (20.5%) were not able to afford those medications or had difficulty accessing them at pharmacies.

4.11 Patient's satisfaction with management

Two hundred and two (62.2%) of the study participants said they were moderately satisfied with the way they are attended to at the hospital, ninety eight (30.2%) were very satisfied, twenty three (7.1%) were not satisfied and two(0.6%) declined comment.

CHAPTER 5

DISCUSSION

5.1 Demographics of Study Participants

In this study, the mean age was 58.2 ± 9.4 years, with 83.7% of the participants aged more than 50 years. 67.4% were females whereas 32.6% were males. This observation is comparable to a study carried out in outpatient diabetic clinic at St. Raphael of St. Francis Hospital Nsambya in Kampala, Uganda where out of 250 patients 62% of them were females. The reason for this may be that females have good health seeking behavior compared to males as reported by Busari et al 2010

A greater number of the participants (42%) were unemployed. This may be related to the age distribution of the disease because about 49% of the study participants were above 60 years which is retirement age and most of the participants would not be any active work.

More than two thirds (78%) of the study participants were either obese or overweight with 54 %(n=174) being females and 24 %(n= 77) being males but there was no statistical significance in BMI between males and females (p=0.202). Obesity is a known major risk factor for hypertension and there is an established correlation between weight gain and hypertension and diabetes.((Innocent et al. 2013; Kahn 1994)

5.2 Diagnosis of hypertension or diabetes or both

Having diabetes predisposes the individual to the development of hypertension if the diabetes is not controlled well controlled and vice versa. In the study 37.50% of the participants had diabetes diagnosed before hypertension implying that, the diabetes may be the cause of the HPT. It is known that diabetes potentiates artherogenesis which makes the arteries develop more plaques thereby narrowing the arteries which eventually leads to cardiac dysfunction.

Of the participants, slightly more than 10% of patients were diagnosed hypertensive before being diagnosed as diabetic. New onset diabetes is associated with the use of certain anti hypertensives

such as therapeutic doses of thiazide diuretics. The probability that these patients developing diabetes after prolonged treatment is very high(Jong et al. 2009).

Forty percent of the patients indicated that they got to know they had both hypertension and diabetes on the same day when they visited the hospital for ill health. It is a common observation by physicians because patients will only report when there are alarming symptoms of the underlying condition that require urgent medical attention.

5.3 Pharmacological management of Hypertension

In the algorithmm of managing hypertension, lifestyle modification is the first line. Inability to achieve blood pressure targets leads to the introduction of drug therapy. Initial therapy is usually a monotherapy and if monotherapy fails, combination therapy is introduced.

Upon review of baseline and next review antihypertensive medication of patients ,the most commonly prescribed dual therapy combinations were CCB+ACEIs/ARB combination accounting for 45.2% and 39.4% of prescription respectively which showed a similar pattern in a study done by Kibirige et al. (2014) and Ibrahim et al. (2010). The most frequently prescribed agents being Nifedipine+Lisinopril, Nifedipine+Losartan, Amlodipine+Losartan and Amlodipine+Lisinopril in that order.

The predominant monotherapy class was ACEIs or ARB accounting for 28% and 27.4% of prescriptions respectively. In a similar study by Kibirige et al. 2014, ACEIs/ARB montherapy accounted for 24.5% of patients prescription. Lisinopril and Losartan were the mostly prescribed with Lisinopril+Nifedipine+Methyldopa being the highly prescribed triple therapy combination seen in that study.

Upon the next review of antihypertensive medication of patients, the number of patients on dual therapy reduced by 9.2%, those on monotherapy also reduced by 4.3%. Most patients were now moved on to triple therapy and quadruple therapy combination. This shows that more patients had their blood pressure uncontrolled. Efficient and effective blood pressure control among diabetic hypertensive's is very difficult to achieve with one agent alone (Mancia et al. 2011;

Ganesh et al. 2011) and so most patients are put on combination therapy to achieve BP control (Pool 2003)

JNC-7 guidelines recommend that, an ACE inhibitor or ARB (if an ACE inhibitor is not tolerated or is contraindicated) be given to diabetes patients with hypertension. Common combinations include an A CE inhibitor or ARB plus a calcium channel blocker or a diuretic. Diuretics are less costly and have proven benefits of reducing all-cause and cardiovascular mortality. The combination of a diuretic and an ACE inhibitor is a good starting point if combination therapy is the selected option.

