PREVALENCE OF COGNITIVE IMPAIRMENT IN AMBULATORY PATIENTS WITH TYPE 2 DIABETES ATTENDING DIABETIC CLINIC AT KENYATTA NATIONAL HOSPITAL

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DECLARATION

This thesis is my original work and has not been submitted for any academic award or published in any other university or any other institution of higher learning for the award of a degree.

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LIST OF ACRONYMS

AB	Amyloid Beta
AGEs	Advanced Glycosylated End products
ANA	Antinuclear antibodies
CI	Cognitive Impairment
CSF	Cerebrospinal Fluid
DM	Diabetes Mellitus
DPP4	Dipeptidyl peptidase-4 inhibitor
FDA	Food and Drug Administration
GI	Gastro-Intestinal
GLP-1	Glucagon-Like Peptide 1
GSK-3B	Glycogen synthase 3beta
HIV	Human Immune Deficiency Virus
HBA1c	Glycosylated Hemoglobin
IDE	Insulin-Degrading Enzyme
KNH	Kenyatta National Hospital
MCI	Mild Cognitive Impairment
MMSE	Mini-Mental State Examination
MOCA	Montreal Cognitive Assessment
NPH	Neutral Protamine Hagedorn
PHQ9	Patient Health Questioner 9
RUDAS	Rowland Universal Dementia Assessment scale
SLE	Systemic Lupus Erythematosus
T2D	Type 2 Diabetes
TSH	Thyroid Stimulating Hormone
UoN	University of Nairobi
UTI	Urinary Tract Infection
Vit-B12	Vitamin B12
WHO	World Health Organization

DEFINITION OF TERMS

Diabetes Mellitus	A metabolic disorder associated with abnormal levels of high sugar glucose in the blood as a result of inadequate insulin production or inadequate sensitivity of cells to insulin action.
Cognitive impairment	It is a condition in which an individual has difficulties remembering, learning new things, concentrating, or making decisions that affect their daily activities, and it ranges from mild to severe forms.
Type 2 Diabetes	Previously known as adult-onset diabetes and is characterized by high blood sugar, insulin resistance, and relative lack of insulin action.
Mini-mental State Examination	Is a brief examination comprising of eleven questions intended to evaluate an adult patient's level of cognitive functioning.
Dementia	A chronic or persistent mental disorder caused by brain disease or injury characterized by memory disorders, personality changes, and reasoning impairment.

ABSTRACT

Background: Type 2 diabetes (T2D) cases have increased significantly in the recent past with more than 422 million diagnoses in 2016. With rise in the number of cases, there is expected increase in diabetic complications. Researchers have provided a greater emphasis on the existing relationship between T2D and cognitive impairment globally. However, there is no information on the prevalence of cognitive impairment among T2D patients in Kenya.

Objective: To determine the prevalence of Cognitive impairment in ambulatory patients with T2D attending the diabetic clinic at Kenyatta national hospital (KNH).

Methods: The study used a cross-sectional research design. Consecutive sampling technique was used to select participants based on the outlined inclusion criteria. Data collection was done using a survey questionnaire which included study proforma and Mini-Mental State Examination (MMSE). A Sample of 369 participants attending the diabetic clinic at Kenyatta National Hospital were recruited at a 5% margin of error of which 367 successfully filled in the study proforma showing a 99.5% response rate. MMSE was done to determine cognitive dysfunction among T2D. Chi-square test for association and multiple regression analyses were conducted at 0.05 level of significance.

Results: A total of 367 respondents were analyzed. Majority of the respondents, 60.8% were female, 48.2% had secondary school education, 75.7% were married and the mean age was 57.7 (SD=11.3) years. The mean duration since diagnosis of T2D was 10.8 (SD = 8.4) years. Results also showed that 70% of the respondents had hypertension. The mean HBA_1c was 8.45 (SD = 2.6) %. The prevalence of cognitive impairment was 32%: mild cognitive impairment in 27% and 5% had moderate cognitive impairment. The results showed that age, ($p < 0.001$), level of education ($p < 0.001$) and duration of diabetes ($p = 0.034$) were significantly associated with cognitive dysfunction. Age ($p<0.001$), level of education ($P<0.001$) and HBA1c ($p=0.025$) were statistically significant predictors of cognitive impairment in T2D patients.

Conclusion: The prevalence of cognitive impairment among T2D patients is increasing with age and off target HBA1c levels (poor glycemic control). There is an inverse relationship between low formal educational level and cognitive impairment among T2D patients. Optimizing adequate glycemic control and improving formal education up to tertiary level are essential in limiting cognitive dysfunction among T2D patients. Older adults are at increased risk hence should be prioritized in screening of cognitive dysfunction.

1. CHAPTER ONE: INTRODUCTION

1.1. Background

Cognitive impairment (C.I) has been a key outcome among patients with type 2 diabetes (T2D) globally. However despite the increasing prevalence of cognitive impairment among T2D, the prevalence in outpatient clinics has not been effectively defined (1). Cognitive function forms an important part of individual wellbeing considering that it helps define individual processes. There are several cardio metabolic risk factors responsible for cognitive impairment which includes- diabetes mellitus, hypercholesterolemia, hypertension, metabolic syndrome, smoking, etc. T2D is a disorder that is linked with extremely high sugar levels in the blood which are produced because of inadequate production of insulin.

T2D has been increasing in recent times resulting in a global prevalence of 422 million. The rate of T2D is expected to rise up to 552 million globally by 2030 (2). Cognitive dysfunction among T2D patients has also been increasing. Mild cognitive impairment has been the most prevalent among T2D patients and studies have shown that T2D patients are more likely to develop dementia or Alzheimer disease (3).

Diabetes mellitus (DM) is one of the common non-communicable diseases in the 21st century. In Kenya, the prevalence of diabetes is 3.3% although the figure is based on national projections which are likely to be an underestimation. Approximately 60% of these incidences were identified when a patient attended a healthcare facility with a completely different health issue. Around 75% of the diabetic population does not know they have the disease (4).

The burden of diabetes in Kenya has been increasing significantly with current rates indicating that 1 in 17 has diabetes (5). According to the World health organization (WHO), approximately 1% of deaths in Kenya were attributed to diabetes in 2012 (6). In 2014, approximately 12,890 patients died from diabetes and related complications (7).

Management of diabetes is a complex process which is based on a strong evaluation of important elements which define individual development and the presence of cognitive dysfunction limits the ability to manage diabetic patients. Cognitive impairment includes diverse aspects such as memory, learning, mental flexibility, executive functions, as well as attention (2) (9). Cognitive dysfunction occurs across different levels which vary from mild to severe and depending on the level of progression, patients are influenced differently. Mild cognitive dysfunction has limited influence on patient wellbeing. Diabetic patients are at increased risk of cognitive impairment especially executive functions which involve individual behavior such as problem-solving, judgment, changing habits as well as starting new habits (10).

Ng et al. conducted a study in Singapore, which sought to determine whether prolonged metformin usage has an influence on cognitive function among older adults with diabetes. The findings highlighted that metformin use showed a statistically significant inverse association with cognitive impairment (11). The findings in the study showed that increase in the use of diabetes treatment decreases the risk of cognitive impairment among patients. In another study that was conducted by Seetharaman et al., it highlighted that there had been a sharp increase in T2D and dementia in the United States (12). It was also determined that T2D shares common genes as well as underlying pathology with Alzheimer and Vascular dementia. Thus the cognitive decline in older adults is significantly associated with T2D (13).

Cognitive impairment is an increasing challenge among patients with T2D. The prevalence is much higher in older adults considering the reduced cognitive abilities. Studies have shown relationship between T2D and cognitive impairment (14). Reduced cognitive function has been considered as a major marker in brain aging as well as development of dementia. The major functions that are commonly influenced include episodic memory and

executive functionality. Executive functions have a major influence on individual performance (15).

Understanding the relationship between T2D and Alzheimer disease provide a strong influence of this condition on individual cognitive performance (16). The increased prevalence of Alzheimer in patients with T2D is mainly due to the cognitive function which is reduced based on the different processes. Approximately 56% of patients with T2D develop Alzheimer and dementia diseases (17). The increased risk of cognitive dysfunction among T2D patients is independent of other factors.

Eze et al. conducted a study that aimed at determining the prevalence of cognitive impairment among T2D patients in Nigeria by using Mini-Mental State Examination (MMSE) a validated questionnaire. The Scale was grouped where scores between 25- 30 were considered as normal while ≤ 24 were associated with mild, moderate or severe cognitive impairment. The study revealed a cognitive dysfunction prevalence of 40% among T2D patients. The study further showed that there an increase in association between diabetes and cognitive impairment (18).

Cognitive impairment and Diabetes Mellitus (DM) are disorders that occur commonly among older citizens. Thus, older adults are at a high risk of developing cognitive impairment (19). Brain infarcts, white matter disease, hyperinsulinemia and Lipoprotein linked proteins have been shown to have a detrimental influence on cognitive impairment (20). Diabetes has also been associated with poor glycemic control and development of chronic episodes of hyperglycemia which create an increased risk of brain microangiopathy and cognitive impairment (21).

1.2. Problem statement

Self-care forms a large proportion of diabetes care, which is essentially an important aspect of normal cognitive function. Quality of diabetic control locally is sub-optimal for multiple

reasons and cognitive impairment is a possible contributor. However, the burden of cognitive impairment is not known locally.

2. CHAPTER TWO: LITERATURE REVIEW

2.1. Prevalence of cognitive impairment in patients with type 2 diabetes

In a cross-sectional study conducted in Tianjin, China aimed at investigating the prevalence of mild cognitive impairment among T2D patients using Mini-Mental State Examination (MMSE), the prevalence of mild cognitive impairment was 13.5%. The prevalence of mild cognitive impairment was higher among diabetic patients compared to the general population (22). The prevalence of T2D in 1980 was 108 million globally. In 2016, the number had increased substantially to 422 million which shows that from 1980 to 2016, there has been a significant increase which can be attributed to increased risk factors. There are an estimated 4.6 million new cases of cognitive impairment among T2D patients annually. However, the cognitive decline is expected to increase significantly based on the current trends with an estimated 42 million cases of cognitive impairment among T2D patients by 2020 and 81 million in 2040 (6). In a study conducted in Nigeria investigating the prevalence of cognitive impairment among T2D patients attending a clinic in South East Nigeria using MMSE, it was determined that 40% had cognitive impairment (18).

In a study done in Romania, the prevalence of mild cognitive impairment was 42.03% based on MMSE scale. The average age of the participants was 63 years. (23). A Japanese study which sought to assess cognitive function among elderly persons by utilizing the MMSE determined that the prevalence of cognitive dysfunction among T2D patients was 15.5% (24).

In a cross sectional study that was conducted in Saudi Arabia using RUDAS scale in assessing cognitive impairment in T2D patients, it was found that 16% of the patients had cognitive impairment compared to 3% cognitive impairment among individuals without T2D (10).

