

**GLYCEMIC CONTROL,
CARDIOVASCULAR RISK PROFILE
AND THERAPEUTIC
INTERVENTIONS IN TYPE 2
DIABETES MELLITUS PATIENTS
AT THE NEW NYANZA
PROVINCIAL GENERAL
HOSPITAL,
KISUMU**

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Medicine in Internal Medicine by

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LIST OF ABBREVIATIONS

- ADA- American Diabetic association
- ACE- Angiotensin Converting Enzyme
- ACR- albumin creatinine excretion ratio
- ACP- American College of Physicians
- AHA- American Heart association
- ARB- Angiotensin Receptor blocker
- BMI- Body mass index
- BP- blood pressure
- CVD- cardiovascular disease
- DBP- diastolic blood pressure
- DAG- di-acyl glycerol
- DCCT- Diabetes Control and Complications Trial
- eGFR- estimated glomerular filtration rate
- FPG- fasting blood glucose
- HDL- high density cholesterol
- IGT- impaired glucose tolerance.
- KNH- Kenyatta National Hospital
- LDL-C- low density cholesterol
- UKPDS- United Kingdom Prospective Diabetes Study.
- NNPGH- New Nyanza Provincial General Hospital.
- OHA- oral hypo glycaemic agent.
- PPG- post-prandial glucose
- PCP- Pneumocystis jirovecii pneumonia
- SMBG- self monitoring of blood glucose
- TG- triglycerides
- WHO- World Health Organization

ABSTRACT

Background: The number of people with type 2 diabetes around the world is estimated to rise from 251 million in 2000 to 380 million by 2025¹. This rise will disproportionately affect the least developed countries of the world. While the prevention of diabetes is imperative, strict glycemic control-(treatment to target), is critical in reducing the onset and or progression of complications for those already afflicted by diabetes mellitus²⁻³. HBA1c, fasting and post-prandial glucose levels are vital indicators of the adequacy of glycemic control. Arterial blood pressure, the fasting lipid profile and urinary albumin excretion are parameters that can be used to make decisions regarding interventions in these patients, especially for coronary artery disease risk reduction-the most important cause of morbidity and mortality.

Study questions: How well is Type 2 diabetes mellitus controlled at a provincial (level 5) hospital, what coronary artery disease risk factors are prevalent and what pharmacotherapeutic interventions are being utilized?

Objective of the study: The study was designed to determine the demographic characteristics, cardiovascular risk factors, level of glycemic control and the pharmaco-therapeutic strategies utilised for CAD risk reduction in Type 2 Diabetes Mellitus patients attending the Outpatient Diabetic clinic at New Nyanza Provincial Hospital in Nyanza Province, Kenya.

Study design: The study was a cross-sectional hospital based observational study:

Site: at the Diabetes Outpatient Clinic at the New Nyanza Provincial General Hospital in Nyanza Province.

Subjects: The study looked at Type 2 diabetes mellitus patients on follow up for at least 6 months at the clinic.

Materials and methods: 119 patients consecutively sampled over nine months provided the data sought by the study. The data was categorized as follows: *Socio-demographic, Clinical, Laboratory or Therapeutic strategies data.*

Results: The study population was rural with 65.5% (78) of the patients living outside the municipal boundaries. The median age was 58.4 (SD 8.9) years. Seventy (58.8%) of the patients were female. Cigarette smoking and alcohol use were low, nineteen (16%) and eight (6.7%) respectively. The patients were generally overweight (68.9%), with a mean body mass index of 27.0 (SD5.6) kg/m².

Twenty three (19.3%) had excellent control with a fasting plasma glucose of less than 6mMol/L. Only 13 patients (10.9%) had a well controlled postprandial profile of less than 10mMol/L. One

hundred and four (87.4%) of the patients had good glycemic with HBA1c of less than 7%. Ninety five (79.8%) had excellent control of less than 6%. All patients except two (1.7%); were on pharmacologic management for glycemic control. One hundred and nine (91.5%) of the patients were OHAs with or without insulin. Twenty six (21.8%) were on insulin only, while eight (6.7%) were on both insulin and OHAs.

The mean SBP and DBP were 129.6(SD20.0) mmHg and 77.7(SD11.0) mmHg respectively. Ninety five (79.8%) were on antihypertensive medications. The RAAS blocking anti hypertensive agents (ACEI and ARBs) were the most frequently used agents, with sixty eight (57.1%) using them. Forty five (47.4%) of those on treatment were at target blood pressure of less than 130mmHg systolic and 80mmHg diastolic.

With regard to lipids, seventy two (60.5 %) had elevated LDL cholesterol above 2.6mmol/L. The utilization of lipid lowering agents was low with only nine (7.6%) patients on them. Antiplatelet agents were used in eleven (9.2%) patients.

The mean estimated glomerular filtration rate was 70.5 ml/min (SD 27.2). Ninety seven (81.5%) patients had deranged renal function; with an estimated GFR below 60ml/min. The median albumin-creatinine excretion ratio was 15.0 (IQR 10-50). Forty four (37%) patients had microalbuminuria, with no patient having macro-albuminuria. Twenty three (52.3%) of patients with microalbuminuria were on RAAS blocking agents. There was no statistically significant difference in the choice of agents for blood pressure control between the patients with microalbuminuria and those with normo-albuminuria.

There was no statistically significant socio-demographic predictor of glycemic control in this study population. Fasting glucose was found to independently predict blood glucose control from our data. There was a trend towards significance with the waist hip ratio.

Conclusion: The level of glycemic control in the study population was good. This is however negated by the high prevalence of elevated LDL cholesterol, poorly controlled blood pressure, obesity and low up take of interventions for cardiovascular risk factor reduction.

1.0. LITERATURE REVIEW

1.1. BACKGROUND

The number of people with type 2 diabetes around the world is estimated to rise from 251 million in 2000 to 380 million by 2025 ¹. Diabetes mellitus is associated with a significantly compromised life expectancy and the quality of life. This has grave implications on healthcare and social support systems with regard to the expected morbidity and mortality (UKPDS) ²⁻³. In *this regard*, intensive therapy targeting normoglycaemia has been shown to have beneficial effects in both type 1 (KUMAMOTO) ⁴ and type 2 diabetes mellitus (DCCT and UKPDS) ⁵⁻⁶.

Several mechanisms have been postulated to lead to the myriad complications in Diabetes mellitus. These include; the overproduction of superoxide by the mitochondrial electron-transport chain, diabetic dyslipidemia, platelet activation, impaired fibrinolysis, and altered endothelial metabolism. Hyperinsulinemia on its own has been implicated in the acceleration of atherosclerosis and genesis of hypertension in diabetics.

The synergistic effect of CAD risk factors and the multiple pathophysiologic processes results in an exponential increase in morbidity and mortality in diabetic patients. There is therefore need for a comprehensive therapeutic strategy to mitigate against these multiplicative effects.

1.2. INTRODUCTION TO DIABETES MELLITUS

Diabetes mellitus refers to a group of metabolic diseases characterized by hyperglycemia arising from defects in insulin secretion, insulin action, or both. The resulting chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs through varied mechanisms⁶⁻⁷

Coronary artery disease risk factors occur in clusters of some or all the following: obesity, dyslipidemia, hypertension and microalbuminuria. Obesity, particularly abdominal obesity, is associated with heightened resistance to the effects of insulin with consequent hyperinsulinemia and hyperglycemia. Adipokines may also lead or contribute to vascular endothelial dysfunction, an abnormal lipid profile, hypertension, and vascular inflammation, all of which promote the development of atherosclerotic cardiovascular disease (CVD).

To promote and sustain good health and quality of life in these patients, all these risk factors must be managed in totality at all levels of health care services.

1.3. THE CLASSIFICATION OF DIABETES MELLITUS

The current classification of diabetes mellitus is based on etiopathogenesis. The classification of diabetes includes four clinical classes:⁸

- a. **Type 1 diabetes** results from β -cell destruction, usually leading to absolute insulin deficiency
- b. **Type 2 diabetes** results from a progressive insulin secretory defect on the background of insulin resistance.
- c. **Other specific types of diabetes** due to other causes, e.g., genetic defects in β -cell function, genetic defects in insulin action, diseases of the exocrine pancreas such as cystic fibrosis, and drug- or chemical-induced such as in the treatment of AIDS or after organ transplantation.
- d. **Gestational diabetes mellitus (GDM)** is diabetes diagnosed during pregnancy.

1.4. TYPE 2 DIABETES MELLITUS

This form of diabetes, accounts for 90–95% of the total diabetes mellitus burden. Type 2 diabetes frequently goes undiagnosed for many years because the gradual onset of either pancreatic dysfunction or insulin resistance and the subsequent hyperglycemia.

Most patients with this form of diabetes are obese; those not obese by traditional weight criteria may have an increased percentage of body fat distributed predominantly in the abdominal region. The patients have insulin resistance and usually relative (rather than absolute) insulin deficiency. Insulin secretion is defective in these patients and insufficient to compensate for insulin resistance. Initially, the hyperglycemia is not severe enough for the patient to notice any of the classic symptoms of diabetes. The hyperinsulinemia, hyperglycemia, and the associated metabolic dysregulation, however, put these patients at increased risk of developing micro and macrovascular complications.

The causes of this form of diabetes are many and varied. The specific etiologies are however, unknown. Its frequency varies in different racial/ethnic subgroups. Type 2 diabetes is associated with a strong, complex and generally poorly defined genetic predisposition. The risk of developing this form of diabetes increases with age, obesity, and lack of physical activity. Insulin resistance may improve with weight reduction of more than 10%.

Despite pharmacological treatment, diabetes is a progressive condition and normo-glycemia is seldom restored.

1.5. DIAGNOSIS OF DIABETES MELLITUS

Table 1 Diagnostic Criteria for Diabetes Mellitus⁹

1.	FPG of 7.0mmol/l. Fasting is defined as no caloric intake for at least 8 h.*
	OR
2.	Symptoms of hyperglycemia and casual plasma glucose of 11.1Mmol/l. The classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss.
	OR
3.	2-h plasma glucose of 11.1mmol/l during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
	NB: Casual is defined as any time of day without regard to time since last meal.

In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day⁹

The diagnosis of type 2 diabetes mellitus is usually made on the basis of phenotype. Individuals with type 2 diabetes exhibit the following features: Onset after the age of 30 years, obesity (80% are obese, though elderly individuals may be lean), requirement for insulin therapy as the disease progresses; and the presence of conditions such as insulin resistance, hypertension, cardiovascular disease, dyslipidemia or polycystic ovarian syndrome.

Although most individuals diagnosed with type 2 diabetes mellitus are older, the age at diagnosis is declining. This has been attributed to the increase in the incidence and prevalence of obesity in children and adolescents; and a much more sedentary lifestyle.

It remains difficult to unequivocally categorize all individuals. Some individuals (5-10%) with the phenotypic appearance of type 2 diabetes do not have absolute insulin deficiency but have autoimmune markers (ICA, GAD auto-antibodies) suggestive of type 1 diabetes mellitus termed; The Latent Autoimmune Diabetes of the Adult (LADA). Such individuals are more likely to be less than 50 years of age, have normal BMI and or have a family history of auto-immune disease. They are much more likely to require insulin treatment within 5 years.

1.6. THE COMPLICATIONS OF DIABETES MELLITUS

Diabetes mellitus is associated with a plethora of complications. These are divided into acute and chronic complications. The chronic complications are responsible for the majority of the morbidity and mortality associated with diabetes mellitus. They are in turn divided into vascular and nonvascular complications. Vascular complications are further divided into micro and macrovascular complications. The microvascular complications are retinopathy, neuropathy and nephropathy. The macrovascular complications include coronary artery disease, cerebrovascular disease and peripheral vascular disease. Nonvascular complications affect the following systems; the GI tract, genitourinary tract, cataracts, glaucoma and skin.

Complications in diabetes correlate with fasting and postprandial glycemia as well as HBA1C. This has been demonstrated conclusively for the microvascular complications in various trials including the landmark DCCT, UKPDS and Kumamoto trials. Evidence for the beneficial effect of intensive glycemic therapy on macrovascular complications is less conclusive; the beneficial effects of interventions targeting the other coronary artery disease factors such as hypertension, dyslipidemia and microalbuminuria, have been conclusively demonstrated. The UKPDS showed a significant reduction in both micro and macro vascular complications (by between 32-56%) in patient on strict blood pressure control therapy.

Globally, Diabetes is the leading cause of coronary artery disease, chronic kidney disease, non-traumatic extremity amputations and blindness in the west.

The incidence and prevalence of these complications has been steadily rising locally, congruent with the growing diabetes epidemic.

1.7. PATHOGENESIS OF MICROVASCULAR COMPLICATIONS:

Microvascular complications are thought to arise through several mechanisms. These include:

Formation of advanced glycosylation end products (AGEs): Non-enzymatic glycosylation occurs when glucose interacts with the amino groups on proteins. Through a series of reactions between glucose and the free amino terminals of proteins, lipids or nucleic acids, glycated end products are made. These products cross-link proteins, accelerate atherosclerosis, promote glomerular dysfunction, reduce nitric oxide synthesis, induce endothelial dysfunction, and alter extracellular matrix composition and structure.¹⁰

Increased glucose metabolism, via the *sorbitol pathway*: Intracellular glucose is predominantly metabolized by phosphorylation and subsequent glycolysis. At high blood levels, some glucose is converted to sorbitol by the enzyme aldose reductase that requires NADPH as a co-factor for its normal function. Increased activity of this pathway reduces the availability of NADPH for the recycling of glutathione and thus the capacity of diabetics to handle oxidative stress.¹¹

Increased formation of diacylglycerol leading to activation of *protein kinase C (PKC)*: Among other actions, PKC alters the transcription of genes for fibronectin, type IV collagen, contractile proteins, and extracellular matrix proteins in endothelial cells and neurons.

Increased the glucose flux through the *hexosamine pathway*: Increased flux through this pathway is associated with increased generation of fructose-6-phosphate. Fructose-6-phosphate is a substrate for O-linked glycosylation and proteoglycan production. The resultant increase in glycosylation of proteins may lead to altered function of proteins such as endothelial nitric oxide synthase. It may also lead to by changes in the gene expression of transforming growth factor β (TGF- β) or plasminogen activator inhibitor-1 (PAI-1).

Growth factors appear to play an important role in DM-related complications, and their production is increased by most of these proposed pathways. These factors include: *Vascular endothelial growth factor* (VEGF) increased locally in diabetic proliferative retinopathy; *Transforming growth factor- β* is increased in diabetic nephropathy. Other growth factors, such as platelet-derived growth factor, epidermal growth factor, insulin-like growth factor I, growth hormone, basic fibroblast growth factor, and even insulin, have been suggested to play a role in diabetes mellitus related complications. Although hyperglycemia serves as the initial trigger for the complications in diabetes, it is still unknown whether the same pathophysiologic processes are operative in all complications or whether some pathways predominate in certain organs.

