SERUM URIC ACID LEVELS IN PATIENTS WITH TYPE 2 DIABETES AT KENYATTA NATIONAL HOSPITAL

A CROSS SECTIONAL DESCRIPTIVE STUDY

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A thesis submitted in part fulfillment of the degree of Master of Medicine, Internal Medicine.

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DECLARATION

This research thesis is my original work and has been presented as a prerequisite for a Master's degree to the Department of Clinical Medicine and Therapeutics, University of Nairobi, Kenya. It has not been presented for any degree to any other university

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DECLARATION

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DEDICATION

I lovingly dedicate this work to my family to whom I owe the gift of persistence and courage

Special dedication goes to my wife and life's companion Munira

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I convey heartfelt thanks to the many people who made this project a success. First, heartfelt gratitude to my supervisors: Prof Omondi Oyoo, Dr. Edna Kamau, and Dr. Eugene Genga for constantly guiding me throughout the research process.

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To my wife Munira, the mere sight of you ignites passion and the desire to be better in my work.

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LIST OF ABBREVIATIONS

2-hpg	2hour plasma glucose
DCCT	Diabetes Control and Complications Trial
DR	Diabetic Retinopathy
FPG	Fasting plasma glucose
HBa1C	Hemoglobin A1C glycated
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose tolerance
IR	Insulin Resistance
KNH	Kenyatta National Hospital
NGSP	National Glycohemoglobin Standardization Program
T2DM	Type 2 Diabetes
OGTT	Oral Glucose tolerance test
PI	Principal Investigator
RBS	Random blood sugar
UA	Uric Acid
WHO	World Health Organization
XDH	Xanthine Dehydrogenase
XO	Xanthine Oxidase

SYMBOLS

mg/dL	milligram per deciliter
kg	kilogram
µmol/L	micromole per liter
mmol/L	millimole per liter
ml/min	milliliter per minute
cm	centimeter
mm	millimeter
N	number
±	Plus minus
>	Greater than
<	Less than
=	equal
M	male
F	female

ABSTRACT

Background: The prevalence of hyperuricemia has been increasing around the world accompanied by a rapid increase in obesity and diabetes. There has been a growing interest in the association between elevated uric acid and other metabolic abnormalities of hyperglycemia, abdominal obesity, dyslipidemia, and hypertension. Hyperuricemia has been positively associated with hyperglycemia. Diabetic patients tend to have higher levels of serum uric acid levels as compared to the normal population. The direction of causality between hyperuricemia and metabolic disorders, however, is uncertain and the prevalence of hyperuricemia still needs to be delineated in population samples. This study has been carried out to see the prevalence, especially, in Kenya where we have limited data on prevalence of hyperuricemia in diabetes.
Objective: To determine the prevalence of hyperuricemia among ambulatory patients with Type 2 Diabetes at Kenyatta National Hospital.

Methods: This was a descriptive cross-sectional study. We employed simple random sampling to recruit eligible participants. We took height, weight and blood pressure from participants, and drew 6-8mls of peripheral blood to determine serum uric acid and HbA1c levels. We used descriptive statistics, especially means to analyze serum levels of measured variables. We employed Pearson product – moment correlation to assess the relationship between levels of serum uric acid with duration of diabetes and glycemic control.

Results: A total of 150 participants were recruited, with 66% females, 34% males, and a mean (SD) age of 56.4 years. The mean (SD) duration of follow-up for diabetes was 10.3 years. Hypertension was a comorbidity in 65.3% of the participants, and obesity in 36%. The mean (SD) HbA1c levels were 7.76% and 42.7% had good glycemic control. We found a prevalence of hyperuricemia at 19.3%. The mean (SD) serum uric acid levels were 5.02mg/dl ±1.84 (299µmol/L). We found no correlation between hyperuricemia and duration of diabetes and glycemic control. Relationship between hyperuricemia and the variables of Age, BMI and hypertension did not achieve statistical significance. Female gender achieved significance with a P value of 0.046.

Conclusion: There is a high prevalence of hyperuricemia at 19.3% in this study population especially in the females above the age of 40 years. Patients were on long-term follow-up for diabetes. The glycemic control was average to good. This forms a basis for regularly screening patients for serum uric acid levels in the clinics. Further studies with larger number of patients with diabetes are needed to explore the relationship of hyperuricemia to other clinical and laboratory parameters.

1.0 CHAPTER ONE: INTRODUCTION

Uric acid is a product of the metabolic breakdown of purine nucleotides, and it is a normal component of urine. Hyperuricemia is defined as a serum urate level of 6.8 mg/dL (404μmol per liter) or more (1).The rising incidence and prevalence of hyperuricemia are probably related to the increased life expectancy of the population, increasing levels of obesity, sedentary lifestyles and change in dietary habits (2).

Type 2 diabetes mellitus consists of an array of dysfunctions characterized by hyperglycemia and resulting from the combination of insulin resistance, inadequate insulin secretion, and excessive or inappropriate glucagon secretion. Type 2 diabetes mellitus is less common in Non-Western countries where the diet contains fewer calories and daily caloric expenditure is higher. However, as people in these countries adopt western lifestyles, weight gain and Type 2 diabetes mellitus are becoming almost epidemic. Prevalence of diabetes is increasing worldwide. The International Diabetes Federation predicts that the number of people living with diabetes will rise from 366 million in 2011 to 552 million by 2030 (3).

It has been shown that serum uric acid is positively associated with serum glucose levels in healthy subjects (4). Recent studies have demonstrated that uric acid levels are higher in subjects with Type 2 diabetes than in healthy controls (5). Furthermore, an elevated serum uric acid level was found to increase the chances and predispose to developing Type 2 diabetes in individuals with impaired glucose tolerance (6). Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance and/or increased insulin secretion in metabolic syndrome (7). An elevated uric acid levels, as reported, often precedes the development of obesity, hyperinsulinemia, and diabetes (8).

Studies related to uric acid levels in diabetes are few and deserve further analysis on prevalence of hyperuricemia in our country as it confers a poor prognosis on the patients. This study will help to add knowledge on the prevalence of hyperuricemia in our set up, and the relationship of hyperuricemia to duration of diabetes, glycemic control and some risk factors such as age, sex BMI and hypertension.

2.0 CHAPTER TWO: LITERATURE REVIEW

2.1 Definitions

2.1.1 Diabetes

Diabetes is a term that describes several diseases of abnormal carbohydrate metabolism that is characterized by hyperglycemia. It is associated with a relative or absolute impairment of insulin secretion, together with differing degrees of peripheral resistance to the actions of insulin.

According to the American diabetes association (ADA) diagnosis of diabetes is based on one of four abnormalities (Table 1) (3). Impaired glucose tolerance describes individuals who during oral glucose tolerance test (OGTT) have blood sugar values between those in normal subjects and those in patients with overt diabetes 7.8 to 11mmol/l (3). Impaired fasting glucose is defined as a fasting blood sugar of 5.6 to 7mmol/l (3).

Table 1: ADA Criteria for the Diagnosis of Diabetes (3)

1	A1c greater or equal to 6.5 %. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay. **OR**
2	FBG >/=7.0mmol/l. Fasting is defined as no caloric intake for at least eight hours **OR**
3	Two-hour plasma glucose >/= 11.1mmol/l during an OGTT. The test should be done as described by WHO, using a glucose load containing equivalent of 75-gram anhydrous glucose dissolved in water. **OR**
4	In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose >/=11.1mmol/l

2.1.2 Uric Acid

UA is a product of purine metabolism and is related to the purine bases of the nucleic acids in humans. Humans are exposed to higher serum UA levels than other mammals due to absence of urate oxidase that converts UA to allantoin (9). The serum UA level is determined by the balance between intake of purines and UA production on one hand and UA elimination by renal and extrarenal routes on the other. Approximately two thirds of total body urate are produced endogenously; the remaining one third is accounted for by dietary purines. The kidneys,

however, excrete approximately 70% of the urate produced daily. The intestines eliminate the rest.

Normal serum UA levels are less than 420-450μmol/l in men and 330-360μmol/l in women (10). UA levels are lower in premenopausal women because estrogen is uricosuric. After menopause, UA levels in women are similar to men (11). UA levels also increase with age, and furthermore**,** UA levels may vary in the same individual by as much as 59 to 119μmol/l during the course of a day, due to the effects of diet and exercise but this are not so obvious variations on doing the levels (12)**.** No test preparation is needed and the blood sample can be taken at any time of the day.

Hyperuricemia is arbitrarily defined as a serum UA concentration in excess of urate solubility, which is about 420μmol/l in men and 360μmol/l in women

Hyperuricemia may occur from excessive production of urate (overproduction). Causes include a purine rich diet, and in some conditions like tumor lysis syndrome and Lesch-Nyhan syndrome. Hyperuricemia also occurs due to decreased elimination (underexcretion), Causes include genetic mutation in the SLC2A9 gene that encodes a transport protein which helps to transport UA in the kidney, and also use of drugs such as diuretics, salicylates, pyrazinamide, ethambutol, nicotinic acid, and cytotoxic agents. Hyperuricemia is frequently a combination of both processes occurring in the same individual and its causes include, high intake of ethanol and fructose rich foods among others.

Potential clinical consequences of hyperuricemia include gout, urate crystal deposition disorders, chronic kidney disease, nephrolithiasis and non-crystal deposition disorders such as hypertension and coronary artery disease.

2.2 Epidemiology of Diabetes and Hyperuricemia

The increase in serum UA levels, or the prevalence of hyperuricemia, appears to be associated with the economic development (13). It has also been noticed that serum UA levels tend to be higher in some populations with certain phenotypes (obesity, metabolic syndrome), and with special diets (meat eaters).

Incidence and prevalence of DM is increasing throughout the world. In 2014 the global prevalence of diabetes was estimated to be 9% among adult age 18 years and above (14). The information to worry about was that more than 80% of the diabetes deaths occur in low and middle income countries (15)(15)

The morbidity and mortality of diabetes is increased by hyperuricemia. It confers a poor prognosis on the diabetic complications. There is increased prevalence of diabetic peripheral neuropathy and it shows a significant correlation with increased UA levels (16). UA concentration has been shown to be associated with an increased severity of diabetic retinopathy in a study done over a three-year period in patients with T2DM (17). Hyperuricemia is also associated with accelerated disease progression in the early stage of diabetic nephropathy (18).

The prevalence of DM in Kenya was at 4.5% in 2010 and is still on the rise. The overall prevalence of hyperuricemia in the general population in Kenya is unknown and data on the prevalence in diabetics is limited. Studies have been done to see the prevalence of hyperuricemia in hypertensive patients. Locally Sylvia et al found a total prevalence of 44% in the hypertensive patients on follow up at Moi Teaching Referral Hospital in Eldoret with a prevalence of 18.2% in the diabetic subgroup (19). Old data from Kenyatta National Hospital found a prevalence of hyperuricemia among untreated patients with essential hypertension to be 27.5% and among those on treatment to be 58% (20).

The prevalence of hyperuricemia in the general population varies markedly depending on the difference in ethnic groups, geographic regions and survey years as seen in Table 2.

The prevalence of hyperuricemia ranged from 0.05% in Chinese women in Shandong in 1995-1996 to 82.0% in male aborigines in Taiwan in 1993-1996. The prevalence was lowest among Mainland Chinese and Indians in the Amazon region of Brazil and highest among aborigines in Taiwan Mountainous area and Maori in New Zealand in both men and women.

The urban African black populations have higher serum UA levels than those with the same ethnicities, but living in the rural community seen in a study done at Seychelles, but there is still paucity in data on the uric acid levels in the general population of Africa especially in Kenya.

Table 2: Prevalence (%) of Hyperuricemia in Different Ethnic Groups and Geographic Regions

Ethnicity	Survey Year	Geographic Location	Age (Years)	Number Men/Women	Prevalence % Men	Prevalence % Women	Reference
Caucasian	1970	Birmingham	Adult	849/254	7.2	0.4	Sturge et al 1977
Caucasian	1989	Southern Germany			28.6	2.6	Gressar et al 1990
Caucasian	1990-1992	New Zealand	>19	139/176	9.4	10.5	Klemp et al 1997
Chinese	1980	Beijing	>20	267/235	1.4	1.3	Fang et al 1983
Chinese	1987-1988	Beijing	40-58	1062/951	15.4	11.0	Li et al 1997
Chinese	1995-1996	Shandong	>20		5.8	0.05	Jiang et al 1999
Chinese	1998	Shanghai	>15	913/1124	14.2	7.1	Chen et al 1998
Chinese	2004-2006	Hangzhou	Adult	1468/906	19.1	3.4	Chen et al 2007
Chinese	2006	Beijing	Adult	1217/780	13.8	6.0	Fang et al 2006
Chinese	1991-1992	Taiwan	>30	1515/1670	25.8	15.0	Lin et al 2000
Chinese	1993-1996	Taiwan	>19	1348/1498	42.1	27.4	Chang et al 2001
Taiwanese	1993-1996	Taiwan Metropolitan	>19	204/201	48.0	20.7	Chang et al 2001
Taiwanese	1993-1996	Taiwan Mountainous	>19	206/233	82.0	64.3	Chang et al 2001
Taiwan Aborigine	1990	Taiwan Mountainous	>18	145/197	53.8	30.7	Chou et al 1998
African Descent	1994	Seychelles	25-64	482/529	35.2	8.7	Conen et al 2004

Studies that have investigated the prevalence of hyperuricemia in Type 2 diabetes are the following

- Fouad et al. performed a case-control study in Egypt at Zagazig University Hospital and reported an overall prevalence of 32% of subjects with type 2 diabetes demonstrated hyperuricemia. He studied 986 participants according to presence and duration of diabetes. The mean (SD) age of the population was 47.9 ± 11.8years. Male gender represented by 49% and females at 51%. He concluded that the patients with long duration of diabetes of more than 5 years had a higher prevalence of hyperuricemia and more severity of diabetic complications. He attributes the hyperuricemia to presence of longer duration of diabetes and its related complications, and also presence of other risk factors such as hyperlipidemia and hypertension in his study population (21).
- T. Murali Venkateswara Rao et al performed a case control study in India and reported, among diabetic cases, the proportion of subjects with hyperuricemia was 11.43% and among the controls, none of the controls had hyperuricemia. The mean (SD) uric acid level increased from 4.30 ± 0.77 mg/dl in people with duration of diabetes 2 to 4 years to 4.57±1.01 mg/dl in people with duration of diabetes 5 to 8 years. Among people who had diabetes for 9 to 12 years, the mean (SD) uric acid level was 6.47 ± 1.07 mg/dl. The association between duration of diabetes and serum uric acid level was statistically significant. He confirms that longer duration of diabetes is a risk factor for hyperuricemia and seen more in patients with obesity and hypertension (22) .
- Ogbera et al reported a 25% prevalence of hyperuricemia in Nigerian patients with Type 2 Diabetes Mellitus. He recruited 601 patients with Type 2 DM aged between 34-91 years for the study. Males were at 44% and the females at 56%. Mean (SD) age was 59.9 ± 10.3years. The prevalence rates of hyperuricemia and the metabolic syndrome were 25% and 60% respectively. The frequency of occurrence of hyperuricemia was comparable in both genders (59% vs 41%, p = 0.3). His population had a high prevalence of obesity and dyslipidemia giving them hyperuricemia and concluded that possible predictors of hyperuricemia are potentially modifiable (23).
- Woyesa et al has reported a 33.8% prevalence of hyperuricemia in patients with Type 2 Diabetes attending Hawassa University Hospital in South West Ethiopia. He recruited 319 patients with type 2 diabetes. 67.0% of the study subjects were males. The mean

(SD) age of the study subjects was 49.8 ± 9.8 years. The serum uric acid concentration was higher among male study subjects when compared to female (22.3% versus 11.5% respectively). Higher prevalence of serum uric acid concentration was determined among study subjects with less or equal to 10year duration of diabetes as compared to the study subjects with greater duration of diabetes (26.4% versus 7.3% respectively). He did not find hypertension as a risk factor for hyperuricemia in his study population, and reported obesity and metabolic syndrome as a predisposing factor (24).

- Sylvia et al reported a prevalence of 18.2% of hyperuricemia in patients with Type 2 diabetes in a study done locally in Kenya at Eldoret at Moi Teaching and Referral Hospital. She was studying the prevalence of hyperuricemia in patients with hypertension. A sample size of 275 of patients was used. 66% were females. Mean (SD) age of 54 ±12.5years. The overall prevalence of hyperuricemia reported is 44%. The diabetics in the study population were of 44 patients in whom 18.2% had hyperuricemia. The risk factors in the population that attributed to hyperuricemia in her study are female sex, obesity and presence of hypertension (19)

2.3 Hyperuricemia and Hyperglycemia

The biologic plausibility between serum uric acid and hyperglycemia has been shown in the Bruneck Study, it reported that the prevalence of IR is 62.8% in subjects with hyperuricemia (25). The increased purine biosynthesis and turnover, with consequent increases in serum UA concentrations caused by the increased activity of the hexose monophosphate shunt, may be linked to IR and/or hyperinsulinemia (26). Especially, the impairment of the glycolytic pathway can increase the flux of glucose-6-phosphate through the hexose monophosphate shunt, resulting in the accumulation of ribose-5-phosphate and other intermediates, which are major substrates for UA production (27).

Insulin can enhance renal proximal tubular UA reabsorption in humans due to an active transport mechanism closely linked to the tubular reabsorption of sodium (28). Whatever the site of the tubular effects of insulin, the possible mechanisms linking hyperinsulinemia (a consequence of IR) with hyperuricemia include the direct stimulations of tubular ion (UA-Na) exchange or the acceleration of cellular metabolism (29).

2.4 Risk Factors for Hyperuricemia in Diabetics

2.4.1 Non Modifiable Risk Factors

Non-modifiable risk factors for hyperuricemia include genes, age, sex, and ethnic group. Some studies of restricted populations (i.e., racially selected, geographically isolated, or families of gouty probands) have shown a bimodal distribution of serum urate values, supporting a single dominant gene hypothesis(30). Nevertheless, abundant data indicate that serum UA concentration is continuously distributed in both male and female general populations (31). Whether a single or multiple genes determine the UA level in primary gout patients remains controversial.

2.4.2 Metabolic Risk Factors

2.4.2.1 Obesity

Obesity has reached epidemic proportions in the past decade and possibly represents the most important component of the metabolic syndrome and an important risk factor for type 2 diabetes.
In obesity, hyperuricemia is attributable to the overproduction of UA and impairment in the renal clearance of UA owing to the influence of hyperinsulinemia secondary to IR (32). Weight reduction is associated with a modest lowering of serum UA concentration and a decrease in the rate of de novo purine synthesis (33). In addition, the weight loss associated with moderate calorie and carbohydrate restriction and increased proportional intake of protein and unsaturated fat (as recommended for insulin-resistant states) is reported to be accompanied by a decrease in serum UA levels and dyslipidemia in gout patients (34).

A possible role of leptin in the relationship among hyperuricemia, obesity, and IR has been addressed recently. Leptin, a hormone product of the OB (obese) gene, is expressed in adipocytes and acts through the hypothalamus to regulate food intake and energy expenditure. Bedir et al. have discussed the role of leptin as a possible regulator of UA concentrations in humans and suspect that it might be a candidate for the missing link between obesity and hyperuricemia (35).

Obesity trends have been linked to increase in fructose consumption, Fructose is known to induce uric acid production by increasing ATP degradation to AMP, a uric acid precursor and thus, within minutes after fructose infusion, serum uric acid levels rise. Furthermore, de novo purine synthesis is accelerated, further potentiating uric acid production (36).

2.4.2.2 Hypertension

The relationship of UA to hypertension is independent of obesity, renal function, or antihypertensive medications; especially thiazide diuretics (37). Hyperuricemia is common in patients with essential hypertension. It appears that overall about 25% of hypertensive individuals have hyperuricemia and this figure increases to 75% in those with malignant hypertension (38). Univariate associations of hyperuricemia with both systolic and diastolic BP were observed, but these relationships were attenuated after adjustment for BMI, suggesting a major role of adiposity in this association (39). The underlying mechanisms of increases in the UA level with essential hypertension are still not well understood. Recent studies proposed the role of IR being the possible pathophysiological link between an altered tubular sodium handling and UA metabolism in humans (40). A commonly prescribed antihypertensive, Angiotensin II receptor blocker Losartan has been shown to reduce uric acid levels, proved in the COMFORT study and has been recommended to be used in patients with hyperuricemia and hypertension (41).

2.5 Pathogenesis of Underlying Mechanisms and Pathophysiology of Hyperuricemia

2.5.1 Oxidative Stress

Serum UA in the early stages of the atherosclerotic process is known to act as an antioxidant and may be one of the strongest contents of plasma antioxidative capacity (42). Intriguingly, the simple concept is that serum UA in patients with cardiovascular disease, the metabolic syndrome, type 2 diabetes, hypertension, and renal disease may reflect a compensatory mechanism to counter oxidative stress. This is not, however, able to explain why higher serum UA levels in patients with these diseases are generally associated with worse outcomes (43). Unfortunately, later in the atherosclerotic process when serum UA levels reach above the normal range 357μmol/l in females and 387–416μmol/l in males, the previously antioxidant (UA) paradoxically becomes prooxidant (44).

This antioxidant – prooxidant UA redox shuttle seems dependent on its surrounding environment such as timing (early or late in the disease process), location of the tissue and substrate, acidity (acidic, basic or neutral PH value), the surrounding oxidant milieu, the depletion of other local antioxidants, and the supply and duration of oxidant substrate and its oxidant enzyme. Depletion of local antioxidants with an underlying increase in oxidative-redox stress is associated with the

uncoupling of the endothelial nitric oxide synthase enzyme, then a decrease in the locally produced naturally occurring antioxidants, endothelial nitric oxide and endothelial dysfunction (45). This process is also occurring within the microvascular bed at the level of the capillaries within various affected hypertensive and diabetic end organs (46).

2.5.2 Inflammation

Increased serum UA was closely associated with systemic inflammation, such as elevated C-reactive protein, stimulation of release of chemokine monocyte chemoattractant protein-1, interleukin-6, and tumor necrosis factor-alpha synthesis (47). In spite of the evidence that UA might contribute to the development of human vascular disease and atherosclerosis, through a proinflammatory pathway, the relationship between UA and inflammation has been less investigated and needs further exploration.

2.5.3 Endothelial Dysfunction

The endothelium represents a single layer of cells that line all vessels in the body, including the conduit vessels, the resistance vessels, precapillary arterioles, and capillaries. By virtue of its direct contact with the circulating blood, the endothelial layer provides a critical interface between the elements of blood and the tissues. The function of each vessel and the role of its respective endothelium vary according to its location in the body. Vascular endothelial dysfunction may occur at any level in the arterial system and contributes to the development and progression of atherosclerosis by favoring coagulation, cell adhesion and inflammation, through promoting inappropriate vasoconstriction and/or vasodilation, and by enhancing transendothelial transport of atherogenic lipoproteins.

Since one of the major sites of the production of UA in the cardiovascular system is the vessel wall and particularly the endothelium. UA has the ability to inhibit endothelial function through inhibiting nitric oxide bioavailability and causing dysfunction (48). SUA also leads to endothelial dysfunction, the progression of which causes vascular lesions and even death. A 0.1mmol/l increase in SUA leads to a 28% increase for the risk of vascular complications in T2DM and a 9% increase for the risk of mortality.

2.6 Justification

Few studies have examined the association between serum uric acid and diabetes mellitus. The association of high serum uric acid with insulin resistance has been known since the early part of the 20th century.

There is no data in Kenya on prevalence of hyperuricemia in diabetic populations.

Hyperuricemia has been implicated in type 2 diabetes with associated poor glycaemic control and diabetes-related complications causing increased morbidity and mortality.

Only one study has been done locally on prevalence of hyperuricemia in hypertensive populations in Eldoret and found a high prevalence of 44%.

This is an important study because if uric acid prevalence is high in our diabetic population, it will help form local guidelines and can be incorporated to form a policy to regularly screen patients. It will also be a key intervention for early detection and lowering high serum uric acid levels utilizing urate lowering therapy agents already readily available in the market as proven by other studies, leading to optimal care, improved quality of life, reduction in morbidity and mortality.

2.7 Research Question

What is the burden of hyperuricemia in ambulatory patients with type 2 diabetes attending the diabetic outpatient clinic at Kenyatta National Hospital?

2.8 Objectives

2.8.1 Broad

To determine the prevalence of hyperuricemia among ambulatory patients with Type 2 Diabetes at Kenyatta National Hospital

2.8.2 Specific

- To determine the prevalence of hyperuricemia in patients with Type 2 Diabetes Mellitus

2.8.3 Secondary

- To correlate serum uric acid levels with duration of diabetes and glycemic control in patients with Type 2 Diabetes Mellitus.
- To describe the association between serum uric acid levels and Age, Sex, BMI and Hypertension in patients with type 2 Diabetes.

3.0 CHAPTER THREE: METHODS

3.1 Study Design and Setting

This was a hospital based cross-sectional descriptive study, conducted among Type 2 diabetic patients attending the diabetes outpatient clinic at Kenyatta National Hospital. The diabetes outpatient clinic runs every day, and caters for 200 to 250 patients per week. Nurses, podiatrists, medical residents and consultants operate the clinic

3.2 Study Population

Inclusion criteria was all Type 2 diabetic patients above 18 years of age, newly diagnosed and treatment naïve or already on treatment or only lifestyle modification with normal urea and creatinine, no dyslipidemias and who consented to the study. Patients were selected by simple random sampling to join the study, until the sample size was attained.

Patients' files were scrutinized and the latest renal function tests (which are routinely performed) checked to calculate the eGFR and excluded those with <90mL/min. A Urinalysis test to check for microalbuminuria or overt proteinuria was not done. A similar approach was used for lipid profile tests. Patients without renal and lipid profile tests done in the last 3 months were excluded from the study.

The following patients were excluded from the study

- On long-term diuretics and steroids. (Thiazide diuretics as they are known to cause hyperuricemia)
- On antimetabolite and chemotherapy drugs
- Pregnancy and lactating mothers
- Patient with uricosuric drugs and urate lowering agents

3.3 Sample Size Estimation

This study used the prevalence from a hospital based study carried out in the Diabetic Clinic of NRI Medical College and General Hospital at Guntur, India by Murali et al. from December 2014 to November 2015 among type 2 diabetic patients who were divided into two groups: 70 patients with diabetes and 30 healthy controls

In the diabetic arm, prevalence of hyperuricemia was at 11.43% while in control group prevalence of hyperuricemia was at 0%.

The study used the prevalence from the above to calculate the sample size groups using the formula (Daniel 1999) below:

$$n = \frac{Z^2 x\ P(1-P)}{d^2}$$

Where,

n = Desired sample size

Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

P = expected true proportion (estimated at 11.43%, from the above study.)

d = desired precision (0.05)

$$n_0 = \frac{1.96^2 x\ 0.11(1-0.11)}{0.05^2} = 150$$

A Sample size of 150 patients was required for the study.

3.4 Study Procedures

3.4.1. Sociodemographic Variables

A pre-designed questionnaire was used to collect data on patient's age, gender, marital status, level of education, duration since diagnosis of diabetes, co-morbidities like hypertension, and current treatment for diabetes mellitus.

3.4.2. Anthropometric Measurements

We performed anthropometric measurements of all eligible study participants in light clothing and without shoes.

• Height and weight were measured to the nearest 10^{th}cm and kg respectively. Body Mass Index was calculated from the two measurements, in kg/m^2

•For all anthropometric indices, measurements were taken twice and the average calculated

3.4.3. Laboratory Parameters

5-6mls of blood was collected from the ante-cubital fossa in each study participant. 2mls were put in the EDTA vacutainer (purple top) for estimation of glycated hemoglobin level and the remaining amount was put in the plain vacutainer (red top) for estimation of serum uric acid levels. The samples were then delivered to the KNH Biochemistry laboratory at the end of the days' collection and were analyzed on the same day hence storage at cool temperatures was not a requirement

Laboratory analysis was performed as follows:

•HbA1C was analyzed in whole blood using Roche clinical chemistry analyzer known as COBAS INTEGRA 400/400 PLUS/800 analyzer using COBAS INTEGRA hemolysing reagent Gen.2.

Quality of glycemic control was determined using HbA1c: Good control was taken as HbA1c < 7%, 7-8% as moderately controlled and poor control at HbA1c > 8%.

• Serum uric acid was estimated using the uricase method. It is a manual assay that quantifies uric acid by absorbance. The co-efficient variation of this method is 2.6%. Category of Serum uric acid was taken as low <3.4mg/dl (<202µmol/L), Normal 3.4 -7.2mg/dl (202µmol/L - 428µmol/L) and high > 7.2mg/dl (>428µmol/L)

3.5 Quality Assurance

We ensured quality of the collected data by training research assistants on the objectives of the study and how to take anthropometric measurements. The research assistant and the principal investigator took these measurements twice, to ensure quality, with the average being recorded. We used calibrated weighing and height machines. Laboratory parameters were done by qualified personnel, and machines calibrated and new standards and controls used.

3.6 Statistical Analysis

Data was coded, entered into SPSS version 23.0 (IBM), and cleaned. Continuous variables like age, BMI, HbA1c, serum uric acid levels were expressed in means ±SD, or median

(Interquartile range). Categorical variables like hyperuricemia and glycemic control were analyzed as proportions, n (%).

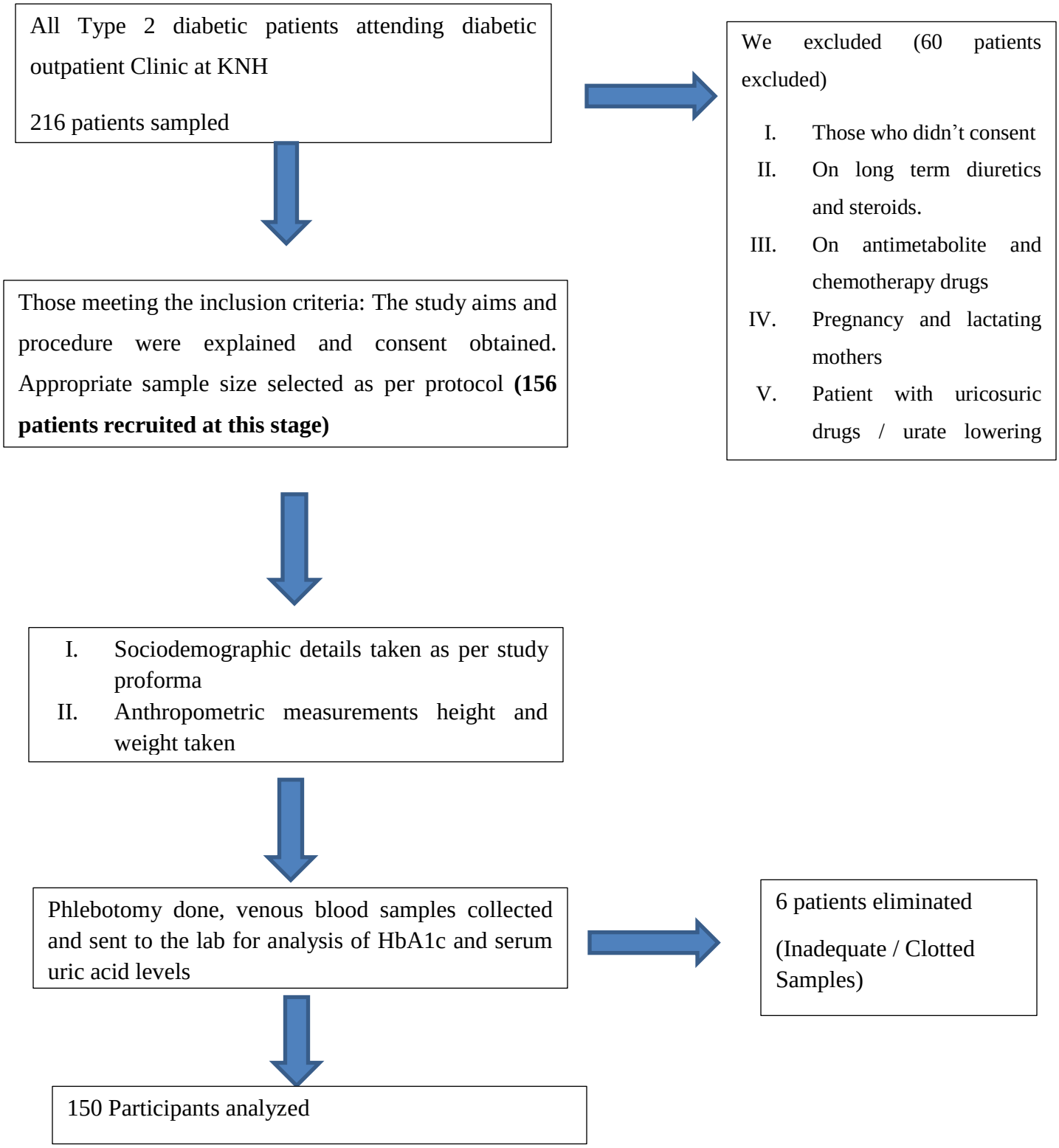
Comparison and correlation of serum uric acid with duration of diabetes, glycemic control, age, sex, BMI and Hypertension were done using the Pearson product- moment correlation, with level of significance set at $p<0.05$. Pearson Chi-squared and Fischer exact tests were used to analyze relationships between categorical variables such as BMI and hyperuricemia. We performed a bivariate analysis to see the relationship between serum uric acid levels and duration of diabetes and glycemic control.

3.7 Ethical Considerations and Authority

Ethical approval was sought from the University of Nairobi/Kenyatta National Hospital Ethics and Review Committee, Research approval number P724/12/2017. The study was clearly explained to potential participants in a language they could understand (English, Kiswahili, and in instances, vernacular). All identifiers were removed and each patient assigned a study number. Strict confidentiality was maintained for all the data. We emphasized to the patients that participation was voluntary, and they did not stand to lose anything if they declined to participate in the study. Further, no monetary gains would be forthcoming to participating patients. We only drew 7mls of blood from the antecubital vein of the patient using aseptic technique. The patient did not bear any costs for the investigations related this study. The serum samples were transported to the biochemical lab immediately after the clinic was over. The results were disseminated to the health care providers to aid in patient care

4.0 CHAPTER FOUR: RESULTS

4.1 Study Flow Chart



4.2 Sociodemographic Characteristics of the Study Participants

Between January and May 2018, we recruited a total of 156 study participants. We excluded 6 because of incomplete records or inadequate blood samples.

The study population had a mean (SD) age of 56.47 ± 13.43 years and a median of 57years with majority between the ages of 46 – 65 years at 52%. The population was predominantly females at 66% and most had attained primary school education at 45.3%

Table 3: Demographic Information of the Patients

Characteristic	**N = 150** **Frequency n (%)**
Age group (Years)	
18 – 25	1 (0.7)
26 – 35	7 (4.7)
36 – 45	26 (17.3)
46 – 55	36 (24.0)
56 – 65	42 (28.0)
66 – 75	26 (17.3)
76+	12 (8.0)
Sex	
Male	51 (34.0)
Female	99 (66.0)
Marital status	
Single	7 (4.7)
Married	122 (81.3)
Separated/Divorced	3 (2.0)
Widowed	18 (12.0)
Education level	
None	6 (4.0)
Primary	68 (45.3)
Secondary	54 (36.0)
Tertiary	22 (14.7)

4.3 Clinical and Anthropometric Characteristics

In the study population the mean (SD) duration since diagnosis of diabetes was 10.3 years with majority having been on follow up for 1-10 years. The most common mode of treatment was oral hypoglycemic agents only in 47.3%.

The study population had comorbidities of hypertension at 65.3% whose mean (SD) blood pressure of 140/78mmHg (±20.8mmHg) and obesity at 36% as shown in table 4.

Table 4:Clinical and anthropometric characteristics of the study population

CLINICAL CHARACTERISTICS	ALL STUDY PARTICIPANTS	
	N	%
DURATION SINCE DIAGNOSIS OF DM (YEARS)	Mean (SD) 10.3 ±7.8years	Median 10.0 years
DURATION OF DIABETES		
1-10 YEARS	87	58
11-20 YEARS	51	34
21-30 YEARS	7	4.7
31-40 YEARS	5	3.3
HISTORY OF HYPERTENSION		
YES	98	65.3
NO	52	34.7
CURRENT DIABETIC MEDICATION		
INSULIN INJECTIONS	23	15.2
INSULIN AND ORAL HYPOGLYCAEMICS	55	36.7
ORAL HYPOGLYCAEMIC AGENTS ONLY	71	47.3
NONE	1	0.7
BMI CATEGORY		
NORMAL	37	24.7
OVERWEIGHT	59	39.3
OBESE	54	36.0

4.4 Laboratory Characteristics

We found hyperuricemia in 19.3% of the study participants. The mean (SD) serum uric acid level was 5.02 mg/dl (299µmol/L). Glycemic control was good as the mean (SD) HbA1c was 7.76% with 42.7% having a HbA1c below 7%.

Table 5: Laboratory characteristics of the study population

LABORATORY PARAMETER	**MEAN±SD (n = 150)**	**MEDIAN**
HBA1C	7.76% ± 2.3	
SERUM URIC ACID LEVELS	5.02 ± 1.84 mg/dl (299µmol/L)	4.60 mg/dl (274µmol/L)
CATEGORIES OF PARAMETERS	**N**	**%**
HBA1C CATEGORY		
GOOD (< 7%)	64	42.7
MODERATE (7 TO 8 %)	32	21.3
POOR (> 8 %)	54	36.0
SERUM URIC ACID LEVEL CATEGORY		
LOW (< 3.4 MG/DL / <202µmol/L)	16	10.7
NORMAL (3.4 – 7.2 MG/DL / 202 - 428µmol/L)	105	70.0
HIGH (> 7.2 MG/DL / >428µmol/L)	29	19.3

Figure 1: Pie chart Showing glycemic control

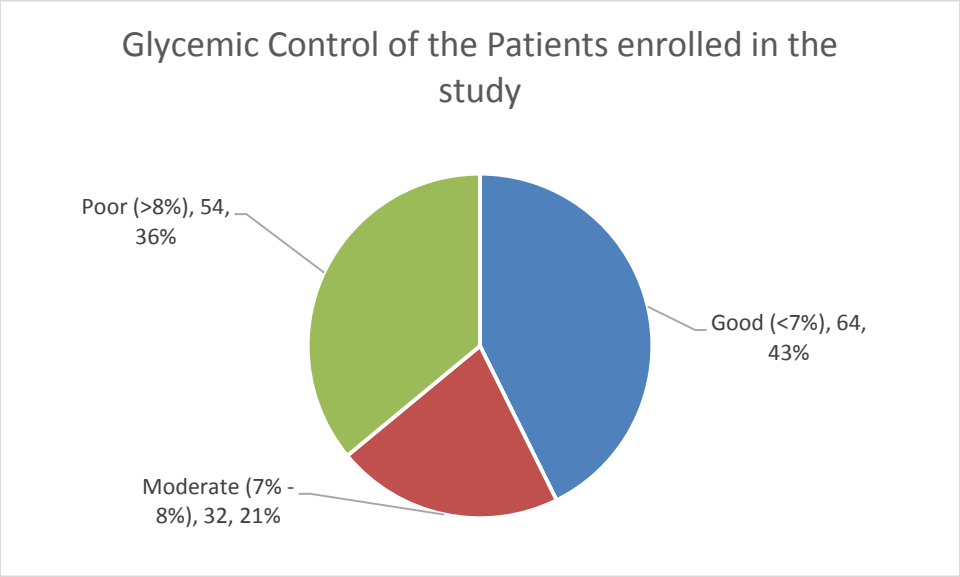


Figure 2: Distribution of Glycated Hemoglobin Concentration (%)

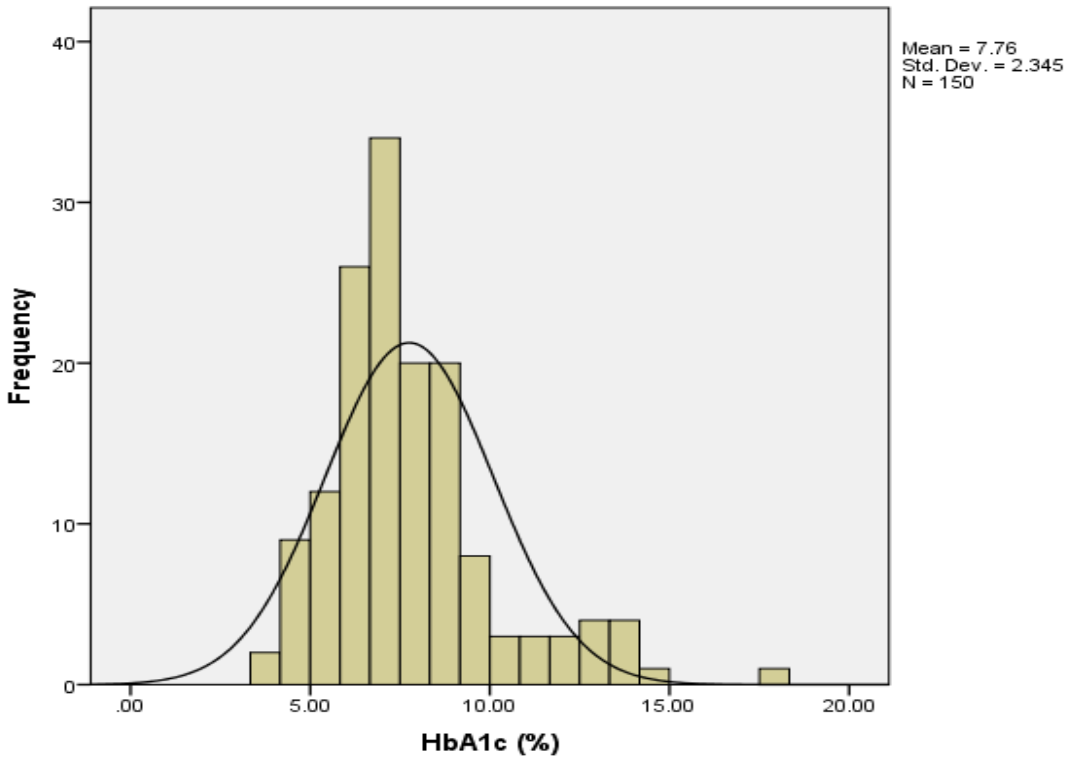


Figure 3: Distribution of Serum Uric Acid Levels (MG/DL)

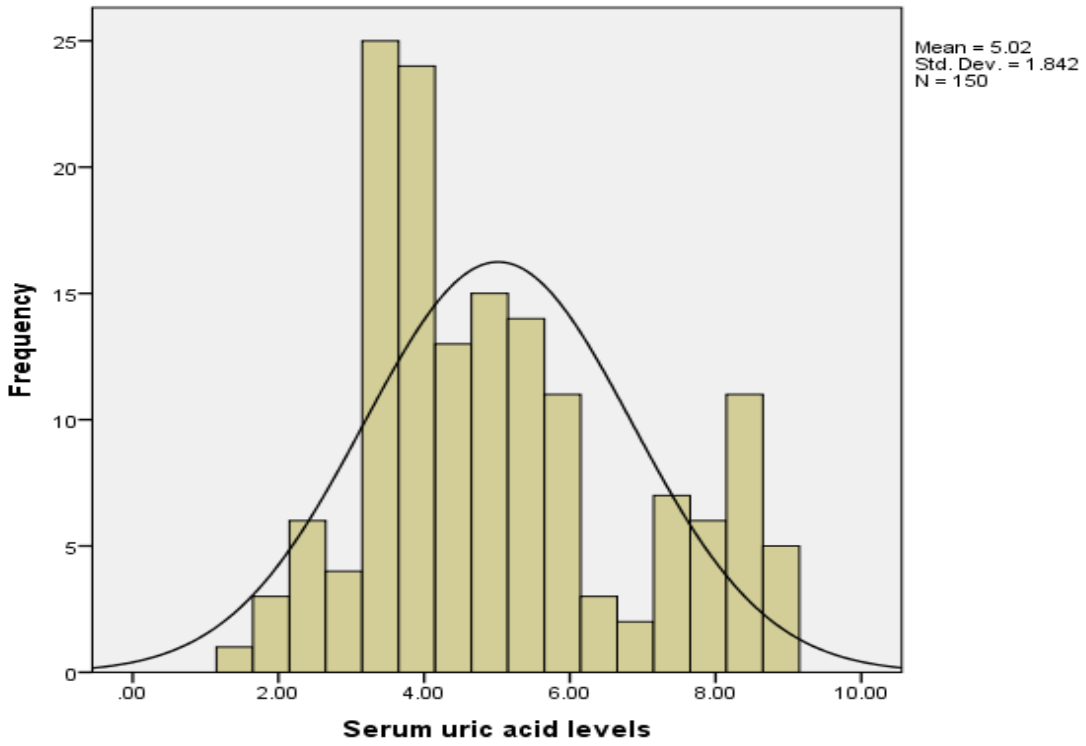


Table 6: Correlation Analysis of Serum Uric Acid Levels with Duration of Diabetes and Glycemic control among the study participants

PEARSON CORRELATION		
VARIABLE	COEFFICIENT (R VALUE)	P VALUE
DURATION OF DIABETES	0.019	0.816
HbA1C (%)	0.203	0.013

There is no correlation between serum uric acid levels and duration of diabetes, r = .019, p = 0.816 and also with glycemic control p = 0.013

The relationship between serum uric acid levels and demographic data is shown by Table 7. Results show that there are no statistical differences between hyperuricemia in respect to Age (p = .067), BMI (p = .100), and History of hypertension (p = .315). Female sex is a risk factor for hyperuricemia in the study (p = 0.046)

Table 7: Correlation of Selected Characteristics with serum uric acid levels among the Study Participants

	Frequency n (%)			Total n (%)	P value
	Hypouricemia	Normouricemia	Hyperuricemia		
Age group (Years)					
18 – 25	1 (6.2)	0 (0.0)	0 (0.0)	1 (0.7)	0.067
26 – 35	0 (0.0)	7 (6.7)	0 (0.0)	7 (4.7)	
36 – 45	4 (25.0)	20 (19.0)	2 (6.9)	26 (17.3)	
46 – 55	5 (31.2)	21 (20.0)	10 (34.5)	36 (24.0)	
56 – 65	1 (6.2)	33 (31.4)	8 (27.6)	42 (28.0)	
66 – 75	3 (18.8)	18 (17.1)	5 (17.2)	26 (17.3)	
76+	2 (12.5)	6 (5.7)	4 (13.8)	12 (8.0)	
Sex					
Male	1 (6.2)	39 (37.1)	11 (37.9)	51 (34.0)	0.046
Female	15 (93.8)	66 (62.9)	18 (62.1)	99 (66.0)	
BMI (Kg/m^2)					
Normal	6 (37.5)	28 (26.7)	3 (10.3)	37 (24.7)	0.100
Overweight	6 (37.5)	43 (41.0)	10 (34.5)	59 (39.3)	
Obese	4 (25.0)	34 (32.4)	16 (55.2)	54 (36.0)	
History of hypertension					
Yes	8 (50.0)	69 (65.7)	21 (72.4)	98 (65.3)	0.315
No	8 (50.0)	36 (34.3)	8 (27.6)	52 (34.7)	

5.0 CHAPTER FIVE

5.1 DISCUSSION

Type 2 Diabetes Mellitus remains a significant cause of morbidity and mortality in Kenya with majority of patients presenting with diabetes-related complications. Hyperuricemia is one of the associated complications giving increased morbidity and mortality to the patients by having detrimental effect on the organs. In Kenya, the prevalence of hyperuricemia in the general population is unknown; few studies that have looked into the prevalence of hyperuricemia are in hypertensive patients but none in diabetic patients. The prevalence of hyperuricemia could mirror population serum uric acid levels. We sought to find out the prevalence of hyperuricemia among ambulatory type 2 diabetic patients at the Diabetes Out-Patient Clinic in Kenyatta National Hospital to know the burden.

We established that 1 in 5 patients with diabetes (19.3%) had hyperuricemia. Hyperuricemia was predominantly seen in females at 62.1% and obese study participants at 55.2%. Studies done in different countries give a prevalence ranging from 11.4 – 32% in type 2 DM patients. The prevalence in our study is lower in comparison to what is reported in studies conducted in Egypt, Ethiopia and Nigeria but has a similar prevalence to the study done locally in Kenya. Table 8 shows the prevalence of hyperuricemia among the studies.

Table 8: Prevalence of hyperuricemia reported in previous studies among diabetic patients

AUTHOR	YEAR	POPULATION	% OF HYPERURICEMIA
Fouad et al (21)	2016	Egyptians	32
Murali et al (22)	2015	Indians	11.43
Ogbera et al (23)	2010	Nigerians	25
Woyesa et al (24)	2017	Ethiopians	33.8
Sylvia et al (19)	2015	Kenyans	18.2
Mufaddal et al	2018	Kenyans	19.3

The variation in prevalence can be attributed to differences in population profiles such as different dietary habits and choices, as well as geographical / environmental and genetic differences. Some of the differences observed in prevalence of hyperuricemia across in the above studies are attributable to the difference in sample sizes and cut off value for defining hyperuricemia used by the authors. Our study excluded patients with deranged renal function tests based on calculating eGFR, dyslipidemias and any drug, that would potentially influence serum uric acid levels. These exclusion criteria may have contributed to our low prevalence. In our study hyperuricemia is defined as serum uric acid levels above 7.2mg/dl (428µmol/l). The mean (SD) age of our study population was 56.47 years (13.4 years) and the mean (SD) duration of DM was 10.3 ± 7.8 years.

Ogbera et al (23) used a cut point of 7.0mg/dl for hyperuricemia, did not exclude dyslipidemias and used a large sample size of 601 patients. It has been shown that serum uric acid is positively associated with serum triglycerides and total cholesterol. Fouad et al (21) also found a high prevalence, however he did not exclude patients with deranged renal function tests and used a large sample size of 986 patients. Patients with low eGFR tend to have hyperuricemia due to poor excretion (17). Woyesa et al (24) also found a high prevalence rate of hyperuricemia at 33.8%, however his sample size was larger than our study. Majority of his sample population were obese and he did not exclude dyslipidemia. Murali et al (22) found a low prevalence as he had a small sample size of 70 patients. Locally Sylvia et al (19) found hyperuricemia in 44% of hypertensive patients attending Moi Teaching and Referral Hospital. She further looked into those with diabetes and found a prevalence of 18.2%. She had similar findings to our study as her diabetic patients with hyperuricemia were predominantly female, obese and in similar age bracket.

Obesity has been found to contribute to hyperuricemia (32). BMI is highly dependent on the individual's genetic composition, dietary habits and level of physical activity. Majority of our population were obese and overweight at 75.3%. In the hyperuricemia group 89.7% were in the overweight and obese group. The mean (SD) BMI among the patients with hyperuricemia was 29.2 kg/m² This is similar to majority of the studies. Ogbera et al (23) found a mean (SD) BMI of 28.9 kg/m² and Fouad et al (21) found a mean (SD) BMI of 30 kg/m² in the patients with hyperuricemia. Locally Sylvia et al (19) found a mean (SD) BMI of 30.2 kg/m² in the hyperuricemia patients and achieved statistical significance. Murali et al (22) found a low

prevalence, his study had lower number of obese participants. In our study we did not reach a statistical significance between serum uric acid levels and BMI, p = 0.100. Though we did not entirely screen for metabolic syndrome in our study, it seems like most of our patients would fall in this category; considering that the prevalence of obesity and metabolic syndrome is rapidly increasing in developing countries due to urbanization, unhealthy food options and physical inactivity. Metabolic syndrome causes insulin resistance which enhances renal urate reabsorption via stimulation of urate-anion exchanger and/or the sodium dependent anion co-transporter in brush border membranes of the renal proximal tubule. Our population needs to be screened for fructose consumption habits. The epidemic trend of obesity in recent years has also coincided with the increasing use of fructose especially in beverages. Fructose intake contributes to insulin resistance, impaired glucose tolerance, and hyperinsulinemia predisposing to hyperuricemia by increasing ATP degradation to AMP, a uric acid precursor and also de novo purine synthesis is accelerated (36).

Hyperuricemia has been strongly associated with male gender (21,24). There was a female preponderance in the hyperuricemia group, 37.9% were males and 62.1% females, with a gender ratio of 1:1.6. This goes against what is known that gout is largely a male dominated disease. The difference can be explained by the possible reason that more females were recruited as they have a better health seeking behavior than the males. More females have diabetes in our setup, also proven by other studies looking into diabetes (49). The age of women was significantly higher as most of them were older than 50 years, and may have been menopausal losing the protective effect of estrogen, and majority were in the overweight and obese group. The same has been shown in the study done by Sylvia et al (19) in Eldoret ,who also had a female preponderance at 66% and hyperuricemia was seen in 71.1% of the females and is explained by the same possible reason of older age, and most being obese. Our study achieved a statistical significance between female gender and serum uric acid levels at p = 0.046.

Our study shows that majority of the patients with hyperuricemia were in the older age group, between the age of 46 and 65 years at 62.1% and is comparable to the other studies. All the other studies achieved a statistical significance between old age and hyperuricemia confirming that the prevalence of hyperuricemia is more with advancing age. Though our study did not achieve a statistical significance, p = 0.067. This is in keeping with the study done locally by Sylvia who

found a mean (SD) age of 54 years and also did not achieve a statistical significance. The mean (SD) age of the overall population in our study was 56.47 ± 13.4 years. It is comparable to the age obtained by Ogbera et al (23) in Nigeria who recorded a mean (SD) age of 59.9 years. However, Woyesa et al (24) in Ethiopia reported a lower mean (SD) age of 49.8 years and Fouad et al (21) in Egypt recorded a mean (SD) age of 47.9 years.

Hyperuricemia has been found to be prevalent in hypertension (19). In our study, 65.3% had a documented diagnosis of hypertension with 72.4 % being hypertensive in the hyperuricemia group. Only 34% of the patients had adequate BP control. It is also quite evident that diabetes and hypertension do co-exist in many of our patients. Diabetic patients with hypertension are more vulnerable to both cardiovascular and renal complications compared to diabetic non-hypertensive patients; hence, BP control is paramount in this patient population. We excluded patients on Losartan due to its urate lowering effects and thiazide diuretics which increase serum uric acid levels. Our study did not achieve statistical significance between serum uric acid and hypertension, $p = 0.315$.

The mean (SD) duration of DM in our study is 10.3 ± 7.8 years. This is higher in comparison to the other studies. Ogbera et al reported a mean (SD) duration of 6.9years and Woyesa et al reported a mean (SD) of 7.2years. Longer duration of disease predisposes to a higher likelihood of diabetic complications predisposing to hyperuricemia and also requiring intensified treatment, such as use of injectable as a viable treatment option to achieve good glycemic control, this has been shown in the study that 53% were on insulin based therapy either as monotherapy or in combination with the oral drugs. The relationship of hyperuricemia with duration of diabetes needs more studies as the other studies done have found different results. Woyesa et al (24) reported patients with duration of diabetes with less than 10 years had more hyperuricemia as compared to patients with a diagnosis of a longer duration. Fouad et al (21) found the converse where patients with a diagnosis of 10 years and more had more hyperuricemia. Most of the patients with hyperuricemia in our study had a mean (SD) duration of more than 10 years. There was no correlation between serum uric acid levels and duration of diabetes $P = 0.816$.

Glycemic control was generally good at 42.7% having HbA1C below 7% based on the ADA criteria (3). This shows improvement to other studies done, Omari et al (KNH 2013) found 29.2% with HbA1C below 7%; and Otieno et al (KNH 1998) found 39.5% of patients with

HbA1C less than 8%. Patients with poor glycaemic control are more likely to have hyperuricemia as compared to those with good glycaemic control and this was found to be statistically significant in the other studies. We did not achieve a statistical significance in our study ($p = 0.013$) as the glycemic control was largely good and the population sample size was small. Poor glycemic control is associated with hyperinsulinemia that enhances uric acid reabsorption in the kidneys (25).

5.2 Conclusion

We found a relatively high prevalence of hyperuricemia in our study population.

Females have been shown to have a higher prevalence and those in the age group of 40 – 60 years should be routinely screened.

5.3 Study Limitations

This was a cross-sectional study hence no causal inference or temporal association could be drawn. It would have been ideal to compare the serum uric acid levels obtained in our study with those generated from the local population; however, there is lack of locally generated data on serum uric acid levels.

We were unable to investigate for other causes of hyperuricemia among our diabetic patients due to limited resources. Our study did not factor in genetics, which significantly affect the serum uric acid levels.

This was a single center study with a relatively small sample size so these results may not be generalizable to the entire population of patients with type 2 diabetes in Kenya.

Patients included in the study are not representative of all the patients with Type 2 diabetes as confounding factors like deranged renal functions and dyslipidemias were excluded and the lack of a control group to compare with serum uric acid levels in the general population

5.4 Recommendations

The following are our recommendations from this study:

i. Studies should be conducted to determine serum uric acid levels in the normal population. This will show the prevalence of hyperuricemia, as well as give normal population values in the local population.

ii. Regular screening for serum uric acid levels in the patients on follow up in the diabetic clinic especially female patients in the age of 45 to 60 years.

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APPENDICES

Appendix I: Informed Consent Form (English)

Study Title: SERUM URIC ACID LEVELS AMONG TYPE 2 DIABETIC PATIENTS AT KENYATTA NATIONAL HOSPITAL

Study number:

Investigator: Dr. Mufaddal Shokat (H58/80708/2015)

Registrar in Internal Medicine, the University of Nairobi

Phone: 0722176970, email mufaddal00@hotmail.com

Supervisors:

Prof G Oyoo

Professor, Department of Clinical Medicine and Therapeutics

University of Nairobi

Dr Eugene Genga

Lecturer, Consultant Physician, Department of Clinical Medicine and Therapeutics,

University of Nairobi

Dr. Edna Kamau

Lecturer, Consultant Physician, Department of Clinical Medicine and Therapeutics,

University of Nairobi

Purpose and Benefits

We wish to conduct a research on patients attending the diabetic outpatient clinic at Kenyatta National Hospital, to identify those with increased serum uric acid. This study aims to determine the serum uric acid levels among type 2 diabetic patients and draw possible comparison with their blood sugar control. We will include patients aged 18 years and above. If you are found to have hyperuricemia, we shall prescribe the relevant treatment for your benefit and give you the required counseling.

Participation

Participation is voluntary and you have the right to withdraw at any point. You will not be victimized if you refuse to participate in the study, and you will still get management

Cost

All the tests will be done for free and you will be reimbursed your fare if you are required to come another day

Procedures

This study will be conducted through a questionnaire administered with the assistance of a trained study assistant. We will also take measurements of your height, weight, and blood pressure. 7mls of venous blood will be drawn from a peripheral vein in your forearm using an aseptic technique.

Safeguarding Privacy

The interviewer has signed a pledge to keep all information about you secure. Your name will be removed from all records involved in the study. A number will be assigned to the survey questionnaire instead. Only project staff will have access to the study data. We will not use your name when we report results of the study.

Benefits

Your taking part in this study will help us determine how prevalent hyperuricemia is in the diabetic population, and help advance knowledge on possible future interventions that might benefit these patients, e.g., initiating early treatment.

There are no direct benefits to you. There will be little or no discomfort while drawing blood. However, the overall impact for the diabetic population may be great because new data on prevalence of hyperuricemia will be found, and form a basis for future research on whether

early screening and treatment reduce the outcome of diabetic complications.

Risks

Compensation

There is no compensation, either monetary or otherwise, for participation in this study

Enquiries

If you have any questions about this research, you may call Dr Mufaddal Shokat on 0722176970. If you have any questions on your rights as a research participant you can contact Professor Chindia M.L, secretary, KNH/UoN- ERC by calling Tel. 2726300, ext. 44102, Nairobi.

CONSENT CERTIFICATE

Respondent Agreement

The Study has been explained to me. I consent to participate. I have had a chance for my questions to be answered. I know that I may refuse to participate or to stop the interview at any time without any loss of health care benefits that I am otherwise receiving. I understand that if I have questions about this study or my rights in taking it, I may contact Dr Mufaddal Shokat on 0722176970. Further, I understand that the information recorded by the investigator will be confidential

Respondent Signature_____ Date_____

Interviewer Signature_____ Date_____

Contacts of the investigator

Dr Mufaddal Shokat

The University of Nairobi, P.O. Box 30197-00100

Email mufaddal00@hotmail.com, Phone: 0722176970

Lead Supervisor:

Prof G Oyoo, Dr Eugene Genga and Dr Edna Kamau

The University of Nairobi, P.O. Box 30197-00100

Kenyatta National Hospital/University of Nairobi Ethics & Review Committee contacts

Prof L Chindia, Tel. 2726300, ext. 44102

Email: uonknh_erc@uonbi.ac.ke

FOMU INAYOELEZA IDHINI

UTANGULIZI

Mimi ni Dkt. Mufaddal Shokat, kutoka Chuo Kikuu cha Nairobi. Kwa sasa nasomea uzamili katika Tiba ya Ndani. Kama sehemu ya masomo yangu ya uzamifu, nahitajika kufanya mradi wa utafiti. Ninafanya uchunguzi kuhusu viwango vya chembe chembe ya Uric Acid katika wagonjwa wa kisukari, katika Hospitali Kuu ya Kenyatta.

Lingo kudu yam utility

Lingo la utility hue in kumara swap wagonjwa wa kisukari wana viwango vya juu ya Uric Acid. Hii ni sababu viwango vya juu waweza kutatiza tiba yao na kuharakisha madhara ya ugonjwa huo.

Taratibu zitakazohusishwa

Lazima kukubali kushiriki katika utafiti sisi kuuliza maswali machahe kulingana na utafiti profoma. Ndipo tutakuwa kufanya mtihani wa kimwili ambayo inahusisha uchunguzi wa uzito wa mwili, urefu na kupima kiwango cha Blood pressure. Tutatoa damu mililita saba kwa utaratibu na bila majeraha ili kufanya utafiti wa viwango vya Uric Acid.

Ukipatikana na viwango juu vya Uric Acid, tutakueleza jinsi ya kutumia madawa kutibu shida hiyo.

Haki yako kama mshiriki katika utafiti huu

Ushiriki wako katika utafiti huu ni wa kujitolea. Hata ukichagua kushiriki au ukatae kushiriki haitaathiri matibabu yako. Una uhuru wa kujiondoa katika utafiti huu wakati wowote. Una uhuru wa kuuliza maswali kabla ya kutia sahihi katika fomu ya idhini na wakati wa utafiti. Maswala yote yatahifadhiwa kwa siri wakati wote.

Hasara za ushiriki

Hakuna hasara yoyote utakayopitia au kupata. Unawezashuhudia uchungu kidogo wakati wa kutoa damu, lakini hakuna uwezekano wa madhara yoyote. Ikiwa na uchungu mwingi, tutagharamia dawa ya maumivu.

Manufaa ya kushiriki

Mwishoni mwa utafiti huu, nitawasilisha matokeo ya utafiti katika idara ya Tiba ya Ndani katika Chuo Kikuu cha Nairobi. Habari zozote muhimu zitakazotokana na utafiti na ambazo zitafanya tiba kuwa bora, wagonjwa watafahamishwa ili hatua mwafaka ichukuliwe.

Siri

Habari zote zitakazokusanywa wakati wa utafiti zitahifadhiwa kwa siri. Ni watafiti pekee ndio wanaoweza kufikia habari za kibinafsi. Habari zitakazokusanywa zitaandikwa na kuainishwa bila kutaja washiriki.

Ikiwa una swali lolote wakati wa utafiti, unaweza kuwasiliana na wafuatao: DKT. Mufaddal Shokat, chuo kikuu cha nairobi, idara ya mafundisho ya udaktari na matibabu ya magonjwa, Simu ya mkono 0722176970 ***AU*** mwenyekiti, knh/uon kamati inayoshughulikia maadili, Nambari ya same: 020-2726300/0722829500/0733606400/EXT 44102. P.O. Box 20723, Nairobi.

CHETI CHA IDHINI

Kabala sijakuhusisha katika utafiti wangu, naomba utie sahihi katika fomu ya idhini iliyopo hapo chini. Fomu hii ya idhini haitahusishwa na majibu yako.

Kauli ya ridhaa: Nimesoma habari hapo juu na nimepata majibu ya maswali yoyote

SAHIHI……TAREHE……

JINA …….

MKUU WA UCHUNGUZI

SAHIHI ……TAREHE……

JINA ……

Ahadi ya mhusika

Ninakiri ya kwamba nimeelezwa na kufafanuliwa muktadha wa utafiti huu, na nimeelewa ya kwamba ni hiari yangu kuhusika. Pia, nimeelewa ya kwamba naweza kujiondoa kwenye utafiti huu wakati wowote bila kuhatarisha matibabu yangu. Aidha, nimeelewa ya kwamba maswali yote nitakayozua kuhusiana na utafiti huu yatajibiwa na mtafiti mkuu, Dkt Mufaddal Shokat (kupitia simu ya rununu) 0722176970, au barua pepe mufaddal00@hotmail.com. Pia, ninaweza kuwasiliana na kamati ya Ethics ya Hospitali ya Kenyatta kupitia Prof Chindia 020-2726300/0722829500/0733606400/EXT 44102. P.O. Box 20723, Nairobi.

Mkuu wa uchunguzi

Dr Mufaddal Shokat

Chuo Kikuu cha Nairobi, P.O. Box 30197-00100

Barua pepe mufaddal00@hotmail.com, Simu: 0722176970

Msimamizi wa uchunguzi:

Prof G Oyoo, Dkt. Eugene Genga ,na Dkt. Edna The University of Nairobi, P.O. Box 30197-00100

Appendix 2: Data Collection Tool

Study Title: Serum Uric Acid Levels Among Type 2 Diabetic Patients at Kenyatta National Hospital

Sociodemographic information

1. Study ID number_____
2. Age (years)_____
3. Gender: Male ☐ Female ☐
4. Marital status: Single ☐ Married ☐ Separated/divorced ☐ Widowed ☐

Education level None ☐ Primary ☐ Secondary ☐ Tertiary ☐

Past/current medical History

5. Duration of Diabetes_____
6. History of hypertension: Yes ☐ No ☐
7. Current diabetic medications
   - Insulin injections ☐
   - Insulin and oral hypoglycaemic ☐
   - Oral hypoglycaemics only ☐
   - None ☐

Anthropometric measurements

8. Height (m) _____
9. Weight (kg)_____
10. BMI_____
11. BMI category <18.5 (below normal) ☐
    - 18.5-<25 (normal) ☐
    - 25-<30 (overweight) ☐
    - 30-<40 (obese) ☐

Blood Pressure reading _____

Laboratory parameters

1. Serum Uric Acid levels_____
2. Category of Serum Uric Acid

   Low <3.4mg/dl ☐

   Normal 3.4 – 7.2mg/dl ☐

   High > 7.2mg/dl ☐

HbA1c (%)_____