

**CARDIOVASCULAR RISK FACTORS ASSOCIATED WITH
TYPE 2 DIABETES MELLITUS AS SEEN AT THE
KENYATTA NATIONAL HOSPITAL**

**A dissertation submitted in part fulfilment of the requirements for
the degree of Master of Medicine in Internal Medicine by:**

Dr. V. P. Vaghela

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DECLARATION

I certify that this dissertation is my own original work and has not been presented for a degree at any other university.



Dr. V. P. Vaghela, MB, ChB

This dissertation has been submitted with our approval as supervisors:



Prof. E. N. Ogola, MB, ChB, MMed
Associate Professor and Chairman, Department of Medicine,
University of Nairobi.



Dr. C. F. Otieno, MB, ChB, MMed
Lecturer, Department of Medicine,
University of Nairobi.

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ABBREVIATIONS

BMI	Body Mass Index
CHD	Coronary Heart Disease
CVD	Cerebrovascular disease
DBP	Diastolic blood pressure
ECG	Electrocardiogram
FBG	Fasting blood glucose
HbA _{1c}	Glycated haemoglobin level
HDL	High density lipoprotein
KNH	Kenyatta National Hospital
LDL	Low density lipoprotein
MAL	Microalbuminuria
MRFIT	Multiple Risk Factor Intervention Trial
NO	Nitric oxide
OHA	Oral hypoglycaemic agent
PVD	Peripheral vascular disease
SBP	Systolic blood pressure
UAC	Urinary Albumin-to-Creatinine ratio
UAE	Urinary Albumin Excretion
UKPDS	United Kingdom Prospective Diabetes Study
USA	United States of America
VLDL	Very low density lipoprotein
WHO	World Health Organization

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ABSTRACT

BACKGROUND There is an emerging epidemic of cardiovascular disease and type 2 diabetes in developing countries with rising associated morbidity and mortality. Diabetes has its greatest impact throughout the vascular system with, macrovascular disease being the leading cause of death and reduction in quality of life of individuals with type 2 diabetes. There is often clustering of multiple risk factors for vascular disease that often predates the clinical diagnosis of type 2 diabetes. No data exist on the prevalence of established cardiovascular risk factors in patients with type 2 diabetes at Kenyatta National Hospital (KNH).

OBJECTIVES The aim of the study was to determine the prevalence of certain established cardiovascular risk factors, specifically, cigarette smoking, obesity, hypertension, poor glycaemic control, dyslipidaemia, hyperhomocysteinaemia and microalbuminuria, in patients with type 2 diabetes seen at the diabetic outpatient clinic at KNH.

METHODS A random sample of type 2 diabetics seen at the diabetic outpatient clinic at KNH was selected and data obtained on age, sex, duration of diabetes, history of cigarette smoking and personal and family history of hypertension and vascular disease in first-degree relatives. Body mass index (BMI), waist circumference, waist-hip ratio (WHR) and resting blood pressure were recorded. A fasting venous blood sample was taken to determine glycated haemoglobin level, fasting lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides), fasting blood glucose, and homocysteine level,

and a spot specimen of urine was screened for microalbuminuria.

RESULTS 108 type 2 diabetics were studied, 54 males and 54 females, with mean age 55.7 years and mean duration of diabetes 7.5 years. Fifty-two patients (48.1%) were on oral hypoglycaemic agents (OHA), 6 (5.6%) on insulin alone and 50 (46.3%) on combined OHAs and insulin treatment. Age and sex as vascular risk factors (males \geq 45 years and females \geq 55 years) were found in 28 males (51.9%) and 50 females (92.6%). There were 6 (5.6%) current smokers, all males. The mean BMI was 26.9 kg/m², with 70 patients (64.8%) being either overweight or obese. The mean WHR was 0.88 and the mean waist circumference was 91.4 cm, females being more likely than males to have an abnormal WHR and WC ($p < 0.001$). Seventy patients (64.8%) were hypertensive, all poorly controlled. The mean glycated haemoglobin level (HbA_{1c}) was 8.8% with 75 patients (70.1%) having HbA_{1c} $> 7.0\%$, while the mean fasting blood glucose (FBG) was 9.4 mmol/l with 88 patients (81.5%) having FBG > 6.0 mmol/l. Dyslipidaemia was found in 101 patients (93.5%), 93 (86.1%) having raised total cholesterol and 88 (81.5%) having raised LDL-cholesterol. Fifty-eight patients (53.7%) had hyperhomocysteinaemia with a mean homocysteine level of 11.6 μ mol/l. Microalbuminuria was found in 17 patients (15.7%). All patients had at least two cardiovascular risk factors present (excluding diabetes itself), with 86 patients (79.6%) having at least five risk factors present, more in males than females.

CONCLUSIONS There is a high prevalence of vascular risk factors, frequently multiple, in patients with type 2 diabetes seen at KNH.

1 LITERATURE REVIEW

1.1 HISTORICAL PERSPECTIVE

Diabetes mellitus has been known since the second century AD when Arataeus the Cappadocian first applied to it the Greek word "diabetes" meaning to run through a siphon, mistakenly believing that the internal milieu dissolved away and passed out as urine, thus wasting away the affected individual. Cotunnus in 1770 and Rollo in 1798 recognized that the urine of some diabetics contained protein. In 1836 Richard Bright noted that the presence of albumin in urine was a sign of serious kidney disease. These findings led Rayer in 1840 to postulate that patients with diabetes may also develop "Bright's disease"(1). After the discovery and isolation of insulin in 1921(2) and its synthesis in crystalline form by Abel in 1926(3), the long term effects of diabetic disease were seen with increasing frequency, these being renal disease, neuropathy, cataracts, peripheral vascular disease, cerebrovascular accidents and myocardial infarction.

1.2 INTRODUCTION

Diabetes mellitus exerts its greatest impact throughout the vascular system (4), with increased morbidity and mortality caused by its vascular complications both in the microcirculation and in the large vessels(5). Indeed, the consequences of large vessel disease are the most common causes of death, and are associated with significant reduction in the quality of life of

patients with diabetes.

Cardiovascular disease is a leading cause of death in diabetic patients, accounting for almost 80% mortality(6), with the prevalence of cardiovascular disease risk two to five times higher in individuals with diabetes compared to those without diabetes(7), and risk of cardiac death three times higher in the same population(8).

The development of large vessel disease is accelerated with type 1 diabetes and often presents at diagnosis with type 2 diabetes, seen predominantly at three major sites of the cardiovascular system, namely the coronary, cerebral and peripheral arteries. Susceptibility to large vessel disease is determined by a complex interaction of various factors including hereditary predisposition, disturbance of metabolic state, and exposure to risk factors within the environment(4). Some of these risk factors may in turn be directly dependent on disturbance of the diabetic state such as hyperlipidaemia, glycosylation and alterations of blood constituents including platelet adhesiveness. Other factors may be part of the genetic predisposition such as hypertension and obesity, while others may be truly avoidable factors such as cigarette smoking, poor diet or sedentary lifestyle(4).

1.3 EPIDEMIOLOGY

Diabetes mellitus is one of the most common chronic diseases in the world with a prevalence that approaches eight percent of the adult populations of the

United States of America (USA) and much of Europe(9). The predominant clinical form of diabetes mellitus is type 2, which accounts for more than 90% of all cases.

Type 2 diabetes occurs with an equal frequency in men and women and most commonly in overweight individuals older than 40 years(9). Cardiovascular disease, which includes coronary heart disease (CHD), cerebrovascular disease (CVD) and peripheral vascular disease(PVD), also occurs with higher than normal frequency in diabetes and is the major cause of mortality and death in diabetic patients worldwide. In the USA, where diabetes is the fourth most common cause of death, cardiovascular disease, and CHD in particular, accounts for as much as 75% of all mortality in type 2 diabetes(10). In the United Kingdom Prospective Diabetes Study (UKPDS)(11), after nine years of follow-up fatal cardiovascular disease events were 70 times more frequent than fatal microvascular complications. International survey data from World Health Organisation (WHO) also show CHD prevalence rates in diabetes between 26% and 35%, with higher rates in women and older people(12).

Certain risk factors for cardiovascular disease were found in Tanzanian adolescents including hypertension, obesity, dyslipidaemia and diabetes(13). The adult mortality rates associated with diabetes were 34 and 21 per 100,000 per year in males and females respectively and the percentages of all adult deaths associated with diabetes was 2.6% in males and 1.7% in females, in Dar es Salaam, Tanzania(14).

The risk of CHD is increased even in patients with newly diagnosed diabetes, probably the result of the long latent period that precedes the clinical diagnosis of type 2 diabetes, during which symptom-free individuals may be exposed to the atherogenic effects of multiple coronary heart disease (CHD) risk factors (the "ticking clock" phenomenon)(15), and especially in women whose normal premenopausal advantage and protection from CHD is lost in the presence of diabetes(4). People with type 2 diabetes are more likely to have risk factors for CHD than are age-matched non-diabetic individuals. In the population-based Framingham Study, the prevalence of established CHD risk factors was 1.4 to 4.1 times higher among patients with than those without clinically diagnosed type 2 diabetes(16). Moreover, individuals with type 2 diabetes are also more likely to have multiple risk factors for CHD ("clustering"). In the Multiple Risk Factor Intervention Trial (MRFIT), men with diabetes alone had an absolute excess risk of CHD death of about 25 per 10,000 person-years; diabetes and any one of hypertension, hypercholesterolaemia or cigarette smoking increased this risk to 47 per 10,000 person-years, and with all of these risk factors the risk was 78 per 10,000 person-years(17).

The clinical and health problem of CHD among people with type 2 diabetes is enormous and a worldwide increase may be expected in the coming years as industrialised societies age and become more obese and sedentary, and as less industrialised societies adopt more "westernized" lifestyles.

1.4 RISK FACTORS

1.4.1 HYPERTENSION

Many type 2 diabetics are hypertensive at the time of the diagnosis of diabetes, which suggests that hypertension may be secondary to a common underlying mechanism such as obesity or insulin resistance or that hypertension may exacerbate glucose intolerance. In patients with diabetes, hypertension increases the risk of coronary events, stroke, congestive heart failure, PVD and microvascular complications(9). Features of hypertension in diabetic patients include increased plasma volume, increased peripheral vascular resistance, low plasma renin activity and commonly, hyperinsulinaemia and insulin resistance(18). Hyperinsulinaemia produces renal sodium retention and increases sympathetic activity, potentiates vascular smooth muscle hypertrophy secondary to mitogenic activity of insulin and modifies ion-transport across the cell membrane, thereby potentially increasing the cytosolic calcium levels of insulin sensitive vascular or renal tissues, all leading to increase in arterial pressure(19).

The prevalence of hypertension in type 2 diabetes is higher than that in the general population especially in younger patients(20). In an Ethiopian study by Seyoum et al., the prevalence of hypertension in patients with type 2 diabetes was 33.3%(21) and was 29.2% in patients at presentation of diabetes in urban Tanzanian(22). At the age of 45 years around 40% of patients with type 2 diabetes are hypertensive, the proportion increasing to 60% by the age of 75

years.

The UKPDS revealed that among patients with hypertension and type 2 diabetes, intensive lowering of blood pressure achieves clinically important reduction in the risks of deaths and complications related to diabetes(23). A similar benefit was observed in the Hypertension Optimal Treatment study among hypertensive patients with diabetes(24), hence the importance of optimal blood pressure control in diabetic subjects.

1.4.2 DYSLIPIDAEMIA

All patients with diabetes have the potential to develop abnormal lipid profiles, and at any one time as many as 25% of patients attending the diabetic clinic will demonstrate dyslipidaemia(4).

Hypertriglyceridaemia and low HDL concentrations are the dominant features. When the catabolism of triglyceride-rich lipoproteins is impaired, they become cholesterol enriched and possibly directly atherogenic. Hypertriglyceridaemia has many metabolic consequences, such as postprandrial hyperlipoproteinaemia, preponderance of small dense LDL and a shift from large and buoyant to small and dense HDL subclasses, which are all potentially atherogenic(25).

Plasma cholesterol concentration is an independent variable in diabetes, and is predictive of coronary events in patients with diabetes. Total cholesterol was

a significant predictor of coronary mortality in the Paris Prospective Study of 943 men with diabetes or impaired glucose tolerance, followed up for 11 years(26). However, hypertriglyceridaemia was an even a stronger predictor of coronary mortality. At the 15-year follow-up, triglyceride concentration was still the strongest independent predictor of coronary death(27).