1.8. MACROVASCULAR COMPLICATIONS

The dysglycemia in type 2 diabetes is characterized by two forms of dysglycemia; sustained chronic hyperglycemia and acute glucose fluctuations. This variability leads to activation of oxidative stress and excessive protein glycation around a mean value¹²⁻¹³. Brownlee proposed a unifying theory for the major role that hyperglycemia plays in the activation of oxidative stress in the pathogenesis of diabetic complications.¹⁴⁻¹⁵ These metabolic alterations predominantly affect the endothelial cells leading to progressive vascular damage¹⁵.

The role of hyperglycemia in macrovascular complications: Epidemiological evidence suggests that postprandial hyperglycemia is an independent risk factor for mortality, including cardiovascular mortality. The DECODE Study Group evaluated the relationship between mortality and glucose levels in the fasting state and 2 hours after a 75-g oral glucose tolerance test. After mean 7.3 year follow-up, postprandial hyperglycemia (11.1mmol/L) in individuals not previously known to have diabetes was found to be associated with a 2- to 3-fold increase in the risk of death, independent of FPG level⁷. In an 11-year follow-up to the Diabetes Intervention Study, a greater incidence of death was observed in subjects with increased PPG levels at baseline compared with subjects who had good to borderline PPG levels (7.8-11.1 mmol/L versus 11.1 mmol/L)¹⁶.

A number of studies have found a relationship between PPG and the risk of diabetes related complications. These findings inform the need for the control of postprandial hyperglycemia in order to prevent or delay complications¹⁷⁻²³. The Framingham Offspring Study²⁴ showed that post challenge hyperglycemia may be much more associated with an increased risk of cardiovascular events more strongly than fasting hyperglycemia. This association is independent of A1C or FBG.

It is possible that postprandial hyperglycemia leads to the highest diurnal levels of glucose despite normal fasting levels. This in turn has a more damaging effect on vasculature, heart function and lipid profile. This translates into increased cardiovascular risk in these individuals²⁵⁻²⁷. In the DCCT/EDIC trial, Intensive treatment reduced the risk of any cardiovascular disease event by 42% and the risk of nonfatal myocardial infarction, stroke, or death from cardiovascular disease by 57%. The decrease in glycosylated hemoglobin values during the DCCT was significantly associated with most of the positive effects of intensive treatment on the risk of cardiovascular disease²⁸.

A global anti-diabetic strategy is thus essential and should aim at reducing to a minimum the different components of dysglycemia (i.e. A1C, fasting and postprandial glucose, as well as glucose variability).²⁹⁻³¹

1.9. RISK FACTORS FOR CARDIOVASCULAR DISEASE IN DIABETES.

Diabetes mellitus patients have a greater burden of atherogenic risk factors when compared to non-diabetics. These factors include hypertension, obesity, lipid abnormalities, hyperinsulinemia, and elevated plasma fibrinogen³²⁻³⁵. Many of these risk factors are also present in the pre-diabetic state³⁶. The CAD risk in diabetics varies widely with the intensity of these risk factors and their effect is multiplicative. The evidence is strongest for hypertension, elevated low density lipoprotein, smoking, the metabolic syndrome, hyperglycemia and microalbuminuria.

Hypertension: Hypertension is present at diagnosis in many patients with type 2 diabetes, but generally does not occur until after the onset of renal disease in patients with type 1 diabetes³⁷. In Africa, prevalence studies have found of 33.3% and 29.2% in Ethiopia and urban Tanzania respectively³⁸⁻³⁹. The most compelling evidence for the importance of hypertension in diabetes comes from the United Kingdom Prospective Diabetes Study (UKPDS)⁴⁰. In this study, each 10 mmHg reduction in updated mean systolic pressure was associated with a 12 percent risk reduction in any complication related to diabetes (including cardiovascular disease); the lowest risk occurred at a systolic pressure below 120 mmHg. The incidence of myocardial infarction fell from 33.1 per 1000 patient years at an updated mean systolic pressure 160 mmHg to 18.4 per 1000 patient years at an updated mean systolic pressure below 120 mmHg. Based upon these and other observations, aggressive antihypertensive therapy is warranted in all patients with diabetes and the recommended goal blood pressure is less than 130/80 mmHg⁴¹. Since hypertension places diabetic patients at very high risk of cardiovascular complications, all diabetics with blood pressures above 140/90 mmHg should also be immediately begun on antihypertensive drug therapy.

Dyslipidemia: There are a number of differences in the lipid profile between diabetics and non diabetics that may contribute to the increase in atherosclerosis⁴²⁻⁴³. Among patients with type 2 diabetes, insulin resistance, relative insulin deficiency, and obesity are associated with hypertriglyceridemia, low serum HDL cholesterol concentrations, and occasionally high serum LDL cholesterol and lipoprotein (a) values⁴³. This pattern of lipid abnormalities can be detected before the onset of overt hyperglycemia and is thought to be due in part to hyperinsulinemia and/or insulin resistance⁴⁴⁻⁴⁵. For any serum lipoprotein concentration, diabetic patients have

more coronary disease than nondiabetic patients. This increase in risk may be due in part to qualitative differences in the lipoprotein fractions or to the presence of other proatherosclerotic metabolic changes. Among these changes are high serum concentrations of small dense LDL particles, enhanced oxidative modification of LDL, and elevations in serum lipoprotein (a) ⁴⁵.

The association of elevated LDL cholesterol with cardiovascular risk in many epidemiologic studies has been reinforced by randomized clinical trials including the MRC/BHF Heart Protection Study, showing that statin therapy improves outcomes in diabetics, including those without clinical evidence of CAD and those with values below 3mmol/L ⁴⁶⁻⁴⁷. Non-HDL cholesterol appears to be a particularly strong predictor of CAD in both men and women with diabetes ⁴⁷.

Smoking: Smoking is an independent risk factor for all-cause mortality, due largely to coronary artery disease ⁴⁸. There is a dose-response relationship between current smoking status and risk of coronary artery disease in women with diabetes ⁴⁹. Smoking is associated with increases in the serum concentrations of total cholesterol and very-low-density lipoprotein cholesterol, a decrease in serum high-density-lipoprotein cholesterol, and a greater degree of insulin resistance ⁵⁰. Smokers, via an uncertain mechanism, have poorer glycemic control ⁵¹. Smokers with either type 1 or type 2 diabetes are at increased risk for neuropathy, an effect that persists after adjusting for glycemic control ⁵². Smoking is associated with an increased risk of end-stage renal disease and with decreased survival once dialysis is commenced ⁵³⁻⁵⁵.

Sex: The risk for coronary artery disease is much higher in female patients with longstanding diabetes than in men ⁵⁶. The magnitude of this effect was illustrated in a meta-analysis of 37 studies of almost 450,000 patients with type 2 diabetes.

Microalbuminuria: Microalbuminuria is the earliest clinical manifestation of diabetic nephropathy and is associated with an increased risk of coronary artery disease in both diabetics and non-diabetics. Microalbuminuria may be a marker for both vascular disease and for a greater likelihood of other cardiovascular risk factors. The magnitude of the predictive value of microalbuminuria was illustrated in a review of over 9000 participants in the HOPE (Heart Outcomes Prevention Evaluation) trial ⁵⁷. The presence of microalbuminuria was associated with an increased relative risk of myocardial infarction, stroke, or cardiovascular death in those with and without diabetes ⁵⁸. The risk of an adverse cardiovascular event increased progressively with increased absolute levels of microalbuminuria.

A similar impact of microalbuminuria was found among participants in the UKPDS trial⁵⁹. Ten years following diagnosis of diabetes, the prevalence of microalbuminuria was 24.9%, of macroalbuminuria was 5.3%, and of elevated plasma creatinine or RRT was 0.8%. Patients with elevated plasma creatinine or RRT had an annual death rate of 19.2% (95% confidence interval, CI, 14.0 to 24.4%). There was a trend for increasing risk of cardiovascular death with increasing nephropathy ($P < 0.0001$), with an annual rate of 0.7% for subjects in the stage of no nephropathy, 2.0% for those with microalbuminuria, 3.5% for those with macroalbuminuria, and 12.1% with elevated plasma creatinine or RRT. Individuals with macroalbuminuria were more likely to die in any year than to develop renal failure.

Exercise: Regular exercise is associated with a lower risk of both CHD and cardiac death for both primary and secondary prevention. Recommendations are; People with diabetes should be advised to perform at least 150 min/week of moderate-intensity aerobic physical activity to achieve 50–70% of maximum heart rate. In the absence of contraindications, people with type 2 diabetes should be encouraged to perform resistance training at least three times per week. In a study in 3316 Finnish patients with diabetes, both occupational and leisure time physical activity were associated with a significant reduction in cardiovascular mortality⁶⁰.

Light to moderate alcohol intake: The effect of light to moderate alcohol consumption in diabetic patients was evaluated in the Physicians' Health Study and Nurses Health Study. These men and women had a significantly lower risk of death from CHD than those who rarely or never consumed alcohol. The risk reduction was similar to that seen in non-diabetics⁶¹⁻⁶³.

Hyperhomocysteinemia: An elevated serum concentration of homocysteine is a known risk factor for atherosclerosis and is associated with an increased risk of myocardial infarction and death. The risk appears to be greater in patients with diabetes for each 5 $\mu\text{mol/L}$ increment in serum homocysteine concentrations, the odds ratio for diabetics and non-diabetics was 1.60 and 1.17, respectively⁶⁴.

Obesity: The association of obesity with the insulin resistance syndrome and cardiovascular risk is not only related to the degree of obesity but also seems to be critically dependent on body fat distribution. Thus, individuals with greater degrees of central adiposity develop this syndrome more frequently than do those with a peripheral body fat distribution.⁶⁵

1.10. MECHANISMS OF INCREASED RISK

A variety of mechanisms may contribute to the increase in CHD risk in patients with diabetes in addition to the effects on blood pressure and lipid metabolism.

Endothelial dysfunction: Endothelial dysfunction has been documented in diabetic patients who have normal coronary arteries and no other risk factors for coronary disease⁶⁶⁻⁷⁰. The degree of impairment is related to the duration of diabetes, but a defect can occur acutely in patients who develop postprandial hyperglycemia despite having normal fasting plasma glucose⁷¹. The presence of insulin resistance alone may be associated with coronary endothelial dysfunction.

Platelet activation: Diabetes has a number of effects on platelet function that may predispose to coronary thrombosis. These include increased primary and secondary platelet aggregation⁷²⁻⁷⁶, increased platelet activation and degranulation⁷⁷, and enhanced binding of fibrinogen to the glycoprotein IIb/IIIa complex. The altered platelet function in diabetics may be mediated in part by elevated blood glucose. This relationship is continuous and graded and is even evident in a range of glucose levels considered to be normal.

Coagulation abnormalities: In addition to platelet activation, diabetes also predisposes individuals to abnormalities in various pathways involved in coagulation, hemostasis, and fibrinolysis⁷⁸. Diabetes is associated with an increase in plasma fibrinogen, which is a cardiovascular risk factor associated with older age, increased body mass, smoking, total cholesterol, and triglycerides. Fibrinolytic activity is reduced⁷⁹⁻⁸⁰ because of increased plasma concentrations of and enhanced binding of tissue plasminogen activator to its inhibitor, plasminogen activator inhibitor (PAI-1). Elevations in PAI-1, probably due to increased synthesis, are also found in atheromata obtained from type 2 diabetic patients undergoing atherectomy⁸¹. Hyperglycemia may contribute to impaired fibrinolysis via non-enzymatic glycosylation of certain proteins. LDL cholesterol normally stimulates the production of PAI-1 and reduces the generation of tPA; these effects are enhanced by glycosylated LDL.

Plaque composition: Plaque composition may differ in diabetics and affect coronary risk. In a histologic study of atherectomy specimens from patients with and without diabetes, coronary tissue from diabetics contained a greater amount of lipid-rich atheroma, more macrophage infiltration, both of which are associated with a greater risk for plaque rupture, and a higher incidence of thrombosis⁸¹.

1.11. THERAPEUTIC STRATEGIES IN TYPE 2 DIABETE MELLITUS

As outlined in the risk factor profile 1.9 above and research findings 1.12 below, the therapeutic strategies in type 2 diabetes must be multi-pronged.

These strategies must include: glycemic control with lowering of blood sugar; therapeutic diabetes education; blood pressure control; lipid lowering and evaluation and management of any microvascular, macrovascular and neurologic complications; and avoidance of drugs that can aggravate abnormalities of insulin or lipid metabolism.

Hyperglycemia: Treatments to achieve normoglycaemia focus on increasing insulin secretion, responsiveness, or both, or decreasing the rate of carbohydrate absorption. All available antihyperglycemic agents reduce HbA1c level. Only a few agents have been shown to specifically lower both FPG and PPG concentrations. These agents include; *short-acting insulin analogues*, *α-glucosidase inhibitors*, *the short-acting insulin secretagogues* (nateglinide and repaglinide), and *glyburide-metformin tablets* for postprandial hyperglycemia. *Repaglinide* and *glyburide-metformin* combination lower FPG level effectively, in addition to their effect on PPG. The other agents only lower FPG concentration significantly when used in combination⁸⁴. If goal glycemic control is not achieved, combined therapy with oral agents and or the early addition of insulin must be explored.

Therapeutic diabetes education must include: dietary changes and diet counseling; physical activity and weight reduction. These changes in lifestyle including modest alcohol use and smoking cessation, have been shown to slow down the progression of impaired glucose tolerance to overt diabetes and improve glycemic control in diabetic patients.

Dyslipidemia: There is evidence for the additive cardiovascular risk of hyper-glycemia and dyslipidemia. Regular assessment of and treatment of lipid abnormalities is recommended as part of comprehensive care in diabetes mellitus. The ADA and the AHA⁸² recommend the following prioritization order in treating dyslipidemia; lowering the LDL, raising the HDL and then decreasing triglycerides levels. The HMG CoA reductase inhibitors are the agents of choice for the lowering of LDL cholesterol as shown in a metaanalysis of 14-randomised control trials⁸³. They have led to a significant reduction in fatal and non fatal myocardial infarctions.

Hypertension: The UKPDS and HOT studies⁸⁴ showed that tight blood pressure control leads to substantial reduction in the cardiovascular events and death. Targeting the goal blood pressure to less than 130/80 mmHg should be accompanied by life-style modifications such as weight

reduction, exercise, restrictions in sodium chloride intake and stress management⁸⁵. The ADA recommends RAAS blocking agents as the first line agents. Subsequently, other beneficial agents can be added. These agents include; beta blockers, thiazide diuretics, and calcium channel blockers. Dietary salt restriction is vital in reversing the underlying tendency to volume expansion⁸⁵. ACE inhibitors and ARBs prevent the progression to macroalbuminuria and end stage kidney disease⁸⁶.

Exercise: Exercise has been shown to improve insulin sensitivity, lower HBA1C and raise the HDL cholesterol⁸⁷. Exercise may be occupational or leisurely as seen in the Finnish study.

Smoking cessation: it has been demonstrated to improve insulin sensitivity, improve glycemic control and slow down the progression of atherosclerosis⁸⁸.

Anti-platelet therapy: there is no clear proof for the utility of these agents for primary prophylaxis. They are however recommended in diabetics over 40 years of age with other CAD risk factors such as hypertension, dyslipidemia, smoking cigarettes and a family history of CAD⁸⁹.

1.12. TREATMENT GOALS FOR ADULT PATIENTS DIABETES MELLITUS

ADA recommended therapeutic targets include but are not limited to the following.

Table 2 Summary of glycemic parameters and treatment goals ⁹⁰

Parameter	Level
HB A1C	< 7.0%*
Pre-prandial capillary plasma glucose	(3.9–7.2 mmol/l)
Peak postprandial capillary plasma glucose	(<10.0 mmol/l)
Blood pressure	<130/80mmHg
LDL cholesterol	<2.6mmol/l
HDL cholesterol	>1.1mmo/l
Triglycerides	<1.7mmol/l
Key concepts in setting glycemic goals: <ul style="list-style-type: none"> ▪ A1C is the primary target for glycemic control. ▪ Postprandial glucose may be targeted if A1C goals are not met despite reaching pre-prandial glucose goals 	

Hemoglobin A1C: This is the most widely used clinical test in monitoring long term glycemic control. A1C reflects mean blood glucose over the entire 120 day life span of the red blood cell, and correlates best with mean blood glucose over the previous 8 to 12 weeks. Red cells are freely permeable to glucose which becomes irreversibly bound to the hemoglobin at a rate dependent upon the prevailing blood glucose. Due to the high red cell turnover, the average amount of A1C is dynamic and indicates the mean blood glucose concentration over the life span of the red cell. ^{91-93,}

Interpretation of HBA1C: The A1C test is subject to certain limitations. A disparity between the A1C value and blood glucose; may suggest that the patient is falsifying blood glucose results or has made an effort to improve glycemic control in the 2 weeks before the appointment. It may also imply uncontrolled inter-prandial hyperglycemia. Some of the factors which can falsely elevate the A1C should be sought for include: hemoglobinopathies, untreated iron deficiency anemia, or renal failure. If the A1C value is lower than expected, it is possible that the patient has prolonged episodes of undetected hypoglycemia for example undetected nocturnal

hypoglycemia. Lower than expected HBA1C may arise with reduced red cell survival as in hemolysis or in conditions in which a disproportionate number of red cells are young as in with chronic bleeding, venesection, treatment of anemia⁹⁴

Recommendations on HBA1C in type 2 diabetes: Type 2 diabetes has less variability in blood glucose concentrations. As a result, the fasting blood glucose correlates fairly well with the A1C value and can be used with the A1C to estimate glycemic control. Lowering A1C to an average of 7% has clearly been shown to reduce microvascular and neuropathic complications of diabetes and, possibly, macrovascular disease⁹⁵. The A1C goal for non-pregnant adults in general is <7%. (A). The HBA1C goal for selected individual patients is as close to normal (<6%) as possible without significant hypoglycemia⁹⁵. From a practical standpoint however, pushing HBA1C lower may be attended by certain challenges such as, increased risk of hypoglycemia, weight gain, and the cost of using multiple drugs to achieve the goal. Each patient should be encouraged to get his or her A1C as close to the non-diabetic range as is practically possible.

Fasting blood sugar: The fasting blood glucose concentration is often used to monitor control in type 2 diabetes since it correlates well with A1C values⁹⁶⁻⁹⁷. It however, may vary by about 15 percent from day to day, and therefore changes in therapy should be based on an average over several days⁹⁷. Some have argued that non-fasting blood glucose measurements are a better marker of glycemic control than fasting values⁹⁸. A meta-analysis of eight randomized trials of SMBG in type 2 diabetes (one of which included patients taking insulin) concluded that SMBG has no definitive benefit⁹⁹ it may however be effective in improving glycemic control in those who are diet-treated or who are treated with oral agents not associated with hypoglycemia. The ADA recommends that patients with type 2 diabetes who are treated with insulin or oral hypoglycemic drugs monitor blood glucose daily¹⁰⁰.

Postprandial blood glucose: In type 2 diabetes patients, peak insulin levels are delayed and are insufficient to control PPG excursions adequately. Abnormalities in insulin and glucagon secretion, hepatic glucose uptake, suppression of hepatic glucose production, and peripheral glucose uptake contribute to higher and more prolonged PPG excursions than in non-diabetic individuals. Emerging data now support the relationship between glycemic control and macrovascular disease. Many patients with type 2 diabetes have difficulty attaining the recommended HbA1C targets despite normal or near-normal FPG levels; thus, pharmacologic treatment targeting PPG levels may prove beneficial¹⁰¹.

Fructosamine: Many proteins other than hemoglobin undergo non-enzymatic glycation, leading to the formation of advanced glycosylation end products which may play a direct role in the development of diabetic microvascular complications. The term fructosamine has been applied

to the ketoamines formed in this process. Several methods are available for measuring serum fructosamine¹⁰².

Most (including colorimetric assays) are simpler, cheaper, and more precise than assays for A1C. There is generally a good correlation between serum fructosamine and A1C values¹⁰³. Several potential problems emerge with the use of serum fructosamine measurement. These include; the higher within-subject variation for serum fructosamine compared to A1C; as a result, serum fructosamine concentrations must change more before a significant change can be said to have occurred¹⁰⁴.

The turnover of serum albumin is more rapid than that of hemoglobin (28 days versus 120 days). Thus, serum fructosamine values reflect mean blood glucose values over a much shorter period of time (one to two weeks). Serum fructosamine values must be adjusted if the serum albumin concentration is abnormal¹⁰⁵. Furthermore, falsely low values in relation to mean blood glucose values will occur with rapid albumin turnover as occurs in patients with protein-losing enteropathy or the nephrotic syndrome. These limitations plus the superfluous need to follow changes in mean blood glucose concentrations every one to two weeks means that A1C is usually preferable for estimating mean blood glucose concentrations¹⁰⁶.

1.13. ADEQUACY OF CARE

Despite extensive data suggesting significant clinical and outcome benefits with the use of preventive and treatment strategies, and increasing media attention, there has been little improvement in diabetes management in the US. Surveys of patients aged 18 to 75 years with diabetes, comparing the US NHANES databases for 1988 to 1994 and 1999 to 2002¹⁰⁷, indicate that glycemic control has improved only minimally (nonsignificant decrease in proportion of patients with A1C > 9 percent, no change in mean A1C, increase in patients with A1C between 6 and 8 percent), and blood pressure distribution has remained unchanged.

Improvements were seen in the proportion of patients with LDL cholesterol <130 mg/dL (3.4 mmol/L); using aspirin; and receiving annual influenza vaccination, lipid testing, eye examination, and foot examination. About 20 percent of patients in 1999 to 2002 had A1C >9 percent, 33 percent had blood pressure >140/90 mm, and 40 percent had LDL cholesterol >130 mg/dL (>3.4 mmol/L). Even when patients are achieving goals for individual components of diabetes care, the proportion of patients who are simultaneously at goal for all measured targets is low.

In a study of 80,000 diabetic patients receiving care in a Veterans Affairs system, only 4 percent were simultaneously at ADA goal for A1C, LDL cholesterol, and blood pressure, though rates for individual targets ranged from 23 to 41 percent. Nevertheless, small improvements in diabetes management and cardiovascular risk factor reduction have decreased cardiovascular and all-cause mortality rates in some patients¹⁰⁸.

THE SCENARIO AT THE KENYATTA NATIONAL HOSPITAL

Several studies have been on type 2 diabetes patients at KNH, among these are those by Mwendwa¹⁰⁹, Vaghela¹¹⁰, and Nguchu¹¹¹. They all demonstrated a high prevalence of coronary artery disease risk factors and poor uptake of risk factor reduction strategies. Good glycemic control was in a small proportion of these patients. Vaghela et al found 29.9% of patients at the KNH Diabetic outpatient clinic had good glycemic control with an HBA1c of <7%. 71% had either normal BP or Grade 1 hypertension. Based on ADA Guidelines, 93% had hypercholesterolemia with a female preponderance (P value of <0.009). Only one patient was on a lipid lowering agent, 18% had albuminuria, 15.7% of patients had micro-albuminuria (30-300mg/g) and <1% had macro-albuminuria. Excluding the diabetic state, 79.6% had five or more risk factors. Males had more risk factors than females. 72.2% had age and sex as risk factors for CAD with a female preponderance (p value <0, 0001). 63.8% were either overweight or had class 1 obese. 5.6% were on going cigarette smokers (all male). 77.8% and 66.7% had family history of diabetes 15.7% had a history of sudden cardiovascular or cerebrovascular death.

2.0. JUSTIFICATION OF THE STUDY

Diabetes mellitus is an epidemic that is dramatically unfolding before us. As our country urbanizes, chronic illnesses such as diabetes are expected to equal if not co-exist with infectious diseases as a major cause or contributor to morbidity and mortality.

The outlying hospitals that serve the larger population of Kenya will bear the most of this burden. Provincial (level 5) hospitals will be critical in offering guidance and even mentoring lower level facilities as to mitigate against the ravages of this epidemic. The New Nyanza Provincial General Hospital is one such hospital.

The New Nyanza Provincial General Hospital is located in Kisumu, the third largest city in Kenya. It is the main referral hospital for the Western, Nyanza and central parts of the Rift Valley provinces. Kisumu city has witnessed phenomenal growth over the last couple of years. Due to its location, the city and hospital serve communities that are a minority at the Kenyatta National Hospital, Nairobi, where most of research in type 2 diabetes has been done.

There is significant data on diabetes from the Kenyatta National Hospital, but none from the western region of this country. The patients served by this hospital or this geographical region have not been characterized as yet. It is clear that various regions vary in their population characteristics, socio-economic activities and thus status, healthcare seeking behavior. With regard to diabetes, self care and access to quality care may also vary.

This study was therefore designed to characterise type 2 diabetes mellitus patients in this setting, evaluate the care accorded them, particularly, the therapeutic strategies employed in their care, and establish the level of control of diabetes and the associated cardiovascular risk factors.

This study also set out to generate data that would hopefully justify the strengthening of programmes targeting non-communicable diseases, with an emphasis on programmes in peripheral facilities or emphasise the need for decentralization of care.

Embodied in this study is the passionate desire to stimulate interest in research beyond the confines and comfort of the Kenyatta National Hospital

3.0. RESEARCH QUESTIONS

What are the characteristics of type 2 diabetes patients attending the diabetic clinic at New Nyanza Provincial General Hospital? How well is diabetes being controlled at a provincial (level 5) hospital? What are the prevalent coronary artery disease risk factors and what pharmaco-therapeutic strategies are being utilised?

4.0. OBJECTIVES

4.1. Broad objective

To determine the patient characteristics, level of glycemic control and pharmaco-therapeutic strategies utilised for both glycemic control and cardiovascular risk reduction in type 2 diabetes mellitus patients at the Nyanza Provincial Hospital in Nyanza Province, Kenya.

4.2. Specific objectives

- 1) To describe demographics of type 2 diabetes mellitus, including: age, gender, educational attainment, employment status, and residence.
- 2) To describe the socio-demographic risk factors in these patients (family history of diabetes mellitus or hypertension, obesity, hypertension, alcohol use and smoking); including biochemical; lipid profile, Estimated GFR, Urine albumin to creatinine ratio.
- 3) To determine the level of glycemic control using; HBA1C, fasting blood glucose, 1hr post glucose load blood profile and the predictors of glycemic control.
- 4) To determine the pharmacologic regimens used in glycemic control.
- 5) To determine the proportion of patients on pharmacologic interventions for risk reduction; lipid-lowering, anti-platelet and anti-hypertensive agents.
- 6) To determine factors associated with glycemic control.

5.0. METHODS AND MATERIALS.

5.1. **Study design:** Hospital based cross-sectional study.

5.2. **Study site:** Diabetes Clinic at the New Nyanza Provincial General Hospital, Nyanza province, Kenya.

5.3. **Study population:** Type 2 Diabetes Mellitus patients at the Outpatient Diabetic Clinic.

5.4. **Inclusion criteria:** Patients on follow-up for at least six months from diagnosis of type 2 diabetes mellitus or who had a diagnosis at >30years of age on the basis of random blood sugar greater than 11.1mmol/L or fasting blood sugar greater than 7mmol/L.

5.5. **Exclusion criteria:**

- Patients with a documented diagnosis of hemoglobinopathies,
- Known to have chronic kidney disease
- Known to have lead poisoning.
- Known to have secondary causes of diabetes from their medical records,
- Those who declined consent or

5.6. **Sample size:** Based on a prevalence of good control (HBA1C <7%) of 30%, Vaghela 2001, minimum sample size will be 118 patients.

Sample size for prevalence studies:

$$N = \frac{Z_{1-\alpha/2}^2 * P * (1-P)}{d^2}$$

N =Minimum sample size

$Z_{1-\alpha^2} = 1.96$ (95% confidence interval)

P =estimated prevalence-30%

d = margin of error will be 8%

Two-sided test.

N=118

5.7. **Sampling technique:** Entry into the study was by consecutive sampling

5.8. Conduct of the study

The principal investigator scrutinized the files before the start of the clinic to exclude any ineligible patients. The study concept, procedure was explained to all patients as a group and individually. Consent was then obtained in writing from those who qualified or their next of kin.

5.8.1. Clinical procedure:

Each patient had a complete history taken. Information sought included: age, gender, marital status, residence, employment status, level of education, history of alcohol use and or cigarette smoking. In the drug history I sought to establish the various medications the patient was on based on the last prescription and or file entry; the choice was assumed to reflect the ideal choice for treatment to target. Family social history included family history of diabetes mellitus, hypertension or premature cardiovascular disease or death.

Physical examination included¹¹²⁻¹¹⁵;

1. **Blood pressure** measurements were done at the upper arm using a manual sphygmomanometer as per the WHO guidelines¹¹². With the patient sitted, the back reclining on the chair after a 15 minute rest, the systolic blood pressure was determined by the first perception of the 1st Korotkoff sound (phase 1) diastolic blood pressure was determined by the perception of disappearance of the 5th Korotkoff sound. Two measurements were taken and the average of these two readings was noted. Hypertension was defined as a systolic Bp of more than 140mmHg and or a diastolic BP of more than 90mmHg or if the patient was on anti-hypertensives for hypertension from records in the file.
 2. **The body mass index**¹¹³⁻¹¹⁴ was calculated as weight (in kilograms) divided by height (in metres) squared and was categorised as per the WHO criteria. **Height:** the exact value was used in computations. The patient stood without shoes with the back square against the wall tape, eyes looking straight ahead with a set square resting on the scalp and against the wall. Weight was measured once without shoes using a lever balance to the nearest 100 milligrams.
- 5.9. **Waist circumference**¹¹⁴ in centimetres was taken using a tape measure with the subject standing; at the level of the umbilicus, measuring in the horizontal plane at the end of gentle expiration. **Hip circumference** was taken at the maximum circumference in the horizontal plane, measured over the buttocks. **The waist to hip** ratio (WHR) was calculated as the ratio of the Waist circumference to the Hip circumference.

5.8.2. Laboratory methods:

Specimens:

1. Fasting blood sugar and Post-prandial blood sugar were measured in capillary samples.
2. HBA1C was measured in venous blood.
3. Serum lipid profile and Serum creatinine were measured in venous samples
4. Urinary microalbumin was measured in early morning spot urine.

Specimen collection and handling:

The patients came on appointed day after an 8-12 hour overnight fast. Venous samples were then drawn from the cubital fossa on the clinic day under strict aseptic technique. The samples were obtained using 10 millilitre syringes and transferred to clot activated vacutainers for serum and lipid profile and into EDTA vacutainers for HBA1C. These were then stored and transported at 2-8°C in cool boxes with dry ice-carbon dioxide on the same day by the principal investigator. The samples were delivered to the Nairobi University Clinical Chemistry and Clinical Medicine Laboratories.

Fasting blood sugar was measured in capillary blood obtained using a lancet on the lateral aspect of any finger of the left hand. The blood glucose level was then be measured by the ACCU-CHECK Softclix glucometer from Roche Diagnostics at the clinic in Kisumu.

HBA1C was measured in venous blood collected in EDTA bottles. It was processed by the Glycohemoglobin Ion Exchange Resin Method from ERBA MANNHEIM GmbH at the Department of Clinical Medicine and Therapeutics, University of Nairobi.

Post-prandial glucose was measured in capillary blood obtained by a lancet one hour after a 75g oral glucose load. This will done using the ACCU-CHECK Softclix glucometer from Roche Diagnostics, GmbH at the clinic in Kisumu.

Lipid profile was analyzed in The Department of Clinical Medicine and Therapeutics, University of Nairobi, using the Human GmbH Kit. LDL-cholesterol was computed from the values of the other lipid parameters (Total cholesterol-HDL-TG/2.2 Mmol/L). HDL-cholesterol was measured using the Human cholesterol liquicolor Phosphatungstic Acid Method, Endpoint kit. Triglycerides were measured using the GPO-PAPA Method, a colorimetric, enzymatic method with glycerophosphate oxidase. Total cholesterol was measured using the CHOD-PAP Method

based on Trinders' Methodology, a calorimetric, enzymatic test for cholesterol with Lipid Clearing Factor.

Serum creatinine was measured using the Modified Jaffes' Reaction without de-proteinization at the Department of Clinical Medicine and Therapeutics, University of Nairobi. The Kit is supplied by Human GmbH. Estimated creatinine clearance will then be calculated using the Cockcroft-Gault formula. For females, the result was multiplied by a factor of 0.85

The Cockcroft-Gault formula for estimation of creatinine clearance:

$$\frac{(140 - \text{age}) \times \text{lean body weight (Kg)}}{\text{Cr (mg/dl)} \times 72}$$

The urine albumin-creatinine ratio was assayed using the CLINITEK Microalbumin Reagent Strips- semi-quantitative screening test at the Department of Clinical Chemistry University, of Nairobi.

6.0 QUALITY ASSURANCE

All aspects of Quality assurance were adhered to. Specimen collection, handling and storage were done observing quality control measures to minimize pre-analytical errors.

Commercial reagents were used for all analyses and manufacturers' instructions were followed. Laboratory analyses were done in batches. Commercial controls were run before each batch. Patient samples were only run if the control materials were within acceptable limits.

7.0 DATA MANAGEMENT AND ANALYSIS

Data was collected using structured questionnaires (Appendix 18.2). Data entry, cleaning and analysis was done using SPSS 15.0.

Descriptive statistics were used to summarise continuous data such as age, duration of illness-into frequencies, means, median, SD, percentages.

Comparisons of means of continuous data with normal distribution were made using the student t-test. For data normally distributed, comparison was made by the Mann Whitney U test.

Any associations of categorical data such as BMI, HBA1c, were made using Chi-square test or Fischer's exact test.

Statistical significance was defined as two-tailed p value of less than or equal to 0.05 for all data analysed.

8.0 ETHICAL CONSIDERATIONS

Study approval was sought and obtained from the Department of Medicine and Therapeutics, University of Nairobi, the Ethics Committee of the Kenyatta National Hospital and from the New Nyanza PGH Ethics and Scientific Review Committee.

Patients gave informed written consent, used thumb print or assented if illiterate. Each patient had a brief interactive session of education on diabetes, complications of diabetes, therapeutic approaches in diabetes and the importance of treatment to target of blood pressure, blood sugar and serum lipids.

As far as was practicable based on study findings, guidance on therapeutic strategies was offered to the patient in conjunction with the physician during study period.

Feed back on results was given to the Nyanza Provincial Hospital with appropriate recommendations.

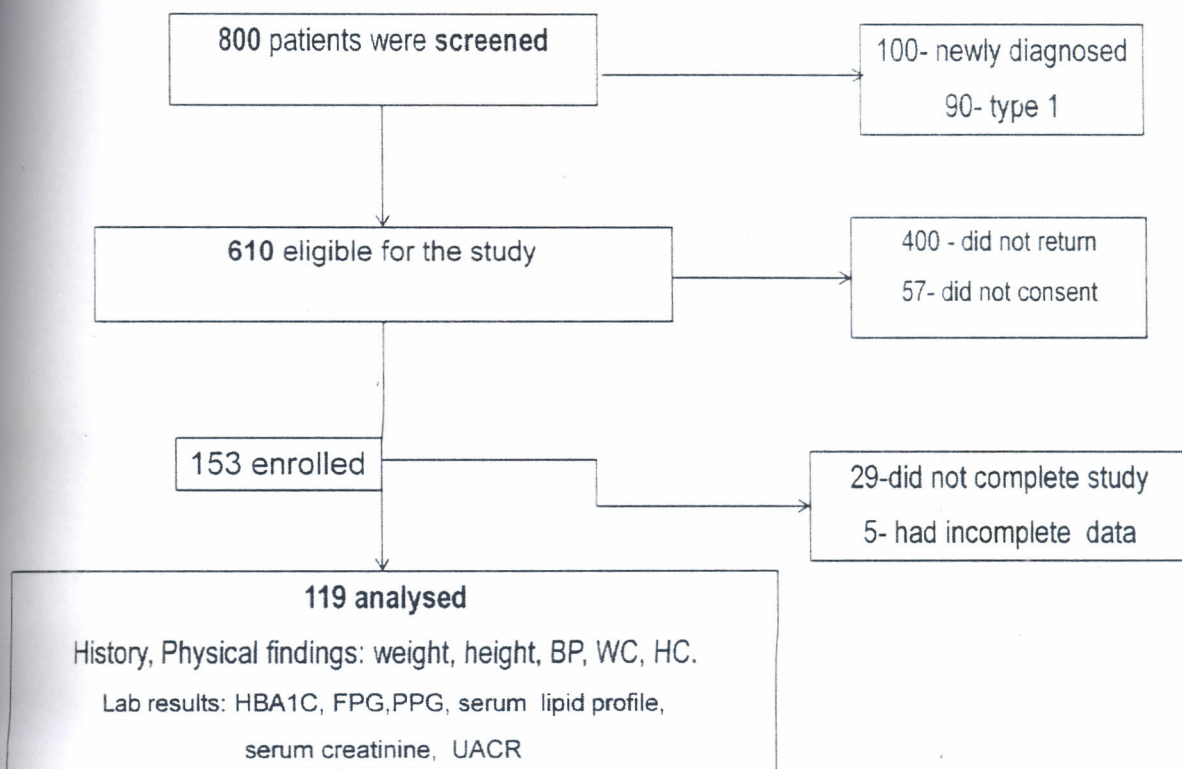
9.0 RESULTS

The study was planned to run from 19th September 2008 to 19th December 2008. Due to unavoidable and unforeseen logistical hurdles, the study period was extended to 24th July 2009.

A total of 800 patients were screened during the study period. At the end of the study and after receipt of all study results, 119 patients had complete study data. They were subsequently analyzed. The findings are presented below.

9.1 ACTUAL FLOW OF STUDY

Figure 1 study flow

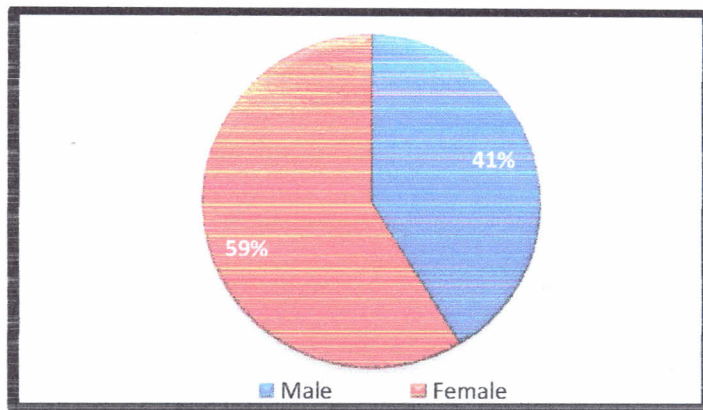


9.2 SEX AND AGE IN THE STUDY

Table 3 Categorization of the study population by sex

Total n-119	Female n-70	Male n-49	Male to Female ratio
100 %	58.8 %	41.2 %	1:1.7

Figure 2 Categorization of the study population by sex



The study population had a larger female component at (70)58.8%. The male to female ratio was 1:1.7 (Table 3 and Figure 2).

Table 4 Categorization of the study population by Age

Variable	Study mean	Range	Male	Female	P Value
Age	58.4 (8.9)	32 – 87	59.3	57.8	0.365

The mean age was 58.4 years (8.9 years SD) with a range of 32 to 87 years. There was no statistically significant difference in age between the two sexes (Table 4). The majority of patients were 50 to 69 years of age, with no significant difference in proportions between the sexes (Table 5).

Table 5 Categorization of the study population by age and sex

Age	Sex		P value
	Female	Male	
30-39	2 (2.9%)	1 (2.0%)	0.549
40-49	10 (14.3%)	4 (8.2%)	
50-59	24 (34.3%)	22 (44.9%)	
60-69	30 (42.9%)	17 (34.7%)	
70-79	4 (5.7%)	4 (8.2%)	
80-89	0 (0.0%)	1 (2.0%)	

9.3 SOCIO DEMOGRAPHIC CHARACTERISTICS

This study population was predominantly rural with seventy eight (65.5%) living outside the municipality-our definition of rural. There was no significant difference in residence by sex. Ninety five (79.8%) patients were in a marital union. Twenty two (18.5%) were widowed with the majority being females. Only twenty three (19.3%) were in formal employment. Eighty eight (73.9%) had basic education, fourteen (11.8%) had some form of tertiary education. Most female patients (42.5%) had attained primary school education while most of the male patients (53.1%) had attained secondary school education. Those with no formal education constituted 14.3% of the study population. (Tables 6 and 7)

Table 6 Socio demographic characteristics of the study population

	Characteristic	Frequency (%)	
Sex	Male	49	41.2
	Female	70	58.8
Marital status	Married	95	79.8
	Widowed	22	18.5
	Divorced	2	1.7
Residence	Urban	41	35.5
	Rural	78	65.5
Employment status	Employed	23	19.3
	Never employed	20	16.8
	Retired	53	44.5
	Unemployed	23	19.3
Level of education	None	17	14.3
	Primary	45	37.8
	Secondary	43	36.1
	Tertiary	14	11.8

Table 7 Socio-demographics characteristics by sex

Variable	Characteristic	Sex	
		Male (%) n-(41.2)	Female (%) n-70 (58.8)
Marital status	Divorced	0 (0.0%)	2 (2.9%)
	Married	46 (93.9%)	49 (70.0%)
	Widowed	3 (6.1%)	19 (27.1%)
Residence	Rural	31 (63.3%)	47 (67.1%)
	Urban	18 (36.7%)	23 (32.9%)
Employment status	Employed	11 (22.4%)	12 (17.1%)
	Never employed	1 (2.0%)	19 (27.1%)
		34 (69.4%)	19 (27.1%)
	Retired	3 (6.1%)	20 (28.6%)
	Unemployed		
Level of education	None	1 (2.0%)	16 (22.9%)
	Primary	15 (30.6%)	30 (42.9%)
	Secondary	26 (53.1%)	17 (24.3%)
	Tertiary	7 (14.3%)	7 (10.0%)

9.4. SOCIO DEMOGRAPHIC FACTORS RELATED TO CARDIOVASCULAR DISEASE

Table 8 Family history, cigarette smoking and alcohol consumption in this study population.

Variable	Category	Characteristic	Number	Frequency%
Family history of DM HTN	Relative specified (diabetes) (n=56)	1 st degree	43	76.8
	Relative specified (hypertension) (n=43)	1 st degree	35	81.5
Cigarette use n=119	Smoking status	Never smoked	100	84.0
		Ever-smoked	19	16.0
Alcohol consumption N=119	Drink alcohol	Yes (male-5)	8	6.7
		No	111	93.3

Forty three (76.8%) patients had first degree relatives with diabetes mellitus. Thirty five (81.5%) had first degree relatives with hypertension (Table 8).

Nineteen (16%) of patients in the study had a ever smoked and fourteen (73.6%) of them were male (Table 8). Five (26.3%) of them could quantify their level of indulgence at less than two pack years.

Eight (6.7%) of patients had a history of alcohol consumption, of these 5(62.5%) were male. Those who could quantify the mount of alcohol consumed gave amounts that are generally acceptable for the general population. (Table 8)

9.5. PREVALENCE OF CAD RISK FACTORS

Table 9 Overall means and medians for CAD risk factors by sex.

Variable	Mean (SD)/ Median (IQR)	Min-Max	Normal values	Sex		P value
				Male	Female	
Median duration of disease	6.0 (3 -11)	0.5 – 37	N/A	10.3	6.9	0.014
BMI Kg/m ²	27.0 (5.6)	15.5 - 48.8	18-25	25.9	27.8	0.073
WC-cm	95.6 (12.9)	60 – 125	<102(M),<88(F)	95.4	95.8	0.888
WHR	0.96 (0.09)	0.76 - 1.24	<0.9(M),<0.85(F)	0.98	0.94	0.012
Median ACR mg/dl	15.0(10-50)	2.7– 300	30-300mg/dl	29.7	39.5	0.272
FBG- mmol/l	8.8 (4.0)	2.6 – 26.4	<7	8.6	9.1	0.484
1HR PPG- mmol/l	15.5 (4.9)	6.7 - 29.2	<10	14.8	16.0	0.197
Systolic BP- mmHg	129.6(20.0)	80.0- 180.0	<140	129.0	130.1	0.782
Diastolic BP mmHg	77.7 (11.0)	50.0- 105.0	<90	77.7	77.7	0.996
Total cholesterol- mmol/l	4.9 (1.3)	2.1 - 9.2	<5.17	4.6	5.1	0.038
HDL- mmol/l	1.4 (0.5)	0.3 - 3.4	>1.1	1.3	1.4	0.075
TG- mmol/l	1.5 (0.95)	0.2 - 6.1	<1.7	1.6	1.4	0.304
LDL- mmol/l	2.9 (1.1)	0.3 - 5.8	<2.6	2.7	3.0	0.134
GFR- ml/min	70.5 (27.2)	8.2 - 174.9	>90	68.2	72.0	0.452

The median duration of disease was 6.0years with an inter-quartile range of 3-11 years and a range of 0.5 to 37 years. There was a statistically significant difference between the sexes with males having a median duration of 10.3 years versus 6.9 years for the female patients with a significance level of 0.014 (Table 9).

Further explanation of the various variables in the tables is captured below.

Table 10 Categorization of CV risk factors (frequencies) (N=119)

Variable	Categorization. N=119	Number	Frequency %
BMI	Underweight	6	5.0
	Normal weight	31	26.1
	Overweight	58	48.7
	Obesity	24	20.2
WC M>102; F=88	High	71	59.7
	Normal	48	40.3
Waist hip ratio M>0.9; F>0,85	High	107	89.9
	Normal	12	10.1
Blood pressure	Normal	32	26.9
	Pre-hypertension	47	39.5
	Stage 1 HTN	21	17.6
	Stage 2 HTN	3	2.5
	Isolated systolic HTN	16	13.4

9.5.1 Obesity

Figure 3 Categorization of the overall study population by BMI

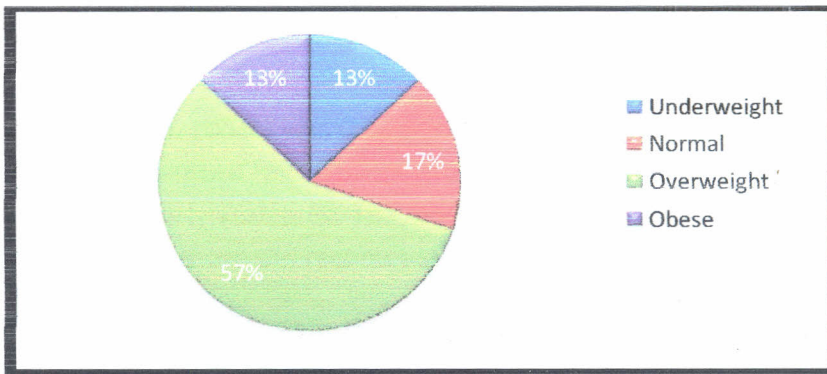
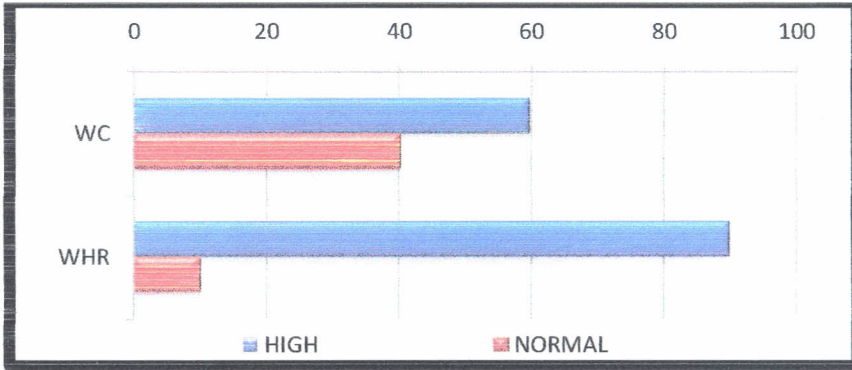


Figure 4 WC and WHR for the study population



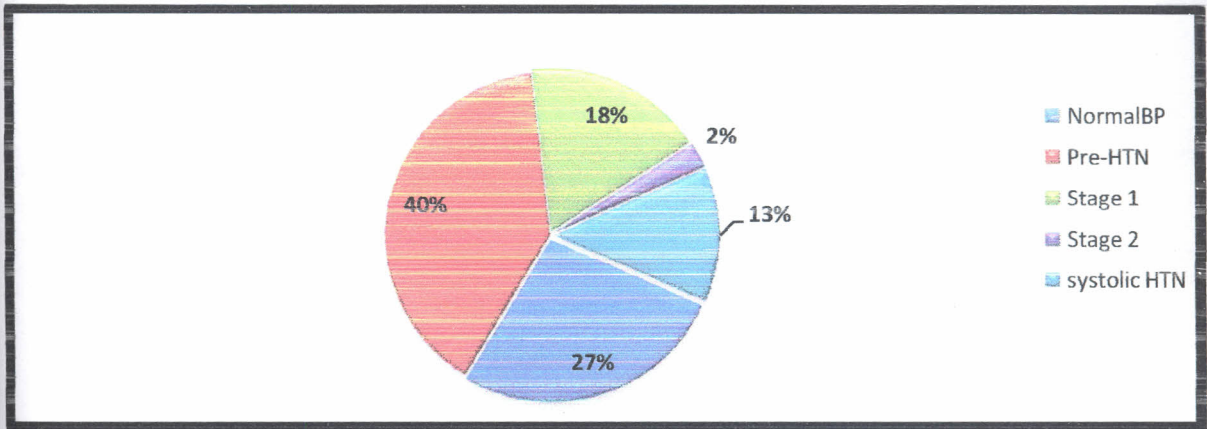
The mean body mass index (BMI kg/m^2) was 27.0 with a standard deviation of 5.6. The range was 15.5 to 48.8. The females tended to be much heavier with BMI of 27.8 compared to 25.9 for the male patients (table 11). This did not attain statistical significance though. 5.5% of the population was underweight with a BMI less than 18.5, while 68.9% were either overweight (48.7%) or obese (20.2%). There was no statistically significant difference between the male and female patients (Table 9).

Waist circumference; the sexes had similar mean values of 95.4 and 95.8 for males and females respectively. The mean for the females was however way above the cut off value for females. The mean was 95.6cm. 59.7% of the study population had waist circumference above the cut off for each sex (Table 9).

The mean waist to hip ratio (WHR) was 0.96(SD0.09) with a range of 0.76 to 1.24. There was a statistically significant difference ($p=0.012$) between the male and female patients with values of 0.98 and 0.94 respectively (Table 9). The WHR ratio revealed 89.9% of the population as being obese; having values above the recommended values for male and female patients (Table 9 and figure 4).

9.5.2. Hypertension

Figure 5 Categorization of hypertension using the JNC VII Guidelines



The mean blood pressure was 129.6 mmHg systolic and 77.7mmHg diastolic. This was within the acceptable levels for type 2 diabetes patients.

The mean SBP was 129.6 (SD20.0) mmHg with a range of SBP was 80-180 mmHg. The means for the male and female patients were 129.0 and 130.1 mmHg respectively. There was no statistically significant difference between the two sexes ($p=0.782$).

As regards the diastolic pressure, the mean was 77.7 (SD 11.0) mmHg with a range of 50 to 105mmHg. The mean of the diastolic blood pressures was similar for the sexes with no statistically significant difference (Table 9).

Seventy nine (66.4%) of the patients had blood pressure values below the 140/90mmHg cut off for the general population (Table 10 and Figure 5). Sixty six (55.5%) had BP values equal to or below the recommended 130/80mmHg for persons living with diabetes. Sixteen (13.4%) had isolated systolic hypertension. (Figure 5)

Ninety five (79.8%) were on treatment for hypertension. Treatment and attainment of target blood pressure levels is discussed later.

9.5.3. Biochemical risk factors

Table 11 Biochemical risk factors for CVD (N = 119)

Variable		Categorization (n=119)	Number (n=119)	Frequency %
Fasting blood sugar		<5.9	23	19.3
		6.0 - 10.9	66	55.5
		>11	30	35.2
Postprandial glucose		Desirable <10mmol/l	13	10.9
		High \geq 10mmol/l	106	89.1
Lipids	Total cholesterol	Desirable <5.17mmol/l	67	56.3
		Borderline High (>5.17-6.18mmol/l)	32	26.9
		High >6.2 mmol/l	20	16.8
	LDL	Desirable <2.6mmol/l	46	38.7
		High \geq 2.6mmol/l	72	60.5
		Missing	1	0.8
	HDL	Low <1.1	35	29.4
		Desirable \geq 1.1	84	70.6
	TG	Desirable <1.7mmol/l	89	74.8
		High \geq 1.7mmol/l	30	25.2
Albuminuria		Normal	75	63.0
		Microalbuminuria	44	37.0
Estimated GFR		Stage 0	14	11.8
		Stage 1	8	6.7
		Stage 2	55	46.2
		Stage 3	38	31.9
		Stage 4	2	1.7
		Stage 5	2	1.7

9.5.3.1. Fasting, 1 hour Post glucose load plasma glucose and HBA1C

Figure 6 Categorization of study population by FPG.

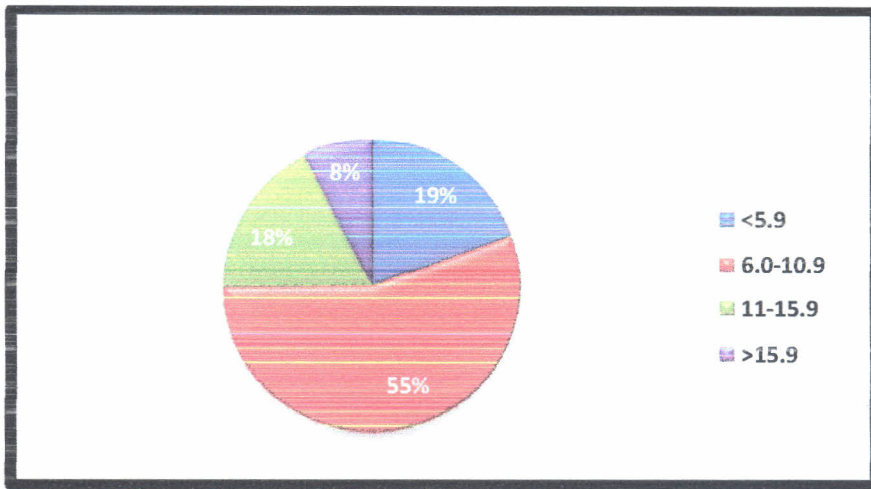
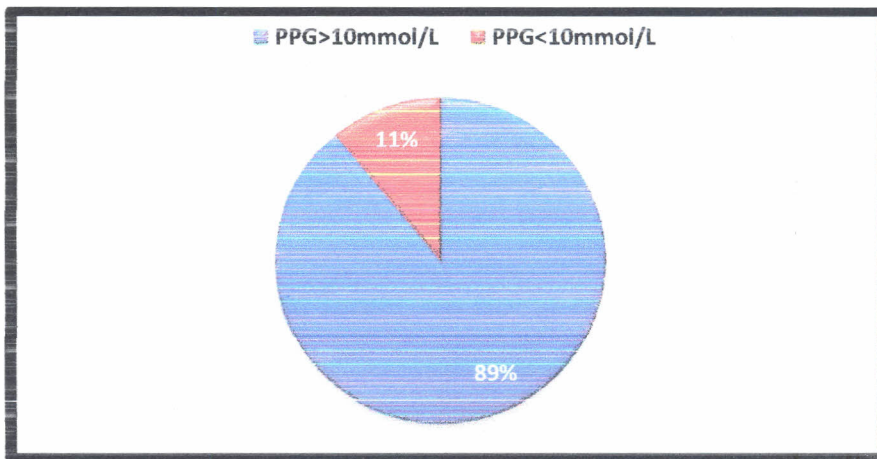


Figure 7 Categorization of the study population by 1HR PPG control

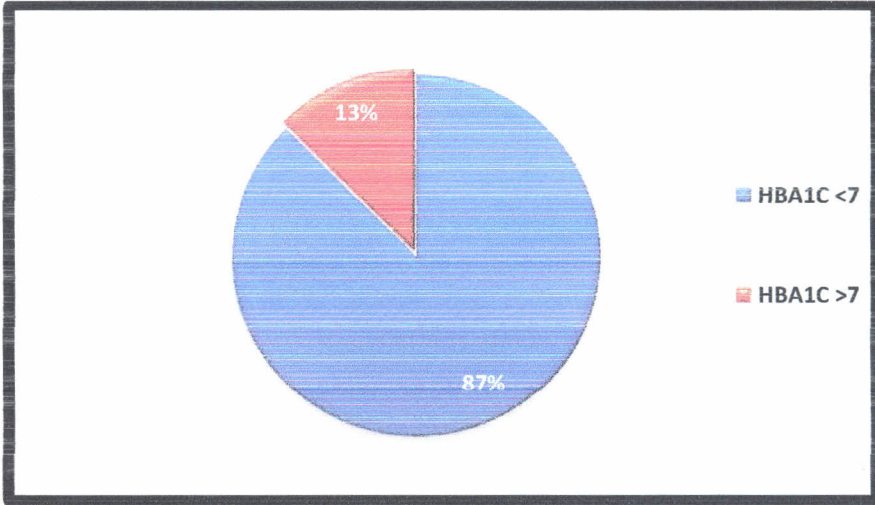


The study population had a mean FBG of 8.8 (SD4.0) with a range of 2.6 to 26.4mmol/l. There was no statistically significant difference between the sexes.

Twenty three (19.3%) had well controlled fasting glucose levels of less than 6mMol/l. Thirty (35.2%) had poorly controlled fasting glucose levels exceeding 11mMol/l. (Tables 11; Figure 6).

The mean 1Hr PPG was 15.5(SD4.9) mmol/l; with a range of 6.7 to 29.2mmol/l. The mean 1Hr PPG values were similar between the sexes. Thirteen (10.9%) of patients had a well controlled postprandial profile of less than 10mMol/L (Table 11; Figure 6).

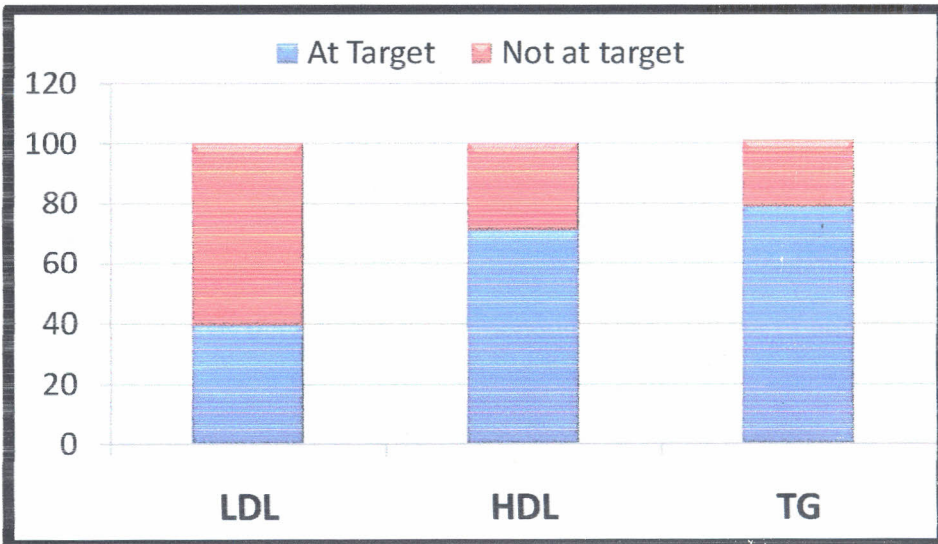
Figure 7 Level of glycemc control as measured using HBA1C



One hundred and two patients (87.4%) had good glycemc control (<7%); as assessed using the HBA1C. 79.8% had excellent control (<6.0%). According to the ADA criteria, 80% had excellent glycemc control with 3% having poor control. (Table 11 and figure 7)

9.5.3.2. Lipid profile

Figure 8 Categorization of HDL, LDL and TG at target levels



The mean total cholesterol was 4.9 (SD1.3) with a range of 2.1 to 9.2. There was a statistically significant difference ($p=0.038$) between the sexes; with the females having a higher level. The mean for the male and female patients was 4.6 and 5.1 mmol/l respectively.

