ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF MEDICAL BIOCHEMISTRY

ASSESSMENT OF RENAL FUNCTION AND HEMATOLOGICAL PROFILE AMONG KHAT *(CATHA EDULIS)* CHEWER AND NON CHEWER TYPE 2 DIABETES MELLITUS PATIENTS ATTENDING HARAR JUGOL HOSPITAL, EASTERN ETHIOPIA.

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Thesis submitted to Department of Medical Biochemistry, School of Graduate Studies, College of Health Sciences, Addis Ababa University in partial fulfillment of the requirements for the degree of Master of Science (MSc) in Medical Biochemistry.

February, 2021
Addis Ababa, Ethiopia

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ADDIS ABABA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

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Declaration Sheet

This is to clarify that thesis prepared by Tewekel Reshid entitled "Assessment of renal function and hematological profile among khat *(catha edulis)* chewer and non chewer type 2 diabetes mellitus patients attending Harar Jugol Hospital, Eastern Ethiopia." is submitted in partial fulfillment of the requirement for the Degree of Master of Sciences in Medical Biochemistry complies with the regulations of the university and meets the accepted standards with respect to the originality and quality.

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Chair of the department or graduate program coordinator

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LIST OF ABBREVIATIONS AND ACRONYMS

CBC	Complete blood count
DDT	Dichlorodiphenyltrichloroethane
DM	Diabetes mellitus
DKD	Diabetic Kidney Disease
FBS	Fasting blood sugar
HCT	Hematocrit
HGB	Hemoglobin
LYM%	Lymphocyte percentage
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MPV	Mean Platelet Volume
NEU%	Neutrophil percentage
PLT	Platelets
QC	Quality control
RBC	Red Blood Cells
RDW	Red cell Distribution Width
ROS	Reactive oxygen species
SOP	Standard operational procedure
T2DM	Type 2 diabetes mellitus
WBC	White Blood Cells
WHO	World Health Organization

ABSTRACT

Back ground: Diabetes mellitus (DM) is a common endocrine disorder characterized by the presence of chronic hyperglycemia and it's the leading cause of end stage renal disease (ESRD). In addition to DM some factors suspected to be the cause of the renal problems are drug abuse. World Health Organization (WHO) classified khat *(Catha edulis)* as a substance of abuse. Khat interferes with normal body functions, which could lead to adverse health effects on organs and systems of the body.

Objective: The aim of this study was to compare fasting blood sugar (FBS), renal function and hematological profile among khat chewer and non chewer type 2 DM (T2DM) patients attending at Harar Jugol Hospital, Eastern Ethiopia.

Methodology: Comparative cross sectional study was conducted on a total of 100 T2DM patients that are divided into two groups (khat chewers and non chewers). Socio demographic data were collected by using standardized questionnaire. Blood sample collection was done through standardized techniques. Automated COBAS 6000 and Sysmex KX-21N hematology analyzers were used to analyze the samples. Statistical data analysis was held by SPSS version 25 model.

Result: Serum FBS and creatinine concentration showed statistically non significant elevation among kaht chewers ($p > 0.05$). White blood cell (WBC), Platelet (PLT) and hematocrit (HCT) of the khat chewers were significantly higher than non chewers ($p<0.05$). On the other hand Mean Corpuscular Hemoglobin Concentration (MCHC) and Mean Platelet Volume (MPV) of the khat chewers were significantly lower than non chewers ($p<0.05$).

Conclusion: Chewing khat among T2DM patients might have an effect on FBS, kidney function and hematological profile. Therefore further study is recommended on the effect of khat chewing among DM patients.

Keywords: Khat, *Catha edulis*, Diabetes mellitus, Renal function, Hematology

1. INTRODUCTION

1.1 Back Ground

Diabetes mellitus (DM) is a common endocrine disorder that affects more than 100 million people worldwide (Saeedi *et al.*, 2019). It is caused by deficiency or ineffective production of insulin by pancreas which results in increase or decrease in concentrations of glucose in the blood. It is found to damage many of body systems particularly blood vessels, eyes, kidney, heart and nerves (Ozougwu and Soniran, 2011).

The number of patients with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity (Debecho *et al.*, 2017). Diabetes is the leading cause of end stage renal disease (ESRD) in both developed and developing nations. Chronic diseases such as diabetes are major public health problems in Ethiopia and kidney disease is one of the commonest complaints in any Ethiopian hospital diabetic outpatient department (Teshome,2019). In addition to DM some factors suspected to be the cause of the renal problems are drug abuse (Gitonga *et al.*, 2017). World Health Organization (WHO) categorized khat as an illegal drug and indicated that its abuse may cause a range of health problems (Badedi *et al.*, 2020). Khat interferes with normal body functions, which could lead to serious liver and kidney disorders in animals and even in humans (Mworia *et al.*, 2016).

Khat *(Catha edulis)* is an evergreen plant that belongs to the *Celastraceae* family. It is predominantly cultivated in East Africa and the Arabian Peninsula (Al-Maweri *et al.*,2018)**.** Khat originated from Ethiopia, specifically in Hararghe with a gradual expansion to different parts of Ethiopia, Yemen and other parts of the world (Gashaw and Getachew, 2014). More than 20 million people worldwide are

using Khat for euphorizing and psychostimulating effect (Kindie *et al.*, 2015; Gitonga *et al.*, 2017).

The effect of khat chewing in diabetic patients is unclear till now. Some believe that the overall effect of khat in diabetic patients is deleterious, because the user is less likely to follow dietary advice, and the consumption of sweetened beverages with khat raises blood sugar. While other believe that khat has hypoglycemic effect responsible for significant reduction in blood glucose level (Debecho *et al.*, 2017). Moreover, the mechanism of khat toxicity on liver and kidney is uncertain. However, the generation of free radicals and oxidants is now seriously implicated in khat toxicity (Kennedy *et al.*, 2020). Kidney damage due to drugs toxicity leads to a fall in creatinine and urea clearance causing elevation of creatinine & urea concentration in the blood (Gitonga *et al.*, 2017).

Hematological derangements have been used as a major test in assessing the toxicity of plant extracts (Kennedy *et al.*, 2020). Only few studies were done to assess the effect of khat on blood, there were reports that khat hydro-ethanol extract caused significant derangement in hemopoiesis and in gross hematological indices (Ismaeel *et al.*, 2014).

1.2 Khat (*Catha edulis forsk*)

1.2.1 Botanical description of khat

Khat refers to the leaves and the young shoots of the plant *Catha edulis forsk* (Kindie *et al.*, 2015). Khat is an evergreen shrub, which is cultivated as a bush or small tree (figure 1). The leaves have an aromatic odour, the taste is astringent and slightly sweet. The plant is seedless and hardy, growing in a variety of climates and soils. Khat can be grown in droughts where other crops have failed and also at high altitudes. It is harvested throughout the year (Wabe, 2011) .

Figure 1: *Catha edulis* (khat) tree, adapted from (Al-Maweri *et al.*, 2018)**.**

The khat tree was first described by Peter Forskal (1736- 1763), (Al-Motarreb, *et al.*, 2002)**.** There are several names for the plant, depending on its origin: qat-Yemen, chat-Ethiopia, qaad/jaad-Somalia, miraa-Kenya, mairungi-Uganda, Muhulo- Tanzania and Hagigat-Hebrew (Kindie *et al.*, 2015; Al-Maweri, *et al.*, 2018)**.** It is habitually used in formal meetings where the participants are engaged in discussions and maintain social contact. It is used to improve performance, stay alert and increases work capacity (Al-Habori, 2005)**.** Khat is mainly grown in Ethiopia, Kenya, Yemen, Somalia, Sudan, South Africa and Madagascar. Khat leaves were available only near to where they were grown. Recently, improved roads and air transport have allowed a much wider distribution (Cox and Rampes, 2003; Mulugeta, 2013; Al-Maweri, *et al.*, 2018).

1.2.2 Khat use in Ethiopia

Ethiopia is thought to be the country of origin of khat use (Gashaw and Getachew, 2014)**.** The chewing of khat leaves probably pre-dates the use of coffee (Cox and Rampes, 2003). In Ethiopia, Khat is commonly used for social and religious

purposes. Furthermore, it considered as a recreational substance. Recently, khat chewing becomes a common practice among high school, College and University students (Mulugeta, 2013). In Ethiopia, a number of local brands are available, including Aweday, Beleche, Abo mismar, Gelemso and Wondo. It is claimed that the Aweday variety cultivated in Harar highlands of Eastern Ethiopia is the most potent and expensive among the local brands, and hence chosen for export (Shewamene and Engidawork, 2014). Khat is a high-cash income crop (figure 2). It is profitable to the huge number of people involved in its production and marketing including farmers, distributors and merchants (Al-Hebshi and Skaug, 2005).