The American Diabetes Association guidelines recommended the initiation of ACE Inhibitors as first line agents in the management of hypertension in diabetes patients. These agents have shown to reduce the progression of micro vascular and macro vascular complications in patients with diabetes (ADA 2014;Ganesh et al 2011) .They have also been shown to slow the progression of diabetic renal disease and more effective than the other drugs in slowing the onset of renal failure. ACE inhibitors has been shown to improve survival in patients with diabetes who present with coronary disease, microalbuminuria and nephropathy (Chobanian et al. 2003). ARBs are useful alternatives in patients who cannot tolerate ACE inhibitors, ACE inhibitors and ARBs have proved superior to CCBs in improving cardiovascular outcomes and delaying progression of diabetic renal disease (Bakris et al. 2000).

Comparing the prescribing pattern from baseline medication and next review, ACEIs and ARBs predominated in most of the prescriptions followed by CCBs. From baseline and next review of patients medication ,ACEIs and ARBs accounted for over 97% and 99.9% of all patients prescriptions respectively either alone or in combination with other agents, this is in tandem with a similar study by Ibrahim et al. 2010 where about 87.4 % patients received an ACEI or ARB as alone or in combination with other antihypertensive therapy and Kibirige et al. 2014 where 76% of patients received ACEI or ARBs. CCBs was the second most prescribed either as alone or in combination with other agents accounting for 66.8% and 70% of baseline therapy and next review therapy of patient's respectively.

Of the ACEIs and ARBs, lisinopril and losartan predominated with prescription in 61% and 36 % of patients respectively on review of baseline medication and 57.5% and 42.4% respectively on next review of patient's medication. The prescribing pattern were in line with ADA guideline

of prescribing which recommends ACEIs and ARBs as first line agents in management of hypertension in diabetes patients and the addition of CCBs as add-on in those not achieving blood pressure targets.

5.4 Level of control of blood pressure

Table 9: Blood pressure targets set in two (2) standard guidelines often consulted at the hospital

Guideline	Target systolic BP	Target diastolic BP
Standard treatment guidelines 2010	<130	<80
American diabetes association 2014	<140	<80

Optimal control of BP as per the 2014 (table 9)ADA guidelines was evident in the 48% of patients by reviewing their baseline blood pressure readings and 44% from next review of their blood pressure readings which was lower than reported in a similar study where 56% of patients achieved optimal control (Kibirige et al. 2014) but higher than what has been reported in some African studies (Kohner et al. 1998). This variation might be due to definition of the optimal B.P control used. The phased out recommended ADA blood pressure target of <130/80 mmHg was used by most of these African studies and that was the recommendation set out by the standard treatments guidelines 2010 for which 35.7% of patients obtained optimal control by reviewing their baseline blood pressure reading and 34% from their next review of their blood pressure reading which was comparable also to similar studies which reported optimal control in 36.5% and 38.2% of patients (Uloko et al. 2012; Sobngwi et al. 2012)

5.5 Pharmacological Management of Diabetes

The most common monotherapy prescribed from review of previous anti-diabetic medication of the patients visit was metformin which also showed a similar pattern in patient current therapy.

For monotherapy in diabetics, Metformin is recommended as an initial therapy for newly diagnosed diabetics by the ADA and STG guidelines. If there are contraindications to its use, a sulphonylurea can be used (ADA 2014). Metformin has a high safety profile in most patients except a small proportion of people who get gastrointestinal side effects. Since 77.5% of the patients were either overweight and obese and was only advisable to start metformin since it has been shown to have cardio protective effect in especially type 2 diabetic patients and does not encourage further weight gain(Calvert et al. 2008). Current published studies has also shown the effectiveness of metformin in reducing cancer related morbidity aside glucose lowering (Mazzone et al. 2012; Chaiteerakij et al. 2013)

The most prescribed dual combinations from baseline therapy were Metformin+Gliclazide, Metformin+Pioglitazone, Mixtard+Metformin, Insulatard+Metformin in that order. Also a similar pattern of prescribing was observed from the next review therapy with Metformin+Gliclazide and Insulatard+Metformin predominating. This pattern of prescribing was similar to that observed in a similar study by Danquah et al. 2012

From the baseline and the next review of drug therapy of patients, patients who received triple therapy had the most commonly prescribed combinations being metformin+gliclazide+pioglitazone, insulatard+metformin+pioglitazone and metformin+glimeperide+pioglitazone. In a similar study by (Nandy et al. 2012) the most common three-drug combinations used included metformin+ glimepiride + thiazolidinedione and insulin+metformin+ thiazolidinedione.

Quadruple therapy accounted for minority of the combinations used and this was also evident is a similar study by (Nandy et al. 2012)

From the baseline anti-diabetic medication of patients most of them were on dual therapy (49%) and triple therapy (30.1%) and next review, those on dual therapy reduced by 3.5% and more patients were now on triple therapy increasing by 7.4% meaning that most patients were not achieving set targets or had poor control of the condition necessitating the need to put more patients on triple therapy regimen.

From baseline and next review of patient's medication, metformin accounted for about 88.6% and 91%of all prescription respectively either as alone or in combination with other antidiabetics.

This goes to confirm the preference for Metformin by prescribers as first line in most patients with diabetes in line with recommendation by the ADA and which is also in consonance with a study by Nandy et al. 2012, where it was found out that Metformin was the highest prescribed antidiabetic drug among prescribed in 80% of patients . Another study also showed metformin was the most prescribed antidiabetic (Rekha et al. 2014)

Sulfonylurea's accounted for 57.8% of prescription from baseline and 48.9% on the next review of patients either as alone or in combination with other agents. This was on the low side compared to a study by Rekha et al. 2014. The study also showed the minimal prescribing of newer agents in the management of diabetes. The only newer agent prescribed was vildagliptin which accounted for only 0.9% of patients upon review of baseline therapy.

Prescribers mostly focus their attention on cost-effectiveness and availability because in most Africans countries there is lack of access to newer agent because of their high cost (Raz 2013).

5.6 Level of Control of blood sugar

Goals for glycaemic targets must be individualized for each patient and this should be based on age, disease duration, severe hypoglycaemia risk and the presence or absence of cardiovascular risk and life expectancy. Even though targets should be individualized; general recommendation has been set by the American diabetes association and Standard treatment guidelines as shown in the table below.

Table 10: Blood sugar targets in two (2) standard guidelines often used at the hospital

Guideline	Optimal target(fasting blood glucose) mmol/L
American diabetic association 2014	≤7.2
Standard treatment guideline 2010	≤ 6

The standard treatment guideline set a glycemic control target of ≤6mmol/l. Using this guidelines 24.9 % (n=81) of patients had their fasting blood glucose levels reaching optimal

target compared to 75% (n=244) who did not reach optimal target from baseline review of their fasting blood sugar. Whereas upon next review of fasting blood sugar of patients 20.9 %(68) of the patient reached the target set and 79% (257) had poorer control. This was lower compared to that of a study where 33.9% of patients reached optimal target of <6mmol/l(Uloko et al. 2012)

Using the recommendation of the ADA guidelines, 42.5 % of the patients had their baseline fasting blood sugar levels reaching optimal target but upon next review, the number who reached optimal target reduced to 36 % which was comparable to results obtained from a study in Saudi Arabia where 40% of patients achieved optimal target(Al-Rowais 2014), in Uganda where 42.8% of patients achieved optimal target (Kibirige et al. 2014) and in Nigeria where 52.6% achieved optimal target (Uloko et al. 2012).There was a statistical difference between baseline and next medical review ($p<0.05$). Most participants for the study had poorly controlled fasting blood glucose level representing 57.7 % (n= 187) at baseline and 64 %(n= 208) upon next review consistent with a study where 60% where of patients had poorly controlled fasting blood sugar of >7.2mmmol/l (Al-Rowais 2014).

5.7 Use of Cholesterol Lowering Agents in Diabetics Hypertensives

Statin use has proved beneficial in the reduction of overall morbidity and mortality in patients at high risk aside it's lipid lowering effects**.** Moderate intensity statin is recommended in all patients 40 years and over even without risk factors. For those high risk patients such as those with hypertension, overweight, obesity and smoking, statins in high doses are recommended (ADA 2014). All of the participants for this study were hypertensive and 77.5% (n=252) of the study participants were either obese or overweight, meaning all the participant had high risk for cardiovascular disease and therefore the need for inclusion of statin in the therapy of these patients. Of all the patients only 35.7 % were put on statins which was not in conformity with current guidelines of the American diabetes Association.

5.8 Use of Aspirin in Diabetic Hypertensives

From the study 106 patients (30.2%) which is less than one third of patients with diabetes and hypertension were given low dose aspirin. A study by Tarawneh et al.(2015) reported a 43% intake of aspirin among diabetes patients in Jordan and (Sweileh et al) also reported a 31.5% use of aspirin among diabetic hypertensives in Palestine. The recommendation set out by the ADA guidelines and other clinical trials are not being adhered to. The American diabetic association guidelines recommend the initiation of aspirin as a primary intervention in diabetic patients who have a greater risk for cardiovascular events (10-year risk >10%) especially men who are 50 years and over and women who are 60 years and over with a least one of these risk factors namely hypertension, dyslipidaemia, those who smoke, those with family history of cardiovascular disease (Pignone et al. 2010) without risk of bleeding. In our current study all the patients had at least one risk factor which was hypertension. Lack of up to date information about current guideline recommendation by prescribers might have cause the low rate of prescribing Aspirin.

From the study 106 of the study participant were males of which 91 of them were above the age of 50 years. Of these, only 29 of them representing about 32% were receiving aspirin therapy. The number of females for the study was 219, of which 100 were above 60 years of age but of these only 37 of them representing 37% were receiving low dose aspirin. All the patients had hypertension which is a cardiovascular risk factor, most were overweight and obese predisposing them to dyslipideamia and therefore there was the need for more patients to be reassessed for the suitability of inclusion of aspirin in their therapy to protect them from cardiovascular accidents.

The HOT study showed the benefit of low dose 75mg/day aspirin in reducing myocardial infarction risk but with no effect on stroke and fatal bleeds (Hansson et al. 1998)

5.90 Patients Knowledge about non pharmacological approaches in Management of Diabetes and Hypertension

Modifiable risk factors of both diabetes and hypertension can be pursued to achieve better therapeutic and non therapeutic outcomes. These modifiable factors include lifestyle modifications. A study which was conducted over a 16 year period involving 84,941 healthy nurses reported 3300 new cases of type 2 diabetes. The study showed that being obese and overweight was a predominant risk factor for diabetes. Increased risk of diabetes and hypertension are associated with factors such as alcohol consumption, poor exercise habits,poor diet and smoking(Hu et al. 2001).

Several trials including the DASH trail proved that these lifestyle changes such as low salt diet, exercise, low saturated fat, cholesterol, high fibre diet significantly lowers blood pressure (Moore et al. 2001)

In this current study, All (100%) of the participants were knowledgeable about simple lifestyle and dietary modifications to help improve the management of diabetes and hypertension.

Just a few had no knowledge about not adding salt at table being able to help improve the blood pressures. In Malaysia, a study done by Ambigapathy et al. 2003 showed that the majority of participants were knowledgeable about lifestyle modifications. In contrast another study done by Okonta et al. 2014 majority of the respondents in their study were not knowledgeable. The reasons for this knowledge could be as a result of level of education of most of the patients and education and counseling programmes they are taking through at the diabetic/hypertensive centre whenever they visit. Even though majority of the patients knew about these lifestyle/non pharmacological approaches, that didn't translate to better control of their blood sugar or blood pressure. The reason for this could be due to lack of adherence to these non pharmacological measures.

6.0 Availability, Accessibility and Affordability of medicines

The main aim of the National Health scheme is the achievement of universal health coverage. Majority of patients who are dealing with chronic disease usually registers with the scheme, so that they can access health care at any point in time.

In this current project all the participants were interviewed 100 % (n=325) were registered with National health insurance and were benefiting. But over the years, remittances to the various institutions after work done do not go and care providers are forced to resort to suspend or sop health care being given to non faculty members. Another development is the copayment system that some service suppliers have adapted. This system requires patients to top up with an amount of money before drugs and services are rendered.

In this current study, majority of patients 58.8% (n=191) had to do copayment before insured drugs are given at accredited facilities outside KATH. Cost of drugs keep rising and so most NHIA accredited facilities require subscribers to pay the difference on certain drugs that falls outside the price range of the NHIA and these are mostly Antihypertensives, Antidiabetics, statins and Insulins

Majority of insured patients are the more vulnerable especially the poor and older population. These groups of people are more likely not to adhere to therapy when required to pay some amount of money(Moore et al. 2001).

Prescriptions were given to patients who could not get the required drugs in the hospital for them to take drugs from premises outside the hospital. Due to delays in reimbursement by NHIA, the hospital is unable to stock adequately to meet the demand and needs of the clients. Of the 325 participants interviewed. 57.5 % (n=187) said pharmacy cards were given to them once a while.42.5% (n=138) said they way given pharmacy cards anytime they come to the hospital. Most of the patients are not able to afford when asked to do copayment for certain drugs. Most of these over 22.5 %(n=73) complained of the difficulty they encounter when asked to collect their drugs from outside the hospitals. This poor blood sugar and pressure control could be due to institutional and individual factors including drug cost and availability, health policy disparities (Sinnott et al. 2013).

Limitations

A retrospective approach was used for the study. Patients could only be tracked and interacted with, only on their next visit. Baseline medication and level of control were obtained from the patients folders where there was missing information; these were obtained from the patients themselves or their caregivers.

The medication, blood pressure and blood glucose levels of the patients were only reviewed once aside the baseline due to time constraints. If more data on subsequent reviews were to have been taken, that would have given a true picture of the medications and levels of control.

CHAPTER 6

6.1 CONCLUSION

Majority of the patients exhibited adequate knowledge about lifestyle modifications, medications and dietary approaches to improve Blood pressure and glucose control, therapeutic outcomes observed in the clients who sought care at KATH was not optimal, based on the targets recommended in the standard guidelines (ADA 2014/STG 2010).

The majority of the patients (Both males and females) involved in the study were either overweight or obese, in particular the female subjects

Majority of the patients involved in the study were prescribed ACEI/ARBs (i.e. lisinopril/losartan) and a biguanide (Metformin) for the management of hypertension and diabetes respectively.

Cholesterol lowering therapy and Aspirin prescribing was inadequate in the study population.

All the patients were NHIS registered clients and majority of them were given prescription always or at least once a while to collect their drugs at other NHIS accredited Pharmacies due to unavailability of their drugs in KATH.

6.2 RECOMMENDATIONS

Further study should be carried out to assess and understand other reasons for the sub-optimal outcomes observed in the patients, despite the use of standard guidelines by the clinicians to manage the patients.

Efficient weight management strategies with input from dieticians must be adopted by both patients and the health care team to aid optimal weight control in the patients. This may contribute to improvement in glycaemic and blood pressure control for the patients.

Patients should be counseled efficiently on their condition and medications, and also monitored closely to ensure adherence to the appropriate pharmacological and non-pharmacological interventions used in their care.

The hospital should stock most of the commonly used drugs for the management of diabetes and hypertension so that patients can access all drugs at the hospital.

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APPENDICES

APPENDIX 1: DATA COLLECTION TOOL

UNIQUE CODE……

Clients background information

Age….. Sex: Male ☐ Female ☐

Weight (kg) ……. Height (cm) ……..

Marital status: Single ☐ Married ☐ Divorced ☐ Widow/Widower ☐

Religion: Christian ☐ Islam ☐ Traditional ☐ Other…….

Educational status: None ☐ Primary- 1, 2, 3, 4, 5, 6 JHS -1, 2, 3 SHS- 1, 2, 3

Tertiary- University, Polytechnic, other…….

Occupation …….

HYPERTENSION AND DIABETES

Information obtained from patient

1. How long have you been diabetic……..
2. How long have you been hypertensive …….
3. How long did it take for you to be started anti-diabetic management?

Immediately ☐

1-3mths ☐ 4-6mths ☐ 7mths-1year ☐ other (specify) ……..

4. How long did it take for you to be started on antihypertensive management?

Immediately ☐

1-3mths ☐ 4-6mths ☐ 7mths-1year ☐ other (specify)……..

5. How long have you been on anti-diabetic treatment?

1-2years ☐ 3-6years ☐ 7-9years ☐ 10 years and over ☐

6. How long have you been on antihypertenive treatment?

1-2years ☐ 3-6years ☐ 7-9years ☐ 10 years and over ☐

Current Weight (kg)…….. Height (cm)……..

7. Baseline Antihypertensives and Antidiabetic medication of the patient

Class of antihypertensive	Name of drug	Dosage/Dosage form	Class of antidiabetics	Name of drug	Dosage /Dosage form
Diuretics eg. Bendrofluazide furusemide			Insulin eg. Mixtard, Insulatard(isophane) Actrapid(soluble insulin)		
AC E Inhibitors eg. Lisinopril Ramipril, Enalapril			Biguanide eg. Metformin		

Calcium channel blockers eg.Nifedipine(nifecard),Amlodipine			Sulphonylureas eg. Glibenclamide(daonil) Gliclazide, Glimeperide		
ARB' s eg. Losartan,candesartan(Atacand)			Thiazolidinediones eg. Pioglitazone(glizone)		
Beta- blockers eg. Atenolol,bisoprolol, carvedilol			Dipeptidylpeptidase-4 inhibitor eg. Vildagliptin, Sixagliptin		
Centrally acting agents eg. Methyldopa(aldomet)			Others		
Vasodilators eg. Hydrallazine,ISDN					
Alpha blockers eg. Prazosin, Doxazosin					

Other drugs of patients which are not listed above

Name	Dosage/dosage form

8. Blood glucose and blood pressure readings of patient

Parameter	Baseline review	Next review
Fasting Blood glucose HbA1c		
Blood pressure		

NB. 8 and 9 were Information obtained from patients medical records

9. Next review Antihypertensive and Antidiabetic medication of the patient.

Class of antihypertensive	Name of drug	Dosage/Dosage form	Class of antidiabetics	Name of drug	Dosage /Dosage form
Diuretics eg. Bendrofluazide furusemide			Insulin eg. Mixtard, Insulatard(isophane) Actrapid(soluble insulin)		
AC E Inhibitors eg. Lisinopril Ramipril, Enalapril			Biguanide eg. Metformin		
Calcium channel blockers eg.Nifedipine(nifecard),Amlodipine			Sulphonylureas eg. Glibenclamide(daonil) Gliclazide, Glimeperide		
ARB' s eg. Losartan,candesartan(Atacand)			Thiazolidinediones eg. Pioglitazone(gliz		

			one)		
Beta- blockers eg. Atenolol,bisoprolol, carvedilol			Dipeptidylpeptidase-4 inhibitor eg. Vildagliptin, Sixagliptin		
Centrally acting agents eg. Methyldopa(aldomet)			Others		
Vasodilators eg. Hydrallazine,ISDN					
Alpha blockers eg. Prazosin, Doxazosin					

NB. Information obtained from patient interview and confirmed from patients prescription.

Comments

……

……

……

PATIENTS KNOWLEDGE ABOUT NON PHARMACOLOGICAL APPROACHES IN MANAGEMENT OF DIABETES AND HYPERTENSION

Do you know you have to exercise at least 30minutes a day? Yes ☐ No ☐

Do you know you have to eat diet high in fruits and vegetables? Yes ☐ No ☐

Do you know you have to eat high fiber diets and low cholesterol diets? Yes. ☐ No ☐

Do you know you have to cut the consumption of high levels of energy rich diets? Eg. soft drinks

Yes ☐ No ☐

Do you know you have to limit the intake of salt? Yes ☐ No ☐

Do you know you do not have to add salt at table? Yes ☐ No ☐

Do you know you have to drink alcohol in moderation eg.two unit per day for women and three units per days for men? Yes ☐ No ☐

Do you know you have to avoid cigarette smoking? Yes ☐ No ☐

AVAILABILITY, ACCESSIBILITY AND AFFORDABILITY

INSURED ☐ **NON INSURED** ☐

1. How many drugs were prescribed for you today ……..

2. How many of the drugs prescribed for you were obtained at the hospital

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ All ☐ None ☐

3. How frequent are prescription cards filled for you to take the insured drugs outside KATH

Always ☐ Every other visit ☐ Once a while ☐

4. Are drugs easily accessible when prescription cards are filled for you
Easily accessible ☐ Get with difficulty ☐ Do not get them at all ☐

5. Which pharmacy outlet(s) do you normally take your pharmacy card to for medication.....
.....

6. Are you sometimes asked to do co-payment before drugs are given to you?
Yes ☐ No ☐

7. Do you sometimes refuse to take medicines because of the difficulty in getting them?
Yes ☐ NO ☐

8. Of the drugs prescribed, are any of them non-insured.
Yes ☐ No ☐

9. If YES to question 8, are you able to buy the non-insured drugs
Yes ☐ No ☐

IF NO to question 8, why

Don't have money to buy ☐ Drug difficult to get ☐ Drugs too expensive ☐

10. Overall, how would you grade your satisfaction with the management of your health condition?

1 ☐ 2 ☐ 3 ☐ 4 ☐

1. No idea
2. Not satisfied
3. Moderately satisfied
4. Very satisfied

APPENDIX 2: ETHICAL APPROVAL LETTER

KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICAL SCIENCES / KOMFO ANOKYE TEACHING HOSPITAL
COMMITTEE ON HUMAN RESEARCH, PUBLICATION AND ETHICS

Our Ref: CHRPE/AP/140/15 — 22nd April, 2015.

Mr. Kofi Osei
Post Office Box 205
KNUST-KUMASI.

Dear Sir,

LETTER OF APPROVAL

Protocol Title: "Management of Hypertension in Patients with diabetes Mellitus."

Proposed Site: Komfo Anokye Teaching Hospital Diabetic and Hypertensive Clinics.

Sponsor: Principal Investigator.

Your submission to the Committee on Human Research, Publications and Ethics on the above named protocol refers.

The Committee reviewed the following documents:

- A notification letter of 16th January, 2015 from the Komfo Anokye Teaching Hospital (study site) indicating approval for the conduct of the study in the Hospital.
- A Completed CHRPE Application Form.
- Participant Information Leaflet and Consent Form.
- Research Protocol.
- Questionnaire.

The Committee has considered the ethical merit of your submission and approved the protocol. The approval is for a fixed period of one year, renewable annually thereafter. The Committee may however, suspend or withdraw ethical approval at any time if your study is found to contravene the approved protocol.

Data gathered for the study should be used for the approved purposes only. Permission should be sought from the Committee if any amendment to the protocol or use, other than submitted, is made of your research data.

The Committee should be notified of the actual start date of the project and would expect a report on your study, annually or at close of the project, whichever one comes first. It should also be informed of any publication arising from the study.

Thank you Sir, for your application.

Yours faithfully,

Osomfuor Prof. Sir J. W. Acheampong, MD, FWACP
Chairman