There was a trend towards statistically significant difference with regard to HDL ($p=0.075$). The study mean was 1.4 (SD 0.5) with a range of 0.3 to 3.4. The triglyceride mean was 1.5(SD0.95) with a range was 0.2 to 6.1. The mean LDL was 2.9(SD 1.1) and a range of 0.3 to 5.8 mmol/l (Tables 11).

Fifty two (43.5%) patients had elevated total cholesterol levels of more than 5.17mMol/l. forty six (38.7%) patients had LDL cholesterol below 2.6mmol/L. Eighty four (70.6%) of the patients had HDL cholesterol levels at or above the recommended levels of 1.1mmol/L. eighty nine(74.8%) of the patients had triglycerides below the recommended level of 1.7mmol/L (Figure 8).

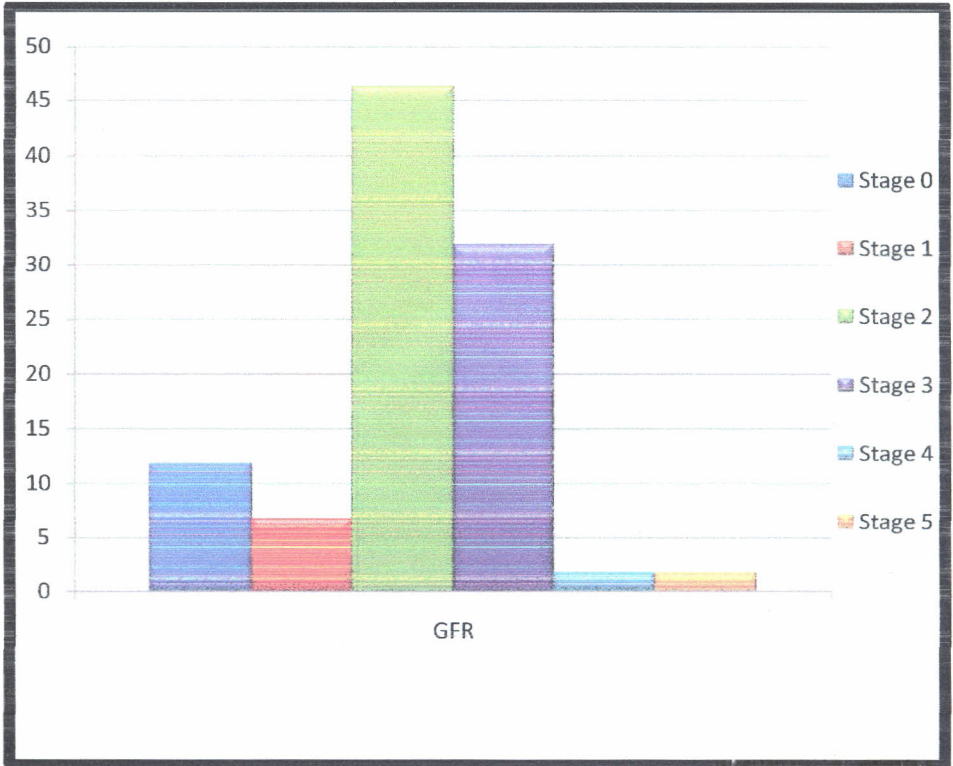
Table 12 Clustering of lipid abnormalities

Variable	Abnormality	No of patients	Proportion
No Lipid abnormality	0	30	25.2%
One lipid N=49; (41.2%)	High LDL	35	71.4%
	Low HDL	9	18.4%
	High TG	5	10.2%
Two lipids N=32; (26.9%)	LDL+TG	14	43.8%
	LDL+HDL	15	46.9%
	HDL+TG	3	9.4%
Three lipids N=8; (6.7%)	LDL+HDL+TG	8	100%

Forty (33.6%) of the patients had more than two lipid abnormalities. Thirty seven (31.1%) had two or more abnormalities in addition to an elevated LDL cholesterol. Eight (6.7%) had all three parameters; HDL, LDL, TGs outside the recommended ranges (Tables 11 and 12).

9.5.3.3. Estimated GFR

Figure 9 Categorization by estimated GFR



The mean estimated glomerular filtration rate was; 70.5ml/min (SD 27.2) and a range of 8.2 to 174.9ml/min. That for the sexes was 68.2 and 72 ml/min for the male and female patients respectively. The difference was not statistically significant.

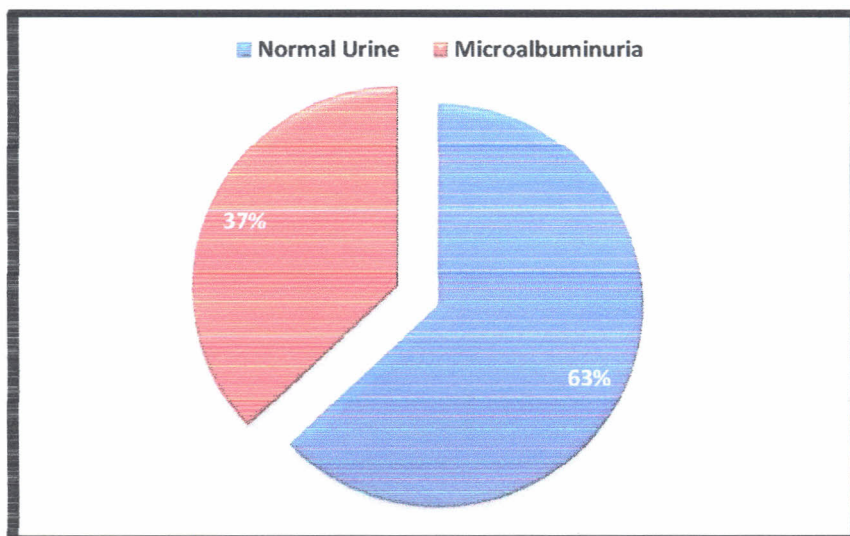
Ninety three (78.2%) of the patients had stage 2 and 3 Chronic Kidney dysfunction with an estimated GFR of less than 60ml/min.

There were four (3.4%) patients with estimated glomerular filtration rates reflecting stage 4 and 5 CKD; this state of severe renal dysfunction was not previously known.

Twenty two (18.5%) patients had a normal estimated GFR. (Tables 11; Figure 9)

9.5.3.4. Albuminuria

Figure 10 Categorization by Albuminuria status



Forty four (37%) of the study population had microalbuminuria (Table11, Figure 10).

The median albumin to creatinine excretion ratio was 15.0 with an inter-quartile range of 2.7 to 300.0 (Table 11).

The female patients had a higher mean level within the microalbuminuria range with a mean of 39.5.

The difference between the male and female patients was not statistically significant.

9.6.0. PHARMACOTHERAPEUTIC INTERVENTIONS FOR CARDIOVASCULAR RISK FACTOR REDUCTION

Table 13 Modifiable Risk factor clustering

Assessment of clustering of modifiable cardiovascular risk factors; hyperglycemia, obesity, hypertension, dyslipidemia, microalbuminuria and renal dysfunction was done. As shown in table 13 below.

Risk factors combinations	Frequency n=119	Percent 100%
0	3	2.5%
1	17	14.3%
2	28	23.5%
3	37	31.1%
4	26	21.8%
5	5	4.2%
6	3	2.5%

The median number of risk factors was three.

Eighty nine patients (83.1%) had more than two risk factors. Thirty four (27.5%) had more than four risk factors.

Table 14 Proportions of study patients on various agents for CAD risk reduction (n= 119)

Characteristic		Number	Frequency (%)
1. Anti-diabetic Drugs	OHA only	83	69.7
	Insulin only	26	21.8
	Both OHA & Insulin	8	6.7
	Diet only	2	1.7
2. Anti-hypertensive drugs	Yes	95	79.8
	No	24	20.2
	a. ACE I/ARB	68	71.6
	b. Other drugs	27	28.4
3. Lipid lowering agents (statins)	Yes	9	7.6
	No	110	92.4
4. Anti-platelet agents	Yes	11	9.2
	No	108	90.8

Most patients were on some glucose lowering treatment. Ninety five (79.8%) were hypertensive and on treatment. Few patients were on lipid lowering and anti-thrombotic treatment (Table 14).

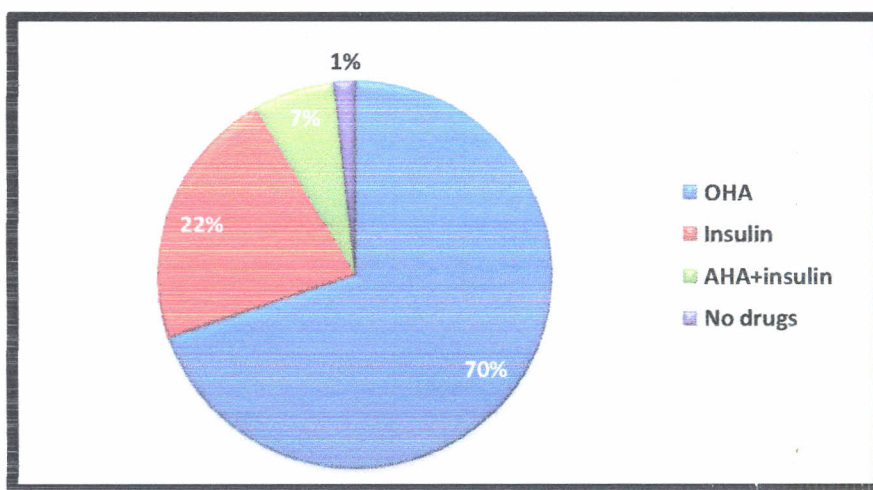
Table 15 Proportion of patients at target on interventions for CV risk factor reduction

Variable	Target level	On treatment	
		Number	Proportion
HBA1C (n=119)	<7 %	102	87.2%
BP (n=95)	<130/80mmHg	45	47.3%
LDL (n=9)	<2.6mmol/l	5	55.5%

Over one hundred and two (87%) of the patients had an HBA1C less the 7%. Less than 50 % of patients on treatment for hypertension were at target blood pressure for the general diabetic patient. With regard to LDL cholesterol, 55.5% of those on treatment were at target. (Table 15)

9.6.1. Glycemic control

Figure 12 Prevalent drugs used for glycemic control



All the patients were on various modalities for their diabetes management.

The most prevalent therapeutic strategy was the use of oral hypoglycemic at 76.4%. These were used either alone or in combination with insulin. Eighty three patients (69.7%) were using oral hypoglycemic agents only; twenty six patients (21.8%) were on insulin only; eight patients (6.7%) on both insulin and OHAs.

1.7 % of patients were not of any pharmacologic treatment for glycemic control. (Table 14)

9.6.2. Hypertension

Ninety five patients (79.8%) were on blood pressure lowering medication.

The renin-angiotensin blocking anti hypertensive agents (ACEI and ARBs) were the most frequently used agents with sixty eight patients (57.1%) using them for the management of hypertension (Table 14)

9.6.3 Dyslipidemia

The utilization or prescription of lipid lowering agents was low, with nine patients (7.6%) on statins.

9.6.4. Antiplatelet Agents

Antiplatelet agents were in eleven patients (9.2%) (Table14)

9.6.5. Microalbuminuria

Table 16 Antihypertensive drug choices, blood pressure and glycated hemoglobin in patients with microalbuminuria (n=44)

Variable		Microalbuminuria (n=44)	Normal (n=75)	P value
Blood pressure drugs	ACE I/ARB	23 (52.3%)	46 (61.3%)	0.334
	Other drugs	21 (47.7%)	29 (38.7%)	
	ACE I/ARB	6 (13.6%)	17 (22.7%)	0.425
	ACE I/ARB + Other	17 (38.6%)	29 (38.7%)	
	Other drugs	21 (47.7%)	29 (38.7%)	
	BP <125/75	19(43.2%)	20(26.7%)	0.064
BP >=125/75	25(56.8%)	55(73.3%)		
	HBA1C<7%	34(77.3%)	70(93.3%)	0.011
	HBA1C>7%	10(22.7%)	5(6.7%)	

Forty four patients (36.9%) had microalbuminuria. Twenty three (52.3%) of these patients were on the renin-angiotensin-aldosterone system (RAAS) inhibiting agents. Of these six (13.6%) were on these agents exclusively, while seventeen (38.6%) were on a combination with other agents such as calcium channel blockers, beta blockers, diuretics, vasodilators and other centrally acting drugs such as Aldomet.

In patients without albuminuria, seventeen (22.7%) were on RAAS blocking agents, twenty nine (38.7%) were on combination therapy, while another twenty nine (38.7%) were on other blood pressure lowering agents.

There was no statistically significant difference in the choice of agents for blood pressure control and attained blood pressure between the patients with or without microalbuminuria (Table 16).

Patients with microalbuminuria were more likely to have a higher HBA1c than those with normal urine ($p=0.011$) (Table 16).

9.7.0. SOCIO-DEMOGOGRAPHIC PREDICTORS OF GLYCEMIC CONTROL

Table 17 Correlation of socio-demographic characteristics and glycemic control (Chi-square)

Variable		HBA1C Category		P value
		<7%	>=7%	
Duration of diabetes	Years of illness	6.0	7.0 years	0.128
		3 – 11 years(IQR)	5 – 13 years(IQR)	
Age	Chronological age	58.6	57.5	0.677
Sex	Female	59 (56.7%)	11 (73.3%)	0.222
	Male	45 (43.3%)	4 (26.7%)	
Marital status	Divorced	2 (1.9%)	0 (0.0%)	0.258
	Married	85 (81.7%)	10 (66.7%)	
	Widowed	17 (16.3%)	5 (33.3%)	
Residence	Rural	68 (65.4%)	10 (66.7%)	0.922
	Urban	36 (34.6%)	5 (33.3%)	
Employment status	Employed	22 (21.2%)	1 (6.7%)	0.200
	Never employed	16 (15.4%)	4 (26.7%)	
	Retired	48 (46.2%)	5 (33.3%)	
	Unemployed	18 (17.3%)	5 (33.3%)	
Educational attainment	None	15 (14.4%)	2 (13.3%)	0.196
	Primary	36 (34.6%)	9 (60.0%)	
	Secondary	39 (37.5%)	4 (26.7%)	
	Tertiary	14 (13.5%)	0 (0.0%)	

The patients with poor glycemic controlled only differed from the rest of the study group with regard to the duration of the disease. They had a median duration of 7 years compared to 6.0 years of the well controlled group. We did not find a statistically significant association between socio-demographic characteristics and glycemic control in this study population (Table 17).

