RELATIONSHIP BETWEEN IMPAIRED ELECTROLYTES, GLYCATED HEMOGLOBIN AND POOR ADHERENCE TO ANTIDIABETICS AMONG PATIENTS ATTENDING SAMBURU COUNTY REFERRAL HOSPITAL, KENYA

FRANCIS LENGASU LENGEIYA (BSc. MLS)

P154/20276/2021

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF SCIENCE IN MEDICAL LABORATORY SCIENCES (CLINICAL CHEMISTRY OPTION) IN THE SCHOOL OF HEALTH SCIENCES, KENYATTA UNIVERSITY.

JUNE, 2024

DECLARATION

This thesis represents my original work and has not been previously submitted for the award of a degree or any other honor at any other university.

Signature……………………. …………………………. Date………………………

Francis Lengasu Lengeiya

P154/20276/2021

Medical Laboratory Sciences, Kenyatta University**.**

We confirm that the work reported in this thesis was carried out by the student under our supervision as university supervisors:

Signature……………………. …………………………. Date………………………

Dr. Scholastica Mathenge

Department of Medical Laboratory Sciences

Kenyatta University

Signature……………………. …………………………. Date………………………

Dr. Patroba Ojola

Department of Biochemistry, Microbiology and Biotechnology

Kenyatta University.

DEDICATION

This thesis is dedicated to those individuals who have supported my personal and academic growth, my wife Nicole Lengeiya, our lovely daughter Lakeisha Lengeiya and my parents Mr. David Lengeiya and Mrs. Rosemary Lengeiya for their valuable effort to enable me attain this level of education.

ACKNOWLEDGEMENTS

I wish to sincerely acknowledge my supervisors Dr. Scholastica Mathenge and Dr. Patroba Ojola for tirelessly guiding me through the entire process of proposal and thesis writing. I am grateful to Samburu County Referral Hospital laboratory department for providing support during data collection. Special thanks to all those who participated in the study for their patience and cooperation.

TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

DALYs	-	Disability-Adjusted Life Years
DM	-	Diabetes Mellitus
DPP-4	-	Dipeptidyl Peptidase-4
ERC	-	Ethics Review Committee
FBS	-	Fasting Blood Sugar
GLP-1	-	Glucagon-like Peptide-1
HBA1C	-	Glycated hemoglobin
HPLC	-	High Performance Liquid Chromatography
IQR	-	Interquartile range
ISE	-	Ion Sensitive Electrode
K2-EDTA	-	Dipotassium Ethylenediaminetetraacetic Acid
KU	-	Kenyatta University
MCQ	-	Medication Compliance Questionnaire
MEQ/L	-	Mill equivalents per liter
MMAS	-	Morisky Medication Adherence Scale
NACOSTI	-	National Commission for Science, Technology and Innovation
OGTT	-	Oral Glucose Tolerance Test
OHAs	-	Oral Hypoglycemic Agents
RPM	-	Revolutions Per Minute
SCRH	-	Samburu County Referral Hospital
SOPs	-	Standard Operating Procedures
SPSS	-	Statistical Package for the Social Sciences
T1DM	-	Type 1 Diabetes Mellitus
T2DM	-	Type 2 Diabetes Mellitus
WHO	-	World Health Organization

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

ABSTRACT

Type 2 Diabetes mellitus is a persistent metabolic disorder that can have devastating effects on patients, resulting in numerous healthcare challenges in terms of its management and the associated cost burden. Adherence to antidiabetics has been consistently sub-optimal in previous studies and remains a significant clinical issue in the management of diabetes. Patients having uncontrolled blood glucose levels often exhibit electrolyte imbalance which greatly influences their treatment. Glycated hemoglobin test, assessing average blood glucose levels over a period of roughly three months, is widely regarded as the gold standard for diagnosing diabetes. The aim of this research was to study the relationship between electrolytes and glycated hemoglobin among diabetic patients with poor adherence to antidiabetics. The study was carried out at Samburu County Referral Hospital, employing a descriptive cross-sectional study design and convenience sampling technique involving adult diabetic patients aged 18 years and above who attended the diabetic clinic. Seventy-two patients, (48.6% females, 51.4% males) who were on antidiabetics for at least three months and demonstrated poor adherence, participated in the study. Adherence levels were assessed using the Morisky Medication Adherence Scale-8. Those with adherence scores <6 was categorized as having low adherence and further assessed using a questionnaire to identify factors contributing to poor adherence to antidiabetics. Blood samples were collected to measure glycated hemoglobin levels and serum electrolytes levels, including potassium, sodium, calcium, magnesium, phosphorus, and chloride. Serum electrolytes were analyzed using the Selectra Prom biochemistry analyzer while glycated hemoglobin levels were measured using the standard F200 HbA1c analyzer. The relationship between electrolytes and glycated hemoglobin was visualized using scatter plots, and correlation coefficients were determined using the Karl Pearson correlation method. Several factors contributing to poor adherence were identified, with lack of money to buy drugs being the most frequently reported factor (69%) among study participants. A significant correlation was observed between glycated hemoglobin and calcium ($r=-0.2398$ $P \leq 0.05$) as well as sodium ($r=-0.31369$ $P \leq 0.05$). However, no significant correlation ($P \geq 0.05$) was observed between phosphorus, magnesium, chloride and potassium r=, -0.04, -0.07,0.05 and -0.01 respectively, with HbA1c levels. This study revealed that calcium and sodium electrolytes imbalances were significantly present in diabetic patients with poor adherence to antidiabetics. Therefore, routine monitoring of serum electrolytes levels among diabetic patients is paramount. The results highlight the importance of comprehensive diabetes management strategies that address both glycemic control and electrolyte status. The findings from this study can inform policy makers on ways to enhance management of Type 2 Diabetes mellitus as well as inform into causes of non-compliance with antidiabetic medications.

CHAPTER ONE: INTRODUCTION

1.1 Background of the study

Type 2 Diabetes mellitus (T2DM) stands as one of the most prevalent metabolic disorders, marked by heightened blood sugar levels (hyperglycemia). It constitutes 90% of all diabetes cases, featuring impaired insulin production and the body's resistance to insulin (Hameed *et al.*, 2015). Additionally, it is ranked as the main cause of death among patients with cardiovascular diseases (Joseph.,2014). According to WHO, between 1980 and 2017, the global prevalence of diabetes surged from 108 million individuals to 462 million (Standl *et al.*, 2019). The numbers are estimated to rise to around 700 million by 2030 and close to 900 million by 2045. The incidence of T2DM has been increasing over the years in low-income nations, surpassing the numbers seen in high-income countries (WHO, 2018).

Presently Type 2 Diabetes mellitus is among the top leading causes of global mortality, ranked ninth in 2017, contributing to up to 1 million deaths (Demoz *et al.*, 2020). In 2019, it was estimated that the number of diabetes-related deaths reached approximately 1.5 million, a worrying trend of increasing cases and deaths compared to the 1990 when it was ranked eighteenth as a leading cause of death. In terms of causing human suffering, Disability-Adjusted Life Year (DALYs), it is ranked seventh in the world. (Hailu *et al.*, 2019).

Glycated hemoglobin becomes chemically bonded to sugar in blood. It is formed when there are deposits of glucose on hemoglobin (McIntyre *et al.*, 2019). Normal sugar levels result in normal HbA1c and increased blood sugar causes HbA1c levels to be elevated. Therefore, HbA1c levels can be used to determine and predict level of blood sugar. Glycated hemoglobin test is among the best methods for checking treatment of T2DM and compensation because it gives average blood glucose over the preceding 3 months (Hameed *et al.*, 2015).

There are several T2DM antidiabetics and majority are administered orally while a few are taken as injections (Paschou *et al.,* 2018). These medications can be categorized as insulin and insulin analogs, oral hypoglycemic agents, dopamine agonists and amylin mimetics. Some patients may also require to be administered with insulin. For instance, alpha-glucose inhibitors mechanism of action is by breaking down table sugar and starch thus lowering blood sugar (Nakrani *et al.,* 2020). Examples include; acarbose and miglitol. Biguanides improve body`s sensitivity to insulin, help muscles absorb glucose and also reduce the amount of sugar made in the liver. Metformin is the most common biguanide and can be administered in combination with other drugs (Hameed *et al.*, 2015).

Electrolytes play significant roles in the human body by controlling acid-base balance, muscle relaxation and contractions and blood clotting. The levels of electrolytes are mostly determined to assess patients` clinical conditions and any imbalance results in electrolyte disorders. Dysregulation of electrolyte distribution caused by hyperglycemic osmotic fluid shift results in electrolyte imbalance (Timerga *et al.*, 2020) limiting T2DM treatment. It is therefore necessary to explore the relationship between electrolytes and extended blood sugar level status through testing of glycated hemoglobin levels in diabetic patients who do not comply with diabetes management and treatment regimen.

1.2 Problem statement

Type 2 Diabetes mellitus constitutes a persistent condition which results in numerous health care challenges in terms of its management and the cost burden among the affected. Anyone can get T2DM regardless of the age but it is prevalent in older people and the middle-aged. There is lowered immunity among diabetic patients resulting in increased risk of being affected by other opportunistic diseases. Adherence to antidiabetics has been found to be sub-optimal across all previous research and it is well recognized that poor adherence to antidiabetics results in poor glycemic control (Demoz *et al.*, 2020). Evidence from the data at Samburu County Referral Hospital (SCRH) traced from patients` individual files and medical records, showed that there were increasing cases of poor adherence to antidiabetics among diabetic patients. The cause of T2DM is multifactorial (including genetics) and studies amongst the marginalized Samburu community have not been previously explored. There is need to research and identify contributing factors to poor adherence among the Samburu population which exhibits unique traditional diets and nutritional practices. The information is important in treatment and management of diabetes cases at SCRH.

Electrolyte imbalance among T2DM has a bearing on the choice. To date, limited studies have specifically examined the relationship between electrolytes and glycated hemoglobin among patients with poor adherence to antidiabetics in Kenya. Globally, this relationship remains under investigated, particularly in patients with suboptimal adherence. Determination of the frequency and pattern of electrolyte imbalance among diabetic patients will also provide basis for improving pathophysiology directed treatment.

1.3 Justification of the study

Diabetes mellitus ranks as one of the primary global causes of mortality. Research findings from this study will provide necessary knowledge to health workers and policy makers in the relevant health sectors in order to guide the former on ways to enhance effective treatment and management of T2DM. Assessing electrolyte levels in diabetic patients could potentially serve as a valuable diagnostic approach in clinical practice, with notable implications for the risk of developing other medical conditions. Many of these studies were done in Asia and western countries having different race and genetics and since the cause of T2DM is multifactorial (including genetics) it is therefore necessary to determine the relationship between glycated hemoglobin and electrolytes due to poor adherence to antidiabetics among Africans.

1.4 Research questions

1. What are the demographic and socio-economic factors that contribute to poor adherence to antidiabetics among diabetic patients attending Samburu County Referral Hospital?
2. What is glycated hemoglobin (HbA1c) levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital?

3. What are the levels of electrolytes (sodium, calcium, phosphate, magnesium, potassium and chloride) and their correlation with HbA1c levels among diabetic patients attending Samburu County Referral Hospital?

1.5 Research objectives

1.5.1 General objective

To determine the relationship between electrolytes and glycated hemoglobin among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital, Kenya.

1.5.2 Specific objectives

1. To determine the demographic and socio-economic factors that contribute to poor adherence to antidiabetics among patients attending Samburu County Referral Hospital
2. To determine glycated hemoglobin (HbA1C) levels among diabetic patients with poor adherence to antidiabetics.
3. To determine the levels of chloride, potassium, calcium, magnesium, phosphate and sodium electrolytes and their correlation with glycated hemoglobin levels among diabetic patients with poor adherence to antidiabetics.

1.6 Significance of the study

Research findings will be disseminated to Policy makers in the Ministry of Health to guide the health care workers in management and treatment of patients with T2DM (This will be done by distributing copies of the research findings to the relevant health departments).

Findings from this research will also provide a pool of knowledge for researchers regarding the relationship between electrolytes and glycated hemoglobin among diabetic patients with poor adherence to antidiabetics.

CHAPTER TWO: LITERATURE REVIEW

2.1 Epidemiology of Type 2 Diabetes mellitus

Type 2 Diabetes mellitus represents a major global health concern. In 2021, around 537 million adults aged 20-79 years worldwide were affected by Diabetes, with T2DM making up 90-95% of these cases (Hameed *et al.*, 2015). The highest prevalence rates are found in regions like the Middle East, North Africa, South Eastern Asia, and the Western Pacific, influenced by aging populations, urbanization and lifestyle shifts. In Africa, T2DM is on the rise. According to, (Standl *et al.*, 2019) approximately 24 million adults in Africa in 2021, and this number is projected to increase to 55 million by 2045. Kenya mirrors this trend with a prevalence of about 3.0% (Mkuu *et al.*, 2019).

2.2 Pathophysiology of Type 2 Diabetes mellitus

Type 2 Diabetes mellitus arises from two primary factors: impaired secretion of insulin by pancreatic beta cells and decreased sensitivity to insulin by tissues sensitive to insulin. Insulin is important in glucose regulation, and consequently, the molecular mechanisms governing its production and release are tightly regulated. Failure of any of these mechanisms may result in metabolic imbalance, hence development of T2DM (Galicia *et al.*, 2020).

Body cells require sugar for energy production which is enhanced by insulin which facilitates sugar movement from bloodstream into them, thus lowering blood sugar levels. Usually, sugar from food causes blood sugar levels to rise due to its failure of transportation into cells. If blood sugar drops, glucagon hormone triggers stored sugar release from the liver with subsequent transportation into bloodstream (Nakrani *et al.*, 2020). Glucagon-like peptide-1 hormone is also involved in blood sugar regulation. It modulates the pancreatic beta cells production of optimal amount of insulin to enhance movement of sugar into cells besides lowering liver gluconeogenesis rate (Fu Z *et al.*, 2013). In the case of inability of the body to produce insulin, glucose is locked out of these cells and its levels become elevated in bloodstream causing hyperglycemia (Freeman., 2022). Symptoms common with T2DM include; hyperglycemia, thirstiness, polyuria, hyperphagia, fatigue, blurred vision, weight gain or weight loss and poor healing of wounds (Michael., 2020). The risk factors for T2DM are environmental, genetic and metabolic conditions. These factors interact together resulting in disease prevalence (Galicia *et al.*, 2020).

2.3 Risk factors of Type 2 *Diabetes mellitus*

The risk of developing T2DM dependent on lifestyle and genes. Risk factors related to family history, age and race cannot be changed while those related to lifestyle can be avoided by ensuring a normal body mass index (BMI) which is used to calculate a healthy body weight, and being physically fit (Barrett *et al*., 2014).

Physical activity lowers chances of getting T2DM as it helps one to control weight and utilize energy thus making cells sensitive to insulin. Exercise increases uptake of glucose by muscles (Grontved *et al.,* 2014) while obesity would trigger adipose tissue production of fatty acids, hormones, glycerol and some sort of cytokines which result in resistance of body to insulin. When resistance to insulin is followed by dysfunction of beta cells of the pancreas, it leads to inability to control insulin. However, not all obese people develop T2DM (Wang *et al.,* 2012).

The risk of T2DM increases after 45 years of age. As people get older, there is decreased physical activity and decrease of muscle mass. The production of insulin by pancreas decreases due to death of pancreatic beta cells (Cuensca-Garcia *et al.*, 2012).

Heavy drinking is known to cause pancreatitis in some cases causing pancreatic beta cells to decrease production of insulin hence lowering body sensitivity to insulin (Wang *et al.*, 2012). Alcohol also has high calories and may cause one to become overweight hence increasing chances of developing diabetes. Moderate drinking of alcohol lowers the diabetes-getting chance while excessive drinking heightens the risk (Barrett *et al.*, 2014).

A person with a close relative with T2DM has a higher risk of developing it. The risk is mediated by both genetic makeup and components of shared environment. The study by InterAct Consortium., 2013 found that there is increased risk of developing T2DM among people whose biological parents suffered from same than in adoptees. Therefore, genetic influence mediates a significant portion of the family history association compared to shared environment components.

Gestational diabetes occurs in pregnant women and normally recognized at the third trimester and resolves after childbirth. However, women experiencing this type of diabetes have a higher chance of getting T2DM later in their lives (Paschou *et al.*, 2018). Gestational diabetes mellitus is essentially similar to type 2 diabetes in that there is hyperglycemia and insulin related problems. Presently, it is the most prevalent pregnancy complication (McIntyre *et al.*, 2019).

In gestational diabetes, there is usually very high decrease in insulin sensitivity, thus insulin resistance causing hyperglycemia in maternal circulation which flows into fetal circulation causing high blood glucose levels (McIntyre *et al.*, 2019). As a result, the fetal pancreas then produces its own insulin and the fetal tissues take up more glucose from the circulation making fetal growth rapid. Symptoms of gestational diabetes include polyuria, polyphagia, paresthesia (not common) and polydipsia (McIntyre *et al.*, 2019).

Diagnosis of gestational diabetes is usually done during screening at the third trimester using oral glucose tolerance test (OGTT) as well as fasting blood sugar. An OGGT of above 10mmol/l after 1 hour of taking glucose or above 8.5 mmol/l after 2 hours of taking glucose may indicate gestational diabetes. This test can help diagnose gestational diabetes (McIntyre *et al.*, 2019) if fasting blood glucose is above 5.1mmol/l.

Complications of gestational diabetes are grouped into maternal, fetal and infant complications while the latter comes with hypertensive disorders, increased risk of infections and insulin-related hypoglycemia (Dhatariya *et al.*, 2020). Fetal complications occur due to fetal hyperglycemia resulting in increased glucose uptake in tissues causing macrosomia (newborns larger than normal). Congenital abnormalities or still birth may also occur (McIntyre *et al.*, 2019).

2.4 Management of Type 2 Diabetes mellitus

Oral hypoglycemic agents that are currently used to manage T2DM are grouped into six classes; sulfonylureas, alpha-glucosidase inhibitors, biguanides, meglitinides, dipeptidyl

IV inhibitors and thiazolidinediones (Rorsman *et al.*, 2014). For effective management, these medications are combined with lifestyle modifications. Oral hypoglycemic agents are grouped into various classes according to their mechanism of action to lower blood glucose level in the body (Noale *et al.*, 2016).

2.4.1 Mechanism of action of antidiabetics

It refers to the specific biochemical reactions that drugs undergo in the body to produce effect. These involve binding with enzymes, receptors and other biomolecules. The mechanism of action of antidiabetic medications varies depending on the class of the drug. (Moon *et al.*, 2017).

Sulfonylureas is a group of drugs that bind to adenosine triphosphate potassium sensitive channels on the cell membrane found in the pancreatic beta cells (Szeto *et al.*, 2018). This in turn impairs the resting potential of the cell thus preventing potassium from exiting the cell and calcium influx thereby activating insulin production (Rorsman *et al.*, 2014). Adverse effects of these drugs include; depression, syncope, nervousness, pain, dyspepsia, flatulence, pruritus, anxiety and vomiting (Moon *et al.*, 2017).

Meglitinides' mode of action is same as sulfonylureas as they bind to adenosine triphosphate-potassium channels, hence blocking potassium exit and causing influx of calcium (Moon *et al.*, 2017) resulting in stimulation of insulin release. Dipeptidyl IV inhibitors (DPP-4) prevent DPP-4 action in the plasma thus blocking inactivation of peptide hormone (GLP-1) in circulation (Rorsman *et al.*, 2014). Incretins are gut hormones whose role is to regulate insulin amount in the body and are usually produced after taking a meal. Examples of DPP-4 inhibitors include; sitagliptin, alogliptin, saxagliptin and linagliptin. Adverse effects of DPP-4 inhibitors include; urinary tract infection, headache usually common with saxagliptin, rhinitis and cold (Noale *et al.*, 2016).

Biguanides reduce the amount of glucose production by decreasing glucose absorption from food after eating. They also prevent conversion of fats to glucose and enhance release of sugar by kidneys (Szeto *et al.,* 2018). Metformin, a common example of biguanide, increases the activity of Aden monophosphate activated protein-kinase reducing gluconeogenic enzyme expression and lipogenesis therefore increasing uptake of glucose in the muscles. Phenformin is another example of biguanide (Moon *et al.*, 2017).

Thiazolidinediones reduce fatty acid circulating in muscle and liver by reducing lipid availability in these organs, thus increasing sensitivity to insulin improving its uptake. Examples of thiazolidinediones include; rosiglitazone and pioglitazone. Adverse effects of these drugs include; weight gain, cancer of the bladder, congestive heart failure and edema (Noale *et al.*, 2016). Alpha-glucosidase inhibitors inhibit absorption of carbohydrates by inhibiting alpha-glucosidase enzymes that digest it in the intestines thus preventing metabolism of sucrose to glucose and fructose (Moon *et al.*, 2017). Acarbose and miglitol are common examples and adverse side effects of alpha-glucosidase inhibitors are abdominal pain, flatulence and diarrhea (Moon *et al.*, 2017).

2.5 Demographic and socio-economic factors influencing adherence to antidiabetics

It is well recognized that poor adherence to prescribed antidiabetics may lead to poor glycemic control, which could result in micro-vascular and macro-vascular complications (Aminde *et al.*, 2019). Inadequate commitment to and compliance with antidiabetic medication places patients at risk of complications, potentially leading to failure in achieving glycemic control objectives. The issue hinders optimal diabetes mellitus management and remains a significant challenge to address (Faisal *et al.,* 2021). With the production of effective oral hypoglycemic agents, adherence to antidiabetics has remained to be a great challenge in treatment and management of T2DM (Lee *et al.*, 2013) therefore, identification of factors associated with poor adherence is warranted. Morisky Medication Adherence Scale-8 (MMAS-8) is a simple and quick method with reference to its acceptable validity and reliability and is the most effective method for assessment of adherence to antidiabetics among diabetic patients in a busy clinical setting (Lee *et al.,* 2013).

Diabetes necessitates individuals to stay self-motivated in adhering to a lifelong regimen that involves both medication and non-pharmacological approaches. While adherence to this combination is pivotal, it hasn't been given adequate focus by health workers (Faisal *et al.,* 2021). Xie *et al.,* (2020) revealed noteworthy connections between specific socio-demographic factors and adherence to various self-management behaviors for diabetes and hypertension. The study also indicated that self-efficacy played a crucial role in mediating age and diet therapy adherence correlation. (Wibowo *et al.*, 2022) further argued that factors which result in poor medication adherence among diabetic patients differ among different population, owing to distinctions in education background, cultural convictions, social and economic status, and a number of other aspects.

Forgetfulness has been reported from many previous studies (Kassahun *et al.,* 2016) to be among the main causes of non-adherence to antidiabetics. Some patients only tend to remember taking medication when they are unwell and ignore when they are feeling okay (Aminde *et al.*, 2019). Number of drugs to be taken and frequency of administration determine complexity of drug regimen. Previous studies for example, demonstrated that patients were adhering better to a once-daily drug than a three-time daily drug (Lee *et al.*, 2013). Patients who are illiterate find it difficult to read and understand prescription instructions and generally fail to understand the real essence of taking medication and this affects adherence to medication (Kassahun *et al.*, 2016). Aminde *et al.,* (2019) showed that severe drug side effects discouraged some patients from taking medications as required. For example, patients who took metformin which is an antidiabetic drug experienced diarrhea, vomiting and nausea. These side effects influenced adherence to medications among some diabetic patients.

2.6 Glycated hemoglobin

Glycated hemoglobin is a form of hemoglobin bonded to sugar by a chemical process. Normal sugar levels result in normal HbA1c and increased blood sugar causes HbA1c levels to be elevated (Katsarou *et al.*, 2017). Therefore, HbA1c levels can be used to determine and predict level of blood sugar. It estimates average blood glucose preceding 3 months and serves as a diagnostic test (Sacks., 2013). Higher amounts of glycated hemoglobin indicate poor glycemic control and since HbA1c levels below 5.7% is normal while a level between 5.7% and 6.4% is regarded as pre-diabetic. 6.5% and above indicates diabetes (ADA., 2021).

Elevated levels of HbA1c among diabetic patients, have been associated with peripheral neuropathy, cardiac diseases, retinal vascular disease and renal diseases (Katsarou *et al*., 2017). The ADA recommends that HbA1c test be done twice a year among diabetic patients who are adhering properly to diabetes medication and at least every 3 months for those who have changed medication or are not adhering well. This test is not appropriate for those who have recently donated or lost blood, hemolytic anemia, and change of diet or treatment within a period of six weeks. This is because the test assumes a normal process of wearing out of erythrocytes (ADA., 2021).

2.7 Roles of Serum electrolytes in a diabetic patient

Electrolytes are electrically charged ions that dissolve in body fluids and are important in many body functions including control of acid base balance, contraction of muscles and helping in blood clotting (Bohara *et al.*, 2021). The main serum electrolytes are sodium, phosphate, chloride, calcium, potassium and magnesium (Shrimanker., 2019).

2.7.1 Sodium (Na)

Sodium normal range in blood is usually between 135-145mEq/L. Its reabsorption occurs in the kidneys to maintain the body's electrolyte balance and blood pressure, regulating fluid levels and supporting various physiological processes (Sterns., 2015). In diabetic patients, sodium levels can fluctuate based on the type of diabetes and its management (Araki *et al.*, 2015). Poorly controlled diabetes with hyperglycemia can cause polyuria, leading to dehydration resulting in electrolyte imbalances, including sodium loss which could potentially result in lower sodium levels (hyponatremia) (Bohara *et al.*, 2021). On the other hand, diabetic patients taking certain medications like diuretics to manage blood pressure or kidney-related issues might experience increased sodium excretion, leading to elevated sodium levels (hypernatremia) (Unachukwu *et al*.,2018). Sodium levels have been found to be lowered in most T2DM cases because higher glucose concentration in the body results in osmotic force which draws fluids to extracellular space causing lowered sodium concentrations in plasma (Datchinamoorthi *et al.*, 2016).

2.7.2 Chloride (Cl)

Chloride is the body's second-most plentiful electrolyte after sodium and is essential in maintaining body pH and also important in maintaining extracellular and intracellular fluid (Khan *et al.*, 2019). Chloride levels are usually elevated in T2DM because of ketoacidosis which lowers the pH of blood causing higher amounts of chloride (Sterns., 2015). Ketoacidosis can also occur in patients with T2DM although it is less common than in Type 1 diabetes and arises due to multiple factors, such as insulin deficiency, increased production of counter-regulatory hormones like glucagon, and elevated blood glucose levels (Jiskani *et al.,* (2022). In T2DM, ketoacidosis typically arises during episodes of severe illness, infection, or extreme stress and during these times, the body's demand for insulin increases, and if there is not enough insulin available or if the insulin resistance is severe, it can lead to a relative insulin deficiency. The combination of insulin resistance, elevated blood glucose levels, and a relative lack of insulin can trigger the body to release counter-regulatory hormones, like glucagon, which stimulate the liver to convert stored glycogen into glucose, further resulting in hyperglycemia

(Datchinamoorthi *et al.,* 2016). As a result of limited insulin and the cells inability to utilize glucose, the body seeks alternative sources of energy and it begins breaking down fat and convert into ketones. This process takes place in the liver. Ketones accumulation in the blood leads to a drop in blood pH, causing ketoacidosis (Jiskani *et al.*, (2022). If left untreated, ketoacidosis can become life-threatening, disrupting normal physiological functions and resulting in severe complications, including dehydration, electrolyte imbalances, and organ damage (Sterns., 2015).

2.7.3 Potassium (K)

Potassium is an electrolyte essential for the body to function properly and is used by cells together with sodium and when there is an inflow of potassium into the cells, sodium flows out (Datchinamoorthi *et al.,* 2016). In individuals with T2DM, hyperglycemia occurs in the blood due to the body's inability to use insulin effectively or produce enough of it (Khan *et al.,* 2019). The kidneys are important in regulating blood glucose as well as maintaining electrolyte balance and when elevation of blood glucose levels occur, kidneys attempt to eliminate the excess glucose through urine, leading to glucosuria (Gilon *et al.*, 2014). Consequently, there is an increased osmotic load in the renal tubules, leading to impaired reabsorption of water and electrolytes, including potassium. Under normal circumstances, the kidneys enhance reabsorption of almost all of the filtered glucose back into bloodstream, along with essential electrolytes like potassium, sodium and calcium (Araki *et al.,* 2015). However, in diabetic patients experiencing hyperglycemia, the excess glucose overwhelms the kidney's reabsorption capacity and this results in osmotic diuresis, a condition where water and electrolytes, including potassium, are excreted in the urine and as a consequence of increased potassium loss, diabetic patients may develop hypokalemia, a deficiency of potassium in the blood (Chatterjee *et al*., 2012). Hypokalemia can give rise to various symptoms and complications, such as muscle weakness, fatigue, muscle cramps, cardiac arrhythmia, and neuromuscular issues (Qadeer *et al.,* 2020). Khan *et al.*, (2019) showed a significant association between hyperglycemia and serum potassium in uncontrolled T2DM ($P \leq 0.05$).

2.7.4 Calcium (Ca)

Calcium is mainly found in the extracellular fluid and food is its main source in the body. It is important in transmission of nerve impulses, blood coagulation and is also needed for muscle contraction, as it enables muscle fibers to move and slide over each other (Fang *et al.,* 2016) among other functions within the body. Calcium metabolism may be affected due to a number of factors related to T2DM. Firstly, T2DM is characterized by insulin resistance, wherein the body's cells have reduced responsiveness to insulin effects. Insulin enhances intracellular calcium uptake in different tissues (Lorenzo *et al.*, 2014). When insulin resistance occurs, it may hinder the transport of calcium into cells, potentially affecting muscle function and insulin signaling pathways. This disruption in calcium metabolism can have significant implications for the overall health and management of T2DM (Gilon *et al.,* 2014). Secondly, diabetic nephropathy is associated with diabetes and affects kidneys, causing proteins leakage in the urine and impaired kidney function and this condition can disrupt the normal reabsorption of calcium in the kidneys, causing an increased excretion of calcium in the urine. As a result, there can be a negative calcium balance in the body, which might contribute to further complications related to bone health (Fang *et al.,* 2016). There is decreased serum calcium level in

T2DM due to production of end products of glycation, which cause misalignment of collagen fibers and weakening of bone (Wongdee *et al.*, 2017).

2.7.5 Phosphorus (P)

Phosphorus constitutes about 1% of body weight and is important in bone and teeth mineralization (Khan *et al.*, 2019). It also plays a role in cellular functions by taking part in several enzymatic reactions taking place within the cells. In individuals with T2DM when cells become resistant to the action of insulin, glucose uptake is impaired, leading to high blood glucose levels, however, insulin resistance not only affects glucose metabolism but also impacts the handling of other nutrients, including phosphorus (Liamis *et al.*, 2014). Fang *et al.*, (2016) found out that serum phosphate levels were significantly lower among T2DM patients compared to healthy people. Increased blood glucose concentration results in depolarization of brush border membrane of kidneys responsible for reabsorption of phosphate and this consequentially lowers phosphate inside cells and causes hyperphosphaturia (Khan *et al.*, 2019).

2.7.6 Magnesium (Mg)

Magnesium, being an important mineral, it plays part in various metabolic processes within the human body and is involved in over 300 enzymatic reactions contributing to numerous biochemical functions which include; enzyme activation, energy production, cardiovascular health, bone health and glucose metabolism (Kumar *et al.*, 2019). In T2DM, there is often a concurrent loss of renal calcium and magnesium (Feng *et al.*, 2020), however, the precise mechanisms responsible for this loss have not been fully explained. In addition, hyperglycemia can decrease the reabsorption of magnesium in the kidney tubules, leading to its excretion in the urine (Barbagallo *et al.*, 2015).

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study area

The study was carried out at Samburu County Referral Hospital in Samburu County with GPS coordinates 1.0981^o N, 36.6962^o E. The hospital is a level 5 hospital serving residents across Samburu County and remains the largest hospital in the county with a 200 inpatient bed capacity and a specialized diabetes clinic.

3.2 Study design

The study used a descriptive cross-sectional study design to adult diabetic patients who attended Samburu County Referral Hospital Outpatient diabetes clinic.

3.3 Study population

The study involved adult diabetic patients who attended diabetic outpatient clinic at Samburu County Referral Hospital.

3.3.1 Inclusion criteria

Diabetic patients aged above 18 years under antidiabetics for at least the preceding 3 months and should have low adherence to the medications (score≤6) on Morisky Medication Adherence Scale.

3.3.2 Exclusion criteria

This study excluded diabetic patients under 18years of age as well as those who had not been under antidiabetic treatment for at least 3 months and diabetic patients who were unwilling to give consent to participate in the study. Additionally, individuals with a Morisky Medication Adherence scale score of ≥ 6 were also excluded.

3.4 Sampling technique

The study employed a convenience sampling technique on adult diabetic patients who attended the outpatient diabetic clinic.

3.5 Sample size determination

The sample size determination was done using Fisher et al., (1998) formula.

$$\mathbf{n=} \frac{Z^2pq}{d^2}$$

Where; n=the desired sample

Z = 95% confidence interval or 1.96

d = degree of accuracy set at 0.05 levels.

P = proportion in target population estimated to have characteristics being measured where P= 0.05 (A recent study done in Kenya reports T2DM prevalence to be at 5%

(Mkuu *et al.*, 2019).

q = 1.0-p

n = [(1.96*1.96) (0.05) (0.95)] / [(0.05*0.05)] = 72

3.6 Morisky Medication Adherence Scale-8 Data collection Instrument

Data on adherence levels was collected by use of Morisky Medication Adherence Scale (Appendix III). Those with adherence score of below 6 were assessed further on the second questionnaire on Factors associated with poor adherence to antidiabetics (Appendix IV).

3.6.1 Validity and reliability of MMAS-8

Morisky Medication Adherence Scale (MMAS-8) is a tool for measuring adherence to medications across patient populations. The tool uses a number of behavioral questions that are structured to prevent yes-saying responses that may result in biased outcomes. Morisky Medication Adherence Scale-8 contains 8 questions, each item elicits either a "yes" or "no" response, making all responses for every item dichotomous in nature (0 and 1 scores). Scores range from 0 to 8. Adherence was then gauged; a high adherence level was indicated by a score of 8 whereas below 6 signified low adherences. A score falling between 6 and 8 was considered as demonstrating medium adherence. For those patients who did not understand English language, the questions were interpreted into languages they best understood for instance, Samburu or Swahili languages.

3.7 Laboratory Analysis of HbA1c

The Standard Operating Procedures (SOPs) were adhered to, in pre-analytical phase by collecting sufficient amount of sample, at least 3mls of blood for measuring serum electrolytes and at least 3mls for measuring glycated hemoglobin levels. Request forms were filled properly with unique patient identification numbers. Blood samples for measuring HbA1c levels were collected in vacutainers containing dipotassium ethylenediaminetetraacetic acid (K2-EDTA) and transported to the laboratory for analysis using automated HbA1c analyzer machine which uses a high-performance liquid chromatographic (HPLC) technique to determine HbA1c concentration. It was manufactured in the Republic of Korea.

3.7.1 Specimen analysis

The “standard test” mode was selected on the analyzer and operator ID was input after which the test device was inserted into the slot. Five microliter of blood was collected with the foil automatically through capillary action. The edge of foil was inserted into the extraction buffer and mixed well by pressing and releasing rubber for 6-8 times carefully and slowly to avoid bubble from forming. All the specimen was collected and applied on the well of the test device already inserted into the analyzer. And pressed “TEST START” button. The analyzer displayed results immediately after 3 minutes.

3.8 Laboratory Analysis of Electrolytes

Venous blood for determination of serum electrolytes was collected in plain red-top vacutainers, labeled properly and delivered into the laboratory immediately. Upon delivery to the laboratory the samples were allowed to settle to allow complete clotting then put in a centrifuge and spun at 3000rpm for 5 minutes, the serum was transferred into sample cups and labeled appropriately. The samples were analyzed for electrolyte levels (sodium, calcium, phosphorus, potassium and chlorides). This was done by use of automated Selectra prom biochemistry analyzer manufactured in the Netherlands. is based on Ion Selective Electrode (ISE) method. The results were then recorded.

3.8.1 Quality Assurance

Samburu County Referral Hospital Biochemistry Laboratory runs daily internal and external quality control on all tests. To ensure quality of analysis two levels of Internal Quality Control (IQC) were conducted by first calibrating the Selectra prom biochemistry analyzer and doing control check using a control sample which had to meet the acceptable values before the samples were analyzed. Calibration set tests were performed to ensure standard F HbA1c analyzer produced accurate results. External quality control tests were run to ensure performance of analyzer and test device and production of quality results.

3.8.2 Data analysis

The completed questionnaires on medication adherence were numbered and coded for the case of handling. Data on factors contributing to poor adherence to antidiabetics were summarized by use of descriptive statistics. The findings were displayed using scatter plots, bar graphs and frequency tables. Relationship between electrolytes and glycated hemoglobin among diabetic patients with poor adherence to antidiabetics was determined using Pearson correlation. This method of correlation is effective for evaluating this relationship due to its ability to detect linear associations efficiently, its ease of interpretation, and its compatibility with parametric assumptions often observed in medical tests. Data analysis including correlation coefficients calculations were done by use of Microsoft excel.

3.9 Ethical considerations

Approval for this study was sort from the KU Ethical Review Committee, NACOSTI and from SCRH Administration. Confidentiality was observed by not sharing information with any unauthorized person and the patient identity was protected by using assigned unique numbers instead of names. All interviews and the examinations were conducted in a private room within the clinic which was well lit and ventilated.

The participants were aware that their participation in the study was entirely voluntary, and they have the right to decline. Their decision would not impact the medical care and treatment they would receive on that day or at any other clinic in the future. They should feel free to ask any question related to the study.

They had the right to decline answering questions or terminate the interview at any time without facing any consequences in their current or future interactions with the clinic or any other organizations. The patients benefitted from the glycated hemoglobin and serum electrolytes examination.

CHAPTER FOUR: RESULTS

4.1 Socio-demographic characteristics of the study participants

Seventy-two study participants comprising of 48.6% (35) females and 51.4% (37) males were enrolled to take part in the study (Table 4.1). They were aged between 21 and 88 years while their mean and median were 53.9 and 53.5 years, respectively. Majority of the study participants, 83.3% (60) were married, 58.3% (42) were rural residents and 37.5% (27) were educated at least up to secondary school level.

Table 4.1: Socio-demographic characteristics of the study participants

Variable	**Features**	**Frequency**	**Percentage**
Gender	Male	37	51.4%
Gender	Female	35	48.6%
Age (Years)	18-29	2	2.8%
Age (Years)	30-49	24	33.3%
Age (Years)	50-64	26	36.1%
Age (Years)	65and above	20	27.8%
Marital Status	Married	60	83.3%
Marital Status	Single	12	16.7%
Education Level	No education	10	13.9%
Education Level	Primary level	17	23.6%
Education Level	Secondary level	27	37.5%
Education Level	Tertiary level	18	25.0%
Residence	Urban	30	41.7%
Residence	Rural	42	58.3%

4.2 MMAS-8 Questionnaire scores among study participants

MMAS-8 scores for the 72 study participants ranged from 1-6 while majority of them (20) got a score of 5 the least number (6) scored 1 as shown in figure 4.1 below. Also 7 individuals scored 2, 9 got a score of 3 while 16 scored 6.

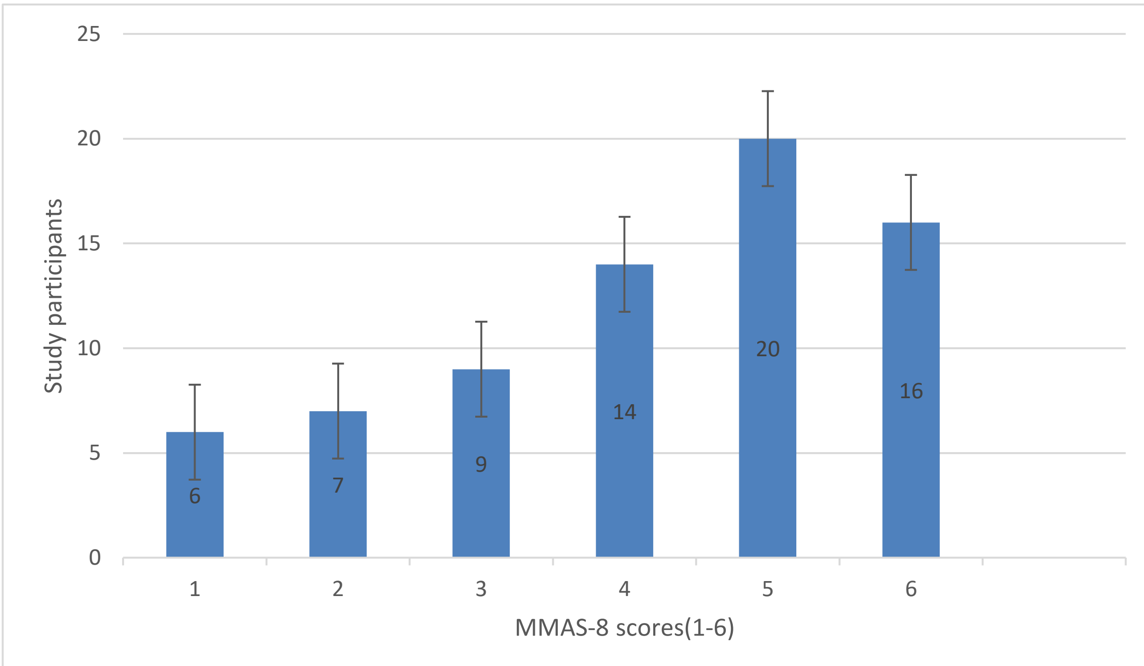


Figure 4.1: A Bar graph showing diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital against MMAS-8 scores

4.3 Distribution of HbA1c across the age groups of diabetic patients with poor adherence to antidiabetics

The dot plot below (Figure 4.2) represents HbA1c levels at different ages. The highest level of HbA1c was 15% and it occurred in three instances, where the age values were 42, 50 and 55 years. The oldest individual was aged 88 years, and the corresponding HbA1c level was 12.2%. On the other hand, the youngest individual was aged 21 years and the corresponding HbA1c was 11.9%. Additionally, the lowest HbA1c level was 5.1% which was observed at the age of 61 years. The data points appear to be scattered without a distinct pattern, and for the majority of the data points, HbA1c levels seem to vary across different age groups as there are individuals with both high and low HbA1c levels across all age groups.

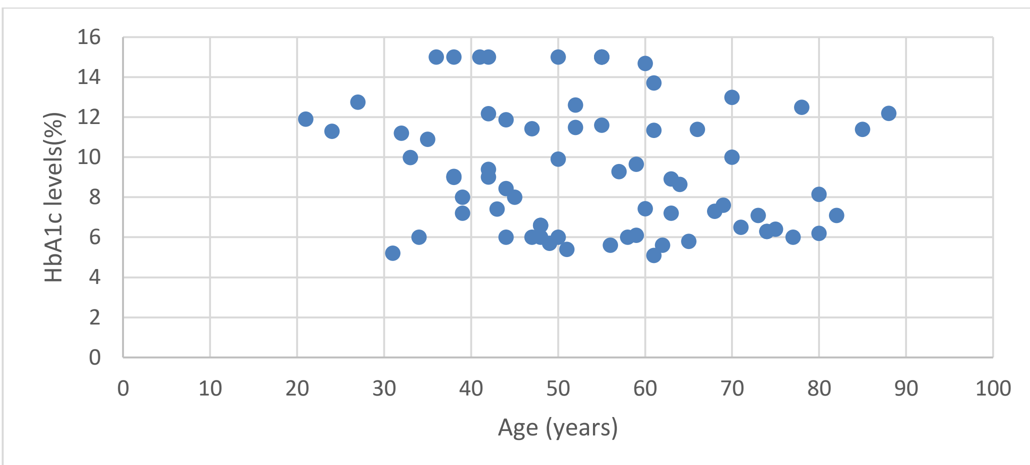


Figure 4.2: A scatter plot diagram showing the distribution of HbA1c and Ages of diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

4.4 Distribution of electrolyte levels and HbA1c

Scatter plots were created to visualize the relationship between HbA1c levels and various electrolytes (sodium, potassium, chloride, phosphorus, magnesium and calcium). The scatter plot on Figure 4.3 presents data on the relationship between HbA1c and sodium. The HbA1c levels ranged from 5.1% to 15% while the lowest sodium level was 122mmol/l and the highest being 149mmol/l. The lowest HbA1c level of 5.1% corresponded with sodium level of 127mmol/l while the highest HbA1c level of 15% corresponded with multiple instances of sodium levels. On the other hand, the lowest sodium level of 122mmol/l corresponded with HbA1c level of 9.4% while the highest sodium level of 149mmol/l corresponded with HbA1c level of 8%.

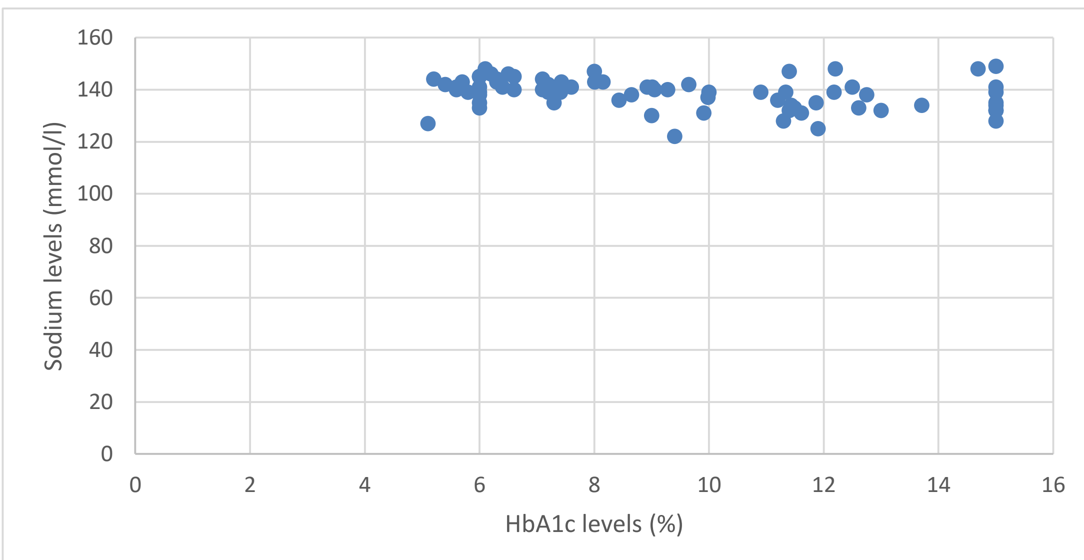


Figure 4.3: A scatter plot diagram showing the distribution of HbA1c and sodium levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

There is scattered distribution of data points in the scatter plot for HbA1c and potassium as shown in Figure 4.4. The lowest HbA1c level was 5%, and its corresponding potassium level was 5.1mmol/l. On the other hand, the highest HbA1c level was 15% and its corresponding level was 5.2mmol/l. Conversely, the lowest potassium level was 3.3mmol/l, and it corresponded to an HbA1c level of 5.7%. The highest potassium level was 5.56, and it was associated with an HbA1c level of 8.15%.

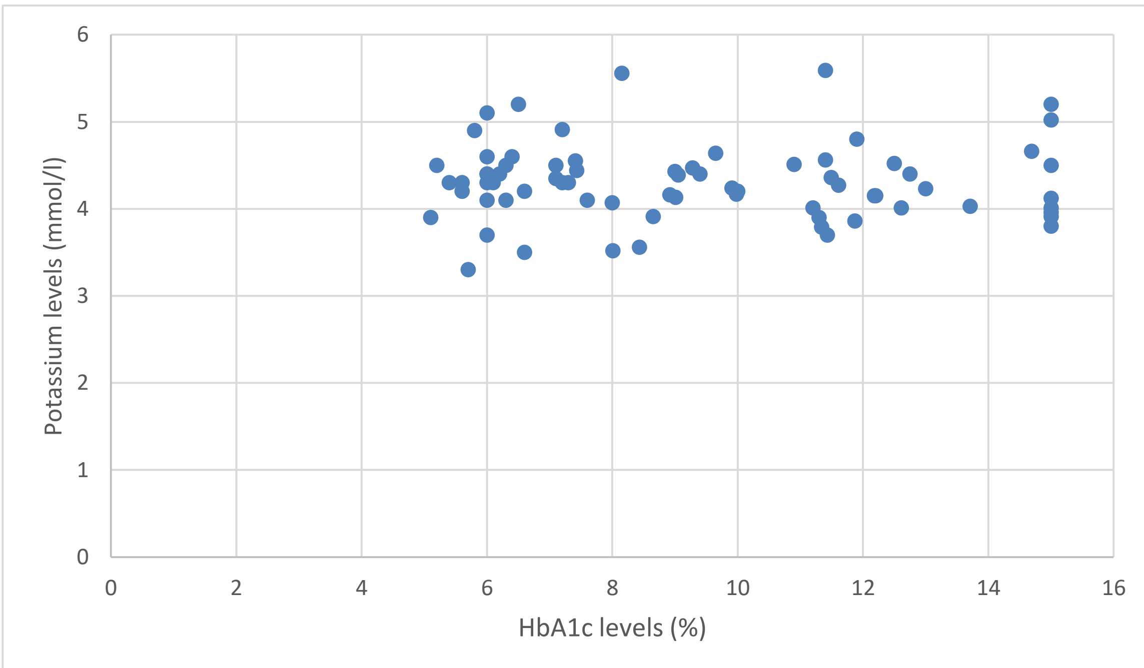


Figure 4.4: A scatter plot diagram showing the distribution of HbA1c and potassium levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

The scatter plot for HbA1c and chloride (Figure 4.5) reveals a slightly more clustered pattern compared to sodium and potassium. The highest chloride level observed was 111mmol/l, which corresponded to an HbA1c level of 6%. On the other end, the lowest chloride level was 93mmol/l, and it was associated with an HbA1c level of 11.3%.

Additionally, the lowest HbA1c level noted was 5.1% and it corresponded to a chloride level of 97mmol/l. Finally, the highest HbA1c level observed was 15%, which was linked to a chloride level of 102mmol/l.

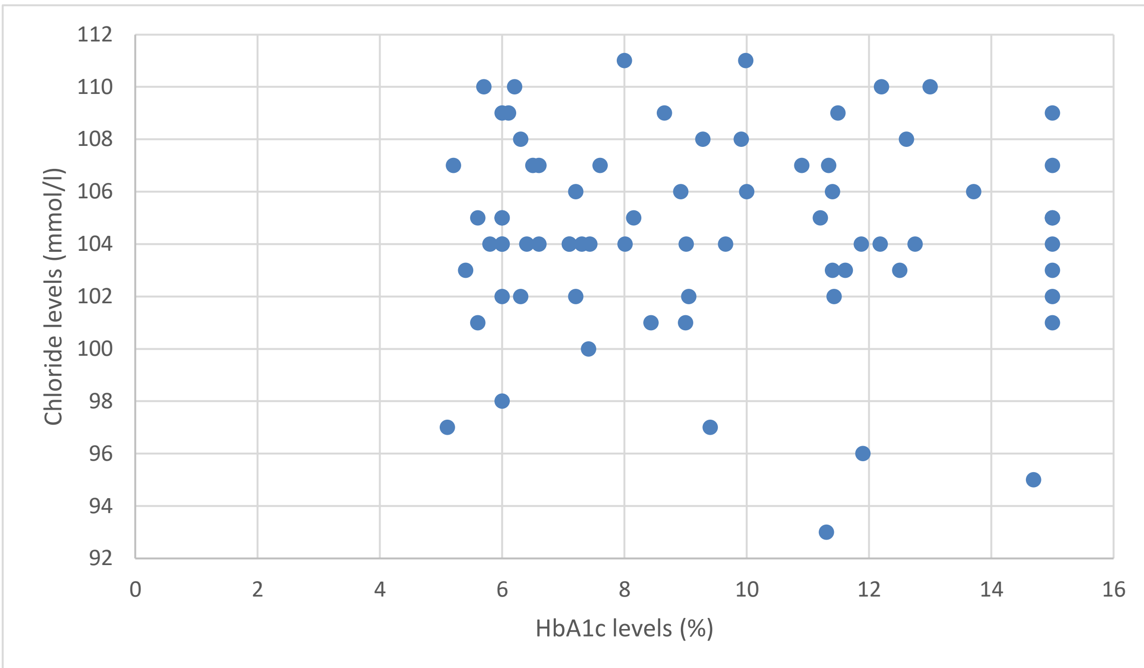


Figure 4.5: A scatter plot diagram showing the distribution of HbA1c and chloride levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

The scatter plot for HbA1c and calcium displays a slightly similar clustered pattern as seen in the HbA1c and sodium relationship, as shown in Figure 4.6. The highest HbA1c level observed was 15%, and its corresponding calcium level was 2.65. On the other hand, the lowest HbA1c level recorded was 5.1mmol/l, and it was linked to calcium level of 2.06mmol/l. Moving on to calcium levels, the highest calcium level was 2.7, which matched an HbA1c level of 6.3%. Conversely, the lowest calcium level observed was 2.0mmol/l, and it was associated with an HbA1c level of 11.4%.

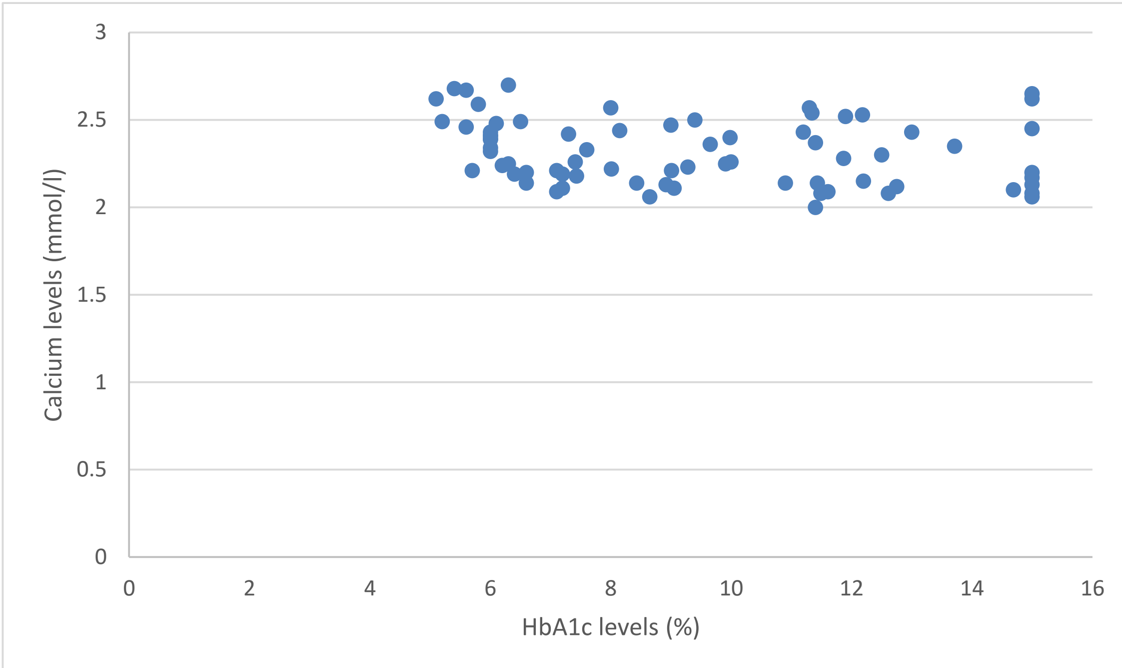


Figure 4.6: A scatter plot diagram showing the distribution of HbA1c and calcium levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

The scatter plot for HbA1c and magnesium shown in Figure 4.7 showcases a relatively dispersed distribution of data points. The highest magnesium level was 1.3mmol/l which corresponded with an HbA1c level of 14.69% while the lowest magnesium level was 0.6 and was linked to an HbA1c level of 15%. Additionally, the lowest HbA1c level observed was 5.1% and corresponded with a magnesium level of 0.6mmol/l.

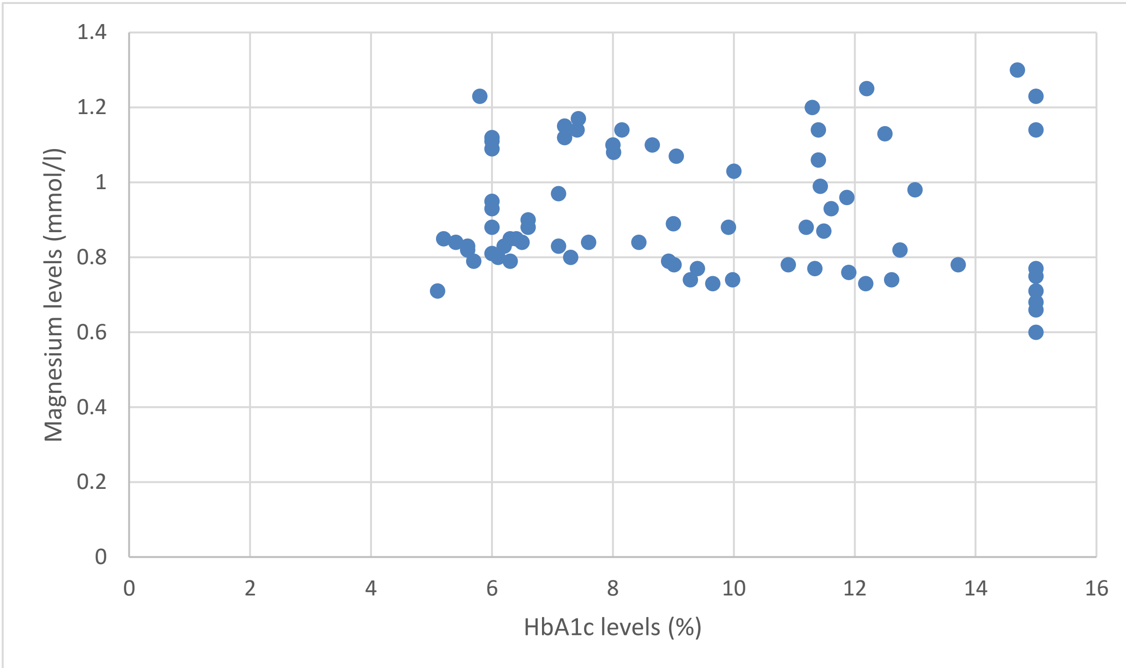


Figure 4.7: A scatter plot diagram showing the distribution of HbA1c and magnesium levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

The scatter plot for HbA1c and phosphorus (Figure 4.8) exhibits a scattered distribution similar to sodium and potassium. HbA1c levels ranged from 5.1% to 15% while phosphorus levels ranged from 0.7mmol/l to 1.60mmol/l. The highest and lowest HbA1c levels corresponded with 1.5mmol/l and 1.02mmol/l phosphorus levels respectively. Shifting the focus to phosphorus levels, the highest and lowest phosphorus levels corresponded with HbA1c levels of 5.8% and 15.0% respectively.

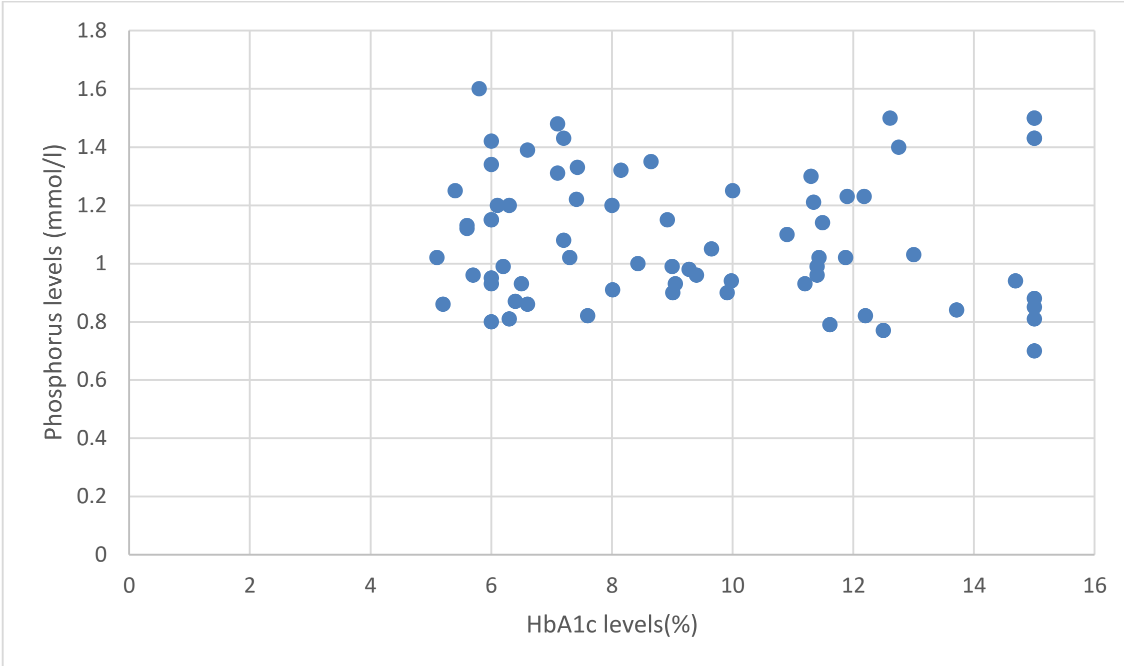


Figure 4.8: A scatter plot diagram showing the distribution of HbA1c and phosphorus levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

4.4.1 Distribution of the selected electrolyte levels among diabetic patients with poor adherence to antidiabetics

The results regarding electrolyte levels, including sodium, potassium, chloride, calcium, magnesium and phosphorus were presented in Table 4.4 below. The sodium range was recorded between 127-149mmol/l, which was slightly broader from the optimal range of 135-145mmol/l. The mean, median and standard deviation of sodium level were calculated as 136.96mmol/l, 139mmol/l and 5.85 respectively, indicating a moderate level of variability in the sodium levels among the participants.

Similarly, for potassium, the observed range in our study extended from 3.3-5.59 mmol/l which was slightly broader from the optimal range of 3.5-5.1mmol/l. The mean, median and standard deviation of potassium level were 4.30mmol/l, 4.3mmol/l and 0.44 respectively, suggesting a relatively low degree of variability in potassium levels. As for chloride, the observed range fell within 93-111mmol/l which was slightly larger than the optimal range of 98-110mmol/l. The mean and median of chloride level were calculated as 104.21mmol/l and 104mmol/l respectively, while the standard deviation indicated a moderate level of variability, measuring 3.72 as shown in Table 4.

For calcium, this study observed a range from 2.06-2.65mmol/l which was slightly different from its normal range of 2.10-2.60mmol/l. The mean and median calcium levels were calculated as 2.35mmol/l and 2.37mmol/l respectively, while the standard deviation was 0.18. The observed range of magnesium in this study ranged from 0.6-1.23mmol/l while typical optimal range at 0.70-1.15mmol/l. The standard deviation was calculated to be 0.17 while the mean and median level were 0.88 and 0.84mmol/l respectively. Lastly, for phosphorus, the observed range ranged from 0.7-1.48mm0l/l and was slightly broader from its optimal range of 0.80-1.40mmol/l while the mean phosphorus level was 1.05 mmol/l, with a median of 1.00 mmol/l. The standard deviation reflected a moderate level of variability, measuring 0.22.

Table 4.2: Distribution of the selected electrolyte levels among diabetic patients with poor adherence to antidiabetics *attending Samburu County Referral Hospital*

Electrolytes	**Reference Range**	**Study Range**	**Mean**	**Standard deviation**
Sodium (mmol/l)	135-145	127-149	136.96	5.85
Potassium (mmol/l)	3.5-5.1	3.3-5.59	4.30	0.44
Chloride (mmol/l)	98-110	93-111	104.21	3.72
Calcium (mmol/l)	2.10-2.60	2.06-2.65	2.35	0.18
Magnesium (mmol/l)	0.70-1.15	0.6-1.23	0.88	0.17
Phosphorus(mmol/l)	0.80-1.40	0.7-1.48	1.05	0.22

4.5 Correlation between HbA1c and electrolytes levels

The correlation between HbA1c levels and electrolyte levels was examined among the 72 study participants. Table 4.5 below presents Pearson correlation coefficients and corresponding significance levels for each electrolyte parameter. For sodium, a moderate negative correlation of -0.32 and a significance level of less than 0.05 was observed. In the case of potassium (K+), a very weak negative correlation of -0.01 was found. However, the correlation lacked statistical significance ($p > 0.05$). Chloride showed a weak negative correlation of 0.05 but the correlation lacked statistical significance ($p > 0.05$). Additionally, calcium, magnesium and phosphorus exhibited correlations of -0.24, -0.07 and -0.04 respectively and their correlations lacked statistical significance ($p > 0.05$).

Table 4.3: Correlation between HbA1c and electrolytes levels among diabetic patients with poor adherence to antidiabetics attending Samburu County Referral Hospital

		Na+	**K+**	**Cl-**	**Ca**	**Mg**	**Phos**
HbA1c levels	Pearson correlation	-0.32	-0.01	0.05	-0.24	-0.07	-0.04
	Sig.	<0.05	>0.05	>0.05	<0.05	>0.05	>0.05
	N	72	72	72	72	72	72

Sig. =Significance N=Number

4.6 Demographic and socio-economic factors contributing to poor adherence to antidiabetics among diabetic patients attending Samburu County Referral Hospital

The study reported several factors contributing to poor adherence among respondents with T2DM as shown in Table 4.6. The most commonly cited reasons were unaffordability of the diabetes drugs (69%), diabetes medications interfering with meal plan (51%), side effects of the medication (41.7%), and forgetting to take diabetes drugs (40.3%). Additionally, other factors that significantly contributed to poor adherence included complexity of the drug regimen (38%), perceived ineffectiveness of diabetes medication (25%) and lack of support from family reported by 14% of the respondents. Furthermore, a smaller proportion of respondents reported the dose being too high (11%), being unable to travel long distances to access medication (11.1%) and the use of herbs such as Aloe Vera as contributing factors, as outlined in the same table below.

Table 4.4: Demographic and socio-economic factors contributing to poor adherence to antidiabetics.

Factors	Percentage (%)	Number
Lack of support from family	14%	10
Forgetting to take diabetes drugs	40.3%	29
Side effects of the medication	41.7%	30
Complexity of the drug regimen	38%	28
Diabetes medication not being effective enough	25%	18
The dose is too high (Experiencing hypoglycemia symptoms)	11%	8
Diabetes medications interfere with meal plan (limiting intake of carbohydrates with added sugars)	51%	37
Lack of money to buy drugs	69%	50
Others; Being unable to travel long distances to access medication	11.1%	8
Use of herbs such as Aloe Vera	5.5%	4

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Socio-demographic characteristics of the study participants

In this study, the highest number of participants were in the age bracket of 50-64 years, making up 36.1% of the total. The lowest number of participants, at 2.8% belonged to the 18-29 years age group. Those aged 65 years and above accounted for 27.8% of the study participants, as shown in Table 4.1. Older participants in the age groups of 50-64 years and 65 and above are more likely to have had diabetes for a longer duration. This extended duration of the condition can introduce challenges related to comorbidities, polypharmacy (the use of multiple medications), and age-related cognitive decline, all of which may impact their ability to prescribed medications.

The table also shows that the participants are almost evenly distributed by gender, with 51.4% males and 48.6% females. Studies have shown that men and women may have different approaches when it comes to managing chronic conditions. For instance, females might be more diligent in taking medications regularly, while males may be less adherent. In addition, a larger number of the study participants resided in the rural areas (58.3%) compared to urban resident (41.7%). Urban and rural participants may encounter distinct challenges regarding access to healthcare resources and medications. Generally, urban residents typically have better access to healthcare facilities, potentially facilitating their diabetes management. On the other hand, individuals in rural areas may encounter challenges related to transportation and limited access to healthcare services, factors that could impact their ability to adhere to prescribed medications. Also, a high number of study participants (83.3%) were married. A significant number (37.5%) reached secondary level of education.

5.1.2 Glycated hemoglobin (HbA1C) levels among diabetic patients with poor adherence to antidiabetics

The results indicate that a substantial proportion (58.3%) of the study participants demonstrated suboptimal glycemic control, as evidenced by elevated HbA1c levels (%). Among the participants, only 41.7% had HbA1c levels within the target range of 5-7%, while the remaining 58.3% had high HbA1c levels ranging from 8% to 16%. This finding is comparable to the results by Yeemard *et al.*, (2022) which reported 54.8% of suboptimal glycemic control among diabetic patients. Kibirige *et al*., (2017) reported a slightly higher percentage where inadequate glycemic control was observed in 311 study participants, constituting 73.52% of the study's subjects and this indicates that a significant majority ($P \leq 0.05$) of patients who had poor adherence to their antidiabetics had difficulty achieving and maintaining optimal glycemic control.

When examining the relationship between age and HbA1c levels (refer to figure 4.2), there is no definite correlation ($r=-0.19238$) observed as the HbA1c levels appear to be distributed across various age groups. This suggests that age may not serve as the primary predominant factor in determining HbA1c levels in this study and other factors, such as individual health conditions and lifestyle choices, may have stronger influence on HbA1c levels than age alone. This finding contradicts results of a study by Yeemard *et al.*,(2022) where it was found that diabetic patients aged <49 years had 3.32 times greater odds of having suboptimal glycemic control than those aged above 70 years. He explained that physiologically, older individuals often experience a decline in beta-cell function and reduced insulin requirements. These age-related changes make it easier for older individuals to maintain stable blood glucose levels. In contrast, younger individuals generally have more robust beta-cell function and higher insulin requirements. The higher insulin requirements in younger patients can pose challenges in achieving optimal glycemic control, contributing to the increased odds of suboptimal glycemic control in this age-group.

The finding that 22.2% of the participants had HbA1c levels ranging from 8-10% (Table 4.3) suggests a moderate level of hyperglycemia among this population. The percentage of study participants within that range was reported to be slightly lower (13.24%) by Kibirige *et al*., (2017). It implies that many individuals who were non-compliant with their antidiabetic medications experienced challenges in controlling their blood glucose levels. This finding emphasizes the detrimental impact of poor adherence on glycemic control and highlights the need for interventions to improve medication adherence and enhance overall treatment outcomes.

Furthermore, 23.6% of the participants had HbA1c levels between 11-13% (Table 4.3), indicating poor glycemic control and a higher risk of developing complications associated with diabetes. Kibirige *et al*., (2017) reported a slightly lower percentage (17.97%) of study participants within the range. This finding underscores the significance of addressing medication adherence issues among this subgroup. Effective interventions aimed at enhancing patient education, support and motivation to adhere to their prescribed antidiabetic medications are crucial to achieving better glycemic control and reducing the risk of long-term complications.

The data also reveals that 12.5% of the study participants had HbA1c levels ranging from 14-16%, indicating significantly elevated blood glucose levels as shown in Table 4.3, signifying extremely poor glycemic control. This finding highlights the critical nature of the problem of poor adherence among this population. Intensive interventions, including close monitoring, education, and involving family members or caregivers, are necessary to support patients in achieving better medication adherence and improving their glycemic control.

5.1.3 Levels of electrolytes (Chloride, potassium, calcium, magnesium, phosphorus and sodium) and correlation with HbA1c among diabetic patients with poor adherence to antidiabetics

Electrolyte imbalance is usually common among patients who adhere poorly to antidiabetics. This depends on many factors but most common causes are hyperglycemia and diabetic ketoacidosis (Liamis *et al.*, 2014). This study showed a statistically significant ($P \leq 0.05$) negative correlation of -0.32 between sodium level and glycated hemoglobin (Table 4.5). It can therefore be stated that an increase in glycated hemoglobin has a consequent decreasing effect on the level of sodium among type 2 diabetes patients. Similarly, (Khan *et al.*, 2019) observed a decrease in serum sodium in uncontrolled diabetes mellitus and observed sodium levels to be highly significant (p-≤0.05). These findings can be explained by several underlying mechanisms. Firstly, the kidneys respond to high blood glucose by initiating osmotic diuresis, increasing urine production to eliminate excess glucose. As a consequence, water and electrolytes, including sodium ions, are excreted in higher amounts, leading to a reduction in serum sodium levels. Moreover, the increased urine production can result in dehydration if fluid intake does not match the elevated fluid loss. Dehydration also lowers the concentration of sodium in the blood, further contributing to lower serum sodium levels.

The scatter plot for HbA1c and chloride (Figure 4.5) reveals a slightly more clustered pattern compared to sodium and potassium. In this study, it was found that there was a negative correlation between HbA1c and chloride levels, r=-0.05 (refer to Table 4.5). However, the correlation is not statistically significant ($P \geq 0.05$) indicating that changes in chloride levels are unlikely to have a notable impact on HbA1c levels. These findings are comparable with results by Santhosh *et al.*, (2021) which showed insignificant alterations of chloride levels in type 2 diabetic individuals. A contrasting finding was seen in a study conducted by Ogunleye.,2016 whereby his study had shown that type 2 diabetic patients had lower levels of chloride, potassium, magnesium and sodium and phosphorus and he explained that the loss of serum electrolytes occurred due to increased excretion of those electrolytes in urine or as a result of lowered absorption. This study comprised of mostly stable individuals with relatively well-controlled diabetes and this might have minimized potential interference of chloride levels.

There is scattered distribution of data points in the scatter plot for glycated hemoglobin and potassium as shown in Figure 4.4. A negative correlation between potassium electrolyte and glycated hemoglobin was observed, r=-0.01188 ($P \geq 0.05$) as shown in

Table 4.5. It can therefore be stated that increase in glycated hemoglobin is inversely related to the potassium level in the body. The lack of statistical significance suggests that changes in potassium levels are not strongly associated with changes in HbA1c levels and since our study participants were on diabetes treatment regimens, this could contribute to heterogeneity and obscure potential alterations in potassium levels. This observation is in agreement with a study by Khan *et al.*, (2019) which also found no correlation between potassium level and glycated hemoglobin. Although significant variations have been shown in a study conducted by Santhosh *et al.*, (2021) whereby increased serum potassium levels were found to be statistically highly significant ($P \leq 0.05$) and he explained that the movement of potassium from the inside of cells to the outside, can result in hyperkalemia which is due to renal dysfunction, insufficient insulin levels, or hypertonicity.

A statistically significant ($P \leq 0.05$) negative correlation coefficient of -0.2398 between HbA1c concentration and calcium level was observed in this study (Table 4.5). This suggests that higher calcium levels may be associated with lower HbA1c levels. Insulin resistance can disrupt calcium metabolism (Wongdee *et al.*, 2017). Normally, insulin promotes calcium uptake by cells, including bone cells. However, in a state where there is insulin resistance, insulin activity is reduced, leading to impaired calcium transport into cells. As a result, type 2 diabetic patients may experience lower calcium levels. Additionally, chronic kidney disease (CKD), a prevalent complication associated with type 2 diabetes further contributes to decreased calcium levels. Chronic kidney disease affects the kidney's ability to regulate calcium levels by impacting filtration, reabsorption, and excretion of calcium. Consequently, kidney dysfunction in individuals with type 2 diabetes can disrupt calcium homeostasis and lead to lower calcium levels. These findings are comparable with a study done by Eshetu *et al.,* (2023) where it was shown that mean serum calcium level for type 2 diabetes mellitus individuals reduced when compared to that of the controls and showed a significant negative correlation between serum calcium levels and glycated hemoglobin.

This study showed a negative correlation, r=-0.06897, between magnesium level and HbA1c concentration although the association was not statistically significant ($P \geq 0.05$) (refer to Table 4.5). Therefore, suggesting that changes in magnesium levels may not strongly influence HbA1c levels. The statistically non-significant correlation ($P \geq 0.05$) between magnesium level and HbA1c concentration observed in this study may be because most of our participants are stable patients who visit the outpatient clinic hence limited cases of renal failure. This study is in contrast with some studies which found a significant negative correlation between glycated hemoglobin and magnesium level. Wang *et al.,* (2013) observed a decrease in serum magnesium levels and a significant negative correlation with HbA1c (Std β=-0.34 $P < 0.01$) in Chinese subjects with diabetes. The study further explained that in insulin-resistant states, the impaired insulin function may disrupt magnesium transport into cells, leading to lower magnesium levels in the bloodstream. It therefore, concluded that diabetic patients who experienced macrovascular complications had significantly lower serum magnesium levels compared to those without macrovascular complications.

The serum level of phosphorus was found to have a negative correlation of -0.04016 with HbA1c levels but the alteration was not statistically significant (P>0.05), refer to table 4.5. This implies that alterations in phosphorus levels are unlikely to have a significant effect on HbA1c levels. A study by Fang.,2016 similarly found no significant correlation between the level of blood glucose and phosphorus in type 2 diabetic group, however, he observed that the blood glucose and serum levels of phosphorus were positively correlated (r= 0.226, P=0.042) and concluded that there was noticeable decrease in serum phosphorus levels, suggesting a potential disturbance in phosphorus metabolism. The treatment of diabetic patients often involves medications and interventions targeting blood glucose management. These treatments can have an impact on phosphorus metabolism, as certain antidiabetic medications or adjunct therapies can directly or indirectly affect phosphorus levels. The complexity of treatment approaches and medication regimens introduces additional variability, which may mask the correlation between serum phosphorus and HbA1c levels as observed in our study.

5.1.4 Demographic and socio-economic factors that contribute to poor adherence to antidiabetics among diabetic patients attending Samburu County Referral Hospital

Lack of money to buy drugs was the prevalent factor associated with poor adherence to antidiabetics in this study with 69% of the respondents (Table 4.6) indicating that they were unable to afford the cost of their diabetes medications and some individuals may skip doses or reduce their prescribed dosage to make their medication last longer, leading to poor glycemic control. Lack of money to buy drugs has been shown to be a contributing factor to non-adherence across various studies. In a study conducted by Aminde *et al.*,(2019) in Western Region Hospital of Cameroon, lack of finances was reported by

17.4% of study participants as the main reason for non-adherence to antidiabetics and implied that the cost of medication and their affordability pose significant challenges in managing T2DM, particularly in low-income settings like ours. Krass. *et al.,* (2015) also showed that depression and medication cost were the leading factors associated with poor adherence to antidiabetics and both factors were potential predictors for type 2 diabetes adherence to medications behavior. Similarly, (Rwegerera., 2014) reported failure to afford medication as the most prevalent reason for failure to adhere to medication and demonstrated that individuals with T2DM who received financial assistance through the Medicare Part D encountered reduced out-of-pocket and showed improved adherence to medication compared to those who did not receive financial assistance. This underscores the need for affordable and accessible healthcare services, including subsidized medication costs or financial assistance for patients with limited resources.

Diabetes medication interfering with meal plan and side effects of the medication were reported by 51% and 41.7% of the participants respectively as a reason for poor adherence (Table 4.6). A variety of side effects were reported in our study and hypoglycemia was the most common one. Some patients taking metformin which is an oral antidiabetic drug complained of experiencing diarrhea and vomiting and this side effect discouraged them from taking the drug. Similarly, Kassahun *et al.,* (2016) showed that side effect was significantly associated with nonadherence (P=0.024) however, the most common reported side effects were related to the gastrointestinal system, followed by symptoms of hypoglycemia, weight gain and headaches. In contrast to our study, only 11.6% of patients reported drug side effects as their reason for non-adherence according to a report by Rwegerera ., (2014). This finding emphasizes the importance of patient education and counselling about potential side effects and their management as well as providing guidance regarding medication administration in relation to meals.

Forgetfulness was reported as a significant factor, with 40.3% of the respondents (refer to Table 4.6) indicating that the participants sometimes or often forget to take their diabetes medications. Some individuals admitted to forgetting to take their diabetes drug when they are feeling okay and only remember to take it when they are unwell. Numerous studies have consistently identified forgetfulness as a common factor contributing to non-adherence to medication. In a study conducted by Aminde *et al.,* (2019), close to a third (30.2%) of study participants highlighted forgetfulness to be the main reason for poor adherence and suggested that the finding may be attributed to the lack of sufficient health education provided to patients or lack of family support. This finding is comparable to results by Domez *et al.,* (2020) which reported forgetfulness as one of the most prevalent self-reported causes for poor adherence. This highlights the need for interventions to improve medication adherence, such as reminder systems, pill organizers, or involving family members in medication reminders.

Complexity of the drug regimen was reported by 38% of the participants as a contributing factor. (Table 4.6). Unsurprisingly, adhering to and persisting with medication become increasingly difficult when the treatment is perceived as arduous or demanding. This finding is in agreement with results by Jackson *et al.,* (2015) which showed a correlation between adherence and complexity of regimen (P=0.001). Similarly, Kassahun *et al.,* (2016) found that individuals on multiple and complex drug regimens were non-adherent compared to patients on single medication. However, a study by Murwanashyaka *et al.*, (2022) contradicts this finding. Surprisingly, their study found that patients receiving both OHA and insulin medications had a lower likelihood of non-adherence compared to patients on a single OHA medication. The odds ratio (OR) for non-adherence among patients receiving both OHA and insulin was 0.59, indicating a reduced likelihood of non-adherence. Additionally, patients receiving insulin only also had a lower likelihood of non-adherence with an OR of 0.26 compared to patients on a single OHA. Diabetes management often involves multiple medications, dosing schedules, and dietary adjustments. The complexity can lead to confusion and difficulties in adhering to the prescribed regimen. Simplifying the drug regimen and providing clear instructions can help patients better comprehend and follow their treatment plan.

Approximately 25% of the participants perceived their diabetes medications as not being effective enough (Table 4.6). This perception may lead to frustration or a lack of motivation to continue taking the prescribed medications since patients tend to adhere more to their medication schedules when they genuinely believe that the prescribed drugs are delivering favorable and relatively swift outcomes. Polonsky *et al.*, (2016) conducted a study involving 477 individuals with T2DM who initiated treatment with a new class of antidiabetics. Self-reported medication adherence over a 6-month period was found to be connected with significant weight loss (≥3kg: 29.9% adherent vs. 24.2% non-adherent) and an increased likelihood of achieving the HbA1c target (<7.0%:47.5% adherent vs. 32.7% non-adherent). This suggests patients' recognition of improvement and partial attribution it to their medications play a role in fostering their commitment to adherence.

It is therefore, important for healthcare providers to regularly assess treatment effectiveness, address patient concerns and adjust the treatment plan when necessary.

Lack of support from family accounted for 14% of the responses (Table 4.6). This suggests that some patients may not receive the necessary encouragement, understanding, or assistance from their family members in managing their diabetes and adhering to their medication regimen. These findings align with several prior studies. Murwanashyaka *et al.,* (2022) further demonstrated that people with T2DM who feel like they are imposing burdens on their family members are more prone to showing non-compliance with their diabetes medications, compared to patients where their loved ones are involved as well as caring about managing the condition and its effects on their lives. Additionally, a high proportion of such individuals may experience decline in their life quality and face social stigma. Family support therefore plays a crucial role in promoting adherence by providing reminders, helping with medication administration, and creating a conducive environment for maintaining a healthy lifestyle.

Surprisingly, 11% of the respondents mentioned that dosage of their diabetes medication was excessively high (Table 4.6), raising questions about their understanding of the prescribed dosage. Some patients reported mild to moderate symptoms of hypoglycemia whenever they take the medication. This in turn discourages them from adhering to medication as they choose to keep their blood glucose at a higher level as the hypoglycemic events will be less likely. Similarly, cross-sectional research conducted by Polonsky *et al.,* (2016) involving patients with T2DM receiving treatment involving both metformin and a sulfonylurea medication, the study revealed that individuals who experienced more severe hypoglycemia symptoms demonstrated lower adherence to medications when compared to those who reported less severe hypoglycemia symptoms (MPR>80%: 46% vs 67%, P<0.01). Healthcare providers should therefore ensure that patients receive proper education on dosing instructions and regularly evaluate and adjust the dosage based on individual needs.

Lastly, there were other miscellaneous factors mentioned by a small number of respondents, including difficulties in travelling long distances to access medications and the use of alternative treatments such as herbs (e.g., aloevera), (Table 4.6). When patients have to travel long distances to reach the clinic, it can potentially impact their motivation to obtain medication refills from the healthcare institutions. These factors have been highlighted in previous studies assessing factors affecting nonadherence to anti-diabetic medication. Kassahun *et al.,* (2016) revealed that patients residing in remote areas, particularly those with limited transportation options and inadequate infrastructure, displayed lower adherence rates compared to participants living closer to healthcare facilities. These factors highlight the unique difficulties experienced by certain patients when trying to access healthcare services and their potential reliance on alternative or traditional remedies.

5.2 Conclusion

1. A high proportion of individuals 40 (58%) with poor adherence to antidiabetics had elevated HbA1c levels, indicating poor glycemic control among the study participants.
2. There are statistically negative significant correlations ($P \leq 0.05$) observed between glycated hemoglobin levels with sodium ($r=-0.31369$) and calcium ($r=-0.2398$) levels in diabetic patients with poor glycemic control. There was statistically insignificant correlation observed between phosphorus, potassium, chloride and magnesium.
3. A key challenge to adherence to medication among diabetic patients in the study population is cost of the prescribed antidiabetic medications.

5.3 Recommendations

1. Targeted interventions and educational programs should be developed to enhance adherence to medication in individuals with diabetes exhibiting elevated HbA1c levels. These interventions could include provision of reminders for medication intake and patient education on the importance of adherence.
2. There should be incorporation of routine monitoring of serum electrolytes into the management of diabetic patients to help identify and address any imbalances promptly.
3. The challenge of unaffordability of antidiabetic medications ought to be addressed by exploring options for financial support, subsidization of medication costs and insurance options for diabetic patients.

5.4 Suggestions for future studies

1. Further research should be conducted to investigate the specific mechanisms through which high HbA1c levels may lead to impairment of serum electrolytes.
2. To address the issue of unaffordability of medications, it is imperative to conduct additional research aimed at identifying suitable financial support solutions for these patients.

REFERENCES

Aminde, L. N., Tindong, M., Ngwasiri, C. A., Aminde, J. A., Njim, T., Fondong, A. A., & Takah, N. F. (2019). Adherence to antidiabetic medication and factors associated with non-adherence among patients with type-2 diabetes mellitus in two regional hospitals in Cameroon. *BMC endocrine disorders*, *19*(1), 1-9.

Araki, S. I., Haneda, M., Koya, D., Kondo, K., Tanaka, S., Arima, H., …& Maegawa, H. (2015). Urinary potassium excretion and renal and cardiovascular complications in patients with type 2 diabetes and normal renal function. *Clinical Journal of the American Society of Nephrology: CJASN, 10*(12), 2152.

Barbagallo, M., M., & Dominguez, L. J. (2015). Magnesium and type 2 diabetes. *World Journal of diabetes,* 6(10), 1152.

Barrett, H. L., Dekker Nitert, M., Mclntyre, H. D., & Callaway, L. K. (2014). Normalizing metabolism in diabetic pregnancy: is it time to target lipids? *Diabetes care, 37*(5), 1484-1493.

Bohara, J., Kunwar, S., Poudel, G.A., Joshi, S.R., & Gurung, S. (2021). Serum Electrolytes Disturbances in Type 2 Diabetic Patients.*Int J Health Sci Res, 11*(7), 105-110.

Chatterjee, R., Colangelo, L. A., Yeh, H. C., Anderson, C. A., Daviglus, M. L., Liu, K., & Brancati, F. L. (2012). Potassium intake and risk of incident type 2 diabetes mellitus: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Diabetologia, 55,* 1295-1303.

Cuensca-Garcia M., Jago, R, Shield, J. P. H., & Burren, C. P. (2012). How does physical activity and fitness influence glycaemic control in young people with type 1 diabetes? *Diabetic Medicine, 29*(10),e369-e376.

Datchinamoorthi, S., Vanaja, R., & Rajagopalan, B. (2016). Evaluation of serum electrolytes in type II diabetes mellitus. *Int J Pharm Sci Rev Res, 40*(1), 251-253.

Demoz, G. T., Wahdey, S., Bahrey, D., Kahsay, H., Woldu, G., Niriayo, Y. L., & Collier, A. (2020). Predictors of poor adherence to antidiabetic therapy in patients with type 2 diabetes: a cross-sectional study insight from Ethiopia. *Diabetology & Metabolic syndrome*, *12*, 1-8.

Dhatariya, K. K., Glaser, N. S., Codner, E., & Umpierezz, G. E. (2020). Diabetic ketoacidosis. *Nature Reviews Disease Primers*, 6(1), 40.

Eshetu, B., Worede, A., Fentie, A., Chane, E., Fetene, G., Wondifraw, H.,…& Fasil, A. (2023). 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*,127-1220.

Faisal, K., Mekuriya, T., & Tusiimire, J. (2021). Factors Associated With Non-Adherence To Antidiabetic Medication Among Patients at Mbarara Regional Referral Hospital, Mbarara, Uganda. *Patient Prefer Adherence*, 16:479-491

Fang, L., & Li, X. (2016). Level of serum phosphorus and adult type 2 diabetes mellitus. *Zhong nan da xue xue bao. Yi xue ban= Journal of Central South University. Medical Sciences*, *41*(5), 502-506.

Feng, J., Wang, H., Jing, Z., Wang, Y., Cheng, Y., Wang, W., & Sun, W. (2020). Role of magnesium in type 2 diabetes mellitus. *Biological trace element research, 196*, 74-85.

Freeman, A. M. , & Pennings, N. (2022). Insulin resistance. In *StartPearls [Internet]*. StartPearls Publishing, 2022.

Fu, Z., R Gilbert, E., & Liu, D. (2013). Regulation of insulin synthesis and secretion and pancreatic Beta-cell dysfunction in diabetes. *Current diabetes reviews*, 9(1), 25-53.

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B.,..& Martin, C. (2020). Pathophysiology of type 2 diabetes mellitus. *International journal of molecular sciences*, 21(17), 6275.

Gilon, P., Chae, H. Y., Rutter, G. A., & Ravier, M. A. (2014). Calcium signaling in pancreatic β-cells in health and in Type 2 diabetes. *Cell calcium, 56*(5), 340-361.

Grontved, A., Pan, A., Mekary, R. A., Stampfer, M., Willett, W. C., Manson, J. E., & Hu, F. B. (2014). Muscle-strengthening and conditioning activities and risk of type 2 diabetes: a prospective study in two cohorts of US women. *PLoS medicine, 11*(1), e1001587.

Hailu, F. B., Moen, A., & Hjortdahl, P. (2019). Diabetes self-management education (DSME)-Effect on knowledge, self-care behavior, and self-efficacy among type 2 diabetes patients in Ethiopia: A controlled clinical trial. *Diabetes, metabolic syndrome and obesity: targets and therapy*, 2489-2499.

Hameed, I., Masoodi, S, R., Mir, S. A., Nabi, M., Ghazanfar, K., & Ganai, B.A. (2015). Type 2 diabetes mellitus: from a metabolic disorder to an inflammatory condition. *World Journal of diabetes*, 6(4), 598.

InterAct Consortium Robert. scott@ mrc-epid. Cam.ac.uk. (2013). The link between family history and risk of type 2 diabetes is not explained by anthropometric, lifestyle or genetic risk factors: the EPIC-InterAct study. *Diabetologia, 56*, 60-69.

Jackson, I. L., Adibe, M. O., Okonta, M. J., & Ukwe, C. V. (2015). Medication adherence in type 2 diabetes patients in Nigeria. *Diabetes technology & therapeutics, 17*(6), 398-404.

Jiskani, S.A., Khawaja, S.I., & Talpur, R.A. (2022). Disturbances in Serum Electrolytes in Type 2 Diabetes Mellitus. *National Journal of Health Sciences, 7*(1), 4-7.

Joseph, J. J. & Golden, S.H (2014). Type 2 diabetes and cardiovascular disease: what next? *Current opinion in endocrinology, diabetes, and obesity* 21(2), 109.

Kassahun, A., Gashe, F., Mulisa, E., & Rike, W.A. (2016). Nonadherence and factors affecting adherence of diabetic patients to anti-diabetic medication in Assela General Hospital, Oromia Region, Ethiopia. *Journal of pharmacy and bio allied sciences*, 8(2), 124.

Katsarou, A., Gudbjornsdottir, S., Rawshani, A., Dabelea, D., Bonifacio, E., Anderson, B. J.,…& Lernmark, A. (2017). Type 1 diabetes mellitus. *Nature reviews Disease primers*, 3(1), 1-17.

Khan, M. A. B., Hashim, M. J., King, J. K.,Govender, R. D., Mustafa, H., & Al Kaabi, J.(2020). Epidemiology of type 2 diabetes-global burden of disease and forecasted trends. *Journal of epidemiology and global health,* 10(1), 107.

Khan, R. N., Saba, F., Kausar, S. F., & Sidiqqui, M. H. (2019). Pattern of electrolyte imbalance in Type 2 diabetes patients: Experience from a tertiary care hospital. *Pakistan Journal of Medical Sciences, 35*(3), 797.

Kibirige , D., Akabwai, G. P., Kampiire, L., Kiggundu, D. S., & Lumu, W. (2017). Frequency and predictors of suboptimal glycemic control in an African diabetic population. *International journal of general medicine,* 33-38.

Krass, I., Schieback, P., & Dhippayom, T. (2015). Adherence to diabetes medication: a systematic review. *Diabetic Medicine, 32*(6), 725-737.

Kumar, P., Bhargava, S., Agarwal, P. K., Garg, A., & Khosla, A. (2019). Association of serum magnesium with type 2 diabetes mellitus and diabetic retinopathy. *Journal of family medicine and primary care, 8*(5), 1671.

Lee, W. Y., Ahn, J., Kim, J. H., Hong, Y. P., Hong, S. K., Kim, Y. T.,...& Morisky, D. E.(2013). Reliability and validity of a self-reported measure of medication adherence in patients with type 2 diabetes mellitus in Korea. *Journal of International Medical research 41, no. 4(2013):*1098-1110.

Liamis, G., Liberopoulos, E., Barkas, F., & Elisaf, M. (2014). Diabetes mellitus and electrolyte disorders. *World Journal of Clinical Cases: WJCC 2,* no. 10 (2014): 488.

Lorenzo, C., Hanley, A. J., Rewers, M. J., & Haffner, S. M. (2014). Calcium and phosphate concentrations and future development of type 2 diabetes: the Insulin Resistance Atherosclerosis Study. *Diabetologia, 57,* 1336-1374.

Mclntyre, H. D., Catalano, P., Zhang, C., Desoye, G., Mathiesen, E. R., & Damm, P. (2019). Gestational diabetes mellitus. *Nature reviews Disease primers*, *5*(1), 1-19.

Michael Dansinger (2020). Medically reviewed online journal on Type 2 diabetes mellitus. https://webmd.com>diabetes.

Mkuu, Rahma S., Gilreath, T. D., Wekullo, C., Reyes, G. A., & Harvey, I. S. (2019). Social determinants of hypertension and type 2 diabetes in Kenya: a latent class analysis of a nationally representative sample. *PloS one*, *14*(8), e0221257.

Moon, M. K., Hur, K. Y., Ko, S. H., Park, S. O., Lee, B. W., Kim, J. H., ... & Kim, N. H. (2017). Combination therapy of oral hypoglycemic agents in patients with type 2 diabetes mellitus. *Diabetes & metabolism journal*, *41*(5), 357-366.

Murwanashyaka, J. D. D., Ndagijimana, A., Biracyaza, E., Sunday, F. X., Umugwaneza, M. (2022). Non-adherence to medication and associated factors among type 2 diabetes patients at Clinique Medicale Fraternite, Rwanda: a cross-sectional study. *BMC Endocrine Disorders, 22*(1), 1-14.

Nakrani, M. N., Wineland , R. H., & Anjum, F. (2020). Physiology, glucose metabolism. *StartPearls Publishing*

Noale, M., Veronese, N., Cavallo Perin, P., Pilotto, A., Tiengo, A., Crepaldi, G., & Maggi, S. (2016). Polypharmacy in elderly patients with type 2 diabetes receiving oral antidiabetic treatment. *Acta diabetologica*, *53*, 323-330.

Ogunleye, A., & Asalou, M. (2016). Evaluation of macro minerals in patients with type II diabetes mellitus in southern Nigeria. *International Journal of Biochemistry Research & Review, 9*(2), 1-9.

Paschou, S. A., Papadopoulou-Marketou, N., Chrousos, G. P., & Kanaka-Gantenbein, C. (2018). On type 1 diabetes mellitus pathogenesis. *Endocrine connections*, *7*(1), R38.

Polonsky, W. H., & Henry, R. R. (2016). Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. *Patient preference and adherence*, 1299-1307.

Qadeer, H. A., & Bashir, K. (2020). Physiology, phosphate. *StatPearls Publishing*

Rorsman, P., Ramracheya, R., Rorsman, N. J., & Zhang, Q. (2014). ATP-regulated potassium channels and voltage-gated calcium channels in pancreatic alpha and beta cells: similar functions but reciprocal effects on secretion. *Diabetologia, 57*, 1749-1761.

Rwegerera, G. M. (2014). Adherence to anti-diabetic drugs among patients with Type 2 diabetes mellitus at Muhimbili National Hospital, Dar es Salaam, Tanzania-A cross-sectional study. *The Pan African Medical Journal*, *17.*

Sacks, D. B. (2013). Hemoglobin A1c in diabetes: panacea or pointless?. *Diabetes, 62*(1), 41-43.

Santhosh, V., Gomathi, D. M., Khadeja-Bi, A., Suganya, S., & Gurulakshmi, G. (2021). Study of Serum Electrolytes in Type 2 Diabetes Mellitus Individuals in Rural Tertiary Care Hospital in Kancheepuram District. *Biomedical and Pharmacology Journal, 14*(2), 691-694.

Shrimanker, I., & Bhattarai, S. (2019). Electrolytes. *StatPearls Publishing*

Standl, E., Khunti, K., Hansen, T. B., & Schnell, O. (2019). The global epidemics of diabetes in the 21st century: Current situation and perspectives. *European journal of preventive cardiology, 26*(2-suppl), 7-14.

Sterns, R. H. (2015). Disorders of plasma sodium-causes, consequences, and correction. *New England Journal of Medicine*, *372*(1), 55-65.

Szeto, V., Chen, N. H., Sun, H. S., & Feng, Z. P. (2018). The role of KATP channels in cerebral ischemic stroke and diabetes. *Acta Pharmacologica Sinica*, *39*(5), 683-694.

Timerga, A., Kelta, E., Kenenisa, C., Zawdie, B., Habte, A., & Haile, K. (2020). Serum electrolytes disorder and its associated factors among adults admitted with metabolic syndrome in Jimma Medical Center, South West Ethiopia: Facility based cross-sectional study. *PloS one*, *15(*11), e0241486.

Unachukwu, M. N., Engwa, G.A., Nwalo,F.N., Attama,T.J.C., Abonyi, C.,Akaniro-Ejim, E. N., …& Ubi,B.E (2018). Influence of type 2 diabetes on serum electrolytes and renal function indices in patients. *Journal of clinical and Diagnostic Research, 12*(6).

Wang, S., Hou, X., Liu, Y., Lu, H., Wei, L., Bao, Y., & Jia, W. (2013). Serum electrolyte levels in relation to macrovascular complications in Chinese patients with diabetes mellitus. *Cardiovascular diabetology, 12*(1), 1-10.

Wang, Y., & Lim, H. (2012). The global childhood obesity epidemic and the association between socio-economic status and childhood obesity. *International review of psychiatry, 24(3),* 176-188.

Wibowo, M. I. N. A., Yasin, N. M., Kristina, S. A., & Prabandari, Y. S. (2022). Exploring of determinants factors of anti-diabetic medication adherence in several regions of Asia- A systematic review. *Patient preference and adherence,* 197-215.

Wongdee, K., Krishnamra, N., & Charoenphandhu, N. (2017). Derangement of calcium metabolism in diabetes mellitus: negative outcome from the synergy between impaired bone turnover and intestinal calcium absorption. *The journal of Physiological sciences*, *67(1), 71-81.*

Word Health Organization. (2018). Global report on diabetes. 2016. *World Health Organization*

Xie, Z., Liu, K., Or, C., Chen, J., Yan, M., & Wang, H. (2020). An examination of the socio-demographic correlates of patient adherence to self-management behaviors and the mediating roles of health attitudes and self-efficacy among patients with coexisting type 2 diabetes and hypertension. *BMC Public Health, 20*(1), 1-13.

Yeemard , F., Scrichan, P., Apidechkul, T., Luerueang, N., Tamorpark, R., & Utsaha, S. (2022). Prevalence and predictors of suboptimal glycemic control among patients with type 2 diabetes mellitus in northern Thailand: A hospital-based cross-sectional study. *Plos one, 17*(1), e0262714.

APPENDICES

Appendix I: Questionnaire 1

Patient Name :

Age :

Gender :

Morisky Medication Adherence Scale (MMAS-8) (Lee *et al*, 2013)

Your participation is voluntary and information collected will be handled with utmost confidentiality.

Instructions

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)

1. Do you sometimes forget to take your medications? Yes ( ) No ( )
2. 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? Yes ( ) No ( )
3. Have you ever cut back or stopped taking your medications Without telling your doctor, because you felt worse when you took it? Yes ( ) No ( )
4. When you travel or leave home, do you sometimes forget to bring along your medications? Yes ( ) No ( )
5. Did you take your medications yesterday? Yes ( ) No ( )
6. When you feel like your health condition is under control, do you sometimes stop taking your medications? Yes ( ) No ( )
7. Taking medications every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan? Yes ( ) No ( )
8. How often do you have difficulty remembering to take all your medications? Yes ( ) No ( )

Appendix II: Questionnaire 2

Factors associated with poor adherence to antidiabetic medications

Instructions

1. Fill or tick appropriately
2. Answer all questions provided
3. Do not write your name

Section A

Biodata

Unique identifier:

1. How old are you?
    a) 18-29
    b) 30-49
    c) 50-64
    d) 65 and above
2. What is your marital status?
    a) Single
    b) Married
3. Sex?
    a) Female
    b) Male
4. What is your education level?
    a) No education
    b) Primary level

c) Secondary level

d) Tertiary

5. Residence

a) Urban

b) Rural

Section B: Factors associated with poor adherence to antidiabetic medications

Instructions

Please circle (Yes/No) for each of the items below no. 1-8. For additional reasons for not taking medications as prescribed by the doctor, please indicate in no. 9

1. I lack support from family Yes ( ) No ( )
2. I forget to take my diabetes drugs Yes ( ) No ( )
3. Side effects of the medications Yes ( ) No ( )
4. The drug regimen is complex Yes ( ) No ( )
5. I feel the diabetes medication is not effective enough Yes ( ) No ( )
6. I feel the dose is too high Yes ( ) No ( )
7. Diabetes medications interfere with my meal plan Yes ( ) No ( )
8. I lack money to buy drugs Yes ( ) No ( )
9. Any other reasons for not taking diabetes medications as advised by the doctor

   Please list below

Appendix III: Informed consent

My Name is Francis Lengeiya, and I am a MASTER'S student at Kenyatta University. I am currently conducting a research study titled 'The relationship between electrolytes and glycated hemoglobin among diabetic patients with poor adherence to antidiabetics, attending Samburu County Referral Hospital." The data collected in this study will be utilized by the Ministry of Medical Services, Public Health and Sanitation to enhance the accessibility and quality of Type 2 Diabetes mellitus management and treatment at the hospital and in other regions of Kenya.

The research procedures involve asking you some questions and conducting examinations to assess your glycated hemoglobin levels and serum electrolyte levels. We will also collect specimens from you for these tests, and your responses will be recorded in a questionnaire.

Please be aware that your participation in this study is entirely voluntary, and you have the right to decline. Your decision will not impact the medical care and treatment you receive today or at any other clinic in the future. Feel free to ask any questions related to the study at any time.

You have the right to decline answering any questions or terminate the interview at any point without facing any consequences in your current or future interactions with this clinic or any other organizations.

Potential discomforts and risks

Certain questions during the interview may cause discomfort. If this occurs, you have the option to refuse to answer those questions or to conclude the interview. Please note that the interview may extend your waiting time for routine services by approximately half an hour

Benefits

Your participation in this study will contribute to our understanding of effective diabetes management and the reduction of electrolyte disorders. Additionally, you will benefit from the glycated hemoglobin examination, and if any issues are detected, you will receive guidance on treatment.

Confidentiality

All interviews and examinations will be conducted in a private setting within the clinic. Your name will not be recorded on the questionnaire, which will be securely stored at Kenyatta University. Your information will be kept confidential.

Contact information

If you have any questions, you may contact Dr. Scholastica Mathenge on 0722936884 or Dr. Patroba Ojola on 0722939090, or the Kenyatta University Ethical Review Committee Secretariat at chairman.kuerc@ku.ac.ke,

Participant's statement

I fully understand the information provided regarding my participation in this study. I have had the opportunity to ask questions, and my queries have been satisfactorily addressed. My involvement in this study is entirely voluntary, and I comprehend that my decision will not affect the quality of care I receive today or in the future from any clinic.

Participant’s code: ………………

Signature or thumb print: …………….

Date: ……………….

Investigator`s statement

I, the undersigned, have explained the study procedures, associated risks, and benefits to the participant in a language they understand.

Name of interviewer: ………………………………………..

Interviewer signature: …………………..

Date: ……………………………

Appendix IV: NACOSTI permit letter

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **909792**

Date of Issue: **05/December/2022**

RESEARCH LICENSE

This is to Certify that Mr.. Francis Lengasu Lengeiya of Kenyatta University, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act, 2013 (Rev.2014) in Samburu on the topic: RELATIONSHIP BETWEEN IMPAIRED ELECTROLYTES, GLYCATED HEMOGLOBIN AND POOR ADHERENCE TO ANTIDIABETICS AMONG PATIENTS ATTENDING SAMBURU COUNTY REFERRAL HOSPITAL, KENYA for the period ending : 05/December/2023.

License No: NACOSTI/P/22/22125

909792

Applicant Identification Number

Director General

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

See overleaf for conditions

Appendix V: KU ERC Approval letter

KENYATTA UNIVERSITY
CENTRE FOR RESEARCH ETHICS AND SAFETY

Fax: 8711242/8711575
Email: chairman.kuerc@ku.ac.ke
Nairobi, 00100

P. O. Box 43844,

Tel: 8710901/12

Website: www.ku.ac.ke

Our Ref: **KU/ERC/APPROVAL/VOL.1**

Date: 10th /11/2022

Francis Langasu Lengeiya
P.O Box 43844, 00100
Nairobi.

Dear Mr. Lengeiya,

APPLICATION NUMBER: PKU/2619/I1740 - RELATIONSHIP BETWEEN IMPAIRED ELECTROLYTES, GLYCATED HEMOGLOBIN AND POOR ADHERENCE TO ANTIDIABETICS AMONG PATIENTS ATTENDING SAMBURU COUNTY REFERRAL HOSPITAL, KENYA.

This is to inform you that ***KENYATTA UNIVERSITY ETHICS REVIEW COMMITTEE*** has reviewed and approved your above research proposal. Your application approval number is **PKU/2619/I1740.** The approval period is **10th /11/*2022 to 10th /11/2023***

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***KENYATTA UNIVERSITY ETHICS REVIEW COMMITTEE***
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***KENYATTA UNIVERSITY ETHICS REVIEW COMMITTEE*** within 72 hours of notification
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***KENYATTA UNIVERSITY ETHICS REVIEW COMMITTEE*** within 72 hours
v. Clearance for export of biological specimens must be obtained from relevant institutions.

vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.

vii. Submission of an executive summary report within 90 days upon completion of the study to ***KENYATTA UNIVERSITY ETHICS REVIEW COMMITTEE***

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

To serve you better, researchers are kindly requested to access and complete a customer feedback form and sent it back online as you continue with research and upon completion of data collection found on the following website link; ;(https://docs.google.com/forms/d/1ytWefDwvyz5h1oz_VIn0xbxg3uGdlDzMXFWNDsMrRPQ/edit?usp=sharing

Yours sincerely

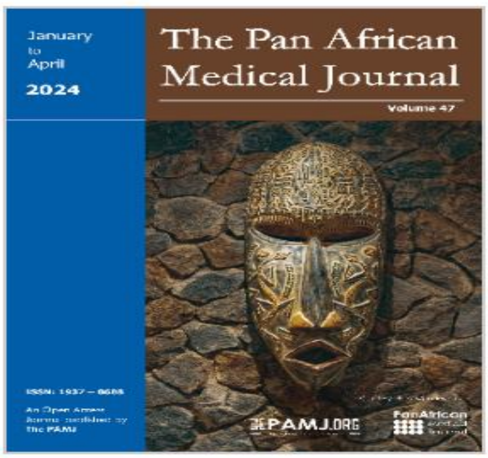
KENYATTA UNIVERSITY OFFICE OF THE CHAIRMAN
10 NOV 2022
ETHICS REVIEW COMMITTEE
P.O. BOX 43844 - 00100 NAIROBI

Prof. Judith Kimiywe

Director: Centre for Research Ethics and Safety

Appendix VI: Publication

Production - M... Jan 30
to me, MATHENGE.S...



Dear authors,

We are glad to inform you that your manuscript is now published in its final version in the Pan African Medical Journal; note however that it may take few days for the manuscript to appear on the journal main page. Your article is accessible online at:

Research
Relationship between electrolytes and glycated hemoglobin among diabetic patients with poor adherence to antidiabetic medications: a cross-sectional study
Francis Lengeiya, Scholastica Mathenge, Patroba Ojola
Pan African Medical Journal. 2024;47:37. Published on 30 Jan 2024
[PDF in process]

Correction of errors

Take time to carefully review your article. If you notice errors (typographical, grammatical, omissions, wrong character, author names etc..) in your publication, ensure that they are corrected within the next 5 days, before your manuscript is sent for long term preservation to several long term preservation bodies.