ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF MEDICAL LABORATORY SCIENCES

Comparative Assessment of Serum Electrolyte level Among Controlled and Uncontrolled Type 2 Diabetes Mellitus Patients Attending Armed Force Comprehensive Specialized Hospital, Addis Ababa, Ethiopia

By: Bezawit Fekadu Setegn (BSc)

Advisors: 1. Prof . Mistire Wolde (PhD)

2. Gobena Dedefo (PhD Candidate)

3. Dr. Theodros Aberra (Endocrinologist)

A research thesis submitted to the Department of Medical Laboratory Sciences, College of Health Science, Addis Ababa University, in partial fulfillment of a Master of Science Degree in Clinical Laboratory Sciences (clinical chemistry track)

December, 2025

Addis Ababa, Ethiopia

Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Bezawit Fekadu entitled:

"Assessment of Serum Electrolyte level Among Controlled and Uncontrolled Type 2 Diabetes Mellitus Patients Attending Armed Force Comprehensive Specialized Hospital, Addis Ababa, Ethiopia", and submitted in partial fulfillment of the requirements for Master of Science Degree in Clinical Laboratory Sciences (Clinical Chemistry) complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee:

External Examiner_____ Signature _____ Date _____

Internal Examiner_____ Signature _____ Date _____

Advisor_____ Signature _____ Date _____

Advisor_____ Signature _____ Date _____

_____

Chairman of the Department or Graduate Program Coordinator

Acknowledgements

First of all, I would like to thank the Almighty for giving me the opportunity for this MSc training period. I also extend my gratitude to my advisors Prof. Mistire Wolde, Dr Theodros Aberra and Mr. Gobena Dedefo for their invaluable guidance rendered to me and for taking time from their busy schedule to read through my work. I'm also grateful for their tireless comment and suggestions. I would also like to thank Addis Ababa University for providing me the opportunity to carry out this research. I would also like to express my sincere appreciation to Armed Force Comprehensive Specialized Hospital for helping, and anyone who contributed in one way or the other to the completion of this research thesis are gratefully acknowledge

Table of Contents

List of Tables

List of figures

Abbreviations

American Diabetes Association	ADA
Armed force comprehensive specialized hospital	AFCSH
Controlled Diabetes mellitus	CD
Diabetes mellitus	DM
Electrolyte imbalance	EI
Fasting blood glucose	FBS
Gestational Diabetes	GD
Hemoglobin A1c	HbA1c
International Diabetic Federation	IDF
Type 1 diabetes mellitus	T1DM
Type 2 diabetes mellitus	T2DM
Uncontrolled diabetes mellitus	U

Abstract

Background: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose due to insufficient insulin production, reduced insulin sensitivity, or both. Poorly controlled T2DM can lead to complications such as electrolyte imbalance (EI), resulting from hyperglycemia-induced increased plasma osmolality and impaired kidney function. This study aimed to assess the prevalence of electrolyte imbalance(EI) in controlled and uncontrolled T2DM patients to support improved diabetes management

Objective: To assess serum electrolyte levels in controlled and uncontrolled type 2 diabetes mellitus patients attending Armed Force comprehensive specialized hospital from December 2024 to August 2025, Addis Ababa, Ethiopia.

Methods: A comparative cross-sectional study was conducted from December 2024 to August 2025 at Armed Force Comprehensive Specialized Hospital, Addis Ababa, among 128 adults with T2DM (64 controlled and 64 uncontrolled based on HbA1c) selected using consecutive sampling. Demographic and clinical data were collected through interviews and patient charts. Blood samples were drawn, processed, and analyzed for serum electrolytes, fasting glucose, and HbA1c using the Cobas c311 analyzer following standard procedures. Data were coded, cleaned, and analyzed in SPSS v27, and logistic regression was used to identify variables with $p < 0.05$ as statistically significant.

Result: This study included 128 T2DM patients equally divided into controlled and uncontrolled groups (n = 64 each). Overall, 81 participants had electrolyte imbalance, which was more frequent in uncontrolled patients (73.4%) compared to controlled patients (53.1%). When abnormalities were pooled, 44 participants (34.4%) had one electrolyte abnormality, while 84 (65.6%) had two or more abnormalities. Hyponatremia was identified in 39 participants and hypochloremia in 13 individuals. Uncontrolled glycemic status was associated with increased odds of electrolyte imbalance, and imbalance was more common among obese participants ($p < 0.05$). Mean serum sodium and chloride levels were significantly lower in uncontrolled T2DM patients ($p < 0.05$)

Conclusion: Electrolyte imbalances, particularly hyponatremia and hypochloremia, were more common in uncontrolled T2DM patients. Routine monitoring of electrolytes should be integrated into diabetes management to prevent complications and improve patient outcomes

Keywords: electrolyte imbalance, controlled type 2 diabetes, uncontrolled type 2 diabetes

1. Introduction

1.1 Background

In the twenty-first century, diabetes mellitus (DM) is a widely recognized metabolic disorder that is characterized by persistent hyperglycemia brought on by decreased insulin secretion and/or activity, which in turn impedes the metabolism of fats, carbohydrates, and proteins (1). There are three major types of diabetes mellitus which are classified based on their differences in pathophysiology. Type 1 diabetes typically develops in children and is characterized by autoimmune destruction of the pancreatic islet cells that secrete insulin. The most common type, according to the American Diabetes Association, is type 2 diabetes, which typically appears in adulthood and it is related to insulin resistance and decreased insulin production, therefore, it does not typically need to be treated with insulin to survive (2).

T2DM is commonly described interms of how well a patients blood glucose is controlled over time (3), this is assessed using glyceated hemoglobin (HbA1c) which reflects the average blood suger level for the previous two to three months and is most commonly clinical measure of long term glycemia, in the routine follow-up monitoring of diabetes (4). Gestational diabetes (GDM) refers to varying degrees of glucose intolerance initially identified during pregnancy (5).

Controlled T2DM refers to a state in which a patients blood glucose levels are maintened with recommende therapeutic targets and HbA1c below 7% also implies that fasting glucose, post-prandial glucose, symptoms, treatment adherence, and risk of complications are all being effectively managed (6). Patients with controlled diabetes generally have improved metabolic stability , and lower risk of microvascular and macrovascular complications (3).

Uncontrolled T2DM indicates persistant hyperglycemia despite treatment and is commonly defined as HbA1c $\geq$7% , also includes poor regulation of fasting and post-prandial glucose levels, medication non adherence and accelerates development of neuropathy, nephropathy,retinopathy and cardiovascular disease (3, 7).

In diabetes mellitus, electrolyte balance may be disrupted as a result of persistent hyperglycemia and altered insulin action. Hyperglycemia promotes osmotic diuresis, leading to increased urinary loss of electrolytes, while insulin deficiency and resistance interfere with normal electrolyte transport (8, 9) Additionally, diabetes-related renal dysfunction and the use of certain medications can further contribute to electrolyte abnormalities(10) ,These disturbances may adversely affect

neuromuscular function, cardiac conduction, and fluid balance, highlighting the importance of monitoring electrolyte status in patients with diabetes mellitus (11).

Uncontrolled hyperglycaemia may cause osmotic diuresis, causing increased urine output and electrolyte loss. This can aggravate diabetes problems and contribute to conditions such as hypokalaemia and hyponatraemia (12).

On the other hand, despite the adequate glucose regulation and nutritional adherence, those with well-controlled type 2 diabetes may exhibit reduced electrolyte imbalances, due to diverse factors, including underlying comorbidities, dietary practices, and adverse drug reactions. Therefore, in order to minimize potential problems and enhance general wellbeing, routine electrolyte level testing is crucial for both controlled and uncontrolled T2DM patients (1, 13, 14).

Hemoglobin A1c (HbA1c) is a reliable marker of long-term glycemic control, reflecting average blood glucose levels over the previous two to three months. Poor glycemic control, indicated by elevated HbA1c, is associated with sustained hyperglycemia that can disrupt renal electrolyte handling and promote electrolyte imbalance in patients with diabetes mellitus (15).

Despite the increasing burden of type 2 diabetes mellitus in Ethiopia, routine electrolyte monitoring is not consistently incorporated into outpatient diabetes care. Most available local studies focus on glycemic control and chronic complications, with limited comparative evidence on electrolyte disturbances between controlled and uncontrolled T2DM patients. This study was therefore conducted to address this gap by providing comparative data on serum electrolyte patterns and associated factors among T2DM patients attending a tertiary hospital in Addis Ababa.

1.2. Statement of the problem

Diabetes mellitus is an increasing global health concern. According to the International Diabetes Federation, approximately 537 million adults were living with diabetes worldwide in 2021, and the number is expected to rise substantially in the coming decades, with the majority of cases occurring in low- and middle-income countries (16, 17).

In Africa, the burden of type 2 diabetes mellitus (T2DM) has increased significantly, with an estimated regional prevalence of 10.9% among adults (18).

Ethiopia was estimated by the WHO to have 800,000 cases of diabetes in 2000; by 2030, that figure is expected to increase to 1.8 million cases. A study carried out in Northwest Ethiopia found that 5.1% of individuals in urban areas and 2.1% of those aged 35 and over had diabetes mellitus (19).

T2DM is chronic illness that can result a number of medical problems, which needs long-term care to avoid consequences. Vascular degeneration, metabolic imbalance, and electrolyte imbalance are among the complications that can arise (20).

When blood glucose is well controlled, electrolyte levels tend to remain stable, reducing the risk of diabetes-related complications. On the other hand, persistent hyperglycemia in people with uncontrolled diabetes can cause osmotic diuresis and changes in renal function, which can seriously disrupt electrolyte balance. Hyponatremia is common in diabetics, increasing morbidity and mortality. Hypomagnesemia has been reported in 11–47.7% of non-hospitalized DM patients. Hypomagnesemia accelerates the progression of diabetes and increases the risk of complications. This include macrovascular disorders such as cardiovascular disease and peripheral artery disease (21).

Despite the known implication of electrolyte imbalance in diabetes management there remain a gap in understanding the extent and nature of these imbalance in patients with varying degree of glycemic control, In Ethiopia, studies examining electrolyte disturbances among patients with diabetes are limited, leaving important questions unanswered regarding which specific electrolytes increase or decrease in controlled versus uncontrolled diabetic patients.

1.3 Significance of the study

One of the non-communicable diseases that kill millions of people globally is diabetes mellitus (22), which is particularly prevalent in low-income nations like Ethiopia (23). Since most diabetic patients have uncontrolled diabetes mellitus, controlling blood sugar levels and glycated hemoglobin as much as possible reduces the risk of macro- and micro-vascular issues. Disturbance in electrolyte levels are frequently observed in individuals living with diabetes, especially when glycemic control is poor resulting in morbidity and mortality.

This study provides comparative evidence on serum electrolyte patterns among controlled and uncontrolled T2DM patients, which may help clinicians identify patients at higher risk of adverse outcomes. The findings may support the use of routine electrolyte assessment as a supplementary prognostic and monitoring tool in diabetic care. In addition, the results can inform hospital-level planning, guide clinicians in timely intervention, and contribute to local evidence for researchers and policy-makers concerned with improving electrolyte imbalance in diabetes.. The prevalence of DM is increasing, although only limited data on serum electrolytes are available. The hospital may plan for the continued availability of serum electrolyte tests once the extent of the problem has been identified and communicated.

2. Literature review

2.1 Pathophysiology and biochemistry of type 2 diabetes mellitus

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from insulin resistance and progressive pancreatic β-cell dysfunction. In this condition, body tissues become less responsive to insulin, while pancreatic β-cells fail to produce sufficient insulin to maintain normal glucose homeostasis. These metabolic disturbances lead to impaired carbohydrate, lipid, and protein metabolism and contribute to the development of both acute and chronic complications (24).

2.2 Role of electrolytes in body systems

Electrolytes are chemicals that, when dissolved in water, can become charged particles. They are classified as cations and anions. The major cations in body fluids are sodium (Na+), potassium (K+), calcium (Ca2+), and magnesium (Mg2+); and chloride (Cl-), the major anion (13).

Electrolytes are essential for maintaining fluid balance, neuromuscular activity, acid–base equilibrium, and cardiac function. In individuals with diabetes mellitus, persistent hyperglycaemia and metabolic dysregulation may disturb electrolyte homeostasis through multiple physiological mechanisms. Elevated glucose levels increase plasma osmolality, causing shifts of water and electrolytes between intracellular and extracellular compartments, which may alter serum electrolyte concentrations. These changes can affect nerve conduction, muscle function, and cardiovascular stability, highlighting the importance of electrolyte monitoring in diabetic patients (11, 25).

In addition, osmotic diuresis resulting from hyperglycaemia promotes increased urinary loss of water and electrolytes such as sodium and potassium. Insulin deficiency or resistance may also influence electrolyte transport across cell membranes, particularly potassium distribution, while renal impairment and certain medications used in diabetes management may further contribute to electrolyte disturbances. These biochemical and physiological alterations increase the risk of metabolic complications, making routine evaluation of electrolyte status an important component of diabetes care (11, 26).

2.3 Association of serum glucose and electrolyte

In diabetes mellitus, alterations in serum glucose levels are closely linked to disturbances in electrolyte and acid–base balance. One important biochemical indicator in this context is the anion

gap, which reflects the balance between measured cations and unmeasured anions in the blood. The anion gap represents major unmeasured anions such as lactate, ketones, phosphate, sulfate, and albumin (27).

In diabetic patients, an elevated anion gap has important clinical significance, as it may indicate the presence of metabolic acidosis, particularly diabetic ketoacidosis or lactic acidosis, which can occur in severe hyperglycemia, infection, or sepsis. Therefore, assessment of the anion gap provides valuable insight into the metabolic status of diabetic patients beyond routine electrolyte measurement (26).

Electrolyte imbalance is common in patients with diabetes and is related to hyperglycaemia and can be attributed to altered electrolyte distribution. This can result in cationic imbalance and changes in osmotic fluid or deficits in the body osmotic diuresis, or the excretion of large amounts of urine, occurs when the blood contains elevated glucose levels, which is then filtered by the kidneys and collects in the tubules, preventing water reabsorption and thereby increasing the water content of the blood. The excess water in the blood distorts the normal electrolyte balance of the body. Loss of water and electrolytes due to increased urination results in loss of salt and potassium from the body (28-30).

Insulin is a peptide hormone that primarily regulates glucose, but also affects electrolyte balance by stimulating the Na+K+ pump in cell membranes (31).

The Na+K+ ATPase enzyme actively maintains the gradients of sodium and potassium across the cell membrane by exchanging three sodium ions on the outside for two potassium ions on the inside, keeping the cell excitability and ion homeostasis intact. Changes in this transport system are linked to many of the complications of DM, most notably oxidative stress, insulin resistance and hyperglycaemia. The activity of Na+K+ ATPase is essential to preserve the membrane potential and therefore cell function, and general ion homeostasis as it helps to maintain the balance of sodium (Na^+) and potassium (K^+) in the membranes of cells. Thus, diabetes affects this enzyme. This can negatively influence the secretion function of the beta cell and may compromise normal insulin release, especially in the face of glucose loads Mg2+ deficiency reduces glucose binding to glucokinase and secondarily impairs insulin secretion, insulin resistance and macrovascular risk (32).

Glycaemia that is not controlled is linked to several serious long-term complications, including peripheral neuropathy, retinopathy and nephropathy, vascular constriction and cardiovascular problems. Nevertheless, uncontrolled glycaemia in patients with type 2 diabetes is associated with an unhealthy diet, a sedentary lifestyle, medication adherence and abnormal blood glucose tests, all of which can be linked to osmotic diuresis associated with SGLT2 inhibition. Even in patients with controlled diabetes, mild electrolyte disturbances may occur because of a variety of causes, including renal insufficiency and drug-related adverse reactions (SGLT inhibitors) (33, 34).

Micronutrient status, including vitamin C intake, has been suggested to influence metabolic regulation and oxidative stress in individuals with type 2 diabetes mellitus. Vitamin C acts as an antioxidant and may contribute to improved endothelial and renal function, which are important in maintaining electrolyte balance. Some studies have indicated that adequate vitamin C levels may support glycaemic control and reduce metabolic complications. Therefore, vitamin C intake was included as a potential factor associated with electrolyte disturbances in this study (35, 36).

These findings suggest that, in comparison to controlled diabetes, uncontrolled DM is linked to a more substantial change in electrolyte levels. Regular monitoring of electrolytes is essential in monitoring complications of diabetes because electrolyte variations in those with poor glycemic.

2.4 Previous studies on association of electrolytes and HbA1c in diabetic patients

The 2013 China study found that 26 (2.2%), 11 (2.8%), and 4 (1.2) patients had hypocalcaemia (P = 0.09), while 9 (0.5%), 0 (0.0) and 2 (0.6) patients had hypokalaemia (P = 0.02). Serum Na + , Mg2+ and Ca 2+ levels were significantly higher (P<0.01) in the DM, IGR and NGR groups as compared to the NGR group, and Ca 2+ levels were significantly higher (37).

A 2016 study involving 100 patients (50 diabetic and 50 age-matched healthy controls) in India reported statistically significant increases in HbA1c (P<0.05) in diabetic patients compared to non-diabetic healthy controls. Levels of sodium were higher in diabetic patients compared to controls, which was also statistically significant (P<0.05). Potassium and chloride levels were observed to be slightly elevated compared to controls, but the P(P* 0.017 and r(R)* -0.233) and r(R) values were statistically significant. FBS correlated positively with potassium. The P(P*>0.05 and r(R) = 0.016) and P* and r values were also found to be significant. FBS correlated positively with chloride and P* and r values were also statistically significant (P*0.04 and r*0.21) (38).

In Saudi Arabia, diabetic patients had significantly reduced serum sodium and elevated potassium and chloride concentrations compared with non-diabetic controls (29).

A 2019 study conducted in Pakistan showed that In uncontrolled diabetes mellitus, decrease in serum sodium and chloride levels were observed to be statistically highly significant (p-value less than or equal to 0.05) while that of potassium and magnesium showed insignificant alterations. Sodium level was also observed to decline with increasing pattern of urine for micro albumin (1).

A study conducted at the University of Jimma showed that the prevalence of one or more serum electrolyte abnormalities is high in diabetic patients. The overall prevalence was 42.0 percent (n=116,276), with hyponatraemia being the most common, followed by hypochloremia at 40.6 percent, hypokalaemia at 14.9 percent and hypercalcaemia at 10.9 percent (39).

A study conducted at the University of Gondar showed tha electrolyte imbalance affected 83.07% of diabetic patients, compared to 52.31% of the control group. Central value of Na^+ and median Mg^{2+} and Ca^{2+} levels decreased significantly. However, the average Cl^- levels within the diabetic population were significantly higher than in the control groups (40).

Regarding electrolyte disturbances in diabetes mellitus, the literature presents a mixed picture, with patients being considered to be important factors. These mixed results highlight the need for further research.

The analysis of the study was based on the following modified conceptual framework

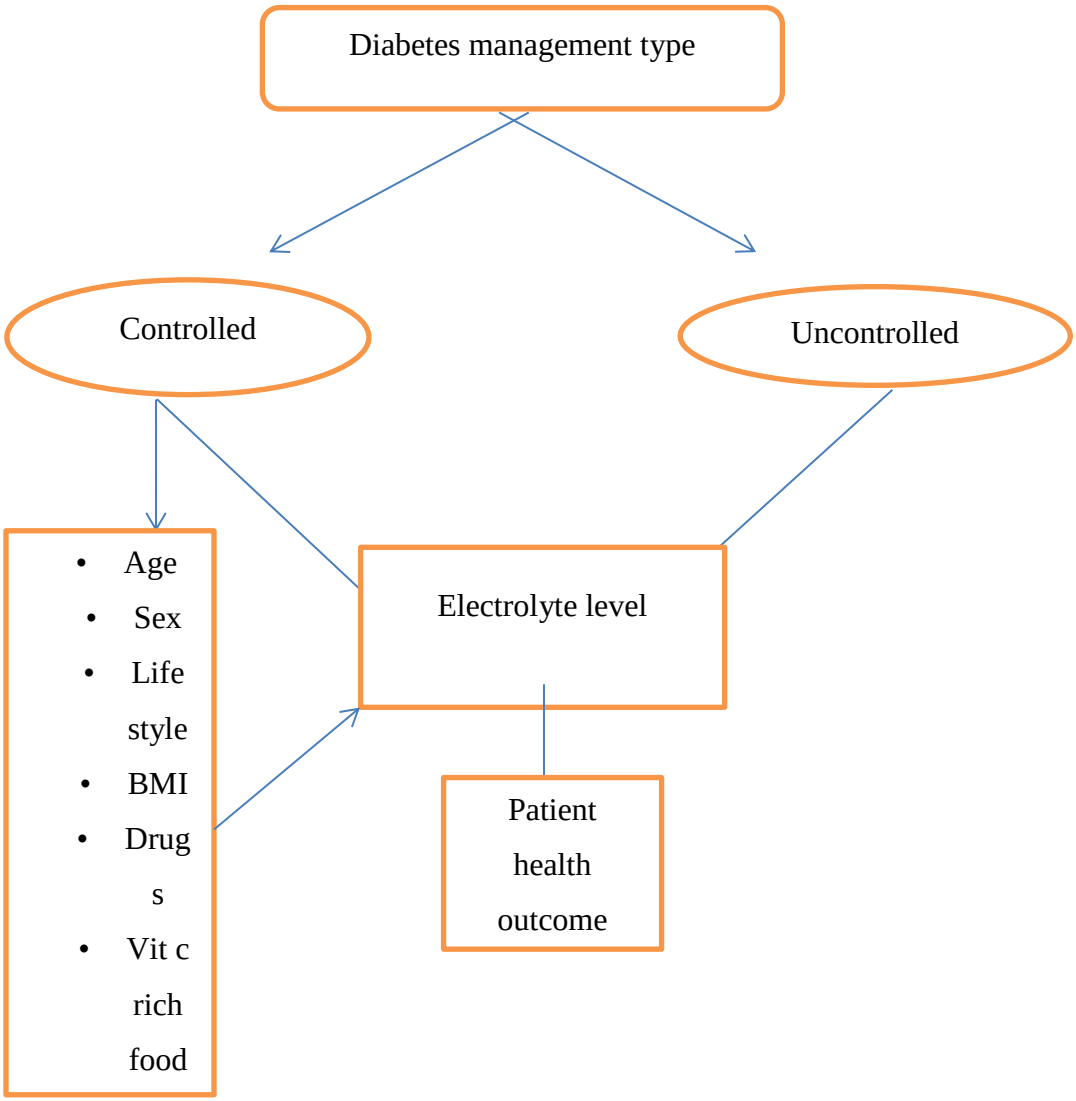

Figure 1 Conceptual framework of the study

3. OBJECTIVE

3.1 General Objective

To assess level of serum electrolyte in controlled and uncontrolled type 2 diabetic patients attending Armed force comprehensive specialized hospital from December 2024 to August 2025, a comparative cross-sectional study, Addis Ababa, Ethiopia.

3.2 Specific objectives

- ✓ To determine the level of serum electrolytes among controlled & uncontrolled T2DM patients
- ✓ To compare serum electrolyte patterns between controlled & uncontrolled T2DM patients
- ✓ To assess risk factors associated with electrolyte imbalances among T2DM patients

4. Hypothesis

Null hypothesis: The electrolyte profiles of both controlled and uncontrolled T2Dm patients are the same.

5. Materials and method

5.1 Study area

The study was conducted at the diabetes outpatient clinic of Armed force Comprehensive Specialized Hospital (AFCSH), formerly known as princess Tsehai memorial hospital which was renamed after the 1974 revolution. Emperor Haile Selassie I founded the hospital in memory of his daughter princess Tsehai Haile Selassie. It is a prominent health care organization delivering specialized medical services serving for huge number of patients. Clinical records indicate that the annual follow-up visits of 5,769 eligible visits per year.

5.2 Study design and period

A comparative cross-sectional study was carried out within a hospital setting to evaluate the electrolyte profiles of the participants from December, 2024 to August, 2025 in Addis Ababa, Ethiopia

5.3 Population

5.3.1 Source population

All DM patients with controlled and uncontrolled glycemic status attending at AFCSH throughout the research period were considered as the source population

5.3.2 Study population

All T2DM patients attending the follow-up at AFCSH during the study period and those who satisfied the inclusion criteria were considered as study population.

5.4 Eligibility criteria

5.4.1 Inclusion criteria

- ✓ T2DM patients' ≥18 years of age and follow-up at AFCSH
- ✓ T2DM patients with <**7% HbA1c** level for controlled T2DM group
- ✓ T2DM patients with ≥7% HbA1c level for uncontrolled T2DM group

5.4.2 Exclusion criteria

This study excluded patients with diarrhea, chronic vomiting, and gestational diabetes mellitus and known kidney disease because all of these situations will change serum electrolyte levels.

5.5 Study variables

5.5.1 Dependent variables

- Serum electrolytes level

5.5.2 Independent variables

- **Sociodemographic factors:** age, gender, educational level, occupation, , residence.
- **Clinical features:** duration of DM, BMI, mode of therapy, presence of comorbidity, biochemical values.

Behavioral factors: compliance with prescribed medication, diet adherence, engagement in regular physical activity, tobacco use

5.6 Measurement and Data collection

5.6.1 Sample size determination

Using the double population proportion method, we calculated the required sample size for the study. A study done at Gondar, Ethiopia, reported the proportion of electrolyte abnormality (Sodium (Na+)) for Diabetic groups (P1=39.2%) and control groups (P2=16.9%)(40), Power (80%), r = ratio of control to case (1:1), and 95% CI. This gives a total of 128 after adding 10% non-response rate, 64 diabetic patients with good glycemic control and 64 diabetic patients with poor glycemic control were included in the study.

By substituting these figures to the formula; $\frac{(\frac{Za}{2}+z\beta)2\ x\ (\mathrm{P1}(1-\mathrm{p1})+\mathrm{P2}(1-\mathrm{P2}))}{(P1-P2)2XR}$

N = $(1.96+ 0.84)^2$ x(0.392(1-0.392)+ 0.169(1-0.169))/ $(0.392-0.169)^2$x 1= 59+5=64 per group.

- P1=Proportion 1, P2= Proportion 2, R=ratio(1:1)
- Zα/2 = Z0.05/2 = Z0.025 = 1.96 (From Z table) at type 1 error of 5%
- Zβ = Z0.20 = 0.842 (From Z table) at 80% power

5.6.2 Sampling method

Participants were selected using a practical convenient based sampling approach to ensure representative inclusion at AFCSH.

5.6.3 Data collection procedure

After each participant provided informed consent, socio-demographic, behavioural and clinical data were collected via face-to-face interviews using a structured and pre-filled questionnaire. which was based on the Ethiopian Demographic and Health Survey (EDHS) data collection tool and other relevant literature, which included variables of interest. Calculated sample size was collected for both the controlled and uncontrolled groups

5.6.4 Specimen collection

Fasting blood samples (5 mL) were collected from all patients with diabetes mellitus after 8-12 hours of fasting for glucose, sodium (Na), potassium (K) and chloride (Cl). Blood samples for serum analysis were collected in serum separator tubes (SST) and serum was obtained through centrifugation of the blood cells at 3500 rPs for 5 min. These tubes are suitable for the majority of routine chemical tests, such as electrolyte panels and glucose-levels. Glycosylated haemoglobin (HbA1c) was detected using the ethylene diamine tetraacetic acid (EDTA) tube.

The process includes preparing the patient, which involves informing the patient of what the procedure will entail and any fasting requirements. Materials were gathered, including syringes, needles, alcohol swabs, tourniquets, gauze, gloves, and stickers. A suitable location for venipuncture, such as the antecubital fossa or the dorsal vein of the arm, is selected and cleaned with an alcohol swab that is moved in a circular pattern outwards from the center of the area and allowed to dry completely in order to minimize discomfort and to avoid haemolysis.

5.6.5 Principle of laboratory test

Principle of FBG: The analysis was performed with the Cobas C 311 laboratory analyser, which uses the hexokinase (HK) approach for quantification of glucose in blood or plasma samples. This method oxidises glucose and converts it to glucose-6-phosphate by enzymatic reaction, resulting in a change that is detectable and proportional to the amount of glucose present in the solution.

Principle of Na, K, Cl: The electrical potential (voltage) generated by this process is directly proportional to the concentration of ions and depends on the ion's selective binding to specific membrane materials in the ISE.The ion-selective electrode (ISE) concentrations were measured in the Cobas c 311 analyser, which detects the ion concentration through selective membrane interactions.

Principle of Hba1c: HbA1c is determined using a turbidimetric inhibition immunoassay (TINIA) blood test using the Roche Cobas c 300 analyzer. It works on the principle that specific antibodies bind to HbA1c in the sample, and excess antibody binds to polyhapten in the buffer and polyhapten reagent to produce insoluble antigen-antibody complexes.

5.7 Data quality assurance and management

The data collection tool was first developed in English, and then translated into the local Amharic language. The demographic characteristics of the study population, including (name, age and gender), family history, medical history, medications, occupation, physical activity and lifestyle patterns, were obtained by a structured questionnaire, which was translated back into the original text with clarity, coherence and precision.

One data collector with the occupation of nurse and one with the profession of medical laboratory technologist were assigned to the study area for data collection and blood sampling respectively. The consistency and completeness of the data collected was checked for completeness immediately after data collection before attempting to enter and analyse them.

Pre-Analytical: information on the Socio-demographic and clinical profile of participants was collected with high quality by data extraction from the registries using a standardised data collection form and the socio-demographic data collected for the control group was collected with high quality by the careful completion of a separate standardised questionnaire for data collection and checked for completeness and followed up during data collection and data compilation and analysis by the PIs. Blood samples were taken using the appropriate tubing and volume, were labelled correctly and integrity of the data was maintained through proper collection and processing in accordance with approved operating guidelines.

Analytical: All reagents and controls used in the test have been stored and handled as per manufacturer's instructions. The analysing machines have been checked for their correct functioning before use. All samples were analysed after daily controls.

Post analytical:

The principal investigator reviwed the cocollected data daily for completeness and accuracy. When entering data, it was cross-checked to ensure that the correct data was entered.

5.8. Data analysis and interpretation

The collected data was coded, entered, cleaned and stored for analysis in the SPSS version 27 software. Descriptive statistics such as frequency, percentage, mean and standard deviation were used to summarise the data after checking for normal distribution. The association between the independent variables and electrolyte imbalance was first evaluated by bivariate logistic regression with variables with a p-value <0.25 included in the multivariate logistic regression model. Adjusted odds ratios (AOR) calculated with 95-percent confidence limits (CI), and $p<0.05$ was regarded as statistically significant.

5.9 Ethical considerations

Ethical approval for this study was secured from the Department Research and Ethical Review Committee of the Department of Medical Laboratory Sciences, College of Health Sciences, Addis Ababa University before any data collection began. A formal permission letter was issued and submitted to the Armed Forces Comprehensive Specialized Hospital to allow the study to be carried out. The purpose of the study was clearly explained to each participant, and written informed consent was obtained. Participants were informed that their participation was entirely voluntary and that the study would not pose any risk or negative consequences to them.

5.10 Dissemination of Result

The completed research findings will be presented to the Department of Medical Laboratory Sciences, College of Health Sciences, Addis Ababa University, as part of the requirements for the Master's degree in Clinical Chemistry.Furthermore, it will be shared to AFCSH to develop interventional strategies. Finally,a manuscript based on the study will be prepared and submitted to appropriate peer reviewed scientific journals for possible publication.

5.11 Operational Definitions

Glycemic control: fasting blood glucose (FBG) level, participants will be classified as with good glycemic control (FBG <130 mg/dl) and poor glycemic control (FBG ≥130 mg/dl)

Poorly-controlled DM: Patients with an HbA1c level of more than 7%

Well-controlled DM: patients with an HbA1c level of equal to or less than 7%

Uncontrolled Type-2 Diabetes Mellitus (T2DM): Patients with confirmed T2DM and who have HbA1c ≥7% during the past three months of follow-up visits.

Controlled Type-2 diabetes: Patients with confirmed T2DM and who have HbA1c <7% during the past three months of follow-up visits.

Electrolyte Imbalance: the presence of one or more abnormal serum electrolyte levels (hyponatremia, hypernatremia, hypokalemia, hyperkalemia, hypochloremia, or hyperchloremia) compared to the reference ranges used by the Armed Forces Comprehensive Specialized Hospital laboratory

6. Result

6.1 Socio-Demographic, Behavioural, and Anthropometric Characteristics of controlled and uncontrolled T2DM patients

This study included 128 patients with type 2 diabetes mellitus were included, with an equal number of controlled (n = 64) and uncontrolled (n = 64) participants. The mean age of controlled and uncontrolled patients were 52.97 ± 10.89 and 53.48 ± 11.24 years, respectively, showing no significant difference (p = 0.621). Males constituted the majority in both groups (71.9% and 75.0%), with no statistically significant variation (p = 0.685).

Based on educational status, 31 (24.2%) of controlled T2DM and 25 (19.5%) of uncontrolled T2DM had secondary education. Based on the lifestyle conditions 30 (23.4%) of controlled group and 25(19.5%) of uncontrolled T2DM group had alcohol-drinking habits. Fifty five (43%) of the total study participants fell within the normal BMI level. The Mean ± SD of systolic blood pressure for controlled and uncontrolled T2DM groups were 125.01 ± 5.38 and 138.5 ± 3.7 p=<0.001, respectively. (Table 1)

Table 1 Socio-Demographic, Behavioural, and Anthropometric Characteristics of controlled and uncontrolled T2DM patients (n = 128)

Variables		**Study participants (n= 128)**		**P-value**
		Controlled t2dm	**Uncontrolled t2dm**	
		n= 64	**n= 64**	
Age group (years)	25-45	21(32.8%)	11(17.2%)	**0.471**
	46-65	32(50.0%)	47(73.4%)	
	>65	11(17.2%)	6(9.4%)	
Sex	Male	46 (71.9%)	48 (75.0%)	0.689
	Female	18 (28.1%)	16 (25%)	
Educational level	Primary	3 (4.7%)	7 (10.9%)	0.129
	Secondary	31 (48.4%)	25 (39.1%)	
	College/ university	27 (42.2%)	32 (50.0%)	
	Postgraduate	3 (4.7%)	0 (0.0%)	
Alcohol consumption	Yes	30 (46.9%)	25 (34.4%)	0.372
	No	34 (53.1%)	39 (65.6%)	

Physical exercise	Yes	41 (64.1%)	22 (34.4%)	**<0.001**
	No	23(21.9%)	42(65.6%)	
Vit c intake	Yes	50 (78.1%)	35 (54.7%)	0.005
	No	14(21.9%)	29(45.3%)	
BMI category	Normal	32 (50.0%)	23 (35.9%)	0.033
	Overweight	30 (46.9%)	31 (48.5%)	
	Obese	2 (3.1)	10 (15.6%)	
SBP	Mean ± SD	125.01 ± 5.38	138.5 ± 3.7	<0.001
DBP	Mean ± SD	79.5 ± 3.0	83.7 ± 2.3	<0.001
Cigarette smoking	Yes	3(4.7%)	7(10.9%)	0.188
	No	61(95.3%)	57(89.1%)	
Treatment regimen	Oral hypoglycemics	46 (71.9%)	46 (71.9%)	0.347
	Insulin	16 (25.0%)	18 (28.1%)	
	Both	2 (3.1%)	0 (0.0%)	
Duration of DM	(<1 year)	28 (43.8%)	25 (39.1%)	0.392
	(1–5 years)	16 (25.0%)	23 (35.9%)	
	(>5 years	20 (31.2%)	16 (25.0%)	
Presence of Comorbidity	Hypertension	0	19(29.7%)	<0.001
	None	64(100%)	45(70.3%)	

6.2 Prevalence of Electrolyte Imbalance Among controlled and uncontrolled type 2 DM Patients

In the present study, electrolyte abnormalities were more common among patients with uncontrolled glycemia compared to those with controlled blood glucose levels, although none of the differences were statistically significant. For sodium levels, hyponatremia was observed in 11.7% of controlled and 18.8% of uncontrolled patients (p = 0.116). Hypernatremia was uncommon in both groups (3.1% vs. 0.8%), while the majority (65.6%) maintained normonatremia.

Similarly, for chloride levels, hypochloremia was more common in uncontrolled patients (7.0%) than in controlled patients (3.1%), while hyperchloremia occurred in 10.2% and 7.8% of

uncontrolled and controlled patients, respectively (p = 0.308). Normochloremia remained predominant (71.9%). Overall, while electrolyte derangements were consistently higher among uncontrolled T2DM patients across sodium, potassium, and chloride parameters, the differences were not statistically significant. (Table 2)

Table 2 Prevalence of Electrolyte Imbalance Among controlled and uncontrolled type 2 DM Patients (n=128)

Electrolyte parameter	Category	Controlled T2dm	Uncontrolled T2dm	Total N=128	P value
NA	Hyponatremia	15 (11.7%)	24 (18.8%)	39 (30.5%)	0.116
	Hypernatremia	4 (3.1%)	1 (0.8%)	5 (3.9%)	
	Normonatremia	45 (35.2%)	39 (30.5%)	84 (65.6%)	
K	Hypokalemia	12 (9.4%)	20 (15.6%)	32 (25.0%)	0.086
	Hyperkalemia	5 (3.9%)	9(7.0%)	14 (10.9%)	
	Normokalemia	47 (36.7%)	35 (27.3%)	82 (64.1%)	
Cl	Hypochloremia	4 (3.1%)	9 (7.0%)	13 (10.2%)	0.308
	Hyperchloremia	13 (10.2%)	10 (7.8%)	23 (18.0%)	
	Normochloremia	47 (36.7%)	45 (35.2%)	92 (71.9%)	

6.3 Overall electrolyte abnormality

The number of electrolyte abnormalities was similar between patients with controlled and uncontrolled T2DM. In the controlled group, 29.7% of participants had a single electrolyte abnormality, while 70.3% had two or more. Among uncontrolled T2DM patients, 39.1% had one abnormality and 60.9% had two or more. (Table 3)

Table 3 Overall electrolyte abnormality burden among controlled and uncontrolled T2DM patients (n = 128)

Number of Electrolyte Abnormalities	Controlled T2DM n (%)	Uncontrolled T2DM n (%	Total n (%)	P-value
One electrolyte abnormality	19 (29.7%)	25 (39.1%)	44 (34.4%)	
≥Two electrolyte abnormalities	45 (70.3%)	39 (60.9%)	84 (65.6%)	
Total	64 (100%)	64 (100%)	128 (100%)	0.264

6.4 Comparison of Electrolyte Imbalance Among controlled and uncontrolled type 2 DM Patients

The average fasting blood glucose and HbA1c were statstically significant higher among uncontrolled patients compared to controlled patients ($p < 0.005$). The mean serum sodium level was lower among uncontrolled patients than among controlled patients ($p > 0.005$) despite this, there was no statistically significant variation in serum potassium levels between the groups (4.33 ± 0.79 vs. 4.32 ± 0.68 mmol/L, $p = 0.892$). (Table 4)

Table 4 Comparison of Electrolyte Imbalance Among controlled and uncontrolled type 2 DM Patients (n=128, independent t-test)

Electrolyte	Study participant		P value
	Controlled T2DM (Mean ± SD)	Uncontrolled T2DM (Mean ± SD)	
HA1c % (4.0–5.6)	5.1 ± 0.79	8.19 ± 1.3	<0.001
FBS(mg/dL) (70–99)	109.3 ± 4.3	181.4 ± 7.7	<0.001
Serum Sodium (mmol/L) (135–145)	139.4 ± 9.6	135.7 ± 11.11	0.047
Serum Potassium (mmol/L) (3.5–5.1)	4.3 ± 0.79	4.34 ± 1.03	0.796
Serum Chloride (mmol/L) (98–107)	105.2 ± 8.3	101.9 ± 10.6	0.05

6.5 Bivariate logistic regression analysis of factors associated with electrolyte imbalance among T2DM patients

After performing bivariate logistic regression analysis, glycemic control, BMI category, and duration of diabetes showed statistically significant associations with electrolyte imbalance. Patients with uncontrolled glycemia had significantly higher odds of electrolyte imbalance compared to controlled T2DM groups (COR = 0.37; 95% CI: 0.17–0.79; p = 0.010). Obesity was also significantly associated with electrolyte imbalance, with obese individuals showing nearly ten times more likely than normal (COR = 9.86; 95% CI: 1.19–81.71; p = 0.034). Additionally,

patients with 1–5 years duration of diabetes had significantly higher odds of electrolyte imbalance (COR = 2.97; 95% CI: 1.18–6.43; p = 0.024).

Other variables—including physical exercise (p = 0.076), smoking (p = 0.102), overweight BMI (p = 0.113), and presence of comorbidity (p = 0.134) also showed significant difference in electrolyte imbalance among T2DM patients. (Table 5)

Table 5 Bivariate logistic regression analysis of factors associated with electrolyte imbalance among T2DM patients (n = 128)

Variable	Category	EI	COR (95% CI)	p-value
		Yes n (%)		
Age	25-45	10(7.8%)	I	
	45-65	27 (21.1)	0.875(0.36, 2.11)	0.767
	>65	7(5.5%)	0.649(0.19, 2.20)	0.488
Glycemic control status	Controlled	15 (11.7%)	I	
	Uncontrolled	29 (22.7%)	0.37(0.17, 0.79)	**0.010**[x]
Physical exercise	Yes	19 (14.8%)	I	
	No	28(21.9%)	0.52(0.25, 1.07)	**0.076** [x]
Vitamin C intake	Yes	29 (22.7%)	I	
	No	18 (14.1%)	0.719 (0.34, 1.53)	0.391
Alcohol consumption	Yes	20(15.6%)	1.03 (0.497, 2.12)	0.942
	No	27(21.1%)	II	
BMI category	Normal	26 (20.3%)	I	
	Overweight	20 (15.6%)	1.84(0.87, 3.90)	**0.113** [x]
	Obese	1 (0.8%)	9.86(1.19, 81.71)	**0.034** [x]
Smoking	No	46(35.9%)	I	
	Yes	1(0.8%)	5.75(0.71, 46.9)	**0.102** [x]
Education	Primary	4 (3.1%)	I	
	Secondary	18(14.1%)	1.41(0.35, 5.62)	0.628
	College/University	23(18.0%)	0.40 (0.266, 4.10)	0.951
	Postgraduate	2(1.6%)	1.04(0.33, 0.02)	0.427

Duration of diabetes	<1 year	23 (18.0%)	I		
	1–5 years	8 (6.3%)	2.97 (1.18–6.43)		**0.024** x
	>5 years	16 (12.5%)	0.96 (0.46–2.23)		0.922
Presence of comorbidity	Hypertension	4 (3.1%)	15 (11.7%)	II	
	None	43 (33.6%)	66 (51.6%)	2.44 (0.76, 7.86)	**0.134** x

Note: * Statistically Significant association. Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; CI, confidence interval; BMI, body mass index; DM; diabetes mellitus; EI,electrolyte imbalance; SBP, systolic blood pressure; DBP, diastolic blood pressure; 1, referenc

6.6 Multivariable logistic regression analysis of factors associated with electrolyte imbalance among Type 2 DM patients

After adjusting for potential confounders, two factors remained independently associated with electrolyte imbalance: glycemic control status and obesity. Patients with uncontrolled glycemia were 80% more likely to have electrolyte imbalance compared with those with controlled blood glucose (AOR = 0.20; 95% CI: 0.08–0.49; $p < 0.001$).

In the same way, obese patients had significantly higher odds of electrolyte imbalance compared with individuals of normal BMI (AOR = 9.06; 95% CI: 1.05–78.38; $p = 0.045$). In contrast, overweight status was not significantly associated with electrolyte imbalance (AOR = 1.52; $p = 0.314$).

Smoking (AOR = 6.20; $p = 0.095$) and intermediate diabetes duration of 1–5 years (AOR = 2.36; $p = 0.095$) demonstrated elevated odds but did not reach statistical significance. (Table 6)

Table 6 Multivariable logistic regression analysis of factors associated with electrolyte imbalance among Type 2 DM patients (n = 128)

Variable	Category	Electrolyte imbalance	AOR (95% CI)	p-value
		Yes n (%)		
Glycemic control status	Controlled	15 (11.7%)	I	
	Uncontrolled	29 (22.7%)	0.20(0.08, 0.49)	**<0.001** x
BMI category	Normal	26 (20.3%)	I	
	Overweight	20 (15.6%)	1.52 (0.67, 3.43)	0.314
	Obese	1 (0.8%)	9.06 (1.05, 78.38)	**0.045** x
Smoking	No	46(35.9%)	I	
	Yes	1(0.8%)	6.20 (0.73, 52.78)	0.095
Duration of diabetes	<1 year	23 (18.0%)	I	
	1–5 years	8 (6.3%)	2.36 (0.86, 6.46)	0.095
	>5 years	16 (12.5%)	0.71 (0.28, 1.81)	0.476

Note: *Stastically Significant association.

Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; EI, electrolyte imbalance; SBP, systolic blood pressure; DBP, diastolic blood pressure; 1, reference category

7. Discussion

This study demonstrated that electrolyte disturbances were common among patients with T2DM and were more frequently observed in individuals with uncontrolled glycemic status. Hyponatremia and hypochloremia were the predominant abnormalities, whereas potassium levels did not show a meaningful difference between the groups. When electrolyte disturbances were assessed collectively, many participants presented with multiple concurrent abnormalities rather than isolated changes, highlighting the complex metabolic effects of diabetes on fluid and electrolyte regulation. Poor glycemic control and obesity emerged as important independent predictors of electrolyte imbalance, supporting the role of chronic hyperglycemia, insulin resistance, and altered renal handling of electrolytes in the development of these disturbances.

The predominance of hyponatremia in this study aligns with findings from Jimma University, Ethiopia, where hyponatremia was also the most common electrolyte disturbance among diabetic patients (39). Similarly, studies from Pakistan reported significantly lower sodium and chloride levels among uncontrolled diabetics compared to controlled patients (1). In China, decreased serum sodium and chloride were observed in patients with diabetes and impaired glucose regulation compared to normoglycemic individuals (41). These findings can be explained by hyperglycemia-induced osmotic diuresis, which promotes renal loss of water, sodium, and chloride (42). Insulin deficiency or resistance may further impair renal tubular electrolyte reabsorption and alter Na^+/K^+-ATPase activity, contributing to potassium shifts between intracellular and extracellular compartments, although potassium levels were not significantly altered in our cohort.

Our study demonstrated significantly lower serum chloride levels among uncontrolled T2DM patients. The lower serum chloride levels observed in uncontrolled T2DM are physiologically expected, as chloride closely follows sodium to maintain extracellular electroneutrality. Therefore, the hyponatremia observed in uncontrolled diabetes is commonly accompanied by parallel reductions in serum chloride rather than representing an independent abnormality. This contrasts with the University of Gondar, Ethiopia, where mean serum chloride was significantly higher in diabetic patients compared to non-diabetic controls (40). Several factors may explain this discrepancy: the Gondar study included non-diabetic controls, whereas our study compared only controlled versus uncontrolled T2DM; variations in hydration status, dietary chloride intake, comorbidities such as renal impairment, and use of medications like diuretics or ACE inhibitors may influence chloride differently; laboratory methods and reference ranges may also contribute; and population-specific genetic, environmental, or lifestyle factors may affect chloride

homeostasis. Therefore, while hypochloremia is frequently observed in uncontrolled diabetes in our study, the magnitude and direction of chloride changes may vary across populations.

Regarding potassium, our study found no significant differences between controlled and uncontrolled T2DM patients, although insulin facilitates intracellular potassium uptake via activation of the Na^+/K^+-ATPase pump, patients with stable type 2 diabetes typically do not experience marked serum potassium changes unless severe insulin deficiency, metabolic acidosis, or renal impairment is present (43). In such cases, renal potassium excretion compensates for minor intracellular–extracellular shifts, maintaining near-normal serum potassium concentrations (11). The absence of significant potassium abnormalities in this study therefore suggests preserved renal potassium handling and metabolic stability among the study participants. This aligns with findings from Darul Sehat Hospital, Karachi, Pakistan, where potassium levels remained largely unchanged despite significant reductions in sodium and chloride among uncontrolled diabetics (1). Within Ethiopia, results are variable: The University of Gondar reported 22.3% hypokalemia and 9.2% hyperkalemia among diabetics, indicating considerable variation rather than a consistent trend (40). and the Jimma Medical Center study found that most patients were normokalemic, with only 20.7% showing hypokalemia (39).). In contrast, studies from India and Saudi Arabia reported slightly elevated potassium levels in diabetic patients, likely due to differences in insulin deficiency, metabolic acidosis, medication use, and disease stage (29, 38). The absence of significant potassium changes in our cohort likely reflects preserved renal function, stable acid–base status, and limited use of potassium-altering medications.

Obesity was a significant predictor of electrolyte imbalance, supporting evidence that higher BMI and insulin resistance exacerbate poor glycemic control and increase susceptibility to osmotic diuresis(44). Bivariate analysis indicated that shorter disease duration was initially associated with electrolyte imbalance, but this lost significance after adjusting for glycemic control, suggesting that glycemic instability rather than disease duration per se drives electrolyte disturbances. Patients with shorter disease duration may experience more fluctuations in glucose levels during treatment initiation, predisposing them to renal sodium and chloride loss.

Overall, our findings indicate that electrolyte disturbances, particularly hyponatremia and hypochloremia, are common among T2DM patients, especially those with poor glycemic control and obesity. While hyponatremia is consistently reported across studies, chloride and potassium alterations vary depending on study population, comorbidities, and methodology. These results

underscore the importance of routine monitoring and management of electrolytes in T2DM care to prevent complications associated with osmotic diuresis and impaired renal electrolyte handling.

8. Limitation of the study

Medication use that may influence serum electrolyte levels, such as diuretics and renin–angiotensin system inhibitors, was not specifically assessed in this study. Including these variables could have provided a more comprehensive understanding of factors affecting electrolyte status among patients with type 2 diabetes mellitus.

9.Conclusion and Recommendation

9.1 conclusion

In conclusion, this study highlights the complex factors that contribute to electrolyte imbalance in diabetes mellitus, with glycemic control status, the length of diabetes, obesity, and educational attainment showing up as important predictors. In order to maximize therapeutic results, these findings support comprehensive treatment approaches that incorporate metabolic monitoring and patient-centered educational initiatives.

9.2 Recommendation

Individuals with type 2 diabetes, especially those exhibiting inadequate glycemic managment, should have routine monitoring of important serum electrolytes, especially salt and chloride, as part of their follow-up care. To avoid difficulties, the hospital should guarantee that electrolyte testing is consistently available. Clinicians are also encouraged to interpret the results in conjunction with glycemic markers. To support the evidence and direct diabetic care in Ethiopia, future research with bigger, multicenter cohorts and a wider variety of electrolytes is advised.

10. References

1. Khan RN, Saba F, Kausar SF, Siddiqui MH. Pattern of electrolyte imbalance in Type 2 diabetes patients: Experience from a tertiary care hospital. Pakistan Journal of Medical Sciences. 2019;35(3):797.
2. Lebovitz HE. Type 2 diabetes: an overview. Clinical chemistry. 1999;45(8):1339-45.
3. Ma J, Yang W, Fang N, Zhu W, Wei M. The association between intensive glycemic control and vascular complications in type 2 diabetes mellitus: a meta-analysis. Nutrition, Metabolism and Cardiovascular Diseases. 2009;19(9):596-603.
4. Soundarya T, Kumar PA. A study of lipid profile in controlled vs uncontrolled type 2 DM with special reference to HBA1C levels. International Archives of Integrated Medicine. 2021;8(11).
5. Buchanan TA, Xiang AH. Gestational diabetes mellitus. The Journal of clinical investigation. 2005;115(3):485-91.
6. Aranaz P, Navarro-Herrera D, Zabala M, Miguéliz I, Romo-Hualde A, López-Yoldi M. American Diabetes Association 2010. Diagnosis and classification of diabetes mellitus. Diabetes Care, 33 (1): S62-69. Declaration of originality. 2023;33(1):189.
7. Al-Dwairi A, Alfaqih MA, Saadeh RA, Al-Shboul O, Alqudah M, Khanfar M, et al. Lack of glycemic control in type two diabetes mellitus patients is associated with reduced serum epidermal growth factor level and increased insulin resistance. Biomedical Reports. 2024;22(1):5.
8. Khanduker S, Ahmed R, Khondker F, Aharama A, Afrose N, Chowdhury M. Electrolyte disturbances in patients with diabetes mellitus. Bangladesh Journal of Medical Biochemistry. 2017;10(1):27-35.
9. Al-Hassan AMA, Hatif RA, Dhari RH, Edan EH. Study on Diabetes Mellitus and the Balance of Electrolytes. J Babylon Uni. 2016;24(7):1947-53.
10. Harring TR, Deal NS, Kuo DC. Disorders of sodium and water balance. Emergency Medicine Clinics. 2014;32(2):379-401.
11. Palmer BF, Clegg DJ. Electrolyte and acid–base disturbances in patients with diabetes mellitus. New England Journal of Medicine. 2015;373(6):548-59.
12. Balcı AK, Koksal O, Ataman Kose EA, Ozdemir F, Inal T, Oner N. General characteristics of patients with electrolyte imbalance admitted to emergency department. World journal of emergency medicine. 2013;4(2):113.
13. Waled A, Ahmed AA. Disturbance of Electrolytes (Na, K and Cl). Homeostasis among Patients with Type II Diabetes Mellitus. Libyan Journal of Medical Research. 2022;16(2):153-60.
14. Pawar BG, Eerike M, Pyati AK, Varatharajan S, Mali K, Konda VGR. Correlation of Serum Electrolyte Imbalances With Diabetic Duration and Medication Use: A Cross-Sectional Comparative Study. Cureus. 2024;16(9):e70065.
15. Campbell MR, Shokrani M. Comparison of HbA1c and glycated protein methodologies. Clinical Laboratory Science. 2016;29(2):114-21.
16. Duncan BB, Magliano DJ, Boyko EJ. IDF diabetes atlas 11th edition 2025: global prevalence and projections for 2050. Oxford University Press; 2025. p. gfaf177.
17. Aldaghi T, Muzik J. Multicriteria Decision-Making in Diabetes Management and Decision Support: Systematic Review. JMIR Medical Informatics. 2024;12:e47701.
18. Hellebo A, Kengne AP, Ademi Z, Alaba O. The burden of type 2 diabetes on the productivity and economy in Sub-Saharan Africa: a life table modelling analysis from a South African perspective. Pharmacoeconomics. 2024;42(4):463-73.
19. Seed KSAM, Noor SKM, Mahjaf GM, Nouraldein M, Hamad M. The Correlation of HbA1c with Serum Electrolytes among Type 2 Diabetic Patients in Atbara, River Nile State, Sudan. 2024.
20. Iriana P, Yardes N, Ekarini NLP. Understanding The Risk Of Electrolyte Imbalance In Type 2 Diabetes Mellitus Patients. Innovative: Journal Of Social Science Research. 2024;4(2):1899-906.
21. Ahmed SS, Nur F, Ullah MR, Al Mamun A, Laila TR, Khan MAM, et al. Electrolyte imbalance in admitted diabetic patients: patterns and factors responsible-a cross sectional study. KYAMC Journal. 2014;5(1):458-66.

22. Roglic G. WHO Global report on diabetes: A summary. International Journal of Noncommunicable Diseases. 2016;1(1):3-8.
23. Misganaw A, Mariam DH, Ali A, Araya T. Epidemiology of major non-communicable diseases in Ethiopia: a systematic review. Journal of health, population, and nutrition. 2014;32(1):1.
24. Ohiagu FO, Chikezie PC, Chikezie CM. Pathophysiology of diabetes mellitus complications: Metabolic events and control. Biomedical Research and Therapy. 2021;8(3):4243-57.
25. Adrogué HJ, Madias NE. Hyponatremia. New England Journal of Medicine. 2000;342(21):1581-9.
26. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes care. 2009;32(7):1335.
27. Kraut JA, Madias NE. Serum anion gap: its uses and limitations in clinical medicine. Clinical journal of the American Society of Nephrology. 2007;2(1):162-74.
28. Datchinamoorthi S, Vanaja R, Rajagopalan B. Evaluation of serum electrolytes in type II diabetes mellitus. Int J Pharm Sci Rev Res. 2016;40(1):251-3.
29. Al-Rubeaan K, Siddiqui K, Abu Risheh K, Hamsirani R, Alzekri A, Alaseem A, et al. Correlation between serum electrolytes and fasting glucose and Hb1Ac in Saudi diabetic patients. Biological trace element research. 2011;144:463-8.
30. Attama ct. ELECTROLYTE IMBALANCE IN TYPE II DIABETES: journal of clinical and Diagnostic Research; 2018.
31. Pipeleers L, Wissing KM, Hilbrands R. Acid-base and electrolyte disturbances in patients with diabetes mellitus. Acta Clinica Belgica. 2019;74(1):28-33.
32. Rajagambeeram R, Malik I, Vijayan M, Gopal N, Ranganadin P. Evaluation of serum electrolytes and their relation to glycemic status in patients with T2dm. Int J Clin Biochem Res. 2020;6:10.
33. Pamungkas RA, Chamroonsawasdi K, Vatanasomboon P. A systematic review: family support integrated with diabetes self-management among uncontrolled type II diabetes mellitus patients. Behavioral Sciences. 2017;7(3):62.
34. Chen L, LaRocque LM, Efe O, Wang J, Sands JM, Klein JD. Effect of dapagliflozin treatment on fluid and electrolyte balance in diabetic rats. The American journal of the medical sciences. 2016;352(5):517-23.
35. Jl E. Are oxidative stress-activated signaling pathways mediators of insulin resistance and beta-cell dysfunction? Diabetes. 2003;52:1-8.
36. Evans JL, Goldfine ID, Maddux BA, Grodsky GM. Are oxidative stress− activated signaling pathways mediators of insulin resistance and β-cell dysfunction? Diabetes. 2003;52(1):1-8.
37. Wang S, Hou X, Liu Y, Lu H, Wei L, Bao Y, et al. Serum electrolyte levels in relation to macrovascular complications in Chinese patients with diabetes mellitus. Cardiovascular diabetology. 2013;12:1-10.
38. KARUPPAN A, SAHAY MI, RAVINDRANATHAN R, HARIPRIYA P, SRIRAM DK, GEORGE M. Electrolyte Disturbances among Diabetic Patients Admitted in a Multi-Specialty Hospital in Southern India. Journal of Clinical & Diagnostic Research. 2019;13(2).
39. Timerga A, Kelta E, Kenenisa C, Zawdie B, Habte A, Haile K. Serum electrolytes disorder and its associated factors among adults admitted with metabolic syndrome in Jimma Medical Center, South West Ethiopia: Facility based crossectional study. PloS one. 2020;15(11):e0241486.
40. Eshetu B, Worede A, Fentie A, Chane E, Fetene G, Wondifraw H, et al. Assessment of Electrolyte Imbalance and Associated Factors Among Adult Diabetic Patients Attending the University of Gondar Comprehensive Specialized Hospital, Ethiopia: A Comparative Cross-Sectional Study. Diabetes, Metabolic Syndrome and Obesity. 2023:1207-20.
41. Sang M, Liu Y, Wu T, Zhou X, Wang D, Sun Z, et al. Association of a novel electrolyte index, SUSPPUP, based on the measurement of fasting serum and spot urinary sodium and potassium, with prediabetes and diabetes in Chinese population. Clinica Chimica Acta. 2022;531:426-33.
42. Roumelioti M-E, Ing TS, Rondon-Berrios H, Glew RH, Khitan ZJ, Sun Y, et al. Principles of quantitative water and electrolyte replacement of losses from osmotic diuresis. International urology and nephrology. 2018;50(7):1263-70.

43. Liamis G, Liberopoulos E, Barkas F, Elisaf M. Diabetes mellitus and electrolyte disorders. World Journal of Clinical Cases: WJCC. 2014;2(10):488.
44. Czech MP. Insulin action and resistance in obesity and type 2 diabetes. Nature medicine. 2017;23(7):804-14.

APPENDIXES

APPENDIX I: Information sheet and informed consent

Information sheet

Name of institution; Armed force comprehensive specialized hospital

Name of working out patient department

Greeting;

Good morning/ afternoon; I'm Bezawit Fekadu graduate student in Clinical laboratory science at Addis Ababa University, College of Health Sciences, Clinical chemistry unit and studying on electrolyte imbalance in type 2 diabetes patients at Armed Force Comprehensive Specialized Hospital in AA,2024 " as a part of master's degree in CLS(Clinical chemistry track). Now I will give you more details about the research.

Advisors name:

Dr Mistire wolde
Dr Theodros Aberra
Sponsor: Addis Ababa University

Consent form

Purpose of the research project: This research will help us to assess the electrolyte imbalance of controlled and uncontrolled type 2 diabetes patients.

Procedures: You are randomly selected to participate in this study because you are currently diagnosed in type 2 diabetes disease here. If you agree to participate in this study, you will be asked to answer some questions about yourself and the knowledge you have about T2DM and its association with electrolyte imbalance.

Benefits: Direct advantages to you from this study are not guarented or you will not be given any incentives or payments to take part in this study, but the result of this study will help us as an input to identify the electrolyte imbalance in diabetic patients.

Risk: By participating in this study, there are no anticipated social and physical risks, but it might take 10-15 minutes for the interview.

Confidentiality: The information collected for this research project will be kept confidential stored in a file, without your name. But a code number assigned to it. In addition, it will not be revealed to anyone except the investigator.

The right to refusal: Your participation is voluntary and if you feel discomfort in the interview please feel free to drop it any time you want. If you choose to take part, you have the right to stop at any time. If you are willing to refuse or decide to withdraw later, you will not be subjected to any ill treatment.

Contacts and questions: If you have any question about the study, please ask me now**.** If you have questions and complains later or want additional information pleases contact the investigator based on the address provided below.

Name of principal investigator; Bezawit Fekadu(BSc,CLS)

Email; bezawitfekadu35@gmail.com

Cell phone; +251921550054

Department of Medical Laboratory Sciences

የስምምነት ቅጽ

የምርምር ፕሮጀክቱ ዓላማ፡- ይህ ጥናት ቁጥጥር የሚደረግባቸው እና ከቁጥጥር ውጪ የሆኑ ዓይነት 2 የስኪር ህመምተኞችን የኤሌክትሮላይት ሚዛን መዛባት ለመገምገም ይረዳናል።

ሂደቶች፡- በዚህ ጥናት ላይ ለመሳተፍ በዘፈቀደ ተመርጠሃል ምክንያቱም በአሁኑ ጊዜ እዚህ ዓይነት 2 የስኪር በሽታ እንዳለብህ ስለታወቀህ። በዚህ ጥናት ውስጥ ለመሳተፍ ከተስማሙ, ስለራስዎ አንዳንድ ጥያቄዎችን እና ስለ T2DM እና ከኤሌክትሮላይት አለመመጣጠን ጋር ስላለው እውቀት መልስ እንዲሰጡ ይጠየቃሉ.

ጥቅማ ጥቅሞች፡- ለእርስዎ ቀጥተኛ ጥቅም ላይኖረው ይችላል ወይም በዚህ ጥናት ውስጥ ለመሳተፍ ምንም አይነት ማበረታቻ ወይም ክፍያ አይሰጥዎትም ነገር ግን የዚህ ጥናት ውጤት በስኪር ህመምተኞች ላይ ያለውን የኤሌክትሮላይት ሚዛን መዛባት ለመለየት እንደ ግብአት ይረዳናል።

ስጋት፡ በዚህ ጥናት ውስጥ በመሳተፍ ምንም የሚጠበቁ ማህበራዊ እና አካላዊ አደጋዎች የሉም ነገር ግን ለቃለ መጠይቁ ከ10-15 ደቂቃ ሊወስድ ይችላል።

ምስጢራዊነት፡- ለዚህ የምርምር ፕሮጀክት የተሰበሰበው መረጃ ያለ እርስዎ ስም በፋይል ውስጥ በሚስጥር ይከማቻል። ግን ለእሱ ኮድ ቁጥር ተመድቧል. በተጨማሪም ከመርማሪው በስተቀር ለማንም አይገለጽም።

እምቢ የማለት መብት፡ የእርስዎ ተሳትፎ በፈቃደኝነት ነው እና በቃለ መጠይቁ ላይ ምቾት ከተሰማዎት እባክዎን በፈለጉት ጊዜ ለመልቀቅ ነፃነት ይሰማዎት። ለመሳተፍ ከመረጡ በማንኛውም ጊዜ የማቆም መብት አለዎት። እምቢ ለማለት ፈቃደኛ ከሆኑ ወይም በኋላ ለመውጣት ከወሰኑ ምንም ዓይነት ሕመም አይኖርብዎትም.

እውቂያዎች እና ጥያቄዎች፡ ስለ ጥናቱ ምንም አይነት ጥያቄ ካለህ እባክህ አሁን ጠይቀኝ። ጥያቄዎች ካሉዎት እና በኋላ ቅሬታ ካሰሙ ወይም ተጨማሪ መረጃ ከፈለጉ ደስ ብሎት ከዚህ በታች ባለው አድራሻ መሰረት መርማሪውን ያነጋግሩ።

የዋና መርማሪ ስም; ቤዛዊት ፈካዱ (ቢኤስሲ፣ ሲኤልኤስ)።

ኢሜል; bezawitfekadu35@gmail.com

የሞባይል ስልክ; +251921550054 የሕክምና ላቦራቶሪ ሳይንሶች ክፍል

APPENDEX II: English version of questionnaire

As I have told you before, your answers to the questions will not be given to anyone else and no reports of this study ever identify you in any way. Therefore, I am asking your willingness to participate in this study.

Are you willing to participate in this study?

1. Yes 2. No

Thank you!!

The interview begins once the study subject agrees tp participate..

The respondent has given interviewer signature confirming that informed consent was obtained verbally.

participants signature Date

If not agree, thank him/her and go to the next respondent by writing the reason why not volunteers.

Checked by:

Supervisor name Signature

Date , , E.C

Interviewer; Code , Name , Signature

Date of interview time started Time completed

Name of interviewer

Date , Signature;

Structured questionnaire:

Participant name & Identification Number: _____

Section 1 demographic information

1. Age: _____

2. Sex: ☐ Male ☐ Female

Section 2 medical history

3. How long have you been diagnosed with type 2 DM

- Less than 1 year
- 1-5 year
- More than 5 year

4. what is your current treatment regimen? Select all that apply

- Oral hyoglycemics
- Insulin therapy
- Diet management
- Other (please specify)

5. Do you have any other medical condition? Select all that apply

- Hypertension
- Kidney disease
- Heart disease
- None
- Other (please specify)

Section 3 current health status

6. What is your average blood glucose level? (If known)

- Controlled (HbA1c <7%)

- Uncontrolled (HbA1c ≥7%)

7. Have you experienced any of the following symptoms recently? Select all that apply

- Fatigue
- Muscle weakness
- Cramps
- Nausea/ vomiting
- None

8. Have you had any recent blood test to assess your electrolyte levels?

- Yes
- No

9. If yes please provide the result for the following electrolytes

Sodium_____(mmol/L)

Potassium_____(mmol/L)

Chloride_____(mmol/L)

Calcium_____(mmol/L)

Section 4 life style factor

10. How would you describe your diet?

- Balanced
- High in carbohydrate
- High in sodium
- Other

11. How often do you engage in physical activity?

- Daily
- A few times a week
- Rarely
- Never

12. Do you consume alcohol?

- Yes
- No

13. your educational status

- Secondary school
- College
- Post graduate

14.do you consume vit c regularly

- Yes
- No

15. do you smoke cigarate

- Yes
- no

APPENDEX II፡ የእንግሊዘኛ መጠይቅ ስሪት።

ከዚህ ቀደም እንደነገርኳችሁት ለጥያቄዎቹ የምትሰጡት መልሶች ለሌላ ሰው አይሰጡም እና የዚህ ጥናት ዘገባዎች በምንም መልኩ አይለዩህም። ስለዚህ, በዚህ ጥናት ውስጥ ለመሳተፍ ፍላጎትዎን እጠይቃለሁ.

በዚህ ጥናት ለመሳተፍ ፈቃደኛ ነዎት?

1. አዎ 2. የለም

አመሰግናለሁ!!

የጥናቱ ርዕሰ ጉዳይ በጥናቱ ውስጥ ለመሳተፍ ከተስማማ, ቃለ መጠይቁን ይጀምሩ.

ተጠሪ በመረጃ የተደገፈ ስምምነትን በቃላት የሚያረጋግጥ የቃለ መጠይቅ አድራጊ ፊርማ ሰጥቷል።

ምላሽ ሰጪ ፊርማ ቀን

ካልተስማማ፣ አመሰግናለው እና በጎ ፈቃደኞች የማይሆኑበትን ምክንያት በመጻፍ ወደሚቀጥለው ምላሽ ሰጪ ይሂዱ።

የተረጋገጠ በ:

የሱፐርቫይዘር ስም ፊርማ

ቀን , 1, EC

ጠያቂ; ኮድ , ስም, ፊርማ

የቃለ መጠይቁ ጊዜ የጀመረው ጊዜ ተጠናቀቀ።

የቃለ መጠይቅ አድራጊው ስም

ቀን , ፊርማ;

የተዋቀረ መጠይቅ፡-

የአሳታፊ ስም እና መለያ ቁጥር፡ _____

ክፍል 1 የስነ ሕዝብ አወቃቀር መረጃ

1. ዕድሜ:_____

2. : ☐ ወንድ ☐ ሴት

ክፍል 2 የሕክምና ታሪክ

3. ዓይነት 2 ዲኤም ለምን ያህል ጊዜ እንደታወቀዎት

- ከ1 ዓመት በታች።
- 1-5 ዓመት
- ከ 5 ዓመት በላይ

4. የአሁኑ የሕክምና ዘዴዎ ምንድነው? የሚተገበሩትን ሁሉ ይምረጡ።

ኦራል ሃይዮግሊሲሚክስ።

- የኢንሱሊን ሕክምና።
- አመጋገብ አስተዳደር
- ሌላ (እባክዎ ይግለጹ)።

5. ሌላ የጤና እክል አለህ? የሚተገበሩትን ሁሉ ይምረጡ።

- የደም ግፊት
- የኩላሊት በሽታ
- የልብ በሽታ
- የለም

ሌላ ሆይ (እባክዎ ይግለጹ)።

ክፍል 3 ወቅታዊ የጤና ሁኔታ

6. አማካይ የደምዎ የግሉኮስ መጠን ምንድን ነው? (የሚታወቅ ከሆነ)።

o ቁጥጥር የተደረገበት (HbA1c <7%)።

ኦ ቁጥጥር ያልተደረገበት (HbA1c ≥7%)።

7. በቅርብ ጊዜ ከሚከተሉት ምልክቶች ውስጥ አንዱን አጋጥሟቸዋል? የሚተገበሩትን ሁሉ ይምረጡ።

- ድካም
- የጡንቻ ድክመት

- ክራምፕስ
- ማቅለሽለሽ/ማስታወክ
- የለም

8. የኤሌክትሮላይት መጠንዎን ለመገምገም የቅርብ ጊዜ የደም ምርመራ አድርገዋል?
   - አዎ
   - አይ
9. አዎ ከሆነ እባክዎን ለሚከተሉት ኤሌክትሮላይቶች ውጤቱን ያቅርቡ።

ሶዲየም_____(mmol/L)

ፖታስየም_____(mmol/L)

Chloride_____(mmol/L)

Calcium_____(mmol/L)

ክፍል 4 የአኗኗር ዘይቤ ሁኔታ

10. አመጋገብዎን እንዴት ይገልጹታል?
    - ሚዛናዊ።
    - ከፍተኛ በካርቦሃይድሬት።
    - ከፍተኛ በሶዲየም
    - ሌላ
11. ምን ያህል ጊዜ በአካል ብቃት እንቅስቃሴ ውስጥ ይሳተፋሉ?
    - ዕለታዊ
    - በሳምንት ጥቂት ጊዜ።
    - አልፎ አልፎ
    - በጭራሽ
12. አልኮል ትጠጣለህ?
    - አዎ
    - አይ

13 ሲጋራ ታጨሳለህ

- አዎ
- አይ

Appendix III: principles of each laboratory analysis

Glucose: glucose is converted to glucose-6-phosphate (G-6-P) by hexokinase in the presence of ATP, a phosphate donor. Glucose-6-phosphatedehydrogenase then converts the G-6-P to gluconate-6-P in the presence of NADP+. As the NADP+ is reduced to NADPH during this reaction, the resulting increase in absorbance at 340 nm (secondary wavelength = 700 nm) is measured. This is an endpoint reaction that is specific for glucose

Electrolyte: Ion-selective electrodes usually consist of three main parts: the electrode body, the reference electrode, and the ion-selective membrane. The electrode body contains the measuring part of the electrode and is usually a tiny glass sphere or glass tube filled with an electrolyte solution containing specific ions. The reference electrode is used to provide a stable potential reference to ensure the accuracy and repeatability of the measurement. The ion-selective membrane, located on the surface of the electrode body, is a semi-permeable membrane that selectively reacts chemically with the target ion.

Ion-selective membranes selectively interact with target ions through their special chemical properties. This interaction causes a change in the concentration of ions on the membrane, leading to a corresponding change in the electrolyte within the electrode body, resulting in a change in potential. When the target ion reacts with the ion-selective membrane, the potential inside the electrode body changes and this change can be measured indirectly by measuring the potential of the electrode to measure the concentration of the target ion. Thus, an ion-selective electrode can determine the concentration of a specific ion in solution by measuring the electrode's potential change

HbA1c: The blood sample is diluted and mixed with TRIS buffer to release hemoglobin from the erythrocytes. A fraction of the sample is conveyed into are action chamber where it is mixed with sodium lauryl sulfate (SLS). SLS is used to form the SLS-hemoglobin complex. The concentration of total hemoglobin is calculated by measuring SLS-hemoglobin complex with a wave length of 525 nm. Hemoglobin A1c (HbA1c) in another fraction of the sample is first denatured by potassium ferricyanide and sucrose laurate.The denatured HbA1c bonds with HbA1c antibody on the latex particle. Latex agglutination inhibition reaction then occurs by reacting the agglutinator that has synthetic antigen which can bond with HbA1c antibody. The concentration of HbA1c is

calculated by measuring the latex agglutination inhibition reaction with a wavelength of 625 nm.% hemoglobin A1c value is measured using a ratio of concentrations ofHbA1c to total hemoglobin

Declaration

I, the undersigned, declare that this M.Sc. thesis is my original work, has not been presented for a degree in this or any other university and that all sources of materials used for the thesis have been duly acknowledged.

M.Sc. candidate: Bezawit Fekadu(B.Sc.)

Signature: _____

Date of submission: _____

This proposal has been submitted with our approval as advisors.

Advisor: Dr Mistere Wolde PhD, (Associte professor. Prof)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.

Advisor: Mr Gobena Dedefo (Bsc,Msc clinical chemistry)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia