ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE, DEPARTMENT OF INTERNAL MEDICINE

PREVALENCE OF NEUROCOGNITIVE IMPAIRMENT AND ASSOCIATED FACTORS AMONG TYPE-2 DIABETIC PATIENTS ON FOLLOW UP AT DIABETIC CLINIC, BLACKLION SPECIALIZED HOSPITAL, ADDIS ABEBA, ETHIOPIA.

Investigator:

Bikila Gedefa Bekana (Internal Medicine Resident)

Advisor:

Dr. Getahun Tarekegn (MD, Consultant Internist and Endocrinologist)

A proposal to be submitted to Department of Internal Medicine , College of Health sciences, Addis Ababa university; in partial fulfillment of the requirements for Internal Medicine Specialty.

December, 2021

Addis Ababa, Ethiopia

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Declaration

This is to certify that the thesis entitled "Prevalence of Neurocognitive Impairment and Associated Factors among Type-2 Diabetic Patients on Follow Up at Diabetic Clinic, Tikur anbessa Specialized Hospital, Addis Ababa, Ethiopia

The thesis comprises only my original work for specialty certificate in Internal medicine. Due acknowledgment has been made in the text to all other materials used.

This thesis is submitted for the qualification of "Specialty in Internal Medicine" complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Name: Bikila Gedefa Bekana **Signature__ _____Date:-December 8, 2021.**

Acknowledgement

First and foremost I would like to thank God, who has given me the power to believe in myself and pursue my dreams. I could never have done this without the faith I have in you, the Almighty.

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Finally, I am very great full to all my friends whose encouraging words kept me going and finally, but by no means least, thanks go to my family for their unbelievable support.

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List of Abbreviations and acronyms

AAU _____ Addis Ababa University

BLH_____ Black Lion Specialized Hospital

CDC_____ Center for Disease Control

CHS_____ College Of Health Science

CKD_____ Chronic Kidney Disease

DALY_____ Disability-adjusted Life Years

DKA_____ Diabetic Keto Acidosis

DM_____ Diabetes Mellitus

DSM_____ Diagnostic and Statistical Manual of Mental Disorders

FBS_____ Fasting Blood Sugar

HDL_____ High Density Lipoprotein

HgA1C_____Glycated Hemoglobin

HHS_____ Hyperglycemic Hyperosmolar State

HIV_____ Human Immunodeficiency Virus

IDF_____ International Diabetic Federation

LDL_____ Low Density Lipoprotein

MCI_____ Mild Cognitive Impairment

MetS_____ Metabolic syndrome

MMSE_____ Mini Mental State Examination

MOCA_____ Montreal Cognitive Assessment

NCI_____ Neurocognitive Impairment

PPBS_____ Post Prandial Blood Sugar

RBS_____ Random Blood Sugar

TGA_____ Triglyceride

TASH _____ Tikur Anbessa Specialized Hospital

US _____ Ultrasound

WHO_____ World Health Organization

WHR_____ Waist to Hip Ratio

Abstract

Background:-*Neurocognitive disorders in patients with type 2 Diabetes Mellitus has spectrum manifestation which might range from subtle executive dysfunction to memory loss and overt dementia. Diabetes patients are at higher risk of all types of cognitive impairment, mainly because some diabetes complications results in cognitive impairments and they are also being considered as disease of the same spectrum. Even though it is estimated that more than 50 million peoples live with dementia worldwide, there is no enough data from low and middle income countries, including Ethiopia, where the number is projected to increase to 152 million by 2050. Hence this study will focus on assessing the overall prevalence, potential determinant and contributing factors among patients with type 2 DM over a period of two months at Black Lion Specialized Hospital, Ethiopia.*

Objective: - *To assess the neurocognitive impairment and associated factors among diabetic patients on follow up at diabetic clinic, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July 1- August 30, 2021*

Methods

A hospital based Cross-sectional study was conducted on total of 338 type 2 diabetic patients on follow-up at BLH. The sociodemographic, anthropometric and clinical data was collected by trained final year medical students. Both face to face interview and medical record reviews were used for data collection. A validated Mini Mental Status Examination tool was used to assess cognitive impairment. Data was entered to epi-data cleared and analyzed by SPSS version 26.0. Finally, Descriptive analysis was carried out and presence of statistical association between neuro-cognitive impairment and associated factors was assessed using logistic regression and associations with p-value of < 0.05 will be considered to be statistically significant.

Results

The overall prevalence of neurocognitive impairment among type 2 diabetic patients on follow up at black lion specialized hospital was 38.75%. From Socio-demographic factors low educational level [AOR=3.65(1.855-7.188)] was associated with increased odds of encountering cognitive impairments. While some clinical characteristics like being on oral hypoglycemic agents [AOR=0.786 (0.370-1.669)] or oral hypoglycemic agents combined with insulin [AOR=1.87(1.054-4.264) were associated with decreased likelihood of cognitive impairments. Total duration of DM [(AOR=1.95(0.987-3.877)] and overall glycemic control [AOR= 2.21(1.238-3.947)] had significant association with NCI. additionally coexisting hypertension [AOR= 0.53(0.314-0.918)] and presence of diabetic eye disease [AOR=1.84(1.056-3.229)] were also associated with increased odds of encountering impairment.

Conclusion: - *The finding indicated high prevalence of neurocognitive impairment among respondents who had low level of education, prolonged duration of DM, poorly controlled DM, diabetic eye disease and coexisting hypertension.*

Key words: - *T2DM, Neurocognitive impairments, cross-sectional study, MMSE*

CHAPTER ONE

Introduction

1.1 -Background Information

The global number of people living with dementia more than doubled from 1990 to 2016, mainly due to increases in population ageing and growth. Worldwide around 50 million people live with dementia, and this number is projected to increase to 152 million by 2050, rising particularly in low and middle income countries (LMIC) where around two-thirds of people with dementia live. Dementia affects individuals, their families, and the economy, with global costs estimated at about US$1 trillion annually (1,2).

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. DM is classified on the basis of the pathogenic process leading to hyperglycemia. Generally there are two broad categories of DM, designated as either type 1 or type 2 DM. But there is increasing recognition of other forms of diabetes. Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production (3).

The metabolic dysregulation associated with DM causes secondary patho-physiologic changes in multiple organ systems, such as brain, that impose a tremendous burden on the individual with diabetes and on the health care system. Generally diabetes related chronic complications are classified as macro vascular complications (coronary heart disease, peripheral arterial disease and cerebrovascular disease), microvascular complications (retinopathy, macular edema, neuropathy and nephropathy) and others (i.e. cognitive impairment). The presentation of cognitive impairment ranges from subtle executive dysfunction to memory loss and overt dementia (3,4).

Neurocognitive Disorders (NCDs) encompasses the group of neuropsychiatric disorders in which the primary clinical deficit is in cognitive function. Only disorders whose core features are cognitive are included in this neuropsychiatric disorder. Neurocognitive disorders include delirium and syndromes of major Neurocognitive disorders and mild Neurocognitive Disorder (with their etiological subtypes).Neurocognitive disorders are acquired rather than developmental. The impairments in cognition has not been present since birth or within very early life(representing a decline from a previously attained level of functioning) (5).

There are twelve modifiable risk factors for neurocognitive disorders: less education, hypertension, hearing impairment, smoking, obesity, depression, physical inactivity, diabetes, infrequent social contact, excessive alcohol consumption, head injury, and air pollution. People with diabetes have higher incidences of all-cause dementia, Alzheimer disease and vascular dementia than people with normal glucose tolerance. Compared to people without diabetes, people with diabetes have a greater risk of cognitive decline, especially memory and executive functions. There is also evidence for an elevated risk of both vascular dementia and AD in patients with type 2 DM (1,4,6,7).

Brain was initially identified as an always insulin-sensitive organ, with tremendous evidences that revealed insulin action in the brain producing multiple behavioral and metabolic effects that influence peripheral metabolism, cognition and eating behavior. But since recently brain insulin sensitivity and insulin signaling within the brain has been receiving more attention. Disturbances in brain insulin action were recently observed in obese and type 2 diabetic patients, as well as in aged and dementic patients. Decreases in insulin sensitivity of central nervous pathways, i.e., brain insulin resistance, may therefore constitute a joint pathological feature of metabolic and cognitive dysfunctions (8,9).

1.2 -Statement of the Problem

Dementia is a rapidly growing public health problem affecting around 50 million people around the world. There are nearly 10 million new cases every year and this figure is set to triple by 2050. Dementia is a major cause of disability and dependency among older people and can devastate the lives of affected individuals, their care givers and families. Additionally, the disease inflicts a heavy economic burden on societies as a whole, with the costs of caring for people with dementia estimated to rise to US$ 2 trillion annually by 2030 (10).

More than 16 million people in the United States are living with cognitive impairment. An estimated 5.1 million Americans aged 65 years or older may currently have Alzheimer's disease, the most well-known form of cognitive impairment; this number may rise to 13.2 million by 2050. Alzheimer's disease and related dementias alone are estimated to be the third most expensive disease to treat in the United States with estimated medical expenditure per state(in 2010) $647 million (11).

Another trend study done in Canada focusing on comparing dementia rates and the financial burden of dementia in Manitoba with other parts of Canada and the rest the world from 2012 to 2048 has predicted that the number of Manitobans (65+) with dementia in 2045 will be 47,021, representing 2.58% of the Manitoban population, which will be 2.3 times that of the year 2015 (20,235). According to this trend study the number of cases of dementia in Manitoba grew by 20.7% from 2015 to 2025, 68.16% from 2015 to 2035 and at an alarming rate of 125% from 2015 to 2045. The total economic burden of dementia in Manitoba is close to one billion USD and is expected to grow more than 28 billion USD during the year 2038 (12).

A computer simulation study aimed at evaluating developments in the costs of treating and caring for people suffering from Alzheimer's disease (AD) in the 28 countries in European Union by 2080 has assumed that the total cost of care for all persons with AD will increase even with a consideration of introduction of medicines (including the newer one) at different disease stages. This mathematical model has predicted the percentage of patients and costs increased as follows: Mild by one year, ~10.61%; Mild by two years, ~17.73%; Moderate by one year, ~16.79%; Moderate by two years, ~34.88%; and Severe by one year, ~23.79%. But according to this simulation test prolonging the stay in the MCI stage reduced the cost (13).

Africa is estimated to have 15.9 million adults living with DM which is a regional prevalence of 3.1%. The African continent has the greatest proportion of people with undiagnosed DM and global projections show that it will experience the greatest future increase in the burden of DM of about 156% by 2045. This unprecedented anticipated increase in diabetes would be followed by significant increase in neurocognitive impairment (14).

In Ethiopia there is an ongoing epidemiological shift from infectious diseases to non communicable disease. In 2015, diabetes was the ninth leading cause of premature death and disability (causing 1,106 DALYs per 100,000). The national estimates of the prevalence of non communicable disease metabolic risk factors showed high rates of raised blood pressure (16%), hyperglycemia (5.9%), hypercholesterolemia (5.6%), overweight (5.2%) and Obesity (1.2%) (15).

There is one dilemma for researchers dealing with these disease entities; whether glycemic control predicts cognitive function or cognitive functions predict glycemic control. Although the fact diabetes causing cognitive impairment is well established; there are also plenty of studies that showed the other way round. In a cohort study that involved 1091 participants it was demonstrated that cognitive function at early adolescence (as early as age 11 years) predicts both HbA1c levels and cognitive function at age 70 years. They also found that lower cognitive function at age 70 is associated with an increase in HbA1c from age 70 to 79 years (16,17).

Although handful of clinical trials have not been able to show whether improved glycemic control results in regained cognitive abilities, some studies elaborated that intensified treatment improved the cognitive score, and an improvement in electro-physiological measures, suggesting increased availability of compensatory mechanisms in subjects with improved glycemic control. This may indicate that the underlying disease process may be partly reversed with appropriate treatment (18–20).

1.3 -Significance of the Study

Diabetes mellitus with its complications is one of non communicable disease with significant burden as an entity and is risk factor for many other non communicable diseases. Although there is foreseeable epidemiological shift from infectious causes of diseases to non communicable diseases, we believe that there is lack of governmental and nongovernmental organizations attention towards non communicable diseases. Additionally, there is a paucity of studies done on non-communicable diseases as a general and diabetes mellitus specifically.

We believe that this study will provide information on neurocognitive impairment in type 2 diabetes mellitus in the study area specifically and in Ethiopia as a general and, it may help for further studies and used as in put for different institutions and government sectors.

CHAPTER TWO

2.1 -Literature Review

2.1.1 Prevalence and incidence of cognitive impairments among type 2 diabetic patients

Data from a Meta analysis that included 54 primary studies, eight reviews and three guidelines, showed that high proportion of people (up to 20%) older than 60 years with type 2 diabetes might have dementia. Diabetes is prevalent co-morbidity in people with dementia, with a prevalence of up to 39% depending on the type of sample studied. The general prevalence of diabetes in people with dementia is most likely to be around 13%. A ten year cohort study also showed, incidence rate of dementia in people with type 2 diabetes can range from 83 per 10,000 person/years in those aged between 60 years and 64 years to as high as 1000 per 10 000 person-years in those older than 85 years of age (21,22).

Longitudinal cohort study of 918 American participants revealed that about 36.38% of the participants had incident MCI (47.9% amnesic MCI, and 52.1% had non amnesic MCI. Diabetes was related to a significantly higher risk of all-cause MCI and amnesic MCI and the risk of MCI attributable to diabetes was 8.8% for the whole sample and was higher for African American persons (8.4%) and Hispanic persons (11.0%). Another cohort study from USA, Atherosclerosis Risk in Communities (ARIC), also showed that African Americans with prevalent diabetes experienced 41% greater annual decline in processing speed scores and 50% greater annual decline in verbal fluency scores than those without diabetes (23,24).

From cross sectional study that involved 367 type 2 diabetic patients on follow up at Kenyatta national hospital, the prevalence of cognitive impairment was 32% (27% mild cognitive impairment and 5% moderate cognitive impairment). The prevalence of cognitive impairment as per hospital based cross sectional study done in Nigeria was 40%. In addition to age and level of education, unskilled occupation and presence of diabetic complications were the identified risk factors for cognitive impairment among type 2 diabetic patients in the latter study (25,26).

Although neurocognitive impairment in diabetes is one the least studied disease entities in Ethiopia, there were few studies done at some teaching hospitals with large catchment areas. A cross sectional study done at Black Lion hospital, DM clinic with 384 study participants selected by simple random sampling demonstrated the overall prevalence of neurocognitive impairment(measured by MMSE) of about 45%(mild and moderate impairment were 29.6% and 15.4% respectively). The mean score of MMSE was found to be 24.32 ± 3.5, ranging from 13 to 30 points. After stratifying to the educational cognitive impairment was twenty five percent (27).

2.1.2 Socio-demographic characteristics of type 2 diabetics and NCI among type 2 Diabetics

Generally from different studies neurocognitive impairment including dementia is much common in elderly than the young population. A review of eleven cross sectional studies from five African countries (Benin, Botswana, Central African Republic, Congo and Nigeria) showed a prevalence of cognitive impairment among elderly that ranges from 6.3% in Nigeria to 25% in Central African Republic. Studies from different part of India support the same notion. In one study the prevalence of neurocognitive impairment was significantly associated with almost all socio-demographic parameters: age, sex, education, occupation, and socioeconomic status and the anthropometric measurement (waist-to-hip ratio) ($P<0.05$). But according to Egyptian study there was weak negative relationship between age of the patients and the cognitive function (28–30)

Study which has involved 450 type 2 diabetic Nigerian patients found that; cognitive impairment with male to female sex distribution of 28.9% and 48.1% respectively. Advanced age, low education attainment, unskilled occupation and presence of diabetic complications were also found to be risk factors for cognitive impairment. As per study done in JUMC DM patients aged ≥62 yrs (compared to age <45 yrs) and farmers (compared to employees) had 7.5 higher odds for cognitive impairment. The American ARIC Brain MRI Study revealed that African Americans with prevalent diabetes experienced 41% greater annual decline in processing speed scores and 50% greater annual decline in verbal fluency scores than those without diabetes; while among whites, diabetes was not associated with cognitive decline (24,25,31).

2.1.3 Duration of diabetes and types of treatment and NCI among type 2 Diabetics

The effect of the duration of diabetes was also studied and the outcomes of the studies were controversial. As per Indian hospital based cross sectional study, there were striking difference between those with shorter duration (</= 5 yrs) of diabetes and longer duration (>5 yrs), with cognitive impairments being more common in the latter. However according to randomized trial participants with impaired fasting glucose had worse baseline cognitive scores compared to other participants, indicating patients my encounter cognitive impairment even before overt diabetes. But another population based longitudinal study demonstrated that, at baseline, there were no significant differences in the neuropsychological tests related to diabetes (32–34).

From a Meta analysis of 14 multinational longitudinal population-based studies of variable methodological quality, the incidence of any dementia was increased in people with diabetes. Overall diabetic patients have an increase in risk of Alzheimer's disease of 50–100%, and an increase in risk of vascular dementia of 100–150%. One of the studies assessed the effect of diabetes duration on the risk of dementia, and observed no effect. However, two other studies showed that screening identified cases of diabetes, which presumably have a shorter or less severe exposure to hyperglycemia, had a lower risk of dementia than people with a known history of diabetes (35).

A prospective analysis of 5,099 participants to know association of glycemic control, diabetes duration, and biomarkers of hyperglycemia with incident mild cognitive impairment (MCI) and incident dementia illustrated that the risk of incident mild cognitive impairment of up to 60%. Another meta analysis of 24 studies and modeling study of type 2 diabetes and pre-diabetes showed that these disease entities are associated with progression from cognitive impairment to dementia; indicating that prevention of diabetes might have a substantial effect on population incidence of dementia after a time lag of decades (36–38).

According to study done by JU researchers which showed high prevalence of NCI (53.3%) among type 2 DM patients; in addition to some socio-demographic factors, FBS level and treatment options were predictors of cognitive impairment. Additionally cognitive impairment among type 2 diabetic patients who had FBS ≥126 and/or on oral hypoglycemic agents were 4.4

times and 5.4 times odds of cognitive impairment among those patients who had FBS<126 Mg/dl and those who were using insulin respectively (31).

2.1.4 Dyslipidemia, insulin resistance & other MetS components and NCI among type 2 Diabetics

Some studies demonstrated that hypercholesterolemia increases the risk of Alzheimer's disease and vascular dementia. A retrospective cohort study demonstrated that high midlife cholesterol (240mg/dl) was associated with an increased risk of developing AD 3 decades later (the HR was 1.57 with 95% CI: 1.23-2.01). Another comparative, community-based epidemiologic study showed increasing levels of cholesterol and LDL was associated with increased risk of AD in individuals without the *APOE*-ε4 allele, but not in those with *APOE*-ε4. According this study there was no significant association between levels of triglycerides and AD risk in those without *APOE*-ε4 (39,40)

Systemic review of a total of 20 studies, 10 for adults and 10 for adolescents done on impact of Metabolic Syndrome on Cognition and Brain had found multiple cognitive domains impairment among adults; even after control-ling for medical factors, such as cardiovascular disease and T2DM, silent brain lesions, education and socioeconomic status, depressive mood, coronary heart disease, and magnetic resonance imaging findings. According to this review MetS has been linked to deficits in memory, visuospatial abilities, executive functioning, processing speed, and overall intellectual functioning (41).