In a study by Laakso and colleagues who followed-up 313 type 2 diabetics for 7 years, a low HDL-cholesterol concentration was the most important single predictor of coronary events, and in the subgroup of patients with HDL-cholesterol concentrations below the median, raised VLDL-triglyceride concentrations were still predictive of future coronary events, thus suggesting that these two features of dyslipidaemia in type 2 diabetes have a strong combined adverse effect(28).

Small dense LDL particles are part of the dyslipidaemia of type 2 diabetes and glycation of LDL and other lipoproteins is a special characteristic of diabetes (29). Glycation of apolipoproteins makes them susceptible to oxidation, which increases their atherogenicity and leads to immune processes that may also enhance atheroma formation(30).

The findings of the Scandinavian Simvastatin Survival Study (4S)(31) and the West of Scotland Coronary Prevention Study (WOSCOPS)(32) showed the benefit of treatment dyslipidaemia using lipid-lowering agents with significant reductions in coronary events, cardiovascular events and all cause mortality,

with the former study showing this benefit clearly in diabetes.

1.4.3 OBESITY

Unfavourable fat distribution may be an independent indicator of circulatory risk. Central adiposity with increased underlying visceral fat is associated with increased predisposition to premature circulatory disorders. In gynaecoid obesity, cardiovascular complications are relatively less common. There is evidence that the obesity (*ob*) gene product, leptin, may have a central role in insulin resistance(33). The metabolic and circulatory changes associated with visceral obesity lead to the development of insulin resistance and increased lipoprotein synthesis(34). Increased body mass index (BMI) appears to be associated with endothelial dysfunction, which is a major factor in atheroma plaque formation and development of thrombosis(34). Compared with lean men, men with BMI of 25 to 29 have been observed to have a 70% greater risk of CHD whereas men with BMI of 29 to 33 had almost a three-fold greater risk of CHD(35).

Weight loss in patients with type 2 diabetes is associated with improved glycaemic control, lipid profile and reduced coronary events(36).

1.4.4 CIGARETTE SMOKING

Cigarette smoking in diabetes has been linked with increased risk of developing microangiopathic complications such as retinopathy and

nephropathy but the greatest adverse affect is on vascular morbidity and mortality(4).

Cerebrovascular episodes and coronary heart events occur more frequently and with greater severity in diabetics who smoke, the relationship being most evident with peripheral arterial disease of the legs(4).

Cigarette smoking not only exerts a detrimental effect on the circulation but also adversely influences diabetic control partly as a consequence of the direct pathopharmacological effects of smoking together with other associated aspects of unhealthy lifestyle(4).

In an Ethiopian study(21), 9.3% of subjects with type 2 diabetes were current smokers compared to other Western studies that reported the prevalence of smoking in the diabetic population to range from 25-35%(37). The relative risk of all cause mortality is about twice as high for smoking compared to non-smoking diabetic population(38), and it must be stressed that patients with diabetes should abstain from smoking.

1.4.5 MICROALBUMINURIA

The term microalbuminuria (MAL) was introduced by Viberti et al.(39) to refer to a subclinical rise in urinary albumin excretion (UAE) greater than 30 mg/24hrs in patients with type 1 diabetes. A conference on early diabetic

nephropathy defined microalbuminuria as UAE between 20-200 $\mu\text{g}/\text{min}$ (30-300 mg/24hrs)(40).

The association between MAL and cardiovascular disease risk has been studied closely in patients with hypertension. Prevalence of MAL in hypertension varies in different studies from 11%(41) to 40%(42) or greater, depending upon the number of patients studied, severity of hypertension, age, race and coexistence of renal impairment(43). Hypertensives with other risk factors such as smoking or dyslipidaemia show greater target organ damage in patients with MAL, with cardiovascular disease being 50% higher in these patients(44).

A local study by Twahir(45) reported the prevalence of microalbuminuria to be 36.4% and 40.5% in type 1 and type 2 diabetes respectively.

Mortality in type 2 diabetes with microalbuminuria is 60% at 8 years and is mainly due to cardiovascular disease(46). Changes in MAL in various cardiovascular disorders suggests that it is of value as an index of vascular damage, especially in hypertension and diabetes, and its association with peripheral markers of endothelial damage or dysfunction suggests the possibility that MAL may be a simple, cheap, and reliable marker of endothelial abnormalities in cardiovascular disease.

1.4.6 HYPERHOMOCYSTEINAEMIA

There is increasing evidence that elevated plasma homocysteine level is a novel independent risk factor for atherothrombotic disease in the general population(47).

Homocysteine is an intermediate compound formed during metabolism of methionine and a number of enzymes, essential cofactors, and the availability of the substrate methyltetrahydrofolate regulate the total plasma homocysteine level. It has been shown that that the in-vitro activity of the rate-limiting enzyme for homocysteine metabolism, cystathionine synthase, declines with age(47). Epidemiological studies have demonstrated an inverse correlation between homocysteine and plasma vitamin B levels, especially in patients with CHD(48), as well as strong positive correlations of homocysteine level with age(49) and with serum creatinine level(50).

Raised plasma total homocysteine level may enhance coronary arteriosclerosis in patients with diabetes by accelerating the direct cytotoxic effects of glucose and the oxidative modification of glucose in endothelial cells. In a study by Molgaard et al.(51), homocysteine has been shown to facilitate the modification of LDL-cholesterol in-vitro. In addition, a very low level of homocysteine markedly increases the binding of lipoprotein(a) to fibrin providing a potential link between thrombosis and atherogenesis. In-vitro studies by Harpel et al.(52), Upchurch et al.(53), and others have shown that homocysteine promotes coagulation. It has been proposed that homocysteine

causes severe endothelial cell injury and that this injury, in turn, leads to platelet activation (by reducing endothelium-derived relaxing factor/nitric oxide (NO) production), smooth muscle proliferation and thrombosis(54,55). Homocysteine-induced attenuation of bioavailable NO has been shown to cause attenuation of the antithrombotic properties of the endothelium and causes platelet activation as well as thrombin generation(56). In diabetic patients, lipoproteins in the arterial wall are subject to oxidative modification via the action of myeloperoxidase or reactive nitrogen species derived from NO (57).

In a study by Okada et al.(58), there seems to be clear relation between hyperhomocysteinaemia and an increased risk of coronary arteriosclerosis in Japanese patients with type 2 diabetes. Hoogeveen et al.(59) found an interaction effect of fasting hyperhomocysteinaemia and type 2 diabetes in terms of risk of macrovascular disease.

Homocysteine lowering treatment with folic acid and vitamin B6 in healthy siblings of patients with premature atherothrombotic disease has been associated with decreased risk of atherosclerotic coronary events in that population(60). Hence, dietary supplementation with vitamins to lower homocysteine concentrations may provide a simple, effective and inexpensive means of reducing CHD risk.

1.4.7 POOR GLYCAEMIC CONTROL

Poor glycaemic control is associated with an increased frequency of microvascular complications and macrovascular cardiac events in patients with type 2 diabetes(61). Hyperglycaemia could contribute to accelerated atherogenesis and to increased clinical CHD events through various mechanisms, which include: glycation of collagen, other vessel wall proteins and lipoproteins; accelerated generation of reactive oxygen species and heightened oxidative stress on glycated end-products, LDL-cholesterol and vascular endothelial cells; alteration in haemorheological characteristics(62); or changes in vascular reactivity(63).

In the Whitehall study(64), two-hour postload glucose values in the upper 5% range were associated with increased cardiovascular mortality, as were values in the upper 20% range in the Paris Prospective Study(65). Knuiman et al. also found an independent relation between hyperglycaemia and overall macrovascular disease(66).

The UKPDS showed that intensive blood glucose control reduces the risk of diabetic complications in type 2 diabetes, the greatest effect being on microvascular complications(67).

2 JUSTIFICATION OF THE STUDY

Diabetes mellitus and its long-term complications including cardiovascular problems are major and growing health problems locally, these being important causes of morbidity and mortality in Kenya.

There are no local data on the prevalence of co-existing cardiovascular risk factors amongst our diabetic population. There are, however, some available data from within the African continent. However, most data emanate from the developed world and this might not directly reflect on our situation due to major socio-cultural, economic and environmental differences.

This study was designed to determine the prevalence of some established risk factors of cardiovascular disease in patients with type 2 diabetes. The data generated from this study will assist in assessing the burden of established major cardiovascular risk factors in our type 2 diabetics, in planning and conducting further detailed studies on cardiovascular morbidity in this population, and in setting up of public health intervention programs for primary and secondary prevention of cardiovascular disease in these patients, this being a far more cost-effective measure than treatment of established CHD, especially in developing nations like ours with extremely limited resources.

3 OBJECTIVES

3.1 BROAD OBJECTIVE

To determine the prevalence of certain established cardiovascular risk factors, and to describe possible associations of these risk factors, in patients with type 2 diabetes attending the diabetic outpatient clinic at KNH.

3.2 SPECIFIC OBJECTIVES

- A. To determine the prevalence of the following cardiovascular risk factors amongst type 2 diabetic patients attending the diabetic outpatient clinic at the KNH:
1. Cigarette smoking
 2. Obesity
 3. Systemic arterial hypertension
 4. Dyslipidaemia
 5. Glycaemic control
 6. Hyperhomocysteinaemia
 7. Microalbuminuria
- B. To describe the possible associations of these risk factors amongst patients with type 2 diabetes.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

Hospital based, cross-sectional descriptive study.

4.1.1 STUDY AREA

The diabetic outpatient clinic at KNH.

4.1.2 STUDY POPULATION

Patients with type 2 diabetes mellitus, seen and followed up at the diabetic outpatient clinic at KNH during the study period.

4.1.3 SAMPLING TECHNIQUE

All patients who satisfied the inclusion criteria were assigned a number, after which, using a table of random numbers, 10 patients on each clinic day were randomly selected for recruitment into the study.

4.2 SAMPLE SIZE

The sample size for this study had been estimated using the following sample size formula for a one-sample situation:

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

where: n = minimum sample size
 $Z = 1.96$ at 95% confidence interval
 P = estimated prevalence from other studies
 d = margin of precision error

The prevalence of each of the risk factors that was to be determined in this study is indicated in table 1, having been established from previous studies(21,45,58,68) and the sample size needed for determining the prevalence of the most prevalent risk factor variable was selected.

Thus the minimum sample size necessary was 96 patients and the study recruited 108 patients.

Table 1. Sample size estimation for various risk factor variables

VARIABLE	PREVALENCE (%)	ESTIMATED SAMPLE SIZE d=0.10
Obesity	36.4	89
Hypertension	33.3	85
Cigarette smoking	9.3	32
Hypercholesterolaemia	30.2	81
Hypertriglyceridaemia	22.8	68
Hyperhomocysteinaemia	39.3	92
Microalbuminuria	40.5	93
Poor glycaemic control	50.0	96

4.3 PATIENT SELECTION

4.3.1 INCLUSION CRITERIA

1. Patients with a diagnosis of type 2 diabetes based on the modified World Health Organisation(69) and/or the National Diabetes Data Group criteria(70), attending the diabetic outpatient clinic at the KNH (see Appendix II).
2. A duly signed informed consent from the patient.

4.3.2 EXCLUSION CRITERIA

1. Patients with urinary tract infection (diagnosed on the basis of history, urine dipstick examination or urine culture) or a febrile illness.
2. Patients with proteinuria based on urine dipstick examination.
3. Pregnant women.
4. Patients with or suspected to suffer from conditions which may interfere with the assay of the glycated haemoglobin fraction, such as haemoglobinopathy or lead poisoning.
5. Patients on drugs such as methotrexate, carbamazepine or phenytoin, which may affect plasma homocysteine concentration, and cimetidine, which may affect the microalbuminuria assay.
6. Any patient who refused to enter the study (this did not jeopardise patient management).

4.4 METHODS

All the files of type 2 diabetic patients booked for the clinic were scrutinised, the files having been obtained from the medical records officer before starting the clinic each day (Friday every week). The medical records were examined for pertinent demographic and clinical data. Files of patients with any of the exclusion criteria were left out, ultimately remaining with the files of patients likely to be eligible for this study. A table of simple random numbers was used to select 10 cases. For each of the recruited patients the following were done.

4.4.1 CLINICAL METHODS

i) A complete medical history was taken as per the proforma outlined in appendix I.