Figure 2: Khat trade at Awadai market, Hararge region in Eastern Ethiopia. Adapted and modified from (Wabe, 2012).

1.2.3 Active constituents of khat leaf

Several different phytochemicals are found in the leaves of khat and these include alkaloids, terpenoids, sterols, flavonoids, glycosides, tannins, more than 10 amino acids including tryptophan, glutamic acid, alanine, glycine and threonine (Cox and Rampes, 2003), trace quantities of vitamins including ascorbic acid, thiamine, riboflavin, niacin, and carotene and elements including calcium, iron, manganese,

zinc, copper and toxic metals like lead and cadmium and a negligible amount of fluoride (Gashaw and Getachew, 2014; Kindie *et al.*, 2015). The leaves of khat plant contain alkaloids like cathinone, cathine and norephedrine which are structurally and pharmacologically related to amphetamine (figure 3) (Al-Motarreb *et al.*, 2010).

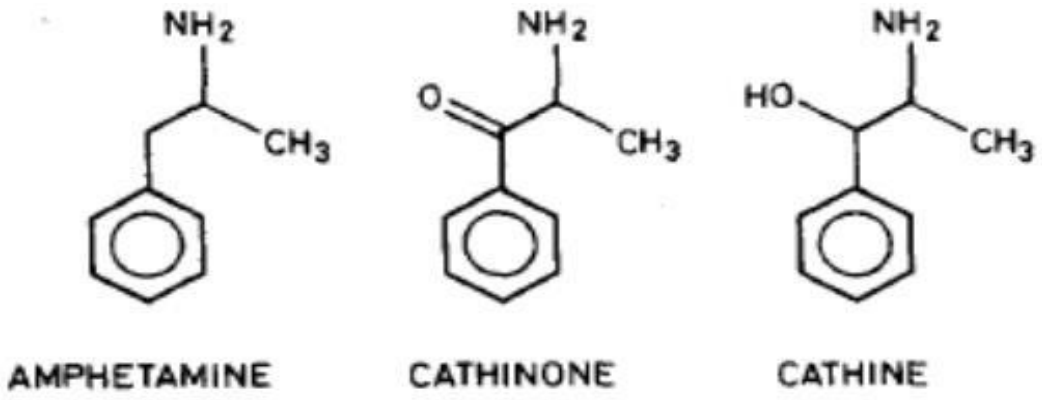


Figure 3: The chemical structure of khat alkaloids in comparison with amphetamine. Adapted from (Tewodros *et al*, 2020).

Cathinone is the principal active constituent of khat responsible for the stimulant effects that have led khat to be known as a 'natural amphetamine' (Wabe, 2011). Considering the nature and content of the various substances known to be present in khat, it is evident that compounds of the amphetamine type and the tannins are those that are particularly relevant to the effects of consumption of khat observed in man (Kindie *et al.*, 2015).

Modes of action Cathinone

The constituents of khat have been shown to exert their effects on two main neurochemical pathways: dopamine and noradrenalin. It has also been postulated that, like amphetamine, cathinone releases serotonin in the central nervous system

(Cox and Rampes, 2003). Both cathinone and amphetamine induce release of dopamine from central nervous system dopamine terminals and thus increase the activity of the dopaminergic pathways. Cathinone has a releasing effect on noradrenalin storage sites, thus cathinone facilitates noradrenalin transmission (Cox and Rampes, 2003; Fantaye *et al.*, 2020).

1.2.4 Health hazards related to chat chewing

Khat chewing has major effect on the gastro-intestinal system, central nervous system, cardiovascular system and urinary system (Gashaw and Getachew, 2014). Central nervous system effects of khat chewing are alertness, dependence, tolerance, anxiety, depression, manic, delusion and insomnia (Al-Motarreb *et al.*, 2010). Gastro-intestinal system effects of khat chewing are dental problem, stomach ulcer, constipation, oral and esophageal cancer (Al-Habori, 2005; Al-Maweri *et al.*, 2018). On cardiovascular system habitual use of khat causes hypertension, arrhythmia, myocardial infarction, stroke and death (Wabe, 2011). On urinary system habitual use of khat causes urinary retention (Mulugeta, 2013). Khat chewing causes impotence. It is known to cause spermatorrhoea usually at the first micturition after the session ends (Mwenda *et al*, 2013).

1.2.5 Khat and type 2 DM

Cathinone the main active constituent of khat induce dopamine release from central dopaminergic nerve terminals thus increasing the activity of dopaminergic pathways. These catecholamines would increase blood glucose levels by activation of glycogenolysis in skeletal muscles and the liver; β- adrenoceptor-mediated response. There is also inhibition of insulin release from the pancreatic β -cells via α-adrenoceptor stimulation which would also elevate blood glucose levels as shown in figure 4 below (Debecho *et al.*, 2017).

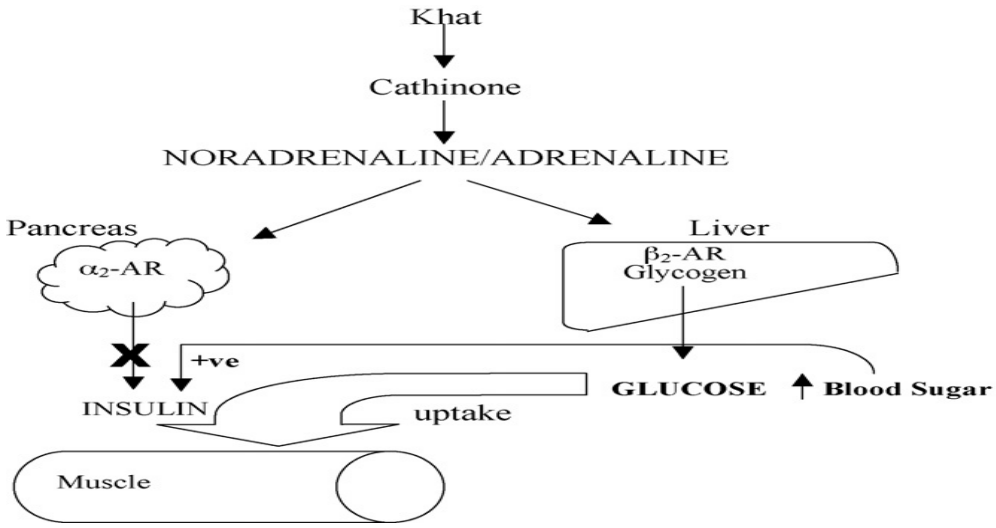


Figure 4. Diagram of the hypothetical effects of khat and cathinone on blood sugar level adapted from (Al-Motarreb *et al.*, 2010) **.**

In addition to cathinone effect on FBS level, chewing DDT sprayed khat influences carbohydrate metabolism, the exact mechanism by which DDT induce hyperglycaemia is not clear, however, DDT inhibit pancreatic secretary activity by increasing the activity of gluconeogenic enzymes. Promoting hepatic glycogenolysis by activating glycogen phosphorylase. DDT reduce calcium permeability and hence insulin secretion (Hadrani and Hoot, 2000). On the other hand a study done by Debecho *et al.*, (2017) showed khat chewing has hypoglycemic potential due to the presence of flavonoids, flavones, flavonols, saponins and trace elements like magnesium, chromium, manganese, zinc, iron, vanadium, copper, nickel, lead and strontium contained in it.

1.2.6 Nephrotoxicity effects of Khat

Regular khat chewing in human may cause kidney damage, as total serum protein levels were reduced in khat consumers, while the levels of urea and creatinine were greatly increased (Naji *et al.*, 2012; Shewamene and Engidawork, 2014)**.** Khat extract contains an oxidizing agent that causes suppression of glutathione

(GSH) synthesis leading to increased production of reactive oxygen species and induction of oxidative stress (Masoud *et al.*, 2014) .

Oxidative stress is among the main path way leading to khat-induced kidney injury. During active oxidative stress, the endogenous antioxidant defense systems fail to curtail the khat-induced production of reactive oxygen species (ROS) (Shewamene and Engidawork, 2014). Some of the khat-induced ROS generation in the kidney and the liver may be attributed to the pesticide and herbicide sprayed on khat such as dichlorodiphenyltrichloroethane (DDT) (Hadrani and Hoot, 2000), glyphosate, paraquat and 1, 2-dibromo-3-chloroporopan (DBCP). Exposure to these results in kidney necrosis which leads to acute and chronic kidney failure (Kennedy *et al.*, 2020).

Khat produced deleterious effect on renal function. This may be explained by decrease in glomerular filtration rate due to khat induced renal vasoconstriction as a result of indirect sympathomimetic action which is mediated by increase in release of norepinephrine from presynaptic storage vesicles in peripheral sympathetic nerve endings which stimulate α 1 and β1 receptors (Al-mahdar *et al,* 2009).

1.2.7 Effect of khat on hematological profile

Certain medicinal herbal preparations, drugs and other chemicals have been shown to adversely affect blood components (Ismaeel *et al.*, 2014). Blood composition alterations were observed among khat users (Alsalahi *et al.*, 2012). Experimental studies in rodents and primates have demonstrated that khat and its components reduce the red blood cells (RBCs) and consequently affect its indices leading to macrocytic anemia (Ismaeel *et al.*, 2014). On the other hand administration of khat in mouse result in decreased levels of RBCs and its indices which might be a clear indicator of khat-induced normochromic microcytic

anemia (Kennedy *et al.*, 2020)**.** Khat extract caused a statistically significant decrease in total WBC count and regarding WBC deferential except neutrophils count the other leukocytes including lymphocytes, monocytes, basophils and eosinophils showed significant decreases in khat treated rats (Ismaeel *et al.*, 2014).

1.3 Effect of DM on renal function and hematological profile

DM may induce several complications or can co-exist with other diseases. The complications are divided in to microvascular and macrovascular. The macrovascular, which are more severe, are coronary disease, stroke and peripheral neuropathy. The microvascular complications are diabetic retinopathy, diabetic nephropathy and diabetic foot (Okur and Siafaka, 2017).

Diabetic Kidney Disease (DKD)

DKD affects approximately one-third of individuals with DM and carries with it considerable cardiovascular morbidity and mortality. Despite modern management of DM, the prevalence of this clinical entity continues to increase in association with an escalating diabetic population and, surprisingly, the excess mortality risk of DM is exclusively correlated with the occurrence of DKD (Manikowski and Atta, 2015; Tang *et al.*, 2016).

Effect of DM on hematological profile

Diabetic patients are more prone to be anemic and it is worsened further by associated chronic kidney disease. Other hematological features like leukocytosis and platelet abnormalities are also common in T2DM patients (Bharathi, 2016).

Hematological alterations often occur in diabetes mellitus as a result of oxidative stress induced by DM (Yakhchalian *et al.*, 2018). Several hematological changes affecting the red blood cells (RBCs), WBCs, and the coagulation factors are shown to be directly associated with DM (Kachekouche *et al.*, 2017)**.**

1.4 Statement of the problem

Diabetes is a serious, long-term endocrine disorder with a major impact on the lives and well-being of individuals, families, and societies worldwide (Ozougwu and Soniran, 2011). The global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045 (Saeedi *et al.*, 2019).

Ethiopia is among the top four countries with the highest adult diabetic populations in sub-Saharan Africa (Abebe and Addise, 2016). The prevalence of diabetes in Ethiopia ranged 2.0%–6.5% (Bishu *et al.*, 2019). Despite of this the prevalence DM in Harar town is 7.0% which showed an increment from the overall prevalence of the country (Abebe and Addise, 2016). Diabetes and associated complications in Ethiopia are major causes of morbidity and mortality with consequential economic impact. Kidney diseases (18.2%–23.8%), was among the most frequently reported diabetes- associated problems of the country (Bishu *et al.*, 2019).

A large number of people chew Khat leaves worldwide because of its pleasurable and stimulating effects (Masoud *et al.*, 2014). The number of khat chewers has significantly increased over the years in Ethiopia (Haile and Lakew, 2015). WHO reported that Khat consumption has become a common problem that affects the health aspects of life (Alsalahi *et al.*, 2012). Moreover, many adolescents have low knowledge towards adverse effects of khat chewing (Gashaw and Getachew, 2014). Daily chewing khat for long time leads to alter in the biochemical composition of blood and enhancing oxidative state, these may contribute in the failure of the body organs, such as liver and kidney (Naji *et al.*, 2012).

In Harar, Eastern part of Ethiopia, Khat chewing is a regular practice among the population. However, many adolescents have low awareness towards adverse

effects of chewing khat on health. Reports are contradictory about the effect of khat on FBS, renal function and hematological profile among DM patients. The inconsistent body of evidence in the literature calls for more investigations to be made on the effects of khat chewing among DM patients. Moreover, no previous human study had been conducted so far to show the effect of chewing khat on FBS, renal function and hematological profile among DM patients. Hence, the aim of this study was to investigate the effect of khat chewing on FBS, renal function and hematological profile among T2DM patients.

1.5 Significance of the study

Limited studies are available regarding the effect of khat chewing on FBS, renal function and hematological profile among T2DM patients. Hence, the present study was done to investigate the effect of khat chewing on FBS, renal function and hematological profile among T2DM patients. The result of this study will provide a clear picture of FBS level, kidney related outcome and hematological profile among khat chewer and non chewer T2DM patients. It also creates awareness about the effect of khat chewing on FBS, renal function and hematological profile. To our knowledge, this is the first time study and believed to be preliminary data for other broad and nationwide research that shall be undertaken on this area.

1.6 Hypothesis of the study

HO: Means of serum FBS, renal function and hematological profile among khat chewer and non chewer T2DM patients are similar.

HA**:** Means of serum FBS, renal function and hematological profile among khat chewer and non chewer T2DM patients are significantly different.

2. OBJECTIVE

2.1 General Objective

To compare FBS, renal function and hematological profile among khat *(Catha edulis)* chewer and non chewer T2DM patients attending Harar Jugol Hospital, Eastern Ethiopia.

2.2 Specific Objective

- To determine fasting blood glucose level among khat chewer and non chewer T2DM patients.
- To asses renal function test (serum creatinine and urea) among khat chewer and non chewer T2DM patients.
- To asses hematological profile {Red blood cells (RBC), Hematocrit (HCT), Hemoglobin (HGB),Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean Corpuscular hemoglobin Concentration (MCHC), Red cell distribution Width (RDW), White blood cell (WBC) count, Lymphocyte percentage (LYM%), Neutrophil percentage (NEU%), Platelet (PLT) and Mean Platelet Volume (MPV)} among khat chewer and non chewer T2DM patients.
- To compare fasting blood glucose level among khat chewer and non chewer T2DM patients.
- To compare renal function test among khat chewer and non chewer T2DM patients.
- To compare hematological profile among khat chewer and non chewer T2DM patients.

3. MATERIALS AND METHODS

3.1 Study Area

The study was conducted at Medical Biochemistry Department, Collage of Health Science, Addis Ababa University in collaboration with Harar Jugol Hospital, Eastern Ethiopia. Harar town is located at 526 km from the capital city, Addis Ababa.

3.2 Study Design and Period

Comparative cross sectional study was conducted from June to September 2020.

3.2.1 Source population

The source population for this study was all T2DM patients who were attending at diabetic clinics of Harar Jugol Hospital during the study period.

3.2.2 Study population.

The study population consisted of 50 khat chewer and 50 non chewers T2DM patients who were on oral hypoglycemic therapy attending at diabetic clinics of Harar Jugol Hospital in the time interval of the study period. Hence a total 100 T2DM patients were enrolled in the study

3.3 Sample Size Determination and Sampling Technique

The sample sizes was determined by using a single proportion formula and calculated as follows.

$$n = Z^2pq / d^2$$

- P= assumed the highest population proportion prevalence of diabetes mellitus in Harar town 7%, (Abebe and Addise, 2016). 5% marginal error (d) to get sample size and Confidence interval (CI) of 95%.

n = Sample size

p = Proportion of DM= 0.07

d = Margin of error =0.05

q = 1-p =1- 0.07=0.93

Z = 1.96 at 95% Confidence Interval (CI)

n = 100 (50 khat chewer and 50 non chewer T2DM patient)

To recruit study participants simple random sampling technique was applied.

3.4 Variables

3.4.1 Dependent variables

- Fasting blood sugar level
- Renal function test
- Hematological profile

3.4.2 Independent variables

- Socio-demographic characteristics
- Anthropometric indicators
- Khat chewing
- Duration of diabetes
- Type of anti diabetic drugs
- Family history of kidney disease

3.5 Inclusion and Exclusion Criteria

3.5.1 Inclusion criteria

- All adult T2DM patients receiving oral hypoglycemic agent.