A prospective cohort study evaluating 1,674 participants without dementia showed that statins therapy decreased the risk of dementia during the 5-year follow-up period after adjustment for conventional risk factors for dementia. Persons who had used statins were about half as likely as those who did not use statins to develop dementia. However a systemic review of eight studies in dementia, and two meta-analyses that covered 1372 cases of dementia from 14,430 participants from the USA and UK on protective effect of statins on dementia was demonstrated only in a nested case–control study of lower quality and one cohort study. In most other cohort and high quality studies, statins use did not show a beneficial effect (42–44).

2.1.5 Relatively higher indicators of hyperglycemia and NCI among type 2 Diabetics

Different studies done in India have also revealed the causative relationship of diabetes and cognitive impairment. In a cross sectional study (hospital based) done in India involving seventy type 2 diabetic patients the prevalence of mild neurocognitive disorder was found to be 54.29%. In this study, those with MCI had higher HbA1c, higher FBS, and PPBS and all were statistically significant. Another cross sectional study with 194 diabetic subjects, 50.5% were cognitively impaired. In the latter study, although socio-demographic characteristics and anthropometric measurement(WHR) were significantly associated with cognitive impairment, blood pressure showed no significant association (29,45).

2.1.6 Hypertension, cardiovascular disease and other co-morbidities and NCI among type 2 diabetics

Comparative cross sectional study done in Egypt revealed that patients with type 2 diabetes had three times increased risk of having MCI compared to non-diabetics. Although this study also demonstrated the effect of other factors and frequency of hypoglycemic episodes on cognitive impairment in diabetic patients; hypertension and cardiovascular diseases are found to be other risk factors for cognitive impairment among type 2 diabetic patients. The presence of hypertension significantly associated with MCI (39.1%) compared to 19.4% among non-hypertensive with MCI patients. Another study found that 19.3% of diabetics with ischemic heart diseases had MCI compared to 11.5% among those without heart diseases (30,46).

Study done in southern India to assess the prevalence of mild cognitive impairment among patients with non-communicable i.e. hypertension, diabetes and asthma diseases has found that the proportion of cognitive impairment was 10.8%. But this study fails to consider co-morbidities like patients having both diabetes and hypertension. Another Chinese study which has involved 256 type 2 DM revealed that depression was a risk factor for mild cognitive impairment (47,48).

2.2 -Conceptual Framework

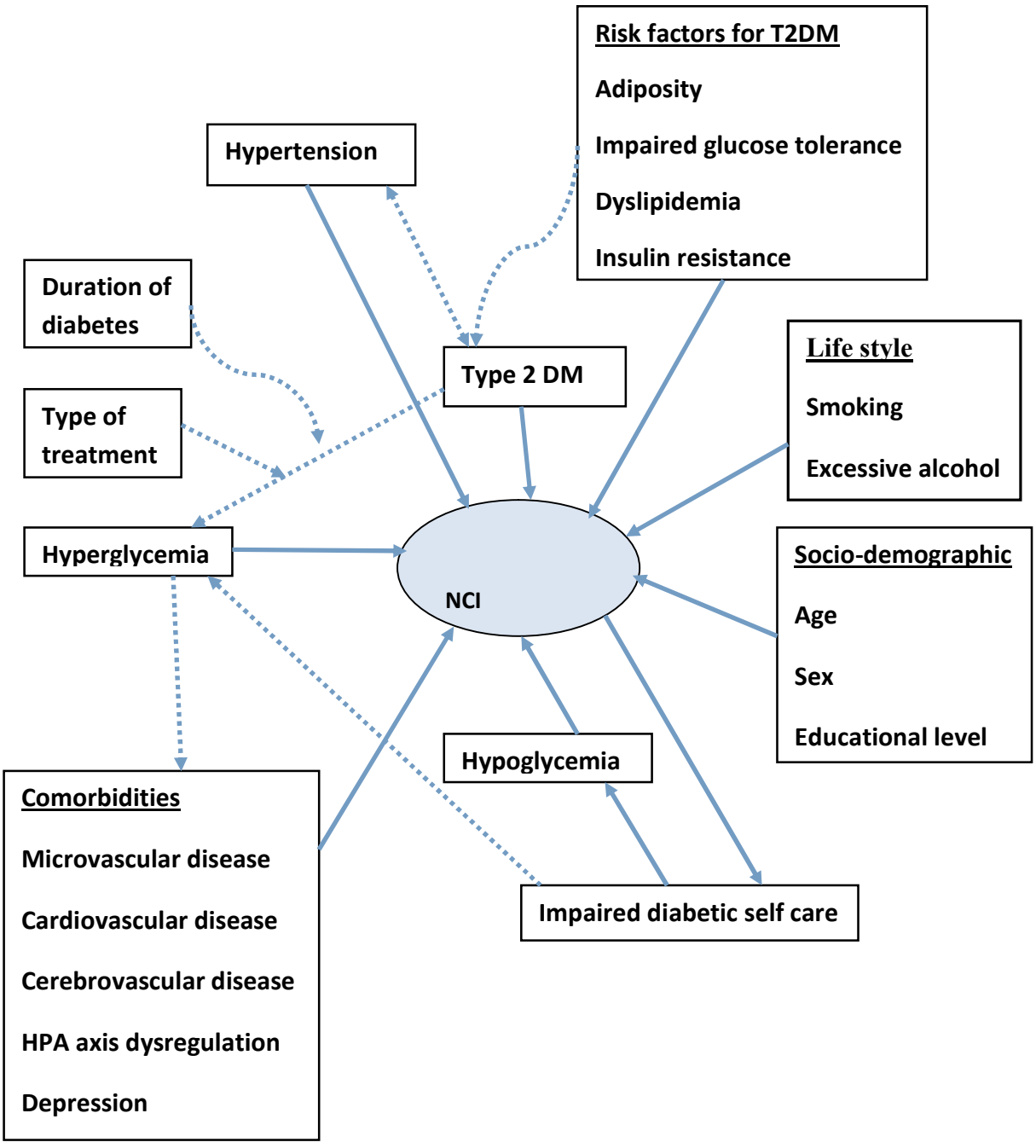

Figure 1:-Conceptual framework showing NCI and associated factors among of type 2 DM (adapted from the literatures and books) (3,8,9,49)

CHAPTER THREE

3. Objectives

3.1. General Objective

To assess neurocognitive impairment and identify associated factors among diabetic patients on follow up at diabetic clinic, Tikur Anbessa Specialized Hospital, Addis Abeba, Ethiopia from July 1- August 30, 2021.

3.2. Specific objectives

- To determine the overall prevalence of neurocognitive impairment among type 2 diabetic patients on follow-up at diabetic clinic, Tikur Anbessa Specialized Hospital.
- To identify factors associated with neurocognitive impairment among type 2 diabetic patients on follow up at diabetic clinic, Tikur Anbessa Specialized Hospital.

.

CHAPTER FOUR

Method and Materials

4.1 Study area and period

The study was conducted from July 1- August 30, 2021 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. Tikur anbessa specialized hospital is the first and largest tertiary hospital in the country and provides specialty services for nearly half a million patients per year coming from every corner of the country.

Black lion hospital provides both inpatient (with total of 800 beds) and outpatient services. Department of internal medicine is one of well organized unit and provides its care through its major subspecialty units. Endocrine unit is one of those subspecialty units which was established back in 1994 GC and currently provides specialty care for more than10, 000patients/year by residents, fellows and consultant endocrinologists. T2DM patients accounts for majority of patients attending follow-up at OPD.

4.2 Study design

Hospital based Cross-sectional study will be conducted.

4.3 Population

Source population:-will be all type 2 diabetic patients on follow up at DM clinic, TASH.

Study population: - will be selected type 2 diabetic patients on diabetic follow up clinic during the study period (from July 1- August 30, 2021) at TASH.

Inclusion criteria:-type-2 diabetic patients on follow up for ≥1 year (FBS on three visits is required to know glycemic control and at TASH diabetic clinic appointment is every 03 months) with complete medical records will be included.

Exclusion criteria: - patients with RVI, previous history of cerebrovascular accidents, previous history of severe traumatic brain injury, known psychiatric illnesses, severe medical illnesses, Alzheimer disease and, those with visual, hearing, and speech difficulty will be excluded. Patients with incomplete medical records will also be excluded.

4.4 Sample size and sampling technique

4.4.1 Sample size

4.4.1.1 Sample size for the first specific objective

Sample size will be determined by using the single population proportion formula considering the following assumptions: 95% confidence interval with 5% margin of error and 53.3% proportion of neurocognitive impairment among type-2 diabetic patients (33).

Sample size is calculated using the formula

$$n=\frac{Z^2 1-\alpha/2\ P\ (1-P)}{d^2}$$

$$n=\frac{(1.96)^2(0.533)\ (0.467)}{(0.05)^2}=381$$

Where, n = sample size

Z= confidence level (1.96) p= estimated prevalence (0.533)

d= Margin of error to be tolerated (0.05).

4.4.1.2 Sample size for the second specific objectives

For associated factors (glycemic Control, duration of diabetes since diagnosis and hypertension)sample size will be calculated using epi info version 7, under the cohort & cross sectional sample size calculation tab; with a consideration of confidence interval of 99.99% (gradually increased from 95% to 99.99% to increase sample size) power of 85% and different ratios, percent outcome in unexposed group, percent out come in exposed group, risk ratios and odds ratios the sample size for each associated factors will be 137, 184 and 92 respectively (52).

Associated factors	Confidence interval and power	Ratio Un-Exposed /exposed	%Outcome in un-exposed	%Outcome in exposed	Risk ratio	Odds ratio	SS
Poor glycemic control (HgA1C≥7%)	99.99% and 85%	3.31	72.7%(53)	23.2%(36)	0.32	0.11	137
Duration of DM(≥10yrs)	99.99% and 85%	0.7	43.4%(27)	10.6%(54)	0.24	0.15	184
Hypertension	99.99% and 85%	0.16	19.6%(55)	86.36%(56)	4.41	25.97	92

From the two sample sizes calculated for the two specific objectives we will take the largest sample size (353) and because the total population is <10,000 the finite population correction formula will be used to determine the final sample size.

N (actual sample size) = n/ (1+ (n/N)) n = sample size

N = total number of adult type 2 diabetic patients who are attending DM clinic of TASH, (N=2800).

Therefore, the sample size will be: Nf = 382/ (1+ (382/2800)) = 336

By adding 5% contingency, a total of 353 patients will be sampled.

4.4.2 Sampling technique

Systemic random sampling technique will be applied after having the list of monthly patient flow to the follow up clinic. Most patients have appointment every two/three months (1400 patients/month) and about 70 patients visit diabetic clinic on daily basis. The first patient will be selected randomly and every 4th patient on the list will be chosen as a participant.

4.5 Data (socio-demographic, life style, clinical and anthropometric) collection process

A total of three data collectors (all psychiatric nurses) will be employed. Data will be collected by a face-to-face interview using structured questionnaire and review of medical records using checklist. A validated MMSE tool which was translated into local languages (Afan Oromo and Amarigna), was used to screen for cognitive impairments. Each components of Mini-Mental State Examination: orientation (10 points), registration (3 points), attention and calculation (5 points), recall (3 points), and language and praxis (9 points) will be evaluated. The data collectors will also measure patients' weight (to the nearest 0.1kg), hip and waist circumferences (to the nearest 0.1cm), and BP (to the nearest 0.5mmHg).

4.6 Variables

4.6.1 Dependent variable Neurocognitive impairment

4.6.2 Independent variable

Socio-demographic characteristics	Life style	Co-morbidities	Clinical	Anthropometry
Age	Smoking	Hypertension	Type of treatment	WHR
Sex	Alcohol	Dyslipidemia	Duration of DM	
Educational level	Chewing khat		Glycemic control	
Income level				
Marital status				

4.6.3 Measurements

Waist to Hip Ratio (WHR):- the waist circumference should be measured at the midpoint between the lower margin of the last palpable ribs and the top of the iliac crest using a stretch-resistant tape that provides a constant 100 g tension. Hip circumference should be measured around the widest portion of the buttocks, with the tape parallel to the floor. According to World Health Organization (WHO), a healthy WHR is: 0.9 or less in men and 0.85 or less for women (57).

Dyslipidemia:- total cholesterol ≥ 200 mg/dl and/or HDL ≤ 45 mg/dl and/or LDL ≥ 100 mg/dl and/or triglycerides ≥ 150 mg/dl and/or use of statins (58).

Uncontrolled RBS:-if the average three months fasting blood glucose measurement(both at home and on visits) is > 130 or < 70 mg/dL and/or HgA1c≥7% (59)(4).

Uncontrolled Hypertension:- Is defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg in patients taking anti-hypertensive treatment (60).

Mini-Mental State Examination scoring:-Total score is out of 30 and generally normal score is ≥24 points. But as per validation study done in Ethiopia different cutoffs will be used depending on educational level: 22, 24 and 26 points for those 5-8 years of education, 9-12 years of education and college/university education respectively. Because patients with no formal education and 1-4 years of education were not included in this study (validation study for MMSE in Ethiopia), the Brazilian study which has found 21 and 22 cutoff points for subjects with no formal education and low educational level respectively will be used(61,62).

Alcohol consumption:-is reported consumption of alcohol 12 months prior to data collection and excessive alcohol consumption is daily alcohol consumption> 20 g/day in women and > 30 g/day in men for 6 months or more (3)

4.6.3 Operational definitions

Moderate hypoglycemia:-is hypoglycemic state where patients can't think clearly, properly control their body, had to stop what they are doing, but they still able to treat themselves; while

Severe hypoglycemia:-is where they need someone's help and are unable to treat themselves (63).

Neurocognitive impairment:-is defined according to educational level as per definition of MMSE scoring explained above.

Fasting blood sugar(FBS):-is blood sugar measured from venous blood after at least 08 hours of fasting (4).

Statins intensity (64)

High intensity	**Moderate intensity**	**Low intensity**
Atorvastatin , 40- 80 mg Rosuvastatin, 20 (40) mg	Atorvastatin, 10 (20) mg Rosuvastatin, (5) 10 mg Simvastatin, 20 to 40 mg Pravastatin, 40 (80) mg Lovastatin , 40 mg Fluvastatin XL, 80 mg Fluvastatin, 40 mg twice daily Pitavastatin, 2 to 4 mg	Simvastatin, 10 mg Pravastatin, 10 to 20 mg Lovastatin, 20 mg Fluvastatin, 20 to 40 mg Pitavastatin, 1 mg

4.7 Data analysis plan

Collected data will be cleaned, edited, and coded before entering into epi-data manager version 4.02. The data entered into epi-data will be cleared and double entry verification will be made and exported to SPSS windows version 27 for data processing and analysis. The data will be explored to check outliers, missing data and assumptions. Descriptive analysis will be carried out using frequency distributions, central tendency and dispersion measures. The stratification of the cut-off points of MMSE will be done in accordance to years of study in order to prevent the possibility of education level to mask the performance in this test, MMSE. Cross tabulations and bivariable analysis will be performed to select variable for multivariate analysis. Hence variables with p-value <0.25 will be taken as a candidate for multivariable analysis. Presence of statistical association between outcome variables and the associated factors will also be assessed using multivariable logistic regression. Association with p- value of < 0.05 will be considered to be statistically significant. Odds ratio (OR) and confidence interval (CI) will be used to determine the presence of significant association between dependent and independent variables. The model

fitness for Logistic regression will be tested using Hosmer-Lemeshow goodness of fit test at P-Value >0.05.

4.8 Data quality control

The questionnaire will be translated from English to local languages (Afan Oromo and Amarigna) and then retranslated back to English to maintain its consistency. Training will be provided for the data collectors before the actual data collection date. Pretest of the questionnaire will be done among 10 type 2 diabetic patients at SPHMMC Hospital to see the validity of the instrument and the questionnaires will be modified accordingly. Supervision will be undergone for the data collection process (for completeness and consistency), data entry process, data storage and management.

4.9 Ethical consideration

Ethical clearance will be obtained from Institutional Review Board of Addis Ababa University (CHS), Ethiopia. . A letter of permission to conduct the study will be obtained from Addis Ababa University, CHS, clinical director's office and research head of endocrine unit. Each participant will be informed about the purpose of the study and his/her right not to participate in the study will be respected. Information obtained from the records will be kept confidentially by not recording participants name and their phone number on questionnaires. Data will be collected after obtaining written informed consent from the participants.

4.10 Dissemination plan

After research completion and finalizing report, it will be submitted to graduate programs coordinating office and College of Health Sciences of Addis Ababa university, Diabetic associations, ministry of health and other concerned institutions and stake holders for possible application and publication of the study.

CHAPTER FIVE: RESULTS

A total of 353 questioners were distributed for Type-II DM patients, of which 338 questioners were recollected and analyzed (15 cases were excluded after data collection because of incomplete data) during the study period making the response rate of 95.75%. Beside the questioners filled by the trained interviewer's, data checklist was prepared and additional data were collected from medical record of the patients.

5.1. Socio-demographic factors

Among the total of 338 Type-II DM cases included in this study the majority were males (n=191, 56.5%) and the remaining patients were females contributing to 43.5 % (n=147) of the cases. With respect to residential areas nearly 3/4th selected cases where from urban areas while the remaining cases are from rural parts of the country. Regarding occupation majority are government employees accounting for 28.1% followed by house wives (23.1%) while the other 23.7% have other source of income.

Majority of patients were in the age category of 55-64 years accounting for 43.8% of the cases and followed by the age category of 45-54 accounting for nearly one third of the cases. The median age of respondents was 53. The age range was 49, the minimum being 29 and the maximum was 78.

Academically one forth (25.7%, n=87 N=338) attended school to level of college/university while majority (38.8%, n= 131, N=338) attended only elementary school level (grade1-8). A total of 26 (7.7%) individual didn't have any formal education. Regarding religion, 191(56.5%) were orthodox Christians followed by Muslims and protestant Christians, accounting 27.5% and 15.1% of the studied cases respectively. All the socio-demographic findings were summarized in the table 1 below.

Table 1Socio-demographic characteristics of selected Type 2 DM patients on follow up at BLH, AA, Ethiopia, **(N=338).**

Variables	Category	Frequency	Percent
Sex	Female	147	43.5
	Male	191	56.5
Marital status	Unmarried	36	10.7
	Married	264	78.1
	Divorced	18	5.3
	Widowed	20	5.9
Religion	Orthodox	191	56.5
	Muslim	93	27.5
	Protestant	51	15.1
	Other	3	0.9
Educational level	No formal education	26	7.7
	Grade 1-8	131	38.8
	Grade 9-12	94	27.8
	College/university	87	25.7
Occupation	Farmer	48	14.2
	Merchant	37	10.9
	Government employee	95	28.1
	House wife	78	23.1
	Other	80	23.7
Age category	25-34	11	3.3
	35-44	70	20.7
	45-54	98	29.0
	55-64	148	43.8
	>=65	11	3.3
	Total	338	100%

5. 2. Substance use pattern of respondents

Regarding substance use pattern among selected patients in this study, the predominant substance use identified was alcohol use as 28.7% (n=97) of the patients had history of alcohol use previously and 7.5% (n=25) of the studied patients are currently drinking alcohol.

Regarding cigarette smoking a total of 53 patients had history of smoking (of these patients 30 patients used to smoke on daily bases) and additionally seven patients are passive smokers and five patients are still active smokers.

A total of 55 patients from total studied population (16.5%) had been khat chewers but only 7 patients are active khat chewers (2.1%). The behavioral habit of substance use among respondents with type 2 DM are summarized by table 2 below.

Table 2Substance use habit of selected Type 2 DM patients on follow up at BLH, AA, Ethiopia. (N=338).

Variables	Category	Frequency	Percentage
Past smoking history	Daily	23	6.8
	Less than daily	30	8.9
	Total	53	15.7
Current smoking	Almost daily	4	1.2
	Less than daily	1	0.3
	Total	6	1.5%
History of Alcohol drinking	No	241	71.3
	Yes	97	28.7
	Total	338	100.0
Passive smoking	Yes	7	2.1
	No	331	97.9
	Total	338	100.0
Current Active Alcohol drinker	No	313	92.6
	Yes	25	7.4
	Total	338	100.0
Past History of Khat chewing	No	283	83.7
	Yes	55	16.3
	Total	338	100.0
Current active Khat chewing	No	331	97.9
	Yes	7	2.1
	Total	338	100.0

5.3 Clinical characteristics of the respondents

Most of the studied cases (n=229, 67.8%) had lived with diabetes mellitus for 05 years or more since the diagnosis. (The median duration after diagnosis of type II diabetes mellitus was 06 years (range=30, max=31 and min=1 years.) The commonest type of treatment the patients receiving were oral anti-diabetic agents (n=164, 48.5%) followed by combination of oral anti- diabetic agents with insulin therapy (n=111, 32.8%).

A total of 130 patients were hypertensive's, of these 85.3% of were on antihypertensive agents but 10.7% were on life style modification and 3.8% were not started on life style modification nor on medication.

A total of 273 (80.7%) patients had unhealthy Waist for hip ratio, of these 43.2% were females (n=118) and males accounted for the majority of the cases with abnormal waist for hip ratio of ≥0.95. (n=155, 56.77%).

Table 3 Clinical characteristics of selected type 2 DM patients on follow up at BLH,AA, Ethiopia.(N=338).

Variables	category	Frequency	Percent
Duration of diabetes	less than five years	109	32.2
	five and above years	229	67.8
Type of treatment for DM	OHA	164	48.5
	Insulin+ OHA	63	18.6
	Insulin only	111	32.8
Treatment of hypertension	on antihypertensives	111	85.3
	on life style modifications	14	10.7
	has never been on treatment	5	3.8
WHR Female	≤0.85	29	19.7
	>0.85	118	80.2
WHR Male	≤0.9	36	18.8
	>0.9	155	81.1
Statin therapy	Yes	107	31.7
	No	155	45.9

5.4. Complications of type 2 DM related complications among the respondents

Among the respondents 75.1% of patients had episodes of moderate hypoglycemia and 22.8% of patients had episodes of severe hypoglycemia where they needed support of other individuals to correct their status in the last 01 year before data collection.

Among the chronic complications peripheral neuropathy was the commonest finding (32.2%) followed by Diabetic kidney disease which accounted for 19.7% of the cases.

Table 4 DM related complications of selected type 2 DM patients on follow up at BLH, AA, Ethiopia. (N=338).

Variables	Category	Frequency	Percent
Control of DM over the last 03 months	Good control	93	27.5
	Poorly controlled	245	72.5
Diabetic neuropathy	No	229	67.8
	Yes	109	32.2
Cardiovascular diseases	No	271	80.2
	Yes	67	19.8
Diabetic kidney disease	No	271	80.2
	Yes	67	19.8
Diabetic eye disease	No	247	73.1
	Yes	91	26.9
Diabetic foot	No	310	91.7
	Yes	28	8.3
Episodes of severe hypoglycemia	No	274	81.1
	Yes	64	18.9
Episodes of moderate hypoglycemia	No	254	75.1
	Yes	84	24.9

5.5. Socio-demographic and clinical characteristics of respondents with NCI

Overall a total of 131 patients had neurocognitive impairment (38.75%). Among group of respondents having NCI 61 patients were females accounting 46.56% of the cases and the remaining are males (43.3%, n=70). Regarding the age category among patients with NCI, the majority are in the age category of 55-64 years (54.19%, n=71) followed by age category of 45-54(29% (n=38) while there is no cases with NCI in the age category of 25-35years. Only 2 patients with NCI are in the age category of >=65.

Regarding the residential areas, 63.3 % of patients with NCI are urban dwellers while the remaining lives in rural area. Most of respondents with NCI are Christian orthodox religion followers (n=69, 52.6%) followed by Muslim religion followers (40, 30.53%) Regarding educational level and occupation, those who have attended school to grade 8 only (n=72, 54.96%) and government employees (n=34, 25.95%) have highest number of neuro-cognitive impairment respectively.

Table 5 sociodemographic parameters with respect to neurocognitive status of selected T2DM patients on follow-up at BLH, AA, Ethiopia (N=338)

Socio-demographics variables	Category	NCI		Total
		No	Yes	
Sex of the patient	Female	86 (41.5%)	61 (46.56%)	147
	Male	121(58.5%)	70 (53.4%)	191
Age category of the patient	25-34	11 (5.3%)	0 (0.00%)	11
	35-44	50 (24.2%)	20 (14.49)	70
	45-54	60 (29%)	38 (29%)	98
	55-64	77 (37.2%)	71 (54.19%)	148
	>=65	9 (4.3%)	2 (1.44%)	11
Residential place	Urban	169 (81.6%)	83 (63.4%)	252
	Rural	38 (18.4%)	48 (36.6%)	86
Religion of the patient	Orthodox	122 (58.9%)	69 (52.6%)	191
	Muslim	53 (25.6%)	40 (30.535)	93
	Protestant	30 (14.5%)	21 (15.21%)	51
	Other	2 (1%)	1 (0.76%)	3
Occupation of the patient	Farmer	21 (10.1%)	27 (20.6%)	48
	Merchant	26(12.6%)	11 (8.39%)	37
	Government Employee	61 (29.5%)	34 (25.95%)	95
	House Wife	39 (18.8%)	39 (29.77%)	78
	Other	60 (29%)	20 (15.26%)	80
Educational level	No Formal Education	16 (7.7%)	10 (7.6%)	26
	Grade 1-8	62 (30%)	72 (54.96%)	134
	Grade 9-12	62 (30%)	31 (23.66%)	93
	College/University	67 (32.4%)	18 (13.74%)	85
Marital status of the patient	Unmarried	29 (14%)	7 (5.3%)	36
	Married	156 (75.4%)	108 (82.4%)	264
	Divorced	11 (5.3%)	7 (5.3%)	18
	Widowed	11 (5.3%)	9 (6.9%)	20

5.6 Behavioral characteristics of patients with NCI

Among patients with NCI with respect to previous substance use, the majority had previous history of alcohol drinking (n=36, 27.48%) followed by khat chewing (n=17, 12.97%). Currently only 7 patients are alcohol drinkers while 2 patients are still active khat chewers among the respondents with NCI.

Table 6 behavioral characteristics of selected type 2 DM patients with NCI on follow up at BLH, AA, Ethiopia. (N=338).

Variables		NCI		
		No	Yes	Total
Past history smoking	No	170 (82.1%)	115(87.8%)	285
	Yes	37 (17.9%)	16 (12.2%)	53
Active current smokers	No	203 (98.1%)	129 (98.5%)	332
	Yes	4 (1.9%)	2 (1.5%)	6
Passive smokers	No	204 (98.6%)	127(96.9%)	331
	Yes	3 (1.4%)	4 (3.1%)	7
Past history of alcohol drinking	No	146 (70.5%)	95(72.5%)	241
	Yes	61 (29.5%)	36 (27.5%)	97
Current alcohol drinker	No	189 (91.3%)	124 (94.7%)	313
	Yes	18 (8.7%)	7 (5.3%0	25
Past history of khat chewing	No	169 (81.6%)	114 (87%)	283
	Yes	38 (18.4%)	17 (13%)	55
Current khat chewing	No	202 (97.6%)	129 (98.5%)	331
	Yes	5 (2.4%)	2 (1.5%)	7

5.7 Clinical characteristics of patients with NCI

Majority of patients with NCI had been diabetic for more than five years (n=91, 69.46%) and the most of the patients (n=79, 60.3%) were receiving OHA alone for treatment followed by insulin therapy alone (n=29, 22.9%). As a coexisting co morbidities nearly one third of patients with NCI (30.53 %, n=40) had hypertension additionally 29% of patients are on statin therapy regardless of the indication. .

The clinical characteristics of T2DM respondents with respect to NCI have been summarized in cross-tabulation below.

Table 7 Clinical characteristics of selected type 2 DM patients with NCI on follow up at BLH, AA, Ethiopia. (N=338).

Variables	Category	No NCI	NCI	total
Duration of diabetes	less than five years	69 (33.3%)	40 (30.5%)	109
	five and above years	138 (66.7%)	91 (69.5%)	229
Type of treatment for DM	Insulin	82 (39.6%)	29 (22.1%)	111
	OHA	85 (41.1%)	79 (60.3%)	164
	Insulin+ OHA	40 (19.3%)	23 (17.6%)	63
Control of DM	good control	68 ((32.9%)	25 (19.1%)	93
	poorly controlled	139 (67.1%)	106 (80.9%)	245
History of hypertension	NO	117 (56.5%)	91(69.46%)	208
	Yes	90 (43.5%)	40(30.5%)	130
Treatment of hypertension	on antihypertensive	76 (84.4%)	35 (87.5%)	111
	life style modification only	11 (12.2%)	3 (7.5%)	14
	has never been on treatment	3 (3.3%)	2 (5%)	5
Statin therapy	No	150 (72.5%)	93 (71%)	243
	Yes	57 (27.5%)	38 (29%)	95

5.8 Acute and chronic DM related Complications of patients with NCI

Among the respondents with NCI the majority had diabetic eye disease (35.9 %) followed by peripheral neuropathy (33.6%) from the chronic complications. Nearly 1 out of 3 patients had moderate hypoglycemia in the last 01 year before data collection but only 19.1% had one or more episodes of severe symptomatic hypoglycemia. The complications of T2DM respondents with respect to NCI are summarized in the table below

Table 8 DM related complications of selected type 2 DM patients with NCI on follow up at BLH,AA, Ethiopia.(N=338).

Variables	Category	No NCI	NCI	total
Diabetic eye complications	No	163 (78.7%)	84 (64.1%)	247
	Yes	44 (21.3%)	47 (35.9%0	91
Diabetic nephropathy	No	168 (81.2%)	103 (78.6%)	271
	Yes	39 (18.8%)	28 (21.4%)	67
Diabetic foot disease	No	190 (91.8%)	120 ((91.6%)	310
	Yes	17 (8.2%)	11 (8.4%)	28
Cardiovascular diseases	No	162 (78.3%)	109 (83.2%)	271
	Yes	45 (21.7%)	22 (16.8%)	67
Diabetic neuropathy	No	142 (68.6%)	87 (66.4%)	229
	Yes	65 (31.4%)	44 (33.6%)	109
Clinical episodes of severe hypoglycemia	No	168 (81.2%)	106 (80.9%)	274
	Yes	39 (18.8%)	25 (19.1%)	64
Clinical episodes of moderate hypoglycemia	No	155 (74.9%)	99 (75.6%)	254
	Yes	52 (25.1%)	32 (24.4%)	84

5.9 Determinants of neurocognitive impairments

5.5.9 Socio-demographic factors

On binary logistic regression was used to see possible determinants of NCI in respondents with NCI. Accordingly, bivarable logistic regression showed that educational level and place of residence had overall statistically significant association with neurocognitive impairment. On sociodemographic analysis, the elementary level of education (grade 1-8) [OR=4.32, 95% CI (2.322- 8.046)] is significantly associated with neurocognitive impairment when compared to higher level of education (college/university). From Residential places, being rural dweller, was also statistically associated with increased risk of impairment [OR=2.572, 95% CI (1.560-4.241)] on bivariable analysis.

Table 9 Socio-demographic determinants of neurocognitive impairments of selected type 2 DM patients with NCI on follow up at BLH, AA, and Ethiopia. (N=338).

Variable	Category	NCI		Crude OR(95%CI)	P-Value
		No	*yes*		
sex	female	*86*	*61*	0.816 (0.525-1.267)	0.365
	Male	*121*	*70*		
Age	25-34	11	0	1	
	35-44	50	20	0.000-	0.999
	45-54	60	38	1.8 (0.357-9.073)	0.476
	55-64	77	71	2.85(0.584-13.908)	0.195
	≥65	9	2	4.14(0.867-19.86)	0.075
Occupation	Farmer	21	27	1	
	Merchant	26	11	3.857 (1.799-8.268)	0.001
	Gov't employee	61	34	1.269 (0.533-3.023)	0.59
	House wife	39	39	1.672(0.867-3.227)	0.125
	Other	60	20	3 (1.53-5.88)	0.001
Education	No formal education	16	10	2.326,(0.903-5.992)	0.08
	Grade 1-8	62	72	4.323,(2.322-8.046)*	<0.001
	Grade 9-12	62	31	1.861(0.947-3.658)	0.072
	College/University	67	18	1	
Residence	Urban	169	83	1	
	Rural	38	48	2.043,(1.560-4.241) *	<0.001

Note: * = significantly associated at p<0.05, 1.0=reference

5.9.2 Type of treatment the patient receiving with respect NCI

Regarding type of treatment for diabetes, those patients who were on oral hypoglycemic agents (oral anti-diabetic agents) as sole means of treatment for DM [OR=0.615, 95% CI (0.316-1.196)] and insulin and OHA combined [OR=1.616 95% CI (0.889-2.938)] were also statistically significant on bivariable analysis

Variable	**Category**	**NCI**		**Crude OR (95%CI)**	**P-Value**
Type of treatment		***No***	***Yes***		
	Insulin	82	29	1	0.001
	OHA	85	79	0.615 (0.316-1.196) *	
	OHA & insulin	40	23	1.616(0.889-2.938) *	

Note: * = significantly associated at p<0.05, 1.0=reference

5.9.3 Hypertension and anti-hypertensives with respect to NCI

On bivariable analysis respondents who were hypertensives [OR=0.571, 95% CI (0.571, 0.360-0.907) and paradoxically patients who were on anti-hypertensives doesn't have significant association as a protective factor for neurocognitive impairment

Variable	Category	NCI		Crude OR (95%CI)	P-Value
		No	*Yes*		
Hypertension	No	117	91	1	0.018
	yes	90	40	0.571, (0.360-0.907) *	
Anti-hypertensives	No	14	5	1.289,(0.431-3.861)	0.65
	yes	76	35	1	

Note: * = significantly associated at p<0.05, 1.0=reference

5.9.4 Chronic complications of diabetes

Among chronic complications of DM diabetic eye diseases was the only complication which was statistically significant [OR=2.073, 95% CI (1.272-3.377)] on bivariable regression analysis with increased odds of neurocognitive impairment.

Variable	Category	NCI		Crude OR (95%CI)	P-Value
		Yes	*No*		
Diabetic eye diseases	Yes	47	44	2.073, (1.272-3.377)*	0.003
	No	64	163	1	

Note: * = significantly associated at p<0.05, 1.0=reference

5.9.4 Duration of T2DM since diagnosis and glycemic control with respect to NCI

On bivariable logistic analysis total duration of DM since diagnosis (OR=2.379, 95% CI (1.266-4.472) and overall control of DM [OR= 2.250, (1.317-3.843)] has significant association with neurocognitive impairment.

Variable	Category	NCI		Crude OR (95%CI)	P-Value
		Yes	*No*		
Total duration of DM	≥5	91	138	2.379, (1.266-4.472) *	0.007
	<5	40	69	1	
Overall control of DM	Good control	25	68	1	0.003
	Not controlled	106	139	2.250, (1.317-3.843)*	

Note: * = significantly associated at p<0.05, 1.0=reference

5.10 Determinants of neurocognitive impairments after adjusting for possible confounding factors

On multivariable logistic regression educational level, age, residential place from socio-demographic variables remain statically significant. Total duration of DM since diagnosis, over all glycemic control of DM, type of treatment and presence of diabetic eye diseases have significant association with presence of NCI among respondents.

Table 10 determinants of neurocognitive impairments after adjusting for possible confounders in patients with NCI on follow up at BLH, AA, Ethiopia. (N=338).

Variables	Category	Crude OR (95%CI)	AOR (95%CI)	P- value
Control of DM	Poorly controlled	2.250, (1.317-3.843)*	2.21(1.238-3.947)	0.007
	Well controlled	1		
Hypertension	No	1	1	
	Yes	0.571, (0.360-0.907) *	0.53(0.314-0.918)	0.023
Type of Treatment	Insulin	1	1	0.002
	OHA	0.615 (0.316-1.196) *	0.786(0.370-1.669)	0.531
	OHA & insulin therapy	1.616(0.889-2.938) *	1.87(1.054-4.264)	0.035
Duration	<5	1	1	
	≥5	2.379, (1.266-4.472) *	1.95(0.987-3.877)	0.045
Educational	No formal education	2.326,(0.903-5.992)	1.39(0.497-3.938)	0.525
	Elementary school	4.323,(2.322-8.046)*	3.65(1.855-7.188)	0.000
	High school	1.861(0.947-3.658) *	1.68(0.818-3.452)	0.157
	College/university	1	1	
Residency	Urban	1	1	
	Rural	2.043,(1.560-4.241) *	1.56(0.865-2.816)	0.139
Diabetic eye complications	No	1	1	
	Yes	2.073, (1.272-3.377)*	1.84(1.056-3.229)	0.031

Note: * = significantly associated at p<0.05, 1.0=reference

CHAPTER SIX: DISCUSSION

In this hospital based cross sectional study, overall prevalence of Neurocognitive impairment among patients with Type 2 DM who are on follow-up at BLH is 38.75%. This prevalence of NCI is higher than the one reported from the same hospital (BLH), which reported the prevalence of NCI in T2DM to be 25%. The same study has revealed that the prevalence is higher when corrected for academic level of the respondents. From another cross sectional hospital based study done at black lion specialized hospital, the overall prevalence of NCI was reported to be 45% which is higher than the prevalence this study revealed. A study done at Jimma University Medical College showed the prevalence of NCI among patients with T2DM to be 53.3% which is also higher than the finding of this study. (27, 31)

The prevalence of NCI reported from countries other than Ethiopia are comparable with the results of this study including the study from Kenyatta Hospital of Kenya where the prevalence of NCI was reported to be 32%, and the study done in Nigeria showed prevalence to be 40% (25, 26.)

Unlike study done at Jimma University specialized Hospital, in this study, there is no strong association between age and decline in cognitive and executive function in patients with T2DM. The study done at black lion specialized hospital has also revealed that there is no significant association between increasing age and neurocognitive impairment when adjusted for confounding factors. Similarly, the study done at Netherland and Egypt didn't show any association between age and NCI. (26, 30, 31, 66)

According to this study, the major socio-demographic factor which is associated with neurocognitive impairment was educational level (low level of education). Similar to this study, a study done at TASH and JUMC has clearly showed much increased odds of having impairments among those who attended low level of education. Similarly a Nigerian study which demonstrated attribution of low education attainment to cognitive impairment. (25, 31)

Unlike the effect of acute hyperinsulinemia which might have beneficial effects on cognition, persistently high levels of circulating insulin might have negative impact on memory and other cognitive functions and OHA (oral anti-diabetic agents) also reduces progress of cognitive impairment in T2DM. Accordingly this study has found that, of types of treatments used to treat

DM, patients on oral hypoglycemic agents as a sole treatment for diabetes or combined with insulin were found to have better performance on neurocognitive function than those on insulin only therapies. Findings from other studies also support the finding including; a systemic review of 15 articles on progress of cognitive impairment in diabetic patients showed oral OHA reduced the risk of progression. Additionally, data derived from Sydney memory and ageing study also revealed that of OHAs, metformin specifically was related with slower decline in cognition. (9, 67, 68, 69)

As per this study some microvascular complications of DM, namely diabetic eye diseases, is associated with neurocognitive impairment. There are plenty of studies that showed the association of chronic diabetes related microvascular and macrovascular complications and cognitive impairments. Additionally, Edinburgh Type 2 diabetic study has found that Participants with moderate-to-severe retinopathy had the worst performances on the individual neurocognitive tests even after controlling for other predictors. This relationship supports the hypothesis that NCI has some microvascular component. The other study conducted by Chicago University showed participants with diabetic retinal disease had a 42% increased risk of incident dementia. (22, 75, 76, 77).

Total duration of DM since diagnosis is one of predictor for development of NCI according to this study. This finding was supported by the same results of studies reported from Cairo and Egypt. But these results contradict with the findings from studies done at Jimma University Medical College and Black Lion Specialized Hospital. (27, 29, 30, 31)

As per this study Respondents with Poor glycemic control (hypoglycemia and hyperglycemia combined) had higher odds of NCI when compared to those who had better glycemic control. in support of this finding, an Indian hospital based study has showed that poor glycemic control has strong association with Neurocognitive impairment. (29)

Chapter Seven: Limitations

The study some has limitations due to its inherent nature of being cross sectional study including difficulty of establishing cause effect relationship. There was also lack of full documentations for some respondents as some of investigations were not fully documented on the electronic medical record of the patients. For this, the investigators had no control over the quality or completeness of the data since it was primarily clinical data, not originally recorded for research purposes but for patient care. There were also diagnostic limitations as some investigations were not done universally for all patients (24hr urine protein, ECG, Echo). The study was primarily based on clinical parameters for detection of neurocognitive impairment and it was not meant to exclude possible causative or co-existing organic causes of decline in cognition/executive functions. Additionally the study is also subjected to recall bias.

CHAPTER EIGHT: CONCLUSION

The overall prevalence of neurocognitive impairment among type 2 diabetic patients on follow up at black lion specialized hospital was 38.75%. From Sociodemographic parameters residential area of patient and relatively low level of education were associated with increased odds of encountering cognitive impairments, while some clinical characteristics like being on oral hypoglycemic agents, when compared with being on insulin only, were associated with decreased likelihood of cognitive impairments in among respondents. From chronic complications diabetic eye disease is also associated with higher odds of cognitive impairments. From clinical characteristics being hypertensive, poorly controlled DM, long duration of DM since diagnosis were also associated with Neurocognitive impairment.

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Annex I: Questionnaires-English

Questionnaires to assess the prevalence of neurocognitive impairment and associated factors among diabetic patients on follow up at diabetic clinic, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July 15- August 30, 2021.

Code of interviewee : _____

Address : Region _____District (Woreda) (sub city) _____Town _____

Name of Interviewer: _____

Name of Supervisor: _____

Informed Consent Form

You will be invited to participate in neurocognitive impairment among type 2 diabetes mellitus. This informed consent form provides you with some information. Please read the following information and decide whether to participate in this study.

The main purpose of this study is to assess the overall prevalence of neurocognitive impairment and associated factors among diabetic patients on follow up at diabetic clinic, Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from July 15- August 30, 2021.The survey will be conducted via face-to-face interviews and by reviewing patients' records. The interview will last about 30 minutes.

The information that will be obtained in this survey is only for scientific research without any commercial interests. All our team members are required to keep your personal information confidential and not disclose it to anyone outside the study group without your permission.

Whether or not to participate in the research is entirely up to you. If you have any questions about this research, you can ask the researcher. You can also refuse to participate in the study or withdraw from the study at any time during the study, which will not affect your relationship with the researcher and will not affect your rights.

If you agree to this study, please sign your name below (If you can't sign, you can assign one of your family members or our investigator to sign it).

Signature:-
Date:-

Questionnaires to assess socio-demographic characteristics of type 2 diabetic patients on follow up at diabetic clinic, TASH

S. No	Question	Answer	Skip
1	Age	_____	
2	Gender	1. Female 2. Male	
3	Residence	1. Urban 2. Rural	
4	Marital status	1. Unmarried 2. Married 3. Divorced 4. Widowed	
5	Religion	1. Orthodox 2. Muslim 3. Wakeffana 4. Protestant 5. Other	
6	Educational level	1. Grade 1-4 2. Grade 5-8 3. Grade 9-12	

		4. College/university	
7	Occupation	1. Farmer 2. Merchant 3. Gov't employee 4. Housewife 5. Others	
8	Income	_____	
9	Ethnicity	1. Oromo 2. Amhara 3. Guraghe 4. Tigre 5. Others	

Questionnaires to assess life style of type 2 diabetic patients on follow up at diabetic clinic, TASH

S. No	**Question**	**Answer**		**Skip**
1	Do you have past history of smoking?	1.Yes 2.No		
		If yes, you used to smoke	1.Daily 2.less than daily	
	Are you currently smoking	1.Yes 2.No		

	tobacco?	If yes, you smoke	1.Daily 2.less than daily
	Anyone who smokes at home?	1.Yes 2.No	
		If yes, how frequent?	1.Daily 2.less than daily
2	Did you ever drink alcohol?	1.Yes 2.No	
	Are you currently drinking alcohol?	1.Yes 2.No	
		If yes, what kind of alcohol you usually drink?	1. local arake 2. tella 3. beer 4. other_____
		How many bottles /melekia /kubaya per week?	local arake____ tella_____ beer_____ other_____
3	Have you ever chewed khat?	1.Yes 2.No	
	Are you currently chewing khat?	1.Yes 2.No	

Questionnaires to assess complications (acute and chronic) among type 2 diabetic patients on follow up at diabetic clinic, TASH

S. No	Question	Answer	Skip
1	When you were first diagnosed with DM?	___yrs	
2	Type of treatment patient receiving?	1. Insulin 3. Insulin & OHA 2. OHA 4. none	
3	Is the patient on statins	1. Yes 2. No If yes, type of statin____ _____mg	
4	History of hypertension	1. Yes 2. No If yes 1. On anti-HTN 2. On life style modification 3. Not on any medication	
5	To what extent can you tell by your symptoms that your blood glucose is LOW?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Always	
6	How many times have you had a severe hypoglycemic episode (where you needed someone's help and were unable to treat yourself)?	Since the last visit ____ times In the last year ____ times	
7	How many times have you had a moderate hypoglycemic episode (where you could not	Since the last visit ____ times	

	think clearly, properly control your body, had to stop what you were doing, but you were still able to treat yourself)?	In the last year ____ times
8	How often do you carry a snack or glucose tablets (or gel) with you to treat low blood glucose?	1. Never 2. Rarely 3. Sometimes 4. Often 5. Almost always
9	In a typical week, how many times will your blood glucose go below 70 mg/dL?	_____ per week
10	Average FBS on SMBG over the past 03 months	_____

Mini-Mental State Examination (MMSE)

Patient's card number_____

Questions	**Max. Score**	**Patient's Score**	**Skip**
"What is the year? Season? Date? Day? Month?"			
"Where are we now? State? County? Town/city? Hospital? Floor?"			
The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible			
"I would like you to count backward from 100 by sevens." (93, 86, 79, 72,			

65...) Alternative: “Spell WORLD backwards.” (D-L-R-O-W)

“Earlier I told you the names of three things. Can you tell me what those were?”

Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.

“Repeat the phrase: ‘No ifs, ands, or buts.’”

“Take the paper in your right hand, fold it in half, and put it on the floor.” (The examiner gives the patient a piece of blank paper.)

“Please read this and do what it says.” (Written instruction is “Close your eyes.”)

“Make up and write a sentence about anything.” (This sentence must contain a noun and a verb.)

“Please copy this picture.” (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)

TOTAL	30		

Annex I: Questionnaires-Afan Oromo

Dadhabina(rakkoo) sammuu"neurocognitive impairment" namoota dhibee sukkaaraa gosa lammaffaatiin" type 2 DM" hospitaala Xiquur Anbasaatti hordoffii gochaa jiran irratti mul'atu, Caamsaa 1 hanga Caamsaa 30tti qorachuuf gaaffilee bocaman.

Koodii afgaaffichaa : _____

Teessoo : Naannoo_____Aanaa _____Magaalaa _____

Maqaa nama afgaaffii godhuu: _____

Maqaa suupparvaayizaaraa: _____

Haayyama gaafatamuu

Haayyama gaafatamuu fi waa'ee qorannicha kanaa "prevalence neurocognitive impairment and associated factors among diabetic patients on follow up at diabetic clinic, TASH, AA, Ethiopia from July 15-August 15, 2021" ilaalchisee wantoota armaan gaditti eeraman erga dubbistee booda waan hubatterratti hundaa'uun qorannicha irratti mirga hirmaachuu fi hirmaachuu dhiisuu guutuu qabdu.

Kaayyoon qorannaa kanaa dadhabina (rakkoo) sammuu dukkuba sukkaaraa gosa lammaaffaan wal-qabatee muudatu hubachuuf qorannaa namoota sababa dhukkuba kanaan (dhukkuba sukkaraa gosa lammaffaa) finfinnee hospitaala xiquur anbassa hordoffii godhan irratti adeemsifame yoo ta'u; qorannoon kun afgaaffiilee fi ragaalee kaardii dhukkubsattootaa irraa funaanaman irratti kan hundaa'u ta'a. Afgaaffileen kunniin naannoo daqiiqaa soddomaa fudhatu.

Ragaaleen qorannoo kanarraa argaman fedhii daldalaaf kan hin ollee fi qorannoo saayintifikaa qofaaf ta'uu ibsuu barbaanna. Ragaaleen isinirraa fi kaardilee keessanirraa funaanaman namoota qorannicha gageessaa jiraniin alattii namoota biraatti kan hin himamnee fi iccitiidhan kan qabamu ta'uu isiniif mirkaneessuu barbaanna.

Qorannoo kanarratti hirmaachuu fi hirmaachuu dhiisuuf mirga guutu qabdu. Qorannicha ilaalchisee gaaffiilee qabdan kamuu qorataadhaf dhiyeessuu dandeessu. Erga qorannichi jalqabees mirga qorannich addaan kutuu guutuu qabdu. Murteen isin murteessitan kamuu hariiroo keessanii fi qorataa irratti dhiibbaa kamuu akka hin qabaanne isinii mirkaneessuu barbaadana.

Qorannoo kanarratti hirmaachuuf haayyamama ta'uu koo mallattoo kootin niin mirkaneessa.

Mallattoo: _____
Guyyaa: _____

Haala hawaasummaa, diinagdee fi ragaalee dimogiraafii biroo dhukkubsattoota sukkaaraa gosa lamaffaa Magalaa finfinneetti, hospitala xiquur Anbassatti hordoffiirra jiran qoo'achuuf gaaffilee qophaa'an.

Lakk.	Gaaffilee	Deebii	Irra darbi
1	Umurii_____	25-29 50-54 30-34 55-59 35-39 60-64 40-44 ≥65 45-49	
2	Saala	1. Dubara 2. Dhiira	
3	Bakka jireenyaa	1. Magaala 2. Baadiyyaa	
4	Haala fuudhaa/Heerumaa	1. Kan hin fuune/heerumne 2. Kan fuudhe/heerume 3. Kan hiike/hiikte 4. Kan abbaan/haati manaa irraa du'e/duute	
5	Amantii	1. Ortodoksii 2. Musliima 3. Waqeeffannaa 4. Protestaantii 5. Kan biraa	
6	Sadarkaa barnootaa	1. Kutaa 1-4 2. Kutaa 5-8	

		3. Kutaa 9-12 4. Koollejjii/Yunivarrsiitii	
7	Hojii	1. Qotee bulaa 2. Daldalaa 3. Hojjataa mootummaa 4. Hojii mana keessaa 5. Kan biraa	
8	Galii(Birriidhan)	1. <500 2. 500-1000 3. 1001-1500 4. ≥1500	
9	Saba	1. Oromoo 2. Amaara 3. Guraagee 4. Tigree 5. Kan biraa	

Gaaffilee haala jireenyaa dhukkubsattoota sukkaara gosa lammaffaa magalaa Finfinne, hospiitaala xiquur Anbassatti hordoffii irra jiran gaafachuuf qophaa'e.

Lakk.	**Gaaffilee**	**Deebii**		**Irra darbi**
1	Tamboo ni arsitaa?	1.Eeyyee 2.Lakki		
		Eeyyee yoo jette guyyuu xuuxxaa?	1.Guyyuu 2.Darbee darbee	
	Kanaan dura xuuxaa	1.Eeyyee 2.Lakki		

	turtee?	Eeyyee yoo jette guyyuu xuuxaa turtee?	1.Guyyuu guyyuun 2.Darbee darbee
	Mana keessaa namni xuuxu jiraa?	1.Eeyyee 2.Lakki	
		Eeyyee yoo jette guyyuu xuuxaa/xuuxxii?	1.Guyyuu guyyuun 2.Darbee darbee
2	Alkoolii dhugdee beektaa?	1.Eeyyee 2.Lakki	
	Alkoolii ni dhugdaa?	1.Eeyyee 2.Lakki	
		Eeyyee yoo jette yeroo baay'ee gosa alkoolii kam dhugda?	1. Araqaa 2. Farsoo 3. Biiraa 4. Kan biraa___
		Torbanitti hammam dhugda?	Araqee____ Farsoo_____ Biiraa_____ Kan biraa_____
3	Jimaa qamatee beektaa?	1.Eeyyee 2.Lakki	
	Jimaa ni qamaataa?	1.Eeyyee 2.Lakki	

Rakkoolee dhibee sukkaaraan wal-qabatan yeroo gabaabaa fi dheeraa dhukkubsattoota sukkaaraa gosa lammaffaa magalaa finfinnee, hospitaala xiquur Anbassattii hordoffiirra jiran muudatuu malan qo'achuuf gaaffiilee qophaa'an.

Lakk.	Gaaffilee	Deebii	Irra darbi
1	Dhukkuba sukkaaraa qabaachuu yoom barte?	Waggaa____	
2	Gosa daawwaa fudhachaa jirtuu	1. Insuliinii 2. Kiniinii dhibee sukkaaraa 3. Insuliinii fi kininii 4. Homaa hin fudhadhu	
3	Qorricha kolostoroolii hir'isu ni fudhattuu?	1. Eeyyee 2. Lakki Eeyye yoo jettan Gosa qorichaa___ Mg_____	
4	Dhibee dhiibbaa dhiigaa qabduu?	1. Eeyyee 2. Lakki Eeyyee yoo jettan 1. Qoricha fudhachaan jira 2. Wantoota qorichaan alaatti dhibbaa dhiigaa hir'isanin gochaa jira 3. Homaa fudhachaa hin jiru.	
5	Mallattoolee hanqina sukkaaraa sirratti mul'ataniirratti hundaa'uun rakkoo hanqina sukkaraa kee akkamiin ibsita?	1. Tasumaa 5. Yeroo hundaa 2. Yeroo tokko 3. Darbee darbe 4. Yeroo baay'ee	

6	Yeroo meeqa rakkoon hanqina sukkaraa hamaan si muudate (yeroo itti of wal'aanuu dadhabdee gargaarsa si barbaachise)?	Edda baallama kanaan duraatii___ Waggaa darbe keessa____
7	Yeroo meeqa rakkoon hanqina sukkaraa giddu galeessi si muudate (qajeellootti yaaduu fi qaama kee too'achuu dadhabuu, Garuu ammoo of yaaluu danda'uu)?	Edda baallama kanaan duraatii___ Waggaa darbe keessa____
8	Rakkoo hanqina sukkaraa sodaachuurraa kan ka'e yeroo meeqa nyaata/karamellaa/sukkaara qabattee baata?	1. Tasumaa 2. Yeroo tokko 3. Darbee darbe 4. Yeroo baay'ee 5. Yeroo hundaa
9	Torbanitti (torban ayyaanaan alatti) yeroo meeqa sukkaarri kee 70mg/dL gadii ta'a?	Torbanitti yeroo____
10	Avreejii sukkaara ji'oota 3 darban otuu hin	nyaatiin manatti safaramee _____

Safartoo rakkoo sammuu-Mini-Mental State Examination (MMSE)

Lakkoofsa kaardii_____

Gaaffilee	**Qabxii guddaa**	**Qabxii dhu-kkubsataa**	**Irra darbi**
"Waggaan kuni maali? Maqaa waqtii? Guyyaa lakkoofsaan? Maqaa guyyaa? Maqaa ji'aa?"			
"Ammaan tana eessa jirra? Maqaa naannoo? Maqaa godinaa? Maqaa mgaalaa? Maqaa hospitaalaa? Maqaa kutaa (yuunitichaa)?"			
Wantoota armaan gadii ani isiniif eeru kanniin, erga dhageeffattanii booda irra deebitanii jettu. Wantootni ani eeru yoo isiniif hin galle ta'e, irra isiniif deebi'uun danda'a.			
KONKOLAATAA, HOOLAA, UTUBAA			
Lakkoofsa dhibbarraa torba torbaan hir'isaa duubatti lakkaa'aa (fakkeenya isiniif eeruun danda'a). Yookan ammoo yoo barnoota qabaattanii fi ni beektu ta'e, jecha "rirma" jedhu duubatti dubbisaa			
Armaan olitti, wantoota sadi isiniif eereen ture irra deebitanii natti himuu dandeessuu?			
Wantootan isinitti mul'isu ykn agarsiisu kanniin maqaa naaf dhahaa (Sa'aatii harkaa fi qalama itti mul'isi)			
Gaalee kana na waliin jedhaa: 'yoo ta'es, ta'uu baates, haa ta'u"			
Waraqaan isinitti kennu kana harka mirgaatin olkaasaa,			

walakkatti dachaasaatii lafa kaa'aa. Wanta kanaan gaditti barreefame dubbisaatii, waan barreeffamichi isin ajaju raawwadhaa (Himni ajaa "Ija keessan cufadhaa") "Hima maqaa fi gocha of keessa qabu ijaaraa. Himicha waa'ee waan barbaaddanii ta'uu danda'a. Fakkeenya isiniif eeruun danda'a. Waraqaan isiniif kennurratti fakkiin armaan gadii akkuma mulátu kanatti fakkeessaa kaasaa 			
Qabxii waliigalaa	30		

Annex II: Data registration checklist

Instructions:-Dear data collector the objective of this study is to assess neurocognitive function and associated factors among type 2 diabetic patients on follow up at diabetic clinic, TASH. The results of the study will help as to see the predictors of neurocognitive impairments among type 2 diabetic patients in our study area. So you are kindly requested to revise each chart thoroughly and record on the designed check list.

We kindly request you to fill the provided boxes/spaces clearly.

Part I: Identification, anthropometric measurement and blood pressure of the study participants

1. Research code _____
2. Card number _____
3. WHR _____
4. Blood Pressure_____

Part II: Any documented complications

A. Chronic Complications

1. Diabetic nephropathy□ 2. Diabetic eye complications □
3. Diabetic foot □ 4. Cardiovascular complications□
5. Diabetic neuropathy□ 6. None□
7. Others (specify) _____

B. Episodes (documented) of acute complication in past 03 months

1. Hypoglycemia _____ 2. HHS_____

Part III: Investigations

A. For patients not on statins

1. LDL _____2. HDL_____3. Triglycerides_____4. Total Cholesterol_____

B. For all patients

5. HgA1C_____

6. FBS (in mg/dL) over the past 03 months, _____, _____, _____

Echocardiography(commented by either Radiologist or Cardiologist)_____
_____
_____
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_____

ECG(commented by either Internist or Cardiologist)_____
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