Older adults have higher prevalence of abnormal glucose which provides crucial information on the development of T2D. Approximately 30% of the elderly population has diabetes, while

75% of the elderly population has pre-diabetes or are diabetic. However, the study also highlights that there is a greater proportion of adults with T2D that has not been diagnosed. Around 45.6% of the older adults 65 years and above remain undiagnosed with diabetes (25).

There has been a higher prevalence of diabetes among older adults which is around two times compared to the middle or young adults. Diabetes incidence continues to increase which has a greater influence on the need to understand the distribution based on the age of individuals. The major increase in incidence of diabetes among individuals aged between 65 and 79 years was 6 per 1,000 and has steadily increased to 11.6 per 1,000 in the year 2000 and 12.4 per 1,000 in 2010 (11). The increasing incidence shows that there is also increased chance of occurrence of different complications that are associated with diabetes such as cognitive impairment which limits individual wellbeing since it negatively influences their physical and mental wellbeing (19).

2.2. Associated risk factors of cognitive impairment

2.2.1. Patient-related factors

Cognitive impairment among patients with T2D provides a strong greater significance on the need to understand the underlying factors which are contributing to the increase in prevalence. In a cohort study conducted in the Netherlands to determine whether T2D is associated with greater decline in cognitive dysfunction among middle-aged adults. Cognitive functioning was measured twice within 5 years in 2613 individuals across both genders aged between 43 and 70 years. The results showed that there was a decline in global cognitive function among diabetic patients with 2.6 times greater than individuals without diabetes. However, the extent to which T2D contributes to the decline in cognitive function, as well as the underlying risks factors, has not been effectively studied. The global prevalence of cognitive impairment among patients with T2D has been increasing which provide a strong consideration where there is

need to control these changes through the development of effective management based on a better understanding on the current situation.

Thus, Alzheimer dementia is the most common as well as a chronic neurodegenerative disorder among senior citizens. Approximately 2% of people start to develop dementia before they reach 65 years. Thus based on the Alzheimer, global reports indicated that 44 million people around the world had dementia in 2014 with the figures expected to double by 2030 and triple by the year 2050. In 2014, it was estimated that 5.2 million American citizens had Alzheimer disease. This population of Alzheimer patients includes around 200,000 individuals who are below 65 years. Majority of Alzheimer disease patients are female with approximately 3.2 million patients. Different factors have been associated with an increasing prevalence of Alzheimer disease even in individual below 65 years including genetics, environmental factors, head trauma, depression, diabetes mellitus, vascular factors as well as hyperlipidemia (10).

2.2.2. Duration of diabetes

Studies have found out that there is a significant relationship between duration of diabetes and the development of cognitive impairment among T2D patients. In a study conducted in 2015 that sought to determine the pattern of cognitive impairment concerning the duration of diabetes, revealed that patients with T2D exceeding five years had decreased cognitive function. This study also showed that coexistence of hypertension with T2D increased the risk of cognitive impairment, and the tool used was MMSE (1).

A study conducted in United States revealed that there was a strong relationship between duration of diabetes and the occurrence of CI based on the MMSE score. It was further explained that a duration of T2D of more than 10 years was associated with higher incidence of cognitive dysfunction (26). In another study, it was identified that mild cognitive dysfunction

began slightly before the age of 65 while a period of higher than 10 years with T2D was associated with higher prevalence of mild cognitive dysfunction (27).

2.2.3. Glycemic Control

Different studies have shown that hyperglycemia and T2D have a detrimental influence on cognitive performance. In a cross sectional study conducted by Jana et al. (2017) that focused on relationship between hyperglycemia and cognition, it was determined that the frequency of mild cognitive impairment increased by 1.7fold in subjects with hyperglycemia. The study further highlighted that the HBA1c was negatively correlated with global cognitive performance(28). Thus increase in HBA1c levels increases the development of cognitive impairment.

Whitmer et al. (2009) also sought to understand the association between HBA1c level and risk of developing cognitive impairment in older women without consideration of their diabetes status. The study utilized a prospective longitudinal study design. This study found that for every 1% increase of HBA1c there was a 1.5 chance of developing mild cognitive impairment. The study further determined that when women with diagnosed diabetes were excluded, there was a reduced chance of mild cognitive impairment although the results remained significant(29).

Cognitive functionality is influenced by different factors that need to be assessed and help determine improved outcomes. HBA1c levels are associated with change in cognitive functionality. Sherwani et al. (2016) conducted a prospective cohort study that aimed at examining the association between diabetes and hyperglycemia-assessed by HBA1c as well as change in cognitive function in individuals with and those without diabetes. The findings in the study showed an average HBA1c of 5.7% while it was higher in persons with diabetes at

8.5% compared to 5.5% in persons without diabetes. Logistic model identified that there was no significant link between cognitive decline and depression among diabetes patients(30).

2.2.4. Smoking

Nooyenset al. conducted a prospective study among 2,613 middle aged men and women with a focus on assessing T2D and cognitive decline in a five-year period. The findings showed that the global decline of cognitive function in diabetic patients was 2.6 times higher that individuals without diabetes (31). The results also revealed that there was a significant association between smoking and cognitive impairment among T2D patients. Those who were smokers had 3.2 times decline in cognitive function compared to those who did not smoke. According to Zhang, smoking was also a major risk factor in cognitive impairment among type diabetes patients (32). Cigarette smoking,T2D, and obesity have shown to have a significant influence on cognitive dysfunction (34). However, in another study conducted to determine the prevalence of mild cognitive impairment in type 2 diabetes patients, the results showed that there was no relationship between cognitive impairment and smoking (33).

2.2.5. Hypertension

Majority of patients with diabetes have presenting hypertension. The prevalence of hypertension among diabetes patients is influenced by different factors such as older age, male gender, higher body mass index and the duration of diabetes (35).

According to Stumvollet.al, the existence of both hypertension and T2D is lethal which could lead to the development of other cardiovascular conditions such as stroke as well as kidney diseases and retinopathy (30). Van Gemert also found that impaired cognitive function was associated with increased risk of cardiovascular diseases such as dyslipidemia and hypertension (35). It is also estimated that approximately 50% of T2D patients have hypertension (36). The

study further states that there are several factors that are associated with the presence of both T2D and hypertension (37).

Sun et al, conducted a bidirectional study that aimed at assessing the relationship between hypertension and diabetes(38). The findings from the study showed that T2D might influence hypertension although hypertension to T2D is unlikely. Therefore, in assessing the relationship between hypertension and cognitive impairment among T2D patients, there is an understanding on the existing mechanisms which interact and present a well-organized emphasis on diabetes and hypertension. Nooyens et al, states that there is major association between cognitive decline and hypertension among T2D patients (39).

Cognitive impairment among T2D patients in Africa has not been effectively determined which provide the study with a strong basis under which results can provide a better background for further investigations pertaining T2D and cognitive ability. Determining the prevalence of cognitive impairment is crucial in understanding the influence of the current interventions and management strategies which need to focus on improving the wellbeing of patients through controlled development of cognitive disability(40). An increase in cognitive decline increases the chances of a patient developing other major mental conditions such as vascular dementia and Alzheimer disease. This means that determining the cognitive decline early allows the integration of important changes which improve positive health outcomes.

2.3. Hypoglycemia and cognitive impairment in T2D patients

Studies have showed that presence of cognitive deficit in patients with T2D involve different factors which include duration, severity as well as the frequency of hypoglycemic episodes (29)(41). Older age has been correlated with increased cognitive decline. The findings further show that there was a strong relationship between brain damage and cognitive decline. Brain damage in this context is caused by hypoglycemia (42).

The fundamental aspect to consider when treating diabetes is to maintain the glycemic levels within the standard range which is close to those non-diabetic patients. Lack of a more intense control of glycaemia allows the development of a series of key chronic complications. The identified complications include nephropathy, retinopathy, cerebrovascular accident and peripheral vascular disease. Glycemia is the common causes of insulin therapy management(41).

Hypoglycemia is an adverse reaction as a result of the insulin therapy. During hypoglycemia, there is a heightened release of adrenaline from the adrenal glands which leads to autonomic symptoms which include facial flush, tremors and other symptoms. Patients on insulin therapy have had a severe hypoglycemia case (29).

The term cognition refers to how an individual acquires processes and manages information. Thus, there is need to effectively assess the cognitive alterations in which one or more previously explained mental processes tend to be transformed (43). The intellectual adjustments that are likely to happen during hypoglycemia is due to a higher release of adrenalin, growth hormone as well as higher release of glucagon (44).

2.4. Cognitive dysfunction and self-care

Cognitive impairment has a detrimental influence on individual normal functionality wherein they are unable to perform their tasks effectively. The negative influence on memory and executive functions mean that an individual has challenges in remembering key events in their lives which is injurious to the development of relationships. Individuals with T2D are more likely to develop these complications. The major functional aspects that are evaluated include daily activities and house chores and persona wellbeing. The common activities at home include bathing, dressing and ambulating indoors. Diabetic patients report an increased difficulty in successfully completing these tasks (45). Thus, cognitive impairment is likely to

increase the level of dependency. Patients with diabetes are 1.7 times likely to develop functional impairment. In a study done in Taiwan, it was revealed that 32.5% of diabetic patients had functional impairment of some form(46). The prevalence of C.I was higher across all domains compared to patients older than 65 years without diabetes(47).

2.5. Types of cognitive impairment in Diabetes Mellitus

2.5.1. Alzheimer disease

Alzheimer health condition is highly influenced by the status of patients with diabetes mellitus. Alzheimer is a severe health condition which is common in old age. The influence of the disease varies from one individual to another in creating a greater focus on the existing issues within healthcare. The manifestation of this condition is gradual, and it may appear as normal during the early times since it is usually more comparable to normal forgetfulness that individuals tend to have but as it develops it continues to have a detrimental impact to an individual(48).

Alzheimer is a cognitive dysfunction which is also known as brain fog. It is the loss of cognitive reasoning abilities which make it very difficult for an individual to carry out his or her day to day activities since they can barely make a correct decision concerning the context being considered. Patients having cognitive dysfunction have enormous significant challenges in verbal recall, basic arithmetic, and concentration. Microbes leading to meningitis, encephalitis may cause cognitive dysfunction. The complications in the brain thus have considerable impact, thus influencing some of essential muscle and nerves, which bring about this effect in patients who are having motor dysfunction. Therefore in this case, an individual cannot communicate with the required speed since there are significant differences in the way that they interact with others (49).

2.5.2. Vascular Dementia

Vascular dementia occurs when part of the brain does not get enough blood that is transporting oxygen and nutrients that are critical to brain development. The difficulty in detecting this condition makes it difficult to develop a counter strategy where an individual can be protected from the adverse effects of this condition. The inability of the brain to get enough supply of oxygenated blood increases the risk of developing minor strokes. Vascular dementia therefore occurs over time when silent strokes pile up. Limiting the development of vascular dementia is based on the ability to maintain and control the levels of diabetes, high blood pressure, high level of cholesterol, and smoking. Thus, it is essential to understand that development of dementia does not occur independently (50).

This condition is also known as multi-infarct dementia. It is the second cause of dementia in older people after Alzheimer's. Many people do not have a significant understanding of the development process of vascular dementia since it is generally assumed as being Alzheimer's. This condition is challenging to diagnose and thus it is tough to determine the number of people who are suffering from this condition. However, the current estimates show that approximately 15% of the dementia cases that occur in older adults are vascular dementia (15).

2.6. Pathophysiologic Mechanism

Various postulates have linked cognitive impairment with T2D. These include insulin signaling, vascular etiology, increased advanced Glycosylated end products, Inflammation, and oxidative stress as well as genetics.

2.6.1. Insulin signaling

Neurodegeneration in T2D has been linked to dysregulation of insulin. Insulin has a tendency of binding itself to a specific receptor at the blood-brain barrier where it is transported to the

central nervous system. A significant increase in serum insulin amount is associated with a higher intracellular insulin levels and the cerebrospinal fluid. Previous research's that have been done show that there is significant association between chronic hyperinsulinemia and down regulation of insulin receptor which results in a decrease in insulin levels. This causes acceleration of neural ageing processes as well as neurodegeneration. Hyperinsulinemia causes an increase in Amyloid beta levels and the inflammatory agents which alter the amyloid metabolism in the brain (51). Although it is perceived that insulin is neurotrophic to the brain and thus performs its tasks through binding to insulin receptors on the cell surface, a more fascinating aspect in this context is that insulin receptors that are present in the brain occur mainly on the surface of the cells which are located in anatomical regions and are responsible for memory formation (52). The insulin receptor activates secondary messengers after the binding process with Akt and phosphatidylinositol-3-kinase(52).

However, different studies have showed that under normal conditions, insulin inhibits tau fibril production and tau phosphorylation(52)(53)(54). Lower levels of CSF insulin are linked with higher neurofibrillary tangles that are pathological markers of severe dementia. In addition, amyloid beta protein is disintegrated by different enzymes such as insulin-degrading enzyme (IDE) and neprilysin(55). Thus, both amyloid beta and insulin rival to bind themselves on the IDE. Insulin has a higher affinity which has a higher chance of binding to IDE compared to amyloid beta enzymes. In conclusion, it is presumed that serum hyperinsulinemia is related with lower insulin levels and increased levels of amyloid protein in the brain which lead to more neurofibrillary tangles. The development of these receptors are likely to be associated with impaired cognitive state (56).

2.6.2. Vascular Etiology

The development of atherosclerosis and small vessel disease is positively associated with type 2 diabetes which results in an increased risk of multi-infarct dementia as well as mixed type

dementia. Previous studies have identified that type 2 diabetes patients tend to have increased risk of hypertension, diabetic retinopathy, macrovascular complications and microvascular complications. These conditions increase the risk of dementia development (57).

2.6.3. Glycosylated end products, inflammation, and oxidative stress

Chronic hyperglycemia has been associated with AGEs which are responsible for mediating different complications of diabetes through influencing the level of interaction with receptors for glycosylated end product present in vascular cells. This enhances different inflammatory processes as well as oxidative stress. Thus, a higher AGE results in amyloid development as well as tau phosphorylation in Alzheimer disease(58).

2.6.4. Genetics

Diabetic type 2 patients have been associated with brain changes and cognitive scores. These patients have also been pronounced to have Apo E epsilon 4 alleles which contribute to higher dementia in patients (59).

2.7. Confounders of cognitive impairment

There are different confounders that have been associated with cognitive impairment among T2D patients. These confounders include depression, B12 deficiency, thyroid disorders, autoimmune disease and HIV. Studies have identified that there is an association between depression and a high risk of cognitive decline among older adults (60)(61).

In assessing thyroid disorders, changes in hippocampal volume, increase in thyroid hormone levels also causes cognitive impairment leading to poor concentration, slower reaction time, decrease in spatial organization, and visual processing skills (62).

Autoimmune diseases have been associated with cognitive impairment and the most significant of which is systemic lupus erythematosus (SLE). Others include multiple sclerosis and psoriasis. About 20% of SLE patients have dementia, which is as a result of neuro inflammation

and autoimmune encephalitis (59). A study conducted by Zaheer Bagha at the University of Nairobi (Kenya) in 2011 in determining the prevalence of cognitive impairment in HIV patients at the out patients clinic revealed 26% of patients had cognitive dysfunction of which 75% of them were on HAART, and 50% of them have been on HAART >2years (63).

2.8. Cognitive impairment Assessment tools

The ability to determine whether an individual has cognitive impairment is based on the underlying assessment of individual wellbeing based on different tools. The significant tools that provide a unique understanding of cognitive assessment include MMSE, RUDAS, and M0CA.

2.8.1. Mini-mental State Exam (MMSE)

The MMSE is a structured test that is self-used by doctors and other healthcare professionals to evaluate memory and cognitive functions. The MMSE was introduced in 1975 by Marshall Folstein(64). It includes a set of 30 questions which an individual must answer to the best of their abilities without straining or reference. The maximum score is 30. A score range of 25-30 is considered normal, 20-24 is mild cognitive impairment, 10-19 is moderate cognitive impairment and less than 10 indicates severe cognitive impairment. Scores might be interpreted differently based on consideration of other factors such as age, education and ethnicity (65).

Advantages

- It is easy to perform
- There are no specific or additional equipment required to perform the test.
- Can help in monitoring deterioration over time

Disadvantages

- Unsuitable for individual with low education

- Cannot be used for visually impaired populations
- Poor sensitivity at detecting mild/early dementia
- It is copyrighted and restricted for editing

2.8.2. Rowland Universal Dementia Assessment Scale (RUDAS)

RUDAS focuses on limiting the influence of other factors such as culture and language diversity. It accommodates different languages with a key emphasis on attaining better results. It contains a maximum score of 30 where score below 22 indicates cognitive impairment (66).

Advantages

- It is short and integrates other forms of cognitive domains which include memory, language, attention and visual abilities making it diverse.
- The test can be administered in a short period.
- It is new and multicultural

Disadvantages

- Has limited evidence of reliability
- Cannot be administered independently.

2.8.3. The Montreal Cognitive Assessment (MoCA)

The MOCA test has been significantly used in recent years, which has provided a greater emphasis on important aspects which help understand memory as well as individual cognitive functionality. The test is commonly used in evaluating Alzheimer disease, although it can also be employed to provide focus on diverse cognitive impairment (67).

Advantages

- ❖ It is simple to perform.
- ❖ It tests executive functions accurately.
- ❖ It is available in different languages approximately 35 languages (68).

Disadvantages

- ❖ The integration of this technique integrates important aspects in determining individual mental status as well their ability to perceive information (69).
- ❖ Takes a little longer than MMSE and cannot be administered alone

2.8.4. The most appropriate assessment tool in the study

The study focused on the MMSE to assess the Cognitive dysfunction among patients. The MMSE is a simple test to apply with a crucial focus on a different level of cognitive dysfunction based on the responses of different participants and it's administered by trained health care personnel. The scale is been used globally and was evaluated based on the international standards. A score range of 25-30 is considered normal, 20-24 mild cognitive impairment, 10-19 moderate cognitive impairment and less than 10 severe cognitive impairment. The application of MMSE is easy as long as there is better information on scores and how the respondents was able to perform simple tasks based on the test examination. This method is essential, considering that it is possible to determine the deterioration of individual cognitive wellbeing with time-based on the high level of specificity and accuracy. The questions included in the tests are diverse, which limit the level of bias and improve the level of validity of the findings with a low degree of error. It has been validated& has a sensitivity of 83% & specificity of 98% based on a study conducted on geriatric patients in Slovakia (51). It is composed of 11 major items which contain different points. They include temporal orientation and spatial orientation, attention which contain 5 points each. Immediate memory, delayed

recall ability and verbal comprehension contain 3 points each. Naming has two points, reading sentence , constructional praxis and verbal repetition contain one point each (70).

3. CHAPTER THREE: OBJECTIVES

3.1. Justification of the study

Cognitive impairment has been associated with T2D. Studies have shown through neuropsychological tests that the development of cognitive dysfunction affects individuals across different age groups with diabetes. This study was aimed at evaluating the cognitive status of ambulatory patients with T2D. The study further explored selected risk factors associated with impaired cognitive function. Our findings and recommendations will help in determining vital healthcare interventions that can be integrated in healthcare delivery which can help in making better policies to improve patient's outcome.

3.2. Research Questions

What is the prevalence of cognitive impairment and its associated factors in ambulatory patients with T2D attending the diabetic clinic at KNH?

3.3. Objectives

3.3.1. Broad Objective

To determine the burden of cognitive impairment in ambulatory patients with T2D attending the diabetic clinic at KNH and its associated factors.

3.3.2. Specific Objectives

1. To determine the prevalence of cognitive impairment in ambulatory patients with T2D attending the diabetic clinic at KNH by use of MMSE.

3.3.3. Secondary objectives

To evaluate the association between selected risk factors and cognitive impairment:-

i. Gender

ii. Age of patients

iii. Glycemic control (HBA_{1c})

iv. Duration of diabetes

v. Presence of hypertension

vi. Smoking

4. CHAPTER FOUR: METHODS

4.1. Study setting

The study was carried out at the Kenyatta National Hospital (KNH) diabetic clinic. The facility is both a referral and teaching center housing College of Health Sciences (University of Nairobi). It is located in Upper hill area approximately 3.5KM west from the central business district and off Ngong road. The hospital has a bed capacity of more than 1,800 in patients with about 30 inpatient wards and various outpatient clinics/ specialized units. The diabetic clinic runs from Monday to Friday weekly on an outpatient basis and the study recruited participants from these patients.

4.2. Research design

The study utilized a cross-sectional research design. The respondents were engaged at a single point in time during their appropriate clinic day.

4.3. The study population

The study included ambulatory adult patients aged 30 years and above with T2D attending diabetic clinic at Kenyatta National Hospital.

4.4. Inclusion criteria

- Patients with T2D attending diabetic Clinic at KNH
- Aged 30 years and above
- Able to give informed consent
- Able to read and write

4.5. Exclusion criteria

- Visual impairment
- Profound hearing difficulty
- Inability to understand either English or Kiswahili

4.6. Sample Size Determination

According to a study conducted in Nigeria, the prevalence cognitive impairment in T2D patients was 40% (16).

The sample was calculated based on Cochrane formula:

$n_o = Z^2Pq/e^2$

Where N_o is the sample population

Z^2 is the abscissa of the normal curve (1.96^2)

P is the estimated prevalence (0.40)

q is (1-p) the proportion of an attribute that is absent in the population (0.6)

e is the margin of error included in the study (5%)

$n_o = Z^2Pq/e^2$

$n_o = (1.96^2)\ (0.4*0.6)/0.05^2)$

n_o= 369.

The sample size was 369

4.7. Sampling Method

A consecutive sampling was used to sample the target population based on the inclusion criteria. The principal investigator with the help of the two research assistants consecutively sampled the target population while identifying those who met the inclusion criteria until the sample population was achieved.

4.8. Research instruments

The study included a study proforma, which comprised of- participant demographics and clinical data.

A MMSE was used to determine cognitive dysfunction among patients.

4.9. Recruitment and Consenting of the study participants

The principal investigator, with the help of the two clinical officers as research assistants consecutively went through the files at the diabetic clinic Kenyatta National hospital based on the inclusion criteria every morning (Monday-Friday) until the sample size was attained. The objectives and benefits of the study were explained to patients and only those who consented were recruited.

4.10. Data collection

After receiving approval /consent, the principal investigator and research assistants administered study proforma to the patients to obtain demographic data. The patients were subjected to a MMSE test by the principal investigator and research assistants to determine cognitive impairment.

4.11. Study variables

Dependent variable

- Cognitive impairment (MMSE Scores: Normal: 25 and above; Mild: 20-24; Moderate: 10 – 19; Severe: Less than 10).

Independent variables

- Age (in years)
- Gender (Male, Female)
- Level of education(formal)
- Glycosylated hemoglobin (HBA1c)
- Duration of diabetes (in years)
- Hypertension (Diagnostic label)
- Smoking (Cigarette smoking)

4.12. Glycosylated Hemoglobin

The principal investigator/research assistants collected 3mls of venous blood in EDTA bottles for all patients that met the inclusion criteria. The above investigation was done at the biochemistry laboratory (University of Nairobi) using Siemens DCA vantage analyzer machine. The analysis was done on daily basis based on the samples obtained. It is a measure of how well controlled patient blood sugar has been over a period of three months and essentially gives a good account of how high or low or average of patient blood sugar. The scoring of glycosylated hemoglobin was ≤ 7% for normal target range (Optimal), 7.1 – 8.4% for High (Poor glycemic control) and ≥8.5% for Very high (very poor glycemic control).

4.13. Quality control

HBA1c was done at the Biochemistry laboratory (UoN) using Siemens vantage analyzer machine for all patients that met the inclusion criteria. The vantage analyzer machine is efficient in controlling unauthorized access to patient data with trusted clinically proven results which enhances quality control. Research assistants were trained on how to administer the study proforma.

4.14. Data analysis technique

Descriptive statistics was used to describe the socio-demographic characteristics of the sample population. Among the variables used for this included but not limited to; gender, age, level of education, and marital status. To present the outcome of this analysis, tables and graphs were used which formed part of the report writing. The table generated gave frequencies and percentages to all the demographic items in the questionnaire.

The prevalence of cognitive impairment among T2D

The prevalence of cognitive impairment in ambulatory patients with type 2 diabetes attending the clinic at Kenyatta National Hospital was determined using the formula,

$$\textbf{Prevalence} = \frac{\textbf{\textit{Number of patients with cognitive impairment}}}{\textbf{\textit{number of people included or recruited in the study}}} * \mathbf{100}$$

The association between selected risk factors and cognitive impairment

A chi square test for association was conducted to evaluate the association between presence of selected risk factors and cognitive impairment among ambulatory patients with type 2 diabetes. The selected risk factors that were evaluated in this case included age, gender, duration of diabetes, glycosylated hemoglobin, presence of hypertension; and cigarette smoking.

A multiple regression analysis was also conducted to determine the predictors of cognitive impairment among T2D patients. The multiple regression analysis was performed using enter method where all the independent variables were added into the model in a single step. The data analysis was done using SPSSv26. The level of significance was taken at 95% confidence level, $p<0.05$.

4.15. Ethical issues considerations

The study obtained approval from KNH-UON ERC after authorization from the Department of Clinical Medicine. Authorization from KNH administration was sought to conform to the hospital research guidelines.

The participation in the study was voluntary where every individual from the target population who was willing to participate in the study filled an informed consent form. All information was kept confidential. The patients with mild and moderate cognitive impairments were referred for further neurologic evaluation.

4.16. Feasibility of the study

The study included 369 sample populations of patients with T2D attending diabetic clinic at KNH. The principal investigator with the help of two research assistants recruited patients daily who met the inclusion criteria until the sample size was achieved. Data collection was done from Monday to Friday, which is the time the diabetic clinic is operational and it lasted for eight weeks.

4.17. Flow chart of processes

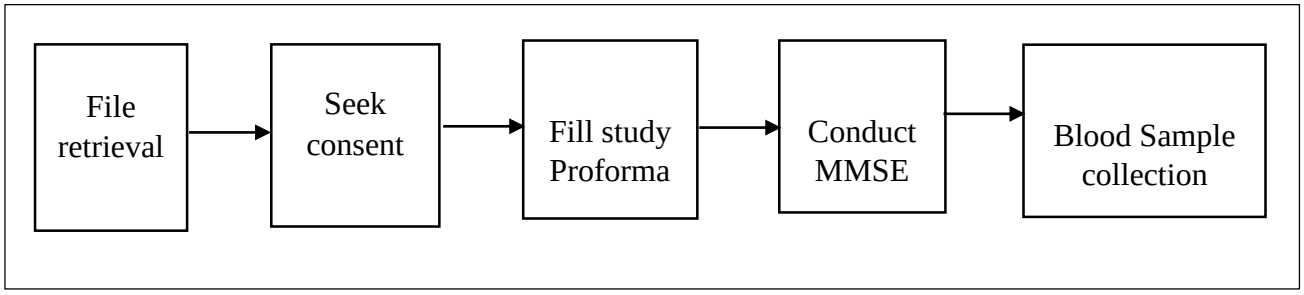

Figure 1: Flow Chart of processes

5. CHAPTER FIVE: RESULTS

5.1. Introduction

Samples of 369 respondents were targeted in the study. A total of 367proformas were successfully and accurately completed representing a 99.5% response rate. Two (0.5%) of the participants did not fully complete the study proforma hence were excluded from the analysis.

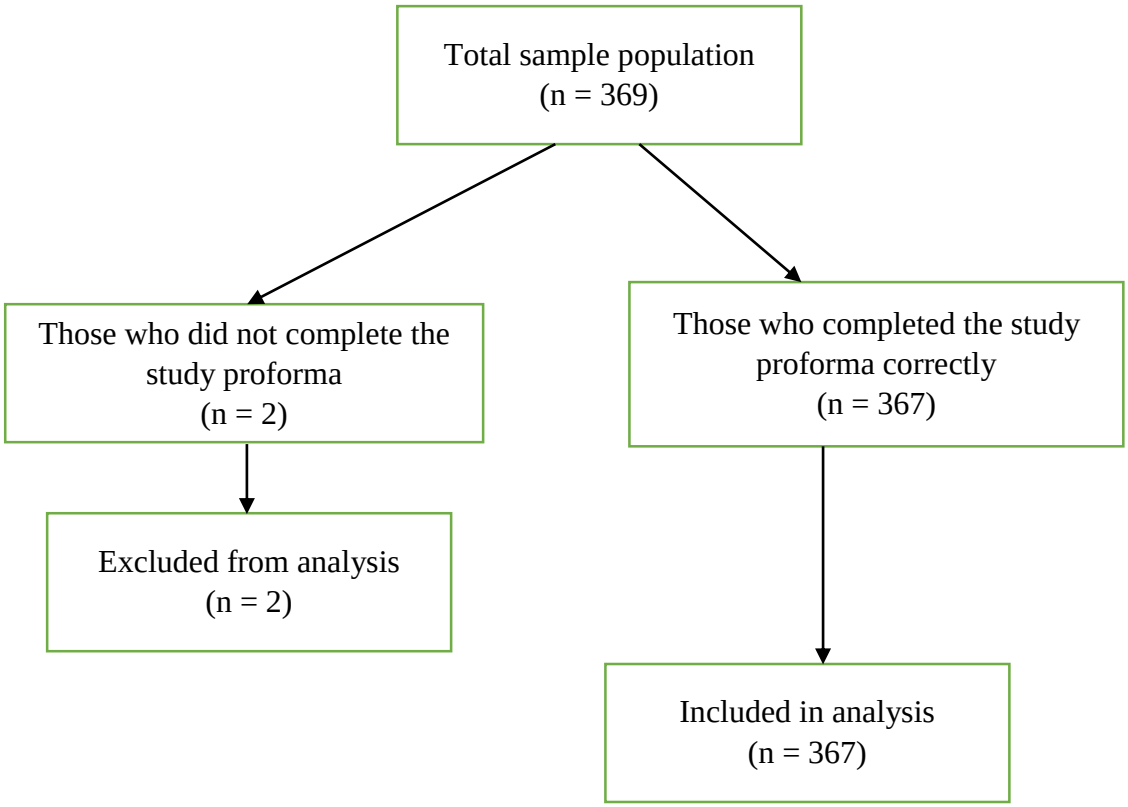

Figure 2: Recruitment of Respondents

5.2. Socio-demographic characteristics

As shown in Table 1, 167 (46.5%) of the respondents, were aged between 50 and 64 years. The mean age for men, M =60.4, SD =10 compared to women, M = 54.5, SD = 11.4. The median age for men was 61 (54 - 69) compared to women 56 (46 – 63.5). Majority of the respondents, 278 (75.7%) were married. More than half of the male respondents, 80 (55.6%) had secondary school education while 90 (40.4%) of female respondents had primary level education.

Table 1: Respondent's socio-demographic characteristics

Socio-demographic characteristics of study participants				
Characteristic		Male (n =144)	Female (n =223)	Total Population(n=367)
Age	<50 years	26 (18%)	68 (30.5%)	94(25.6%)
	50 -64 years	66(45.8%)	103 (46.2%)	167(46.1%)
	>65 years	52(36.2%)	52(23.3%)	104(28.3%)
	Mean (SD)	60.4 (10.9)	54.5(11.4)	57.7(11.3)
.	Median (IQR)	61(54 - 69)	56(46 – 63.5)	58(50 - 66)
Marital status	Married	130(90%)	148 (66.4%)	278 (75.7%)
	Single	7(4.5%)	47(21.1%)	54(14.7%)
	Divorced	7(4.5%)	28(12.5%)	35(9.6%)
Level of formal education	Primary	33(22.9%)	90(40.4%)	123 (33.5%)
	Secondary	80(55.6%)	97(43.5%)	177(48.2%)
	Tertiary	31(21.5%)	36(16.1%)	67(18.3%)

5.3. Clinical characteristics of the study participants

Regarding the duration of type 2 diabetes among the respondents, 222(60.5%) had lived with T2D for less than 10 years since diagnosis. Male respondents had a higher average (SD) duration of diabetes type 2 of 11.6(9.1) years. The median duration was 10 years. Most of the respondents, 257 (70%) had hypertension and 20(5.4%) were cigarette smokers, 164(45%) of the respondents had normal glycemic control, HBA1c (≤ 7%) while 132(36%) of all the respondents had poor glycemic control (≥8.5%). Female respondents had a very high level of

HBA1c with an average of 8.6 (SD=2.6). The median value was 7.8%. More than half of the respondents 68% had normal cognitive function while 32% had cognitive impairment. The average MMSE score in both male and female was 26 (3.7) score as shown in Table 3.

Table 2: Clinical characteristics of study participants

Characteristic		Male (n =144)	Female (n =223)	Total Population(n=367)
Duration of diabetes type 2	<10 years	83(57.6%)	139(62.3%)	222(60.5%)
	11 - 20 years	38(26.4%)	57(25.6%)	95(25.9%)
	>20 years	23(16%)	27(12.1%)	50(13.6%)
	Mean (SD)	11.6 (9.1)	10.3(7.8)	10.8(8.4)
	Median (IQR)	10(5 – 18)	8(4 – 15)	9(4 – 16)
HBA1c	≤7% (Normal)	73 (50.7%)	91(40.8%)	164(44.7%)
	7.1 - 8.4% (Poor)	21(14.6%)	50(22.4%)	71(19.3%)
	≥8.5% (Very Poor)	50(34.7%)	82(36.8%)	132(36%)
	Mean (SD)	8.16(2.6)	8.6(2.6)	8.5(2.6)
	Median (IQR)	7.5(6.2 – 9.6)	7.8(6.9 10.1)	7.8(6.6 – 9.8)
Hypertension	Yes	93(64.6%)	164(73.5%)	257(70%)
	No	51(35.4%)	59(26.5%)	110(30%)
Cigarette Smoking	Yes	15(10.4%)	5(2.2%)	20(5.4%)
	No	129(89.6%)	218(97.8%)	347(94.6%)
MMSE Score	<10	0	0	0
	10–19	6(4.2%)	14(6.3%)	20(5%)
	20 – 24	38(26.4%)	60(26.9%)	98(27%)
	≥25	100(69.4%)	149(66.8%))	249(68%)
	Mean (SD)	26(3.4)	25.6(3.7)	25.75(3.6)
	Median (IQR)	26.6(24 – 29)	26(24 – 28)	26(24 – 28)

5.3.1. Categories of duration of type 2 diabetes

As shown in Figure 3, 222 (60%) of the respondents had T2D for less than 10 years, 95 (26%) of the respondents had T2D between 11-20 years, while 50 (14%) of the respondents have had T2Dfor a period of more than 21 years.

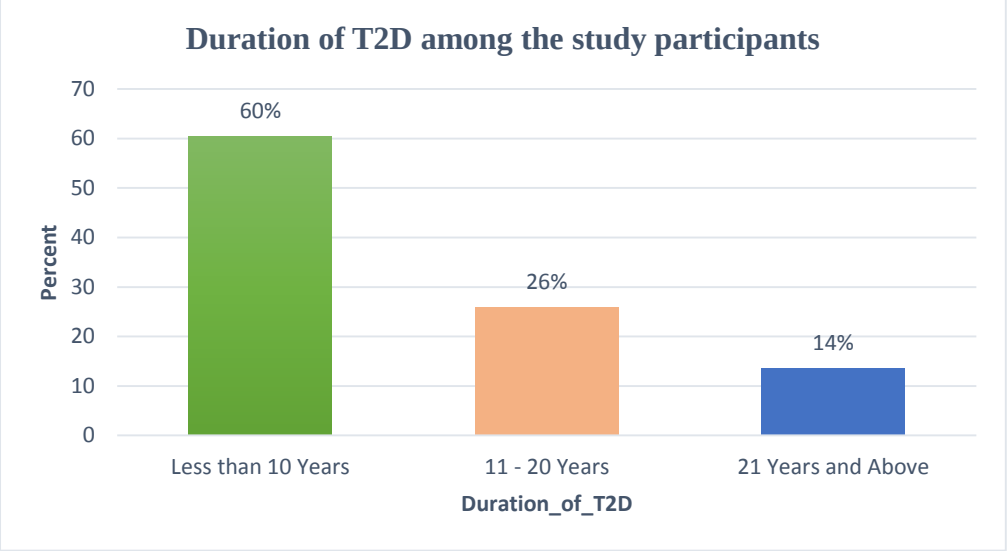

Figure 3: Respondents, duration of T2D

5.3.2. Presence of Hypertension and Cigarette Smoking in respondents

Out of the three hundred and sixty seven respondents, two hundred and fifty seven, 70% of the respondents had hypertension, twenty (5%) had history of cigarette smoking. Ninety (25%) did not have history of hypertension or cigarette smoking as shown in figure 4.

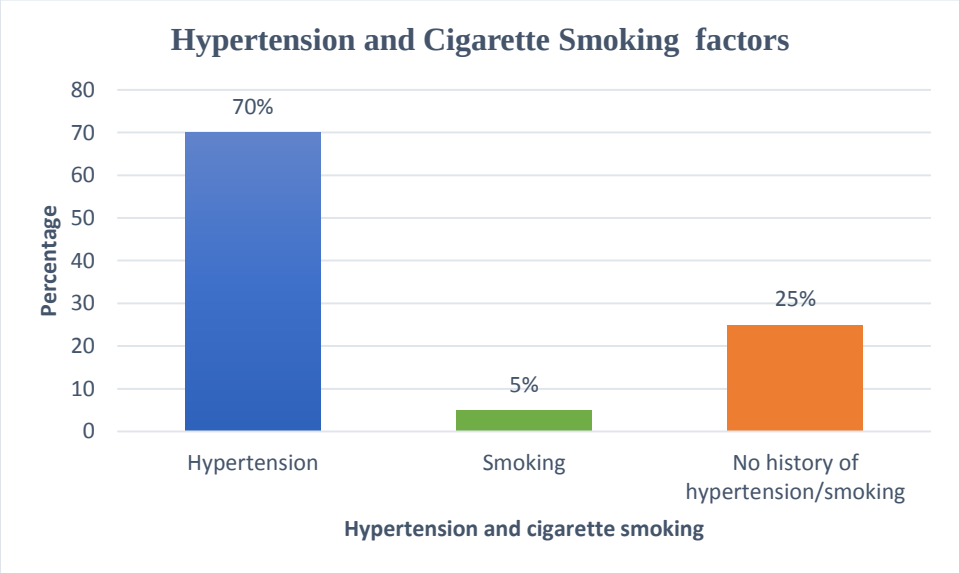

Figure 4: Hypertension and Cigarette Smoking

5.3.3. Categories of HBA$_1$C

The Pie chart (Figure 5) identify that 164 (45%) of the respondents had good/optimal glycemic control levels (≤7%), 71 (19%) of the respondents had moderate glycemic control levels (7.1%-8.4%) while 132 (36%) had poor glycemic control levels (≥8.5%).

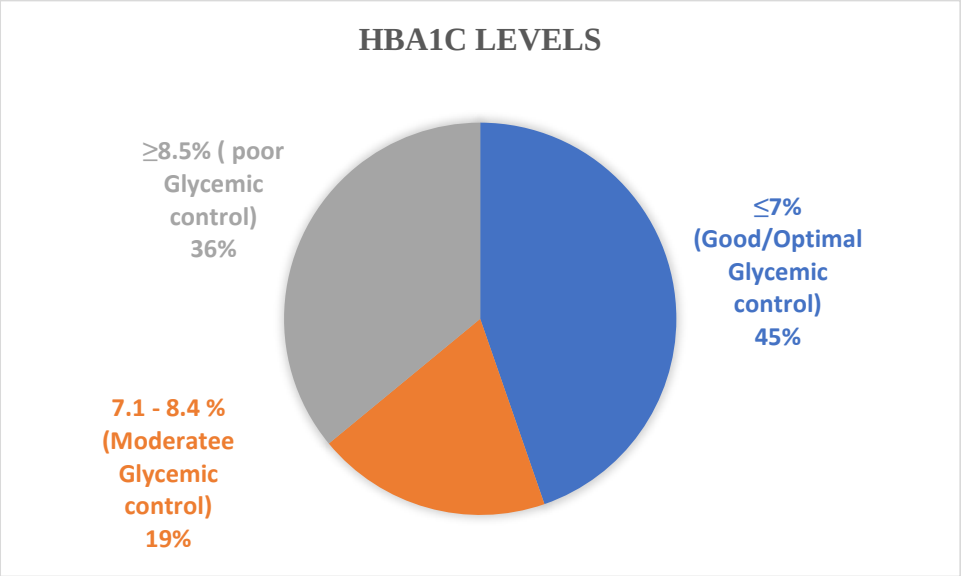

Figure 5: Patterns of HBA1c of the study population

5.4. Prevalence of cognitive impairment by MMSE in study population

Based on the MMSE score, 32% (95% CI 31.1 to 32.9) of the respondents had cognitive impairment. On further analysis and as shown in figure 6, 27% (n=98) had mild cognitive impairment (MMSE score of 20 to 24) and 5%(n=20) had moderate cognitive impairment (MMSE score of 10 to 19). The rest (68%, n=249) had normal cognitive function.

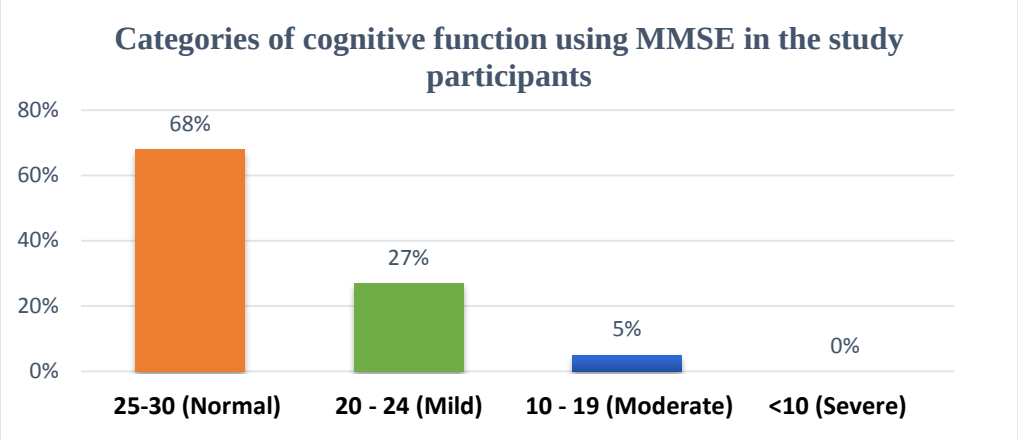

Figure 6: Respondents' MMSE scores

This is alternately presented in tabular form as shown below (Table 3).

Table 3: Prevalence of Cognitive impairment by MMSE in study population

MMSE Scores	Functional interpretation	n(%)
25 - 30	Normal cognitive function	249 (68%)
20 – 24	Mild cognitive dysfunction	98 (27%)
10– 19	Moderate cognitive dysfunction	20 (5%)
<10	Severe cognitive dysfunction	0(0%)

5.5. Correlates of cognitive impairment among type 2 diabetic patients

Correlates of cognitive impairment among diabetes type 2 respondents were investigated and the results showed that advance in age of the respondent ($p< 0.001$), lower level of formal education ($p<0.001$) and longer duration of diabetes in years ($p = 0.034$) were significantly associated with cognitive impairment as shown in Table 4.

Table 4: Association between characteristics of study participants and cognitive impairment

Characteristics	Category	Normal cognitive function	Mild Cognitive impairment	Moderate cognitive impairment	Df	Chi square	p-value
Age group	≤50years	72(28.9%)	20(20.4%)	2(10%)	2	13.98	***P*<0.001**
	51 - 64 years	118(47.8%)	48(49%)	3(15%)			
	≥65 years	59(23.3%)	30(30.6%)	15(75%)			
Gender	Male	100(40.2%)	38(38.8%)	6(30%)	2	0.814	0.67
	Female	149(59.8%)	60(61.2%)	14(70%)			
Level of formal Education	Primary	56(22.5%)	52(53%)	14(70%)	6	44.82	***p*<0.001**
	Secondary	135(54.6%)	36(36.7%)	6(30%)			
	Tertiary	57(22.9%)	10(10.3%)				
Duration of type 2 diabetes	≤10 years	150(60.2%)	64(65.3%)	8(40%)	2	5.837	**0.034**
	11 – 20 years	66(26.5%)	20(20.4%)	9(45%)			
	≥ 21years	33(13.3%)	14(14.3%)	3(15%)			
Quality of glycemic control (HBA1c) %	≤7%	164(65.7%)	42(42.9%)	8(40%)	1	0.056	0.508
	≥ 7.1%	85(34.3%)	56(57.1%)	12(60%)			
Hypertension	None	83(33.3%)	19(19.4%)	3(15%)	1	0.211	0.461
	Hypertension	166(66.7%)	79(80.6%)	17(85%)			
Cigarette Smoking	Smoking	14(5.6%)	5(5.1%)	1(5%)	1	0	0.732
	No smoking	235(94.4%)	93(94.9%)	19(95%)			

5.6. Predictors of cognitive impairment among the type 2 diabetes patients participating in the study

As shown in Table 5, coefficient of determination (r^2) = 0.183 which shows that the independent variables included in the analysis explain 18.3% of the total variance in respondent's cognitive function.

Table 5: Regression Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.428[a]	.183	.172	3.292

a. Predictors: (Constant) age, gender, level of formal education, duration of diabetes, HBA1c, hypertension, cigarette smoking.

An analysis of variance was also conducted to determine the significance of the model. As shown in Table 6, the F (5,361) = 16.178, *p >0.001*. The results show that the model was significant thus, able to predict the dependent variable.

Table 6: Analysis of the Model significance

ANOVA[a]

Model		Sum of Squares	Df	Mean Square	F	Sig.
1	Regression	876.728	5	175.346	16.178	.000[b]
	Residual	3912.705	361	10.839		
	Total	4789.433	366			

a. Dependent Variable: MMSE

b. Predictors: (Constant), age, gender, level of formal education, duration of diabetes, HBA1c, hypertension and cigarette smoking.

The analysis of coefficients in the multiple regression analysis showed that advance in age of the respondents (*P<0.001*), lower level of formal education, (*p<0.001*) and High HBA1c (%) (*p = 0.025*) were the significant predictors of cognitive impairment in patients with T2D as shown in Table 7.

Table 7: Predictors of cognitive impairment among T2D patients enrolled in the study

Coefficients[a]

Model		b	T	P-value	95.0% Confidence Interval for B	
					Lower Bound	Upper Bound
1	(Constant)	27.32	17.739	0	24.291	30.348
	Age	-0.063	-3.549	**0.000**	-0.098	-0.028
	Gender	-0.181	-0.495	0.621	-0.898	0.537
	Level of education	1.813	7.287	**0.000**	1.324	2.303
	Duration of T2D	0.014	0.584	0.56	-0.033	0.06
	HBA1c	-0.133	-1.947	**0.025**	-0.271	0.001
	Hypertension	-0.391	-0.313	0.754	-0.971	0.704
	Smoking	-0.135	-0.943	0.346	-1.206	0.424

a. Dependent Variable: MMSE Scores

6. CHAPTER SIX: DISCUSSION

Cognitive impairment is an important issue among T2D patients. Thus, understanding the prevalence and associated risk factors present a better focus on the increasing cognitive dysfunction among T2D patients. The study enrolled 367 participants, of whom sixty one percent of the respondents were female (n=223) while thirty nine percent (n=144) were male. Female patients were more willing to participate in the study compared to male participants. Most of male patients cited no benefit or action in the previous studies they have participated in hence saw any need to enroll in this study. The results also showed that seventy four percent of the respondents (n=271) were aged 50 years and above with an average age of 57 years (SD =11.3). Almost half of the respondents in the study had secondary education; thirty three percent (n=123) of the respondents had primary school education while eighteen percent of the respondents had tertiary education. These findings are similar to a study conducted in China by Zhang et al. who found that 70% (n=5,749) of the participants had secondary education level with an average age of 59 years (32).

WHO in 2013 conducted a systematic review on the prevalence's of cognitive impairment among general African adults older than 50 years in Sub-Saharan Africa. This review revealed prevalence's ranged between 6.3% in Nigeria and 25% in Central African Republic. The identified common associated factors included increase in age, gender and diabetes (81). Different studies globally have found different prevalence's of cognitive impairment among T2D (32,71). The results in our study showed that the prevalence of cognitive impairment was 32%. The associated factors identified include advance in age above 50 years, lower level of formal education and long duration of type diabetes. Our results are comparable to the findings in a study done in Nigeria which revealed the prevalence of cognitive impairment was 40% (180/450) (18). The high cognitive impairment was associated with increase in age above 50

years, low formal education attainment, unskilled occupation as well as presence of diabetes complications.

However, our prevalence is different from studies conducted in China and Japan. In a study conducted in China, the prevalence of cognitive impairment was 13.5% (1108/8213), of which the underlying factors that were identified as predictors included advance in age, cigarette smoking, long duration of diabetes, insulin use and high levels of glycosylated hemoglobin (HBA1c) (poor glycemic control) (22). In the Japanese study conducted by Umegaki et al, prevalence of cognitive impairment was 15.5%. The associated factors included long duration of diabetes and increasing in age (24). The studies conducted in Asia have shown lower prevalence of cognitive impairment. This can be explained by possibility of higher levels of formal education, better care of patients, early detection of diabetes and frequent monitoring of HBA1c due to accessible, affordable and advanced health care system for their citizens compared to Kenya and Nigeria.

On univariate analysis, this study showed that there was a significant association between age, level of formal education and the duration of T2D with cognitive impairment. On multivariate analysis, age, level of formal education and HBA1c were significant predictors of cognitive impairment. Older patients above 50 years were more likely to develop cognitive dysfunction. These findings compare with those in the study conducted by Malekian et al. that also showed an association between old age and cognitive impairment (77). Nooyens et al. (39) also identified that patients with increased risk of T2D were older and less educated which compares with results of our study.

There was a higher prevalence of cognitive impairment in patients attaining primary and secondary school levels. Participants with primary level of education were more likely to have cognitive impairment. Saedi et al also found a significant association between level of

education and cognitive dysfunction among T2D patients (33). Tsaiet also found that patients with lower schooling were associated with increased incidence of cognitive dysfunction (78). This can be explained by the assumption that diabetic patients with higher education levels are more knowledgeable and comparably able to manage their health status better because they understand the negative implications involved. Education can also protect against neurodegeneration or the onset of dementia might be delayed. This is because it has been postulated to improve neuronal networking so as a result when neurons die others could carry out similar functional tasks, so minimizing decline in cognitive status (63).

Increasing age has been observed as a common predictor of cognitive impairment across different studies highlighted (11 22,24,39) just as we also found in the study. This can be explained as a result of brain aging due to increase in age and also producing similar additive effects with diabetes of reduced resting cerebral blood flow and decrease in functional blood oxygen level thereby affecting cognitive function. The body immune system decreases with age hence allows for development of other degenerative conditions such as Alzheimer which is a common cognitive condition among older adults.

This study showed that majority of the respondents had lived with T2D for less than 10 years but there was a significant association between duration of T2D and cognitive impairment. Our findings are also similar to those of Munshi et al. (74) that duration of 10 years or more was associated with mild cognitive impairment. Another study conducted in the United States also showed that duration of T2D 10 years or longer was associated with increased cognitive dysfunction among T2D patients (12). Hazari et al. (1) found that there were striking differences in cognitive function with the duration of diabetes where patients who had longer than 5 years with T2D showed higher trend of cognitive impairment than patients with lower than five years. Similarly, Taylor et al. (75) found that there was a strong correlation between long duration of T2D and the development of cognitive dysfunction among their study patients.

T2D patients having the condition for more like five years are at increased chance of cognitive dysfunction (39). Longer duration of diabetes coupled with old age increase the development of cognitive dysfunction among patients (12).

Results from this study have shown that longer duration of T2D is vital in the development of cognitive dysfunction among patients. This can be justified by the fact that diabetes is a risk factor for atherosclerosis and small vessel disease resulting in brain infarcts which can affect cognition. Nevertheless, the interaction of metabolic imbalances and other key factors directly can directly lead to altered nervous system as well as impaired cognition (71). Longer durations may increase the risk of cognitive dysfunction through well recognized associations with silent stroke, causing cerebral macrovascular disease and cerebral infarctions (32).

The results from our study also showed that there was no association between hypertension and cognitive impairment. These findings were similar from the study Umegaki (21) which highlighted that there was no association between hypertension and cognitive impairment. Fundamentally, hypertension is having been known to have a greater influence on development of cognitive dysfunction among T2D patients. However, this relationship is less likely to be evident in cross sectional studies focusing on relatively older population as the one evaluated in this study. In contrast, Noovens et al. found that hypertension was a significant predictor of cognitive impairment (31). The difference in Noovens et al and our findings could be as a result of the sample sizes of population recruited and the design of the study. Their study was a five year prospective study including 2613 participants while our study was of cross-sectional design and a smaller sample size (n =367).

This study did not find any association between cigarette-smoking and cognitive dysfunction among T2D patients. These findings are distinct from Ruis et al who found that cigarette-smoking was an independent predictor of cognitive impairment among type 2 diabetes patients

(79). Bruce et al also found that cigarette-smoking was a significant predictor of cognitive impairment (80). The difference can be explained by the smaller sample size of cigarette-smokers. In our study, only 20 respondents were cigarette smokers compared to the above.

The average HBA1c of our study patients was 8.5% which indicates that most of the respondents had poor glycemic levels. HBA1c was found to be a significant predictor of cognitive impairment in T2D patients. Hopkins et al. (71) found that the average HBA1c was 8.5% among T2D patients while normal patients had 5.5% HBA1c. The high average of HBA1c in our study was mainly attributed to inability of patients to routinely do the investigation after every three months which is the standard protocol. However most participants cited high cost of the test as the reason for failure to conduct routine test, hence their anti-diabetic drugs were not optimized. The results further showed that poor glycemic control was a significant predictor for cognitive dysfunction. Our findings are comparable to the Chinese study (22) which found HBA1c as a predictor of cognitive impairment among T2D patients. The negative effects of HBA1c on cognition from this study might have been as a result of long duration of diabetes with poor chronic control of hyperglycemia which may have resulted in brain microangiopathy and cognitive impairment.

7. CHAPTER SEVEN: CONCLUSION AND RECOMMENDATIONS

7.1. Conclusion

This study has identified a prevalence of cognitive dysfunction among type 2 diabetes patients of 32%. On multivariate analysis of patient demographic and clinical characteristics, age above 50 years, lower level of formal education and poor glycemic control measured by HBA1c were identified as key predictors of cognitive impairment.

7.2. Recommendations

- ❖ To optimize adequate glycemic control among T2D patients.
- ❖ All patients 50 years and above with T2D should be routinely screened for cognitive impairment using MMSE.
- ❖ More prospective studies to further identify key predictors of cognitive impairment and its mimics.

7.3. The strengths of the study

- HBA1c is an important predictor of cognitive impairment investigated in this study.
- The assessment of cognitive impairment was easier and quick using MMSE.

7.4. Limitations of the study

- Confounders of CI were not assessed (depression, hypothyroidism). The presence of these can erroneously worsen the MMSE scores and erroneously imply the presence of cognitive impairment, thus pushing up the prevalence figure.
- Many patients were excluded with probable cognitive dysfunction after the sample size was achieved, so true prevalence would have been higher.
- Many potential male participants declined to take part in the study; this may have resulted in a gender bias affecting results interpretation.

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APPENDICES

Appendix I: Consent form

Title of the study: Prevalence of Cognitive Impairment in Ambulatory Patients with type 2 Diabetes in the Diabetic Clinic at Kenyatta National Hospital.

Researcher: Gibril Luseni

Introduction to the study: You are asked to participate in the study which is voluntary and will be conducted in the department of Internal Medicine at Kenyatta National Hospital.

The Purpose of the study: To determine the prevalence of Cognitive impairment in ambulatory patients with type 2 diabetes at Kenyatta National Hospital.

Procedures: If you agree to participate in the study, medical history will be taken, and a test will be performed. The test will involve answering easy questions to provide a better understanding of your cognitive function. Cognitive impairment will be assessed using MMSE. Laboratory investigation will be done (HBA1c) to assess your glycemic control

Time: The study proforma has simplified multiple choice questions expected to guide the researcher. Completing the proforma will take approximately 30 -45 minutes.

Benefit of the study: If the findings indicate cognitive impairment, you will be given priority to get expert management intervention from healthcare service providers within the clinic.

Risks, stress and discomfort: There are no direct foreseen risks in you participating in this study. However, the study will require you to spare about30 minutes of your time and fill the proforma. If there are any questions you do not want to answer, you are obliged to skip. In addition, you have the right to decline giving information.

Cost and risk of loss of Confidentiality: There will be no direct cost incurred by you neither will you receive any money for participating in this study. Data including the proforma and

file from the study will be kept locked in a cabinet during the study period. Your data will be labeled with your unique identity and your name concealed maintaining confidentiality when taking part in the study. Furthermore, your name will not appear in any report or publication of the research and all your personal information will be handled with a high level of confidentiality.

Voluntary Participation and withdrawal: Remember, your participation is entirely voluntarily. Should you consider changing your mind midway, you have the right to do so and you shall not suffer any consequence whatsoever.

Sharing of results: The results of this study may be presented during scientific and academic forums and may be published in scientific medical journals and academic papers.

Participants consent

I confirm that the researcher has explained fully the nature of the study and the extent of activities which I will be asked to undertake. I confirm that I have had adequate opportunity to evaluate and ask questions about this study. I understand that my participation is voluntary and that I may withdraw at any time during the study, without having to give a reason. I agree to take part in this study by filling in the proforma.

Signed by participant…… Date……..

In case of any issues or challenges related to this study, please contact me on **0796557916**

Thank you for sparing your precious time dedicated to participating in this study exercise.

Researcher's statement

Interviewer: I certify that the purpose, potential benefits and possible risks associated with participating in this research have been explained to the above participant and the individual has consented to participate.

Signature_____ Date_____

Appendix II: Fomu ya idhini

Utangulizi

Jina langu ni..., mimi ni mwanafunzi baada ya kuhitimu katika Idara ya Internal Medicine katika Chuo Kikuu cha Nairobi. Utafiti ni sehemu ya programu ambayo kusaidia katika kuelewa mwenendo wa sasa wa matibabu na ugonjwa. Ninachagua kufanya utafiti kuhusu utambuzi kazi na The maambukizi ya utambuzi kudhoofika katika Ambulatory wagonjwa na aina 2 ugonjwa wa kisukari katika kliniki ya kisukari katika hospitali ya Kenyatta.

Madhumuni ya mafunzo

Mahumumi ya utafiti huu ni Kuamua kazi ya utambuzi na maambukizi ya matatizo ya kimwili katika juua na aina 2 ugonjwa wa kisukari katika hospitali ya Taifa ya Kenyatta.

Taratibu

Kama unakubali kushiriki katika utafiti, historia ya matibabu utachukuliwa na kisha utafiti utafanywa. Utafiti huo utahusisha kujibu maswali rahisi ili tuweze kuelewa kwa upana kiwango cha utambuzi. Kuathirika kwa uwezo wa kutambua utatathminiwa kutumia MMSE . Uchunguzi wa maabara (HBA1c) kutathmini udhibitishaji wa kiwango cha sukari utafanwa.

Watakaohusika

Umechaguliwa kama mmoja wa washiriki 93 kulingana na hali yako ya sasa ya matibabu na wewe wamefaulu mahitaji ya ushirikishwaji.

Hatari ya kuhusika

Hakuna hatari inayohusika

Faida ya kuhusika

Kama matokeo ya kuonyesha majonzi au matatizo ya kimwili, utapewa kipaumbele kupata kuingilia kati usimamizi wa mtaalam kutoka kwa watoa huduma ya afya ndani ya kliniki.

Usiri

Majibu yote yatachukuliwa kama siri na matokeo ya mshiriki hayatachukuliwa kibinafsi lakini tu katika hali ya jumla.

Kushiriki katika utafiti huu ni hiari na kutakuwa na hakuna fidia ya fedha.

Washiriki pia kuhifadhi haki zote kujiondoa wenyewe na data zao kutoka kwa kujifunza wakati wowote.

Saini na mtafiti... .....Tarehe.....

Ridhaa ya washiriki

Mimi nathibitisha kwamba mtafiti alielezea kikamilifu asili ya masomo na kiwango cha shughuli ambayo mimi natakiwa kutekeleza. Mimi nathibitisha kuwa na nafasi ya kutosha kwa maswali kuhusu somo hili. Ninaelewa kwamba ushiriki wangu ni wa hiari na kwamba mimi kuondoka wakati wowote wakati wa masomo, bila kutoa sababu. Mimi kukubali kushiriki katika utafiti huu, kwa kujaza hojaji.

Saini na mshiriki..... Tarehe.....

Kwa masuala yoyote au changamoto kuhusiana na somo hili Tafadhali wasiliana nami kwa **0796557916.**

Asante kwa kutenga muda wako wa thamani kujitolea kushiriki katika zoezi hili

Appendix III: Proforma

Section A: Demographics

1. What is your gender

Male ○

Female ○

2. What is your Age

---

3. What is your Marital Status?

Married ○

Single ○

Widowed ○

4. What is your level of education?

Primary ○

Secondary ○

Post-Secondary ○

5. When were you diagnosed with type 2 diabetes?

(In years)……..**:**

6. Which of the following cardiovascular risk factors do you have?

Hypertension ○

Smoking ○

Any other

……

Section B: Testing glycosylated hemoglobin

HBA_1C	**Value (%)**
Glycosylated Hemoglobin	

Section C: Standardized Mini-Mental State Examination (SMMSE)

Please see accompanying guidelines for administration and scoring instructions

1. Say: I am going to ask you some questions and give you some problems to solve. Please try to answer as best you can.

Allow ten seconds for each reply. Say:

a. What year is this? (accept exact answer only) /1

b. What season is this? (during the last week of the old season or first week of a new Season, accept either) /1

c. What month is this? (on the first day of a new month or the last day of the previous month, accept either) /1

d. What is today's date? (accept previous or next date) /1

e. What day of the week is this? (accept exact answer only) /1

2. Allow ten seconds for each reply. Say:

a. What country are we in? (accept exact answer only) /1

b. What city/town are we in? (accept exact answer only) /1

c. <At home>What is the street address of this house? (except a street name and house number or equivalent in rural areas) /1

d) <In facility>What is the name of this facility? (accept the exact name of the institution only) /1 e) <At home>What room are we in? (accept exact answer only) /1

e) <In facility>What floor of the building are we on? (accept exact answer only) /1

3. Say: I am going to name three objects. When I am finished, I want you to repeat them. Remember what they are because I am going to ask you to name them again in a few minutes (say slowly at approximately one-second intervals).

Ball Car Man

For repeated use: Bell, jar, fan; bill, tar, can; bull, bar, pan

Say: Please repeat the three items for me (score one point for each correct reply on the first attempt) /3

Allow 20 seconds for reply; if the person did not repeat all three, repeat until they are learned or up to a maximum of five times (but only score first attempt)

4. Say: Spell the word WORLD (you may help the person to spell the word correctly). Say: Now spell it backwards please (allow 30 seconds; if the person cannot spell world even with assistance, score zero). Refer to accompanying guide for scoring instructions (score on reverse of this sheet) /5

5. Say: Now what were the three objects I asked you to remember? /3

(score one point for each correct answer regardless of order; allow ten seconds)

6. Show wristwatch. Ask: What is this called? /1

(score one point for correct response; accept ‘wristwatch' or ‘watch'; do not accept ‘clock' or ‘time,' etc.; allow ten seconds)

7. Show pencil. Ask: What is this called? /1

(score one point for correct response; accept ‘pencil’ only; score zero for pen; allow ten seconds for reply)

8. Say: I would like you to repeat a phrase after me: No ifs, ands, or buts /1

(allow ten seconds for response. Score one point for a correct repetition. Must be exact, e.g. no ifs or buts, score zero)

9. Say: Read the words on this page and then do what it says /1

Then, hand the person the sheet with CLOSE YOUR EYES (score on reverse of this sheet) on it. If the subject just reads and does not close eyes, you may repeat: Read the words on this page and then do what it says, a maximum of three times. See point number three in Directions for Administration section of accompanying guidelines. Allow ten seconds; score one point only if the person closes their eyes. The person does not have to read aloud.

10. Hand the person a pencil and paper. Say: Write any complete sentence on that piece of paper (allow 30 seconds. Score one point. The sentence must make sense. Ignore spelling errors). /1

11. Place design (see page 3), pencil, eraser and paper in front of the person. Say: Copy this design please.

Allow multiple tries. /1

Wait until the person is finished and hands it back. Score one point for a correctly copied diagram. The person must have drawn a four-sided figure between two five-sided figures. Maximum time: one minute.

12. Ask the person if he is right or left handed. Take a piece of paper, hold it up in front of the person and say the following: Take this paper in your right/left hand (whichever is non-dominant), fold the paper in half once with both hands and put the paper down on the floor.

Takes paper in correct hand_____ /1 Folds it in half_____ /1

Puts it on the floor_____ /1

TOTAL TEST SCORE: /30

Section C: SMME (Swahili version)

Uchunguzi wa hali ya afya wa kiakili (SMMSE)

Tafadhali angalia miongozo inayoandamana kwa ajili ya kuyajibu kiukamilifu

1. **Sema:** Naenda kuuliza baadhi ya maswali na kukupa baadhi ya matatizo unayoweza kutatua kulingana na hali yako. Tafadhali jaribu kujibu kulingana na uwezo wako.
   a. Huu ni mwaka gani? (Kubali Jibu halisi tu) /1
   b. Huu ni msimu gani? (wakati wa wiki ya mwisho ya msimu wa zamani au wiki ya kwanza ya msimu mpya, Kubali jibu moja kati ya haya) /1
   c. Huu ni mwezi gani? (siku ya kwanza ya mwezi mpya au siku ya mwisho ya mwezi uliopita, kubali jibu moja kati ya haya) /1
   d. Tarehe ya leo ni gani? (Kubali tarehe ya awali au inayofuata)
   e. Ni siku gani ya juma? (Kubali Jibu halisi tu)

(*Ruhusu sekunde kumi kwa kila jibu*)

2. Sema:

a. Sisi tupo nchi gani? (Kubali Jibu halisi tu) /1

b. Je, tupo mji upi? (Kubali Jibu halisi tu) /1

c. <Nyumbani> Ni nini anwani ya mitaa unapotoka? (Kubali jina la mtaa na nambari ya nyumba au sawa katika maeneo ya vijijini) /1

d. <Katika kituo > Lipi jina la kituo hiki? (kukubali jina halisi ya taasisi tu)/1 e) < nyumbani > Tupo katika chumba kipi? (Kubali Jibu halisi tu) /1

e. <Katika kituo > Tupo kwenye orofa ya ngapi kwa hili jengo? (Kubali Jibu halisi tu) /1

3. Sema: Mimi nitataja vitu vitatu. Ninapomaliza, Nataka wewe urudie kwa kuvitaja. Vikumbuke vitu vyenyewe kwa maana nitakuomba urudie kuvitaja tena katika dakika chache (Sema polepole kwa kiasi cha moja kwa kila sekunde).

Mpira Gari Mtu

Kwa matumizi yaliyorudiwa: Kengele, chupa, shabiki; muswada, lami, debe; ng'ombe, baa, sufuria

Sema: Tafadhali rudia vitu vitatu nilivyovitaja (alama moja kwa jibu sahihi kwa jaribio la kwanza) /3

Ruhusu sekunde 20 kwa jibu; kama mtu hakuwa ameyarudia yote matatu, msaidie kurudia mpaka ajifunza au hadi juu ya mara tano (lakini pean alama tu kwa jaribio la kwanza)

4. **Sema:** Loga neno dunia (Unaweza kumsaidia mtu ili kutaja neno kwa usahihi).
   Sema: sasa loga kwa nyuma Tafadhali (Ruhusu sekunde 30; kama mtu hawezi loga neno dunia hata kwa msaada, alama sifuri). Rejelea mwongozo wa kuandamana kwa maelekezo ya kupeana alama (weka alama ya kinyume kwenye karatasi hili) /5

5. **Sema:** Kwa sasa vitaje vitu vitatu nlivyokuuliza ukumbuke hapo awali? /3

(Peana alama moja kwa kila jibu sahihi bila kujali utaratibu; Ruhusu sekunde kumi)

6. Onyesha saa ya mkononi. Uliza: Je, hiki inaitwa kitu gani? /1

(Peana alama moja kwa ajili ya majibu sahihi; Kubali ' saa ' au ' saa ya mkononi '; usikubali ' saa ya ukuta, ' nk; Ruhusu sekunde kumi)

7. Onyesha penseli. Uliza: Je, hiki inaitwa kitu gani? /1

(peana alama moja kwa jibu sahihi; Kubali ' penseli ' tu; alama sifuri kwa kalamu; Ruhusu sekunde kumi kwa jibu)

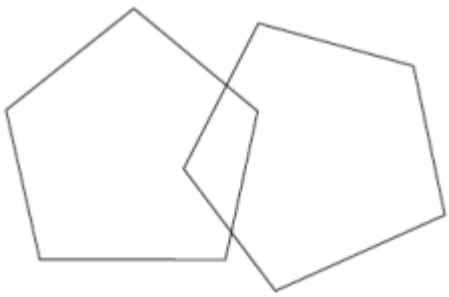
8. **Sema:** Ningependa uyarudie haya maneno baada yangu: *No ifs, ands, or buts* /1

(Ruhusu sekunde kumi kwa majibu. Alama moja ya marudio sahihi. Lazima kauli yote iwe sahihi)

9. Sema: Soma maneno kwenye ukurasa huu na kisha fanya kile hayo maneno yanasema. /1

Kisha, peana karatasi iliyo na maneno "**Funga macho yako**" (Peana alama kinyume kwenye karatasi hili). Ikiwa mhusika anasom maneno hayo tu pasipo kufunga macho. unaweza kurudia: Soma maneno kwenye ukurasa huu na kisha fanya kile hayo maneno yanasema. Tazama nambari tatu katika maelekezo kwa ajili ya usimamizi wa mwongozo wa kuandamana. Ruhusu sekunde kumi; peana alama moja tu kama mhusika aliyafunga macho yake. Sio lazima mhusika asome kwa sauti.

10. Mpe mhusika penseli na karatasi. **Sema:** Andika sentensi yoyote kamilifu kwenye kipande cha karatasi hili (Ruhusu sekunde 30. Peana alama moja. Sentensi lazima iwe na maana. Puuza makosa ya tahajia). /1
11. Weka sanifu (mchoro/umbo) (tizama ukurasa 3), penseli, Kifutio na karatasi mbele ya mhusika. **Sema**: Nakili sanifu hii tafadhali. /1



Ruhusu majaribio mengi. Subiri hadi mhusika amalize and kurusdisha karatasi lake. Peana alama moja ya mchoro ulionakiliwa kwa usahihi. Mtu lazima kuwa na mchoro ulio na pande nne. Muda wa juu: dakika moja.

12. Muulize mhusika kama hutumia mkono wa kushoto au wa kulia. Chukua kipande cha karatasi, Shikilia mbele ya mhusika na aseme yafuatayo: Chukua karatasi hii katika mkono wako wa kulia/kushoto (kwa hakika ni yasiyo ya maana sana), Kunja karatasi nusu mara moja kwa mikono yote miwili na uweke karatasi sakafuni.

karatasi katika mkono sahihi anaoutumia_____ sahihi/1 Kukunja nusu mara moja_____/1 Kuweka karatasi sakafuni_____/1

AlamayaJumla: /30

Asante

Appendix V: Work schedule

ACTIVITY	Jan 2019 – Mar 2019	April 2019 – Sept 2019	Sept2019 – Nov 2019	Dec 2019 - Feb 2020	March - April 2020	May 2020	June 2020
Proposal development and topic submission							
Proposal writing							
Proposal submission and presentation							
ERC Approval							
Data collection							
Data analysis							
Report writing and submission							

Appendix VI: Budget

Item Description	Unit Cost (Ksh.)	Quantity	Total (Ksh.)
Proposal and questionnaire development			
Files	**100.00**	**6**	**600.00**
Pens	**15.00**	**6**	**90.00**
Papers	**500.00**	**5**	**2,500.00**
Flash Disk	**2000.00**	**3**	**6,000.00**
Internet			**15,000.00**
Printing	**10.00**	**1000**	**10,000.00**
Photocopying	**5.00**	**1000**	**5,000.00**
Binding	**100.00**	**10**	**1,000.00**
HBAIC	1@800	369	295,200
Sub-total			**40,190**
Data Collection and Analysis			
Research assistant	**10,000.00**	**2**	**20,000.00**
Data entry and cleaning	**15,000.00**	**1**	**15,000.00**
Statistician	**30,000.00**	**1**	**30,000.00**
Sub-total			**65,000**
Thesis Development			
Printing	**10.00**	**1000**	**10,000.00**
Binding	**100.00**	**30**	**3,000.00**
Photocopying	**5.00**	**1000**	**5,000.00**
Sub-total			**18,000**
Other Expenses			
Travelling	**300.00**	**30**	**9,000.00**
Internet			**15,000**
Airtime	**100.00**	**50**	**5,000.00**
Sub-total			**29,000**
Sum-Total			**152,190**
Contingencies (15%)			**22,828**
Grand Total			**470,218.00**

Appendix VII: Map

Appendix VIII: KNH Ethical Approval Letter

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 03 FEB 2020 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Ref: KNH-ERC/A/52

3rd February 2020

Dr. Gibril Luseni
Reg. No.H58/89128/2016
Dept.of Clinical Medicine and Therapeutics
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Luseni

RESEARCH PROPOSAL - PREVALENCE OF COGNITIVE IMPAIRMENT IN AMBULATORY PATIENTS WITH TYPE 2 DIABETES ATTENDING DIABETIC CLINIC AT KENYATTA NATIONAL HOSPITAL (P938/11/2019)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 3rd February 2020 – 2nd February 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. 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*).
f. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to Discover

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Clinical Medicine and Therapeutics, UON
Supervisors: Dr. J. Kwasa(UoN), Prof. C.F.Otieno(UoN), Dr. Ochanda Mbuya (UoN)

PREVALENCE OF COGNITIVE IMPAIRMENT IN AMBULATORY PATIENTS WITH TYPE 2 DIABETESATTENDING DIABETIC CLINIC AT KENYATTA NATIONAL HOSPITAL

ORIGINALITY REPORT

10%	4%	7%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Elham Saedi, Mohammad Reza Gheini, Firoozeh Faiz, Mohammad Ali Arami. "Diabetes mellitus and cognitive impairments", World Journal of Diabetes, 2016 Publication	1%
2	worldwidescience.org Internet Source	1%
3	Submitted to Kenyatta University Student Paper	1%
4	www.science.gov Internet Source	1%
5	"Minutes of the 44th Genral Assembly of the European Association for the Study of Diabetes", Diabetologia, 2009 Publication	<1%
6	"Posters", International Psychogeriatrics, 2007 Publication	<1%