Table 18 Differences between the well and the poorly controlled diabetes-(student t-test)

Means of Variables	HBA1C category		P Value
	<7% (n=104)	>=7% (n=15)	
Waist circumference (cm)	97.1	85.3	0.001*
Waist-to-hip ratio	0.96	0.93	0.232
Systolic BP(mmHg)	131.2	119.0	0.027*
Diastolic BP (mmHg))	78.7	70.7	0.008*
BMI (Kg/m ²)	27.6	23.3	0.006*
Fasting glucose (mMol/L)	8.3	12.7	0.000*
Postprandial glucose (mMol/L)	15.0	18.7	0.009*
Total cholesterol	5.0	4.5	0.174
HDL	1.4	1.4	0.795
TG	1.6	1.1	0.086
LDL (mMol/L)	3.0	2.7	0.390
Albumin/creatinine ratio	30.0	73.3	0.001*
GFR	70.7	68.7	0.792
OHA & Insulin drugs			
OHA only	74 (71.2%)	9 (60.0%)	0.611
Insulin only	22 (21.2%)	4 (26.7%)	
Both OHA & Insulin	6 (5.8%)	2 (13.3%)	
Diet only	2 (1.9%)	0 (0.0%)	
Blood pressure drugs			
ACE I/ARB	63 (60.6%)	6 (40.0%)	0.131
Other drugs	41 (39.4%)	9 (60.0%)	

On categorizing the study population based on the HBA1C level, certain parameters differed significantly between the well and poorly controlled groups. These included waist circumference, systolic and diastolic blood pressure, BMI, FPG, 1r PPG and UACR. Due to the skewed nature of the study population, detailed analysis was not done (Table 18).

The choice of medications for blood pressure and glycemic control did not differ between the good and poor control groups. (Table18).

Table 19 Logistic regression analysis of predictors of glycemic control

Variable	OR (95% CI)	P value
Waist circumference (cm)	1.0 (0.9 - 1.1)	0.421
Systolic blood pressure	1.0 (0.9 - 1.1)	0.945
Diastolic blood pressure	1.0 (0.9 - 1.1)	0.282
Post-prandial glucose level	1.1 (0.8 - 1.0)	0.124
BMI	1.0 (0.8 - 1.3)	0.930
Albumin – creatinine ratio	0.99 (0.98 – 1.0)	0.111

On logistic regression analysis, there was no statistically significant predictor of glycemic control (Table 19).

10.0 DISCUSSION

The study was designed to assess glycemic control and the prevalent cardiovascular risk factors, but not to determine the predictors of glycemic control or define clustering of the risk factors.

The sampling method was the non-probability convenient sampling method. Confounding factors between the poor control and good control categories thus, were not controlled for. The findings including associations point towards possible predictors of observations made but do not explain causality. The predictors can be teased out much more definitively using case control or cohort study designs.

10.1 SOCIO-DEMOGRAPHIC CHARACTERISTICS

The mean age was 58.4 years (8.9 years SD) with a range of 32 to 87 years. In our population and the associated low life expectancy, this may be considered as an elderly population. This age is frequently afflicted by chronic ailments, diabetes included. These patients are most likely retired and thus less active and are at risk of obesity.

The age distribution was similar to that found in other studies on Diabetes Mellitus at Kenyatta National Hospital. For example, Mwendwa et al found mean age of 53.2 (SD 9.6) years, in type 2 diabetes mellitus patients on follow-up for less than 2 years from diagnosis. Vaghela et al found a mean age of 55.7 with a range of 41 to 87 years; most patients were between 51-60 years.

The mean duration of diabetes was 6.0 years, at KNH the duration in a comparable study was 7.5 years. This might be an underestimate of the actual duration of disease due to the long latency of the disease before diagnosis.

Sex: There were more females than males in our study with 70(58.8%) females versus 49 (41.8%) for the male. This result compares well with established health seeking behaviour between the sexes in Kenya. This can also be explained by the larger proportion of widowed patients being female; fewer men reach the age for the development of diabetes and related conditions or succumb early to the complications. Mwendwa found females to pre-dominate at KNH in newly diagnosed patients at 63% in recently diagnosed type 2 diabetes patients.

Residence of our study population was mainly rural at 65.5% in keeping with the location of the study site and the hospital. There was no difference in residence with regard to sex. In her study, Mwendwa found a mainly urban population at 78%¹⁰⁹. Rural populations are undergoing lifestyle changes with increased caloric intake, more sedentary lifestyles with newer modes of transport among other factors. These factors increase the risk for obesity and diabetes and hypertension.

Educational attainment was mainly basic at 73.9%. These had primary and secondary education in keeping with rural setting of the study site. 11.8 had some form of tertiary

education. Most of the female patients (42.5%) had primary school education while most of the male patients (53.1%) had attained secondary school education. Illiteracy level was low at 14.3% of the study population. It would have long been stated that these are diseases of the learned and thus affluent sectors of society, our findings indicate that it is not so in this population. It may reflect an overall rise in standards of living with the attendant risk factors.

Family history; Type 2 diabetes mellitus has polygenic inheritance and thus a family history is a significant risk factor for its development. In our study, a family history of diabetes and hypertension was found in fifty six (47.1%) and forty three (36.1%) respectively. This was modest considering that; Vaghela¹⁰¹ at KNH found 77.8% and 66.7% for diabetes and hypertension respectively. It suggests that there may be other factors that contribute to elevated risk for the development of diabetes and hypertension in the KNH patients; most probably variations in genetic susceptibility in the various ethnic groups. In those patients with a family history, there was a first degree relative affected in forty three (76.8%) and thirty five (81.5%) respectively. It is thus important to screen the relatives of patients with diabetes and or hypertension as to institute early treatment in the event of disease or institute preventive measures to forestall development of disease. Special emphasis should target the modifiable risk factors that are not capital intensive to deal with and yet can positively impact the reduction in morbidity and mortality.

10.2 MODIFIABLE RISK FACTORS

Eighty nine (83.1%) patients had two or more risk factors for coronary artery disease. The median number of risk factors was three. Thirty four (27.5%) had more than four risk factors.

Duration of disease though not modifiable is important in its interaction with various other risk factors and the adverse outcomes of longstanding diabetes mellitus. The median duration of disease in our study was 6.0 years with an inter-quartile range of 3-11 years; this finding was much shorter than that seen at KNH by Vaghela¹⁰¹ at 7.6 years with a range of 6.4 to 8.5 years. This may reflect a difference in the capacity for early detection of disease or an inherent difference in this population from that seen at the Kenyatta national Hospital-predominantly from Central and Eastern provinces of Kenya

10.2.1 Obesity: body mass index, waist circumference and the waist to hip ratio.

Eighty two (68.9%) of the patients were overweight with BMI greater than 25kg/m². Obesity as defined by BMI >30kg/m² was found in 20.2% of the patients; a much lower prevalence rate when compared to that seen at KNH (65%). This could be related to the genetic and socio-economic differences between the populations seen at KNH and at NNPGRH. For instance, the KNH patients were predominantly urban and from central Kenya; their urban lifestyle would inform their dietary habits, a more sedentary lifestyle and hence the higher increased risk for weight gain. There is evidence for a linear relationship between excess weight and the risk for

developing diabetes and the attendant complications. Obese patients are also most likely to have hyperinsulinemia and dyslipidemia as part of the metabolic syndrome.

The female patients were more likely to be obese than the male patients with a trend towards statistical significance ($p=0.073$). The female patients had a significantly higher WHR compared to the male patients ($p=0.012$).

Using BMI to diagnose obesity, our pick-up rate for obesity was 20.2%, much lower than that seen at KNH by Mwendwa-66%¹⁰⁹ and Vaghela 66.7%¹¹⁰. Obesity was better picked by the waist hip circumference (59.7%) and by the waist to hip ratio (89.9%) though these are less useful with BMIs above 35. Thus in this population, the waist to hip circumference ratio was a much more sensitive measure than BMI and WC. In the absence of stadiometers to measure weight and height, a tape measure which is fairly affordable can be used to help these patients monitor their weight as to keep within the recommended ranges. It is known that visceral obesity is associated with a higher cardiovascular risk compared to peripheral obesity with regard to the development of insulin resistance and diabetes.

Weight loss is associated with better glycemetic control and serum lipid profiles in addition to blood pressure control; changes in the lipid profile include a decrease in LDL cholesterol and triglycerides and a rise in HDL cholesterol.

It is imperative therefore, to target weight reduction in this population to fortify the gains made through glycemetic control.

10.2.2 Hypertension

There was a high prevalence of hypertension at 77.3% with no significant gender difference. The mean systolic and diastolic blood pressures were 129 and 77mmHg respectively.

Ninety five (79.8%) were on treatment for hypertension. Sixty six (55.5%) of those on treatment had blood pressures at the recommended level for persons living with diabetes of 130/80mmHg. Forty five (47.4%) of the patients on anti hypertensive treatment were well controlled; with blood pressures less than 130/80mmHg.

The above findings were much lower when compared to that found by Vaghela¹¹⁰ (143/87.1mmHg) at KNH. The UKPDS trial in particular which had more liberal targets for blood pressure control, showed that good blood pressure control had significant effect on microvascular disease in type 2 diabetes patients. The effect on macrovascular disease however, was not that clear cut.

Hypertension is known to predispose to all the major atherosclerotic cardiovascular disease outcomes including cardiac failure, cerebrovascular accidents, peripheral arterial disease. It is therefore anticipated that the average lower blood pressures in our study population would translate to lower cardio and cerebrovascular disease morbidity and mortality in this population.

The high prevalence of hypertension in the study population may be attributed to the lower age at onset and aggressive nature of hypertension in our African population; most of our patients were in the sixth decade of their lives- a fairly younger population when compared to the west.

The less than fifty percent control rate is a near universal finding with regard to adequacy of blood pressure treatment. It would have been important to evaluate factors such as, compliance to medication, adequacy of drug dosing, drug combinations and the role of factors such as obesity and renal dysfunction. This was not part of this study.

10.2.3 Dyslipidemia

Dyslipidemia was found in this population as outlined; seventy two patients (60.5%) had elevated LDL (>2.6mmol/l); thirty five (29.4%) had a depressed HDL (<1.1 mmol/l) and thirty (25.2%) had elevated Triglycerides (>1.7mmol/l).

The high prevalence of high LDL cholesterol is a marker of significant CAD risk thus the need for increased use of statins. A third of the patients had low HDL and high TG, which is a common finding in diabetes mellitus patients. It is important to note that the prevalence of statin use was very low.

In our study population which is a fairly active rural population, dietary strategies, weight reduction and increased use of HMG CoA reductase inhibitors would probably help more of these patients to attain the required LDL cholesterol levels and thus lower their coronary artery risk.

10.2.4 Alcohol and cigarette smoking

There was a low prevalence of cigarette smoking and alcohol utilization.

The quantities of alcohol used involved were not sufficient to constitute significant risk. Alcohol in small amounts; less than 2 units per day for males and less than 1 unit per day for females is thought to be cardio-protective while, larger amounts may affect compliance to medication in

addition to additive toxicity to various organs. This low consumption rate would be expected to align well with reduced CVD risk. This has however not been studied in our population.

Smoking is an independent risk factor for all cause mortality, and confers increased risk at all levels of cigarette smoking. Smoking hampers glycemic control, promotes dyslipidemia and accelerates atherosclerosis in addition to an increased event and mortality rate. We did not use objective markers of smoking such as breath carbon monoxide and urine nicotine. The low consumption of cigarettes in this population then reduces the cardiovascular disease risk.

From the Framingham studies, smoking was associated with a twofold increase in coronary heart disease when smoking and non-smoking diabetics were compared. It is a highly modifiable risk factor, and should be pursued aggressively if present. We do not know the significance of recall bias if any in our study population.

10.2.5 Microalbuminuria

Forty four (37%) of the patients had microalbuminuria, a marker of cardiovascular risk and mortality risk. None of the patients had macroalbuminuria. This value compares well with that found by Twahir A H¹¹⁹.

Day to day variability of microalbumin may be as high as 40 % in spot urine samples. This variability is lowest with a 24hr urine collection measurement. The design of our study and logistical limitations did not allow us to use the 24 hour urine collection method for urinary albumin estimation. We opted for the more convenient spot urine, CLINITEK microalbumin assay technique.

The detection of microalbuminuria points towards glomerular damage. It predicts the development of overt nephropathy and subsequent ESRD. Twahir A H¹¹⁹ did not find any significant association between microalbuminuria and age, duration of disease, BMI, SBP and DBP. We did not set out to document the predictors of microalbuminuria in our study.

Microalbuminuria is also an important marker of vascular injury. The treatment to target of dysglycemia, hypertension and the use of RAAS blocking agents may mitigate the onset and progression of vascular injury.

10.2.6. Renal dysfunction

Most of the patients were in stage 2 and 3 CKD stage. Only 18.5% of patients had a normal estimated glomerular filtration rate. Without intervention, the risk of progression to ESRD and subsequent mortality is high in the patients with impaired renal function.

The high prevalence of renal dysfunction in this study and paucity of renal replacement services in our country; point towards an increasing burden of renal disease in our diabetic population.

There therefore sufficient reason to urgently and systematically increase the uptake of interventions that ameliorate, delay or prevent the progression of any stage of renal dysfunction to end stage renal disease.

It is also important to start planning for a larger program for renal replacement services in the country.

10.3 CARDIOVASCULAR RISK FACTOR REDUCTION INTERVENTIONS

Local studies done by Vaghela¹¹⁰ and Nguchu¹¹¹ at KNH found the uptake of these CAD risk factor reduction interventions to be grossly inadequate with statins at less than 1% and 8.4% respectively. Antiplatelet agents were used in a paltry 9.3% and 14.7% respectively. This is replicated in our study with only 9 (7.2%) on statins and 11(9.2%) on antiplatelet agents. Attention needs to be paid to these risk factors in order to ameliorate the ravenous effects of this disease.

10.3.1 Glycemic control, therapies and predictors of control

There was good overall glycemic control in the study population with 104 (87.4%) of patients having HBA1c < 7.0%. This was by all standards good control level. Vaghela¹¹⁰ had 30% good control respectively.

It is important to note that over 491 patients were eligible for inclusion into the study, but for various reasons did not participate. The results therefore may have been the outcome of an inherent bias in design of the study-cross sectional study; in which the process selected for a more motivated patient group. The extent however is can not be defined.

The UKPDS study conclusively demonstrated that *improved blood glucose control reduces the risk of nephropathy, retinopathy and possibly neuropathy*. It also showed a 16% non-significant reduction in the incidence of cardiovascular disease-fatal and non-fatal myocardial infarction. As a primary preventive tool for vascular disease, treatment of diabetes to the prespecified HBA1C target is therefore important.

From our study, there was no obvious predictor of glycemic control. Based on the study design and sampling technique, we can only suggest possible associations; waist circumference, SBP; DBP; BMI and PPG. These can be best studied in cohort studies.

Based on our findings, we expect a predominance of macro vascular complications. This is the result of the mixed profile; while glycemic control is good, LDL cholesterol and blood pressure management was suboptimal. Hypertension may cause and exacerbate retinopathy and nephropathy in patients with diabetes mellitus. Hypertension accelerates atherosclerosis and is synergistic with dyslipidemia.

Does the schedule of follow-up affect outcomes? Though we did not set out to study the effect of follow-up visits and intervals, patients in our study population had 1-3monthly visits compared to the 6 monthly to one year visits at KNH. I believe this regular and much more frequent contact offers opportunity for the reinforcement of treatment strategies, goals and early intervention of any abnormalities culminating in better outcomes.

Ninety one (76.4%) of the patients were on oral hypo-glycemic agents, with or without Insulin, thirty four (28.5%) were on insulin only and 2(1.7%) were on undefined treatment.

There was concordance between FPG and HBA 1C. This adds internal validity to the results. It suggests that in the absence of the more costly HBA1C, FPG can be used in resource limited settings to monitor control. This was however not the case as random blood glucose was done for most patients on most occasions.

10.3.2 Pharmacotherapeutic interventions for CVD risk reduction

There were compelling indications for certain therapeutic strategies in these patients.

Of the total population, forty four (37%) had microalbuminuria. In these patients, only twenty three (52.3%) were on ACEI/ARBs. There was no statistically significant difference in the choice of or prevalence of RAAS blocking agents between those with or without microalbuminuria ($p=0.334$). This indicates that the prescription of anti-hypertensive medication was not driven by the presence or absence of compelling risk factors such as microalbuminuria. Indeed, ACEI/ARBs were used in sixty eight (57.1%) of patients only.

LDL cholesterol was elevated in seventy two (60.5%) of patients yet only nine (7.6%) were on statins. The age of the patients, the duration of disease, the lipid profile, the clustering of risk factors would invite the use of statins for CV risk reduction in these patients. The low uptake of HMG-Co-A reductase inhibitors suggests that the risk factor profile including lipid levels, was not the determinant of prescription of these agents. This may point towards a need for continued exposure of clinicians to current treatment concepts. It may be compounded by the lack of the necessary technology to raise this issue to the fore through regular assay of lipids.

Anti-platelet agents were used in only eleven (9.2%) of the patients. Since we did not have data on the prevalence of macrovascular disease, it would be difficult to categorically state the required uptake rate for this intervention for secondary prophylaxis.

1.0 STUDY LIMITATIONS

- The non-probability sampling technique did not control for confounders during the study. This may have selected for highly motivated patients. Such patients are more likely to have the various parameters at target.
- Coupled with the socio-economic and other unknown constraints, some otherwise eligible patients did not return on appointed dates of the study. This may have influenced the results by selecting, willing, highly motivated and financially able patients.
- The definition of type 2 diabetes was by phenotype. Phenotype is not an accurate diagnostic method and thus could result in misclassification of patients with attendant erroneous treatment. For example, no immunological studies were done to diagnose and or exclude Latent Autoimmune Diabetes of the Adult (LADA) in the study. This may have been true in the poorly controlled non obese patients.
- Single HBA1c values may not accurately reflect overall glycemic control over many years. We know that macro and micro vascular complications occur over the longer term thus momentary values of excellent control may, mask existing or ongoing or even longer term poor control and risk.
- Hemoglobinopathies were not tested for, for exclusion purposes. Any haemolytic state would result in a lower than normal haemoglobin level. Nyanza has a high prevalence of sickle cell disease and the sickle cell trait.
- Very poor record keeping led to total dependence on recall with the attendant risk of Recall bias. This may have led to inaccurate information of undefined magnitude. Case in point would be missing records for any prior test or diagnosis for example renal dysfunction.
- Single spot urine samples for urine albumin-to-creatinine excretion ratio may have been affected by the day to day variability in albumin excretion.

12.0 CONCLUSION

This study was the first of its kind designed to determine the patient characteristics, glycemic control, cardiovascular risk factors and the interventions in the Western Kenya.

We thus found the following:

Glycemic control can be achieved in technologically challenged environments. The measurement of fasting blood glucose is a vital tool to this end.

Hypertension was a common problem in diabetes mellitus patients in this region. In this study, treatment to target was achieved in less than half of the patients. Other factors such as availability of the necessary drugs, appropriate sequencing, formulations and dosing may affect control of blood pressure. There is need to evaluate them to establish their role in this setting.

There was a significant familial component in these patients. This information can be exploited to increase the pick up rate of these non-communicable disorders in relatives of patients; as early diagnosis and treatment is most likely to lead to lower cardiovascular morbidity and mortality.

Obesity was common in this rural population. Excessive weight is important in the causation of diabetes, success of treatment and risk of adverse outcomes. More effort is required to deal with the lifestyle therapies in these patients.

Dyslipidemia, particularly raised LDL cholesterol was common. Elevated levels have an additive effect to elevated blood pressure and excess weight. There is thus need for concerted efforts for risk reduction; including dietary therapy, weight reduction and a higher uptake of statins.

Renal dysfunction was very common. This may reflect longstanding diabetes, poor blood pressure control or poor choices in blood pressure medication. More effort is required to enhance evidence based practice in this area. Increased uptake of RAAS blocking drugs for their Renoprotective effects could reduce the prevalence of renal dysfunction.

In general, the uptake of evidence based Interventions for cardiovascular risk factor reduction was low. Strategies must be put in place to address this gap in the care of these patients.

There is need for better designed studies to verify the various determinants of glycemic control

13.0 RECOMMENDATIONS

In resource limited settings without HBA1C technology, the use of FPG is advised. Efforts should however be made to avail appropriate technology to level 5 hospitals in Kenya.

With a single and simple tape measure, WHR can be used to monitor central obesity.

To enhance the uptake of evidence based interventions for biochemical risk factors for CAD appropriate laboratory technology should be made available for the measurement of biochemical risk factors.

Due to the high prevalence of obesity, high LDL cholesterol and hypertension, there is need to encourage evidence based practice in the comprehensive care of diabetes mellitus in our public hospitals including procurement and drug supply.

There is need to study and establish the prevalence of vascular and non-vascular complications on a public health level as to institute the necessary preventive and therapeutic strategies.

Encourage patients to seek care and enhance the provision of care of diabetes mellitus at peripheral health facilities

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15.0 APPENDICES

15.1. STUDY VARIABLES

15.2 Age and sex as cardiovascular risk factors will be defined as >45yr for males, >55yrs for females

15.3 BMI: Kg/m² : weight in kilograms divided by height in metres square and to be categorised as per WHO criteria: Standing height-measured once and rounded to nearest 0.5 cm without shoes and back square to the wall tape, eyes looking straight ahead and set of square resting on the scalp. Weight: Measured once with a lever balance to the nearest 100g without shoes and with light garments on.¹¹⁴

Underweight ----- BMI < 18.5 kg/m²

Normal weight -----BMI 18.5 - 24.9 kg/m²

Overweight ----- BMI 25.0 - 29.9 kg/m²

Class I obesity ----- BMI 30.0 - 34.9 kg/m²

Class II obesity ----- BMI 35.0 - 39.9 kg/m²

Class III obesity ----- BMI 40 kg/m² (This type of obesity is also referred to as severe, extreme, or morbid obesity)

15.3. Waist circumference (WC) ¹¹⁴: To measure waist circumference, locate the upper hip bone and the top of the right iliac crest. Place a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Before reading the tape measure, ensure that the tape is snug, but does not compress the skin, and is parallel to the floor. The measurement is made at the end of a normal expiration. In adults with a BMI of 25 to 34.9 kg/m², a waist circumference greater than 102 cm (40 in) for men and 88 cm (35 in) for women is associated with a greater risk of hypertension, type 2 diabetes, and dyslipidemia, and CHD. Hip Circumference in centimetres: the maximum circumference in the horizontal plane, measured over the buttocks

15.4 Waist Hip ratio: waist-to-hip ratio > 0.9 (male) or > 0.85 (female) ¹¹⁴.

15.5 Blood pressure: measured as per WHO recommendations. With the patient sitting, using a standard cuff and a mercury sphygmomanometer, the patient having rested for 15 minutes, systolic BP will be determined by the first perception of the korotkoff sound (phase 1). Diastolic pressure will be determined by the disappearance of the fifth korotkoff sound (phase 5). Two measurements will be taken at 5minute intervals and an average value computed and recorded. Hypertension will then be defined as Systolic and diastolic pressures above 140mmHg and 90mmHg respectively or patient on antihypertensive medication ¹¹⁵.

- Normal <130/85mmHg
- Borderline 130-135/85-89mmHg
- Grade 1 140-159/90/99mmHg
- Grade 2 160-179/100-109mmHg
- Grade 3 >180/110mmHg

15.4 Glycated haemoglobin, (HbA1C).

As per ADA¹¹⁶ criteria:

- Excellent control 4.5-6.0%
- Good control 6.0-7.0%
- Marginal control 7.0-8.0%
- Poor control >8.0%

15.5 1hour post-prandial glucose¹¹⁶: will be categorized as <10g/l or > 10g/l.

15.6 Fasting blood sugar: will be categorized as; < 5.9, 6.0-10.9, 11-15.9 or > 15.9 g/dl

15.7 Cholesterol levels:

Adult treatment panel III classification of LDL, total, and HDL cholesterol¹¹⁷

Total cholesterol, mmol/L

- 5.17 ----- Desirable
- 5.17 to 6.18----- Borderline High
- 6.20----- High

HDL cholesterol, mg/dL (mmol/L)

- <1.1 -----Low
- >1.1 -----High

LDL cholesterol

- < 2.6 mmol/L ----- Desirable

> 2.6 mmol/L ----- High

Triglycerides:

< 1.7 mmol/L ----- Desirable

> 1.7 mmol/L ----- High

15.8 Estimated Glomerular filtration rate:

Stage	Description	GFR, mL/min per 1.73 m ²
0	At increased risk	90 (CRD risk factors)
1	Kidney damage with normal or increased GFR	90
2	Kidney damage with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Renal failure	15 (or dialysis)

Note: GFR, glomerular filtration rate.

Source: Adapted from Levey, with permission¹¹⁸.

15.9 Urinary Albumin excretion:

- <20 mg/day (15 µg/min) ----- normal
- 30 - 300 mg/day (20 to 200 µg/min) ----- microalbuminuria
- >300 mg/day (200 µg/min) ----- macroalbuminuria.

15.10 Education status categorised as: 1) No formal education. 2) Primary (including adult learning), 3) Secondary. 4) Tertiary: College or university

15.11 Residence will be categorised based on municipal boundary as: Rural, Urban

15.12 Cigarette smoking: never smoked, Ex-smoker or smoker, how many <15> and duration of smoking in years.

15.13 Alcohol use: never used alcohol, ex alcohol user, alcohol user- how many bottles/ week and duration in years.

15.2 STUDY PROFORMA:

1. Registration number-----

2. Date of examination by PI/SA-----

Demographics

3. Date of Birth: mm, yy-----

4. Sex: Male Female

5. Marital status: Single Married Divorced widowed Separated

6. Residence: Urban Rural

7. Employment status: Employed Never employed Retired Unemployed.

8. Level of education: None. Primary Secondary Tertiary Adult education

Past medical history

9. Has a health worker ever told you that you have hypertension? Yes No

10. What is your current smoking status? Never smoked. Ex-smoker Current smoker.

11. How many sticks do you smoke? 1-15/day----- or > 15/day

12. Do you take alcohol? Yes No.

13. How much alcohol? -----, for how long? -----

14. For how long have you been attending this clinic? -----

15. Are you currently on any medications? Yes No Don't know

16. If yes please specify:

a) Oral hypoglycaemic agent drug/ dose-----

b) Insulin formulation/dose-----

c) Blood pressure lowering drugs drug/dose-----

d) Lipid lowering drug drug/dose-----

e) Anti-platelet agents drug/dose-----

f) Others e.g. anti obesity/ multivitamins /analgesics etc-----

Family social history

17. Did or do any of your relatives suffer from diabetes? Yes No

18. Please specify: Parent Parents, Sibling, Other.

19. Did or do any of your relatives suffer from hypertension? Yes No

20. Please specify Parent Parents Sibling, Other.

Physical examination:

21. Height in cm----- Weight in kg-----

22. Hip circumference in cm-----Waist circumference in cm-----
23. Blood pressure while sitting in mmHg- 1st reading-----2nd reading-----

Laboratory data

24. HBA1C level-----
25. Fasting blood sugar level-----
26. Post-prandial glucose level-----
27. Cholesterol g/L: Total cholesterol-----
LDL-----
HDL-----
TG-----
Total/HDL ratio-----
28. Serum creatinine-----
29. Total albumin/ creatinine ratio -----

15.3 CONSENT EXPLANATION.

I **DR WAFULA Z NALWA**, a Post-graduate doctor at The University of Nairobi, Kenyatta National Hospital am conducting a study on how diabetes patients are managed at New Nyanza Provincial General Hospital Kisumu.

Diabetes 2 Mellitus is a growing problem around the world. It results from the inability of the body to produce enough or to respond adequately to insulin. This type of diabetes is increasing due to changes in lifestyle.

This study seeks to establish how well we are treating our patients at the New Nyanza PGH and how well it compares with the Kenyatta National Hospital.

I will take blood from a vein in one of your arms to measure the levels of blood glucose, cholesterol in blood and assess kidney function. I will take some of your urine to measure urinary protein. I will also measure your blood pressure, weight, height, waist circumference and hip circumference. I will also want to know which drugs you are receiving.

Benefits: You will have tests free of charge to establish how well your diabetes is controlled. You will get back your results. You can raise issues regarding your treatment so we can discuss free of charge. The study will give us information about this disease in Nyanza Province.

Risks: You will be exposed to needles as I obtain blood for the tests. I and my assistants will try to ensure adequate care to prevent any infections, unnecessary pain or injury.

All the information you give me will be confidential.

You can however withdraw from the study at any stage and will not be victimised.

Thank you

15.4a Consent form in English

I-----of-----
voluntarily accept to participate in the study as explained by Dr Wafula and/or his Assistant
----- . I give consent to participate in the study, having
understood the purpose and procedure of the study.

Patient----- sign-----date-----

Researcher-----sign-----date-----

15.4b. Consent form in Kiswahili

Mimi-----wa-----nakubali
kushiriki katika shughuli ya kuchunguza vile ambavyo tunatibiwa ugonjwa wa sukari.

Nimeelezwa Na nimeelewa makusudi na mpangilio wa uchunguzi huu kulingana na maelezo ya
(jina)-----

Mgonjwa-----Sahihi-----tarehe-----

Mchunguzi-----sahihi-----tarehe-----

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