Current smokers would have smoked at least 100 cigarettes in their lifetime and are still smoking or would have quit smoking within the preceding year. Former smokers would have smoked at least 100 cigarettes in their lifetime but would have quit smoking more than one year earlier. Subjects who would have smoked less than 100 cigarettes or who would have never smoked were considered never to have smoked(71).

ii) A complete physical examination, including a thorough cardiovascular examination, was undertaken as per the format outlined in appendix I.

Standing height was measured once to the nearest 0.5cm, without shoes, the back square against the wall-tape, eyes looking straight ahead, with a set

square resting on the scalp and against the wall(72).

Weight was measured once with a lever balance, to the nearest 100 grams, without shoes, in light garments.

Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in metres) squared, and was categorised as per the WHO criteria(73).

Waist circumference (WC) in centimetres was taken as the narrowest circumference between the lowest rib and the top of the pelvis, measured in the horizontal plane at the end of a gentle expiration, with the subject standing(74). Hip circumference in centimetres was taken as the maximum circumference in the horizontal plane, measured over the buttocks(74). Waist-hip circumference ratio (WHR) was calculated as the ratio of the former to the latter. WC and WHR were classified as per the Dietary Guidelines for Americans(75,76).

Blood pressure was measured as per the WHO recommendation(77), with the patient in the sitting position and using a standard adult cuff and a mercury sphygmomanometer, after an initial rest period of 15 minutes. The systolic blood pressure level was determined by the first perception of Korotkoff sound (phase 1). Diastolic pressure level was determined by the perception of disappearance of fifth Korotkoff sound (phase 5). Two measurements at five-minute intervals were taken and the average of these two readings was noted.

Hypertension was defined as a systolic or diastolic pressure greater than or equal to 140 mm Hg and 90 mm Hg respectively, or patients on antihypertensive treatment.

III) All patients were subjected to a resting 12-lead electrocardiogram (ECG) using CARDIOFAX ECG 6353 (Tokyo, Japan), as per the standard ECG recording technique(78), at the diabetic clinic, by the principal investigator.

4.4.2 LABORATORY METHODS

Blood

Following 10 to 12 hours of overnight fasting, 12ml blood was withdrawn by venepuncture from each patient for the following investigations:

1. Serum urea, creatinine and electrolyte assays were performed at the Department of Clinical Chemistry, Nairobi Hospital Laboratory, using the enzymatic kinetic method for urea measurement, the alkaline picrate reaction for creatinine assay, and the ion-selective electrode method for the assay of sodium and potassium, all with the Random Access clinical chemistry analyser, RA 1000 (Technicon Instruments, USA).
2. Fasting blood sugar was done at the Department of Clinical Pathology, KNH, using the glucose oxidase colorimetric method on a RA 1000 analyser (Technicon Instruments, USA).

3. Lipid profile assays (total cholesterol, HDL-cholesterol, LDL-cholesterol and Triglycerides) were performed at the Department of Clinical Chemistry, Nairobi Hospital Laboratory, using the ALCYON™ 300/300i Analyser.

Plasma total cholesterol level was determined after enzymatic hydrolysis and oxidation by cholesterol esterase and cholesterol oxidase, using the enzymatic colorimetric test (79).

HDL-cholesterol was assayed by solubilising the HDL lipoprotein particles using a detergent containing polyanion, 4-aminoantipyrine and a buffer solution that released HDL-cholesterol, which was subsequently determined after enzymatic hydrolysis and oxidation as for total cholesterol(79).

LDL-cholesterol was assayed by solubilising the non-LDL lipoprotein particles by enzymatic hydrolysis and oxidation as for total cholesterol. The remaining LDL particles were solubilised using N,N-bis(4-sulfobutyl)-m-toluidine disodium and a buffer solution, and a chromogenic coupler led to colour formation(79).

Triglycerides were determined after enzymatic hydrolysis by lipoprotein lipase to free fatty acids and glycerol. The glycerol was phosphorylated by adenosine triphosphate (ATP) with glycerol kinase (GK) to produce glycerol-3-phosphate and adenosine diphosphate (ADP). Glycerol-3-phosphate was oxidized to

dihydroxyacetone phosphate (DAP) by glycerol phosphate oxidase producing hydrogen peroxide (H_2O_2). In a colour reaction catalysed by peroxidase, the H_2O_2 reaction with 4-aminoantipyrine (4-AAP) and 4-chlorophenol (4-CP) was used to produce a red colour dye, the absorbance of which was proportional to the concentration of triglyceride present in the sample(79).

4. Glycated haemoglobin (HbA_{1c}) assay using the Ion Capture Assay (Abbot IM_x^{SYSTEM}) method on automated immunoassay analyser (IM_x^{SYSTEM}, USA), were performed at the Immuno-Molecular Diagnostic Laboratories Limited.
5. Plasma homocysteine assay was performed at the Immuno-Molecular Diagnostic Laboratories Limited, using the IM_x Homocysteine Fluorescence Polarization Immunoassay (FPI) method, on an automated immunoassay analyser (IM_x^{SYSTEM}, USA).

Urine

10 ml mid-stream specimen of urine was collected in a sterile bottle and the following investigations were performed:

1. Urinalysis was done using the Multistix 10SG (Bayer) reagent strips, as per the standard procedure, at the Department of Microbiology, KNH(80).
2. Urine culture for aerobic bacteria on cysteine-lactose-electrolyte-deficient (CLED) medium, using standard procedures, read every 24 hours for 48

hours, was done at the Department of Microbiology, KNH(80).

3. Screening for microalbuminuria by determining the albumin-to-creatinine ratio using the CLINITEK[®] Microalbumin (Bayer) reagent strips, a CLINITEK[®] 50 urine chemistry analyser was done at the diabetic clinic, by the principal investigator(see Appendix III).

4.5 DEFINITIONS OF STUDY VARIABLES

Age and sex as risk factors were defined as ≥ 45 years in males and ≥ 55 years in females(81).

Waist circumference (cm) was considered abnormal if ≥ 94.0 cm in males and ≥ 80.0 cm in females(75,76). Waist-hip ratio was considered abnormal if >0.95 in males and >0.80 in females(75,76). Body mass index (kg/m^2) was classified according to the WHO classification(73):

Normal	<25.0
Overweight	25.0-29.9
Class 1 obesity	30.0-34.9
Class 2 obesity	35.0-39.9
Class 3 obesity	≥ 40.0

Hypertension was defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, or patients on antihypertensives, and was classified as per the WHO classification(77):

Normal	<130/85
Borderline	130-139/85-89
Grade 1	140-159/90-99
Grade 2	160-179/100-109
Grade 3	\geq 180/110

Dyslipidaemia was classified as per the American Diabetes Association recommendations(81):

Total cholesterol \geq 4.2mmol/l.

LDL – cholesterol \geq 2.6mmol/l.

HDL – cholesterol < 0.9mmol/l in males and <1.15mmol/l in females.

Triglyceride level \geq 2.3mmol/l.

Hyperhomocysteinaemia was defined as homocysteine level >10.0 μ mol/l(82).

Glycated haemoglobin was categorized as(83):

4.5-6.0 Excellent control

>6.0-7.0 Good control

>7.0-8.0 Marginal control

>8.0 Poor control

Microalbuminuria was taken as a ratio of 30-300mg urine creatinine per gram serum creatinine (3.4-33.9 mg/mmol) and clinical albuminuria as a ratio of greater than 300mg/g (>33.9mg/mmol)(84).

4.6 DATA MANAGEMENT

All data from the study was entered into questionnaires and transferred to SPSS 8.0 database, and the data were analysed using SPSS 8.0 software. Continuous data were analysed into means and categorical data into percentages, with their corresponding 95% confidence intervals. Comparisons of continuous data were made using the t test, and of categorical data using the Chi-square test or Fisher's exact test. Correlations between continuous variables were tested using the Pearson correlation coefficient.

Prevalence rates of risk factors were calculated as percentages with 95% confidence intervals. Association of multiple (two or more) risk factor variables were determined, and correlations between some of these variables were also identified as described above. Clustering (co-occurrence) of risk factors was described as number of risk factors present.

Statistical significance was defined as a two-tailed p value of less than or equal to 0.05.

5 RESULTS

A total of 750 patients with type 2 diabetes were screened from 30th May, 2000 to 21st September, 2000. Eight-nine patients were newly diagnosed and 69 had had diabetes for less than two years and were excluded. Out of the 592 patients, 160 were randomised (over 16 weeks) of which 11 did not return for appointment, six were on cimetidine and two refused consent. Of the 141 subjects interviewed, 26 had evidence of proteinuria on urine dipstick examination and seven had urinary tract infection (as evidenced by positive urine cultures for aerobic bacteria) and were excluded. Data for 108 patients were analysed.

There were 54 males and 54 females, giving a male to female ratio of 1:1. The mean age of the population studied was 55.7 years [95 percent confidence interval 54.1 to 57.3]. There was no statistically significant gender difference in age of recruited patients; (56.8 [54.3-59.2] for males and 54.5 [52.4-56.9] for females, $p=0.204$). The patients' ages ranged from 41 years to 87 years, 51 patients (47.2%) being in the 51-60 years age group (Figure 1).

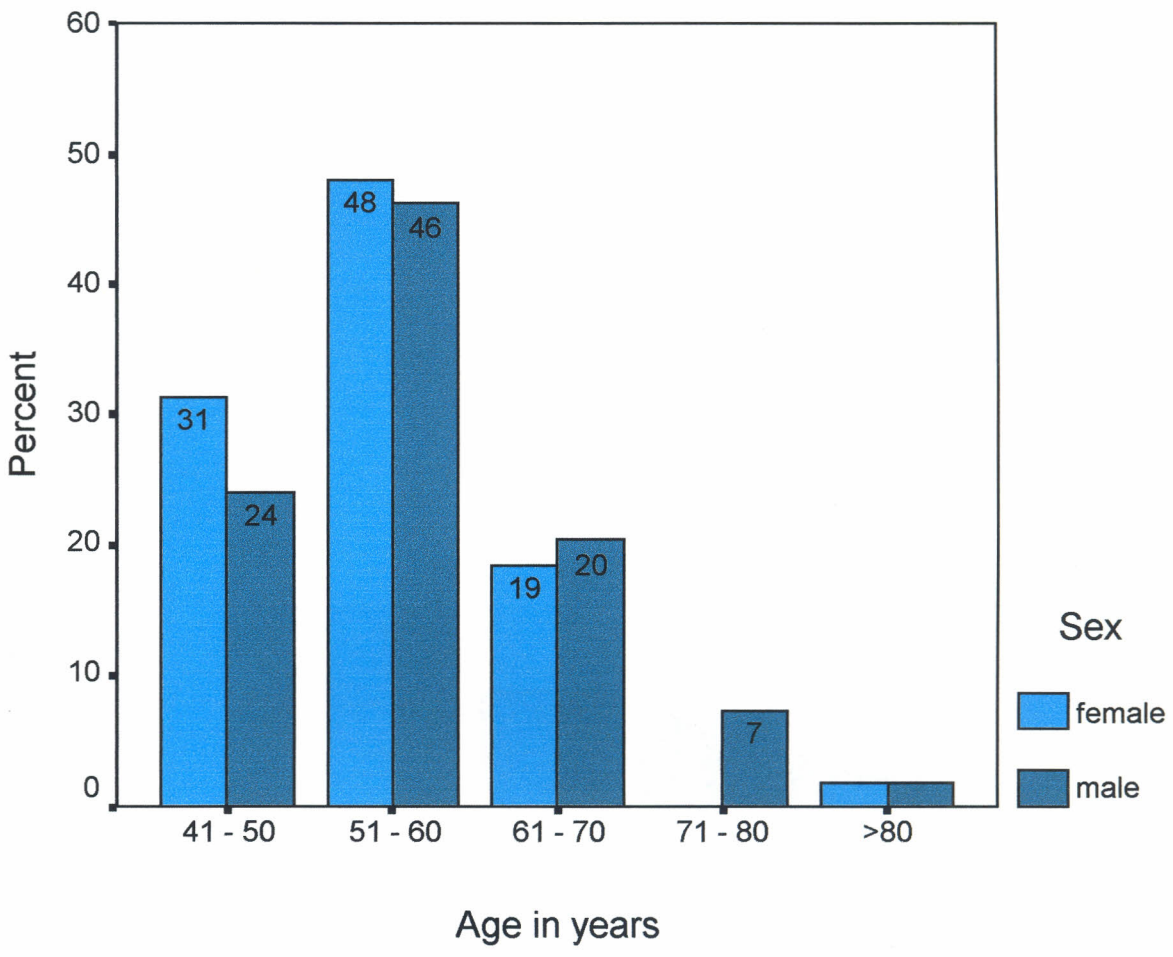


Figure 1. Age and sex distribution of the study population

Duration of diabetes ranged from 2 years to 27 years with a mean of 7.5 years [6.4-8.5], with no statistically significant difference between the genders (8.2 [6.6-9.7] for males and 6.8 [5.4-8.1] for females, $p=0.182$). The majority of the study patients (75.9%) had had diabetes for less than 10 years (Figure 2).

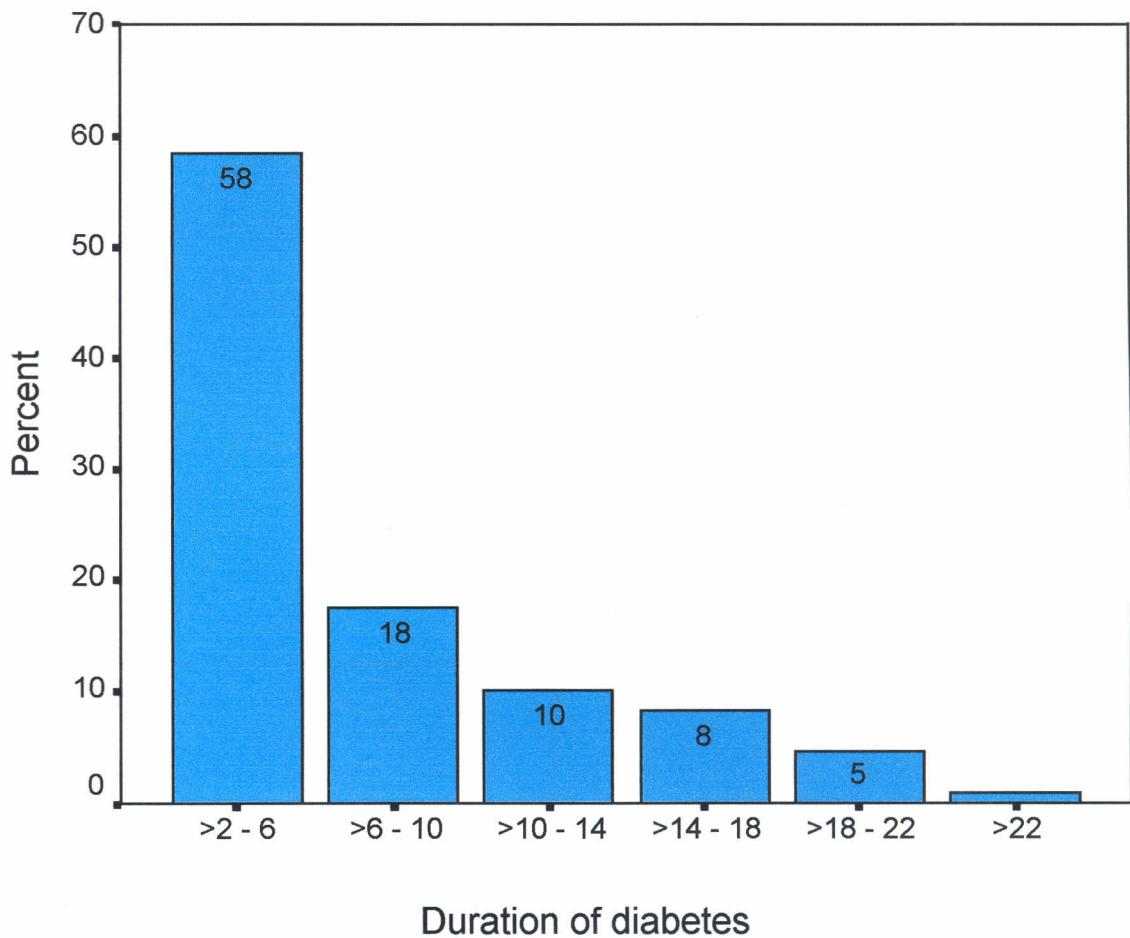


Figure 2. Duration of diabetes of the study population in years

In terms of glycaemic therapy, 52 patients (48.1%) were on oral hypoglycaemic agents alone, of which 27 (51.9%) were on sulphonylureas, three (5.8%) were on metformin, 19 (36.5%) were on both of these and three patients (5.8%) were on other oral hypoglycaemic medications. Six patients (5.6%) were on insulin alone and 50 (46.3%) were on combined oral hypoglycaemic agent(s) and insulin therapy.

BODY MASS INDEX

The mean BMI was 26.9 kg/m² [26.1-27.7] with a range of 17.8-39.5 kg/m².

Fifty patients (47.6%) were overweight, 17 (16.2%) had class 1 obesity, and 3 (2.9%) had class 2 obesity (Figure 3).

Seventy patients (66.7%) were either overweight or obese.

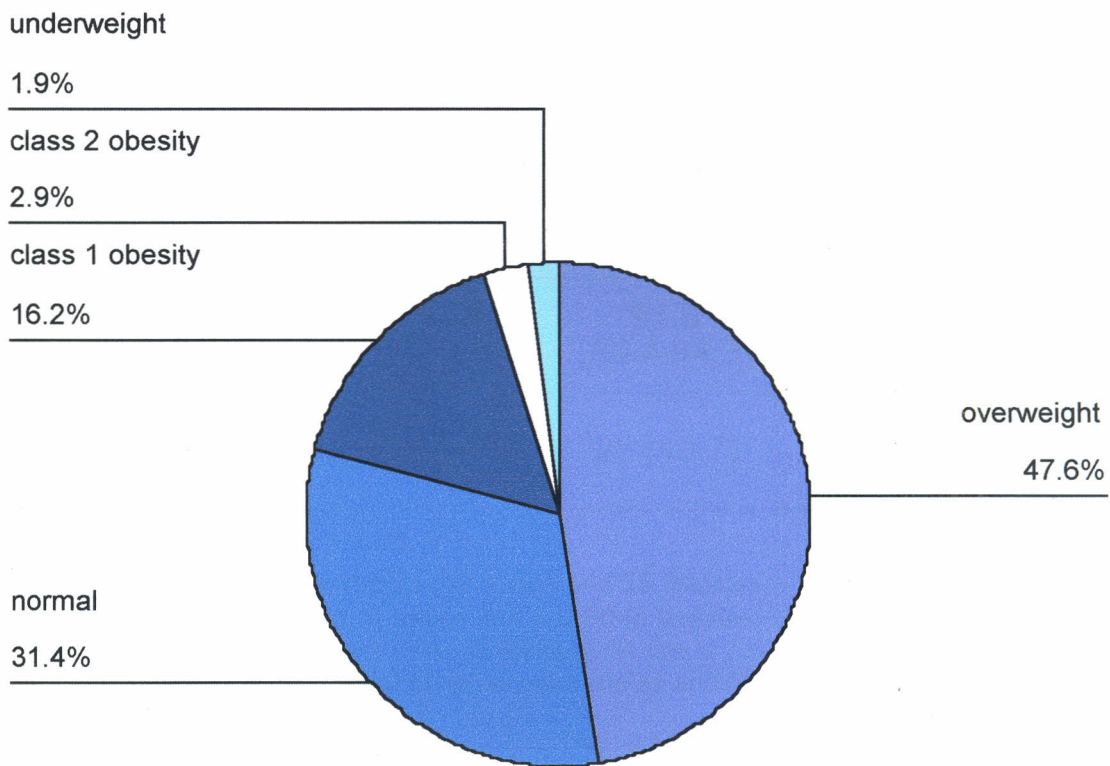


Figure 3. Classification of obesity in the study patients by body mass index

Central obesity was measured using the WHR and WC parameters. Females were significantly more likely to have abnormal WHR or WC than males. There was a statistically significant difference in the absolute values of BMI and WHR

between the genders (Table 2).

Table 2. Mean body mass index, waist-hip ratio and waist circumference and prevalences of obesity using these indices in the study patients

VARIABLE		ALL (n=108)	MALES (n=54)	FEMALES (n=54)	P value*
BMI §	Mean (kg/m ²) [95% CI]	26.9 [26.1-27.7]	25.6 [24.7-26.5]	28.2 [27.0-29.4]	0.001*
	Overweight/Obese No. (%)	70 (64.8)	31 (58.5)	39 (75.0)	0.072
WHR	Mean	0.88 [0.66-0.90]	0.93 [0.92-0.95]	0.84 [0.82-0.85]	<0.001*
	Abnormal WHR ¶ No. (%)	53 (49.1)	11 (20.4)	42 (77.8)	<0.001*
WC	Mean (cm)	91.4 [86.9-93.2]	91.8 [89.4-94.3]	90.6 [88.0-93.3]	0.744
	Abnormal WC † No. (%)	71 (65.7)	22 (40.7)	49 (90.7)	<0.001*

§ Data were available for 105 patients (52 males and 53 females)

¶ Obesity defined by WHR > 0.95 in males and > 0.80 in females

† Central obesity defined by a waist circumference ≥ 94 cm in males and ≥ 80 cm in females

* P value indicating statistical significance between males and females

CIGARETTE SMOKING

The prevalence of current cigarette smoking was 5.6% (six patients). 28 patients (25.9%) were ex-smokers. All of the current smokers were males, while one of the ex-smokers was a female.

FAMILY HISTORY

Eighty-four patients (77.8%) gave positive family history of diabetes and 72 patients (66.7%) gave positive family history of hypertension.

A family history of heart attack, stroke or sudden death amongst first-degree relatives was obtained in 17 patients (15.7%).

HISTORY OF VASCULAR DISEASES

Fifty-one patients (47.2%) had history of vascular disease, of which 41 had history suggestive of PVD, 13 CHD, and two CVD (a number of patients had history of disease in more than one vascular bed). Of the 13 patients with CHD, two had had myocardial infarction and 11 patients had history of angina. Amongst the patients with PVD, one patient had had an amputation and the rest had a history of intermittent claudication. Of the two patients with history of CVD, one had suffered a stroke and one a TIA.

Six patients (5.6%) had history of CHD and PVD. The patient with TIA also had history suggestive of PVD.

A total of 10 patients (9.3%) were on aspirin prophylactically of which four (3.7%) had history of vascular disease (all with CHD).

SYSTEMIC ARTERIAL HYPERTENSION

The mean systolic blood pressure was 143.8 mm Hg [139.4-148.2] with a range of 102-204 mm Hg. The mean diastolic blood pressure was 87.1 mm Hg [84.7-89.5] with a range of 55-115 mm Hg. Thirty-one patients (28.7%) were normotensive and seven (6.5%) had borderline hypertension. Seventy patients (64.8%) were hypertensive, mostly with grade 1 hypertension (40 out of 70 patients), as outlined in Table 3. Thirty-nine females compared to 31 male patients were hypertensives although this did not attain statistical significance ($p=0.109$). SBP was significantly higher in females compared to males (mean 151.2 mm Hg [144.5-157.8] for males and 136.5 mm Hg [131.3-141.7] for females, $p=0.001$). Thirty-two patients (45.7%) amongst the hypertensives were on antihypertensive agent(s) yet none had well-controlled blood pressure, with 35% having grade 3 hypertension.

Table 3. Blood pressure classification and sex

BP \ Sex	Males Number (%) (n=54)	Females Number (%) (n=54)	Total Number (%) (n=108)	P value
Normal (<130/85)	20 (37.0)	11 (20.4)	31 (28.7)	0.056
Borderline (130-139/85-89)	3 (5.6)	4 (7.4)	7 (6.5)	1.000
Grade 1 (140-159/90-99)	20 (37.0)	20 (37.0)	40 (37.0)	1.000
Grade 2 (160-179/100-109)	6 (11.1)	10 (18.5)	16 (14.8)	0.279
Grade 3 (\geq 180/110)	5 (9.3)	9 (16.7)	14 (13.0)	0.252

SBP was positively correlated with BMI and total cholesterol (Table 4).

GLYCAEMIC CONTROL

The mean fasting blood glucose (FBG) was 9.4 mmol/l [8.7-10.2] with a range of 3.1 to 22.1 mmol/l. Eighty-eight patients (81.5%) had FBG \geq 6.0 mmol/l, as shown in Figure 4. Females had significantly higher FBG than males: 10.3 [9.2-11.5] for females and 8.6 [7.5-9.6] for males ($p = 0.028$).

Table 4. Correlations of Systolic and Diastolic Blood Pressure with various factors

VARIABLE	SBP		DBP	
	Pearson correlation coefficient	P value	Pearson correlation coefficient	P value
Age (years)	0.135	0.163	-0.072	0.462
Duration of diabetes (years)	0.030	0.759	-0.166	0.086
BMI (kg/m ²) ††	0.206	0.035	0.087	0.377
WC (cm)	0.104	0.282	0.026	0.786
WHR	-0.145	0.134	-0.111	0.254
HbA _{1c} (%)	-0.066	0.498	-0.124	0.202
Homocysteine level (µmol/l)	0.008	0.938	-0.050	0.607
Total cholesterol (mmol/l)	0.246	0.010	0.098	0.311
HDL-cholesterol (mmol/l)	0.056	0.567	-0.025	0.801
LDL-cholesterol (mmol/l)	0.088	0.366	0.066	0.496
Triglycerides (mmol/l)	0.182	0.060	0.035	0.719

†† Data were available for 105 patients

The mean HbA_{1c} level was 8.76% [8.33-9.20] with a range of 5.37-17.22%. Thirty-two patients (29.9%) had good glycaemic control (HbA_{1c} ≤ 7.0%), whereas 75 patients (70.1%) showed evidence of poor glycaemic control (Figure 5). HbA_{1c} was significantly higher in females at 9.3% [8.6-9.9] compared to 8.3% in males [7.7-8.9] (p = 0.037).

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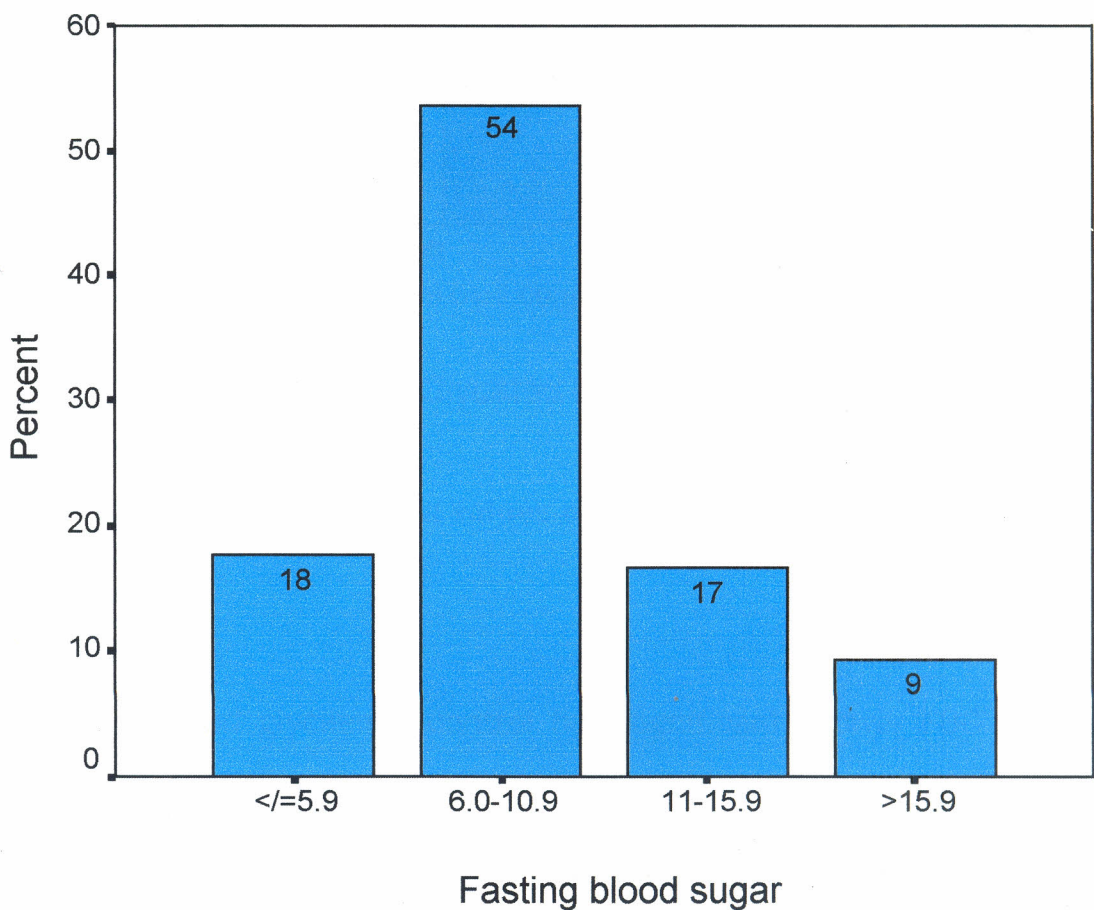


Figure 4. Fasting blood sugar values of study patients

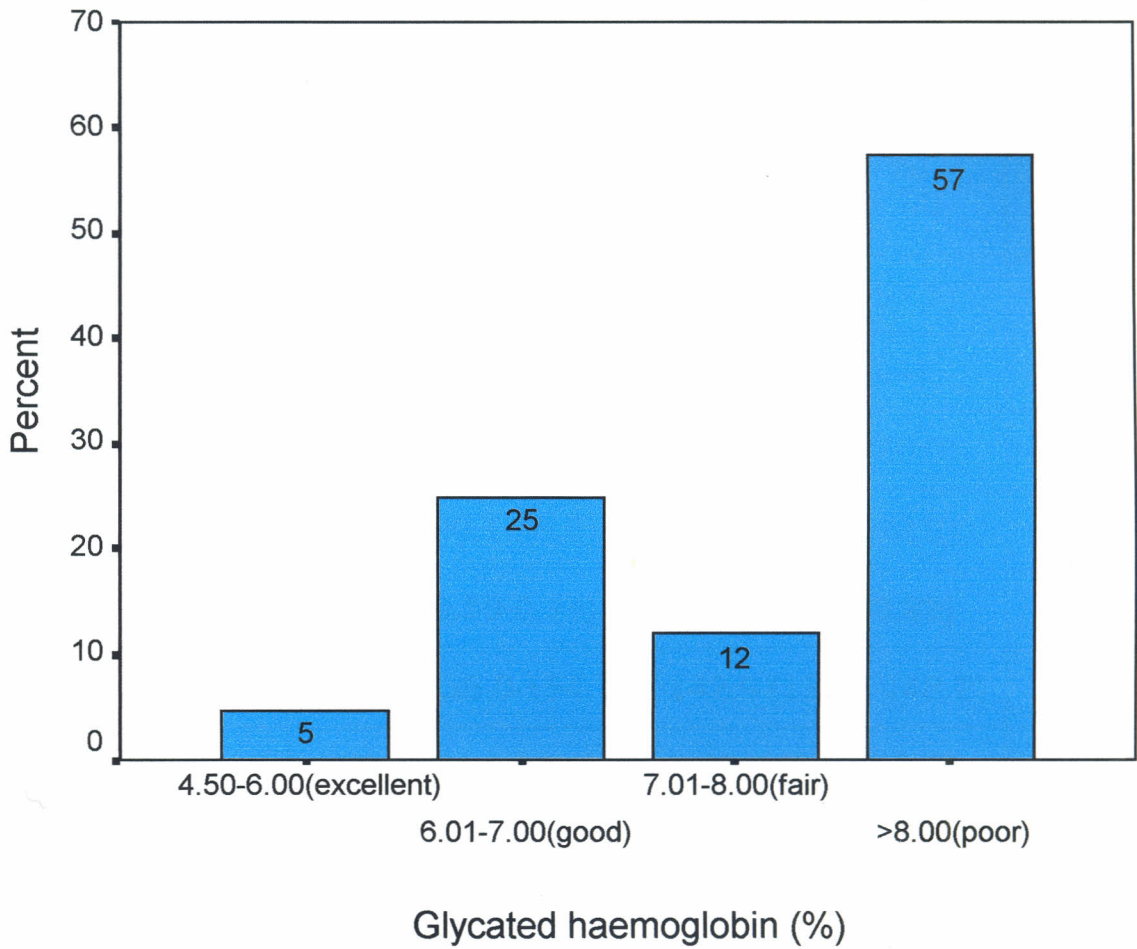


Figure 5. Glycated haemoglobin values of study patients (n=107)

Patients with good glycaemic control had significantly lower FBG ($p < 0.001$) and higher WHR ($p = 0.020$), as outlined in Table 5.

Table 5. Mean values [95 % Confidence Interval] for good and poor glycaemic control against various factors in study population

VARIABLE	Good glycaemic control (HbA _{1c} ≤ 7%) Mean [95% CI] (n = 32)	Poor glycaemic control (HbA _{1c} > 7%) Mean [95% CI] (n = 76)	P value
Age (years)	56.9 [53.5-60.4]	55.2 [53.3-57.1]	0.336
Duration of diabetes (years)	7.8 [5.5-10.1]	7.3 [6.2-8.4]	0.682
† BMI (kg/m ²)	26.6 [25.5-27.7]	27.0 [26.0-28.0]	0.636
WC (cm)	93.1 [90.1-96.0]	90.7 [88.5-92.9]	0.225
WHR	0.91 [0.89-0.93]	0.87 [0.86-0.89]	0.020
SBP (mm Hg)	146.1 [138.0-154.1]	142.9 [137.5-148.2]	0.514
DBP (mm Hg)	88.1 [84.0-92.2]	86.7 [83.7-89.7]	0.598
† FBG (mmol/l)	6.3 [5.8-6.8]	10.7 [9.8-11.7]	<0.001
Homocysteine (µmol/l)	12.6 [10.9-14.4]	11.4 [10.1-12.7]	0.280
Total cholesterol (mmol/l)	5.6 [4.8-6.4]	5.4 [5.1-5.7]	0.510
HDL-cholesterol (mmol/l)	1.1 [1.0-1.1]	1.1 [1.0-1.2]	0.446
LDL-cholesterol (mmol/l)	3.3 [3.0-3.7]	3.5 [3.3-3.7]	0.415
Triglycerides (mmol/l)	1.8 [1.2-2.4]	1.3 [1.1-1.5]	0.130

† Data for good and poor glycaemic control were available for 31 and 74 patients respectively

DYSLIPIDAEMIA

The mean values with 95% confidence intervals for the parameters of the fasting lipid profile are shown in Table 6. Females had a statistically significant higher total cholesterol levels than males (p=0.009), whereas males had significantly lower HDL-cholesterol than females (p=0.017).

Table 6. Mean values [95% Confidence Interval] for lipid profile of the study population

Lipid variable	Total (n=108)	Males (n=54) [95% CI]	Females (n=54) [95% CI]	P value
Total-cholesterol (mmol/l)	5.5 [5.2-5.8]	5.1 [5.2-5.8]	5.9 [5.3-6.4]	0.009
HDL-cholesterol (mmol/l)	1.1 [1.0-1.1]	1.0 [1.0-1.1]	1.1 [1.1-1.2]	0.017
LDL-cholesterol (mmol/l)	3.4 [3.2-3.6]	3.2 [3.0-3.5]	3.6 [3.3-3.9]	0.083
Triglycerides (mmol/l)	1.5 [1.3-1.7]	1.4 [1.1-1.6]	1.6 [1.2-2.0]	0.273

The prevalence of dyslipidaemia based on the National Cholesterol Education Program (NCEP)(85) and the current American Diabetes Association (ADA)(81) criteria is as shown in Table 7.

Table 7. Proportion of patients with dyslipidaemia based on the National Cholesterol Education Program (NCEP) and the American Diabetic Association (ADA) cut-off values

Lipid variable	NCEP cut-off values	Number (%)	ADA cut-off values	Number (%)
Total cholesterol (mmol/l)	≥ 5.20	56 (51.9)	≥ 4.20	93 (86.1)
HDL-cholesterol (mmol/l)	< 0.90	24 (22.2)	< 0.90 (M) < 1.15 (F)	45 (41.7)
LDL-cholesterol (mmol/l)	≥ 3.40	50 (46.3)	≥ 2.60	88 (81.5)
Triglycerides (mmol/l)	≥ 1.70	30 (27.8)	≥ 2.30	12 (11.1)

One hundred and one patients (93.5%) had some form of dyslipidaemia. Ninety-one patients (84.3%) had at least two lipid abnormalities. Most of these patients had elevated levels of either total cholesterol or LDL-cholesterol (Table 7). Only one patient was on a lipid-lowering agent (statin).

HDL-cholesterol was negatively correlated with WHR and triglycerides, and was positively correlated with HbA_{1c}, FBG, total cholesterol and LDL-cholesterol (Table 8). Total cholesterol was strongly correlated with LDL-cholesterol and triglycerides (Table 9).

Table 8. Correlations of HDL-cholesterol and Triglycerides with various parameters

VARIABLE	HDL-CHOLESTEROL		TRIGLYCERIDES	
	Pearson correlation coefficient (n=108)	P value	Pearson correlation coefficient (n=108)	P value
Age (years)	0.119	0.219	-0.130	0.180
Duration of diabetes (years)	0.156	0.108	-0.113	0.244
†BMI (kg/m ²)	-0.031	0.755	0.132	0.179
WC (cm)	-0.161	0.095	0.175	0.071
WHR	-0.201	0.037	-0.073	0.454
HbA _{1c} (%)	0.210	0.030	-0.140	0.149
†FBG (mmol/l)	0.265	0.006	-0.041	0.679
Homocysteine level (µmol/l)	-0.071	0.466	-0.103	0.289
Total cholesterol (mmol/l)	0.203	0.035	0.624	<0.001
HDL-cholesterol (mmol/l)	-	-	-0.209	0.030
LDL-cholesterol (mmol/l)	0.210	0.029	0.049	0.616
Triglycerides (mmol/l)	-0.209	0.030	-	-

† Data were available for 105 patients

Table 9. Correlations of LDL-cholesterol and Total cholesterol with various parameters

VARIABLE	LDL-CHOLESTEROL		TOTAL CHOLESTEROL	
	Pearson correlation coefficient (n=108)	P value	Pearson correlation coefficient (n=108)	P value
Age (years)	0.143	0.140	0.082	0.401
Duration of diabetes (years)	0.070	0.470	0.002	0.985
†BMI (kg/m ²)	0.111	0.258	0.064	0.514
WC (cm)	-0.035	0.716	-0.022	0.822
WHR	-0.036	0.711	-0.154	0.113
HbA _{1c} (%)	0.078	0.426	-0.014	0.888
†FBG (mmol/l)	0.038	0.702	0.006	0.952
Homocysteine level (µmol/l)	-0.061	0.529	-0.121	0.212
Total cholesterol (mmol/l)	0.657	<0.001	-	-
HDL-cholesterol (mmol/l)	0.210	0.029	0.203	0.035
LDL-cholesterol (mmol/l)	-	-	0.657	<0.001
Triglycerides (mmol/l)	0.490	0.616	0.624	<0.001

† Data were available for 105 patients

HYPERHOMOCYSTEINAEMIA

The mean homocysteine level was 11.6 µmol/l [10.7-12.8] with a range of 4.2-43.1 µmol/l. Fifty-eight patients (53.7%) had hyperhomocysteinaemia (>10.0 µmol/l). Males had a significantly higher homocysteine level (13.1 [11.4-14.7] compared to females, 10.4 [9.2-11.6], p=0.010).

MICROALBUMINURIA

A total of 18 patients (16.7%) had albuminuria, of which 17 patients (15.7%) had microalbuminuria (30-300 mg/g) and one patient had macroalbuminuria (>300 mg/g) (not seen on screening during urine dipstick examination).

Microalbuminuria was significantly associated with SBP ($p=0.004$), smoking ($p=0.013$) and LDL-cholesterol level ($p=0.029$),

RISK FACTOR CLUSTERING

The number of cardiovascular risk factors present in individuals in the study population was analysed (Figure 6). These were age and sex (age ≥ 45 years for males and ≥ 55 years for females), family history of vascular disease in first-degree relatives, and smoking, hypertension, poor glycaemic control, obesity, dyslipidaemia, hyperhomocysteinaemia and microalbuminuria. All patients had at least two CHD risk factors present, excluding their diabetic state, with the majority (79.6%) having five or more. Males had more risk factors than females.

Seventy-eight patients (72.2%) had age and sex as risk factors for cardiovascular disease (males ≥ 45 years, females ≥ 55 years), significantly more females than males ($p<0.001$).

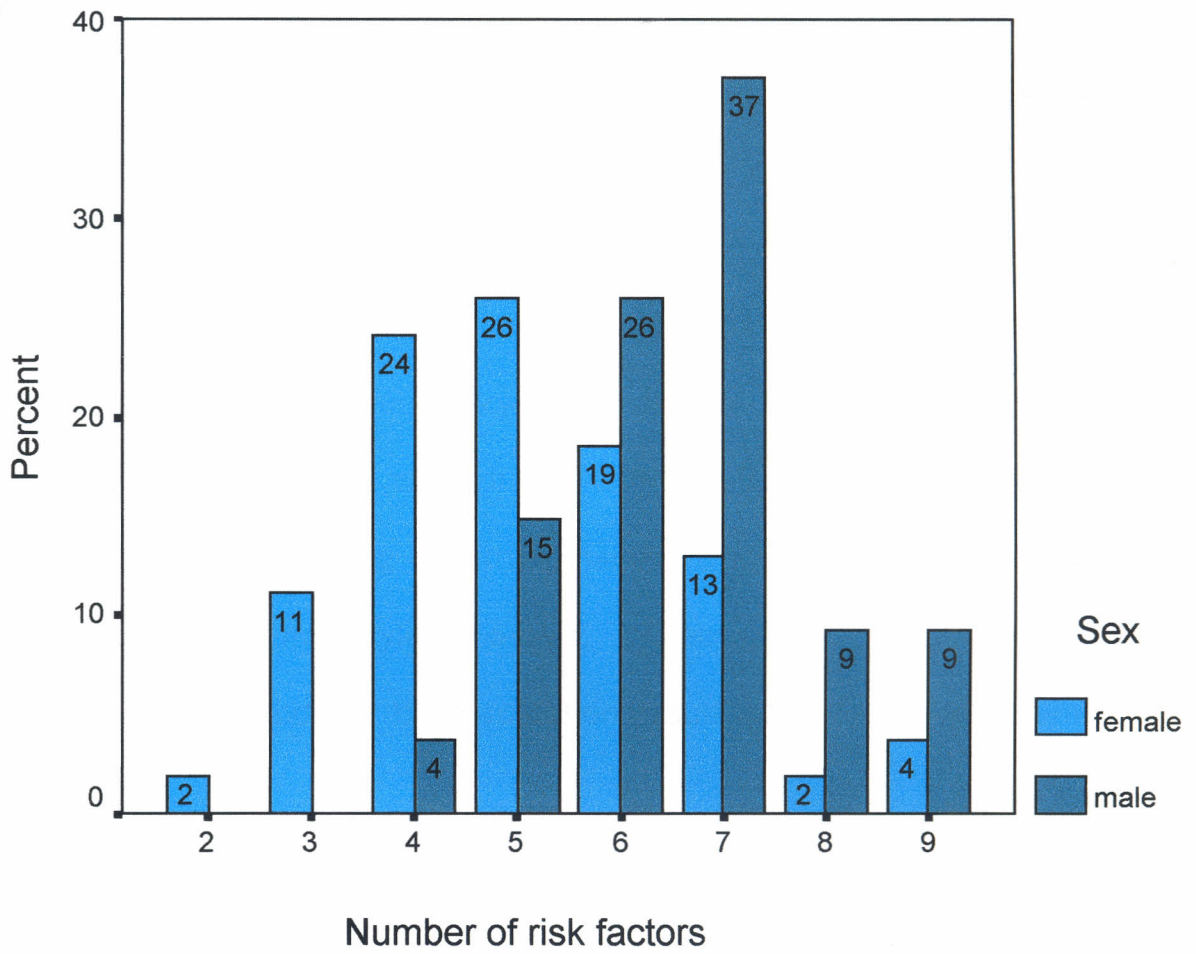


Figure 6. Number of CHD risk factors and sex

6 DISCUSSION

This study was the 'first of its kind' that set out to determine the prevalence of certain established vascular risk factors in type 2 diabetics seen at the diabetic clinic at KNH. There are no local data available, and no studies from the East African region other than an Ethiopian study by Seyoum et al.(21) that looked at the profile of coronary artery disease risk factors in Ethiopian diabetic patients. There is an emerging epidemic of CHD risk factors and CHD in Africa and other developing countries mainly attributable to increasing and rapid urbanisation, life style changes, increased life expectancy and epidemiological transition of the population resulting in the development of new risk factors(86).

The risk of CHD increases markedly in diabetic compared to non-diabetic patients(87). The annual incidence of fatal or non-fatal CHD in type 2 diabetes is 2 to 5% in the U.K.(88). In a WHO project, it has been postulated that, in developing countries, CHD mortality is probably increasing and will continue to rise and become the leading cause of death in a few decades' time(89). In a review on CHD in black Africans by Bertrand, the prevalence of CHD as a percentage of cardiovascular diseases was reported at 1.38% in mid-1960s, increasing to 6.5% in early 1990(90). In a prospective study by Amoah(91) to determine the pattern of cardiovascular disorders in Ghanaian subjects, CAD was the fifth commonest cardiovascular disorder reported with a prevalence of 11.3%.

The study was designed to look at the prevalence of certain established risk factors for cardiovascular disease in a random sample of type 2 diabetics being followed up at KNH. This preliminary data is likely to assist investigators to design studies to evaluate the importance of these prevalent factors and any other novel factors in contributing to the risk of cardiovascular disease in patients with type 2 diabetes in Kenya. However, it should be emphasised that the present study was not designed to test whether an established risk factor (mostly in Western studies) was an actual risk factor in this study population. Neither was it designed to define clustering of the various established CHD risk factors.

A total of 108 patients were recruited into this study, with a male to female ratio of 1:1. This is similar to the sex ratios in other studies on diabetics at KNH(45,92). It is known that type 2 diabetes occurs with an equal frequency in men and women(9). The mean age of the study population was 55.7 years, with over 90% females having age as a vascular risk factor compared to over 50% males with similar risk. This is important, especially in view of the fact that diabetic women carry an increased risk of cardiovascular disease and lose the premenopausal protection from CHD enjoyed by non-diabetic females(9). The relative risk of death from CHD in type 2 diabetics is greater for women than men(9).

The mean duration of diabetes was 7.5 years. This might be an overestimate since patients with diabetes for at least two years without insulin therapy were

recruited, this being one of the inclusion criteria for the epidemiological definition for type 2 diabetes in this study population. However, the duration of diabetes may actually have been underestimated considering the long latent period that precedes the clinical diagnosis of type 2 diabetes(4).

Past history of atherovascular disease (CHD, PVD and CVD) was noted in 47.2% of our patients. This finding was based on history alone, and is likely to be an underestimate since no attempt was made to evaluate patients for clinically silent disease, this being beyond the scope of our study.

Family history of vascular diseases or sudden death among first-degree relatives was found in 16% of the study population. This is a significant proportion, again based on history alone and may be an underestimate (reporting bias). It is imperative to screen relatives of patients with cardiovascular disease for risk factors for vascular disease and appropriate measures to be taken towards prevention of such events, which would be more cost-effective in a resource-poor country like ours with limited facilities available for definitive management of vascular events. Correction of certain modifiable risk factors (smoking, hypertension, dyslipidaemia, weight loss) would lead to decreased morbidity and mortality associated with CHD(87).

Out of the several risk factor prevalences determined in this study, all patients had a minimum of at least two risk factors present, excluding diabetes *per se*. In a review on coronary artery disease in patients with diabetes by Haffner, it

has been suggested that type 2 diabetes may confer the same degree of risk as pre-existing CHD(93). About 80% of the study patients had five or more risk factors present, more so in males than females. It has been established that individuals with type 2 diabetes are also more likely to have multiple risk factors for CHD ("clustering") than age-matched non-diabetic population(17,94). The co-occurrence of multiple CHD risk factors seem to impart a substantial fraction of the increased risk of CHD that accompanies impaired glucose tolerance and type 2 diabetes(95). In most observational studies, the established risk factors confer a similar relative risk of CHD among patients with type 2 diabetes and among non-diabetic individuals, these risks being additive and perhaps multiplicative(95).

The mean glycated haemoglobin level was 8.76%, similar to other local and western data(91,96,97). Approximately 70% of patients had poor glycaemic control ($HbA_{1c} > 7.0\%$). This is lower than the 82% found by Nyamu(91). The difference could be due to the different selection criteria in the latter study, with a majority of their patients having chronic infected foot ulcers, compounding inadequate glycaemic control.

In a local study on cardiac autonomic neuropathy in diabetics at KNH (98), 93% of the patients had good glycaemic control. In that study, there were predominantly younger diabetics (both type 1 and type 2) with no acute illness(es) and/or complications, unlike our study that recruited only type 2 diabetics and did not exclude those with various diabetic complications.

Studies in USA found poor glycaemic control (HbA_{1c} >8.0%) in 50% of non-Hispanic black women and 45% of Mexican-American men(97). In a Finnish study(96), approximately 25% of patients had HbA_{1c} ≤ 7.3%. In the former study, the prevalence of poor glycaemic control was lower compared to our study, mainly due to the higher cut-off criteria of HbA_{1c} > 8.0% that was used. Males had significantly better glycaemic control than females in our study, which is comparable to the findings of the Finnish study(96).

The largest and longest study of patients with type 2 diabetes, the United Kingdom Prospective Diabetes Study (UKPDS), conclusively demonstrated that improved blood glucose control in these patients reduces the risk of developing retinopathy and nephropathy and possibly reduces neuropathy. The overall microvascular complications rate was decreased by 25% in patients receiving intensive therapy versus conventional therapy. Epidemiological analysis of the UKPDS data showed a continuous relationship between the risk of microvascular complications and glycaemic control. These results confirm that in type 2 diabetes lowering blood glucose is beneficial(98).

Several observational studies, including the results of the epidemiological analysis of UKPDS data, have shown strong and statistically significant associations between blood glucose control and the risk of cardiovascular disease morbidity and mortality. The UKPDS showed a 16% reduction (not statistically significant, p=0.052) in the risk of combined fatal or nonfatal myocardial infarction and sudden death in the intensively treated group(98).

Primary prevention of vascular disease in patients with type 2 diabetes is heavily dependent on achieving and maintaining good glycaemic control(99). It is thus imperative to aim for this in any intervention to reduce the risk for vascular disease in our patients. There are many possible factors that may be responsible for the finding of poor glycaemic control in individuals with type 2 diabetes at KNH, but this issue has not been studied at this hospital. Overall, low socio-economic status of many patients attending the diabetic clinic at KNH would be important in influencing other more proximate causes of the patients' failure to achieve optimal glycaemic control: lack of adequate knowledge of the disease, inadequate follow-up in the diabetic clinic (due to the high throughput of patients in this clinic, making for late clinic appointments), inadequate adherence to proper diabetic diets, lack of exercise and improper drug adherence. Lack of education about the disease and unavailability of self-monitoring facilities for blood glucose could also contribute towards long-term poor glycaemic control.

However, only one glycated haemoglobin level was used to assess glycaemic control and this may not reflect long-term glycaemic status of these patients. On the other hand, the agreement between the glycated haemoglobin and fasting blood glucose levels was excellent, suggesting that the former was a good measure of current and possibly past glycaemic status. This is also used as a validity test for glycaemic control using FBG and HbA_{1c}.

The prevalence of hypertension was 65%. There was no significant overall

gender difference, though systolic hypertension was significantly more prevalent in females compared to males ($p=0.001$). Hypertension was undetected in 55% of these patients. Of the 45% known hypertensives and those who were on some form of anti-hypertensive treatment, none had well-controlled blood pressure with 35% having grade 3 hypertension. This shows that our patients with diabetes and hypertension often have poorly controlled blood pressure, compounding further their risk profiles, not only for cardiovascular disease but also for chronic renal impairment.

In the Ethiopian study by Seyoum et al.(21), the prevalence of hypertension in patients with type 2 diabetes was 33.3%. This data cannot be compared to our study as there was no clear-cut definition for hypertension in the former study. Swai et al. found the prevalence of hypertension amongst newly diagnosed diabetic patients in Dar es salaam, Tanzania to be 26.7%(100). The difference is possibly due to the fact that these were newly diagnosed diabetics and hypertension was defined as blood pressure of $\geq 160/95$ mm Hg. In other Western studies, the prevalence of hypertension in diabetic patients has been reported to be between 22 and 54%(101,102), hypertension having being defined as a blood pressure of $\geq 160/95$ mm Hg according to the WHO criteria during that time(103). These figures are lower compared to our results, but then hypertension is now defined as blood pressure $\geq 140/90$ mm Hg, according to the Joint National Committee on Prevention, Detection, Evaluation and Treatment of Hypertension VI (JNC VI) criteria(77).

Hypertension predisposes to all of the major atherosclerotic cardiovascular disease outcomes, including cardiac failure, stroke, CHD and PVD. Coronary heart disease is the most common and lethal sequelae of hypertension(104). The concomitant occurrence of diabetes and hypertension is believed to act synergistically in elevating the risk factor for CHD(105). A number of trials have demonstrated a greater incidence of CHD end-points in diabetic hypertensive patients than in diabetic normotensive patients(105). Furthermore, hypertension is associated with increased risk of cardiovascular mortality and microvascular complications in patients with diabetes (105), by accelerating the natural progression of atherosclerosis (106).

Systolic blood pressure was significantly correlated with BMI and total cholesterol in this study. It is known that hypertension tends to occur in association with other atherogenic risk factors that promote both its occurrence and greatly influence its impact on cardiovascular disease. Patients with hypertension tend to have a higher prevalence of dyslipidaemia, glucose intolerance, obesity, and left ventricular hypertrophy than normotensive patients(107). They are also prone to have hyperinsulinaemia, insulin resistance and hyperuricaemia(107). Thus, hypertension is best regarded as an important component of a comprehensive cardiovascular risk profile that must be considered in judging the urgency for treatment and in formulating optimal therapy.

The recent guidelines from JNC VI emphasised the importance of treating

patients with hypertension and diabetes as if they already had target organ damage(108). Low blood pressure targets of 130/85 mmHg with an optimal goal of 120/80 mmHg are recommended to reduce the risk of events in hypertensive patients with diabetes(108). In the UKPDS trial, in patients with hypertension and type 2 diabetes, intensive lowering of blood pressure provided greater protection against death from cardiovascular causes and major non-fatal events than did less aggressive therapy(23), with similar observations in the Hypertension Optimal Treatment study(24).

A large proportion of our study population had dyslipidaemia (93.5%), the majority having either raised total cholesterol (86.1%) or elevated LDL-cholesterol levels (81.5%). This could be due to the fact that the majority of our patients had poor glycaemic control which tends to impact negatively on lipid and lipoprotein abnormalities, particularly increasing total-cholesterol and LDL-cholesterol levels(109). However, the most common pattern of dyslipidaemia found in patients with type 2 diabetes reported in other studies has been hypertriglyceridaemia with decreased HDL-cholesterol levels(25). Seyoum et al.(21), reported the prevalence of hypercholesterolaemia and hypertriglyceridaemia to be 30% and 23% respectively. The higher prevalence of elevated total cholesterol in our study is probably due to the lower cut-off value used as per the recent ADA recommendations(81). The lower prevalence of hypertriglyceridaemia in this study may also be related to the higher cut-off value for triglycerides recommended by ADA(81), while nutritional or genetic factors may also be responsible for this finding. Various Western studies have

reported the prevalence of hypercholesterolaemia and hypertriglyceridaemia in type 2 diabetics to range from 30 to 77%(110,111). The discordance between our findings and Western data requires further investigation, as the finding of a high prevalence of raised LDL-cholesterol levels would be expected to impart a higher risk of cardiovascular disease as compared to hypertriglyceridaemia or low HDL-cholesterol levels(29), and this finding, if confirmed, could modify the choice and cost of interventions to reduce the said risk.

Only one patient in this study was on a lipid-lowering agent. Data from subset analyses of various trials with lipid-lowering treatment provide some insight into the benefit of treating dyslipidaemia in diabetics, with significant reductions in the incidence of CHD and total mortality(31,112-114). Current evidence suggests that in people with type 2 diabetes, if any lipid abnormality is found, it should be corrected to reduce the risk of vascular disease(81).

About 65% of the patients were obese in this study. This is much higher compared to 36% reported in the Ethiopian study (21) and 14.6% reported in the Tanzanian study by Swai et al.(99). Both these studies included younger and also type 1 diabetic population and in the latter study, the cut-off value to define obesity was higher ($BMI \geq 30 \text{ kg/m}^2$) with all newly diagnosed diabetics. In a recent local study on diabetic foot ulcers (91) about 25% of the patients were obese. In Western studies, the prevalence of obesity in patients with diabetes has been reported to be as high as 70-80% (115), in keeping with our results. There was, however, no significant association between obesity and

form of dyslipidaemia in this study, suggesting the complexity of the relationship between markers of obesity and dyslipidaemia.

males were significantly more likely to be overweight or obese than females. This is in keeping with reports from other studies done regionally and in the developed countries(21, 116). Similarly, females had significantly higher WC and WHR compared to males ($p < 0.001$ in both cases).

Waist circumference alone, because of its greater simplicity, may be a useful index of obesity, closely linked to BMI but in fact better related than the BMI as a predictor of atherosclerosis(117). Ko et al. in their study among a Chinese population concluded that WHR, WC and BMI provide important information in assessing cardiovascular risk(118). Visceral obesity is associated with higher degree of risk than peripheral obesity. The metabolic and circulatory changes associated with visceral obesity lead to the development of insulin resistance and increased lipoprotein synthesis(34). Excessive insulin administration is associated frequently with unacceptable weight gain. Obesity is associated with a progressive increase in cardiovascular mortality, glucose intolerance and insulin resistance(33).

Weight loss has been shown to markedly improve blood glucose control in obese subjects with type 2 diabetes(25,119). A 5-10% weight reduction is also expected to result in a significant loss of visceral adipose tissue and would also significantly improve plasma lipids independent of dietary fat restriction.

Total cholesterol, LDL-cholesterol and triglyceride levels decrease while HDL-cholesterol increases(120). Glucose intolerance and insulin resistance will be ameliorated(120). Therefore, obese diabetic patients should be encouraged to lose weight (through lifestyle modification and/or anti-obesity medication) and increase exercise as well.

Hyperhomocysteinaemia was prevalent in over 50% of the study patients. There is no local comparative data available on normal homocysteine levels in the Kenyan population. Okada et al. found the prevalence of hyperhomocysteinaemia to be 39.3% in Japanese patients with type 2 diabetes(58), a lower figure than in our study, probably related to their use of a higher cut-off value of 14.0 $\mu\text{mol/l}$ used to define hyperhomocysteinaemia. As for studies in type 2 diabetes, higher fasting homocysteine levels are reported in patients with microangiopathy(121) and in association with atherothrombotic disease(121). Males had significantly higher homocysteine levels than females ($p=0.007$). It was also significantly related to fasting blood sugar ($p=0.035$), but no correlation was seen with blood pressure, dyslipidaemia, albuminuria, hypertension or cigarette smoking as has been reported in different studies(58-60). This difference may be due to the fact these studies have been conducted in Western countries with different ethnic groups, larger population size, and differences in genetic (defects in enzymes that control homocysteine metabolism) and nutritional factors (deficiencies of folate and vitamins B₁₂ and B₆). Dietary supplementation with vitamins to lower homocysteine concentrations may provide a simple, effective and

inexpensive means of reducing CHD risks. However, intervention studies are required to determine the importance of such therapy and to formulate a rational approach to the clinical management of type 2 diabetic patients with hyperhomocysteinaemia who are at risk of CHD.

Since the study was designed to determine the prevalence of microalbuminuria as a cardiovascular risk factor, patients with overt proteinuria on screening dipstick examination (and those with urinary tract infection) were excluded. The prevalence of microalbuminuria was 16% in our study. It was much lower than a local study by Twahir(45) and a Central African study by Erasmus et al.(122), which showed prevalences of MAL in type 2 diabetes to be 40.5% and 42%, respectively. The finding of a lower prevalence in our study could be a function of the methodology used (CLINITEK® 50 Microalbumin assay of UACR), which has 87% accuracy and 90% sensitivity in comparison to the UAER method used by Erasmus and colleagues, while Twahir used a different assay for UACR. In this study, spot urine specimen was tested for MAL and it is well known that the MAL rate can vary highly from day to day, by up to 40% (123), with 24-hour urine collection measurement having lowest variability. In developed countries, prevalence of microalbuminuria is in the region of 20% (46), similar to our finding.

The exclusion of patients with macroalbuminuria and urinary tract infection was important for the determination of the prevalence of microalbuminuria in study patients. However, the exclusion of patients with overt dipstick

proteinuria may have affected (under-estimated) the prevalence rates for other risk factor variables by excluding patients with diabetes with overt nephropathy and other accompanying complications and, possibly, a greater burden of cardiovascular risk factors and even atherosclerotic disease. Microalbuminuria is the first manifestation of injury to the glomerular filtration barrier and predicts the development of overt nephropathy which subsequently progresses to end-stage renal disease(124).

Microalbuminuria was significantly associated with systolic blood pressure ($p=0.004$), smoking ($p=0.013$) and LDL-cholesterol level ($p=0.029$), approaching statistical significance with diastolic blood pressure ($p=0.066$) and homocysteine levels ($p=0.066$) in this study. There was no significant association with the duration of the disease, glycaemic control, BMI, HDL-cholesterol levels and triglycerides. Erasmus et al. found significantly higher systolic and diastolic blood pressure measurements, with no significant differences in age, BMI and glycaemic control in diabetic patients with microalbuminuria(122). Similarly, Twahir found no association with age, duration of diabetes, BMI, systolic blood pressure and diastolic blood pressure(45).

MAL should be screened for in all diabetics as it is of value as an index of vascular damage especially in patients with hypertension. Increasing information on its association with traditional cardiovascular risk factors and its prognostic value is becoming available(125). Hence, the attainment of

optimal glycaemic control, optimal blood pressure control and early treatment with angiotensin-converting enzyme inhibitors are effective in reducing MAL(126).

Cigarette smoking was noted in about 6% of the population (all males), this being the least prevalent risk factor determined in this study. In the Ethiopian study, the prevalence of cigarette smoking was found to be 9.3% in type 2 diabetics(21). Gill et al.(127) reported the prevalence of smoking amongst black South African diabetic patients to be 20%. Similarly, in the Western countries, these figures are much higher, with several studies having reported 25-35% prevalence rates(12,37,128), depending on the selection criteria used. Smoking was found to be uncommon in this study possibly due to reporting bias. Objective markers of smoking such as the analysis of breath carbon monoxide and urine cotinine were not measured.

Analyses of the follow-up data from the Framingham study have shown a strong correlation between smoking and CHD, both in patients with or without diabetes(129). Since the relative risk of all-cause mortality is about twice as high for smoking compared to non-smoking diabetic population(38), and it is the most cost-effective to modify, every effort should be made to ensure that diabetic patients stop and abstain from smoking.

The finding of a high prevalence of various established cardiovascular risk factors in type 2 diabetics at KNH reflects a major potential for cost-effective

modification of the risk factor profiles of these patients with a view to primary (and also secondary) prevention of atherosvascular disease. Further work is required to study the risk factor profiles in diabetics in the community and in rural areas, quantify the risk from various known factors and evaluate any putative novel risk factors, as well as assess the burden of clinically silent cardiovascular disease in these patients. Appropriate intervention and cost-benefit analysis studies are also urgently needed to assist in the selection of the optimal preventive program for our patients with type 2 diabetes.

7 LIMITATIONS

1. The data collection was very much dependent on patient recall, which may have been inaccurate, and on patient medical records, which are often incomplete.
2. There may have been selection bias since the study was conducted at a specialist diabetic clinic, in a national referral hospital, and the study was limited to patients who had been diabetic for at least two years.
3. An underestimation of prevalence of cardiovascular disease in this population is possible since no effort was made towards screening for or definitive diagnosis of CHD (no exercise stress test or angiographic studies were done).
4. A single HbA_{1c} measurement was used to assess glycaemic control, and this may not have reflected overall glycaemic control over many years of diabetes.
5. Single spot urine samples were used to determine UACR as this was most practicable in the out-patient setting due to the problems with timed urine collections, though this is not the most accurate method for assessing UAE; however studies have revealed good correlations between UAC ratio and more elaborate methods of assaying UAE.

8 CONCLUSIONS

1. There was a high prevalence of vascular risk factors present in patients with type 2 diabetes seen at KNH.
2. Aggregation of multiple risk factors was the rule, with at least two risk factors (excluding diabetes) being found in study patients.
3. Glycaemic control was inadequate in the majority of patients with type 2 diabetes seen at the KNH.
4. Hypertension was prevalent in two-thirds of the study patients, undetected in approximately 50%, and poorly controlled in all.
5. About 65% of the patients were either overweight or obese, dyslipidaemia was found in the majority (>90%), and about 50% had hyperhomocysteinaemia.
6. Microalbuminuria and cigarette smoking were the least prevalent risk factors determined (17% and 6% respectively).

9 RECOMMENDATIONS

1. Vascular risk factors are prevalent and require urgent attention in patients with type 2 diabetes at KNH.
2. More prospective studies are needed to identify the specific vascular risk factors, and their associated relative risks, in patients with diabetes at KNH, using larger samples with case-control or cohort designs, more active diagnosis of vascular disease, involving accurate screening and diagnostic techniques, and comparison of urban and rural populations.
3. Primary and secondary prevention of cardiovascular disease by institution of comprehensive risk factor modification is essential, of proven medical value and likely to be cost-effective for a resource-poor developing country like ours, where evaluation and management of patients with established disease is often inadequate and certainly cost-intensive.

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11 APPENDICES

11.1 APPENDIX I STUDY PROFORMA

StudyNo _____

Name _____

Date _____ OP No _____

DOB (month, year) _____ Age (years) _____

Date of diagnosis of diabetes (month, year) _____ / _____

Duration of diabetes (months, year) _____ / _____

DEMOGRAPHICS

1. Gender 1= Male 2=Female

2. Marital Status
 1=Single 2=Married 3=Divorced 4=Widowed 5=Separated

3. Usual residence _____

4. Usual occupation _____

Current formal employment status

1=Employed 2=Unemployed 3=Never had formal employment

4=Retired

5. Level of formal education

1=None 2=Primary school 3=Secondary school 4=Tertiary level

5=Other (specify) _____

PAST MEDICAL HISTORY

6. Have you ever had any of the following? (tick response/s)

1 = Been told by a doctor that you have coronary heart disease?

2 = Heart attack

3 = Angina pectoris (chest pain due to insufficient blood flow to the heart).

4 = Coronary bypass surgery

5 = Coronary angioplasty (coronary "balloon" procedure)

6 = Abdominal aortic aneurysm

7 = Blockage of arteries to the limbs

8 = Transient ischaemic attacks (transitory strokes)

9 = Blockage of carotid artery

10 = Stroke

FAMILY HISTORY

7. Did or do any of your relatives suffer from diabetes?

1=Yes 2=No

Father Mother Brother/Sister Children Other (specify)

8. Did or do any of your relatives suffer from hypertension?

1=Yes 2=No

Father Mother Brother/Sister Children Other

Specify _____

9. Did any of your first-degree relatives (father, mother, brothers, sisters or children) suffer from heart attack, stroke or sudden death?, if a male relative before 55years / female relative before 65 years.

1=Yes

2=No

SMOKING HABITS

10. Are you currently smoking cigarettes?

1=Yes

2=No

- a) If "yes" how many cigarettes do you usually smoke per day?

_____ cigarettes/day

- b) How many cigarettes did you smoke per day a year ago?

_____ cigarettes/day

- c) How old were you when you began to smoke cigarettes?

_____ years

11. Did you ever smoke cigarettes?

1=Yes

2=No

- a) If "yes" what is the maximum number of cigarettes you ever smoked per day for as long as a year?

12. Do you drink alcohol?

1=Yes

2=No

Quantify _____ units/day

CURRENT MEDICATIONS

13. Are you currently on any of the following medications?

1=Yes 2=No 3=Don't know

OHA (drug, dose & duration)

Insulin treatment (formulation, dose & duration)

Blood pressure lowering drugs (drug, dose & duration)

Blood lipid-lowering drugs (drug, dose & duration)

Any other drug taken regularly, at least once a day

(drug, dose & duration)

PHYSICAL EXAMINATION

14 Height (cm) _____

15. Weight (kg) _____

16. BMI (kg/m²) _____

17. Waist circumference (cm) _____

18. Hip circumference (cm) _____

19. WHR _____

20. Blood pressure _____ mm Hg

(Average of 2 readings)

21. EYES

Arcus senilis Yes=1 No=2

Xanthelasmata Yes=1 No=2

Pupils: Equal reaction to light and accommodation

 Yes=1 No=2

Pupil abnormality

 Yes=1 No=2

Specify _____

Fundi: Right Left

Normal

Increased light reflex

Narrow arterioles

Tortuous arterioles

A – V compression

Haemorrhage

Exudates-soft

 -hard

Papilloedema

Disc abnormalities

Lens opacities

Other (specify) _____

Retinopathy classification 1 2 3 4

22. NECK

Raised jugular venous pressure

Yes=1 No=2

23. HEART

Apical impulse _____

Thrills Yes =1 No=2

Specify _____

Rhythm Apical rate _____ /min

Regular=1 Irregular=2 Gallop=3 Other=4

Specify _____

Heart tones

Normal Yes=1 No=2

Specify _____

Significant murmurs

Systolic Yes= 1 No= 2

Specify _____

Diastolic Yes=1 No=2

Specify _____

LAB RESULTS

Fasting blood sugar _____ mmol/l

Glycated haemoglobin _____ %

Serum Urea _____ mmol/l

Creatinine _____ μ mol/l

Na+ _____ mmol/l

K+ _____ mmol/l

Homocysteine _____ μ mol/l

Serum Lipid profile

Total cholesterol _____ mmol/l

HDL-cholesterol _____ mmol/l

LDL-cholesterol _____ mmol/l

Triglycerides _____ mmol/l

Urinalysis

Specific gravity

Nitrites

pH

Leucocytes

Glucose

Blood

Protein

Bilirubin

Ketones

Urobilinogen

Urine Culture

Positive Negative

UACR

Normoalbuminuria

Microalbuminuria

Macroalbuminuria

11.2 APPENDIX II CRITERIA FOR DIAGNOSIS OF TYPE 2 DIABETES MELLITUS

1. Symptoms of diabetes plus casual plasma glucose concentration ≥ 200 mg/dL (11.1mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.

or

2. Fasting plasma glucose ≥ 126 mg/dL (7.0mmol/l). Fasting is defined as no calorie intake for at least 8 hours.

or

3. 2-hour plasma glucose ≥ 200 mg/dL (11.1mmol/l) during an oral glucose tolerance test. The test should be performed as described by WHO (69), using a glucose load containing the equivalent of 75-grams anhydrous glucose dissolved in water.

(130).

Type 2 diabetes mellitus was defined based on at least two of the following(58):

age > 40years

no history of ketosis

not on insulin for two years following diagnosis of diabetes

and/or family history of diabetes

11.3 APPENDIX III CLINITEK® Microalbumin

Reagent strips for determining Albumin and Creatinine in Urine

Clinitek Microalbumin Reagent Strips are firm plastic strips that contain two reagent areas that test for albumin and creatinine in urine. An albumin-to-creatinine ratio is also determined, which allows for the use of single-void specimens in testing. This product provides semi-quantitative results and can be used for screening samples for microalbuminuria.

CHEMICAL PRINCIPLES OF PROCEDURES:

Albumin: This test is based on dye binding using a high affinity sulphonaphthalein dye. At a constant pH, the development of any blue colour is due to the presence of albumin. The resulting colour ranges from pale to aqua blue.

Creatinine: This test is based on the peroxidase-like activity of a copper creatinine complex that catalyses the reaction of diisopropyl-benzene dihydroperoxide and 3,3',5,5'-tetramethylbenzidine. The resulting colour ranges from orange through green to blue.

EXPECTED RESULTS:

Albumin: Albumin is normally present in urine at concentrations of less than 20mg/l. Microalbuminuria is indicated with results of 20-200mg/l; results of >

200mg/l indicate clinical albuminuria. These levels have been found to be predictive of albumin excretion rates of 30-300mg/24hours and >300mg/24hours, respectively.

Creatinine: Creatinine is normally present in urine at concentrations of 10-300mg/dL (0.9-26.5mmol/l).

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UNIVERSITY OF NAIROBI

Albumin-to-Creatinine Ratio: Albumin is normally present in urine at concentrations of less than 30mg albumin/g creatinine (3.4 mg albumin/mmol creatinine).Microalbuminuria is indicated at a ratio result of 30-300mg/g (3.4-33.9mg/mmol) and clinical albuminuria at a ratio result of >33mg/g (>33.9mg/mmol)(84).

11.4 APPENDIX IV CONSENT FORM

I, _____, do voluntarily agree to take part in this research study on CARDIOVASCULAR RISK FACTORS ASSOCIATED WITH TYPE 2 DIABETES MELLITUS AS SEEN AT THE KENYATTA NATIONAL HOSPITAL. The nature of the study has been explained to me by Dr. Vinesh P Vaghela.

Signed: _____

Witnessed:

Dated: