Addis Ababa University

College of Health Sciences

School of Medicine

Department of Medical Physiology

The Magnitude of Hyperuricemia and Associated Factors Among Adult Type II Diabetes Mellitus Patients with Central Obesity in Woldia Comprehensive Specialized Hospital, North-East Ethiopia, 2023.

By

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APPROVAL SHEET

This thesis by Habtemariam Mulugeta Abate is accepted in its present form by the board of examiners, satisfying the thesis requirement for the degree of Master in Medical Physiology.

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DECLARATION

I declare that “Magnitude of Hyperuricemia and Associated Factors Among Adult Type Two Diabetes Mellitus Patients with Central Obesity in Woldia Comprehensive Specialized Hospital, Woldia, Ethiopia, 2023” is my work and that all the resources that I have used or quoted have been indicated and acknowledged through complete resources. This work has not been submitted to any other institution.

Principle Investigator

Name	Rank	Signature	Date
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ABBREVIATIONS

AOR	Adjusted Odds Ratio
BMI	Body Mass Index
CBHE	Community-Based Health Insurance
CI	Confidence Interval
CO	Central Obesity
COR	Crude Odds Ratio
DASS-21	Depression Anxiety Stress Scale 21
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
FBS	Fasting blood glucose
HDL	High-Density Lipoprotein
HbA1C	Hemoglobin A1C
HTN	Hypertension
HUA	Hyperuricemia
IQR	Inter Quartile Range
LDL	Low-Density Lipoprotein
MMAS-8	Morisky Medication Adherence Scale-8
SBP	Systolic Blood Pressure
SD	Standard Deviation
SPSS	Statistical Product & Service Solutions
SCr	Serum Creatinine
SUA	Serum Uric Acid
T2DM	Type Two Diabetes Mellitus
TC	Total cholesterol
TG	Triglyceride
WCSH	Woldia Comprehensive Specialized Hospital
WHO	World Health Organization

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ABSTRACT

Background: Hyperuricemia is an abnormally high level of uric acid in the blood. It has been linked to several disease conditions including metabolic syndrome, diabetes mellitus, kidney disorder, and gout both in females and males. Few studies exist that explored the prevalence of hyperuricemia instigated thru Type II diabetes mellitus with central obesity in Ethiopia.

Objective: To assess the magnitude of hyperuricemia and associated factors among adult type-two diabetes patients with central obesity in Woldia Comprehensive Specialized Hospital, North-East Ethiopia, 2023.

Methods: An institution-based cross-sectional study was employed at Woldia Comprehensive Specialized Hospital from May 8 to July 7, 2023, with a total sample size of 423. Convenience sampling was employed. Face-to-face interviews, review of patient's medical records, laboratory tests, anthropometry, and blood pressure measurements were implemented. The data were entered via Epi-Data (version 4.6.0.6), and exported to Statistical Product and Service Solutions (version 26) for analysis. The bivariable and multivariable binary logistic regression analysis model was fitted to determine the associated variables of Hyperuricemia. The adjusted odds ratio (AOR) with a 95% confidence interval (CI) was calculated. Variables having a p-value of < 0.05 were considered statistically significant.

Results: The magnitude of hyperuricemia in the study subject was 37.2 % (95% CI 32.9 – 42.2). Age ≥ 45 years (AOR = 1.670, 95% CI = 1.020 – 2.732), male gender (AOR = 1.754, 95% CI = 1.075 – 2.861), duration of diabetes mellitus ≥ 10 years (AOR = 2.310, 95% CI = 1.074 – 4.972), diastolic blood pressure ≥ 80 mmHg (AOR = 3.437, 95% CI = 1.748 – 6.758), serum creatinine ≥ 1.2 mg/dl (AOR = 2.347, 95% CI = 1.154 – 4.771), total cholesterol ≥ 200 mg/dl (AOR = 2.362, 95% CI = 1.300 – 4.292), alcohol consumption (AOR = 3.320, 95% CI = 1.557 – 7.081) were found to be significantly associated with hyperuricemia.

Conclusion: Results in this study revealed that diabetic patients with central obesity in and around Woldia region demonstrated significantly higher levels of hyperuricemia. Significant associations between hyperuricemia and factors like age, creatinine, diastolic blood pressure, total cholesterol, alcohol consumption, and duration of DM were also recorded. Lifestyle changes, health education, and regular screening shall be implemented to prevent hyperuricemia in centrally obese DM patients in Woldia region.

Keywords: Central Obesity, Diabetes mellitus, Hyperuricemia, Magnitude, Woldia, Ethiopia

1. INTRODUCTION

1.1 Background

Serum uric acid (SUA) levels should not exceed the typical maximum limits of 7.2 mg/dL for males and 6 mg/dL for females; anything above is regarded as saturated, and symptoms may develop. Increased uric acid generation, reduced uric acid excretion, or a combination of both processes are responsible for this excessive level. An abnormally high blood uric acid level is known as hyperuricemia (HUA) (1,2).

Accelerated purine breakdown under conditions of rapid cell turnover and reduced excretion are further signs of elevated SUA. Moreover, it has been linked to conditions including metabolic syndrome, diabetes mellitus (DM), cardiovascular disease, and chronic renal disease as indicators (1,3).

The chronic metabolic disorder commonly referred to as DM has been defined by persistent hyperglycemia. It might be brought on by decreased insulin production, insulin resistance, or both. About 415 million persons between 20 and 79 years old had DM in 2015 (4). By etiology and clinical manifestation, DM may be categorized into type one diabetes, type two diabetes, and gestational diabetes. Monogenic and secondary diabetes are a few of the additional less typical kinds of diabetes (5,6).

Type two diabetes mellitus (T2DM) previously identified as adult-onset diabetes indicated by elevated plasma sugar, resistance of insulin, and a relative shortage of insulin. Amplified thirst, recurrent micturition, and mysterious loss of weight are its typical symptoms. The leading causes of T2DM include being overweight and not exercising. Genetically speaking, some people are more vulnerable than others. Moreover, among all the cases of DM about 90% is T2DM (7,8).

Central obesity (CO) particularly characterized by extra fat build up in the belly to the point that it might harm one's health or cause further medical issues, is closely linked to the manifestation of T2DM (9). CO is linked with insulin resistance, mainly affecting skeletal muscle, adipose tissue, and the liver. In particular, abdominal fat secretes hormones called adipokines, which may reduce glucose tolerance (10,11).

A study conducted in Japan found that CO was linked to HUA in both men and women, especially in those who were normal weight (12). There is a reciprocal relation between obesity and HUA; obesity raises the synthesis of SUA and reduces its excretion, which results in HUA (13). Additionally, oxidative damage, inflammation, and resistance of insulin brought on by obesity might raise SUA levels (14). By speeding up peripheral and hepatic lipogenesis, which results in weight gain and fat deposition, HUA induces obesity. In addition to enhancing hunger and impairing glucose metabolism, HUA can also lead to obesity (15). It is crucial to measure central fat distribution to identify health hazards early on, especially in those who are of normal weight (12).

1.2 Statement of the Problem

The magnitude of HUA has significantly grown globally during the past several decades. The majority of patients with HUA are symptomless, about one-quarter of hospitalized patients and up to 21% of the general population are thought to have asymptomatic HUA (1,16). Various studies have shown diverse instances of HUA in people with T2DM who possess CO, such as in China the overall prevalence of HUA was 32.6% (17). In Africa, T2DM patients as a whole had a prevalence of HUA of 27.28%. The frequency was 33.72% in Central Africa and 24.72% in North Africa, respectively. Regarding gender, 28.02% and 28.20% of T2DM were female and male with HUA, respectively (18). Similarly, in southwest Ethiopia, 33.8% of T2DM individuals had HUA (19).

Hyperuricemia is possibly a serious disorder with risks of mainly complications related to nephrolithiasis and gout but it also possesses some potential ramifications including bone loss, chronic kidney disease, HTN, tophi deposits, skin rashes, allopurinol sensitivity syndrome, loss of mobility, restricted range of motion, joint damage and deformity (1).

Hyperuricemia also leads to an unfortunate prognosis and rise of DM complications including diabetic neuropathy, retinopathy, and nephropathy, raising the risk of morbidity and mortality that can affect their family members financially and emotionally (18). Each 0.1 mmol/l rise in SUA was linked to a 28% increase in the risk of diabetes vascular complications and a 9% increase in the risk of diabetic mortality (2,18,20). Moreover, an estimated 3.4 million people died of poor DM prognosis, among those > 80% of diabetes mellitus demises happen in low- and middle-income nations (7).

HUA might increase medical costs for diagnostic and therapeutic management of complications like diabetes and chronic renal disease, which has a significant impact on healthcare costs. In addition, it could necessitate lifestyle adjustments, including dietary adjustments and medication compliance, which might influence workplace productivity, social activities, and relationships. Furthermore, there could be a need for nutritional limitations, including limiting the consumption of foods high in purines, which might vary depending on national dietary customs (2,17,21).

High blood pressure, hyperglycemia, and abnormal cholesterol levels are some of the major determinant factors affecting HUA among T2DM patients with CO. An increased risk of HUA is shown in T2DM patients who are older, females, and have had diabetes for a more extended period. Hyperuricemia was linked to several cardiovascular risk factors such as HTN, dyslipidemia, and renal failure which in turn are linked to other factors of HUA (2,19,20,22–24).

Lifestyle modifications such as alterations in diet, drop in alcohol intake, and workout, were the first line of treatment for the vast majority of HUA-affected individuals except for the oncologic set that individuals getting cytolytic treatment. Regarding pharmacotherapy, the main aim is to reduce morbidity and prevent complications that also depend on whether patients are overproducers or under-secretors. Furthermore, together with lifestyle interventions, medical treatment options such as non-steroidal anti-inflammatory drugs, glucocorticoids, uricosuric agents, xanthine oxidase inhibitors, recombinant uricase drugs, and more were suggested (1,16).

The research done among different scholars shows inconsistency and contradictions regarding HUA, like the difference in inclusion criteria, and especially the factors that affect HUA; as in some studies, some factors become a significant predictor of HUA & show a positive relation with HUA, whereas in others studies vice versa.

To the best of the authors' knowledge, no similar research has been done in the study area. Furthermore, unlike most related research done in other countries, new predictor variables like medication adherence, khat consumption, depression, anxiety, and stress were added. Moreover, studies in different countries show inconsistency and contradictions and do not profoundly explore factors that may affect HUA. Furthermore, some studies showed

methodological feebleness that can affect the study output, like having a relatively small sample size. Hyperuricemia can harm the quality of life, and daily tasks, and increase expenditure for medication, but the burden of elevated plasma uric acid in T2DM patients with CO and even in the general population of Ethiopia has not been quantified. As a result, the purpose of this study was to determine the magnitude of hyperuricemia and its associated factors among adult type-two diabetes mellitus patients with central obesity in Woldia Comprehensive Specialized Hospital, Woldia, Ethiopia, 2023.

1.3 Significance of the Study

An increased uric acid level in the plasma which is known as hyperuricemia is a common disorder that touches patients of all ages and sex. Various socio-demographic, clinical, behavioral, and psychosocial factors have been identified as risk factors for HUA.

Type 2 diabetes mellitus patients with CO face a variety of routine and psychosocial pressures due to factors including poor healthcare access, comorbidities, and their treatment along with financial burden that can directly or indirectly cause new or aggravate the preexisting problems they possess. Even though hyperuricemia can impair one's quality of life, daily tasks, and financial resources directly or indirectly in T2DM patients with CO, there is no publicly available data on the magnitude of HUA in Ethiopian T2DM patients with CO.

The findings of this study will be valuable for various stakeholders in creating awareness, adding value to the existing literature, filling a research slit, and providing insight into the magnitude of HUA in the T2DM patient with CO. Furthermore, the findings of this study will provide information to stakeholders in the future as they develop prevention strategies, care, and early treatment for the disease. Moreover, the findings of this study will serve as a baseline for other researchers interested in this area.

2. LITERATURE REVIEW

2.1 Overview of Diabetes Mellites & Hyperuricemia

A chronic metabolic condition called diabetes mellitus (DM) is characterized by excessive blood sugar levels brought on by inadequate or resistant insulin. Over 463 million individuals are affected globally, and its prevalence is rising. The three main kinds of DM are type 1, type 2, and gestational diabetes. When insulin-producing pancreatic beta cells are destroyed, type 1 diabetes develops, which results in a complete lack of insulin. Beta cell dysfunction and insulin resistance are the two main characteristics of T2DM, making up 90% of all disease cases. Gestational diabetes develops during pregnancy and typically goes away after delivery, but it raises the possibility of developing T2DM later on. Cardiovascular disease, retinopathy, neuropathy, nephropathy, and foot ulcers are among the side effects of DM. Together with drugs like insulin and oral hypoglycemic agents, lifestyle changes like diet and exercise can help manage DM and stop its consequences (7,8,25).

A plasma uric acid level greater than 6.8 mg/dL is considered to be HUA. It is characterized by increased blood levels of uric acid, which is linked to several illnesses, including gout, kidney stones, heart disease, and DM. Even though uric acid was discovered over 200 years ago, certain pathophysiologic elements of HUA still need to be addressed. For many years, gout has been associated with or assumed to be the same as HUA. Nevertheless, uric acid is a marker for several problems in metabolism and hemodynamics. Uric acid is a weakly soluble end product of purine metabolism in humans as opposed to allantoin, which is the more soluble result of purine metabolism in lower species (1,16,26).

Two-thirds of the body's urate is generated endogenously, with the remaining one-third coming from dietary purines. The kidneys expel around 70% of the daily urate production, while the intestines eliminate the remaining 30%. The intestinal contribution to urate excretion rises with renal failure to compensate for the kidneys' reduced ability to excrete urate. The balance between the rate of uric acid excretion and purine breakdown determines the uric acid levels in the blood. Although most cases of HUA are caused by clinically deficient elimination, changes in this equilibrium theoretically might explain HUA. Patients with T2DM who are centrally obese or overweight frequently experience HUA. Diabetes and its long-term consequences,

such as cardiovascular illnesses, metabolic syndrome, insulin resistance, and diabetic macroangiopathy, are all intimately correlated with HUA (1,16,26).

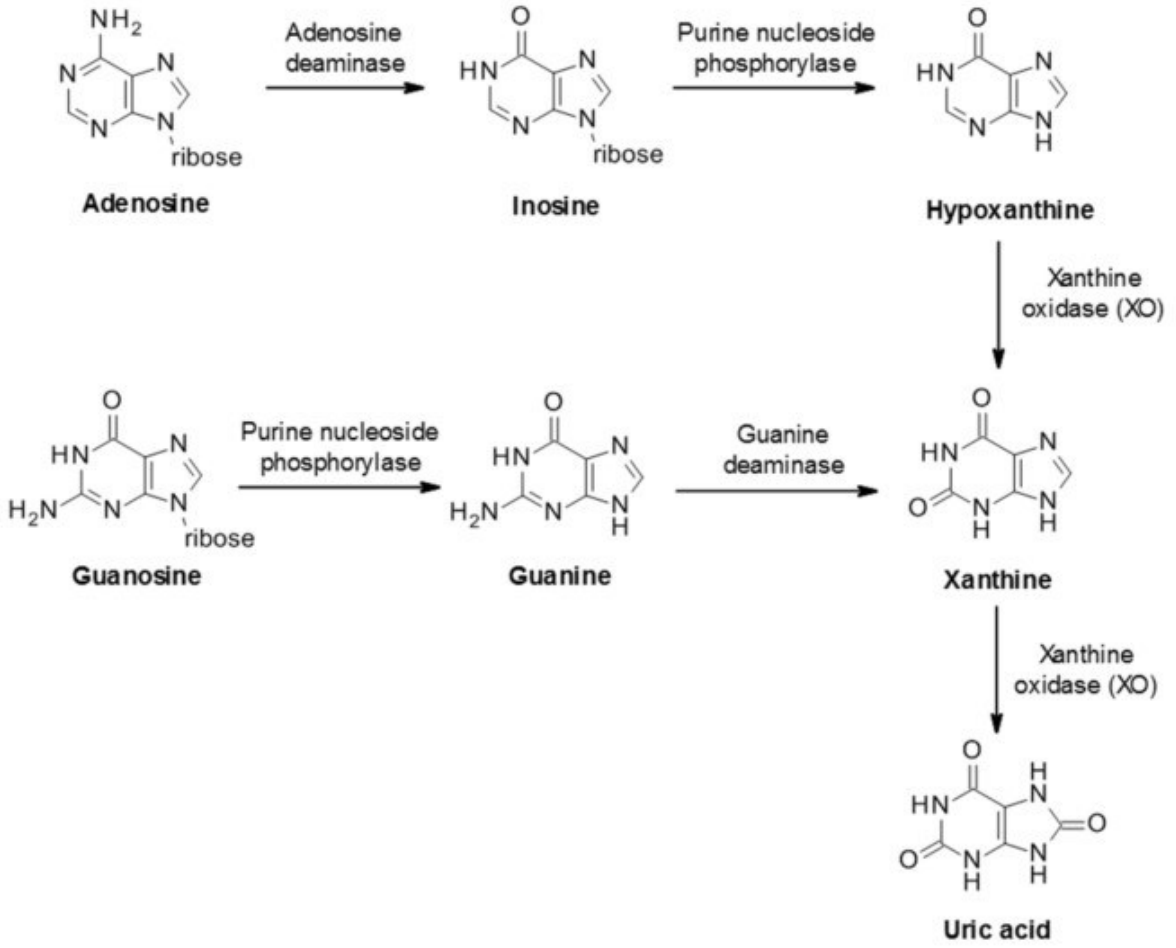

Figure 1: Biosynthesis of uric acid from purines (27).

2.2 Magnitude of Hyperuricemia Among Adult Type Two Diabetes Mellitus Patients

The incidence of HUA significantly varies among places in the world, according to the systematic review of population-based epidemiological studies the incidence of the condition was 22% in females and 21% in males in High Income North America, compared to 9–12%, 5–11%, and 10–16% in Italy, Spain, and Sweden respectively. Although HUA was comparatively more common in Asia (High Income Asia Pacific: Japan 4% in 1980s / 20-26% in 2000s, South Korea 5%, Central Asia: Mongolia 5% in Females & 18% in Males, East Asia:

China 6-25%, Taiwan 10-52%, Southeast Asia: Indonesia 18%, Philippines 25%, Seychelles 25%, Thailand 9-11%), the least reported incidence (Papua New Guinea 1%) and the most remarkable reported occurrence (Marshall Islands 85%) were both in Oceania (28).

The prevalence of HUA was in Italy 54.1% (29), Romania 26.3% (30), India 13.43% (31), New Delhi 46% (32), India 33.8% (33), Jordan 28.1% (34), Saudi Arabia 80% (35), Riyadh 25% (36), Tianjin, 17.25% (37), Guangdong Province 32.6% (17), Africa 27.28%, Inner Africa, 33.72%, North Africa, 24.72 % (18), Casablanca 26.5% (38), West Cameroon 27.5% (39), Cameroon 38.1% (40), Jimma 22% (2), Hawassa 33.8% (19), and Gondar 31.5% (24).

2.3 Factors Affecting Hyperuricemia Among Type Two Diabetes Mellitus Patients

2.3.1 Sociodemographic Characteristics

Studies in China, Taiwan, India, Tianjin, Jordan, Jimma, Hawassa, Gondar, and China showed that age had a positive statistically significant relation with HUA (2,19,24,34,37,41–44). Research led in China, Dschang, India, Casablanca, Jordan, and Saudi Arabia displayed that the female sex had a statistically significant relationship with HUA compared to the male sex (32,34,36,38,39,43,44). Whereas the study done in Maharashtra, Dhaka, and Jimma showed that Male sex had a statistically significant relationship with HUA compared to female sex (2,33,45).

A Center for Disease Control and Prevention study found that DM was more common in low-income populations in the United States between 2001 and 2018, indicating income-related disparities in DM. Furthermore, a survey of a rural population in Brazil discovered that marital status was the only factor independently linked to the incidence of T2DM. Married people were much less likely to get diabetes than divorced people, even though they had meaningfully enlarged their mass. It's also important to remember that DM and HUA are complicated diseases that can impact various variables, such as access to treatment, nutrition, lifestyle, and heredity. Therefore, among the several factors influencing the incidence of HUA among patients with T2DM are characteristics such as residency, CBHI enrollment, average monthly income, occupational status, educational background, and marital status. It's also important to

remember that T2DM individuals' HUA must be reduced by regular health education regarding lifestyle changes, early detection, and HUA therapy (18,19,46–49).

2.3.2 Clinical & Biochemical Factors

Studies in Bengaluru, Tianjin, Italy, Maharashtra, Sivaganga, Gondor, and Jimma showed that SUA levels were significantly and positively associated with the duration of diabetes (50,51) (2,24,29,41,45,52).

The study conducted in Saudi Arabia revealed that among the medications used, including oral hypoglycemic drugs only, insulin only, or both, HUA was meaningfully related with not using oral hypoglycemic medications (36). Meanwhile, the study led in Italy displayed that the proportions of those treated with insulin were significantly advanced in patients with HUA than those without (29).

Tianjin, Saudi Arabia, Cameroon, and Turkey studies showed that SUA was significantly positively associated with HbA1c (35,39,51,53). However, the survey conducted at Nantong University, China, Romania & India showed that SUA levels were contrariwise related with HbA1c in T2DM affected peoples (30,31,37,44,54).

Concerning China, Andhra Pradesh, Saudi Arabia, Gondar, Maharashtra, Taiwan studies, SUA was significantly positively associated with fasting blood glucose (FBS) (24,35,42,45,55,56). However, the study conducted at Nantong University, China, Tianjin First Central Hospital, showed that SUA heights were inversely associated with FBS in T2DM patients (37,44,51,54). Yili Xu et al. meta-analysis report showed that in the pooled approximations for the connection, each 0.1 mmol/l increment in SUA was associated with a 28% upsurge in the hazard of DM vascular problems and a 9% upsurge in the hazard of DM mortality. Without regard to mean age, adjustments for metabolic factors, or medication use, the positive connection between SUA and vascular complications in stratification analysis remained significant. It varied, however, depending on demographics and sample sizes (notably positive in the relatively high sample size [≥1000] but non-significant in the small sample size [<1000] (20).

The research conducted in Taiwan displayed that enlarged SUA level was meaningfully related with Diabetic Retinopathy (42). Similarly, the research conducted in Morocco as well as Cameroon presented that HUA was related with a greater incidence of degenerative

complications, including diabetic retinopathy (38) (40). However, the investigation executed in Saudi Arabia revealed that the most common diabetic complications were nephropathy (57.3%), neuropathy (49.7%), retinopathy (47.3%), and vasculopathy (19.3%), in which HUA was meaningfully related with the presence of diabetic nephropathy (36).

According to the research led in Morocco, HTN, renal failure, and ischemic heart disease were among the factors significantly associated with HUA (38). Similarly, the study led in Italy demonstrated that HTN and enduring kidney ailment incidence was significantly advanced in people with HUA than in those not having HUA. At the same time, the study led in Cameroon showed that HUA was meaningfully related with HTN & history of Stroke (40). Moreover, patients with HUA also had significantly lower left ventricular ejection fraction, higher left atrial volume index, and greater incidence of left ventricular hypertrophy than those without HUA (29). In addition, the study conducted in Sivagangai showed that elevated SUA levels were significantly observed among those with HTN and coronary artery disease (52).

The study in Bengaluru displayed that SUA heights were significantly and positively associated with HTN (50). Furthermore, the study in Guangdong Province binary logistic regression analyses indicated that HTN was a risk factor associated with HUA (17). Correspondingly, in the study in Jordan, HUA was significantly higher in HTN patients than in normotensive patients (34). Similarly, In Gondor, the incidence of HUA was higher among study participants with HTN (24). Likewise, the study led in China revealed that the occurrence of HTN was gradually enlarged through the SUA quartiles (54).

Moreover, the study conducted in Maharashtra showed that 29 of the 38 patients with HUA also had HTN, while nine non-hypertensive patients also had the condition. This distinction was statistically significant (45). However, the research led in Saudi Arabia presented that HUA was significantly associated with the history of HTN (36).

Studies in Tianjin, Nantong University, India, Saudi Arabia, Gondar, Italy, Maharashtra and Taiwan demonstrated that SUA levels in T2DM patients were positively associated with systolic blood pressure (SBP) (24,29,35–37,42,44,45,54,56).

Findings in Tianjin, Nantong University, Saudi Arabia, Jimma, and Maharashtra demonstrated that SUA levels in T2DM patients were positively associated with DBP (2,35,37,44,45,54).

The study conducted in India, Saudi Arabia, Italy, Tianjin showed that SUA shows a strong positive association with serum creatinine (SCr) (29,36,37,54,56).

Studies at Nantong University, Tianjin First Central Hospital of China, Gondar, Saudi Arabia & Guangdong Province demonstrated that SUA levels in T2DM patients were positively correlated with Total cholesterol (TC) (17,24,36,37,44,51,54).

As per the investigation in Romania, China, Nantong University, Yantai Qishan Hospital, Tianjin First Central Hospital, Maharashtra, Bengaluru, Saudi Arabi, Gondar, Guangdong Province, Saudi Arabia, Morocco, Italy, Taiwanese, Tianjin. And Jordan a positive and substantial connection among SUA with Triglyceride (TG) was observed (17,24,43,44,50,51,54,55,57,29,30,34–38,42).

Studies in Bengaluru, Maharashtra, Nantong University, Tianjin First Central Hospital, Yantai Qishan Hospital, Saudi Arabia, Hawassa, Jordan, Guangdong Province, Saudi Arabia, Morocco, and Taiwan showed that SUA was significantly negatively correlated with High-density lipoprotein (HDL) (17,19,51,54,57,34–36,38,42,44,45,50).

Studies in Tianjin First Central Hospital, Bengaluru & Gondar showed a significantly positive relation of HUA with Low-density lipoprotein (LDL) (24,37,50,51).

Studies in Yantai Qishan Hospital, Tianjin First Central Hospital, China, Nantong University, Maharashtra, Sivagangai, Bengaluru, India Romania, Guangdong Province, Cameroon, Jimma, Hawassa, and Gondar showed that a positive and substantial relationship among SUA with BMI was observed (2,17,50–52,54–57,19,24,30,31,37,40,43,44).

The study conducted in Cameroon showed that intake of lipid-lowering drugs, specifically statin intake, was positively associated with HUA (40).

Based on a Japanese study, people with T2DM may change their HbA1c level through independent medication adherence. Similarly, a different study showed that the mean HbA1c dropped by 0.24% for every 10% rise in the medication possession ratio; this shows that medication adherence and glycemic management are positively correlated in T2DM affected people. Furthermore, an Indonesian study found that a significant number of patients did not take their medications as prescribed, which was linked to irregular physical activity. In

addition, medication non-adherence may lead to insufficient glycemic control, raising the risk of complications and mortality from DM. Nevertheless, it's vital to maintain that DM and HUA are multifaceted ailments that can impact a range of variables, such as heredity, routine, diet, and access to care. Medication adherence among T2DM patients who also have CO may have an indirect impact on the development of HUA by influencing variables such as glycemic indices and DM complications (58–61).

2.3.3 Behavioral & Psychosocial Factors

The study in India, Cameroon, Jimma, and Hawassa demonstrated an independent correlation of SUA values with alcoholism status (2,19,40,56).

As of the study of Jordan, Hawassa, Indian the study led in revealed that a history of cigarette smoking was among the determinant variables associated with HUA (19,34,52). While the study led in Cameroon showed that smoking appeared to decrease the hazard of HUA independently (40).

Khat is an evergreen plant that fits to the flowering kind. It is terribly abused for its stimulating-like properties. It has two energetic ingredients: cathine and cathinone. It is a stimulant drug, indicating that it speeds up the communications within the brain and the body. Some social customs in the Middle East, such as those in Saudi Arabia and Yemen, and Eastern Africa, such as those in Somalia and Ethiopia, involve chewing khat (62). Consuming Khat has a substantial link to the onset of T2DM. When compared to non-chewers, those who consumed Khat had a risk of T2DM that was > 3 times higher. Khat consumption has been discovered to affect those with T2DM negatively. Studies in Yemen and the Saudi Arabian region of Jazan displayed that chewing khat is undoubtedly linked to poor glycemic control, a lower BMI, and increased glycemic parameters such as HbA1c heights, FBS, and post-prandial blood glucose. But it's crucial to remember that DM and HUA are complicated ailments that various variables, such as access to healthcare, genetics, food, and lifestyle, can impact. Consuming Khat may have an indirect impact on the pervasiveness of HUA among T2DM patients who have CO by influencing variables including food and lifestyle (63–67).

Depression has been linked to poor glycemic control, a higher risk of complications, higher medical expenses, and a shorter life span. Similarly, microvascular problems connected to T2DM, such as neuropathy and retinopathy, are inversely correlated with anxiety. Likewise,

high blood sugar and insulin resistance can result from psychological and physical stress. In individuals with T2DM, stress levels have been demonstrated to impact both postprandial and FBS levels. Furthermore, It has been demonstrated that anxiety and stress can raise blood sugar levels, which may result in long-term issues for people with diabetes. However, it's essential to remember that HUA and DM constitute complicated conditions that various factors, including lifestyle, diet, genetics, and access to treatment, can influence. By affecting factors like DM complications and lifestyle, stress, anxiety, and depression may indirectly affect the development of HUA among T2DM patients who also have CO (68–70).

In general, in this literature review, the majority of studies addressed SUA as well as HUA. some studies showed variation, contradicting, and inconsistent ideas in their results, especially regarding the factors affecting HUA. The study population is mostly only T2DM patients that don’t specifically focus on those who have CO. Moreover, the studies had a variety of sample sizes, and they had a difference in inclusion criteria, mainly in the age category; the data collection method varied. Also, differences in sampling techniques and study designs were observed. Therefore, in this study, the investigation done was the magnitude of HUA concerning the factors affecting it among T2DM patients with CO and tested variables that had conflicting and inconsistent ideas from previous studies and newly added factors in contrast to most the studies and tried to mitigate the limitation of other studies done.

2.4 Conceptual Framework

After reviewing various HUA & associated factors studies, the conceptual framework was developed below to show the influence of predictor Variables on HUA among T2DM patients with CO.

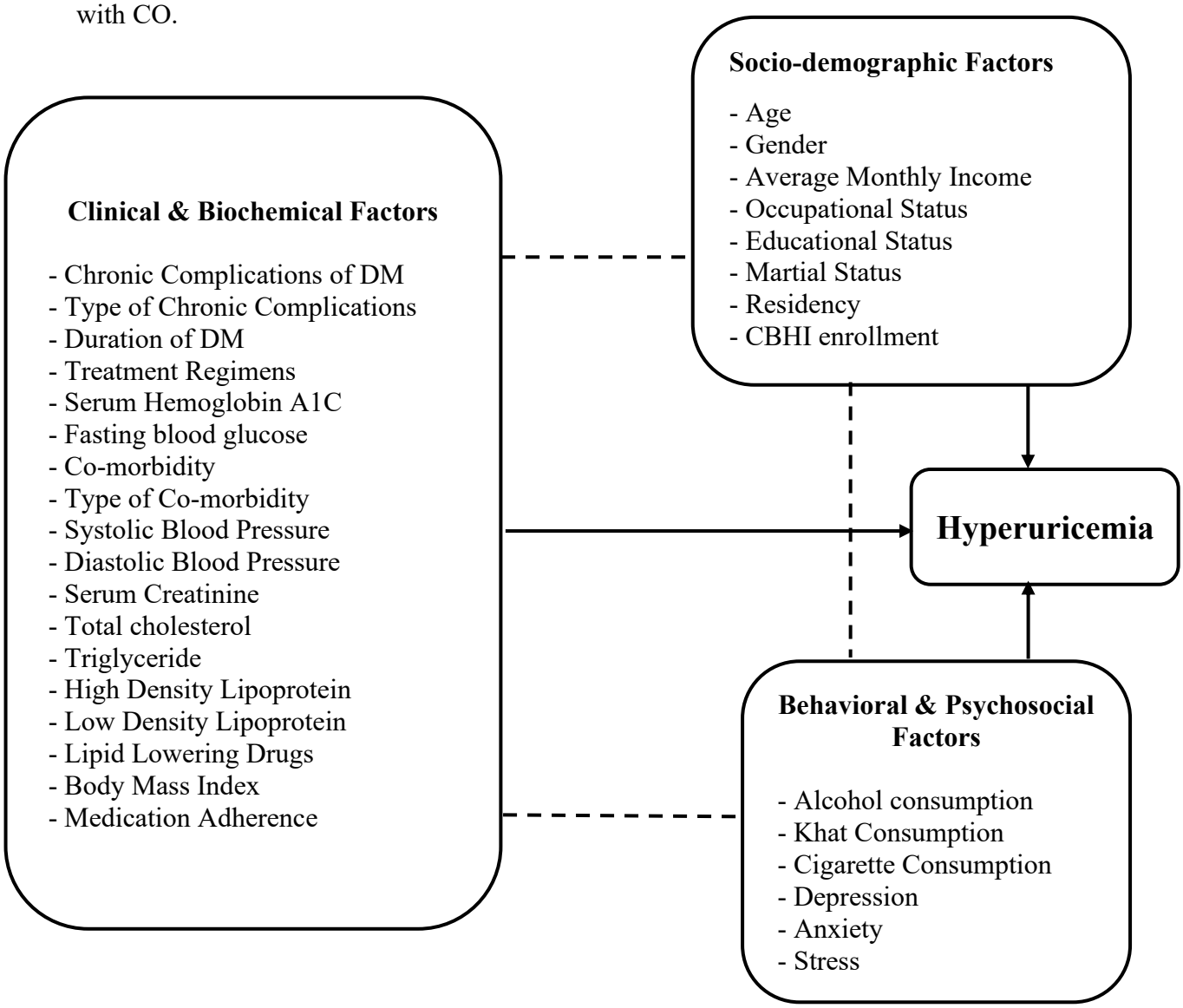

Figure 2: Conceptual framework on Hyperuricemia and associated factors among T2DM patients with central obesity adapted and modified from different works of literature (1,16–20,30–32,34–41,43–45,50,52,53,55,56)**.**

3. OBJECTIVE

3.1 General Objective

- To assess the Magnitude of Hyperuricemia and associated factors among adult type 2 diabetes mellitus patients with central obesity on-diabetic follow-up clinic at WCSH, Woldia, Ethiopia, 2023.

3.2 Specific Objectives

- To determine the Magnitude of Hyperuricemia among adult T2DM patients with CO on-diabetic follow-up at WCSH, Woldia, Ethiopia, 2023.
- To identify the socio-demographic factors associated with Hyperuricemia among adult T2DM with CO on-diabetic follow-up at WCSH, Woldia, Ethiopia, 2023.
- To distinguish the clinical variables associated with Hyperuricemia among adult T2DM with CO on-diabetic follow-up at WCSH, Woldia, Ethiopia, 2023.
- To identify the biochemical factors associated with Hyperuricemia among adult T2DM with CO on-diabetic follow-up at WCSH, Woldia, Ethiopia, 2023.
- To recognize the behavioral variables associated with Hyperuricemia among adult T2DM with CO on-diabetic follow-up at WCSH, Woldia, Ethiopia, 2023.
- To extricate the psychosocial variables associated with Hyperuricemia among adult T2DM with CO on-diabetic follow-up at WCSH, Woldia, Ethiopia, 2023.

4. MATERIAL AND METHODS

4.1 Study Area

The study was conducted in Woldia Comprehensive Specialized Hospital (WCSH), Woldia, North-Eastern Ethiopia. Woldia city administration is the North Wollo Zone & District's capital city in northern Ethiopia, located north of Dessie & southeast of Lalibela in the Amhara Region. It is 351 kilometers from Bahir Dar, the Amhara regional state's capital city, and 521 kilometers from Addis Ababa, Ethiopia's capital city. The town elevates 2112 meters above sea level and its notable landmark is the Woldia St. Gabriel orthodox tewahedo church. The Geographic Coordinate of the city is 11°49′50″North 39°36′0″East (71). Rase Wole Bitul was the early name of WCSH that was established in 1961 and it serves a total of 1.5 million people. It has 406 healthcare and administrative workers, of which 8 are anesthetics professionals, 3 Biomedical Engineers, 34 General practitioners, 14 clinical specialists, 24 Laboratory professionals, 36 Midwives, 145 Nurses, 22 Pharmacists, and four radiologists. The hospital offers a comprehensive range of medical, surgical, obstetric, prenatal, chronic illness management, pediatric, orthopedic, HIV/AIDS treatment, and follow-up treatments, among other healthcare services. The hospital generally works hard to give each patient compassionate, thorough treatment and is dedicated to promoting their health and well-being (72).

4.2 Study Design & Period

The institutional-based cross-sectional study was conducted in the chronic outpatient department of WCSH from May 8 to July 7, 2023.

4.3 Source Population

All adult T2DM patients with CO who had diabetic follow-ups at WCSH.

4.4 Study Population

All adult-T2DM patients with CO who follow their diabetic treatment & have fulfilled the eligibility criteria.

4.5 Study Unit

- Selected Adult T2DM patients with CO.

4.6 Inclusion & Exclusion Criteria

- **Inclusion Criteria:** T2DM patients with CO aged ≥ 18 years and on-diabetic follow-up for at least six months before this study.
- **Exclusion Criteria:**
    - Patients who were unable to communicate due to serious medical illnesses.
    - Patients who are taking anti-hyperuricemia drugs.
    - Patients who are pregnant.

4.7 Study Variable

4.7.1 Dependent Variable

Hyperuricemia

4.7.2 Independent Variable

Socio-demographic Factors: age, average monthly income, occupational status, educational status, gender, marital status, enrollment of CBHI (community-based health insurance), and residency.

Behavioral & Psychosocial Factors: alcohol consumption, khat consumption, cigarette consumption, depression, anxiety, stress.

Clinical Factors: chronic complications of DM, type of chronic complications, duration of DM, treatment regimens, HbA1C, FBS, co-morbidity, type of co-morbidity, SBP, DBP, SCr, TC, TG, HDL, LDL, BMI, lipid-lowering drugs, medication adherence.

4.8 Operational Definitions

Hyperuricemia was defined as respondents having SUA levels of more than 7.2 mg/dl (420 μmol/ L) in males and more than 6.0 mg/dl (360 μmol/L) in females (17,19,36).

Central Obesity was defined as a waist circumference ≥ 90 cm in men and ≥ 85 cm in women (17).

Co-morbidity is an illness or disorder that coexists with diabetes but is mainly unrelated (73).

Body Mass Index was used to categorize the participants as defined by the World Health Organization (WHO) guidelines into Four groups: BMI <18.5, 18.5 – 24.9, 25 – 29.9, and ≥ 30 kg/m2 will be considered as underweight, normal, overweight and obesity, respectively (24,74).

Medication Adherence: The total scores of all the items range from 0 to 8, and it was grouped into two levels: adherent (score of 6 to 8) and non-adherent (score < 6) based on the Morisky Medication Adherence Scale-8 (MMAS-8) (75,76).

Alcohol Consumption: It is defined as the proportion of individuals who have ever used alcoholic drinks such as tela, tej, katicala/areke, beer, wine, or other beverages that can cause intoxication at least once in their lifetime or respondents who drank alcohol during one month preceding the study at least once per month taken as alcohol drinker (77,78).

Khat Consumption: respondent who chewed the leaves of the khat plant during his lifetime in any amount taken as khat chewer (77,78).

Cigarette Consumption: Respondents who practiced smoking cigarettes during the past year, regardless of the amount, while those who had never smoked in their lifetime or who had been smokers before the last year were taken as non-smokers (77,78).

Depression: Based on their score on the Depression Anxiety Stress Scale 21 (DASS-21) questionnaire, the Participant was classified as [No] Depression: 0 – 9, [Yes] Depression: ≥ 10 (79,80).

Anxiety: Based on their score in the DASS-21 questionnaire, the Participant was classified as [No] Anxiety: 0 – 7, [Yes] Anxiety: ≥ 8 (79,80).

Stress: Based on their score in the DASS-21 questionnaire, the Participant was classified as [No] Stress: 0 – 14, [Yes] Stress: ≥ 15 (79,80).

Monthly Income: The individual's monthly income compared to the International Poverty Line - is US$1.90 with the current Ethiopian exchange rate of 104.9325 Ethiopian Birr & multiplied by 30, which equals 3147.975 Ethiopian Birr**,** based on this**,** "Above Poverty Line" an individual's income greater than or equal to the International Poverty Line or "Below Poverty Line": an individual's income less than the International Poverty Line (81).

4.9 Sample Size Determination

The study sample size was initially calculated using Cochran's sample size formula by assuming a prevalence of HUA, 32.6%, taken from the study conducted in Guangdong Province, China (17). The sample size is calculated using the following 95% CI (Confidence Interval) formula.

$$\boldsymbol{n_i = \frac{z^2 p.q}{e^2} \quad n_i = \frac{z^2 p.q}{e^2} = \frac{(1.96)^2(0.326)(0.674)}{(0.05)^2} = \frac{0.8440917184}{0.0025} = 338}$$

However, there is a significant, well-known difference in sociodemographic and other related characteristics between the population of China and Ethiopia. Thus, using a sample size calculated based on such conditions is not recommended. Therefore, this sample size was not used for this study.

Secondly, the study sample size was calculated using Cochran's sample size formula by assuming a prevalence of HUA, 31.5%, from the study conducted in Gondar, Ethiopia (24). The sample size is calculated using the following formula with 95% CI.

$$n_i = \frac{z^2 p.q}{e^2} \quad n_i = \frac{z^2 p.q}{e^2} = \frac{(1.96)^2(0.315)(0.685)}{(0.05)^2} = \frac{0.82892124}{0.0025} = 332$$

In the Gondar study, the prevalence of HUA was determined among adult T2DM patients regardless having CO or not. Even though the sociodemographic characteristics of the population are similar, the study population is distinct from the current study.

Third, considering the present study design, planned statistical analysis, and study subject selection procedure the study sample size was calculated using the second objective and after that via a priori power analysis (below Table 1) and (below Table 2) respectively.

Table 1: Second objectives sample size calculation using Epi-Info version 7.2.5.0

Variables	CI	AOR	Power	% Outcome in the unexposed group	% Outcome in the exposed group	Sample size	Reference
Age	1.1 - 3.2	3.00639	80	9.6	24.2	232	(19)
Metabolic Syndrome	1.5 – 4.6	6.00231	80	6	27.7	110	(19)
HTN	7.9 - 24.6	13.26605	80	14.6	69.4	30	(24)
SBP	2.1 - 9.3	4.26758	80	24.6	58.2	78	(24)

Table 2: A priori power analysis for sample size using G*Power version 3.1.9.7

Variables	Tail	AOR	Pr(Y=1 |x=1) H0	α	Power	R^2	X parm π	Sample size	Reference
Age	2	3.00639	0.5	0.05	80	0.5	0.5	238	(19)
Metabolic Syndrome	2	6.00231	0.5	0.05	80	0.5	0.5	112	(19)
HTN	2	13.26605	0.5	0.05	80	0.5	0.5	79	(24)
SBP	2	4.26758	0.5	0.05	80	0.5	0.5	151	(24)

Generally, all sample size calculation done above wasn't used for this study due to the difference in sociodemographic and other related characteristics of the population, the difference in the study population, and the sample size calculated using second objectives sample size calculation as well as a priori power analysis was inadequate for binary logistic regression analysis, which generally affect the outcome of the current study in an annulling way. Therefore, this study sample size was finally calculated using Cochran's sample size formula by assuming the prevalence of HUA at 50 %. Besides, to the best of the author's knowledge, there is no study conducted in Ethiopia with a similar study population. Furthermore, to amplify the precision, quality, and generalizability of the research as well as to mitigate bias, the sample size was calculated using Cochran's sample size formula with 95% CI assuming the prevalence of HUA at 50 %.

$$\boldsymbol{n_i = \frac{z^2 p.q}{e^2}} \quad \boldsymbol{n_i = \frac{z^2 p.q}{e^2} = \frac{(1.96)^2(0.5)(0.5)}{(0.05)^2} = \frac{0.9604}{0.0025} = 384}$$

Where:

$\mathbf{n_i}$ = initial sample size

n = final Sample size

e = desired level of precision

p = estimated proportion

q = 1- p

p = 50% = 0.5

q= 1 - 0.5 = 0.5

z = the standard normal variables at (1-∂) % confidence level and ∂%

i.e., with a 05% CI = 1.95, p= 0.5

The study sample size was calculated by assuming prevalence of HUA 50% since there is no adequate research done in Ethiopia and to increase and ensure the precision and quality of the research. Adding 10% for contingency the desired sample size becomes **423 (n = 423)**.

4.10 Sampling Technique

The required sample was selected by using a Convenience sampling via the consecutive case principle until the required sample size was fulfilled.

4.11 Data Collection Tool

4.11.1 Data Collection Tools & Procedures

4.11.1.1 Sample Collection and Processing Procedures

After the required materials had been organized, informed consent was obtained from the study participants. After using 70% alcohol to clean the medial cubital vein, a tourniquet was used. Next, 5 mL of each participant's overnight fasting blood was drawn by two trained Laboratory technicians using an aseptic/sterile technique. Once the necessary volume of blood had been drawn, the tourniquet was removed. The venous puncture site was covered with dry gauze, the needle was carefully removed, and the patient was instructed to keep exerting light pressure. Supplies that were contaminated were appropriately disposed of, and the patient's ID number and date were written on the tubes. Hand washing was done and gloves were taken off and thrown into the rubbish pit marked with an infectious disease. For half an hour, the drawn sample was left alone. The obtained blood sample was then centrifuged at 3000 rpm for 10 minutes in a thermostable condition using a Rotanta 960 centrifuge to extract the serum. After that, serum was extracted and kept in the WCSH Biochemistry Laboratory at -20 °C until the biochemical analysis was completed (82).

Laboratory Test Principles

Using an automated chemical analyzer, the ABX Pentra 400, established principles and techniques were used to determine the SUA content. The uricase enzyme oxidizes uric acid to produce hydrogen peroxide and allantoin. Released hydrogen peroxide combines with an aniline derivative and 4-amino antipyrine in the presence of peroxidase to generate a colorful chromogenic compound. The amount of uric acid present in the sample was determined by measuring the colored dye's absorbance at 520 nm. Generally, uric acid levels were measured by performing three replicates per sample according to the uricase-peroxidase method, also known as the uricase method, which is currently recognized as the gold standard for SUA level determination (82). The precision of this method is excellent, with within-set coefficients of variation of 0.08-0.18% and between-set coefficients of variation of 0.02-0.07% for

chromatography/mass spectrometry analyses (83). The accuracy of the measurement can be evaluated by comparing the results with established reference methods (83). The Instrument was correctly calibrated as per the institution standard by initially preparing a set of standard solutions with known concentrations of SUA. These solutions should span the expected range of analyte concentrations for the analyzed samples, which is 3.4 to 7.2 mg/dL (milligrams per deciliter) for men and 2.4 to 6.0 mg/dL for women. Then, the standard solutions onto the ABX Pentra 400 analyzer were loaded and run randomly. The instrument generates a calibration curve by plotting the instrument response (i.e., absorbance) against the known concentrations of the standards. After that, the linearity, accuracy, and precision calibration curves were checked. The curve should be linear over the range of concentrations tested, and the accuracy and precision should be within acceptable limits. If the calibration curve is insufficient, troubleshooting the problem by checking the reagents, cleaning the instrument, or recalibrating as needed is done until the calibration curve is acceptable.

In addition, control samples with known concentrations of SUA are run regularly to monitor the accuracy and precision of the ABX Pentra 400 analyzer over time; this was initially done by preparing control solutions with known concentrations of SUA at low, medium, and high concentrations. Then, run the control solutions along with the samples regularly. The frequency of control testing was run weekly. Next, the control results were analyzed using statistical methods to calculate accuracy and precision. The accuracy was within ±2 standard deviations (SD) of the mean, and the precision was within ±1 SD of the mean, which is an acceptable range. Finally, when the control outcomes are outside of the excellent range, troubleshooting the problem by checking the reagents, cleaning the instrument, or recalibrating as needed is done until the control outcomes are within the acceptable range.

Lastly, quality checks, including verifying that the analyzer meets specific performance criteria and that reagents and consumables are within expiration dates, were done by initially checking the instrument's performance using manufacturer-recommended quality control materials or external proficiency testing programs. Then, verifying that the reagents and consumables are within expiration dates and stored according to the manufacturer's instructions was done. After that, the instrument's cleaning and maintenance logs were checked to ensure it was properly maintained and serviced regularly. Finally, routine checks of the instrument's performance, such as checking the linearity of the calibration curve, verifying the instrument's accuracy and

precision using control samples, and monitoring the instrument's performance over time, were done.

Anthropometry and Blood Pressure Measurements

Stretch-resistant tape was used to measure each study subject's waist circumference after they gave their informed consent and stood with their feet close together, arms at their sides, and body weight evenly distributed. The subjects were instructed to wear light clothing and to stand at the midpoint between the top of the iliac crest and the lower margin of the least palpable rib. When there was a 1 cm discrepancy between the two measurements, the average was calculated. The measurement was taken twice. When there was a difference of more than one centimeter between the two measures, additional measurements were made (84). We measured height and weight in accordance with the WHO guidelines (73). With the use of portable weighing scales, body weight was determined with an accuracy of 0.1 kg. The subjects were dressed simply for indoors, wore no shoes, and had their body height measured by a stadiometer. Weight in kilograms divided by height in meters squared was used to determine BMI [BMI = weight/(height)2 kg/m2]. BMIs of less than 18.5, 18.5–25, 25–30, and more than 30 kg/m2 were categorized as underweight, normal, overweight, and obese, in that order. After the patients had rested for more than 10 minutes and 30 minutes after consuming any hot beverage, such as coffee, SBP and DBP were measured twice, 20 minutes apart, from the left arm at the level of the heart while the subjects were seated. The instruments were an OMRoN M2 oscillometric automated sphygmomanometer. For research participants whose SBP was greater than 140 mmHg (85).

Socio-demographic data and some clinical, biochemical, behavioral, and psychosocial factors questionnaires were adapted, adopted or developed from the literature review, and conceptual framework. Moreover, it was collected with an interview and respondent's medical record review.

Medication adherence: was measured using the Morisky Medication Adherence Scale-8 (MMAS-8), a validated assessment tool with internal reliability of Cronbach alpha 0.47. It has been supported and validated by multiple studies conducted worldwide, with more than 110 versions and more than 80 translations; based on this tool, the total scores of all the items range from 0 to 8, and Items 1 through 7 had response choices of "yes" or "no" whereas item 8 had 5-point Likert scales. Each "no" response was rated as "1," and each "yes" was rated as "0,"

except for item 5 (reversed score), in which the response "yes" was ordered as "1" and "no" was rated as "0". The 5-point Likert scale of item 8, concerned with remembering to take their insulin therapy, was never/rarely = 0, once in a while = 1, sometimes = 2, usually = 3, and all the time = 4. In this scale, if patients choose response "0", the score is "1," and if they select response "1,2,3 or 4", the score is "0". Higher scores indicate higher adherence levels. Finally, by summing all scores for each item, it was grouped into two levels: adherent (score of 6 to 8) and non-adherent (score < 6) based on the Morisky Medication Adherence Scale-8 (MMAS-8) (74,75).

Depression, Anxiety, & Stress were measured using the DASS-21 short form developed by Lovibond. A psychological screening tool called DASS-21 can distinguish between stress, anxiety, and depression symptoms. With 21 items spread throughout three categories, it is a validated and trustworthy tool. The DASS-21 was shown to be very reliable, with excellent Cronbach's alpha values of 0.81, 0.89, and 0.78 for the depression, anxiety, and stress subscales, respectively, and an overall score of $\alpha = 0.91$ for the three domains combined. Each section has seven items that measure stress, anxiety, and depression symptoms. In each domain, participants were asked to rate their symptoms throughout the previous week, with 0 representing "did not apply" and 3 representing "applied most of the time." Every dimension's scores were added up. The final score was then divided by two and classed in accordance with the DASS handbook. However, the DASS-21 scores with normal levels of stress, anxiety, and depression were categorized as "0" [No] in order to assess the incidence of these conditions. On the other hand, people who had levels that were light, moderate, severe, or extremely severe were recorded as "1" [Yes] (78,79,86).

From Woldia Health Center, three BSc nurses and two laboratory technicians with a minimum of two years of clinical work experience were allocated. Two of the nurses were assigned to be data collectors, and one was given the role of supervisor. In addition to reviewing the patient's medical file and conducting in-person interviews, the data collectors also performed laboratory testing, anthropometry, and blood pressure checks. Finally, from May 8 to July 7, 2023, data collection activities were carried out.

4.11.2 Data quality control

For the study, standardized instruments were employed. The surveys were translated from the English version into the Amharic version of the local language, and then back to English to

ensure uniformity and reduce information bias. For two days, supervisors and data collectors received instruction on how to gather the necessary data from research participants. A week prior to the data collection period at Dessie Comprehensive Specialized Hospital, 10% of the population underwent a pre-test. By calculating Cronbach's alpha during the pretest, the Likert scale tools' internal consistency was evaluated. Following the pretest, some adjustments were performed, including typing errors being fixed, data collectors being reoriented, and questionnaires being rearranged. Following the test and modification, data collectors began gathering data. They took great care to prevent data redundancy by collecting the medical record numbers of data collection study participants to distinguish them from non-data collection study participants. Next, the supervisor reviewed the questionnaires with the data collectors at the conclusion of each day of data collection and ensured they were complete. The supervisor gave data collectors feedback daily until the data gathering was completed. Lastly, for any error or ambiguity and incompleteness of the data, the principal investigator took corrective measures.

4.11.3 Procedure for data processing & data analysis

After the data were collected, it was entered into Epi Data version 4.6.0.6 and then, exported into SPSS version-26 software for data cleaning, coding, editing, and analysis. Descriptive analysis was carried out for each of the independent variables and results were presented in the mean, standard deviation (SD), median, interquartile range (IQR), tables, frequencies, and percentages. The normality of the continuous data was checked by the Kolmogorov-Smirnov test (Weight: $P = 0.072$, Age, Income, SUA, DM duration, HbA1C, FBS, SBP, DBP, SCr, TC, TG, LDL, HDL, Height, BMI: $P < 0.001$). The Cronbach's alpha test was used to check the internal consistency of the Likert scale variables. During the pretest, the DASS-21 scale reliability coefficient (Depression: $\alpha = 0.740$, Anxiety: $\alpha = 0.264$, Stress: $\alpha = 0.690$) and the MMAS-8 scale reliability coefficient (Medication adherence: $\alpha = 0.675$) and also for the main study the DASS-21 scale reliability coefficient (Depression: $\alpha = 0.669$, Anxiety: $\alpha = 0.177$, Stress: $\alpha = 0.777$) and the MMAS-8 scale reliability coefficient (Medication adherence: $\alpha = 0.673$) as non-outcome variables which was acceptable for these population.

I used bivariable binary logistic regression analysis to identify the variables that were related to the HUA. The multivariable binary logistic regression model included all variables that had a p-value of less than 0.25 in the bivariable binary logistic regression analysis. Hosmer and

Lemeshow's goodness-of-fit test was used to check the model fitness (p = 0.178). All binary logistic regression assumptions were checked and fulfilled, and multicollinearity was studied using standard error and variance inflation factor. The adjusted odds ratio (AOR) with a 95% confidence interval (CI) was calculated to characterize the degree of the relationship between independent factors and HUA. Variables having a p-value < 0.05 were considered statistically significant.

4.12 Ethical consideration

Ahead of data collection, The ethical approval came from the ethical review committee of Addis Ababa University, College of Health Sciences, Department of Medical Physiology. After ethical approval was received, a letter of administrative authorization was obtained from WCSH's chief executive officer. During the data collection, before the study subjects given consent an information sheet was read and study participants were briefed on the study objectives, its purpose, and the right to withdraw at any point. Verbal and then written informed consent were acquired from every research participant through the sign-on questionnaire paper & their participation was completely voluntary. The confidentiality & privacy of participants was secured by omitting any personal identifier. Most of all, the data was collected anonymously. Generally, this study was conducted per the Declaration of Helsinki in 1964.

4.13 Dissemination of the result

The final report will be disseminated to the Department of Medical Physiology, Addis Ababa University; the study findings will also be issued to the regional health bureau, WCSH & non-governmental health organizations. Lastly, it will be made to publish the results in a reputable scientific journal.

5. RESULT

5.1 Socio-demographic Characteristics of the study participants

Four hundred and nineteen subjects were included in the study and the overall response rate was 99%. The age of the respondents ranges from 22 - 62 years with a median (IQR) of 41 (34 - 50) years. The majority of the respondents were female 244 (58.2%), literate 231 (55.1%) and urban dwellers 261 (62.3%). Most of the respondents were married 281 (67.1%) and had CBHI 276 (65.4%). The median (IQR) of average monthly income was 2793 (1723 - 10556) Ethiopian Birr. (see Table 3 below).

Table 3: Socio-demographic characteristics of type two diabetes mellitus follow-up participants with central obesity attending WCSH, Woldia, Northeast Ethiopia, from May 8 to July 7, 2023 (n=419).

Variable	Category	Frequency (n)	Percentage (%)
Age in Years [a]	≥ 45	154	36.8
	< 45	265	63.2
Gender	Male	175	41.8
	Female	244	58.2
Residency	Rural	158	37.7
	Urban	261	62.3
Educational Status	Illiterate	188	44.9
	Literate	231	55.1
Marital Status	Un-married	138	32.9
	Married	281	67.1
Occupational Status	Un-employed	158	37.7
	Employed	261	62.3
Average Monthly Income	Below Poverty Line	228	54.4
	Above Poverty Line	191	45.6
CBHI enrolment	Yes	276	65.9
	No	143	34.1

a. Age category was adopted from a research article (a study done in Hawassa) (19).

Abbreviation: CBHI, Community-Based Health Insurance

5.2 Clinical & Biochemical Characteristics

The duration of DM of the study sample ranged between 2 and 21 years, with a median (IQR) of 14 (10 - 17) years; regarding treatment regimens, less than half of 20 (4.8%) study participants have used Insulin & Oral anti-diabetic medication, and among the chronic complication of DM, the leading one was diabetic-related hypertension 55 (13.1%). The HbA1c of the study sample was with a median (IQR) of 6.6 (5.9 – 9.8) %. Of the total participants, 93 (22.2%) had developed co-morbidity diseases. Among these co-morbidity diseases, the leading one, 52 (12.4%), was HTN. The median (IQR) of FBS, SCr, TC, TG, LDL, and HDL were 119 (99 - 141), 0.94 (0.71 – 1.17), 208 (181 - 226), 153 (133 - 177), 100 (76 - 108), and 41 (35 - 59) mg/dl respectively. In comparison, the SBP and DBP of the study sample with the median (IQR) were 127 (119 -133) and 74 (70 - 79) mmHg, respectively. In unison, regarding the medication adherence of the study participants, 228 (54.4) of study subjects were non-adherent to medication. The BMI of the study sample ranged between 19.13 and 34.36 Kg/m^2, with a median (IQR) of 27.36 (25.21 – 29.21) Kg/m^2. Whereas the mean (SD) weight of the respondents was 71.51 (± 11.93) Kg, and the study participant's height in median (IQR) was 162 (156 - 169) cm. (see Table 4 below).

Table 4: Clinical & Biochemical characteristics of type 2 diabetes mellitus follow-up participants with central obesity attending WCSH, Woldia, Northeast Ethiopia, from May 8 to July 7, 2023 (n=419).

Variable	Category	Frequency (n)	Percentage (%)
Treatment Regimens	Oral anti-diabetic Medication only	112	26.7
	Insulin Only	284	67.8
	Insulin & Oral anti-diabetic medication	20	4.8
	Only following the dietary plan as recommended	3	0.7
Chronic Complication of Diabetes Mellitus	Yes	82	19.6
	No	337	80.4
Type of Complications	Diabetic Nephropathy	5	1.2
	Diabetic Retinopathy	11	2.6
	Diabetic Neuropathy	11	2.6
	Diabetic Foot Ulcer	-	-
	Diabetic Heart Disease	-	-
	Diabetic Hypertension	55	13.1
	Other	-	-

Duration of Diabetes Mellitus in Years [b]	≥ 10	334	79.7
	< 10	85	20.3
Hemoglobin A1C (%) [c]	≥ 7	161	38.4
	< 7	258	61.6
Fasting Blood Sugar (mg/dl) [d]	≥ 180	71	16.9
	< 180	348	83.1
Co-morbidity	Yes	93	22.2
	No	326	77.8
Type of Comorbidity	Heart-related Disease	19	4.5
	Kidney Disease	24	5.7
	Hypertension	52	12.4
	Other	-	-
Systolic Blood Pressure (mmHg) [c]	≥ 130	167	39.9
	< 130	252	60.1
Diastolic Blood Pressure (mmHg) [c]	≥ 80	98	23.4
	< 80	321	76.6
Serum Creatinine (mg/dl) [c]	≥ 1.2	88	21
	< 1.2	331	79
Total Cholesterol (mg/dl) [d]	≥ 200	273	65.2
	< 200	146	34.8
Triglyceride (mg/dl) [d]	≥ 150	224	53.5
	< 150	195	46.5
Low-density lipoprotein (mg/dl) [d]	≥ 100	215	51.3
	< 100	204	48.7
High-density lipoprotein (mg/dl) [d]	≤ 40	208	49.6
	> 40	211	50.4
Lipid-lowering drugs	No Medication	292	69.7
	Statin Only	127	30.3
	Fibrate Only	-	-
	Statin + Fibrate	-	-
	Other	-	-
Medication Adherence	Non-adherent	130	31
	Adherent	289	69
Body Mass Index	Under Weight	-	-
	Normal Weight	93	22.2
	Over Weight	249	59.4
	Obesity	77	18.4

b. Duration of diabetes mellitus category adopted from research article (study done in Jimma) (2).

c. Hemoglobin A1C, serum creatinine, systolic and diastolic blood pressure categories adopted from research article (study done in Debre Berhan) (23).

d. Fasting blood sugar, total cholesterol, triglyceride, low density, and high lipoprotein categories were adopted from research articles (study done in Jimma) (22).

5.3 Behavioral & Psychosocial Characteristics

Of a total of participants, 271 (64.7%) had Depression, and 227 (54.2%) had Anxiety. At the same time, respondents during the past 30 days of the data collection period used Alcohol and Khat with a median (IQR) of 5 (3 - 9), and 2 (1 - 6) days, respectively. Likewise, among participants who smoked cigarettes on average a day, they consumed with the median (IQR) 5 (2 - 8) number of cigarettes. (see Table 5 below).

Table 5: Behavioral & Psychosocial characteristics of type 2 diabetes mellitus follow-up participants with central obesity attending WCSH, Woldia, Northeast Ethiopia, from May 8 to July 7, 2023 (n=419).

Variable	Category	Frequency (n)	Percentage (%)
Alcohol drinking status	Drinker	330	78.8
	Non-drinker	89	21.2
How often a respondent drink alcohol during the last 13 months	Almost Every Day	-	-
	At Least Once A Week	192	46.1
	Less Than Once A Week	138	32.9
	None in The Last 13 Months	-	-
Khat chewing status	Chewer	42	10
	Non-chewer	377	90
Smoking status	Smoker	34	8.1
	Non-smoker	385	91.9
Depression	Yes	271	64.7
	No	148	35.3
Anxiety	Yes	227	54.2
	No	192	45.8
Stress	Yes	118	28.2
	No	301	71.8

5.4 Magnitude of Hyperuricemia

The Serum Uric Acid of the study sample ranged between 2.7 and 8.6 mg/dl, with the mean (SD) of 5.696 (± 1.674) mg/dl. The overall magnitude of Hyperuricemia in the study subject was 37.2 % (95% CI 32.9 – 42.2) (see Figure 2 below).

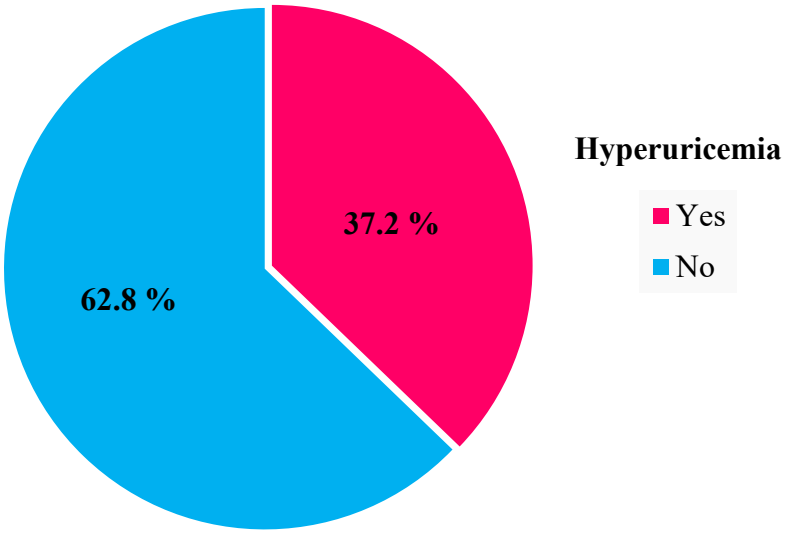

Figure 3: Magnitude of Hyperuricemia among type 2 diabetes mellitus follow-up participants with central obesity attending WCSH, Woldia, Northeast Ethiopia, from May 8 to July 7, 2023 (n=419).

5.5 Factors Associated with Hyperuricemia

The variables that are entered into simple univariable analysis using binary logistic regression model and passed to multivariable analysis using binary logistic regression model with a p-value < 0.25 were Age, Gender, Duration of DM, SCr, FBS, HbA1C, TC, LDL, SBP, DBP, Alcohol Consumption, Medication Adherence, and Stress. Then, multivariable analysis using binary logistic regression model was done using the ENTER selection method and declared that Age, Gender, Duration of DM, SCr, DBP, TC, and Alcohol Consumption are significantly associated with HUA.

Respondents with age ≥ 45 years are 1.670 times more likely to have HUA than respondents with age < 45 years (AOR = 1.670, 95% CI = 1.020 – 2.732). Male respondents were 1.754 times more likely to have HUA than female respondents (AOR = 1.754, 95% CI = 1.075 – 2.861). Respondents with a duration of DM ≥ 10 years are 2.310 times more likely to have HUA than respondents with a duration of DM < 10 years (AOR = 2.310, 95% CI = 1.074 – 4.972). Respondents with DBP ≥ 80 mmHg are 3.437 times more likely to have HUA than respondents with DBP < 80 mmHg (AOR = 3.437, 95% CI = 1.748 – 6.758). Respondents with SCr ≥ 1.2 mg/dl are 2.347 times more likely to have HUA than respondents with SCr < 1.2 mg/dl (AOR = 2.347, 95% CI = 1.154 – 4.771). Respondents with TC ≥ 200 mg/dl are 2.362 times more likely to have HUA than respondents with TC < 200 mg/dl (AOR = 2.362, 95% CI = 1.300 – 4.292). Respondents who consumed alcohol are 3.320 times more likely to have HUA than respondents who don't consume alcohol (AOR = 3.320, 95% CI = 1.557 – 7.081) (**See Table 6 below**).

Table 6: Multivariable binary logistic regression on factors associated with Hyperuricemia among type two diabetes mellitus follow-up participants with central obesity attending WCSH, Woldia, Northeast Ethiopia, from May 8 to July 7, 2023 (n=419).

Variable	Hyperuricemia		COR (95% CI)	AOR (95% CI)	P-Value
	Yes (n)	No (n)			
Age					
≥ 45 years	64	90	1.337 (0.889 – 2.011)	1.670 (1.020 – 2.732)	0.041*
< 45 years	92	173	1	1	
Sex					
Male	83	92	2.113 (1.411 – 3.165)	1.754 (1.075 – 2.861)	0.025*
Female	73	171	1	1	
Duration of DM					
≥ 10 years	130	204	1.446 (0.867 – 2.411)	2.310 (1.074 – 4.972)	0.032*
< 10 years	26	59	1	1	
Hemoglobin A1C					
≥ 7 %	66	95	1.297 (0.855 – 1.945)	1.201 (0.635 – 2.272)	0.573
< 7 %	90	168	1	1	

Fasting Blood Sugar					
≥ 180 mg/dl	36	35	1.954 (1.168 – 3.271)	1.770 (0.874 – 3.582)	0.113
< 180 mg/dl	120	228	1	1	
Systolic Blood Pressure					
≥ 130 mmHg	51	116	0.616 (0.407 – 0.931)	0.512 (0.238 – 1.102)	0.087
< 130 mmHg	105	147	1	1	
Diastolic Blood Pressure					
≥ 80 mmHg	71	27	7.301 (4.394 – 12.132)	3.437 (1.748 – 6.758)	0.000**
< 80 mmHg	85	236	1	1	
Serum Creatinine					
≥ 1.2 mg/dl	62	26	6.012 (3.587 – 10.078)	2.347 (1.154 – 4.771)	0.018*
< 1.2 mg/dl	94	237	1	1	
Total Cholesterol					
≥ 200 mg/dl	116	157	1.958 (1.266 – 3.027)	2.362 (1.300 – 4.292)	0.005*
< 200 mg/dl	40	106	1	1	
Low-Density Lipoprotein					
≥ 100 mg/dl	86	129	1.276 (0.858 – 1.899)	0.731 (0.353 – 1.511)	0.397
< 100 mg/dl	70	134	1	1	
Alcohol Consumption					
Yes	140	190	3.362 (1.876 – 6.025)	3.320 (1.557 – 7.081)	0.002*
No	16	73	1	1	
Medication Adherence					
Non-Adherent	43	87	0.770 (0.498 – 1.189)	0.608 (0.358 – 1.033)	0.066
Adherent	113	176	1	1	
Stress					
Yes	35	83	0.627 (0.397 – 0.991)	0.940 (0.538 – 1.640)	0.826
No	121	180	1	1	

Notes: *Statistically significant ($p<0.05$); **statistically highly significant ($p<0.01$).

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; COR, crude odds ratio; DM, Diabetes Mellitus

6. DISCUSSION

The study aimed to determine the magnitude of hyperuricemia and associated factors among adult type-two diabetes mellitus patients with central obesity in Woldia Comprehensive Specialized Hospital, northeast Ethiopia, 2023. Even though there is little quantity of prior studies on a similar study population other than the Chinese study (17), the comparison of the present study was done with respect to other studies done on a wider study population.

According to this study's findings, 37.2 % (95% CI 32.9 – 42.2) of the respondents with T2DM and CO attending WCSH, Ethiopia, have HUA (**see Figure 3 above**). The current study finding is in line with the study conducted in Dhaka (33.8%) (33), Cameroon (38.1%) (40) and Hawassa, Ethiopia (33.8%) (19). This may be due to similarities in study design, sampling technique (40), resemblances in healthcare provision and system, and likeness in sociodemographic and hereditary attributes (19). However, the magnitude in the current study is higher than the study done in several countries like in Europe, Italy (24.1%) (29), Romania (26.3%) (30), in Asia, Tianjin, China (17.25%) (37), Guangdong Province, China (32.6%) (17), Uttar Pradesh (13.43%) (31), in the Middle East, Jordan (28.1%) (34), Saudi Arabia (25%) (36), in Africa, Casablanca (26.5%) (38), West Cameroon (27.5%) (39), in Ethiopia, Jimma (22%) (2), Gondar (31.5%) (24). This difference in magnitude might be because of the distinction in study population since other than the study led in Guangdong Province, China which has nearly comparable magnitude of HUA (32.6%) and similar study population of adult T2DM patients with CO with the current study but other studies had different study population; only adult T2DM patients regardless having CO or not (2,24,29–31,34,36–39), which might contribute to the difference in magnitude of HUA. Moreover, difference in sociodemographic characteristics and population profiles, such as dietary habits, geographical/environmental factors, genetic factors as well as variance in healthcare support and setup (29,30,37), difference in studies sample size like some studies had 191 (38), 245 (29), and other had 133 study subjects (30), inclusion & exclusion criteria difference like aged over 20 years, lived in the study area for ≥ 1 year to be included in the study (17), excluding patients taking lipid lowering drugs (24), subjects with a pacemaker (29), difference in data collection method & instrument like retrospective electronic records review instead of primary data collection (29), using mercury sphygmomanometer for blood pressure measurement (37), difference in study

design like employing retrospective study (29,36,38), some studies led population-based study (30), instead of institutional and other conducted multicentric study instead of single center study like some studies included 60 hospitals for their research (17), difference in sampling technique may have contributed to the differences in magnitude of HUA, whereas the magnitude of HUA in current study is lower than the studies done in countries such India (46%) (32), Saudi Arabia (80%) (35). This difference in magnitude might be because of the difference in study population, studies in India (46%) (32), and Saudi Arabia (80%) (35) had study populations of only adult T2DM patients regardless of having CO or not, when compared to the present study which might contribute to the difference in magnitude of HUA. Likewise, differences in sampling technique, variation in inclusion & exclusion criteria like in Saudi Arabia only women aged ≥ 35 years old with T2DM included in the study (35), targeting only T2DM patients aged between 35 and 60 years (32), and excluding patients on supplements such as calcium, allopurinol, and vitamin D (35). Differences in sociodemographic characteristics and diverse resident profiles, such as nutritional behaviors, geographical/environmental aspects, genetic issues, and variation sample size, like in India 50 cases of T2DM studied (32), may have contributed to the variances in magnitude.

This study found that there was a statistically significant association between the age of respondents and HUA (***see Table 6 above***), indicating there is a positive relationship between older age and HUA that people with age ≥ 45 years are more likely to have HUA than younger peoples (< 45 years). This study finding is consistent with the study conducted in China (41), Taiwan (42), India (43), Tianjin (37), Jordan (34), Hawassa (19), Gondar (24), and Nantong University, China (44); this may be due to the reason that changes in renal function and body composition may cause a higher risk of HUA with aging. After 40, there is a 10% decline in kidney function for every decade of age beyond that. This results in decreased uric acid excretion, leading to blood uric acid buildup (88). Predisposing variables for HUA and crystal deposition also increase with age, including joint aging, and chronic joint overloading from being overweight. As a result, the burden of HUA could rise (78,89). In addition, comorbid conditions like hypertension, and kidney disease are more common in the older and are linked to a higher risk of HUA (40). HUA may arise due to hormonal changes brought on by age, such as a rise in testosterone levels in males and a fall in estrogen levels in women (90,91).

Furthermore, because of renal problems during aging and age-related increases in the adenosine triphosphate binding cassette transporter sub-family G member 2 protein (24,92), urate reabsorption in the renal ductal tube is stimulated by adenosine triphosphate binding cassette transporter sub-family G member 2 protein activation, leading to an increase in blood uric acid levels and the eventual induction of HUA through urate reabsorption (78,93,94). In conclusion, the mechanism behind the association between aging and HUA is probably complex and includes altered renal function, hormonal fluctuations, lifestyle choices, and a higher incidence of comorbidities (24,78,88–90,92–96).

This study found that there was a statistically significant association between the sex of respondents and HUA (***see Table 6 above***), indicating there is a positive relationship between male sex and HUA that male respondents are more likely to have HUA than female respondents. This study finding is consistent with the study conducted in Maharashtra (45), Dhaka (33), and Jimma (2). Males are more likely than females to experience HUA for a variety of reasons, including the impact of sex hormones, where estrogen, the female sex hormone, aids in the kidneys' elimination of uric acid that might stabilize blood uric acid levels (97,98). Comparatively, men have higher circulating uric acid levels than women and a higher risk of associated comorbidities, women mostly have lower SUA levels and are protected from developing related illnesses, which is suspected to be a result of the suppressive effects of estradiol on xanthine oxidase. However, a study found that the sex difference in uric acid is established during adolescence due to a substantial rise in SUA in boys, coinciding with a rise in testosterone levels, not estradiol levels, and a decrease in sex hormone-binding globulin (99,100).

Furthermore, as a female sex hormone seems to guard against HUA, sex hormones may also regulate how the kidneys handle uric acid, particularly estrogen plays a part in controlling the expression and action of uric acid transporters, such as adenosine triphosphate binding cassette transporter G2 and solute carrier family 2 member 9. Estrogen has been found to increase the expression of organic anion transporter 1 and organic anion transporter 3, encouraging uric acid uptake into renal cells and smoothing its secretion into the tubular lumen. Simultaneously, estrogen downregulates urate transporter 1 expression, decreasing uric acid reabsorption and promoting its excretion. Furthermore, estrogen can affect renal bicarbonate handling by upregulating the renal sodium-bicarbonate cotransporter, which improves bicarbonate

reabsorption, leading to a further alkaline environment that favors uric acid dissolution and excretion (99,101,102).

In addition, men could be more inclined than women to engage in alcohol consumption. Alcoholic beverages can trigger the development of adenosine triphosphate binding cassette transporter sub-family G member 2 protein, which is more expressed in men than women because alcohol, especially beer, has a high purine content. By encouraging the reabsorption of urate in the renal ductal tube, adenosine triphosphate binding cassette transporter sub-family G member 2 protein activation raises blood uric acid levels, which in turn causes HUA by facilitating urate reabsorption (78,93,94). In summary, because of increased testosterone levels, variations in renal function, and the possible impact of sex hormones on uric acid processing, the male sex is a substantial risk factor for HUA (99,101).

This study finding is also inconsistent compared to the study led by Nantong University of China (44), District Hospital of Dschang (39), New Delhi (32), Datta Meghe Medical College of India (43), Casablanca (38), Jordan (34), Saudi Arabia (36), which stated that female sex had a statistically significant relationship with HUA compared to the male sex. This discrepancy may be due to multiple reasons, such as the difference in the age of the female study participants; in the studies stated above (32,34,36,38,39,43,44), feminine partakers were mostly post-menopausal especially in the study of Nantong University of China (44) all female patients enrolled were post-menopausal also the in the Jordan study (34) hyperuricemic women were above 60 years old, that the protective effect of female sex hormone which shield against HUA may diminish in post-menopausal women (102). Nevertheless, in the current study, more than half of the female respondents didn't reach the age of menopause, typically between 49 and 52 years of age (103). Furthermore, the difference in the study population and the variance in sociodemographic characteristics and population profiles, such as dietary habits, geographical/environmental factors, and genetic factors, may have contributed to the discrepancy with the current research findings.

As per the finding of the present study, there was a statistically significant association between the study subject's Duration of DM and HUA (***see Table 6 above***), indicating there is a positive relationship between a higher Duration of DM and HUA that people with a Duration of DM ≥ 10 years more likely to have HUA than peoples with lower Duration of DM (< 10 years). This

study finding is consistent with the study conducted in Bengaluru (50), Tianjin First Central Hospital of China (51), Italy (29), Maharashtra (45), Sivagangai (52), Gondar (24), Jimma (2), and Jing Wang et al. meta-analysis and cohort study (41); this may be due to the reason that long-term DM can cause decreased kidney function or diabetic kidney disease, which inhibits the kidneys' ability to eliminate uric acid and causes HUA (104,105). Also, insulin resistance is linked to DM, and this is made worse by the disease's protracted course. Insulin resistance and hyperinsulinemia can reduce uric acid excretion and increase purine synthesis, which raises uric acid levels (104). Further, as DM progressed, the prevalence of endothelial dysfunction, inflammation, and oxidative stress, all hallmarks of the disease and its complications - rose dramatically. These conditions also played a critical role in developing conditions linked to elevated uric acid levels, which may exacerbate HUA (18,26). In conclusion, a complex association between HUA and an extended duration of DM encompasses several interrelated components, such as insulin resistance, renal impairment, inflammation, and endothelial dysfunction (18,26,104,105).

This study finding is also inconsistent compared to the Jing Wang et al. meta-analysis and cohort study that study subjects with higher SUA concentrations had shorter diabetic duration (41). This discrepancy may be due to the difference in study design, study population, and the variance in genetic, sociodemographic characteristics and population profiles, such as dietary habits, and geographical/environmental factors, which may have contributed to the discrepancy with the current research findings.

As of the current study finding, there was a statistically highly significant association between the DBP of respondents and HUA (***see Table 6 above***), indicating there is a positive relationship between higher DBP and HUA that people with DBP ≥ 80 mmHg are more likely to have HUA than people with lower DBP (< 80 mmHg). This study finding is consistent with the study conducted in Tianjin (37), Nantong University (44), Al Madinah Al Munawarah City (35), Jimma (2), Maharashtra (45), and Ming-Yun Chen et al. study (54). This may be due to the reason that long-standing increase in DBP triggers complex responses in renal physiology and function. The continued rise of the renal perfusion pressure, which is among the stimuli that effect on hyperfiltration as an initial compensatory response, remains sufficient to keep up with the demands of homeostasis. However, lingering elevation of DBP leads to a processive

condition of renal injury and ultimately to insufficient renal perfusion. Additionally, prolonged raise of DBP can disturb renal autoregulatory mechanisms, possibly leading to insufficient regulation of renal blood flow and glomerular filtration rate. Protracted increase of DBP causes structural remodeling within the renal vasculature, primarily through arteriolar sclerosis; thus, integrity mechanisms for proper blood flow and oxygenation in the kidney suffer degradation. As a consequence, glomerular filtration rate demonstrates a gradual reduction as an effect of continuous damage and hardening of the glomeruli. A gross impairment of kidney function occurs, and the person is greatly prone towards the unfurl of chronic kidney disease into a chronic stage of end-stage renal disease. Moreover, a prolonged high DBP compromises the uric acid clearing mechanisms, and thus SUA surges, leading to a highly problematic predisposition towards HUA. It thus becomes clear that there is a complex interplay that underscores the intrinsic relationship between elevated DBP, renal dysfunction, and the development of such metabolic disorders as HUA (106–109). Furthermore, endothelial injury due to enduring exposure of the endothelium to high blood pressure, which produces structural changes in the vasculature that induce endothelial apoptosis, vascular remodeling, and atherosclerosis. Second is renal dysfunction brought about by chronic high blood pressure occurring as microvascular damage in the kidneys that results from long-term elevated DBP, leading to impaired renal excretory and filtration functions of uric acid. Hyperuricemia can arise due to endothelial dysfunction, which can cause increased vasoconstriction, altered renal hemodynamics, and decreased nitric oxide bioavailability (109,110). In broad terms, HTN and elevated DBP are linked to heightened oxidative stress, inflammatory response, and insulin resistance inside the body. HUA can result from insulin resistance, which leads to changes in renal uric acid passage and intensifies uric acid synthesis, patients with selective insulin resistance, such as those with overweightness or lipodystrophy, display normal or somewhat elevated fractional excretion of uric acid signifying that their HUA is not principally triggered by reduced renal excretion of uric acid. Instead, it seems that amplified uric acid synthesis and changed expression of renal uric acid transporters play more significant roles in the progress of HUA in these people. (110–114). In summary, HUA can be influenced by high DBP through its effects on oxidative stress, renal function, and vascular health. The intricate connection between uric acid levels and blood pressure is affected by these processes (109,110,115).

This study found that there was a statistically significant association between the SCr of respondents and HUA (***see Table 6 above***), indicating there is a positive relationship between higher SCr and HUA that people with SCr ≥ 1.2 mg/dl more likely to have HUA than lower SCr people (< 1.2 mg/dl). This study finding is consistent with the study conducted in India (56), Saudi Arabia (36), Italy (29), Tianjin (37), and Ming-Yun Chen et al. study (54); this may be due to the reason that increased SCr levels are frequently linked to kidney impairment but also indicates other conditions like metabolic disorders, muscle breakdown which can impact the body's uric acid levels and cause HUA. There are many possible mechanisms for such circumstances. For instance, when renal function is compromised, as seen by an increased SCr level, about two-thirds of the uric acid in the body is eliminated through the kidneys; this can result in decreased excretion and an accumulation of uric acid in the blood, which is known as HUA. Moreover, renal function and SCr levels are known to be impacted by comorbidity and DM problems, particularly those of the kidney. Moreover, muscle breakdown leads to a surge in the release of intracellular contents, including purines and nucleic acids that can accentuate uric acid production. Myoglobin released from damaged muscle cells could also precipitate in the kidneys, causing renal damage, therefore impairing the excretion of uric acid and subsequent HUA (116–118).

As per the present study finding, there was a statistically significant association between the TC of respondents and HUA (***see Table 6 above***), indicating there is a positive relationship between higher TC and HUA that people with TC ≥ 200 mg/dl are more likely to have HUA than people with lower TC (< 200 mg/dl). This study finding is consistent with the study conducted in Nantong University (44), Tianjin First Central Hospital of China (51), Gondar (24), Saudi Arabia (36), Guangdong Province of China (17), Tianjin (37), and Ming-Yun Chen et al. study (54). A possible reason for the increased likelihood of HUA in elevated TC may be due to the coincidence of communal risk factors such as alcohol consumption (119). Even though the exact mechanisms underlying HUA, dyslipidemia, and increased TC remain unclear. However, several possible mechanisms have been suggested. For instance, nicotinamide adenine dinucleotide phosphate serves as a coenzyme in numerous stages of the cholesterol biogenesis lane. One noteworthy phase in which nicotinamide adenine dinucleotide phosphate is used is during the conversion of 3-hydroxy-3-methylglutaryl-coenzyme A to mevalonate, which is catalyzed by the enzyme β-Hydroxy β-methylglutaryl-coenzyme-A

reductase enzyme that require nicotinamide adenine dinucleotide phosphate as a reducing molecule; this could increase uric acid production because the pentose phosphate pathway is upregulated (120–122). A further potential cause is that high cholesterol might exacerbate HUA by causing inflammation and oxidative stress, which are critical to the onset and course of disorders linked to HUA (78,110). Likewise, hyperuricemia is frequently linked to metabolic syndrome, a collection of illnesses that includes high blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol levels, the disruptions to metabolic processes in people with elevated TC may also have contributed to the production of high levels of uric acid. Consequently, increased cholesterol may be a component of the more extensive metabolic alterations that lead to HUA (19,45,56).

This study found that there was a statistically significant association between Alcohol Consumption and HUA (***see Table 6 above***), indicating there is a positive relationship between Alcohol intake and HUA that people who drink alcohol are more likely to have HUA than people who don't consume Alcohol. This study finding is consistent with the study conducted in India (56), Cameroon (40), Jimma (2), and Hawassa (19); this may be due to the reason that Alcohol use can influence HUA in many ways. Consuming alcohol, particularly beer, is high in purines, which the body converts to uric acid. Furthermore, drinking alcohol causes hyper-lactic acidemia, which lowers the excretion of UA, as well as increases urate and lactate synthesis (2,56,123,124). Increased nicotinamide adenine dinucleotide production from ethanol metabolism causes ethanol to oxidize to acetaldehyde, raising uric acid production (125).

Additionally, ethanol promotes the breakdown of adenine nucleotides, increasing blood levels of lactic acid and potentially exacerbating HUA. Also, purines in alcoholic drinks, particularly beer, might raise the levels of plasma uric acid (126). Drinking alcohol can cause ketoacidosis and dehydration, both of which are linked to ethanol-induced HUA. As well it may raise the plasma concentrations and excretion of xanthine and hypoxanthine in the urine, which may lead to HUA (126). Moreover, alcohol can cause lactic acidosis, a disease that lowers the kidneys' capacity to eliminate uric acid and causes it to build up in the blood (124). The impact of various alcoholic beverages on serum urate levels differs. Wine is the beverage that causes the most significant increases in serum urate levels, followed by beer and whiskey (127).

Conjointly, alcohol is a diuretic, which increases the risk of dehydration. Dehydration can concentrate urine, lowering uric acid excretion and raising blood uric acid levels (124).

6.1 Strength of the study

To the best of the authors' knowledge, there is no similar study conducted in the area as well as the entire country; this is the first large sample size study (n = 423) with a high response rate (99%, n = 419) investigating the magnitude of and risk factors associated with HUA in Ethiopian T2DM patients with central obesity so that it can contribute a lot as source or baseline information for future studies. Use contextually adopted standardized questionnaires and quality control in training, pretesting, and data entry programming. Also, the study used a multivariable analysis to control for confounders and assess the strength of the association of variables with HUA .

6.2. Limitation of the study

Even though the necessary endeavors were made to minimize or avoid possible limitations of the study, the results should be interpreted in light of the following unavoidable limitations.

The present study was cross-sectional; hence, no causal inferences or temporal associations could be drawn because the study design only describes what is happening at present. A face-to-face interview may lead to social desirability bias by overestimating or underestimating the result, and recall bias may be exposed to get inappropriate information from each participant and not complemented with a mixed study design, decreasing the study's strength. Owing to resource limitations, the homeostatic model assessment for insulin resistance test was not performed to determine insulin resistance status and insulin concentration was not measured.

7. CONCLUSION & RECOMMENDATION

7.1 Conclusion

The overall magnitude of HUA results was high, even higher than most studies conducted in other countries. Having an age of ≥ 45 years old, being male, having a duration of DM ≥ 10 years, having SCr ≥ 1.2 mg/dl, having DBP ≥ 80 mmHg, having TC ≥ 200 mg/dl, and alcohol consumption were found to be statistically significant factors associated with HUA.

7.2 Recommendation

Health Policymakers

Based on the present study findings health policymakers are recommended to put an effort into:

- Prioritizing screening, and raising awareness programs by focusing on T2DM patients with CO, especially those who are male, older age, and have had diabetes for a prolonged duration.
- Providing funds for additional research and facilitating long-term studies.

For Hospital Managers

Based on the current study findings hospital managers are recommended to focus on:

- Priority on staff education, training, regular interdisciplinary meetings, and integration.
- Creating patient education initiatives and allocating funding for long-term care plans.

For Health Professionals

As of the present study result health professionals are recommended to give attention to:

- Prioritize ongoing screening and education of patients about the link between T2DM, CO & HUA, and also offer lifestyle modification counseling.
- Taking risk factors into account, and employing multidisciplinary teamwork.

For Researchers

Based on the current study findings researchers are recommended to concentrate on:

- Doing more studies using a stronger study design, huge sample size, and on a multicentered or community level and exploring more predictor variables utilizing relative scrutiny to provide a clear understanding of the disorder's epidemiology and associated factors.
- Disseminating findings through peer-reviewed journals and conferences.

For The Community

As of the finding of the current study, the community is recommended to concentrate on:

- Dynamically involving in civic screening programs and routine health check-ups.
- Forming support groups, and putting society members in touch with pertinent resources.

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ANNEX I. Information sheet and Informed consent form (English version)

Information sheet

Dear participants, my name is _____. I am here to collect data for a study entitled "Magnitude of Hyperuricemia and its associated factors among Type II Diabetic patients with central obesity on follow-up in Woldia Comprehensive Specialized Hospital, Habtemariam Mulugeta conducting the Research project. I am an MSc student in Medical Physiology. The interview will require about 25 to 45 minutes to be completed.

Title of the Research Project: Magnitude of Hyperuricemia and its associated factors among Type II Diabetic patients with central obesity on follow-up in Woldia Comprehensive Specialized Hospital, North East Ethiopia, 2023.

Principal Investigator: Habtemariam Mulugeta Abate (BSc)

Name of advisors: Dr. Diresebachew Haile (MSc, PhD, Associate Professor) & Dr. Abebaye Aragaw (MSc, PhD, Assistant Professor)

The organisation's name is Addis Ababa University, College of Medicine & Health Sciences, School of Medicine, Department of Medical Physiology.

Introduction: Patients with type 2 diabetes and central obesity frequently experience hyperuricemia, but the underlying causes of its onset and persistence are poorly known. This lack of comprehension can make therapy less effective and have a detrimental impact on patient outcomes. To enhance patient treatment and results, it is crucial to understand the related causes of hyperuricemia in this patient population.

Purpose: This study aims to find the Magnitude of Hyperuricemia & associated factors among adult diabetes mellitus patients with central obesity. The information you provide is essential not only for the successful accomplishment of the study but also for producing relevant information that will help improve the provision of medical status to adult diabetic patients & provide research results to the concerned body for intervention.

Procedure & Participation: The research method is a descriptive cross-sectional study & the data collection method is Face-to-face interviews, document reviews, Laboratory Tests, Anthropometry & Blood Pressure Measurements. The expected duration of the participants' contact with the data collector will take 25 to 45 minutes. You will be asked to participate in this Research because the complete trust information is vital for understanding the proposed subject matter. Moreover, the sampling frame's participation is affirmed through the Procedure probability sampling technique, which provides an equal chance of selection.

Confidentiality: I assure you that privacy will be strictly maintained throughout. Your responses to any of the questions will not be given to anyone else & no reports of the study will ever identify you. If an account of the results will be published, only information about the whole group will appear.

Benefit: The information generated from the study will help policymakers change the direction of the strategic plan, continuous monitoring & evaluation of the program according to the study result; improving quality of care, quality of life, & Health Literacy will enable healthcare providers to implement other care beyond metabolic control & will help you to get the quality of medical services from health institutions.

Risk: By participating in this research project, you may feel a little discomfort, especially when spending your time. We hope you will join the study to benefit from the result. I am sure there is no risk of participating in this research project in physical harm, social discrimination, psychological trauma, or economic loss & no discrimination to you. Healthcare professionals in health institutions provide all treatment services. **Inducement, incentive, & Compensation:** This study process has no form of inducement or coercion & the study does not bring any risks that incur compensation.

Results Dissemination: The researcher is responsible for disseminating findings & being fully accountable for providing feedback; the final report will be published to the Department of Medical Physiology Addis Ababa University & the study findings will be issued to the regional health bureau & concerned health facility. The investigator will publish the findings in a scientific journal.

Freedom to withdraw: If you want to participate in the study, you have the full right to withdraw at any time; this would not affect your health benefits from health institutions. Nobody will force you to explain the reason for withdrawal; in other words, refusal to respond to the questions will not affect the services you or any family member may receive from any service providers now or in the future. You have the right to terminate the study for any reason related to the Research or personal defense.

Person to Contact: The participant has the right to ask for information that is unclear about the research context & content before & during the research work. You can contact the principal investigator & supervisor. Moreover, this Research has undergone ethical review & approval by the Addis Ababa University College of Health Sciences ethical research committee. This ethical research committee's main task is to ensure that the moral principles have been adhered to and that & the research participants are protected from harm. If you want additional information & check about this project, you can contact the following people. Addis Ababa University College of Health Sciences Ethical research committee, Secretary Office Tel. +251911012775

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Informed consent form

Title of the project: Magnitude of Hyperuricemia & associated factors among type II diabetic patients with central obesity on follow-up in Woldia Comprehensive Specialized Hospital, North East Ethiopia, 2023. I understand this research undertaking is a post-graduate degree partial fulfilment of Research fully supported & coordinated by the Addis Ababa University Department of Medical Physiology & the designated principal investigator is Habtemariam Mulugeta. I have been fully informed in the language I understand about the research project objective: Magnitude of Hyperuricemia & associated factors among type II diabetic patients with central obesity on follow-up in Woldia Comprehensive Specialized Hospital. I have been informed that all the information I provide to the interviewer will be confidential. I understood that Research has no risk & no composition. I also know that I have the right to withhold information, skip questions to answer, or withdraw from the study any time I am acquainted, and nobody will impose on me to explain the reason for withdrawal. It is also enlightening that health benefits or other administrative effects from health institutions would not affect my health benefits. I have assured you that the right to ask for information that is not clear about the Research before & or during the research work & to contact:

Addis Ababa University, College of Health Sciences Office **Tel**. +251911012775

Principal Investigator's Name: Habtemariam Mulugeta, **Mobile:** +251924314840

Supervisor name & address: Name: Tsgereda Assefa Legesse**,**

Phone Number: +251931882791

I have read this form, or it has been read to me in the language I comprehend & understand the condition stated above. Therefore, I am willing & confirm my participation by verbal consent. Agreed to participate in the study: Yes /No (mark one of them for verbal consent)

Name of witness signature _____ (Data collector, supervisor, any third person),

Signature _____, Date _____

ANNEX II - English version Questionnaires

These questionnaires are designed to assess the Magnitude of Hyperuricemia & its associated factors among Type II diabetic patients with Central Obesity on follow-up in Woldia Comprehensive Specialized Hospital.

Code number_____, starting time _____ in minutes, finishing time _____ in minutes, Data collector name_____		
Part I - Socio-demographic characteristics		
Encircle the coding category number that you choose from the given boxes.		
Code	Questionnaires	Coding Categories
101	What is your gender?	1. Male 2. Female
102	Where are you living now?	1. Urban 2. Rural
103	How many years old now?	_____ in years
104	What is your educational status?	1. Can read and write 2. Cannot read and write 3. Primary school 4. Secondary school 5. College 6. University
105	What is your marital status?	1. Single 2. Married 3. Widowed 4. Divorced
106	What is your occupational status?	1. Unemployed 2. Private employed 3. Governmental employed 4. Housewife 5. Self-employed
107	How much money is your average monthly income per month?	_____ in Ethiopia Birr
108	Are you a member of community-based health insurance?	1. Yes 2. No
Part II – Serum Uric Acid Laboratory Measurement		
code	Questionnaires	
201	**Serum Uric Acid**	_____ in mg/dL
Part III: Factors that affect the Hyperuricemia		
Encircle the coding category number that you choose from the given boxes.		
Code	Questioner	Code categories (Please circle the number)
301	Which drug regimen you are following currently for your diabetes?	1. Oral anti-diabetic medication only 2. Insulin only 3. Insulin and oral ant-diabetic medication 4. Only following the dietary plan as recommended
302	Do you have any diabetic-related long-term Complications? If the answer is "**No,**" **303 and 304 skips and start 305**	1. Yes 2. No
303	If your answer is "Yes" for question No. 302, which type of long-term complications do you have? (Multiple answers are possible)	1. Diabetic Nephropathy 2. Diabetic Neuropathy 3. Diabetic Retinopathy 4. Diabetic foot ulcer 5. Diabetic related heart disease 6. Diabetic related hypertension 7. Other

304	For how long have you had diabetes?	_____ in years
305	Serum HbA1C	
306	Fasting blood glucose	
307	Do you have co-morbidity disease? If the answer is "No," skip question 310 and start 311	1. Yes 2. No
308	If your answer to question number 308 is yes, what type of co-morbidity diseases do you have?	1. Heart disease 2. Kidney disease 3. Hypertension 4. Other
309	Systolic BP	_____ mmHg
310	Diastolic BP	_____ mmHg
311	Serum Creatinine	
312	Total cholesterol	
313	Triglyceride	
314	LDL	
315	HDL	
316	Weight	
317	Height	
319	Lipid Lowering Drugs	1. No Medication 2. Statin only 3. Fibrate only 4. Statin + Fibrate 5. Other

Khat Chewing questionnaires

Encircle the coding category number that you choose from the given boxes.

401	Have you ever chewed Khat? **If the answer is "No," skip 402 and 403**	1. Yes 2. No
402	During the last 30 days, how many days did you chew Chat?	---------- Number of days

Alcohol consumption screening

Encircle the coding category number that you choose from the given boxes.

501	Have you ever taken a drink that contains alcohol (Tella/Tegi/Areke/Beer/Wine, etc...)? **If the answer is "No," skip 502 and 503**	1. Yes 2. No
502	During the last 30 days, how many days did you have a drink that contains alcohol?	---------- Number of days
503	During the last 13 months, how often did you take a drink that contains alcohol?	1. Almost Every Day 2. At Least Once A Week 3. Less Than Once A Week 4. None in The Last 13 Months

Cigarette Consumption

601	Have you smoked a cigarette - even one puff - during the past Year?	1. Yes 2. No
602	If yes, how many cigarettes did you smoke on an average day?	Number of cigarettes: _____

Depression Anxiety Stress Scale 21 (DASS-21) Checklist

Please read each statement and circle 0, 1, 2, or 3, indicating how much the statement applied to you over the past week. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 = Did not apply to me at all - **NEVER**
1 = Applied to me to some degree, or some of the time - **SOMETIMES**
2 = Applied to me to a considerable degree, or a good part of time - **OFTEN**
3 = Applied to me very much, or most of the time - **ALMOST ALWAYS**

S = STRESS, D = DEPRESSION, A = ANXIETY

code		Ratings			
701 (**S**)	I found it hard to wind down	0	1	2	3
702 (**A**)	I was aware of dryness of my mouth	0	1	2	3

703 (**D**)	I couldn't seem to experience any positive feeling at all	0	1	2	3
704 **(A)**	I experienced breathing difficulty (e.g., excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
705 (**D**)	I found it difficult to work up the initiative to do things	0	1	2	3
706 (**S**)	I tended to over-react to situations	0	1	2	3
707 (**A**)	I experienced trembling (e.g., in the hands)	0	1	2	3
708 (**S**)	I felt that I was using a lot of nervous energy	0	1	2	3
709 (**A**)	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
710 (**D**)	I felt that I had nothing to look forward to	0	1	2	3
711 (**S**)	I found myself getting agitated	0	1	2	3
712 (**S**)	I found it difficult to relax	0	1	2	3
713 (**D**)	I felt down-hearted and blue	0	1	2	3
714 (**S**)	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
715 (**A**)	I felt I was close to panic	0	1	2	3
716 (**D**)	I was unable to become enthusiastic about anything	0	1	2	3
717 (**D**)	I felt I wasn't worth much as a person	0	1	2	3
718 (**S**)	I felt that I was rather touchy	0	1	2	3
719 (**A**)	I was aware of the action of my heart in the absence of physical exertion (e.g., sense of heart rate increase, heart missing a beat)	0	1	2	3
720 (**A**)	I felt scared without any good reason	0	1	2	3
721 (**D**)	I felt that life was meaningless	0	1	2	3

Morisky Medication Adherence Scale (MMAS) checklist

Please answer each question based on your personal experience with your medications. Note that there is not right or wrong answer. (Please circle your answer below)

Code		Choices	
801	Do you sometimes forget to take your medications?	(1) No	(0) Yes
802	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your medications?	(1) No	(0) Yes
803	Have you ever cut back or stopped taking your medications without telling your doctor, because you felt worse when you took it?	(1) No	(0) Yes
804	When you travel or leave home, do you sometimes forget to bring along your medications?	(1) No	(0) Yes
805	Did you take your medications yesterday?	(1) No	(0) Yes
806	When you feel like your health condition is under control, do you sometimes stop taking you medications?	(1) No	(0) Yes
807	Taking medications every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?	(1) No	(0) Yes
808	How often do you have difficulty remembering to take all your medications?	4. Never/rarely 3. Once in a while 2. Sometimes 1. Usually 0. All the time	

Thank You!

ANNEX III: Information sheet and Informed consent form (Amharic version)

የመረጃ ወረቀት

ውድ ተሳታፊዎች ስሜ _____ ነው የመጣሁት በወልዲያ ሁለገብ ስፔሻላይዝድ ሆስፒታል ውስጥ ክትትል በሚደረግበት ወቅት በአይነት II የስኳር ህመምተኞች መካከል ያለው የጤና ትምህርት (መሃይምነት) ደርጃ እና ተጓዳኝ ምክንያቶች" በሚል ርዕስ ጥናት ለማሰባሰብ ነው ። ይህ ጥናት በሀብተማርያም ሙሉጌታ የሚካሄድ ሲሆን እርሱም በአዋቂዎች ጤና ነርሲንግ የማስትርስ ተማሪ ነው። ቃለመጠይቁ ለማጠናቀቅ ከ 25 እስከ 45 ደቂቃ ያህል ይጠይቃል ።

የምርምር ፕሮጀክቱ ርዕስ፡ በደም ውስጥ ያለው ከፍ ያለ የዩሪክ አሲድ መጠን እና ተያያዥ ምክንያቶች በወልዲያ አጠቃላይ ስፔሻላይዝድ ሆስፒታል ክትትል በሚደረግባቸው የማዕከላዊ ውፍረት እና የዓይነት ሁለት የስኳር ህመምተኞች መካከል፣ በሰሜን ምስራቅ ኢትዮጵያ ፣ 2015።

ዋና ተመራማሪ፡ ሀብተማርያም ሙሉጌታ (ዲግሪ)

የአማካሪዎች ስም፡ ዶ/ር ድርስባቸው ሃይሌ (ማስትርስ ፣ ፒኤች.ዲ፣ ተባባሪ ፕሮፌሰር) እና ዶ/ር አበባየ አራጋው ((ማስትርስ ፣ ፒኤች.ዲ ፣ረዳት ፕሮፌሰር)

የድርጅቱ ስም: አዲስ አበባ ዩኒቨርሲቲ ፣ ጤና ሳይንስ ኮሌጅ ፣ የህክምና ትምህርት ቤት ፣ የሜዲካል ፊዝዮሎጂ መምሪያ ።

መግቢያ: ዓይነት 2 የስኳር በሽታ እና ማዕከላዊ ውፍረት ያለባቸው ታካሚዎች በደም ውስጥ ያለው ከፍ ያለ የዩሪክ አሲድ መጠን በተደጋጋሚ ያጋጥማቸዋል, ነገር ግን የመጀመሩ እና የመቆየቱ ዋና መንስኤዎች በደንብ አይታወቁም. ይህ የግንዛቤ እጥረት ህክምናን ውጤታማ አያደርገውም እና በታካሚ ውጤቶች ላይ ጎጂ ተጽዕኖ ያሳድራል። የታካሚውን ህክምና እና ውጤቱን ለማሻሻል በዚህ የታካሚ ህዝብ ውስጥ hyperuricemia የሚያስከትሉ ተያያዥ ምክንያቶችን መረዳት በጣም አስፈላጊ ነው.።

ዓላማ: ይህ ጥናት የማዕከላዊ ውፍረት እና በአዋቂዎች አይነት 2 የስኳር ህመምተኞች መካከል በደም ውስጥ ያለው ከፍ ያለ የዩሪክ አሲድ መጠን እና ተያያዥ ምክንያቶች ለማግኘት ያለመ ነው ። የሚሰጡት መረጃ ለጥናቱ ስኬታማነት ብቻ ሳይሆን ለአዋቂ የስኳር ህመምተኞች የህክምና ሁኔታ ጥራትን ለማሻሻል እና ለሚመለከተው አካል የምርምር ውጤቶችን ለማስገኘት የሚረዳ አግባብነት ያለው መረጃ ለማውጣት አስፈላጊ ነው ።

አሰራር እና ተሳትፎ: የምርምር ዘዴው ገላጭ የመስቀለኛ ክፍል ጥናት ሲሆን የመረጃ አሰባሰብ ዘዴው ፊት-ለፊት ነው ። ተሳታፊዎች ከቃለ-መጠይቁ ጋር የሚገናኙበት ጊዜ የሚጠበቀው ጊዜ ከ 25 እስከ 45 ደቂቃዎችን ይወስዳል ። የታቀደውን ርዕሰ ጉዳይ ለመረዳት በጣም የሚያቀርበው የተሟላ የመተማመን መረጃ በጣም አስፈላጊ በመሆኑ በዚህ ምርምር ውስጥ እንዲሳተፉ ይጠየቃሉ ። በተጨማሪም ፣ የናሙና ፍሬም ተሳትፎ በእኩልነት የመምረጥ እድል በሚሰጥ የአሠራር ፕሮዳክሽን አሰራር ዘዴ የተረጋገጠ ነው ።

ሚስጥራዊነት: በአጠቃላይ ምስጢራዊነቱ በጥብቅ እንደሚጠበቅ ላረጋግጥላችሁ እወዳለሁ ። ለማንኛውም ጥያቄዎች የሚሰጡት ምላሾች ለሌላ ሰው አይሰጡም ፣ እናም የትኛውም የጥናት ሪፖርቶች በጭራሽ አይለይዎትም ። የውጤቶቹ መለያ ከታተመ ስለ አጠቃላይ ቡድኑ መረጃ ብቻ ይታያል።

ጥቅም: ከጥናቱ የተገኘው መረጃ የፖሊሲ አውጪዎች የስትራቴጂክ እቅዱን አቅጣጫ ለመቀየር ፣ በተከታታይ ክትትልና የፕሮግራሙን ምዘና በጥናቱ ውጤት መሠረት ይረዳል ፤ የጤና መፃህፍትን ማሻሻል የጤና እንክብካቤ አቅራቢዎች ከሚታቦሊክ ቁጥጥር ውጭ ሌሎች እንክብካቤዎችን ተግባራዊ እንዲያደርጉ የሚያስችላቸው ሲሆን የህክምና አገልግሎቶችን ጥራት ከጤና ተቋማት እንዲያገኙ ይረዳዎታል ።

አደጋ: በዚህ የምርምር ፕሮጀክት ውስጥ በመሳተፍ አንዳንድ ምቾት እንደሚሰማው ይሰማዎታል ፣ በተለይም ጊዜዎን ያጠፋሉ ። ለምርምር ውጤቱ ጥቅም በጥናቱ ውስጥ እንደሚሳተፉ ተስፋ እናደርጋለን ። በአካላዊ ጉዳት ፣ በማህበራዊ አድልዎ ፣ በስነልቦና ቁስለት ፣ በኢኮኖሚ ኪሳራ እና ለእርስዎ ምንም አድልዎ ላይ በዚህ የምርምር ፕሮጀክት ውስጥ የመሳተፍ አደጋ እንደሌለ እርግጠኛ ነኝ በጤና ተቋማት ውስጥ የጤና እንክብካቤ ባለሙያዎች ሁሉንም የሕክምና አገልግሎቶች ይሰጣሉ ።

ማበረታቻ ፤ ጥቅማ ጥቅም እና ማካካሻ፡ ይህ የጥናት ሂደት የማነቃቂያ ፣ የማስገደድ አይነት የለውም ፣ እናም ጥናቱ ካሳ የሚያስገኙ አደጋዎችን አያመጣም ።

የውጤት ስርጭት፡ ተመራማሪው ግብረመልስ ለመስጠት ሙሉ በሙሉ ተጠያቂነት ላለው ግኝቶች የማሰራጨት ኃላፊነት አለበት ፤ የመጨረሻው ዘገባ ለአዲስ አበባ ዩኒቨርሲቲ ለሜዲካል ፊዝዮሎጂ ትምህርት ክፍል የሚሰራጨ ሲሆን የጥናቱ ግኝት ለክልሉ ጤና ቢሮ እና ለሚመለከታቸው የጤና ተቋማት ይሰጣል ። መርማሪው ግኝቱን በሳይንሳዊ መጽሔት ላይ ያትማል ።

የመውጣት ነፃነት: በጥናቱ ውስጥ መሳተፍ ከፈለጉ በፈለጉት ጊዜ ከጥናቱ የመውጣት ሙሉ መብት አለዎት ፤ ይህ ከጤና ተቋማት በሚሰጡት የጤና ጥቅማ ጥቅም ላይ ምንም ተጽዕኖ አያሳድርም ። የመውጣቱን ምክንያት ለማስረዳት ማንም አያስገድድዎትም ፤ ለጥያቄዎቹ መልስ ለመስጠት እምቢ ማለት እርስዎም ሆኑ ማንኛውም የቤተሰብዎ አባል ከማንኛውም አገልግሎት ሰጪዎች በሚያገኟቸው አገልግሎቶች ላይ አሁንም ሆነ ለወደፊቱ ተጽዕኖ አይኖረውም ። በመካከል ከምርምር ወይም ከግል መከላከያ ጋር በተዛመደ በማንኛውም ምክንያት ጥናቱን የማቋረጥ መብት አለዎት ።

የሚገናኘው ሰው፡ ተሳታፊው ከምርምር ሥራው በፊት እና በሚከናወኑበት ጊዜ ስለ ጥናታዊው ዐውድ እና ስለ ይዘቱ ግልጽ ያልሆነ መረጃ የመጠየቅ መብት አለው ። ዋና መርማሪውን እና ተቆጣጣሪውን ማነጋገር ይችላሉ ። በተጨማሪም ይህ ጥናት በወሎ ዩኒቨርሲቲ የጤና ሳይንስ ኮሌጅ የስነምግባር ጥናት ኮሚቴ የስነምግባር ግምገማና ማረጋገጫ አግኝቷል ። ይህ የስነምግባር ጥናት ኮሚቴ ዋና ስራው የስነምግባር መርሆዎች ተጠብቀው አለመኖራቸውን ማረጋገጥ እና የምርምር ተሳታፊዎች ከጉዳት እንዲጠበቁ ማድረግ ነው ። ተጨማሪ መረጃ ከፈለጉ እና ስለዚህ ፕሮጀክት ለማጣራት የሚከተሉትን ሰዎች ማነጋገር ይችላሉ ። የአዲስ አበባ ዩኒቨርሲቲ የጤና ሳይንስ ኮሌጅ ሥነምግባር ጥናት ኮሚቴ ፣ ጸሐፊ ጽሕፈት ቤት ስልክ. +251911012775

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በመረጃ የተደገፈ የስምምነት ቅጽ

የፕሮጀክቱ በደም ውስጥ ያለው ከፍ ያለ የዩሪክ አሲድ መጠን እና ተያያዥ ምክንያቶች በወልዲያ አጠቃላይ ስፔሻላይዝድ ሆስፒታል ክትትል በሚደረግባቸው የማዕከላዊ ውፍረት እና የዓይነት ሁለት የስኳር ህመምተኞች መካከል፣ በሰሜን ምስራቅ ኢትዮጵያ ፣ 2015፡፡ ይህ የምርምር ስራ የድህረ-ምረቃ ድግሪ በከፊል የተሟላ ምርምር ሙሉ በሙሉ የተደገፈ እና የተቀናጀ መሆኑን ተረድቻለሁ ፡፡ በአዲስ አበባ ዩኒቨርሲቲ የሜዲካል ፊዝዮሎጂ መምሪያ እና የተሾመው ዋና መርማሪ ሀብተማርያም ሙሉጌታ ናቸው ፡፡ በወልዲያ አጠቃላይ ሁለገብ ስፔሻላይዝድ ሆስፒታል ውስጥ ክትትል በሚደረግበት የ II ዓይነት የስኳር ህመምተኞች መካከል ስለ ምርምር ፕሮጀክት ዓላማ በተረዳሁበት ቋንቋ ሙሉ በሙሉ ተነግሮኛል ፡፡ ለቃለ-መጠይቅ የማቀርበው መረጃ ሁሉ በሚስጥር እንደሚያዝ ተነግሮኛል ፡፡ ምርምር ምንም ስጋት እና ቅንብር እንደሌለው ተረድቻለሁ ፡፡ እንዲሁም መረጃን የመከልከል ፣ መልስ ለመስጠት ጥያቄዎችን መዝለል ፣ ወይም ጥናቱን የማቋርጥ መብት እንዳገኘኝ የማውቅበትን ምክንያት ለማብራራት ማንም ሰው አይጭንብኝም ፡፡ በተጨማሪም በጤና ጥቅሞቼ ላይ ወይም ከጤና ተቋማት የማገኛቸውን ሌሎች አስተዳደራዊ ውጤቶች እንደማይነኩ ብርሃን ነው ፡፡ በምርምር ሥራው በፊትም ሆነ ወቅት ስለ ምርምሩ ግልፅ ያልሆነ መረጃ የመጠየቅ እና የማግኘት መብት እንዳገኘሁ አረጋግጫለሁ ፡፡

የአዲስ አበባ ዩኒቨርስቲ ፣ ጤና ሳይንስ ኮሌጅ ጽ / ቤት፣ **ስልክ**. +251911012775

የዋና መርማሪ ስም፡ ሀብተማርያም ሙሉጌታ፣ **ሞባይል** +251924314840

ተቆጣጣሪ ስም እና አድራሻ፡ ስም፡ ፀጌረዳ አሰፋ ለገሰ፣ **ስልክ ቁጥር:** +251931882791

ይህንን ቅጽ አንብቤዋለሁ ፣ ወይም ከላይ በተጠቀሰው ሁኔታ በተረዳሁት እና በተረዳሁት ቋንቋ ተነበበኝ ፡፡ ስለሆነም ፈቃደኛ ነኝ እና ተሳትፎዬን በፈቃድ አረጋግጣለሁ ፡፡ በጥናቱ ውስጥ ለመሳተፍ ተስማምተዋል-አዎ / የለም (በቃላት ለመስማማት በአንዱ ላይ ምልክት ያድርጉ)

የምስክር ፊርማ ስም _____ (ዳታ ሰብሳቢ ፣ ተቆጣጣሪ ፣ ማንኛውም ሶስተኛ ሰው) ፣

ፊርማ _____ ፣ ቀን _____

ANNEX IV: Amharic Version Questionnaires

እነዚህ መጠይቆች በወልድያ አጠቃላይ ሁለገብ ስፔሻላይዝድ ሆስፒታል ከትትል በሚደረግባቸው በደም ውስጥ ያለው ከፍ ያለ የዩሪክ አሲድ መጠን እና ተያያዥ ምክንያቶች የማዕከላዊ ውፍረት እና የዓይነት ሁለት የስኳር ህመምተኞች መካከል ለመዳሰስ የተቀየሱ ናቸው ::

መለያ ቁጥር_____, መነሻ ጊዜ_____ በደቂቃ, መጨረሻ ጊዜ _____ በደቂቃ, መረጃ ሰብሳቢዉ ስም_____		
ክፍል አንድ ፡ ማህበራዊ-ስነ-ህዝብ ባህሪዎች		
በሳጠኑ ውሰጥ ከተቀመጡት የመለያ ቁጥሮች ትክክለኛ መልስ ብለው ያሰቡትን ቁጥር ያክቡ		
መለያ ቁጥር	ጥያቄ	መለያ ቁጥር (የመረጡትን ያክቡ)
101	ፆታ?	1. ወንድ 2. ሴት
102	አሁን የምትኖሩበት ቦታ የት ነው?	1. ከተማ 2. ገጠር
103	እድሜ?	_____ አመት
104	የትምህርት ደረጃ?	1. ማንበብ እና መጻፊ የሚችል 2. ያልተማረ 3. አንደኛ ደረጃን ያጠናቀቀ 4. ሁለተኛ ደረጃ ት/ቤት ያጠናቀቀ 5. የኮሌጅ ት/ት ያጠናቀቀ 6. የኒቨርሰቲ ያጠናቀቀ
105	የጋብቻ ሁኔታ?	1. ያላገባ/ያላገባች 2. ያገባ/ያገባች 3. በሞት የተለየ/ በሞት የተለየች 4. የፈታ/ የፈታች
106	የስራ ሁኔታ?	1. ስራ የሌለው/ የሌላት 2. በግል ተቀጥሮ የሚሰራ/ የምሰራ 3. በመንግሰት ተቀጥሮ ሚሰራ/ የምሰራ 4. የቤት እመቤት 5. በራሱ ስራ ፈጥሮ የሚተዳደር
107	የወር ገቢዎ መጠን በአማካኝ ስንት ነው?	_____ የኢትዮጵያ ብር
108	የጤና መድን አባል ነዎት?	1. አዎ 2. የለም
ክፍል ሁለት - የሴረም ዩሪክ አሲድ የላቦራቶሪ መለኪያ		
መለያ ቁጥር		
201	ሴረም ዩሪክ አሲድ	_____በ ሚሊግራም/ደሲ ሊትር
ክፍል ሶስት: በከፍተኛ የሴረም ዩሪክ አሲድ ላይ ተጽዕኖ የሚያሳድሩ ነገሮች		
ከተሰጡት ሳጥኖች ውስጥ የመረጧቸውን የምርጫ ምድቦች ቁጥሮን ያክብቡ		
መለያ ቁጥር	ጥያቄዎች	የምርጫ ምድቦች (እባክዎን ቁጥሩን ያክብቡ)
301	ለስኳር በሽታ ከሚሰጡ መድሀኒቶች መካከል የትኛዋቹን በተከታታይ ይወሰዳሉ?	1. የሚዋጡትን ብቻ 2. ኢንሱሊን ብቻ 3. የሚዋጡትን እና ኢንሱሊን 4. የባለሙያ ምክር የአመጋገብ እቅድ መከተል ብቻ
302	በስኳር ህመሙ ምክንያት ያጋጠምዎት ተጨማሪ የረጅም ጊዜ ተያያዥ የጤና እክል አለበዎት? መልስዎ **"የለም"** ከሆነ ተራ ቁጥር **303** እና **304 ይዘለል** እና 305 ይጀምሩ	1. አዎ 2. የለም
303	ለጥያቄ ቁጥር **302** መልስዎ **"አዎ"** ከሆነ የትኛውን የረጅም ጊዜ ችግሮች አጋጥምዎታል? (ብዙ መልሶች ይቻላል)	1. ከኳስር ህመም ጋር የተያያዘ የኩላሊት ህመም 2. ከስኳር ህመም ጋር የተያያዘ የነርቭ ህመም 3. ከስኳር ህመም ጋር የተያያዘ የአይን ህመም 4. ከስኳር ህመም ጋር የተያያዘ የልብ ህመም 5. ከስኳር ህመም ጋር የተያያዘ የእግር ቁስለት 6. ከስኳር ህመም ጋር የተያያዘ የደም ግፊት 7. ሌሎች
304	የስኳር ህመም ከተገኝብዎት ጀምሮ ምን ያህል ጊዜ ሆነዎት?	_____ አመት
305	ሴረም ሄሞግሎቢን ኤ 1 ሲ	

306	የጾም የደም ስኳር መጠን	
307	ከስኳር በሽታው ሌላ በሀኪም የተረጋገጠ በሽታ አለበዎት? መልስዎ **"የለም"** ከሆነ ተራ ቁጠር **307** ይታለፍ	1. አዎ 2. የለም
308	ተራ ቁጥር 309 መልሰዎ **"አዎ"** ከሆነ የተኛው አይነት በሀኪም የተረጋገጠ በሽታ ነው ያለበዎት? (ብዙ መልሶች ይቻላል)	1. የልብ በሽታ 2. የኩላሊት በሽታ 3. የደም ግፊት 4. ሌሎች
309	ሲስቶሊክ የደም ግፊት	_____ በሚሊ ሜትር ሜርኩሪ
310	ዲያስቶሊክ የደም ግፊት	_____ በሚሊ ሜትር ሜርኩሪ
311	ሴረም ክሬቲኒን	
312	ጠቅላላ ኮሌስትሮል መጠን	
313	ትራይግሊሰርይድ መጠን	
314	ዝቅተኛ እፍግታ ያለው የሊፕቶ ፕሮቲን (ከፕሮቲን እና ቅባት (ቅባት) የተሰሩ ቅንጣቶች) መጠን	
315	ከፍተኛ እፍግታ የሊፕቶ ፕሮቲን (ከፕሮቲን እና ቅባት (ቅባት) የተሰሩ ቅንጣቶች) መጠን	
316	ክብደት	
317	ቁመት	
319	የሰውነት ቅባትን የሚቀንሱ መድኃኒቶች	1. መድሃኒቱን የማይጠቀም 2. ስታቲን ብቻ 3. ፊብሬት ብቻ 4. ስታቲን + ፊብሬት 5. ሌሎች

የጫት መቃም መጠይቆች

ከተሰጡት ሳጥኖች ውስጥ የመረጧቸውን የኮድ ምድቦች ቁጥርን ያክብቡ

401	ጫትን ቅመው ያውቃሉ? መልስዎ **"አይ"** ከሆነ **402 ን ይዝለሉ**	1. አዎ 2. የለም
402	በአለፉት 30 ቀናት ውስጥ ስንት ቀን ጫት ቅመዋል?	---------- የቀኖች ብዛት

አልኮል መጠጥ መለያ መጠይቆች

ከተሰጡት ሳጥኖች ውስጥ የመረጧቸውን የኮድ ምድቦች ቁጥርን ያክብቡ

501	አልኮል በዉስጡ የያዘ መጠጥ (ጠላ / ጠጅ / አረቄ / ቢራ / ወይን ፣ ወዘተ) ጠጥተው ያውቃሉ? መልሱ **"አይ"** ከሆነ **602** እና **603 ን ይዝለሉ**	3. አዎ 4. የለም
502	ባለፉት 30 ቀናት ውስጥ ስንት ቀናት ያህል አልኮል የያዘ መጠጥ ጠጥተዋል?	---------- የቀኖች ብዛት
503	ባለፉት 13 ወራቶች ውስጥ አልኮል የያዘ መጠጥ ምን ያህል ጊዜ ጠጥተዋል?	1. በየቀኑ ማለት ይቻላል 2. ቢያንስ በሳምንት አንድ ጊዜ 3. በሳምንት ከአንድ ጊዜ ያነሰ 4. ባለፉት 13 ወሮች ውስጥ ምንም የለም

የሲጋራ ፍጆታ

601	ባለፈው ዓመት ሲጋራ አጨስሃል - አንድ ፑፍ እንኳን -	
602	አዎ ከሆነ፣ በአማካይ በቀን ስንት ሲጋራ አጨስ ነበር?	የሲጋራዎች ብዛት : _____

የድባቴ (ድብርት)፣ የመንፈስ መሸበር (ቁዘማ) እና ጭንቀት ልኬት መጠይቅ

እባክዎን እያንዳንዱን መግለጫ ያንብቡ እና **ባለፈው ሳምንት** ምን ያህል መግለጫው ለእርስዎ እንደተተገበረ ወይንም እርሶን በይበልጥ የሚግልጸውን የሚያመለክት ቁጥር 0 ፣ 1 ፣ 2 ወይም 3 ያክብቡ :: ትክክለኛ ወይም የተሳሳቱ መልሶች የሉም :: በማንኛውም መግለጫ ላይ ብዙ ጊዜ አይውሰዱ ::

ደረጃ አሰጣጡ እንደሚከተለው ነው፡

0 = በጭራሽ ለእኔ አልተተገበረም (የእኔን ሁኔታ አይገልጽም) - በጭራሽ (አልቀበለውም)

1 = በተወሰነ ደረጃ ለእኔ ተተግብሯል ፣ ወይም በተወሰነ ጊዜ - አንዳንድ ጊዜ (አልፎ አልፎ)

2 = በአብዛህኛው ደረጃ ለእኔ ተተግብሯል ፣ ወይም ብዙ ጊዜ - በተደጋጋሚ

3 = ለእኔ በጣም ተተግብሯል ፣ ወይም እጅግ በጣም ብዙ ጊዜ - ሁልጊዜ

መለያ ኮድ	ጥያቄዎች	ምርጫ			
701	መጨነቅ በማቆም ዘና ለማለት ይከብደኝ ነበር	0	1	2	3
702	አፌ ሲደርቅ ይታወቀኝ ነበር	0	1	2	3
703	ምንም አይነት ጥሩ ስሜት እየተሰማኝ አልነበረም	0	1	2	3

704	ለመተንፈስ እቸገር ነበር (ለምሳሌ ፣ ከልክ ያለፈ ቶሎ ቶሎ መተንፈስ ፣ ያለ ምንም አካላዊ እንቅስቃሴ ትንፋሽ ማጣት)	0	1	2	3
705	ማንኛውንም ነገር ለማከናወን ተነሳሽነትን አጣለሁ	0	1	2	3
706	አንዳንድ ነገሮችን ከተገቢው በላይ አጋንናለሁ	0	1	2	3
707	መንቀጥቀጥ አጋጥሞኛል (ለምሳሌ ፣ እጆቼ ላይ)	0	1	2	3
708	ብዙ የነረቭስ (ስሜታዊነት) ጉልበት እንደተጠቀምኩ ይሰማኛል	0	1	2	3
709	አንዳንድ አጋጣሚዎች ላይ ተጨንቄ እራሴን እንዳላዋርድ እሰጋ ነበር	0	1	2	3
710	ምንም ወደፊት የሚያጓጓ ነገር እንደሌለኝ ይሰማኛል	0	1	2	3
711	የመንፈስ መረበሽ ውስጥ እራሴን አገኘዋለሁ	0	1	2	3
712	የመዝናናት መንፈስ ውስጥ መግባት ይከብደኛል	0	1	2	3
713	የሀዘን ስሜት ይሰማኝ ነበር	0	1	2	3
714	ከማንኛውም እያደረኩት ከነበረው ነገር የሚያስቆመኝን ነገር መታገስ አልችልም	0	1	2	3
715	ልረበሽ ትንሽ የቀረኝ እንደሆነ ይሰማኛል	0	1	2	3
716	ለማንኛውንም ነገር በጥሩ ስሜት ማየት አቅቶኝ ነበር	0	1	2	3
717	እንደ ሰው ምንም የማልረባ መስሎ ይሰማኝ ነበር	0	1	2	3
718	ትንሽ የሚበቃው እንደሆንኩ ይሰማኛል	0	1	2	3
719	የአካል እንቅስቃሴ በሌለበት የልቤን ድርጊት አስተውል ነበር (ለምሳሌ፡ የልብ ምት መጠን መጨመር፣ የልብ ምት መዝለል)	0	1	2	3
720	ያለ ምንም ምክንያት ፍርሃት ይሰማኛል	0	1	2	3
721	ህይወት ትርጉም እንደሌለው ይሰማኛል	0	1	2	3

የሞሪስኪ 8 መድሐኒቶችን በታዘዘዉ መሰረት በአግባቡ ስለመዉሰድ መመዘኛ መጠይቅ

ከመድኃኒቶችዎ ጋር ባለዎት የግል ተሞክሮ ላይ በመመርኮዝ እባክዎ እያንዳንዱን ጥያቄ ይመልሱ ፡፡ ትክክለኛ ወይም የተሳሳተ መልስ እንደሌለ ልብ ይበሉ ፡፡
(እባክዎን መልስዎን ከዚህ በታች ያክብቡ)

መለያ ኮድ	ጥያቄዎች	ምርጫ	
801	አንዳንድ ጊዜ መድኃኒትዎን መውሰድ ረስተው ያውቃሉ?	የለም	አዎ
802	አንዳንድ ሰዎች ከመርሳት ውጪ መድኃኒቶችን ያለመውሰድ ችግር ይታይባቸዋል።ባለፉት ሁለት ሳምንታት ውስጥ መድኀኒት ያልወሰደበት ቀን አለ?	የለም	አዎ
803	መድኃኒትዎን በሚወስዱበት ጊዜ የከፋ ስሜት ስለተሰማዎት ለሐኪምዎ ሳያማክሩ መድኃኒትዎን ቀንሰው ወይም አቁመው ያውቃሉ?	የለም	አዎ
804	ወደ ሌላ ቦታ ሲጓዙ ወይም ከቤት ሲወጡ አንዳንድ ጊዜ መድኃኒትዎን ይዘው መሔድ ረስተው ያውቃሉ?	የለም	አዎ
805	በትላንትናው እለት ሁለንም መድኃኒት በትክክል ወስደዋል?	የለም	አዎ
806	የህመሙ ምልክቶች ቀንሰዋል ወይም ተሸሎኛል ብለው አንዳንዴ መድኃኒትዎን መውሰድ አቋርጠው ያውቃለ?	የለም	አዎ
807	መድኃኒቶችን በየቀኑ መውሰድ ለአንዳንድ ሰዎች ምቾት ይነሳቸዋል። እርስዎ በህክምና ክትትልዎ ወቅት በየቀኑ ወይም አንድም ጊዜ ሳያዛንፉ መድሐኒት በትክክል ለመዉሰድ ተሰላችተዉ ያዉቃለ?	የለም	አዎ
808	ሁሉንም መድሃኒቶችዎን መውሰድ አለመውሰድዎን ማስታወስ የከበደዎት ጊዜ አለ?	4. በፍፁም / አልፎ አልፎ 3. ከብዙ ጊዜ አንዴ 2. አንዳንድ ጊዜ 1. አብዛኛውን ጊዜ 0. ሁል ጊዜ	

አመሰግናለሁ !

ANNEX IV: Map for the study area