3.5.2 Exclusion criteria

- DM patients who were less than 18 years in age.
- Patients who suffer from HIV/AIDS
- Patients with cancer / malignancies
- Pregnant women
- Patient with known history of anemia
- Patient with known history of kidney disease

- Patient with known history tuberculosis and malaria
- Patient with history of drinking alcohol and cigarette smoking
- Patient who had history of blood donation/transfusion with in time period of less than 4 month.

3.6. Data Collection and Measurement

Data collection procedures

Each Patient who visited the clinic during the study period was evaluated for eligibility criteria to be included in the study. Those eligible individuals were included in the study. The selections of patients were continuing until the required number of patients was fulfilled. Structured questionnaires were used to collect the data. The data was collected mainly by using the questionnaire, anthropometric, and biochemical measurements.

A. Questionnaire

Standardized semi-structured questionnaire which is assumed in such a way that it can meet the objectives of this study was used during face-to-face interview and review of documented medical records. Socio demographic variables (age, gender and residence), khat chewing status and family history of kidney disease were collected using face to face interview questions. Variables including duration of diabetes and type of anti diabetic drugs were abstracted from patients' medical records.

B. Anthropometric measurement

Physical measurements such as weight, height, and blood pressure were taken using standardized methods and adjusted equipment. Weight was measured in kilogram with light cloths and no wearing of shoes, the participants' height was measured in centimeter using height board with no shoes wearing and in upright position then body mass index (BMI) was calculated to determine the obesity status (WHO, 2000). Blood pressure was measured according to WHO guideline

using an automated sphygmomanometer at the midpoint of the left arm after participants rest for at least five minutes or 30 minutes for those who took hot drinks like coffee. Three blood pressure readings were taken for all participants then the mean blood pressure was taken as true value (Chalmers, 1999).

Body Mass Index (BMI) was calculated from the body weight (kg) and height (meter) as follows:-

BMI = Weight (in kg) / (Height in m) ^{2}

Based on the National Institutes of Health Guidelines on overweight and obesity (Janssen and Ross, 2002), Subjects with BMI below 18.5 kg/m2 are classified as underweight, BMIs from 18.5 kg/m2 to 24.9 kg/m2 are classified as normal, BMIs from 25.0 to 29.9 kg/m2 are classified as overweight, and BMIs at or above 30.0 kg/m2 are considered obese.

C. Biochemical/ Laboratory tests

Five milliliter (5mL) of blood sample was collected in early morning before breakfast or minimum of eight hour fasting. The process of blood sample collection was through aseptic/sterile technique. About 2mL of the blood was collected in EDTA coated tubes for CBC analysis by using Sysmex KX-21N (Sysmex, USA) machine. Other 3mL of Blood was collected into standardize serum separator tube (SST) without anticoagulant from each participant by trained laboratory technologist and allowed to stand for 30 min at room temperature to allow complete clotting and clot retraction. The sample was then centrifuged at 3500 rpm for 10 min by using HuMax14k centrifuge to extract the serum. Then the serum was transferred from SST tube into Nunc tube and stored at -20^{o}c in the refrigerator. The serum extracted was then used to determine the levels of fasting blood glucose level, creatinine and urea by using COBAS 6000 chemistry analyzer.

D. Sampling technique

A consecutive sampling technique was used until the required sample size was achieved.

3.7 Test Principles of the Laboratory Analysis

3.7.1 Determination of fasting blood glucose level

Test principle

Enzymatic reference method with hexokinase was used to determine serum fasting blood glucose level. Hexokinase catalyzes the phosphorylation of glucose to glucose-6-phosphate by ATP.

$$\text{Glucose} + \text{ATP} \xrightarrow{\text{HK}} \text{G-6-P} + \text{ADP}$$

Glucose-6-phosphate dehydrogenase oxidizes glucose-6-phosphate in the presence of NADP to gluconate-6-phosphate. No other carbohydrate is oxidized. The rate of NADPH formation during the reaction is directly proportional to the glucose concentration and is measured at 340 nm photometrically.

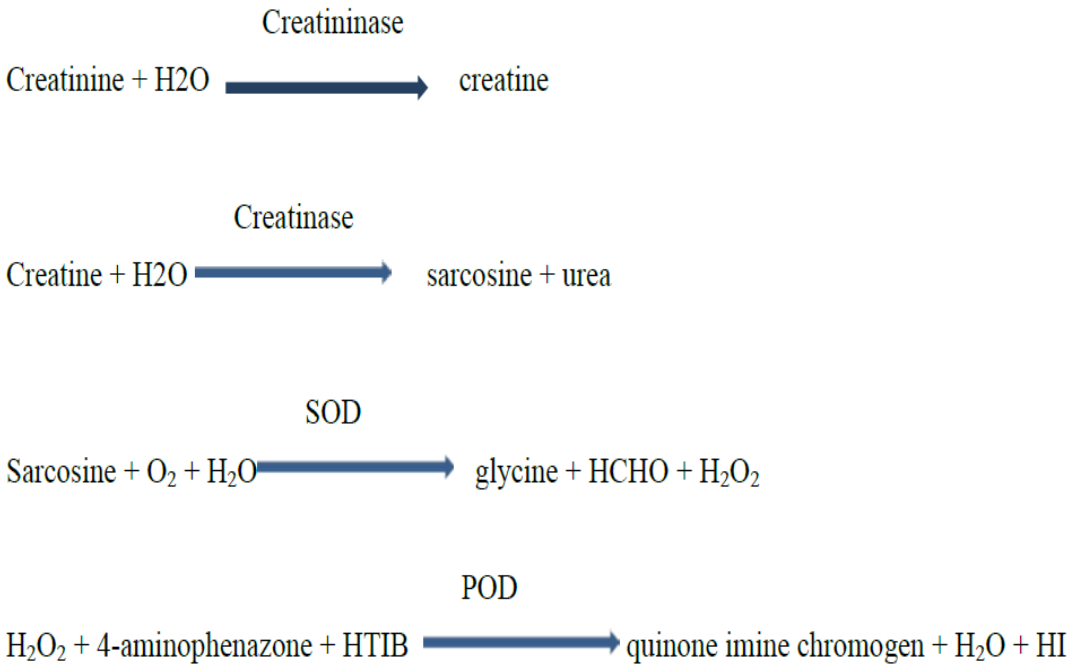
$$\text{G-6-P} + \text{NADP}^{+} \xrightarrow{\text{G-6-PDH}} \text{gluconate-6-P} + \text{NADPH} + \text{H}^{+}$$

Expected normal range of fasting blood glucose concentration is 4.11-6.05 mmol/L (74-109 mg/dL) (WHO, 2006).

3.7.2 Determination of serum creatinine

Test principle

Enzymatic method was used to determine serum creatinine. It is based on the conversion of creatinine with the aid of creatininase, creatinase, and sarcosine oxidase to glycine, formaldehyde and hydrogen peroxide. The liberated hydrogen peroxide reacts with 4-aminophenazone and HTIB (2,4,6-triiodo-3-hydroxybenzoic acid) to form a quinone iminechromogen. The color intensity of the quinone imine chromogen formed is directly proportional to the creatinine concentration in the specimen and is measured at 546 nm photometrically.

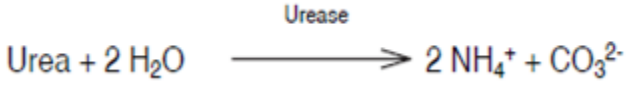


Expected normal values of serum creatinine in adults are**;** 45-84 µmol/L (0.51-0.95 mg/dL) for females and 59-104 µmol/L (0.67-1.17 mg/dL) for males (Dries *et al.*, 2000).

3.7.3 Determination of serum urea

Test principle

Kinetic test with urease and glutamate dehydrogenase was used to determine serum urea concentration. Urea is hydrolyzed by urease to form ammonium and carbonate



In the second reaction 2-oxoglutarate reacts with ammonium in the presence of glutamate dehydrogenase (GLDH) and the coenzyme NADH to produce L-glutamate. In this reaction two moles of NADH are oxidized to NAD+ for each mole of urea hydrolyzed

The rate of decrease in the NADH concentration is directly proportional to the urea concentration in the specimen and is measured at 340 nm photometrically. (fawcett and scott, 1960)

Expected normal values of serum urea for adults is 2.76 - 8.07 mmol/L or (16.6 - 48.5 mg/dL) (Löhr *et al.*, 2009).

3.7.4 Determination of hematological parameters (CBC)

Principally sysmex analyzer is based on the electronic resistance (impedance) detection method for counting and sizing recognition of the leukocytes, erythrocyte, and platelet using three hydraulic systems for, WBC, RBC, platelet and hemoglobin, and displays the results on the liquid crystal displayer (LCD) and will be printed out the results in thermal paper. The analysis was performed by using automated hematology analyzer (Sysmex KX-21N, USA) using EDTA anti coagulated fresh venous blood sample. For each sample of blood the: RBC, HCT, HGB, MCV, MCH, MCHC, RDW, WBC count, LYM%, NEU%, PLT and

MPV were determined using an automated hematological analyzer (Sysmex, 2000).

Table 1: Expected Values for hematological profile

Parameter	Reference Range	Units
WBC	3.0 - 11.0 x 10^3	µl
RBC	2.5 - 5.50 x10^6	µl
HGB	8.0 - 17.0	g/dl
HCT	26.0 - 50.0	%
MCV	86.0 - 110.0	Fl
MCH	26.0 - 38.0	Pg
MCHC	31.0 - 37.0	g/dl
PLT	50 - 400 x10^3	µl
LYP%	5.0 - 55.0	%
NEU%	45- 95	%
RDW-CV	11- 16	%
MPV	9 - 13	Fl

3.8 Data quality control and management

The data quality assessment was started with socio-demographic data collection and has gone through blood sample collection, laboratory test and final data entry and statistical analysis. The blood sample was taken under aseptic techniques with standard operational procedure. In order to maintain the quality of laboratory result every laboratory procedure following SOP and QC were performed to check the performance of chemistry and hematological analyzer by running quality control materials daily before analysis of the samples and analysis of

specimen has been carried out in Ethiopian public health institute (EPHI) and Harar jugol hospital laboratory unit. Results were checked for completeness on daily basis by the immediate supervisor. Great attention in data insertion to software on computer was sought. The complete result was rechecked repeatedly to maintain the overall quality of data.

3.9 Data processing and analysis

Data was obtained from laboratory analysis and questionnaires, statistical data analysis was conducted using statistical package for the social science (SPSS) version 25 software. Categorical variables were presented in numbers and percentages. Continuous variables were expressed as mean ± standard deviation and mean difference was determined by using independent sample t- test for comparison between the groups. Significance is set at $p<0.05$.

3.10 Ethical consideration

Ethical clearance was obtained from Research and Ethical Committee of the Department of Biochemistry, School of Medicine, College of Health Sciences, Addis Ababa University with protocol number: M.Sc. 12/20. Consent form was prepared with detailed explanation of objectives, risks, benefits to the study participants and the confidentiality was presented to the participant and kept. Data was collected after obtaining informed consent and agreement from the patients under study. Sample collection was performed by trained health professionals following ethical steps and scientific procedures. All the necessary precautions were undertaken to prevent COVID-19 transmission.

3.11 Operational definition

Khat chewer-are those who chew khat about 300 gram in average for ≥3 hour daily or those who chew khat every other day for at leat 5 year and above.

Non chewer- are those who never chew khat.

Hematological profile: refers to measurable or quantifiable characters which include WBC, PLT, RBC, HGB, HCT, WBC Diff count (NEU% and LYM%), RBC indecis (MCV, MCH, MCHC, RDW) and MPV.

Mean corpuscular volume (MCV): measures the average red blood cell volume

$$MCV\ (fL) = \frac{HCT}{RBC}$$

Mean corpuscular hemoglobin (MCH): is the average amount of hemoglobin per red blood cell in a sample of blood.

$$MCH\ (pg) = \frac{HGB}{RBC}$$

The mean corpuscular hemoglobin concentration (MCHC): is the average concentration of hemoglobin in red blood cells.

$$MCHC\ (g/dL) = \frac{HGB}{HCT}$$

Red cell distribution width (RDW): is a test that reflects variability in the size of the red blood cells (and is proportionate the standard deviation of the MCV).

$$RDW\ (\%) = \frac{SD\ of\ MCV}{Mean\ MCV} \times 100$$

4. RESULTS

4.1 Socio- demographic characteristics and Anthropometric indicators of diabetic patients in the study

A total of 100 participants diagnosed with T2DM (fifty khat chewers and fifty non chewers) were included in the study. All participants in this study were on oral hypoglycemic drugs. Among the total participants, 45/100 (45%) were males and 55/100 (55%) were females and the numbers of male and female in each group were more or less similar. Out of 50 non chewer participants, 30 (60%) were females and 20 (40%) were males and out of 50 khat chewer participants, 25 (50%) were females and 25 (50%) were males.

The majority of khat chewers (58%) and non chewer (46%) of the study participants were found within the age group of 40-60 years. Most (64%) of khat chewers and 86% of non chewers were living in the urban area of Harar town. Among khat chewer participants, 37/50 (74.0%) had normal BMI, 13/50 (26.0%) were overweight. Among non chewer participants, 39/50 (78.0%) were normal, 9(18.0%) were overweight, 2 (4.0%) were obese and none of the study participants were found to be underweight as shown in table 2. Regarding Blood pressure, 48/50 (96%) of khat chewers and 47/50 (94%) of non chewers had normal systolic (<140 mmHg) and diastolic (<90 mmHg) blood pressure.

Regarding the type of anti diabetic medication among khat chewer participants 31/50 (62%) were on combination therapy taking Biguanides/metformin + Sulfonylurea and 19/50 (38.0%) were taking Biguanides/metformin mono therapy. Among non chewer participants 26/50 (52%) were on combination therapy taking Biguanides/metformin+ Sulfonylurea and 24/50(48%) were taking Biguanides/metformin mono therapy. Concerning duration of DM, 30/50 (60%) of khat chewers and 24/50(48%) of non chewers had DM duration of <5 year, 13/50 (26%) of khat chewers and 19/50 (38%) of non chewers had DM duration

between 5 to 10 year and 7/50(14%) of both khat chewer and non chewers had DM duration of more than 10 years. Regarding family history of kidney disease, most (76%) of our study participants had no family history of kidney disease (table 2).

Table 2: Socio- demographic and anthropometric characteristics

Variable	Khat chewer T2DM patients (n=50)		Non chewer T2DM patients (n=50)	
	Number (n)	Percentage (%)	Number (n)	Percentage (%)
Gender				
Male	25	50	20	40
Female	25	50	30	60
Age in years				
20-40	13	26	10	20
41-60	29	58	23	46
>60	8	16	17	34
Residential area				
Urban	32	64	43	86
Rural	18	36	7	14
BMI in kg/m2				
<18.5	-	-	-	-
18.5-24.5	37	74	39	78
25-29.9	13	26	9	18
>30	-	-	2	4
Systolic BP				
<140mmHg	48	96	47	94
>=140mmHg	2	4	3	6
Diastolic BP				
<90mmHg	48	96	47	94
>=90mmHg	2	4	3	6

Duration of diabetes <5 year 5-10 year >10 year	 30 13 7	 60 26 14	 24 19 7	 48 38 14
Anti diabetic medication Biguanides/metformin Metformine+ Sulfonylurea	 19 31	 38 62	 24 26	 48 52
Family history of kidney disease No Yes	 35 15	 70 30	 41 9	 82 18

4.2. Clinical characteristics of diabetic patients

4.2.1 Fasting blood sugar Level

The mean FBS level was found to be 192.22±98.45 mg/dl for khat chewer participants and 178.95±76.0 mg/dl for non chewers. Independent sample t test showed that among diabetic patients, khat chewer participants had higher level of FBS as compared to non chewers. The difference between the two groups was not statistically significant ($p>0.05$) as shown in table 3.

4.2.2 Renal function test: serum creatinine and urea concentrations

The mean level of serum creatinine was 0.75±0.26 mg/dl for khat chewer participants and 0.73±0.26 mg/dl for non chewers. There is no statistically significant difference between the two group ($p>0.05$). Regarding serum urea concentration, the mean level for khat chewer participants (21.9±10.9 mg/dl) was slightly lower than non chewers (23.4±10.5 mg/dl). But this difference was not statistically significant ($p>0.05$) (table 3).

Table 3: Comparison of renal function test (serum creatinine and urea) and FBS level

Biochemical Parameters	Khat chewer T2DM patients (n=50)	Non chewer T2DM patients (n=50)	P-value
FBS (mg/dl)	192.22±98.45	178.95±76.0	0.531
serum creatinine (mg/dl)	0.75±0.26	0.73 ±0.26	0.723
serum urea (mg/dl)	21.9 ± 10.9	23.4±10.5	0.502

Results are presented as mean ± standard deviation and $P<0.05$ is statistically significant (by Independent Samples Test). mg/dl- milligram per deciliter

4.2.3 Hematological indices

WBC counts of khat chewer participants (7.7±2.9 $x10^3$/ µL) were significantly higher than non chewers (6.7±1.5 $x10^3$/ µL). Among WBC differential, NEU% and LYM% counts showed non-significant reduction among khat chewer participants as compared to non chewers (table 4).

Table 4: Comparison of WBC indices

Biochemical Parameters	Khat chewer T2DM patients (n=50)	Non chewer T2DM patients (n=50)	P-value
WBC ($x10^3$/ µL)	7.7±2.9	6.7±1.5	**0.033***
NEU (%)	51.2±13.7	52.0±12.3	0.760
LYM (%)	36.5±12.5	36.7±9.4	0.922

Results are presented as mean ± standard deviation and P<0.05 is statistically significant (indicated in bold by independent sample t-test). µL-micro litter

PLT counts of khat chewer participants (291.28±77.7 $x10^3$/ µL) were significantly higher than non chewers (250.74±73.0 $x10^3$/ µL). From PLT indices MPV count of khat chewer participants (8.4± 2.2fL) were significantly lower than non chewers (9.6± 2.9fL) (table 5).

Table 5: Comparison of PLT indices

Biochemical Parameters	Khat chewer T2DM patients (n=50)	Non chewer T2DM patients (n=50)	P-value
PLT ($x10^3$/ µL)	291.28±77.7	250.74±73.0	**0.008***
MPV (Fl)	8.4±2.2	9.6±2.9	**0.019***

Results are presented as mean ± standard deviation and P<0.05 is statistically significant (indicated in bold by independent sample t-test). fL-femtolitre, µL-micro litter

Among RBC indices, HCT of khat chewer participants (44.3±5.6%) were significantly higher than non chewers (41.1±5.3%). On the other hand MCHC of khat chewer participants (32.3±2.4g/dl) was significantly lower than non chewers (34.1±1.8g/dl) (table 6).

RBC, HGB and MCV were non- significantly elevated among khat chewer participants as compared to non chewers. But MCH and RDW showed non-significant reduction among khat chewer participants as compared to non chewers (table 6).

Table 6: Comparison of RBC indices

Biochemical Parameters	Khat chewer T2DM patient(n=50)	Non chewer T2DM patient(n=50)	P-value
RBC ($x10^6$/ µL)	4.98±.74	4.70±.68	0.058
HGB (g/dl)	14.3±1.8	14.0±1.9	0.489
HCT (%)	44.3±5.6	41.1±5.3	**0.005***
MCV (FL)	89.9±10.3	87.8±6.8	0.233
MCH (pg)	29.0±3.7	29.9±2.7	0.133
MCHC (g/dl)	32.3±2.4	34.1±1.8	**0.000***
RDW (%)	13.7±3.9	13.9±1.9	0.674

Results are presented as mean ± standard deviation and P<0.05 is statistically significant (indicated in bold by independent sample t-test). fL-femtolitre , g/dl – gram per deciliter, µL-micro litter, pg – picogrem

5. DISCUSSION

DM is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by greater or lesser impairment in the metabolism of carbohydrates, lipids and proteins (Baynest, 2015). The number of patients with diabetes is increasing globally (Debecho *et al.*, 2017) and it is among the top 10 causes of death in adults worldwide (Saeedi *et al.*, 2019).

Ethiopia is among the top four countries with the highest adult diabetic populations in sub-Saharan Africa (Abebe and Addise, 2016). Kidney diseases was among the most frequently reported diabetes- associated problems of the country (Bishu *et al.*, 2019). In addition to DM some factors suspected to be the cause of the renal problems are drug abuse (Gitonga *et al.*, 2017). Due to its medical and socio-economic impact on the society, WHO has classified khat as a substance of abuse (Mwaniki *et al.*, 2014). In Ethiopia, khat chewing has deep rooted history as early as fourteenth century and is commonly used for social and religious purposes. Furthermore, it is considered as a recreational substance (Mulugeta, 2013). Khat has a potential adverse health effect on organs and systems of the body. It affects nervous system, cardiovascular system, reproductive system, gastrointestinal tract, liver, kidneys and others (Kindie *et al.*, 2015)**.**

The results of the present study indicated that the mean serum values of FBS level had shown statistically non-significant elevation among khat chewer participants as compared to non chewers. Our result was in line with studies done by Al-Sharafi and Gunaid (2015) that assessed the effect of khat on T2DM patients. Our result was also supported by Dallak et al. (2010) who reported that there were slight, non significant increases in blood glucose levels of khat extract-treated diabetic rats, as compared to the corresponding untreated rats. The current study contrasts with findings of Debecho et al. (2017) who reported that oral

administration of crude extract of khat exert a hypoglycemic effect in normal and Streptozocin (STZ) induced type 2 diabetic rats.

The elevation of blood glucose level observed in khat chewer T2DM patients could be a result of Sympathomimetic actions of cathinone (Debecho *et al.*, 2017). It might be also due to chewing pesticide and herbicide sprayed khat which would have an influences on carbohydrate metabolism (Hadrani and Hoot, 2000).

Our results regarding serum creatinine showed statistically non-significant elevation among khat chewer participants as compared to non chewers. Even though there was non- significant elevation in serum creatinine concentration among khat chewer, our result was in line with study done by Alam et al. (2014) who reported that the concentration of serum creatinine, urea and uric acid was significantly higher in khat users than the non-users. Our result was also supported by Gitonga et al. (2017) who reported that there was an increased level of serum creatinine and urea in all albino mice exposed to Khat extract. In contrast to this, Mworia et al. (2016) reported that total protein and creatinine concentration were significantly decreased in the serum of khat consumers as compared to non-consumers. The increased serum creatinine concentration in khat chewer T2DM patients could be due to khat induced renal vasoconstriction and decrease glomerular filtration rate (Al-mahdar *et al,* 2009).

Concerning serum urea concentration, the mean level for khat chewer participants was slightly lower than non chewers. This result is in contrary to Alam et al. (2014) who reported that the concentration of serum urea was significantly higher in khat users than the non-users. Our result was also not in line with Al-Mehdar et al. (2009) who reported that the oral administration of khat in guinea pigs resulted in significant increase in plasma urea and creatinine concentrations compared with normal control. A reduction in serum urea concentration among khat chewer

T2DM patients might be due to sympathomimetic action of cathinone in khat which result in khat-induced delay of gastric emptying (Kindie *et al*, 2015). Delay to intestinal absorption contributes to some degree to malnutrition. Tannins and norpseudoephedrine contribute to malnutrition and constipation, the most common medical complaint of the khat user (Gashaw and Getachew, 2014).

Regarding hematological profile, WBC count showed statistically significant elevation among khat chewer participants as compared to non chewers. The result of this study was in line with Kennedy et al. (2020) who reported that WBC count was markedly elevated by khat in mouse model and it also agree with Alsalahi et al. (2012) who reported that there was an elevation in WBC count in both male and female Sprague-Dawley rats group treated with khat. But the current study contrasts with findings of Ismaeel et al. (2014) who reported that khat extract caused a statistically significant decrease in total WBC count in rats. Our result also contrasts with findings of El-amin et al. (2014) who reported that hematological profile were not affected by khat chewing except platelet count in Yemeni individuals.

The significant elevation of total WBC count among khat chewer participants in the current study might imply that khat has immune potentiating property (Ketema *et al.*, 2015). The presences of phytochemicals like flavonoids, alkaloids, tannins and terpenes in khat leaf extracts may be responsible for the haemopoietic stimulating effects (Jorum and Piero, 2016). Flavonids in khat are able to activate immune cells such as mast cells, basophils, neutrophils, eosinophils, T and B lymphocytes, macrophages and others. Alkaloids in khat are supposed to play stimulatory role responsible for immune modulation (Ketema *et al.*, 2015).

Among WBC sub type NEU and LYM counts showed statistically non significant reduction among khat chewer participants as compared to non chewers. The result

of this study was in line with study done by El-amin et al. (2014) who reported that NEU and LYM count showed non-significant decrease in khat chewers group compared to that of control in Yemeni individuals**.** Our result contrast with the finding of Kennedy et al. (2020) who reported that NEU and LYM count were significantly elevated in khat treated mouse model. The decrease in the number of NEU and LYM count in the peripheral blood of khat chewer might be due to the fact that these cells migrate to the affected damaged tissue after khat intoxication (Ismaeel *et al.*, 2014).

Our results regarding platelet count showed statistically significant elevation among khat chewer participants as compared to non chewers. This was in line with Ismaeel et al. (2014) who reported that oral administration of a hydro-ethanol extract of khat to rats induced a statistically significant elevation in platelet count. This study was in contrary to the reports of El-amin et al. (2014) who reported platelets count was significantly reduced among khat chewer Yemeni individuals. The significant increase in platelets count in the current study might suggest that the khat contain compounds and phytochemicals that may have stimulated thrombopoietic process. These indicate that khat phytochemicals had a megakarypoietic stimulatory activity (Muriithi *et al.*, 2015). A significant increase in platelets count among khat chewer participants also might be attributed to presence of tannins in khat which have been shown to confer anti-hemorrhagic properties in animals (Jorum and Piero, 2016)**.** MPV was significantly reduced among khat chewer participants as compared to non chewers. This decrease in MPV might be due to kidney problem associated with khat chewing (Korniluk *et al.*, 2019)**.**

Regarding RBC, HGB and HCT, the result of the present study showed a significant elevation in HCT and non significant elevation in RBC and HGB among khat chewer participants as compared to non chewers. This result was in

line with Ketema et al. (2015) who reported an elevation in RBC count of Swiss albino mice treated with khat and cathinone extract. Our result was also supported by Alsalahi et al. (2012) who reported non- significant increase in HGB in male and female Sprague-Dawley rats treated with khat extract. This result was also supported by El-amin et al. (2014) who reported non- significant elevation in HCT among khat chewer group as compared to control in Yemeni individuals. Our finding was in contrast with Ismaeel et al. (2014) who reported that oral administration of a hydro-ethanol extract of khat to rats induced a statistically significant decrease in RBC, HGB and HCT. It was also in contrast with Kennedy et al. (2020) who reported that exposure to khat resulted in microcytic anemia as depicted by the decreased levels of HCT and RBC indices in mouse model.

The increase in RBC, HGB and HCT concentration among khat chewer participants might suggest that khat may contain phytochemicals and compounds that stimulate the secretion or formation of erythropoietin (Jorum and Piero, 2016). Stimulation of stem cells in the bone marrow to produce red blood cells occurs due to the action of erythropoietin (Gitahi *et al.,* 2015). The presence of antioxidant phytochemicals like flavonoids and tannins in khat may be responsible for the haemopoietic stimulating effects (Jorum and Piero, 2016). RBC might be protected from oxidative damage by flavonoids, tannins and terpenes content of khat (Muriithi *et al.,* 2015).

MCV had shown statistically non-significant elevation among khat chewer participants as compared to non chewers. This result was supported by Ismaeel et al. (2014) who reported that khat treated rats showed a marked increase in the value of MCV. The current study contrasts with findings of Kennedy et al. (2020) who reported exposure to khat resulted in microcytic anemia as depicted by the decreased levels of HCT ,RBC and MCV in mouse model. The increase in MCV

level of our study might be due to an increase in RBC count (Jorum and Piero, 2016).

The results of the present study also indicated that the mean value of MCHC showed statistically significant reduction among khat chewer participants as compared to non chewers and MCH had showed statistically non significant reduction among khat chewer participants as compared to non chewers. The reduction in MCH and MCHC among khat chewer participants might be due to inhibitory effect of plant phytochemicals on hemoglobin incorporation into red blood cells and a consequent reduction in oxygen exchange (Jorum and Piero, 2016).

RDW had showed statistically non significant reduction among khat chewer participants as compared to non chewers. This result agrees with study done by Kennedy et al. (2020) who reported that administration of khat decreased the level of RDW in mouse model. Our result was in contrast with Ismaeel et al. (2014) who reported oral administration of a hydro-ethanol extract of khat to rats induced a statistically significant increase in the value of RDW. The reduction in RDW among khat chewer participants might be due to phenolic and flavonoids content of khat which are responsible for anti-inflammatory action (Abdelwahab *et al.*, 2018).

6. CONCLUSION

The effect of khat chewing on human health is controversial and studying its effect is very important. To this end, the present study on T2DM patients tries to address the effect of Khat chewing on FBS, renal function and hematological profile. The result obtained from this study showed non- significant elevation of serum FBS level and creatinine concentration among khat chewer T2DM patients and this could indicate that khat chewing might have an effect on FBS level and kidney function.

The significant increase in total WBC, PLT and HCT and non significant elevation in RBC, HGB and MCV among khat chewer T2DM patients might indicate that chewing khat may promote the immune-stimulatory activities, erythrocytes and thrombocytes production. However, a significant reduction in MCHC and non significant decrease in MCH among khat chewer T2DM patients might indicate that khat may has inhibitory effect on hemoglobin incorporation into red blood cells and might result in consequent reduction in oxygen exchange.

From this study we can conclude that chewing khat might have an effect on FBS level, kidney function and hematological profile. Hence, it can be taken as a base line study and might require further study on large group of participants to just improve the lives of type 2 diabetic people and also to address other effect of khat chewing on health.

7. STRENGTH AND LIMITATIONS OF THE STUDY

7.1. Strength of the present study

- It was the first study to investigate the effect of khat on FBS level, renal function and hematological profile among khat chewer and non chewer T2DM patients.

7.2. The limitations in the present study include

- Since this is a short cross- sectional study we could not follow up our patients for long duration of biochemical progression due to limitation of money and time.
- We couldn't exclude some factor that might affect renal function and hematological profile such as hypertension, heart failure, hepatitis, respiratory problem, infection and other hematological disorder.

8. RECOMMENDATION

- Health institutions and researcher should plan further study with large sample size to investigate effects of khat chewing on FBS, renal function and hematological profile among healthy individual.
- It will be appropriate to experiment long term effects of crude khat extract on FBS level, kidney function and hematological indices.
- To understand short and long term effect of khat chewing prospective and cohort studies should be in place.
- A proper awareness and health education needs to be given to T2DM patients and the whole public regarding the effect of khat chewing.

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ANNEXS

Annex I: - Information sheet (English version):

Principal Investigator: Tewekel Reshid

Addis Ababa University

College of Health Science

Department of Medical Biochemistry

Dear participant! Here, I the undersigned, at Addis Ababa University College of Health Sciences, Department of Medical Biochemistry, graduate Study Program, currently undertaking a research on a topic entitled as, 'Assessment of renal function and hematological profile among khat *(catha edulis)* chewer and non chewer type 2 diabetes mellitus patients attending Harar Jugol Hospital, Eastern Ethiopia' For this study, you will be selected as a participant and before getting your consent, you need to know all necessary information related to the study whose detail is explained as follows.

Introduction

Privacy is the state of being free from intrusion, and in the context of health care it concerns the responsibility of a care provider to protect a client from any disclosure to third party (i.e., discovery by others), even unintentional, of personal health data, by providing security to the patient and the patient's records. Confidentiality, in contrast, is the limiting of information to only those for whom it is appropriate. Therefore, this information sheet briefly provides the necessary guide to be considered during the study.

Objective: the main aim of this study is to compare FBS, renal function and hematological profile among khat (*Catha edulis)* chewer and non chewer type 2 DM patient attending Harar Jugol Hospital, Eastern Ethiopia during the study period.

Participants to be included: All adult type 2 diabetic patients receiving oral hypoglycemic agent through simple random sampling techniques will be included in the study.

Risks and discomfort: Participant in this project will not cause more discomfort and no need of extra sample other than sample taken for diagnostic purpose. But, there could be minor pain and challenge in color of your skin following the blood drawing. The amount of blood taken from each volunteer throughout the study period is 5ml which will not affect your health. There is no major risk in participating in this research, as the whole procedure is carried out by physician and /or health professionals following the standard good clinical practice.

Benefits:-There is no immediate benefit from participating in this study. However, you will have the chance to know your Kidney health status from the laboratory result. And if your result reveals any incidental health problems that need immediate treatment, you will be referred to an appropriate health facility. In addition, your participation will contribute in improving the health delivery system for DM patients.

Incentive:-There is no financial or material incentive for participating in this study.

Confidentiality: The information that we will collected from this research project will be kept confidential. Information about you that will be collected from the study will be stored in a file, which will not have your name on it, but a code number assigned to it. Which number belongs to which name will be kept under lock and key, and it will not be revealed to anyone except the principal investigator**.**

Participant Rights

Your participation is entirely voluntary and up to you to decide. There is no penalty if you do not agree to participate. Also you have the right not to answer any questions you do not want to. You may also withdraw from the study at any

time. If in the middle you decide to stop filling questions and no longer participate, you can stop without worry.

Persons to contact:

If you have any question, you can ask at any time. If you have additional questions about the study, you can contact the:

Principal investigator: Tewekel Reshid cell phone-0921157600, E-mail tewekelch@gmail.com Thank you for your cooperation.

If you are voluntary to participate in the study we kindly request you to provide your response for the questionnaire in the next page.

Annex II: - Information sheet (Amharic version)

የተሳታፊዎች የፈቃደኝነትና መተማመኛ መረጃ መስጫ ቅፅ

በአዲስ አበባ ዩኒቨርሲቲ የጤና ሳይንስ ኮሌጅ የሕክምና ባዮኬሚስትሪ ትምሕርት ክፍል፡
እኔ □□□□ □□□ በአዲስ አበባ ዩኒቨርሲቲ ጤና ሳይንስ ኮሌጅ የህክምና ባዮኬሚስትሪ የድህረ ምረቃ ተማሪ ስሆን የመመረቂያ ጽሁፌን ‘Assessment of renal function and hematological profile among khat *(catha edulis)* chewer and non chewer type 2 diabetes mellitus patients attending Harar Jugol Hospital, Eastern Ethiopia’ በሚል ርእስ በመስራት ላይ ነኝ። ለዚህ ጥናት ደግሞ እርስዎ የተመረጡ ስለሆነ ክዚህ ቀጥሎ የሚገኘዉነ መረጃ አንብበዉ በጥናቱ ላይ መስማማትዎን ወይም አለመስማማትዎን እንዲያረጋግጡ በትህትና እጠይቃለሁ።

መግቢያ፡- ጥናቱ ከእርሶ የሚወስዳቸዉ ማንኛዉም መረጃወች ሚስጥራዊነት ሙሉ በሙሉ የተጠበቀ ሲሆን እርሶ በጥናቱ አለመሳተፍም ሆነ በማንኛዉም ሰአት ተሳትፎዎን ማቋረጥ ይችላሉ።

የጥናቱ አላማ፡- የጥናቱ ዉጤት ለስካር ህሙማን ጤና እንክብካቤ የሚጠቅም ሲሆን በጥናቱ ላይ የሚያደርጉት ተሳትፎ ሙሉ በሙሉ በእርሶ በጎ ፈቃደኝነት ላይ የተመሰረተ ነዉ። በጥናቱ ለመሳተፍ ፍቃደኛ ሲሆኑ ለናሙና ይሆን ዘንድ አምስት ሚሊ ሊትር ያህል ደም በሆስፒታሉ የጤና ባለሙያዎች አማካኝነት የሚሰጡ ሲሆን ናሙና በሚሰጡበት ጊዜ ሁልጊዜ ለምርመራ ክሚሰጡት የተለየ ህመም እና አለመመቸት የለዉም።
ከጥናቱ ጋር በተያያዘ ጥያቄ ቢኖርዎ ወይም ችግር ቢያጋጥሞ በማንኛዉም ሰአት በሞባይል ቁጥር **0921157600** □□□□ □□□ ብለዉ ይደዉሉ ወይም በኢሜል አድራሻ **tewekelch@gmail.com** መላክ ይችላሉ።

በጥናቱ ለመሳተፍ ፈቃደኛ ከሆኑ እባክዎ ከዚህ ቀጥሎ ባለዉ የስምምነት ቅጽ ላይ በመፈረም ይተባበሩ።
እናመሰግናለን!!!

Annex III: - Consent form English version

In undersigning the aim of the project, I am giving my consent to participate in the study entitled as, 'Assessment of renal function and hematological profile among khat *(catha edulis)* chewer and non chewer type 2 diabetes mellitus patients attending Harar Jugol Hospital, Eastern Ethiopia' I have understood that participation in this study is entirely voluntarily. I have been told that my answers to the questions will not be disclosed to anyone else and no reports of this study never identify me in any way. I have also been informed that my participation or non-participation or my refusal to answer questions will have no effect on me. I understood that participation in this study does not involve risks. I understood that Tewekel Reshid is the contact person if I have any question about the study or about my rights as a study participant.

Respondent's signature_____

Interviewer Name _____

Signature _____Date_____

Annex IV: - Consent form (Amharic version)

የፈቃደኝነት ማረጋገጫ ቅጽ

የምርምር ጥናቱ ክፍል የሆኑ መረጃዎችና ሂደቶች ከተብራሩልኝ በኋላ ‘Assessment of renal function and hematological profile among khat *(catha edulis)* chewer and non chewer type 2 diabetes mellitus patients attending Harar Jugol Hospital, Eastern Ethiopia’ በሚል ርዕስ በተዘጋጀው ጥናታዊ ፅሁፍ ለመሳተፍ ሙሉ ፈቃደኝነቴን አሳይቻለሁ። እኔም በተብራራልኝ መንገድ ተረድቻለሁ። ምርምሩ ምንም የተለየ የገንዘብ ጥቅማ ጥቅም የሌለው፣ አደጋ የማያስከትል መሆኑን እንዲሁም የሚደርገው ተሳትፎ እና መረጃ በሚስጢር የሚያዝና ለማንም ተላልፎ የማይሰጥ መሆኑን ተረድቻለሁ። ስለዚህ በዚህ የምርምር ጥናት ላይ ለመሳተፍ ፈቃደኛ መሆኔን በፊርማዬ አረጋግጣለሁ።

የተሳታፊው ፊርማ ----------

የመረጃ ሰብሳቢው ስም---------- ---------ፊርማ----------ቀን ----------

Annex V: -**Questioner in English**

Part 1: Personal information: please make a circle" on the options that best describes you.

Patient Code; …….

1. Gender: A. Female B. Male

2. Age in year: _____

3. Residential area: A. Rural B. Urban

4. Khat chewing status: A. Frequently B. Sometimes C. Never

Part 2: History of diabetes and kidney diseases

1. Duration of diabetes: A. <5 year B. 5-10 year C. >10 year

2. Treatment Regimens: A. Sulfonylurea B. Biguanides/metformin C. Metformine+ Sulfonylurea

3. Family History of kidney diseases A. Yes B. No

Part 3: Anthropometric measurements

A. Height _____cm

B. Weight _____kg

C. BMI _____kg/m2

D. Blood pressure _____mmHg

THANK YOU FOR YOUR PARTICIPATION!!!

Annex VI: - Questionnaire in Amharic

ክፍል አንድ ;- ግላዊ መረጃ ፡- ከዚህ በታች እርስዎን በትክክል የሚገልጽዎትን ክብ ያድርጉ

የተሳታፊው ሚስጥራዊ ቁጥር፡- .....

1. ፆታ ፡- ሀ. ወንድ ለ. ሴት

2. ዕድሜ በዓመት _____

3. የመኖሪያ ቦታ ;- ሀ. ከተማ ለ. ገጠር

4. ጫ ት ይቅማሉ ;- ሀ. ሁሌ እቅማ ለው ለ.አልፎ አልፎ እቅማ ለው ሐ. አልቅምም

ክፍል ሁለት;- የስኪር የኩላሊት ህመምን በተመለከተ

1. የስኪር በሽታ ካመመዎት ስንት አመት ሆነዎት: ሀ. ከ5 ዓመት በታች ለ. ከ5-10 ዓመት ሐ) ከ10 ዓመት በላይ

2. የሚዎስደት የመድሃኒት አይነት ሀ. ሳልፈነዩሪያ ለ. ሜትፎርሚን ሐ. ሳልፈነዩሪያ + ሜትፎርሚን

3. የኩላሊት ሕመም ታማሚ የሆነ የቤተሰብ አባል አሎት ሀ. አለኝ ለ. የለኝም

ክፍል ሶስት;- አካላዊ ምርመራን በተመለከተ

1.ቁመት (በሜትር) .....

2.ክብደት በኪሎ ግራም.....

3. የሰውነት ክብደት ልኬት (ኪ.ግ./ሜ2).....

4. የደም ግፊት ልኬት .....

ለትብብርዎ በጣም እናመሰግለን!