JIMMA UNIVERSITY
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Neurovascular Diseases of The Lower Extremity and Their Predictors Among Type II Diabetes Mellitus at Jimma University Medical Center, Ethiopia, 2024

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ABSTRACT

Background: Poorly controlled diabetic mellitus has a devastating impact on peripheral nerves and blood vessels and even with good management options, complete prevention remains an ongoing challenge, particularly in T2DM. Thus, researchers need to evaluate the occurrence of neurovascular diseases and predictors of peripheral neuropathy and peripheral arterial in T2DM.
Objective: To determine the prevalence of neurovascular diseases of the lower extremity and their predictors among T2DM at Jimma University Medical Center, 2024.

Materials and Methods: A cross-sectional design with sequential sampling was utilized. the Michigan Neuropathy Screening Index for diagnosing peripheral neuropathy as well as the Edinburgh Claudication Questionnaires in conjunction with the ankle-brachial index to screen peripheral arterial disease. Data were collected via structured face-to-face interviews, anthropometric measurements, and immuno-hematological parameters using the Kobo Toolbox. The descriptive study was followed by bivariate and multivariate regression adjustments, with a 95% confidence interval, and at P-values < 0.25 and <0.05 respectively, utilizing SPSS v27.

Results: The study included 336 T2DM with response rates of 95.8% (322). The majority were male 187(57.9%), females 135(41.8%), and their mean age was (49±16 years). The prevalence of Peripheral neuropathy, Peripheral arterial disease, and Neurovascular disease of the lower extremity was 57.6%, 55.1%, and 76.1%, respectively. Older age (40-49 years, OR:5.43; >50 years, OR:5.52), longer duration of T2DM (5-10 years, OR:4.65; >10, OR:7.72), lower high-density lipoprotein (OR:10.16), increased fasting blood sugar (OR=5.79), elevated glycated hemoglobin (OR:1.55), poor self-care (OR:19.51), and elevated Neutrophil-to-lymphocyte ratio (OR=2.33) were associated to peripheral neuropathy. whereas, urban dwellers (OR:2.00), longer duration of T2DM(5–10years, OR:2.31;>10 years, OR:2.72), elevated glycated hemoglobin (AO: 1.94),Lower high-density lipoprotein (OR:2.90), poor self-care (OR:3.37), elevated platelets-to-lymphocyte ratio(OR:1.17), and increased waist circumference (OR:1.19) were identified risks of Peripheral arterial disease.

Conclusion and Recommendations: The prevalence of diabetes-induced neurovascular diseases of the lower extremity among T2DM was high. Older age, urban residents, prolonged duration, hyperglycemia, dyslipidemia, central obesity, poor self-care, and low-grade inflammation were significant risk factors. Therefore, healthcare professionals should prioritize regular screening for peripheral neuropathy and peripheral arterial disease, early risk factors identification, and implementing interventions such as diabetes self-care educations, frequent monitoring, and early treatment initiation accordingly.

Keywords: Peripheral neuropathy, Peripheral arterial disease, Neurovascular diseases, T2DM, Predictors.

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ABBREVIATIONS AND ACRONYMS

ABI	Ankle-brachial index
ADA	American Diabetes Association
BMI	Body mass index
DFD	Diabetic foot disease
DFU	Diabetic foot ulcers
DM	Diabetics mellitus
DPN	Diabetic peripheral neuropathy
FBS	Fasting blood sugar
HbAlc	Glycated hemoglobin
HDL-C	High-density lipoprotein cholesterol
IDF	International diabetic federation
JUMC	Jimma University Medical Center
LDL-C	Low-density lipoprotein cholesterol
NLED	Neurovascular lower extremity disease
NLR	Neutrophil lymphocyte ratio
OxLDL-C	Oxidation of LDL-C
OxHDL-C	Oxidation of HDL-C
PAD	Peripheral arterial disease
PLR	Platelets lymphocyte ratio
T2DM	Type II diabetic mellitus
TGs	Triglycerides
WC	Waist circumference
WHR	waist-hip ratio

CHAPTER ONE: INTRODUCTIONS

1.1. Background

Diabetic mellitus is a group of metabolic disorders defined as persistent hyperglycemia brought on by insulin defects that affect the metabolism of fat, carbohydrates, and proteins (1). Poorly managed diabetic mellitus progresses to both sudden and chronic/recurring complications. This leads to debilitating vasculopathy, as for chronic complications, both macro- and micro-vascular complications, which impair large, medium, and small-sized blood vessels and nerve cells, were common (2,3).

Diabetic vasculopathy encompasses micro-vascular and macro-vascular complications, posing significant global health concerns since they threaten peripheral nerves and blood vessels. Persistent hyperglycemia and dyslipidemia/hyperlipidemia can directly damage nerve cells through oxidation and glycation while also affecting the inner lining of blood vessels (endothelium) over time, leading to endothelial dysfunction. Chronic inflammation further compromises blood flow to the lower limb, resulting in both neurovascular (especially peripheral neuropathy and peripheral arterial disease) and cerebrovascular complications. Moreover, diabetic cholesterol issues and endothelial dysfunction can advance to atherosclerosis and the formation of plaques, affecting medium- to-large sized blood vessels (4,5).

Diabetic neurovascular diseases of the lower extremities are chronic complications resulting from progressive damage to both blood vessels and injury to nerve function in the legs and feet. The conditions of diabetic peripheral neuropathy(DPN), according to “international consensus guidelines, define DPN as the presence of symptoms or signs of peripheral nerve dysfunction in patients with diabetes after all other causes have been ruled out”. Peripheral arterial disease involves the narrowing or blockage of arteries that supply blood to the legs or feet, leading to reduced blood flow in the lower extremities. Hyperglycemia/dyslipidemia damages the endothelial lining of blood vessels, and platelet activation along with nerve injury contributes to atherosclerosis. The central pathophysiology of PAD in T2DM (5–8).

The development of diabetic-induced neurovascular diseases was multifactorial and involved a combination of (1). Excessive alternative glucose metabolism pathways like the polyol pathway and advanced glycation end product [AGE] (2). Vascular abnormalities such as endothelial dysfunction and atherosclerosis. (3).Neurodystrophic conditions like NGF and decreased IGF (4). Autoimmune injury of nerve tissue (5). Genetic susceptibility (9–11).

Dyslipidemia is a typical medical condition due to consistent economic growth, urbanization, and undesirable dietary patterns. Increased TG and low HDL-C levels; small, dense LDL-C, elevated triglyceride particles have potential atherogenic in T2DM; also, lipid causes oxidative pressure, followed by increased expression of pro-inflammatory cytokines and neuronal apoptosis, which causes neuropathy (4,12–14).

Research has shown that diabetic mellitus is a disease of chronic inflammation and immune system dysfunction, in which its onset is subtle and its progression is slow. Low-grade chronic inflammation is known as a slow-silent killer among chronically ill people, particularly among those with T2DM. On top of its` inevitable effect, the contributions of low-grade inflammation to diabetic-induced peripheral complications were neglected. Thus, platelets lymphocyte ratio [PLR] and the neutrophil-lymphocyte ratio [NLR] were novel hematological surrogate markers for chronic inflammation and endothelial dysfunctions; they could be an integral part of the pathogenesis of PAD, DPN, and progression to DFU (15–18).

Besides poorly controlled T2DM, even with good progress in the control of diabetes mellitus and novel therapeutic options for type II diabetes mellitus, neurovascular complications cannot be fully prevented. Therefore, this study aims to assess the impact and identify risk factors for diabetes-induced peripheral neuropathy and peripheral arterial disease in individuals with T2DM. Various validated screening techniques, such as the Michigan neuropathy screening index, the ankle-brachial index, and the Edinburgh claudication questionnaires, are utilized to detect peripheral neuropathy and peripheral arterial disease, respectively (19,20).

To control debilitating complications such as diabetes-induced foot diseases, increased risk of amputations, elevated cardiovascular morbidity, compromised quality of life, and reduced life expectancy in the general population, screening T2DM and identifying aggravating factors is crucial (21).

1.2. Statement of the problem

The globe has faced a diabetic mellitus pandemic, and it is a disease of the 21st century. The current global prevalence of diabetes mellitus [DM] was 6.1%, 10.5% of which was T2DM, comprising 98% of DM cases. The prevalence of T2DM was reported in South America in 2019 (8.0%), North America in 2020 (11.4%), Europe in 2019 (6.2%), Asia in 2020 (10.9%), and Africa in 2021 (5.0%). In our country, Ethiopia, the prevalence ranged from 2% to 6.5%, and T2DM was 5.2% (22–25).

T2DM was attributed to 12.2% of all global deaths between the ages of 20 and 79 years and 32.6% of all deaths occurring in the productive age group. The African region, especially Sub-Saharan Africa (SSA), was largely inflicted; the International Diabetes Federation reported an estimated 416,163 diabetes-related deaths(26,27).

Diabetic-induced neuropathy is a global healthcare problem for both developed and developing countries. It was the most commonly prevailing chronic complication in T2DM than T1DM, whose estimated prevalence varied from 22–46.5% among type II diabetes globally; in Africa, it was 22–66%. It accounted for 80% of foot ulcerations and 50–60% of non-traumatic limb amputations performed due to diabetic neuropathy, and the problem had been growing (28,29).

Furthermore, patients with distal symmetric sensory peripheral neuropathy [DPN] often suffer from loss or absence of protective sensation, balance, and gait abnormalities, increased risk of foot injuries, and delayed wound healing, which can go unnoticed and untreated, leading to further complications like foot infections, risk of foot ulcerations, disrupted sleep patterns, reduced quality of life, and increased cost of treatments (30–33).

The incidence of DPN in patients with T2DM by treating hyperglycemia yields only a 5–7% reduction; however, it was 50–70% in patients with T1DM. Despite strict glucose control, more than 40% of diabetes patients were eventually diagnosed with peripheral neuropathy, suggesting that hyperglycemia was not the sole instigator of DPN (34–36).

The prevalence of diabetic mellitus [T2DM], along with the incidence of peripheral arterial disease (PAD), has become alarming over the last decades. The worldwide prevalence of PAD was 200 million, which is estimated to range from 20% to 50%; 7–12 million affected

individuals were in the United States; in Africa, 39%–52%; and in Ethiopia, it ranged from 27%–56% (24,37–41).

“Peripheral arterial disease poses a significant challenge in individuals with diabetes’’, as it restricts blood flow to the lower extremities, causing leg pain, non-healing wounds, intermittent claudication, critical limb ischemia, and an increased risk of limb amputation. In additions, the disease affected men, women, and children of all ages in every country, and within the next thirty years, the disease was rising rapidly, which is not only alarming but also challenging for every health system in the world (37,42,43).

T2DM and its consequences also had a significant socio-economic impact on people, families, and governments. Since it was a major cause of productivity loss, morbidities, premature mortality, and increased healthcare utilization, such as having more outpatient visits, a higher probability of being hospitalized, and increased use of more medications. T2DM and its complications like DPN, and PAD also, drive escalating costs of diabetes management, patients’ social incapability, and financial burden on the healthcare system (37,44)

Diabetic-induced lower extremity complications were rising in the world and affecting about 131 million people worldwide, with a global estimate of 1.8%. This means that every 20 seconds, someone loses a leg to T2DM somewhere in the world. 80% of non-traumatic limb amputations were due to T2DM, of which 85% were due to DFU. In Africa, the mortality rate in those late with infection and gangrene is 55%, often leading to limb-threatening conditions like disability, delayed wound healing, being prone to infections, and ulcers in legs and feet (21,45–47).

DFUs were a serious worldwide problem; lifetime risk and burden were high in low- to middle-income countries, and an earlier suggestion was that diabetic neuropathy was mainly responsible, whereas the paradigm shifts to the increasing preponderance of ischemic or neuro-ischemic foot ulcers. However, PAD was underdiagnosed and mainly untreated among Africans, both in ulcer and non-ulcer T2DM (1,45,46,48).

Ethiopia was one of the top four leading sub-Saharan countries after Nigeria in experiencing DM burden and devastating DM complications since the prevalence of T2DM in Ethiopia was rising faster. Besides, DPN ranges from 22.5% to 53.6%. Even if, a lot has been tried to alleviate T2DM exacerbations, neurovascular disease of the lower extremities is still increasing (49,50).

According to a systematic review conducted in 2021 in various regions of Ethiopia, the prevalence of DPN was Addis Ababa(23%), Oromia (27%), southern nation nationalities (16%), and Amhara (15%). Studies done in 2019, 2020, and 2021 in Addis Ababa, Debra Tabor, and Wolaita reported prevalence of PAD as 35.9%, 30.7%, and 27.3%, respectively. Age, duration, poor glycemic control, and dyslipidemia were commonly identified contributors (51–53).

In our country, mortality rate in-hospital was high, ranging from 2% to 21%. Since uncontrolled blood glucose sugar is not the sole determinant, central obesity, dyslipidemia, low-grade chronic inflammation, genetic susceptibility to complications, hypertension, and sedentary lifestyle might be non-glycemic, potentially worsening factors even in those under routine treatment (54–58). Besides, A 2023 meta-analysis study reported that the major predictors of lower extremity amputation (LEA) were DPN, PAD, and obesity. However, there were limited screening studies on how they were prevalent in the study area (49,55).

According to a 2019 JUMC investigation on DFUs; DPN and PAD were prospective risk factors (60). Most patients with PAD are asymptomatic, and might not complain of intermittent claudication due to late clinical manifestations, and diminished pain sensitivity. Due to this, PAD is an underestimated and untreatable in T2DM. As far as we know, there was little information about potential risk factors of diabetic-induced neurovascular disorders of the lower limbs, especially DPN and PAD, in the target population. The prevalence of DPN has been unknown in the same study area since 2018(61), and the prevalence of PAD was hardly known. Besides, the overall occurrence of neurovascular disease in the lower limb was also, unknown.

Therefore, the focus of the current study was to examine the following: the prevalence of DPN, the prevalence of PAD, and the overall prevalence of neurovascular disease and the impact of a biochemical test, diabetic self-care practices, central and general obesity, and low-grade chronic inflammation newly assessed. Moreover, diabetes/clinical information, and socio demographic factors related to diabetes, including medication adherence, and chronic disease comorbidities were also, studied. This study also aimed to close the information gaps on disease prevalence, variables gap, point prevalence variation in earlier researches, and short reporting times.

1.3. Significance of the study

Since this study aimed to assess the prevalence of diabetic peripheral neuropathy and peripheral arterial disease, together with risk factors, in particular, the impacts of biochemical test, hematological parameters and other factors like clinical/diabetes information, behavioral factors such as diabetic self-care, and anthropometric measurement of general and central obesity, were assessed. It is anticipated that the current study's findings will reduce the gap on prevalence and aggravating factors of DPN, PAD, and their overall occurrences in the lower limb (neurovascular diseases).

Besides, covering laboratory costs, it creates awareness and additional knowledge for the study participants. It will also serve medical professionals to create more precise and efficient screening, preventing, risk identifying, and treating diabetes-induced neurovascular disease of the lower limb. Additionally, it will be an asset for researchers as current/existing literature and establish a foundation for future research in related areas.

CHAPTER TWO: LITERATURE REVIEW

2.1. Introduction to Diabetic Mellitus

Diabetes mellitus and its complications pose a major threat to public health throughout the world. According to the International Diabetes Federation (IDF) Diabetes Atlas, the prevalence of diabetes for 2021, projected to 2030 and 2045, for adults aged 20–79 years is estimated to be 537 million, 643 million, and 783 million, respectively. Of these, 80% of these people live in low- or middle-income countries. Thus, the number of people with diabetes is estimated to increase by 46%. In African countries, the magnitude of DM in 2021, 2030, and 2045 ranges from 24 million, 33 million, and 55 million, respectively, with a 134% increase (62,63).

In South America, the prevalence of diabetic peripheral neuropathy ranged from 6.0% to 81.0% in six studies, and the prevalence of peripheral artery disease ranged from 10.0% to 29.0% in Australia. The prevalence of diabetic peripheral neuropathy across African countries over the most recent twenty years has been 84.7% in Tanzania, 68.2% in Sudan, 69% in Egypt, 42% in Libya, 24.9% in Uganda, and 72.0% in Senegal. The prevalence of peripheral arterial disease in Africa went from 20.0% to 55.0%. DFU are mainly associated with DPN and PAD, and DPN is the most common cause of diabetic foot ulcers (63,64).

2.2. Prevalence of Diabetic Peripheral Neuropathy in Type II Diabetes Mellitus

According to a descriptive study in Bokhara, Nepal, the 2018 prevalence of DPN was 45.45% among diabetes, and in the same study period in Jordan, the overall prevalence of DPN based on the MNSI tool was 39.5% among T2DM. In a study in Baltimore in 2019, peripheral neuropathy was estimated to be 51% among adults with T2DM (57,65,66).

A hospital-based study conducted in Larkana, Pakistan, in 2020 reported the severity of peripheral neuropathy was 72.2% of whom 55% were severe, 19% were moderate, and 26% were mild among Puducherry, India, 2021, using MNSI diagnostic criteria reported as DPN was 31.1%, and also, a study in Bushehr, Iran, 2022 reported as DPN in T2DM was 26.2%; on the same period, Beijing, China, 2022 among diabetes was 23.5% and PAD as 11.6% (67–70).

A facility study in Aden, Yemen, in 2019 and Cairo, Egypt, in 2020 reported DPN in 60.48% and 46%, respectively, and also in Damietta, Egypt, in 2021, the severity of peripheral neuropathy was mild(11.7%), moderate(56.7%), and severe(31.7%) of T2DM patients (71,72)

A facility-based cross-sectional study conducted in Paramour Benin in 2015 reported distal sensory polyneuropathy in diabetes as prevalent at 88.7%. In Khartoum, Sudan in 2017, found that peripheral neuropathy was observed in 50% of diabetes patients. Additionally, an institutional study in Lurks, Bosnia, in 2022 concluded that the prevalence of DPN with type II DM using nylon monofilament was 24.2%. In a community-based study in Kampala, Uganda, in 2023, it was reported that the prevalence of DPN was 65.8%. Additionally, 44.8% of participants had mild DPN, 42.4% had moderate DPN, and 12.8% had severe DPN (34,73–75).

2.3. Prevalence of Peripheral arterial disease among Type II Diabetes Mellitus

In 2016 and 2022, a prospective descriptive study was done in Kolkata, India, on people with T2DM. The prevalence of PAD was found by measuring ABI with a handheld Doppler and ABI radiologically with Duplex Ultrasonography was 25% and 72.2%, respectively (76,77).

According to a study conducted in Trujillo, Peru, in 2017, the prevalence of PAD was 40% in 322 T2DM patients, and in Colombo, Sri Lanka, in 2019, among T2DM patients, the reported prevalence of PAD was 15.3%. In another study in coastal Karnataka in 2019, the prevalence of PAD was found to be 8.52% as ABI was done on 317 T2DM (78–80).

In 2018, a cross-sectional prospective study was done in Wenzhou, China. A study using more accurate and noninvasive duplex ultrasonography found that 80.9% of individuals with T2DM had PAD(81). Health facility-based studies were conducted in Rawalpindi, Mardan, and Peshawar, Pakistan, in 2016, 2020, and 2023. Measurements were taken in a supine position using a hand-held Doppler ankle-brachial index. The ABI for the last two studies among individuals with T2DM was 77.6%, 57.8%, and 43.6%, respectively (82–84).

Institution-based studies in Lagos, Nigeria, 2015; Lokoja, Nigeria, 2016; Northern Nigeria, 2020; and south-west Nigeria, 2020, stated that the prevalence of PAD in T2DM used ABI as a

diagnostic tool, and Doppler added that in the last study, 40%, 22.0%, 48.5%, and 59.5%, respectively (20,79,85–87).

2.4. Prevalence of Peripheral Neuropathy and Peripheral arterial disease among T2DM patients in Ethiopia.

In an institution-based study in Bahir Dar, Ethiopia, in 2017, the overall prevalence of peripheral sensory neuropathy among 368 DM was found to be 52.2%. An institution-based study at Jimma in 2019 reported that the prevalence of DPN was 53.6% among 366 T2DM. According to this study, age above 40 years, above 50 years, duration of diabetes above 5 years, duration above 10 years, physical inactivity, and smoking (current smoker; former smoker) were independent predictors of DPN among study participants (61,88,89).

The study conducted on the prevalence of PAD at Tikur Anbessa Specialized Hospital, Ethiopia, in 2019 reported 34.2%. In the same study area, in 2020, the prevalence of DPN among people with diabetes was 56.8% vs. 43.2% (90). Again, in 2021, the prevalence of diabetic PAD in people with diabetes was 32.6%, and also, in the same area, 2022 indicated diabetic neuropathy was as common as 47.5% (91–93).According to a study done in Debra Tabor, Ethiopia, in 2020, the prevalence of PAD in this study was 30.7% among T2DM (94). Another study in 2021 found that the prevalence of PAD diabetes in southern Ethiopia was 32.6% (95).

2.5. Factors Associated with Peripheral Neuropathy and Peripheral Arterial Disease in T2DM

2.5.1. Socio-demographic factors

An institution-based study was conducted in Bahir Dar, in 2017 and JUMC, in 2019 in DPN concluded older age patients and longer duration since DM diagnosis were significant predictors among diabetes individuals (61,96).

2.5. 2. Biochemical parameters

Lipid profile and blood plasma glucose test

In a meta-analysis study done in Hunan, China, in 2021, diabetic neuropathy patients showed higher TG and lower HDL levels than controls. In a study in Iran in 2022, HbA1c,

hyperlipidemia, and hypertension were associated with the prevalence of DPN. Furthermore, people with higher TG and LDL levels had a higher risk of DPN (48,69).

A multi-center study in Beijing in 2022 concluded that risk factors for DPN included: age ≥40 years, ≥10+year duration of diabetes, a body mass index of <18.5 kg/m2 or ≥24 kg/m2, a systolic blood pressure (SBP) of ≥140 mm Hg, a hemoglobin A1c (HbA1c) level of ≥7%, and PAD are also risk factors for PAD, including a 15+ year diabetes duration, a body mass index of <18.5 kg/m2, an SBP of ≥140 mm Hg, and an HbA1c level of ≥7% (68).

On analysis of PAD in Gujrat, 2015, patients were found to have ABI>1, and factors like total cholesterol, triglyceride, and low-density lipoprotein (LDL) were noted to be higher than those for patients having ABI<1, which was statistically and positively associated with significant value for the development of PAD. In Pakistan, the prevalence of peripheral vascular disease [PVD] was stratified as smoking, hypertension, obesity, and hypercholesterolemia to determine if there was any association between these and peripheral vascular disease (97,98).

A study in Rawalpindi, Pakistan, in 2021 stated that there is a significant increase in triglyceride levels and a decrease in high-density lipoprotein cholesterol in patients with diabetic peripheral neuropathy as compared to healthy controls (99,100).

2.5.3. Anthropo-behavioral and clinical information

Anthropometric parameters and clinical factors

In Ecuador, 2020. The prevalence of PAD was 13.98%, and the use of metformin plus insulin, higher HgA1C, and duration of DM are significant factors. Bali, Indonesia, 2021 NLR in uncontrolled type 2 DM was significantly higher than in controlled type 2 DM, and in India in 2023, subjects with higher BMI (overweight and obesity), types of diabetes, diabetic neuropathy, and foot self-care practice were factors significantly associated with diabetes (29,101–103).

In Bahir Dar, Ethiopia, 2017 major factors of DNP identified were age >50 years, overweight and obese; duration of DM; not involved in physical exercise; and male gender. A study done in Addis Ababa identified factors like age, duration of diabetes, poor blood glucose control, hypertension, and dyslipidemia (96,104).

In Bahir Dar, Ethiopia, in 2017, the major factors of DNP identified were age >50 years, overweight and obesity, duration of DM, not being involved in physical exercise and male gender. A study done in Addis Ababa identified factors like age, duration of diabetes, poor blood glucose control, hypertension, and dyslipidemia (95,105).

A study in Jimma, Ethiopia, in 2019 and another study conducted in Debre Tabor, Ethiopia, in 2020 reported that increasing age, duration, high HbA1c, and being a cigarette smoker increased the likelihood of developing peripheral arterial disease and peripheral neuropathy (106,107). A comparative study conducted in Addis Ababa, Ethiopia, in 2022 reported that NLR was significantly higher and associated with DPN than non-DPN in T2DM patients. Therefore, NLR is considered a predictor and a prognostic biomarker of DPN (17).

Behavioral factors, diabetes information, and immune-hematological parameters

A study done in Australia in 2020 concluded that T2DM was an independent and strong predictor of LDL-C (108). Other studies report that predominant lesions in T2DM are associated with changes in lipid metabolism. In India in 2023, a study reported that diabetes duration was significantly correlated with DPN and PAD(109–111). According to a systematic review study conducted in Ethiopia, in 2020, among diabetic patients, a high percentage also had poor dietary practices, self-monitoring of blood glucose, physical activity, and diabetic foot care (112).

A cross-sectional study of SDSCA in DPN at St. Paul Hospital Millennium Medical College, Ethiopia, in 2021 reported that diabetes patients with DPN comorbidities have poorer diabetes self-care than those without DPN comorbidities, and another study from Harar, Ethiopia, in 2022 concluded that the burden of chronic complications was high in poor diabetic self-care(113,114).

An institution-based study conducted in Catalia, Italy, in 2020 reported that both neutrophil-lymphocyte ratio [NLR] and platelet lymphocyte ratio [PLR] were repetitive markers of PAD, and a report from Lattakia, Syria, in 2022 concluded that both PLR and NLR were independent risk factors of DPN (18,115).

Conceptual framework

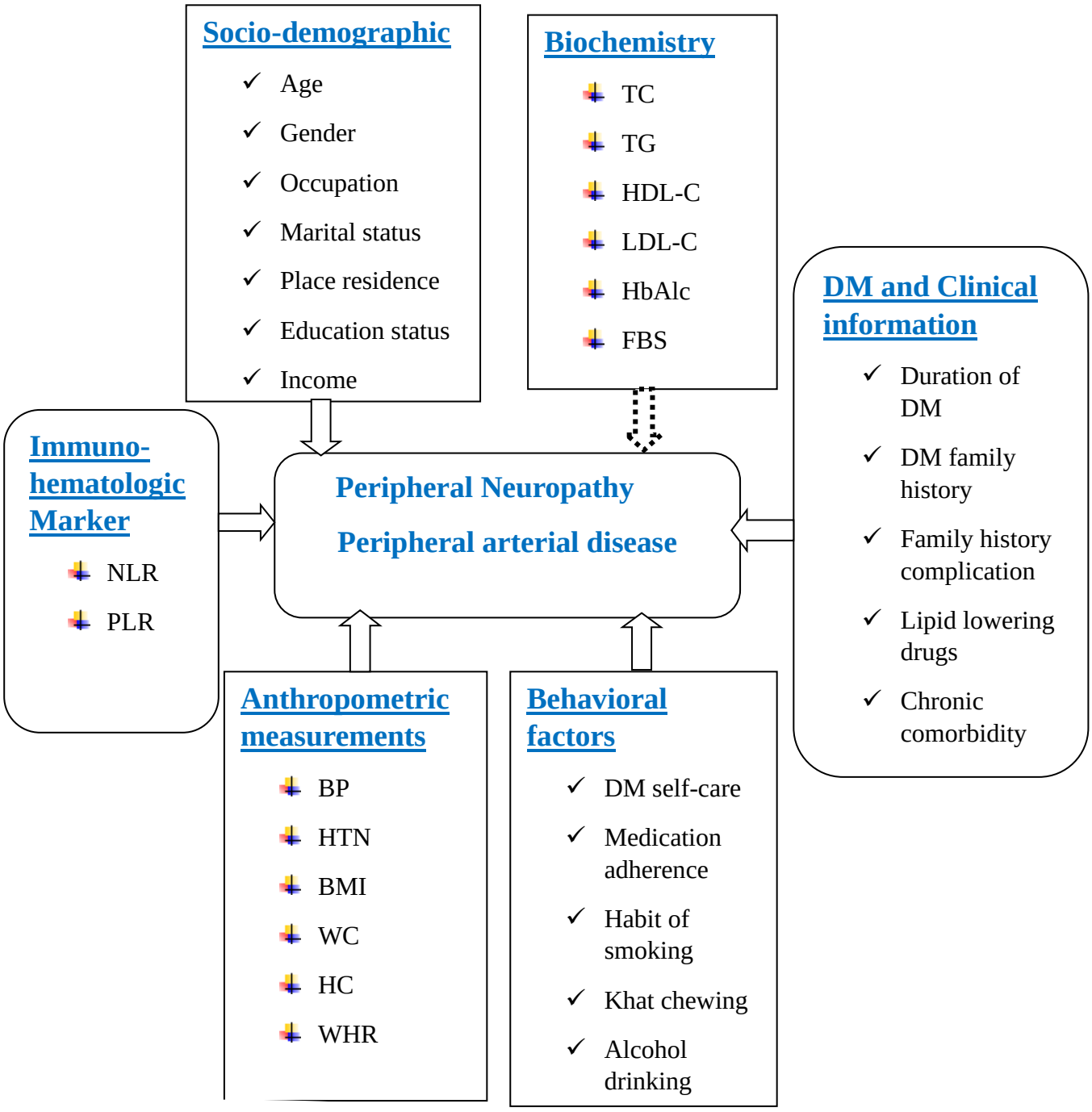

Figure 1 Indicates a conceptual framework designed based on adopted literature of related fields.

CHAPTER THREE: OBJECTIVES

3.1. General Objective

To determine the prevalence of neurovascular diseases of the lower extremity and their predictors among T2DM in follow-up clinic at Jimma University Medical Center, Ethiopia, in 2024.

3.2. Specific Objectives

1. To determine the prevalence of peripheral neuropathy among T2DM at a follow-up clinic in Jimma College Medical Center, Jimma, in 2024.

2. To assess the prevalence of peripheral arterial disease among T2DM at a follow-up clinic in Jimma University Medical Center in 2024.

3. To determine the prevalence of neurovascular disease among T2DM at a follow-up clinic in Jimma College Medical Center, Jimma, in 2024.

4. To assess predictive factors of peripheral neuropathy among T2DM patients at a follow-up clinic in Jimma University Medical Center in 2024.

5. To identify factors that worsen peripheral arterial disease among T2DM at a chronic follow-up clinic in Jimma University Medical Center in 2024.

CHAPTER FOUR: MATERIALS AND METHODS

4.1. Study Area and Study Periods

Jimma is the largest zone in the southwestern Oromia region. It is located in the Jimma zone, a special area within the Oromia region in southwestern Ethiopia, about 220 miles (353 km) to the southwest of Addis Ababa. It is positioned at a latitude of 7040 N and a longitude of 36050 E. Based on the 2007 census conducted by the Central Statistical Agency, this zone has a total population of 3,486,155, an increase of 26.76% over the 1996 census, of 1,750,527 males and 1,735,628 are females, with an area of 15,568.58 km2 (116).

The study was conducted at Jimma University Medical Center, which is one of the oldest public hospitals and the only teaching and referral medical center in the southwestern portion of Ethiopia. JUMC offers a wide range of medical services to the local population of 15 million each year, with 800 beds available in the southwestern region of the country. Service is offered to around 19,000 inpatients,160,000 outpatients attendance, 5000 deliveries, and 11,000 emergency cases annually (117,118).

A chronic follow-up clinic was one of the services provided at JUMC. Approximately 19,000 patients attended regular follow-up clinics, of which around 2256 diabetes patients attended the clinics, 752 diabetes expected in one month, and 1504 diabetes patients were expected in two months at follow-up clinics, as counted from the follow-up record registration book. The study took place between December 15, 2023, and February 20, 2024

4.2. Study Design

A hospital-based cross-sectional study was employed.

4.3. Source Populations

All T2DM attending Jimma University Medical Center.

4.4. Study Population

T2DM adults attend chronic follow-up clinics at Jimma University Medical Center.

4.5. Study Subject

T2DM adults selected according to their routine random attendance at the Jimma University Medical Center follow-up clinic.

4.6. Eligibility Criteria

4.6.1. Inclusion criteria

Type II diabetes patients at the follow-up clinic, according to their random attendance were selected, diabetes patients above 18 years old, on regular follow-up, and residents of Jimma Zone were included.

4.6.2. Exclusion criteria

T2DM patients with lipid profile records greater than one year since the laboratory was done, glycated hemoglobin tests more than three months since last done, those without fasting plasma glucose done on the day of data collection, patients attending follow-up clinics more than once during the data collection period, and patients who were not volunteers or disabled, those with acute inflammation or infections, known hepatic disease patients, those with filariasis or lower limb swelling, gestational diabetes mellitus, pregnant mothers, leprosy, HIV patients, patients with traumatic injury to foot skin, and those with both leg amputation were excluded.

4.7. Sample Size and Sampling Technique

4.7.1. Sample size calculation

Single proportion population sample size was calculated using the epi-info 7.2.5.0 formula.

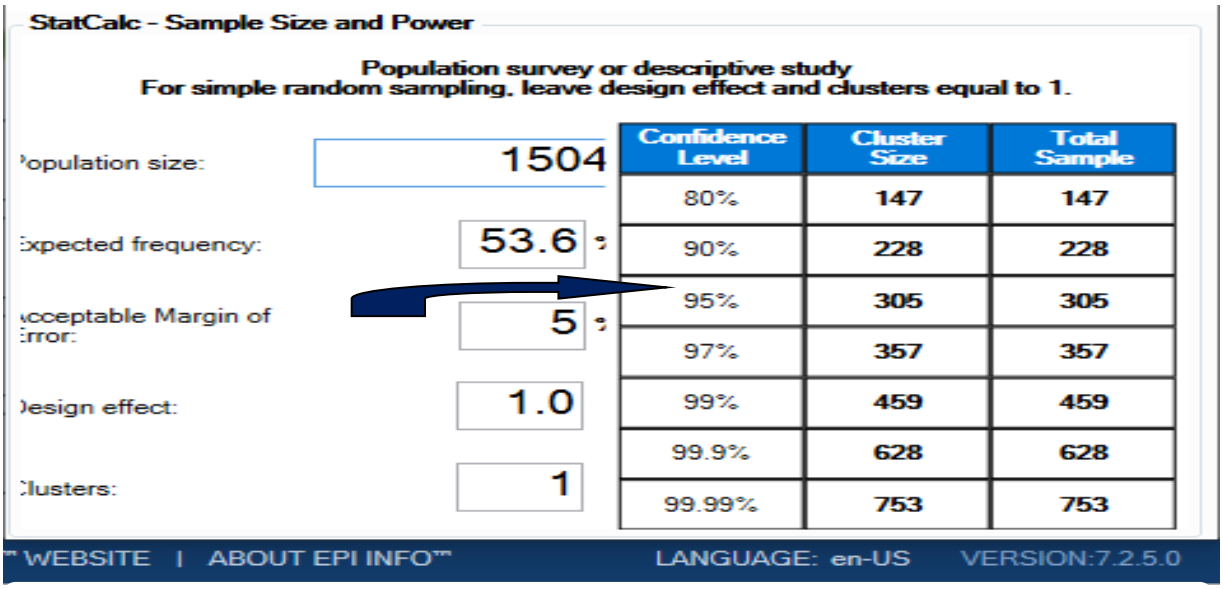

Figure 2. Indicate epi-info version 7.2.5.0 based on sample size estimation for the study population.

The size of the study population [N=1504] and maximum variability from previous studies of the same study area was [p=53.6%](61) using a confidence interval of 95% at a 5% margin of error. The study's sample size was 305, assuming a 10% nonresponse rate [0.1*305 = 30.5~31 and 305+31=336]. Finally, the sample size was [**n=336].**

4.7.2. Sampling technique

For patients who attended a diabetes follow-up clinic and each of them met the inclusion criterion, according to their random attendance [random presentation] at the follow-up clinic; a consecutive/sequential sampling technique was considered and applied.

4.8. Data Collection Tools and Procedures

4.8.1. Data collection instruments/tools

A structured questionnaire was developed, which was adopted from literature related to diabetic-induced neurovascular diseases(10,36,46,58,62,67,87,88,91–93,95,105,108,119–146). Data collection tools had different sections such as socio-demographic, biochemical parameters, hematological parameters, anthropometric measurements, behavioral factors like diabetic self-care and clinical information, and diagnostic tools like the Michigan Neuropathy Screening Index [MNSI], Ankle-brachial Index [ABI], summary of diabetic self-care Activities (SDCSA), Morisky Medicine Adherence Scale (MMAS), and Edinburgh Claudication Questionnaires (ECQ) were adopted to conduct this survey.

4.8.2. Data collection methods

Data were gathered using structured questionnaires through interviews, chart reviews, physical examinations, and measurements of anthropometric and immuno-hematological parameters with internet-based tools created using Kobo Tool Box and collected via Kobo Collect v2023.2.4. Physicians did the Michigan neuropathy screening physical assessment version. However, the ankle-brachial index, anthropometric assessment, summary of diabetic self-care Activities (SDCSA),Morisky Medicine Adherence Scale (MMAS), and Edinburg claudication questionnaires (ECQ) were done and collected by senior nurses at follow-up clinic.

Data collectors received three days of training on how to contact study participants, gather surveys (especially how to use Kobo CollectV2023), and how to transmit data to the primary investigator's server. The investigator and supervisor monitored the data collection process attentively, making sure every day collected data were accurate, comprehensive, and consistent.

4.8.3. Data collection procedures

Diabetic peripheral neuropathy screening procedure

The Michigan Neuropathy Screening Index tool is a validated, noninvasive, and inexpensive measurement tool that evaluates the sensory and motor components of neuropathy. It is a well-known instrument used to assess peripheral neuropathy among patients with type 2 DM, with a sensitivity of 80% and a specificity of 95%. This tool is divided into two sections: a history version with interviewer-administered questionnaires and a physical assessment conducted by a physiotherapist. Nonetheless, in our study, seniors and physicians were considered.

History questionnaires:-

Responses will be tallied to obtain a total score. Each response of "yes" to items 1–3, 5–6, 8–9, 11–12, and 14–15 was counted as 1 point. "No" responses for items 7 and 13 will count as 1 point. Item #4, a measure of diminished circulation, and item #10, a measure of general asthenia, were not included in the scoring. A score greater than seven is indicative of diabetic peripheral neuropathy.

Physical assessment:

Foot inspection: The feet were examined for evidence of extremely dry skin, callous growth, fissures, open ulceration, or abnormalities. Amputation, large metatarsal heads, hammer toes, overlapping toes, hallux valgus, medial convexity (Charcot's foot), and flat feet are examples of deformities.

Vibration sensation: Vibration sensation was assessed bilaterally using 128 HZ by tuning fork the American Diagnostic Corporation (ADC) to detect loss of vibration as placed across the dorsum of the great toe on the bony eminence. The big toe was left unsupported during the vibration sensation evaluation. When they could feel the vibration no more, patients with their eyes closed were asked to respond. Vibration was evaluated as (1). Present if the patient feels the vibration on his or her finger for fewer than 10 seconds (2). Reduced if felt for greater than 10 seconds (3). Absent, if no vibration was felt.

Muscle stretch reflexes: A typical triangular rubber-headed hummer manufactured in China was used to detect the ankle reflexes. If the reflex was obtained, it was scored as present, but the Jendrassic maneuver was instructed to be performed by the patient if there was no reflex, and the responses were classified as "present with reinforcement." If the reflex was absent, even in the face of the Jendrassic technique, the reflex was declared nonexistent.

Monofilament testing: Multiple 5.07/10mg MEDLINE monofilaments manufactured in China were used to detect a decrease in pressure sensation (loss of protective sensation) on the feet. The filament was applied perpendicularly and briefly with uniform pressure. When the filament bends, a force of 10grams is applied. The patient, whose eyes were closed, was asked to respond, yes, if he or she felt the filament. Out of ten applications, eight correctly answered questions were deemed normal; one to seven correctly answered questions indicate decreased sensation and no correctly answered questions indicate absent sensation. Each monofilament was used to evaluate a maximum of 10 patients to avoid over diagnosing mistakes resulting from loss of viscoelasticity owing to frequent buckling. Both feet were independently assessed, and the scores for both feet were put together.

Finally, Peripheral neuropathy was determined by adding together all components of a physical examination score larger than or equal to 2.5 [sign score > 2.5] and/or a history questionnaire score greater than or equal to 7 [symptom score >7]. Furthermore, prior diagnoses of DPNs were also gathered from their medical records and self-reports (148).

Peripheral arterial disease screening process

This procedure was followed by every patient. At first, the patients were made to rest quietly in a supine position before reading. Study employed by mercury sphygmomanometer manufactured in Deka Accoson, England, with suitable cuff size, and required the participants to be positioned either supine or seated. Measurements were taken from the right and left brachial arteries, as well as the dorsalis pedis or posterior tibial arteries of the right and left ankle, to figure out their ankle-brachial index (ABI). A blood pressure cuff was placed over the posterior tibial artery three centimeters above the medial malleolus, with the middle of the bladder placed over the bare ankles, and for the arms, the bottom edge was placed 2.5 cm over the antecubital fossa (149).

By quickly inflating the cuff until the pulse could no longer be felt, the maximum inflation level was ascertained separately for the arm and ankle. The maximal inflation level of 30 mmHg above the audible systolic level was considered. Then the cuff deflated at a rate of roughly 2 mmHg per second until the systolic blood pressure became audible, and the first return sound was recorded as the systolic pressure (150).

Ankle-brachial index [ABI]: ABI was an inexpensive, noninvasive, and reproducible method for assessing lower extremity hemodynamics [peripheral vascular status-PAD], and this was calculated by taking the highest ankle systolic measurement as the numerator and the higher of the two brachial systolic measurements as the denominator after both ankle and brachial blood pressure measurements on sitting or supine position (151).

ABI has a diagnostic accuracy rate range [sensitivity:75-95% vs specificity:70-90%]; even the color Doppler ultrasound has a diagnostic accuracy of 85%, making it a reliable tool for assessing arterial perfusion and diagnosing PAD in clinical practice. According to both standards of the European Vascular Association and the American Diabetes Association [ADA], ABI >1.3 indicates poorly compressible arteries [arterial calcification], $0.9 \leq$ ABI ≥ 1.3 indicates a normal range, and PAD can be diagnosed or abnormal when ABI <0.9. ADA recommends that an ABI test be performed only in T2DM with signs and symptoms of PAD (83,152).

Edinburgh claudication questionnaire(ECQ is a widely used, validated screening tool that evaluates leg symptoms and measures the presence and severity of intermittent claudication, which is the hallmark of peripheral artery disease (PAD), in primary care settings. It has a sensitivity of 50-70% and a specificity of 85-95% for detecting PAD in primary care populations. It consists of a series of five questions and a pain diagram that are self-administered by the patient. Each ECQ-related score is counted as one point if yes to each of [ECQ1, ECQ2, ECQ3, ECQ4], except for ECQ5, which generally continues for less than ten minutes and is counted as one point. The overall score is interpreted as a score: I. Overall scores of zero: No claudication; II. Total Score = 1-2: Mild claudication; and III. A total score of 3-5: Severe claudication.

Using ABI and ECQ in combination can increase the sensitivity, specificity, and accuracy of PAD diagnosis compared to 80-95% of either test. This is so that distinct components of PAD are evaluated by the two tests. While the ECQ measures intermittent claudication symptoms subjectively, the ABI inspects blood flow to the legs objectively. By utilizing both tests, medical professionals can obtain a more complete/accurate view of a patient's PAD status (153,154).

Lipid profile test: Both World Health Organization[WHO] and American Diabetes Association [ADA] suggested lipid profile test screening done at least annually in T2DM (62). Thus, lipid profiles such as total cholesterol [TC], triglycerides [TGs], low-density lipoprotein [LDL-C], and

high-density lipoprotein [HDL-C] measurements collected from patients' records as of the most current, which was less than one year since the last lipid test was done, were utilized.

Calculation of LDL-C and VLDL-C: The LDL cholesterol or any unfilled or unrecorded lipid value was computed using the Fried-Edwald equation. LDL-C=TC-HDL-TG/5, VLDL-C=TG/5. [Only TG<400mg/dl] Third Report of the National Cholesterol Education Program (NCEP) Expert Panel in Adults (Adult Treatment Panel III) Final Report: Low levels of HDL-C are defined as < 40 mg/dl in men and < 50 mg/dl in women. High LDL-C values can be defined as ≥100 mg/dl. Hypercholesterolemia is described TC level of ≥200 mg/dl. Hypertriglyceridemia is again defined as a TG level ≥150 mg/dl. Dyslipidemia is defined as the presence of at least one abnormality in the serum lipid profile [LDL, HDL, TG, TC] (155,156).

Glycated hemoglobin[HbAlc] is a measure of the amount of glucose that is attached to hemoglobin in the red blood cells. It is an average measure of the amount of blood sugar or glucose level over the past 2–3 months. According to the American Diabetic Association, 2023, the normal range for HbAlc is below 5.7%, and controlled blood sugar is recommended to be kept below 7% (157). Thus, in this study, the most recent HbAlc, which was less than three months after being last done, was adopted from the patient's medical records.

A fasting blood sugar test [FBS] is a medical test used to measure glucose or sugar in the blood after an extended period of fasting, usually 8–12 hours. Peripherally small amounts of blood [3-5 ml] were taken from the antecubital vein of the arm after overnight fasting [8–12 hours] and sent for a laboratory analyzer. According to the American Diabetes Association [ADA, 2023], the normal ranges of fasting blood sugar were between 70 and 100 mg/dl. A higher blood sugar level [hyperglycemia] was considered, as FBS was greater than 126 mg/dl (157).

Immuno-hematological parameters:- The collected peripheral blood counts have been reported to have a predictive surrogate effect on low-grade chronic or systemic inflammation. 5 ml of blood was taken from the antecubital vein of patients after consent was given orally, and the dragged blood was centrifuged for about 30 minutes and underwent the Coulter counter method. Blood cell count values, particularly neutrophil count (NC), lymphocyte count (LC), and platelet count (PC), were obtained. Inflammation biomarker ratios like PLR ratio PC to LC, i.e., [PC/LC], and NLR ratio of NC to LC [NC/LC] that accounted as prognostic markers of low-grade chronic inflammation with 90.7% sensitivity and a specificity of 97.6% in T2DM,

including PAD and DPN, were considered. The reference cut-off value considered for NLR prognosis from different studies varies from 2.5–5, and that of PLR was 132.40 (46.79–218.01) (15,155,158,159).

Blood pressure: - systolic and diastolic circulatory pressure levels of the patients (SBP and DBP) were required following 15-30 minutes of rest in a sitting situation from their left arm, while their hands were at the level of their heart using a mercury sphygmomanometer made by deka met Accoson, England with appropriate cuff size. In like manner, the typical SBP and DBP of the two readings recorded as hypertension if SBP ≥ 140, as well as DBP ≥ 90 mmHg, or known hypertensive who had been on antihypertensive drugs, were remembered for the class of patients with hypertension unless normotensive (149,160).

Body mass index [BMI]: -Patients' heights and weights were assessed while they were standing upright using stadiometer in the typical position and just wearing light clothing. A standard height measurement scale of one meter [~0.1m] was approximated by measuring height in centimeters (to the nearest 0.01 cm) via no stretch measuring tape and recording weight in kilograms (to the nearest 0.1 kg). BMI is calculated as [squared height in meters squared divided by deliberate body weight in kilograms]. Participants were assigned to one of the three groups as follows: I. Normal BMI ranges from 18.5-24.59. II. Overweight, BMI = 25 to 29.9 III. BMI (obesity) > 29.9 (157) (161).

Diabetic self-care:- The following five domains of self-care practices—diet, exercise, foot care, blood glucose testing, and medications—are used to assess self-care practice and make up the Rundown Summary of Diabetes Self-Care Activities (SDSCA). We estimated the recurrences of self-care within the last seven days. There are mean values for each domain, with adequate scores arranged above the mean value and unsatisfactory scores, if not precisely equal to the mean value.

Thus, after calculating the average score, patients have a good eating schedule when they score ≥4, acceptable foot care when they score ≥7, good exercise when they score ≥4, and good self-blood glucose testing when they score ≥ 1. If the patient's overall mean score is less than 4, it is categorized as having good self-care practices, and if greater than 4, it is categorized as having poor self-care practices (162).

Adherence to anti-diabetic medications:- Morisky Medicine Adherence Scale(MMAS-4 thing). The scale contains questions requesting that the patient answer "Yes" or "No" to a set of four

inquiries. If patients answered "yes" or “No” to any of the questions, their responses will be coded 1 and 0, respectively. The four items will be added together to get the total score, and if MMAS is 4 (good medication adherence), MMAS is either 2 or 3 (moderate) or 1 (poor) (163).

Waist circumference [WC] and Waist-to-hip ratio [WHR]

Measurement of the waist circumference (in centimeters) was taken halfway between the top of the iliac crest and the bottom edge of the last palpable rib. A measuring tape was used to measure the hip circumference (in centimeters) around the broadest part of the buttocks. By dividing the waist circumference by the hip circumference, WHR is computed. WHR above 0.90 for males and above 0.85 for females is a strong indicator of abdominal obesity, and behavioral variables like smoking, alcohol consumption, and khat chewing were also, assessed based on the WHO stepwise approach for chronic disease. The recommended cutoff waist circumference was 102 cm (40 inches) for men and 88 cm (35 inches) for women, recommended as a cutoff value for increased waist fat accumulation/health risk (164,165)

4.9. Study Variable

4.9.1. Dependent variables

Neurovascular disease of the lower extremity

Peripheral Neuropathy

Peripheral Arterial Disease

4.9.2. Independent variables

Socio-demographic factors

Age Marital status Income

Place of residence Occupation

Gender Education status

Anthropometric measurements

Blood pressure [BP] Body mass index [BMI]

Waist circumference Waist to hip ratio [WHR]

Biochemical profile

Total cholesterol [TC] Low-density lipoprotein [LDL-C]

High-density lipoprotein [HDL-C] Triglyceride [TG]

Glycated hemoglobin[HbAlc] Fasting blood sugar[FBS]

DM and clinical information

Anti-diabetes medications Comorbid Diseases

Hypertension Lipid-lowering drugs

DM Family history Duration since DM diagnosis

Behavioral factors

A habit of smoking Habit khat chewing

Alcohol drinking Medication adherence

Diabetes self-care

Immuno-hematologic parameter

NLR PLR

4.10. Operational Definitions and Standard Definition

Neurovascular disease of the lower extremity is a condition characterized when peripheral neuropathy and/or peripheral arterial disease occurs in the feet or toes of T2DM individuals. It is also known as neurovascular lower extremity disease (NLED) (166).

A. Diagnosis of peripheral arterial disease (PAD): The Edinburgh Claudication Questionnaire item >1 is used to quantify intermittent claudication in combination with the ABI values of less than or equal to 0.9 and/or >1.4 to diagnose peripheral artery disease (167).

B. Diabetic peripheral neuropathy diagnosed based on the MNSI diagnostic criteria; if the score was greater than seven according to the MNSI historic version (symptom score) and/or if the score of the physical examination (sign score) was greater than 2.5 in T2DM (168).

Diabetic foot ulcer is a nontraumatic breaking of the skin of the foot that includes at least the epidermis and/or part of the dermis in type II diabetic mellitus (169).

Fasting blood sugar [FBS] was assumed higher plasma glucose if FBS > 126 mg/dl (63).

Well-controlled glycemic control: According to the American Diabetes Association in known diabetes patients, good glycemic control was whenever the HbA1C level ≤7% (170).

low-grade chronic inflammation:- Leukocyte-derived inflammation biomarkers that show elevated neutrophil-to-lymphocyte ratio(NLR>5.0)and/or elevated platelets-to-lymphocyte ratio (PLR>218.0) are markers of **low-grade chronic inflammation** in diabetes-induced peripheral neuropathy or peripheral arterial disease (18,115).

Foot deformity: Hammer toes, mallet toes, claw toes, hallux valgus, and prominent metatarsal heads are examples of abnormal foot shapes and sizes, as are any of these structural abnormalities in one or both feet (169).

Poor glycemic control in T2DM is said to be poorly managed diabetes mellitus if >7% (170).

Dyslipidemia is defined as the presence of at least one of the previous four lipid abnormalities in the serum lipid profile [LDL, HDL, TG, and TC].

Atherogenic dyslipidemia is defined as a combination of high serum triglyceride ≥ 1.7 mmol/L, high serum LDL cholesterol ≥ 2.6 mmol/L, and low serum HDL cholesterol < 1 mmol/L for men and < 1.30 mmol/L for women (156).

For cigarette smoking status, we included the smoking variable based on its current prevalence in such a way that current smokers and nonsmokers were determined based on whether they currently smoke or not**.**

Diabetic self-care practices are classified as good self-care or poor self-care according to the patient's calculated overall mean score of the dietary plan, physical exercises, self-glucose testing, diabetes medication, and self-foot care less than 4, as having good self-care practice, and if greater than 4, as poor self-care practice (162).

Regular follow-up: a diabetic patient who visited the chronic clinic based on appointments regularly in the previous six months was considered to have a regular follow-up.

Seriously ill patients are those who are unable to communicate and are abnormally conscious.

Comorbidity: the coexistence of two or more related medical conditions or diseases

4.11. Data Quality Control

Before commencing data collection, a pretest was conducted on 5% of the sample size to assess the tools' validity, reliability, data quality, and cultural acceptance. This occurred shortly before the data collection at Shanan Gibe Public Hospital, with no significant alterations made.

Data quality was ensured through standardized collection materials, with the measurement scale aiming for a Cronbach alpha above 0.7. For scales with fewer than ten items, a mean inter-item of 0.2–0.4 was targeted (171). In our investigation, the Edinburgh Claudication Questionnaire [ECQ] and the Michigan Neuropathy Screening Tool demonstrated Cronbach alpha values of 0.825 and 0.856, respectively. Moreover, the Morisky medication adherence tool and the Summary of Diabetic Self-Care Activities tool exhibited Cronbach alpha values of 0.73 and 0.74, respectively.

The tool was initially created in English and validated for the skip condition and validity criteria using the Kobo toolbox. Subsequently, it was fully translated into local languages (Afan Oromo and Amharic), then reconverted to English for clarity and precision in respondents' inquiries, utilizing Google Translation Services. The original and translated questionnaires were compared, and discrepancies were reviewed and resolved accordingly.

A week before data collection, data collectors underwent training on each step of the physical examination procedures. They were thoroughly instructed to adhere strictly to the guidelines during the procedure to minimize interpersonal variations. The same data collectors performed the physical assessments to reduce intra-/interpersonal variation. Additionally, they received training on using the Kobo toolbox and managing data transmission to the server instrument.

Data collectors were also retrained during the data collection period via on-call and supervision. Completed questionnaires were sent by data collectors to the server, either immediately after one patient's data administration was completed or at the end of the day. Every day, investigators checked the collected questionnaire for clarity, consistency, and completeness. As a result, amendments and corrections were made before commencing work on the following day.

4.12. Data Processing and Management

After the data collection period was completed, the data were exported and downloaded from the Kobo Toolbox server in both Excel and SPSS format, and then Excel data was exported and downloaded before being entered into SPSS software. Consecutively, after the SPSS format was displayed, a command was run to combine the SPSS format with Excel data on SPSS software version 27. Finally, data was checked and controlled for any missing values and cleaned from unnecessary data or categories. Variables were coded, recoded, re-categorized, and transformed just before the data analysis phase.

4.13. Data analysis, Presentations, and Interpretations

After controlling the data using various data management methods, both descriptive and inferential analyses were conducted with SPSS version 27. First, descriptive analysis using frequency distributions of variables was done to summarize numerical or diagrammatic data presentation. Frequency tables, graphs, and percentages were utilized to present the univariate analysis and interpret the results accurately. Specifically, the frequency, percentage, or crosstabulation of the variables used to summarize the predictive variables was conducted shortly after measuring the disease prevalence.

The homogeneity test of Chi-Square analysis was used to compare the proportions of categorical variables and their relationships to the research variables. After confirming and validating assumptions like multicollinearity and outliers of logistic regression, we conducted regression analysis with adjustments for confounding variables using sequential bivariate and multivariate analysis (171).

To assess relevant predictive factors related to the study variables, binary logistic regression analysis was used. The robust test and the Lem show-Hosmer test [p-value<0.25] were utilized to validate the model before applying binary logistic regression to identify factors predicting diabetic peripheral neuropathy and peripheral artery disease. Variables with a p-value of <0.05 at 95% confidence interval (CI) were considered statistically significant associations (171).

Moreover, the findings of the epidemiological investigation were analyzed, discussed, summarized, and recommendations were proposed.

4.14. Ethical Consideration

Ethical clearance was obtained from the Ethical Review Board [ERB] of Jimma University, and permission or supportive letters were written to Jimma University Medical Center, Shana Gibe Hospital, and the documentation record office. Data collection began after permission was obtained from the medical director of the hospital and oral informed consent from study participants. Moreover, confidentiality and anonymity were maintained by data collectors and investigators throughout the study period.

4.15. Dissemination of Results

The final report of this study will be communicated to Jimma University Medical Center, the Institute of Health Science and Biomedical Science Department, and the Jimma Zone Health Bureau. This result will also, be presented in a thesis defense, seminars, and probably, at different workshops. Finally, the publication of this finding will be in a reputable journal.

CHAPTER FIVE: RESULTS

5.1. Description of Variables Frequency

5.1.1. Socio-demographic characteristics of participants

The study included a total of 336 individuals diagnosed with Type II diabetes mellitus, with a response rate of 95.8%. Fourteen adults selected as part of the sample were excluded from the study. However, 322 patients, 187(57.9%) male and 135(41.8%) female met the eligibility requirements included in the study.

The participants had a mean age of 49 years with(S.D±16) and were categorized as follows: 148(46.3%) were older than 50 years, 77 (23.9%) were aged 40-49 years, and 64(19.9%) were below thirty years old. Approximately three-fourths of the participants were married 250(77.6%), and two-thirds were urban residents 221(68.6%).

5.1.2. Clinical characteristics and anthropometric parameters of respondents

In the study, 166 individuals (51.4%) had a family history of T2DM. Additionally, the duration of T2DM in the sample was divided into three groups: less than five years (43.2%), 5 to 10 years (24.5%), and over 10 years (32.3%). Two-thirds of the participants had a normal body weight (62.4%), and half of the study sample had comorbidities, with the majority being hypertensive participants (53.3%).

Most research participants had elevated waist-to-hip ratios (WHR) at 281(87.3%), with a mean of 0.97(S.D±0.23), and elevated waist circumferences at 147(45.7%) with a mean of 100.4 cm(S.D±16.5). Diabetes with elevated platelet-to-lymphocyte ratio (PLR) was observed in 60.9% of cases with a mean value of,200.4(S.D±90) while elevated neutrophil-to-lymphocyte ratio (NLR) was present in 56.2% with a mean value of 5.3(S.D±3.5).

5.1.3. Biochemical parameters and behavioral characteristics of respondents

In this study, nearly two-thirds of patients had glycosylated hemoglobin [HbAlc>7%] at 205 (63.7%) and fasting blood sugar [FBS>126 mg/dl] at 177(55%). Their sample mean was 9.6% and 261 mg/dl, respectively. Most individuals had high levels of low-density lipoprotein (LDL-C>100mg/dl) at 288 (89.4%). The study participants also had lower levels of high-density lipoprotein (HDL-C<40mg/dl), elevated triglycerides (Tg>150mg/dl), and increased total cholesterol (TC>200mg/dl) at 201(62.4%), 208(64.6%), and 204(63.4%), respectively.

Sixty percent of individuals with type II diabetes mellitus had poor diabetes self-care (196 out of 322), and more than half of the diabetes sample exhibited poor medication adherence (168 out of 322). Furthermore, 15.8% of respondents were khat chewers (51 individuals) and 33.5% were alcohol users (108 individuals).

Table 1: Frequency of socio-demographic characters` in Neurovascular disease of lower extremity disease among T2DM at JUMC, Jimma, Ethiopia,2024 [n=336].

Name of Variables	Categories of Variables	Frequency of variables	Percent (%)
Gender	Female	135	41.8
	Male	187	57.9
Age categories	<30	64	19.9
	30-39	32	9.9
	40-49	77	23.9
	>50	148	46.3
Marital status	Single	41	13
	Married	250	77.6
	Widowed	22	6.8
	Divorced	9	2.8
Educational status	Illiterate	21	6.5
	Junior school	70	21.7
	Secondary school	129	40.1
	College Level	102	31.7
Occupation	Unemployed	91	28.3
	Farmer	38	11.8
	Gov`t employee	93	28.9
	Merchant	52	16.1
	Retired	48	14.9
Residence	Urban	221	68.6
	Rural	101	31.4
Income status	Low-income	211	65.3
	Middle income	74	22.9
	High-Income	37	11.5

***. NLED**-Neurovascular lower extremity disease /Neurovascular disease of lower extremity
***.DPN-**Diabetic peripheral neuropathy
***.PAD-**Peripheral arterial disease
***. Gov`t –** Government

Table 2: Clinical information and anthropometric parameters frequency in neurovascular diseases of lower extremity among T2DM at JUMC, Jimma, Ethiopia, 2024 **[n=336].**

Name of Variables	Categories of Variables	Frequency of variables	Percent (%)
Duration since T2DM diagnosis [year]	<5	139	43.2
	5-10	79	24.5
	>10	104	32.3
Family history of DM	No	127	39.4
	Yes	166	51.6
	Unknown	29	9.0
Family-DM complications	No	81	25.1
	Yes	77	23.8
	Unknown	9	2.8
Common Comorbid diseases	Not comorbid	151	46.9
	Hypertension	128	39.8
	Cardiac Failure	30	9.3
	Renal Failure	13	4
Lipid-lowering drugs	No	120	37.2
	Yes (statin)	202	62.7
Body mass index	Underweight	8	2.5
	Normal	201	62.4
	Overweight	68	21.1
	Obesity	45	14
Elevated WHR	No	41	12.7
	Yes	281	87.3
Mean±S.D	0.97±0.23		
Elevated WC	No	175	54.3
	Yes	147	45.7
Mean±S.D	100.4±16.5		
Elevated PLR	No	126	39.1
	Yes	196	60.9
Mean±S.D	200.4±90		
Elevated NLR	No	141	43.8
	Yes	181	56.2
Mean±S.D	5.3±3.5		

***WHR**-Waist-to-hip ratio ***.S.D**-Standard deviation

*. **NLR**-Neutrophil-to-lymphocyte ratio

***.PLR**- Platelets-to-lymphocyte ratio

***.WC**- Waist circumference

Table 3: Biochemical parameters and behavioral factors frequency in Neurovascular lower extremity diseases among T2DM at JUMC, Jimma, Ethiopia,2024[n=336].

Name of Variables	Categories of predictors	Frequency of predictors	Percent (%)
Hb-ALC [%]	<7	117	36.3
	>7	205	63.7
Mean[%]±S.D	9.6±4.6		
FBS [mg/dl]	<126	145	45
	>126	177	55
HDL-C [mg/dl]	>40	121	37.6
	<40	201	62.4
Mean[mg/dl]±S.D	38.7±21.6		
LDL-C	<100	34	10.6
	>100	288	89.4
Triglycerides	<150	114	35.4
	>150	208	64.6
Total cholesterol	<200	118	36.6
	>200	204	63.4
Smoking status	No	276	85.7
	Yes	46	14.3
Khat Chewing	No	271	84.2
	Yes	51	15.8
Alcoholics status	No	214	66.5
	Yes	108	33.5
Medication adherence	Good	50	15.5
	Moderate	104	32.3
	Poor	168	52.2
Diabetic self-care	Good self-care	126	39.1
	Poor self-care	196	60.9

***.HbAlc**-Glycated hemoglobin

***.FBS**-Fasting blood sugar

***. HDL-C**-high density lipoprotein

***. LDL-C**-Low-density Lipoprotein

***.NLED**-Neurovascular lower extremity disease

5.2. The Prevalence of Neurovascular Diseases of the Lower Extremity in T2DM

The researcher used a Michigan neuropathy screening index-based combination of patients' historical diagnostic approaches (symptom score) 133(41.30%) and physical assessment approaches (sign scores) 108(33.34%) were estimated using the symptom score to determine the prevalence of DPN. As a result, the overall prevalence of diabetic peripheral neuropathy among individuals with T2DM was 186 cases (57.6%) at a confidence interval of 52.2%-63%.

The researchers also used a diagnostic modality based on the ankle-brachial index (ABI) identified 160(49.5%), while a symptom-based score using the Edinburg claudication questionnaires (ECQ) identified 95(29.4%). Moreover, the overall prevalence of peripheral arterial disease among participants with diabetes was 178(55.1%) at a 95% confidence interval of 49.7%-60.5%.

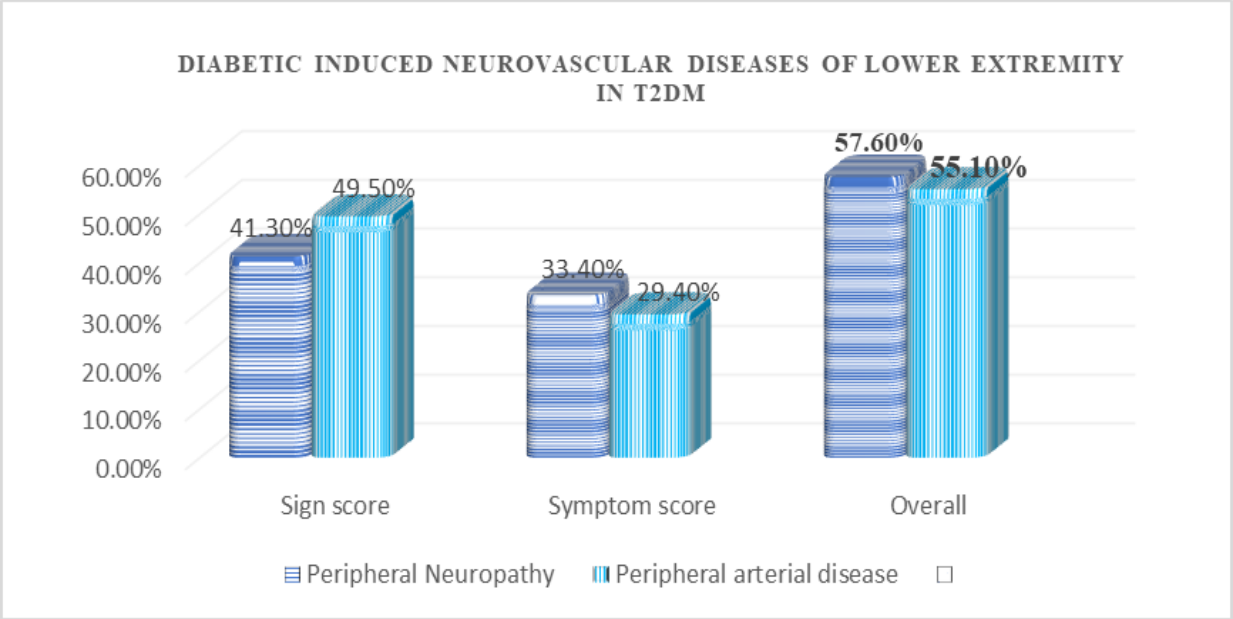

Figure 3. Indicates diagnostic modality-based prevalence of diabetic-induced peripheral neuropathy and peripheral arterial disease among T2DM at JUMC, Jimma, Ethiopia,2024[**n=336**]

Finally, overall occurrences of neurovascular diseases in the lower extremities were calculated from the overall prevalence of DPN and PAD, and it was 245(76.1%) individuals among T2DM at a confidence interval of 71.4%-80.8%.

5.3. The Proportions and Significant Predictors of Peripheral Neuropathy in T2DM

The proportion and significant predictors of diabetic peripheral neuropathy were determined using statistical analyses including the homogeneity test of chi-square, bivariate, and multivariate logistic regression analysis, with p-value <0.05, 0.25, and <0.05, respectively.

During the bivariate evaluation, twelve variables Age, duration of DM, Residence, Comorbidity, Family history, HDL-C, LDL-C, HbAlc, FBS, TC, NLR, and WHR showed a relationship with the DPN at a p-value of <0.25 were consequently included in the multivariate logistic regression analysis.

As a result, the age of patients increased from 40–49 years old to greater than 50 years old, and the proportion of DPN increased from 26.4% to 56.5%, respectively, compared to those without DPN after controlling other factors. With over five times the odds of DPN in both age categories (Age 40–49 years: AOR=5.43, 95%CI:1.20,26.82; For older than fifty years: AOR:5.52, at 95%CI:1.45,21.01) compared to those under thirty years old.

The proportion of DPN in individuals with elevated glycosylated hemoglobin (HbA1c >7%) was 86.6% compared to normal levels. With each 1% increase in HbA1c above the mean value (HbA1c>9.6%), the odds of experiencing DPN were 1.55 times higher (95%CI, AOR=1.55, 1.26-1.90) after all other factors were controlled. Conversely, individuals with fasting blood sugar levels >126 mg/dl had a 75.3% proportion and over five times higher odds of progressing to DPN compared to normal fasting plasma sugar levels (AOR=5.798, CI=1.13-29.70).

Moreover, the proportion of DPN in individuals with T2DM and low HDL-C levels (<40mg/dl) was 92.5%. Additionally, for each 1mg/dl decrease in HDL-C below the mean value (<38mg/dl), the odds of DPN occurrences were more than ten times higher (95%CI, AOR=10.6, 2.26-45.60) compared to those above the mean value after controlling for other factors.

An elevated neutrophil-to-lymphocyte ratio (NLR>5.0) was observed in 91.4% of cases compared to the normal range. It carried twice the odds of progressing to DPN compared to individuals within the normal NLR range (95%CI; AOR:2.33,1.87-2.89). Compared to individuals with normal waist-to-hip ratio (WHR), those with elevated WHR had an 88.2% proportion of DPN and this is evidenced by a 4.7 times higher likelihood of DPN occurrences for

each unit increases beyond the mean value (WHR>0.98) compared to the normal ratio (AOR = 0.21, 95% CI=0.005-0.09) controlling other all other variables.

Individuals with T2DM who exhibited poor diabetes self-care behavior accounted for 81.3% compared to those with overall good diabetes self-care. Furthermore, poor self-care was a significant potential predictor, with more than nineteen times more likely to develop DPN than those with good diabetic self-care [95%CI, AOR:19.51, 6.63,57.44].

Table 4: Significant Predictors and their proportions in Diabetic Peripheral Neuropathy [DPN] as a reference to those without DPN among T2DM at JUMC, Jimma, Ethiopia, 2024 **[n=336]**.

Predictor Variables		**Response variable**			**Binary logistic analysis**				
Name of Variables	**Category of variable**	**Proportions Peripheral Neuropathy(%)**			**Bivariate Analysis**		**Multivariate Analysis**		
		NO	**Yes**	**P-value**	**p-value**	**COR**	**p-value**	**AOR**	**95%CI**
Age of patients [years]	<30	42(32.6)	23(12.4)	1	1	1	1	1	1
	30-39	24(18.6)	9(4.8)	.001	0.02	0.715	0.61	-	-
	40-49	27(20.9)	51**(26.4)**	0.42	.001	3.890	.038	**5.434**	1.10-26.82
	>50	36(27.9)	105**(56.5)**	.001	.001	5.182	.012	**5.518**	1.45-21.01
Duration [years]	<5	89(69.0)	52(28.0)	1	1	1	1	1	
	5-10	23(17.8)	49**(26.3)**	<.001	<.001	3.455	.026	**4.645**	1.28-46.70
	>10	17(13.2)	85**(45.7)**	<.001	<.001	11.07	.046	**7.716**	1.03-21.02
HDL-C [mg/dl] **Mean**	>40	100(80.6)	14(7.5)	1	1	1	1	1	1
	<40 38.7±.02	25(19.4)	172**(92.5)**	<.001	<.001	70.4	0.002	**10.16**	2.26-45.60
HbAlc [%] **Mean±S.E**	<7	93(72.1)	25(13.4)	1	1	1	1	1	1
	>7 9.6+.11	36(27.9)	161**(86.6)**	.001	.001	1.724	0.02	**1.55**	1.26-1.90
FBS [mg/dl]	<126	95(73.6)	46(24.7)	1	1	1	1		
	>126	34(26.4)	140**(75.3)**	.0022	<.001	7.239	.035	**5.798**	1.13-29.70
Elevated NLR Mean±S.E	No	122(94.6)	16(8.6)	1	1	1	1	1	1
	Yes 5.3+.11	7(5.4%)	170**(91.4)**	.002	<.001	2.564	0.00	**2.326**	1.87-2.89
Diabetes self-care	Good	101(78)	31(16.7)	1	1	1	1	1	1
	Poor	**28(21.7)**	155(83.3)	.001	.001	4.488	.000	**19.51**	6.63-57.44

***.95%CI**- Confidence Interval at 95%
***.S.E**-Standard Error

5.4. The Proportions and Significant Predictors of Peripheral Arterial Disease in T2DM

Again, the homogeneity test of chi-square analysis before bivariate and multivariate regression analysis was employed at p-value <0.05, <0.25, and <0.05, respectively to find out what factors are strongly linked to PAD in people with T2DM. Predictors associated through a bivariate analysis were the age of patients, gender, duration of DM, residence, Obesity(WC), khat chewing, Hypertension-C, HDL-C, TG, HbAlc, FBS, NLR, PLR, smoking, and diabetes self-care were transferred to multivariate analysis.

The proportion of PAD in those over 10 years was 39.3%, whereas for those between 5-to-10 years, the duration after T2DM was diagnosed as 27.5%. Likewise, compared to individuals under five years, those age groups had odds of getting PAD that were more than twice as high [95%CI, AOR:2.31,1.15,4.65, and AOR:2.72,1.24-5.94] respectively. Similarly, the proportion of PAD in urban residents was 75.3% as compared to rural inhabitants, and this association was verified as the likelihood of developing PAD was two times greater in urban residents than in rural people [95% CI, AOR:2.00, 1.20, 3.63].

As compared to blood hemoglobin levels below 7%, the percentage of increased hemoglobin (HbAlc > 7%) was 78.7%, and blood hemoglobin level above the mean (HbA1c>9.61%) had a 1.94 times greater chance of getting PAD than someone with a hemoglobin level below the mean[At 95%CI, AOR:1.94,1.33, 2.83]. In the same scenario, lower HDL-C [HDL-C<40 mg/dl] than normal results in 72.5% of PAD. For every unit (1gm/dl) of HDL-C below the mean value (HDL-C<38 mg/dl), there were 2.9 times more chances of getting PAD compared to those above the mean value (95%CI, AOR:2.9, 1.95–18.00).

As compared to their respective normal ranges, the proportion of PAD in an elevated waist circumference(WC) and elevated platelets-to-lymphocyte ratio (PLR) was 60.7% and 91.0%, respectively. As evidence, there were 1.17 and 1.19 chances of PAD compared to those below their mean values [At 95%CI, AOR:1.17, CI:1.01–1.36 and AOR=1.19, 1.09–1.29] for every unit rise in PLR [one-unit ratio] and WC [1cm] above their mean values [PLR>200 and WC>105]. Finally, at a 95% confidence interval (CI), the proportion of people with poor diabetes self-care in T2DM was 72.5%, and they were three times more likely to experience PAD events than those who had good diabetes self-care[At 95% CI, AOR:3.37,1.63-18.05].

Table 5: Significant Predictors and their proportion in Peripheral arterial disease of lower extremity as compared to those without PAD in T2DM at JUMC, Jimma, Ethiopia, 2024[n=336].

Predictor variables		**Response variable**			**Binary logistic analysis**				
Name of variable	**Variable group**	**Proportion of Peripheral arterial disease(%)**			**Bivariate Analysis**		Multivariate analysis		
		NO	**Yes**	**P-value**	**P-value**	**COR**	**P-value**	**AOR**	95%CI
Duration of T2DM [In years]	<5	75(52.1)	59(33.2)	1	1	1	1	1	**1**
	5-10	33(22.9)	49**(27.5)**	0.02	<.001	3.37	.019	**2.31***	1.15-4.65
	>10	36(25)	70**(39.3)**		<.001	6.18	.012	**2.72***	1.24-5.94
Residence	Rural	67(46.5)	44(24.7)	1	1	1	1		
	Urban	77(53.5)	134**(75.3)**	0.001	<.001	2.46	.022	**2.00***	1.10-3.63
Hb-ALC [%]	<7	79(54.9)	38(21.3)	1	1	1	1	1	1
Mean±S.D	**>7** 9.6+.11	65(45.1)	140**(78.7)**	0.01	<.001	1.71	.01	**1.94***	1.33-2.83
HDL-C [Mg/dl]	>40	77(53.5)	49(27.5)	1	1	1	1	1	1
Mean±S.E	**<40** 38+.02	67(46.5)	129**(72.5)**	0.001	<.001	.98	.032	**2.90***	1.95-18.00
PLR-elevation Mean±S.D	No	97(100)	16(9.0)	1	1	1	1	1	1
	Yes 200±.08	0(0.0)	162**(91.0)**	0.001	<.001	1.10	.042	**1.17***	1.01-1.36
Diabetes self-care	Good	83(57.6)	49(27.5)	1	1	1	1		
	Poor	61(42.4)	129**(72.5)**	0.001	<.001	6.31	.016	**3.37***	1.63-18.05
Elevated WC Mean±S.D	No	99(68.8)	70(39.3)	1	1	1	1	1	1
	Yes 100.4±.04	45(31.3)	108(**60.7**)	0.031	<.001	1.11	.000	**1.19***	1.09-1.29

CHAPTER SIX: DISCUSSION

6.1. Prevalence of Neurovascular Diseases of the Lower Extremity in T2DM

This study was conducted on 336 individuals with T2DM achieving a response rate of 95.8%. Fourteen selected individuals with diabetes were unable to participate in the study because they were unwilling, had insufficient medical information, or refused baseline examinations.

A report from 322 T2DM revealed that the prevalence of DPN according to the Michigan Neuropathy Screening-based symptoms score diagnostic modality was 34.60% and according to the sign, score was 42.60%. The discrepancy between the two approaches might be explained by patients' limitations in their self-perception of DPN symptoms and our urge to insist on a sign version of MNSI. Assessment based on the combined effect of symptoms and signs score showed that the overall prevalence of DPN was 57.60% at a confidence interval [95% CI:52.2%-63%]. This finding was consistent with earlier research conducted in China in 2017, Yemen in 2019, Ethiopia Bahir Dar in 2017, Jimma in 2019, Addis Ababa (TASH) in 2020, and Nigeria in 2021(34,61,72,90,96).

Conversely, our study found a higher prevalence than studies carried out in Cairo, Egypt, in 2020; Puducherry, India, in 2021; Beijing, China, in 2022; JUMC, in 2020; TASH, Ethiopia, in 2022; and Adama, Ethiopia, in 2024 (68,70,71,90,93,135,172). This variation could be attributed to different study designs, including those used in TASH in 2021, variations in sampling techniques, smaller sample sizes compared to studies in Egypt in 2020, China in 2022, and Adama in 2024, and the use of different diagnostic tool like monofilament only or Douleur Neuropathique-4. Additionally, the difference in study groups, and type I diabetes, who were part of the study in TASH in 2022, might have influenced the results.

However, the estimates from Benin (2015), Nigeria (2015), Sudan (2016), Pakistan (2020), Mali (2020), and Uganda (2023) (50,67,74,75,173) indicated significantly higher prevalence rates. The differences in estimated disease prevalence within the study group could be attributed to several factors, like inclusion of both T1DM and T2DM, the focus on symptomatic patients with painful polyneuropathy, the inclusion of symptomatic diabetes only, the study conducted among elder diabetes, different study groups, and the smaller sample size considered, the utilization of specific diagnostic tools such as vibration perception and the 10g monofilament only in studies conducted in Benin, Sudan, Egypt, and Pakistan. Furthermore, other diagnostic instruments, such

as the Douleur Neuropathique en 4 questions and the Toronto Clinical Screening Scale (TCSS), were employed in studies in Sudanese and Mali.

The diagnostic criteria used to estimate the prevalence of peripheral arterial disease (PAD) were a combination of subjective [ECQ] and/or objective measurements [ABI]. Researchers believed that using both subjective [ECQ] and objective measurements [ABI] together would improve diagnosis accuracy more than using either tool alone. Thus, the prevalence of peripheral arterial disease [PAD] in T2DM according to the signed score was 49.50% and the symptom score was 29.4%. The difference in disease magnitude using each diagnostic tool may be due to patients' limited self-awareness [lack of subjectivity]. While ECQ tools are less sensitive, but chosen for their higher specificity, ABI is preferred for their sensitivity and objective measurement but lacks specificity and reduced pain perception due to comorbid existence of peripheral neuropathy.

The overall prevalence of PAD was 55.1% at a confidence interval of [95%CI:49.7-60.5%], with a recommendation for the sign score [ABI] as the preferred assessment modality for PAD. Furthermore, previous studies from Thailand in 2020, China in 2021, Northern Nigeria in 2020, and Southern Nigeria in 2010, 2012, and 2020 were confined to this study(80,85,86,168). However, this study reported a higher prevalence of PAD compared to studies conducted in Peshawar, Pakistan, in 2023; Lagos, Nigeria, 2015; Trujillo, Peru, 2017; TASH, 2019; and Debra Tabor, 2020 (147). Variability attributed to factors like larger sample size, the use of combined diagnostic tools (ECQ and ABI) unlike previous studies, different sampling techniques (consecutive sampling), both symptomatic and asymptomatic patients' included variations in diabetes self-care, age, and diabetes duration, time difference, and different study participants.

In contrast to studies conducted in Rawalpindi, Pakistan, in 2016; Wenzhou, China, in 2018; and Kolkata, India, 2022, our study found a lower prevalence of diabetic PAD among participants (77,81,84). The disparity may stem from studies concentrating only on symptomatic patients, elder patients, and those with foot ulcers, as seen in studies from China and India. Additional reasons could involvement of varied diagnostic techniques, like ABI with radiologic duplex ultrasonography and Doppler, different population setups, and challenging sampling methods unsuitable for broad generalizations.

Finally, the prevalence of Neurovascular disease in the lower extremity due to DPN and/or PAD occurrences in the lower extremity was 245(76.1%) at [95% CI:71.4%-80.8%] among T2DM. The mechanism through DPN and PAD is precisely uncertain, the possible integrated pathway is through, IR-mediated hyperglycemia or dyslipidemia triggers a cascade of oxidative stress and microvascular damage (vasa nervorum and vasa vasorum) impairing peripheral nerve tissue—besides, atherosclerotic, and endothelial dysfunction.

6.2. Independent Factors of Neurovascular Diseases of Lower Extremity in T2DM

The number of patients with diabetic peripheral neuropathy (DPN) was found to be rising among advanced age. Individuals in the forty- and fifty-year-old age groups were significantly five times more inclined than those in the thirty-year-old age group to develop diabetic-induced peripheral neuropathy, respectively. These results were comparable to studies published in 2017 in Bahir Dar, Ethiopia; at JUMC in 2019, Ethiopia; in Cairo, Egypt in 2020; and in Kampala, Uganda in 2023(61,71,75,96). Aging is a well-known risk factor, notably T2DM. An explanation could be as people age, bodies become more susceptible to ongoing metabolic stress, a reduced ability to regenerate, increased neuronal degeneration, and peripheral nerves are both length and size-dependent leading to compromised physiological well-being (61,96).

The proportion of DPN with increasing duration of T2DM was a significant predictor, with a higher (more than seven) likelihood of developing DPN in those between five to ten and above ten years than in those under the age of five, even if this was also higher in two other studies conducted in the same study area (61,172). This is confirmed by studies from Benin(2015), Tanzania(2017), Bahir Dar(2017), Egypt(2019), JUMC (2019);2020,and Harar(2022) (59,70,72, 105,116,141,167). The likely mechanism of advanced duration aggravating DPN was exactly uncertain. Alternatively, this is linked to the slow-onset activation and production of an advanced glycosylation end-product (glycosylation and oxidative stress) starting in unmyelinated small peripherally located nerve and vasa nervorum causing neuronal ischemia (61).

Furthermore, compared to people without PAD, the percentage of people with diabetic PAD was higher in those aged 5 to 10 and over 10 years, and the duration of T2DM was an independent predictor of PAD, with odds of more than two. This was confined to studies from north-central

Nigeria (2020) and south-eastern Nigeria (2020 (86,175). However, research conducted in Debra Tabor, 2020; Northern Nigeria, 2020; and Mardan, Pakistan, could not reveal a relationship between the duration of diabetes and PAD (82,87,94). This could be attributed to sample size discrepancies or sample size selection, other factors like dyslipidemia/hyperglycemia were not explored since most of them focused on disease frequency. In addition, most of the patients in our study were older, had dyslipidemia, were hypertensive, and had poor diabetes self-care. It was unclear how precisely and completely the possible mechanisms were. However, Aging intima weakens the endothelium's integrity, reduces nitric oxide availability, accumulates calcium and fats inside the arteries, vasoconstriction, reduced angiogenesis progresses arterial stiffening and thickening over time potentially compromises blood flow (94,176).

Urban dwellers made up the majority of the study population having a two-fold increased risk of PAD. This was consistent with the research reports from Gamo-Gofa Ethiopia, in 2021 and Harar Ethiopia in 2022 (95,113). The rising urbanization among Africans made diabetes the main victim of the past three decades, which is due to the majority of urban lives sedentary lifestyles like less physical activity, table-loaded workers, unhealthy diets, and environmental factors such as psychological stressors are more common (177,178).

Among the study populations, the proportion of T2DM with DPN was 75.3% among those with high fasting plasma glucose levels having a nearly fivefold higher risk of developing diabetic peripheral neuropathy (DPN) compared to individuals with normal blood glucose levels. This study's findings were consistent with studies conducted in Beijing, China, 2022, and Gamo-Gofa, southern Ethiopia,2021;2022 (68,95,105).

The likelihood of developing DPN was 86.6% higher among elevated HbAlc and for each 1% increase in HbA1c above the average value (HbA1c >9.6%), the risk of DPN development was approximately 55% controlling other factors. This was supported by studies conducted in Benghazi, Libya (2019), Saudi Arabia (2020), and Gamo-Gofa, southern Ethiopia (2021) (95, 138,179). High blood sugar levels can lead to an increased production of free radicals (FR). FR aggravates axonal distal polyneuropathy of the limb due to oxidative stress, the accumulation of toxic metabolites, and ischemic hypoxia of the nerve tissue (including vasa nervorum) (5,175,176).

Diabetes with poor glycemic control (HbA1c > 7%) had a 78.7% and for each 1% increase above the average HbA1c value of 9.6%, there was a 94% higher chance of PAD compared to individuals below the average value PAD controlling other factors. Studies in Debra-Tabor, Ethiopia (2020); South-Eastern Nigeria (2020); Egypt (2021); Eastern India (2022); Taiwan, China (2020); and Beijing, China (2022) (68,72,76,86,94,180) have explored this phenomenon. The exact mechanism is still exactly unclear but persistent hyperglycemia leads to oxidative damage to the endothelium, or dyslipidemia-induced atherosclerosis, which leads to vascular stiffening of arteries or vasa vasorum-deprived peripheral artery, promoting PAD (5,180,181).

Moreover, with each 1mg/dl decrease in HDL-C below the average value of 38.7 mg/dl, the likelihood of DPN was ten times more controlling for other factors. These findings align with studies from Egypt in 2019 and Kurnool in 2021(72,182). Individuals with lower HDL-C levels with each 1mg/dl decrease in HDL-C below the average a risk of developing PAD twice compared to those above the average. Yet, the proportion of LDL-C, TG, and TC remained higher at 92.1%, 93.8%, and 65.7% respectively as compared to those without PAD, even if they were not significantly associated. This could confront findings from South-Eastern, Nigeria, 2018, Northern, Nigeria, 2020 (86,87). The possible mechanism is the reduced protective effect of HDL-C progresses to dyslipidemia/hyperlipidemia-induced oxidative pressure (oxLDL-C), atherosclerosis, and endothelium damage. Results in neuronal axonopathy, neuroinflammation, and microcirculations impairments (181,183,184).

Diabetes with elevated waist circumference [WC] 57.7% had PAD and an increase of 1cm in waist circumference above the mean value was associated with a 19% higher risk of developing PAD controlled for other variables. This finding was supported by studies conducted in Nigeria in 2020 and Larkana, Pakistan in 2022 (67,86). The possible mechanism of central obesity was through metabolic, inflammatory, and vascular pathways. Nutrient excessiveness results in visceral adipose tissue expansion, which increases the release of free fatty acid and proinflammatory adipocytokines increases the susceptibility of peripheral blood vessels to oxidative damage, dyslipidemia, and atherosclerosis compromise peripheral arteries (79,184–186).

Poor diabetes self-care was over nineteen times more likely to develop DPN and they also had more than three times more chance to experience PAD after controlling for other predictors. This is reported by studies from Dire Dawa (2020), Debra Markos (2020), and Harar (2022 (112–114) Poor self-care worsens persistent hyperglycemia through pathophysiologic mechanisms that involve a complex interplay of metabolic,vascular, and inflammatory processes. I. Metabolic disorders like glycemic-induced oxidative stress/glycation-mediated nerve injury and/or II.Vascular Insufficiency like microvascular damage [Vasa nervorum] and/or Endothelial dysfunction. This is common in those who do not prioritize proper nutrition and regular physical exercise. III. Hyperglycemia-induced excessive pro-inflammatory cytokines secretions [TNF-α] and immune cell activation [Macrophage] (184,187).

The neutrophil-to-lymphocyte ratio (NLR>5) was associated with a higher risk of DPN in 91.4% of diabetics and for every unit increase the chance of DPN was more than after controlling for other factors. This was confirmed by a study from Bali, Indonesia, 2021; Hefei, China, 2021; Lattakia, Syria, 2022; and Chhattisgarh, India (18,102,183,184). Within the same study group, for each unit increase in PLR over the mean value was associated with a 16.7% greater risk of developing PAD. This is in line with a previously conducted study from Catania, Italy, 2020, and Chhattisgarh, India, 2023 (115,159).

The Precise mechanism is not well stated. however, Insulin resistance-mediated chronic hyperglycemia or dyslipidemia like in our study, causes increased adipose tissue expansion and NF-KB pathway activation-mediated overexpression of proinflammatory molecules, adhesions molecules activations, immune cell activation, and platelets aggregates_creates slowly low-grade chronic inflammatory damage through neurovascular pathological changes like ischemia or hypoxia of nerve tissues, injured peripheral nerves and blood vessel inner linings; worsen both DPN and PAD (15,188).

6.3. Limitations and Strengths of the Study

This study had limitations that should be acknowledged; Inferring incidental correlation is challenging due to the cross-sectional design of the study and time limits. ABI may sometimes give false-positive results. The absence of angiogram and nerve conduction testing, which is the gold standard diagnostic procedure for confirming the diagnosis of peripheral artery disease and peripheral neuropathy, respectively. However, it is invasive and associated with other complications like an allergic reaction to the contrast medium, thrombosis, and embolism. The duration of diabetes in this study may not accurately reflect the actual length of the disease. Patients' record inaccuracy since there were parameters and diagnoses derived from chart reviews even though the most recent and physician diagnosis was adopted.

The sensorimotor component of peripheral neuropathy was only diagnosed. However, vegetative neuropathy, diurnal glucose fluctuations, and long-term plasma glucose variation went undetected, and the incompressibility of peripheral blood vessels might influence tool sample representativeness. For both diagnostic studies, either of the legs were considered. The patient recall bias and limitations in diagnostic tools could affect the performance of the MNSI score and ECQ score. Because the study participants were only chosen from one diabetic center, the results might not be representative of the larger community. Despite these limitations, both symptomatic and asymptomatic diabetes were studied, and the composite of both sign and symptom diagnostic modality of either tool was recognized as it screened both symptomatic and asymptomatic participants and also, increases tools diagnostic accuracy. The diagnostic tools are also, not invasive, have no complications, are readily available, and have inexcusable accuracy.

Data were obtained via face-to-face interviews, directly measured parameters, with very good reliability, validated, and well-controlled tools/instruments. besides, this data will provide information that will inform both JUMC and zone health bureau policymakers and clinicians to reconsider prevention strategies including treatment initiation to reduce the experience of diabetes-induced neurovascular diseases. Low-grade chronic inflammatory biomarker, overall diabetes self-care character, and anthropometric parameters like central obesity were newly assessed among study participants.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

7.1. Conclusion

According to our study, Diabetic Peripheral neuropathy of the lower extremity among T2DM was approximately in more than half of the study participants; Similarly, the other half had PAD and three-fourth of them were those with neurovascular diseases of lower extremity. Finally, the prevalence of peripheral neuropathy, peripheral arterial disease and neurovascular disease in the lower limb of T2DM was high and factors such as advanced age, longer time since diagnosis, urban dwellers, high plasma glucose levels, low HDL-C, poor diabetes self-care, elevated WC, elevated NLR, and elevated PLR were significant predictors identified.

7.2 Recommendation

The sample population in our study showed a relatively high prevalence of neurovascular disease. We also identified older age, urban residents, prolonged duration, hyperglycemia, dyslipidemia, central obesity, poor diabetes self-care, and low-grade inflammation. This might go undetected and underdiagnosed if not screened.

As a result, healthcare professionals should prioritize regular screening for peripheral neuropathy and peripheral arterial disease, identifying risk factors early, and implementing interventions, such as diabetes self-care education, frequent monitoring, and early treatment initiation plans for individuals with identified risk factors accordingly. Besides, Jimma Zone Health system policy maker and Jimma University health service management to reconsider their prevention strategies regarding those identified factors.

Furthermore, conducting longitudinal studies and investigations through stronger casual relationships of possible risks were suggested. Besides, we also, recommend investigating vegetative neuropathy, the impact of diurnal glucose fluctuations, and long-term plasma glucose variation since went undetected.

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ANNEXES

Annexes I. Consent Form

An English version

My name is _____, a Senior Nurse working in JMC and now I am collecting data for the research being conducted to assess Neurovascular Disease of the lower extremity and their predictors among Type II Diabetes mellitus at Jimma University Medical Center, Ethiopia,2024 by Segni Gemechu Hurisa who is the student of Masters in medical physiology in Jimma University. You are selected as one of the study subjects.

The investigator employed me for this data collection to maintain your data strictly confidential, we believe that the findings of this study will have some evidence and information for governmental and non-governmental organizations.

The study will be conducted through Interview questionnaires, physical examination, and blood tests will be done, it will not as such cause any harm to you. Your name and other personal identifier will not be recorded on the data collection form and the information that you give us will be kept confidential and will also be used for this study purpose only. You have full right not to participate in this study.

If you have any questions about this study, you may ask me or the principal investigator Segni Gemechu Hurisa Tel: +251909100289

Are you willing to participate in this study?

1. Yes 2. No (End the interview)

Signature of the interviewer which shows that the respondent has consented (verbally) to take part in the study----------

Annexes II. Questionnaires

English Version

Part I. Socio-demographic factors			
S/N	**Questionnaires**	**Response**	**Remark**
0.	Card number	**…….**	
1.	Age	----------[year]	
2.	sex	A. Male B. Female	
3.	Marital status	A. Single B. Married C. Widowed D. Divorced	
4.	Educational status	A. Cannot read $write B. Junior school C. Secondary school D. College degree	
5.	Occupation	A. Farmers B. Gov`t employee C. Merchant D. Retired E. Daily laborer	
6.	Residence	A. Urban B. Rural	
7.	Income	……...[birr/month]	

	Part II. Diabetes information and Clinical factors		**Remark**
8.	Duration since DM Diagnosed	-------[In Year]	
9.	Do you have a family history of DM	A. Yes B. NO C. Unknown	
10.	If yes to the above QU.12, Is their family history of DM complications	A. Yes B. NO C. Unknown	
11.	Do you have a previous history of foot Ulcer	A. YES B. NO	
12.	Level of Hb ALC [%]		
13.	BMI [kg/m^2]	A. Weight [Kg] B. Height[m]	
14.	Waist-to-hip ratio	A. Waist circumference[cm] B. Hip circumference[cm]	

	Diabetic Peripheral arterial disease		
15.	Maximum Blood pressure[mmhg]	A. Brachial SBP------ B. Brachial DBP------ C. Ankle SBP……. D. Ankle DBP……...	
16.	**Edinburgh Claudication Questionnaire (ECQ)**		
	ECQ1.Do you get pain or discomfort in either leg(s) when you walk?	A. Yes B. NO C. Unable to walk	
	ECQ2.If you "Yes" to question (1) does this pain ever begin when you are standing still or sitting?	A. Yes B. NO	
	ECQ3. Do you get it if you walk uphill or hurry?	A. Yes B. NO	
	ECQ4. Does this pain occur when you walk at an ordinary pace on the level?	A. Yes B. NO	
	ECQ5. What happens to it, if you stand still?	A. Usually continues for more than 10 minutes B. Usually disappears in 10 minutes or less	
	ECQ6.In what part of your leg do you feel the pain?	A. Leg calf B. hamstring C. Thigh D. Buttocks E. Absence	
17.	Do you have any known comorbid diseases	A.YES B.NO	
18.	If yes to the above question, which is common to you? [QU.20]	A. CKD B. CVD C. Stroke D. If other, specify	
19.	Do you take Lipid-lowering drugs	A.NO B. Yes	
20.	If yes to the above QU.20, which is common to you?	A. statins B. Fibrates C. If other, specify	

21.	**Peripheral Neuropathy Assessment [DPN] [Historical Version] [PH]**		
	PNH1. Are your legs and/or feet numb?	A. Yes B.NO	
	PNH2. Do you ever have any burning pain in your legs and/or feet?	A. Yes B. No	
	PNH3. Are your feet too sensitive to touch?	A. Yes B. No	
	PNH4. Do you get muscle cramps in your legs and/or feet?	A. Yes B. No	
	PNH5. Do you ever have any prickling feelings in your legs or feet?	A. Yes B. No	
	PNH6. Does it hurt when the bed covers touch your skin?	A. Yes B. No	
	PNH7. When you get into the tub or shower, are you able to tell the Hot water from the cold water?	A. Yes B.NO	
	PNH8. Have you ever had an open sore on your foot?	A. Yes B.NO	
	PNH9. Has your doctor ever told you that you have diabetic neuropathy?	A. Yes B.NO	
	PNH10. Do you feel weak all over most of the time?	A. Yes B.NO	
	PNH11. Are your symptoms worse at night?	A. Yes B.NO	
	PNH12. Do your legs hurt when you walk?	A. Yes B.NO	
	PNH13. Are you able to sense your feet when you walk?	A. Yes B.NO	
	PNH14. Is the skin on your feet so dry that it cracks open?	A. Yes B.NO	
	PNH15. Have you ever had an amputation?	A. Yes B.NO	
	DX.DPN	**Total** =	
	Peripheral neuropathy Assessment [DPN] [Physical Examination-PE]		
	PNE1. Is the appearance of Feet, normal?	A. Yes B. NO	
	PNE1. If no to PE1, check all that apply:	A. Deformities B. Dry skin, callus C. Fissure D. If other, specify	
	PNE2. Ulceration	A. Absent B. Present	
	PNE3. Ankle Reflexes	A. Present B. Reinforcement C. Absent	
	PNE4. Vibration perception at the great toe	A. Present B. Decreased C. Absent	

	PNE5. Monofilament	A. Normal B. Reduced C. Absent	
	Total score	---------	

	Part III. Behavioral factors and diabetes self-care		**Remark**
22.	History of khat chewing	A. previous B. Current C. Never	
23.	History of alcohol	A. Previous B. Current C. Never	
24.	History of smoking	A. Previous B. Current C. Never	
25.	**Summary of Diabetes Self-Care Activities [DC]**	**Number of days**	
	A. Diet [DCD]		
	DCD1.How many of the last seven days have you followed a healthful eating plan? [0-7 days]		
	DCD2. On how many of the last seven days did you eat five or more servings of fruits and vegetables?		
	DCD3. On how many of the last seven days did you eat high-fat foods such as red meat or full-fat dairy products?		
	The sum of days for diet	=	
	B. Exercise [DCE]		
	DCE1. On how many of the last seven days did you participate in at least 30 minutes of physical activity? (Continuous activity, including walking)		
	DCE2. On how many of the last seven days did you participate in a specific exercise session (such as swimming, walking, biking) other than what you do around the house or as part of your work?		
	Average days of exercise	=	
	C. Blood Sugar Testing [DCS]		
	DCS1. On how many of the last seven days did you test your blood sugar?		
	The sum of days for exercise		
	D. Foot Care [DFC]		
	DFC1. On how many of the last seven days did you check your feet?		
	DFC2. On how many of the last seven days did you inspect the inside of your shoes?		

	DFC3. On how many of the last seven days did you wash your feet?		
	DFC4. On how many of the last seven days did you dry between your toes after washing? [foot soaking]		
	The sum of the days of DFC =		
	E. Diabetics self-care medications		
	On how many of the last seven days did you take your diabetic medications?		
	Average days of DM medications		
26.	**Morisky Medication-Taking Adherence Scale-MMAS (4-item)**		
	MMA1. Do you ever forget to take your (Insulin or pills) medicine?	A. Yes B. No	
	MMA2. Do you ever have problems remembering to take your medication?	A. Yes B. No	
	MMA3. When you feel better, do you sometimes stop taking your medicine?	A. Yes B. No	
	MMA4. Sometimes if you feel worse when you take your medicine, do you stop taking it?	A. Yes B. No	

Part IV. Lipid profile and blood profile			**Remark**
27.	Lipid profile	A. Total cholesterol [mg/dl B. Triglycerides [mg/dl] C. LDL-C [mg/dl] D. HDL-C [mg/dl]	
28.	Blood profile	A. Neutrophil[cell/mm^3] B. Lymphocyte [cell/mm^3] C. Platelets [cell/mm^3]	

Afaan Oromootin

Maqaan koo _____, Narsii Olaanaa taeen gidduu gala yaala fayyaa unibarsiti Jimmaa keessatti hojjedhu yoo ta’uu amma qorannoo dhibee Niwuroovaskularii (dhibee narvii fi hidda dhiiga miilati) qaama gadii dhukkuba sababa Sukkaaraa gosa 2ffaa qorachuuf giddugala yaalaa Yuunivarsiitii Jimmaa, Itiyoophiyatti, barataa digirii 2ffaa mummee fiiziyoloojii (sirna fayyaa qaama) fayyaa kan taee Segni Gemechu Hurisaa gaggeeffamaa jiruuf ragaa walitti qabaa jirra. Ati akka carraa barnoota qo'annoo tokkootti filatamta.

Qorataan daataa keessan cimsee iccitii akka ta’uuf odeeffannoo walitti qabuu kanaaf na qacare, argannoon qorannoo kanaa dhaabbilee mootummaa fi miti-mootummaaf ragaa fi odeeffannoo tokko tokko ni qabaata jennee amanna.

Qorannoon kan gaggeeffamu gaaffilee afgaffii irratti hundaa’an, qorannoo qaamaa, fi qorannoon dhiigaa ni raawwatama, akkasitti miidhaa tokkollee sirra hin geessisu. Maqaan kee fi adda baastonni/icciti dhuunfaa biroo unka daataa walitti qabuu irratti kan hin galmoofne yoo ta’uu odeeffannoon ati nuuf kennitu iccitii ta’ee kan eegamu yoo ta’uu, akkasumas kaayyoo qorannoo kanaaf qofa kan oolu ta’a. Qo’annoo kanaaf hirmaachuu dhiisuuf mirga guutuu qabda.

Waa'ee qorannoo kanaa gaaffii yoo qabaattan ana ykn qorataa olaanaa Segni Gemechu Hurisa Bilbila: +251909100289 kanan gaafachuu dandeessu.

Qo’annaa kanaaf hirmaachuuf fedhii qabdaa?

1. Eeyyee 2. Lakki (Gaaffii fi deebii xumuraa).

Mallattoo gaafataa kan deebii kennaan qorannoo kana irratti hirmaachuuf afaaniin hayyamuu isaa agarsiisuf----------

Dabalata II. Gaaffilee

Afaan oromootin kan qophaae

I. Qabxiilee hawasumma fi dimogiraafi			
Lakk.	**gaaffilee**	**Deebii**	**Yaada kennu**
0.	Lakkoofsa kaardii	**……..**	
1.	Umurii	----------[waggaadhan]	
2.	Saala	A. Dhiira B. Dubarti	
3.	Haala gaa'elaa	A. kan hinfuune B. Gaaelan kan jiruu C. kan hike/hiikkaan D. kan jala duee	
4.	Sadarkaa barnoota	A. Barreesssu fi dubbisu kan hin dandeenye B. Barnoota sadarka 1ffaa kan xumure C. Barnoota sadarka 2ffaa kan barate/tte D. Barnootan sadarka kolleejji kan gahee	
5.	Gahee hojii	A. Hojii dhabeeyyii B. Hojjetaa mootummaa C. Daldalaa D. Soorama bahe	
6.	Iddoo Jireenya	A. Magaalaa B. Baadiyyaa	
7.	Madda galii	……. [Birr/Jiaan]	

	II. Odeeffannoo dhukkuba sukkaaraa fi Qabxiilee Kilinikaalaa		**Yaada**
8.	Turtii erga dhibeen sukkaara qorannon beekame	-------[Waggaadhan]	
9.	Qorichoota wal'aansa dhukkuba sukkaaraaf kennaman	A. Insulini B. Gilukoosii afaanin fudhatamu C. Lachuu	
10	Madaa miila dhukkuba sukkaaraa qabdaa	A. Eyyee B. Lakkii	
11.	Maatii keesan keessa dhukkuba sukkaaraa qabduui?	A. Eyyee B. Lakkii C. Hinbeekuu	
12	Seendubee maatii dhukkuba sukkaara walxaxaa qabduui?	A. Eyyee B. Lakkii C. hinbeekuu	
13	Seenaa Madaa miila sukkaara kanaan dura qabduu	A. Eyyee B. Lakkii	

14.	Sadarkaa Himoogilobiinii A1C [%].		
15.	Indeeksii ulfaatina qaamaa [kg/m2].	A. Ulfaatina [Kg]. B. Olka'iinsa[m].	
16.	Reeshiyoo mudhii fi teessuma[boroo]	A. Naannoo mudhii[cm]. B. Naannoo boroo[cm]	
	Dhukkuba sukkaaraa Dhukkuba arteriin naannoo miila/lukaa [ABI OR SaO_2]		
17.	Dhiibbaa dhiigaa[mmhg].	A. Dhiibbaa dhiigaa sistoolikii harkaa------. B. Dhiibbaa dhiigaa diastolic harkaa------. C. Dhiibbaa dhiigaa sistooliik jilba..... D. Dhiibbaa dhiigaa diastolic jilbaa……..	
18.	Hamma ruqoo oksajinii qubaa miila [%].	A. Kan quba Gudda miila B. Kan qubaa miila	
19.	Dhukkuboota biroo kan sukkara alaa kan beektan jiraa?	A. Lakkii B. Dhukkuba kalee yeroo dheeraa C. Dhukkuba onnee hir`ina dhiiga D. Dhibee sammuu keessatti dhangala'uu dhiigatin dhufuu E. Yoo kan biraa ta'e, ibsi	
19.	Qoricha dhukkuba sukkaaraa gosa 2ffaa irraa kan hafe kan fudhataman	A. lipidii gadi buusu B. Yoo kan biraa ta'e, ibsi	
20.	**Madaallii dhibee narvii Naannoo miila sababa dhukkuba Sukkaaraa gosa 2ffaa.** **[Hiika Seenaa]**		
	1. Miilli kee si hadooda?	A. Eyyeen B. Lakkii	
	2. Miila kee fi/ykn lukaa kee irratti dhukkubbiin gubaa si mudatee beekaa?	A. Eyyee B. Lakkii	
	3.Miilli kee tuquuf garmalee miira qabaa?	A. Eyyeen B. Lakkii	
	4. Miilaa fi/ykn lukaa keessan irratti maashaan ni dhiita'aa?	A. Eyyeen B. Lakkii	
	5. Miila ykn miila kee irratti miira ciniinsuu si mudatee beektaa?	A. Eyyeen B. Lakkii	
	6. Yeroo haguuggiin siree gogaa kee tuqu ni dhukkubaa?	A. Eyyee B. Lakkii	

	7.Yeroo ujummoo ykn shawaariitti seentu, bishaan ho'aa bishaan qabbanaawaa addaa baaste himuu dandeessaa?	A. Eyyeen B. Lakkii	
	8. Miila kee irratti madaan banaa si mudatee beektaa?	A. Eyyee B. Lakkii	
	9. Doktarri kee dhukkuba narvii miila sukkaaraa akka qabdu sitti himee beekaa?	A. Eyyee B. Lakkii	
	10. Yeroo baay'ee guutummaatti dadhabbiin sitti dhaga'amaa?	A. Eyyee B. Lakkii	
	11. Mallattoon kee halkan hammatadhaa?	A. Eyyee B. Lakkii	
	12. Yeroo deemtu miilli kee si dhukkuba?	A. Eyyee B. Lakkii	
	13. Yeroo deemtu miila kee miiran toachuu dandeessaa?	A. Eyyee B. Lakkii	
	14. Gogaan miila keessanii akka malee gogee caccabee banaa?	A. Eyyee B. Lakkii	
	15. Qaamaa miila si irraa citee beektaa?	A. Eyyee B. Lakkii	
	DX.DPN	**Waliigalatti**=	
	Madaallii dhibee narvii Naannoo miila sababa dhukkuba Sukkaaraa gosa 2ffaa [hiika qormaata qaamaa]		
	1. Milli kee maal fakkaata		
	A. Baratamaa/fayyaadha	A. Eyyee B. Lakkii	
	B. Yoo Lakki ta'e, kan ilaallatu hunda ilaali:	A. Mudaa miila[deformities] B. Goggogaa gogaa miila [callus] C. Babaqaqu gogaa miila[fissure] D. Yoo kan biraa ta'e, ibsi	
	2. Madaa'uu miilarra (Ulceration) qabdaai?	A. Hinjira B. Injira	
	3. Buaan qorannoo Rifleeksii jilbaa	A. Injiraa B. Injiraa [Cimsuu] C. Hinjiruu	
	4. Hubannoo raafama quba gudda miila irratti	A. Present B. Decreased C. Absent	
	5. Buaan qorannoo Monofilament	A. Fayyaadha B. Gadii buaadha C. Hinjiruu	
	Qabxiin waliigala	---	

	III. Qabxiilee amala fi dhukkuba sukkaaraaf of kunuunsuu		**Yaada**
21.	Seena Caati nyaachuu qabdaai?	A. kanan duraa	

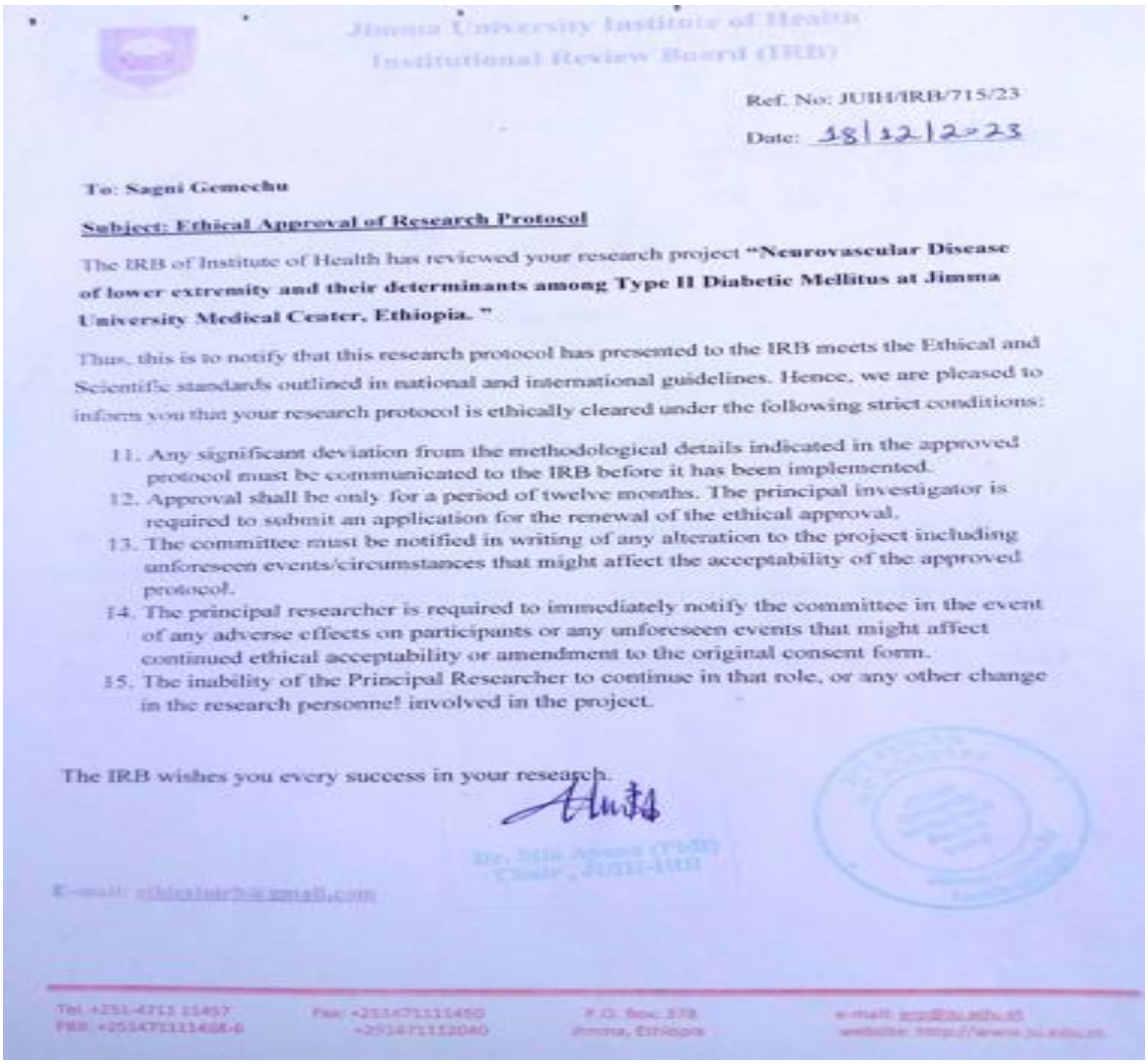
		B. Yeroo ammaa C. Gonkumaa	
22.	Alkooli macheessuu dhugdaai?	A. kanan duraa B. Yeroo ammaa C. Gonkumaa	
23.	Seenaa sigaara/tamboo xuuxuu qabdaai?	A. kanan duraa B. Yeroo ammaa C. Gonkumaa	
24	Quba miila kee gidduutti kiriimii fayyadamtaai?	A. Eyyee B. Lakkii	
25	**Gudunfaa Hojiiwwan Of Kunuunsuu Dhukkuba Sukkaaraa**	**Baay'ina guyyota**	
	A. Nyaata [guyyaa 0-7].		
	1. Guyyoota torban darban keessa guyya meeqa karoora nyaata fayya qabeessa hordofte?[guyyota 0-7].		
	2.Guyyoota torban darban keessaa guyyaa meeqa irratti kuduraa fi muduraa shan fi isaa ol nyaattan?		
	3. Guyyoota torban darban keessaa guyyaa meeqa irratti nyaata cooma baay'ee qabu kan akka foon diimaa ykn oomishaalee aannani cooma guutuu qaban nyaattan?		
	Giddugaleessan guyyoota nyaataa	=	
	B. Sochii qaamaa [guyyaa 0-7].		
	1. Guyyoota torban darban keessaa yoo xiqqaate daqiiqaa 30 sochii qaamaa irratti guyya hirmaatte meeqa? (Sochii qama walitti fufiinsa qabu, deemsa dabalatee)		
	2. Guyyoota torban darban keessaa guyya meeqa irratti waan akka qaama hojii keetti hojjettu malee sochii qaamaa murtaa'e (daakkaa dambalii, deemsa, biskileetii) irratti hirmaatte?		
	Giddu galeessaan guyyoota sochii qaamaa	=	
	C. Qorannoo Sukkaara Dhiigaa		
	1. Guyyaa torba darban keessaa guyya meeqa irratti sukkaara dhiiga kee qoratte?		
	Giddu galeessaan guyyoota qorannoo sukkaara dhiigaa	=	
	D. Kunuunsa Miilaa		
	1. Guyyaa torba darban keessaa guyya meeqa irratti miila kee ilaalte?		
	2. Guyyaa torba darban keessaa guyya meeqa irratti keessoo kophee keetii sakattatee?		

	3. Guyyaa Torba darban keessaa guyya meeqa miila kee dhiqatte?		
	4. Guyyaa Torba darban keessaa guyya meeqa erga dhiqattee booda quba miila kee gidduutti gogsitee? [miila jiidhuu].		
	Qoricha sukkaara		
	1. Guyyoota torban darban keessaa guyya meeqa qoricha dhukkuba sukkaaraa akka gorfamteetti [Insuliinii ykn kiniinii] fudhattee?		
	Waliigala giddu galeessaa Gudunfaa Hojiiwwan of Kunuunsuu Dhukkuba Sukkaaraa =		
26.	**Iskeelii Qajeelfama Qoricha-Fudhachuu Morisky-MMAS (4-item)**		
	1. Qoricha kee (Insulin ykn kiniinii) fudhachuu dagattee beektaa?	A. Eyyee B. Lakkii	
	2. Qoricha kee fudhachuu yaadachuu irratti rakkoon si mudatee beekaa?	A. Eyyee B. Lakkii	
	3. Yeroo miira gaariin sitti dhaga'amu, yeroo tokko tokko qoricha kee fudhachuu ni dhiistaa?	A. Eyyee B. Lakkii	
	4. Yeroo tokko tokko qoricha kee yeroo fudhattu yoo sitti hammaate, fudhachuu ni dhiiftaa?	A. Eyyee B. Lakkii	
	Qabxii MMAS Waliigalaa =		

Part IV. Profaayilii lipidii fi piroofaayilii dhiigaa			**yaada**
27.	Profaayilii lipidii	A. Kolestroolii waliigalaa [mg/dl B. Tiraayigiliisaayidii [mg/dl]. C. LDL-C [mg/dl] D. HDL-C[mg/dl] E. VLDL-C	
28.	Piroofaayilii dhiigaa	A. Niwutiroofiil[seelii/mm3]. B. Limfoosaayitii[seelii/mm3]. C. Pilateleetii[seelii/mm3].	

Annexes III. Permission Letters

Ethical approval letter



Jimma University Institute of Health
Institutional Review Board (IRB)

Ref. No: JUIH/IRB/715/23
Date: 18/12/2023

To: Sagni Gemechu

Subject: Ethical Approval of Research Protocol

The IRB of Institute of Health has reviewed your research project **"Neurovascular Disease of lower extremity and their determinants among Type II Diabetic Mellitus at Jimma University Medical Center, Ethiopia. "**

Thus, this is to notify that this research protocol has presented to the IRB meets the Ethical and Scientific standards outlined in national and international guidelines. Hence, we are pleased to inform you that your research protocol is ethically cleared under the following strict conditions:

11. Any significant deviation from the methodological details indicated in the approved protocol must be communicated to the IRB before it has been implemented.
12. Approval shall be only for a period of twelve months. The principal investigator is required to submit an application for the renewal of the ethical approval.
13. The committee must be notified in writing of any alteration to the project including unforeseen events/circumstances that might affect the acceptability of the approved protocol.
14. The principal researcher is required to immediately notify the committee in the event of any adverse effects on participants or any unforeseen events that might affect continued ethical acceptability or amendment to the original consent form.
15. The inability of the Principal Researcher to continue in that role, or any other change in the research personnel involved in the project.

The IRB wishes you every success in your research.

Dr. Nila Assen (PhD)
Chair, JUIH-IRB

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PBX: +251471111458-6

Supportive letters

JIMMA UNIVERSITY

ጅማ ዩኒቨርሲቲ

ቁጥር
Ref.No [illegible]

ቀን
Date 16 | 04 | 2016

ለ ተከታታይ ህክምና ክፍል (Chronic follow-up clinic)

ጅማ

ትብብር ስለመጠየቅ፡፡

በጅማ ዩኒቨርሲቲ ውስጥ ከሚገኙ ተማሪዎች መካከል "Neurovascular Disease of lower extremity and their Determinants among Type II Diabetic Mellitus at Jimma University Medical Center, Ethiopia " በሚል ርዕስ የምርምር ጥናታቸውን የሚሰሩ መሆኑን እየገለጽን ለተመራማሪ ውጥ [illegible] ለመረጃ ስብሰባዎቻቸው አስፈላጊው ትብብር እንዲደረግላቸው በትህትና እንጠይቃለን። በዚሁ አጋጣሚ ያለንበት የCOVID-19 ወረርሽኝ በመሆኑ ለህብረተሰቡም ሆነ ለመረጃ ሰብሳቢዎች የመከላከያ መንገዶችን ሁሉ በአግባቡ እንዲጠቀሙ እናሳስባለን።

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Recommendation letters

JIMMA UNIVERSITY
ጅማ ዩኒቨርሲቲ

ቁጥር
Ref.No [illegible]
ቀን
Date 24/4/2016

ከባዮሜዲካል ትምህርት ክፍል
ጅማ ዩኒቨርሲቲ
ለ Shenen Gibe Hospital

ጉዳዩ፡- ትብብር ስለመጠየቅ ይሆናል፡፡

ከላይ በርዕሱ ለመጥቀስ እንደተሞከረው በባዮሜዲካል ትምህርት ክፍል የ2ኛ ዓመት ሜዲካል ፊዚዮሎጂ(Medical Physiology) የድህረ ምረቃ ተማሪ "Segni Gemechu Hurisa በNeurovascular disease of lower extremity and their determinants among T2DM at JUMC,Ethiopia " በሚል ርዕስ ላይ ምርምሩን ለማድረግ ‹ርትስት› ፕሮፖዛል አጠናቋል ስለሆነም ለጥናቱ የሚያገለግላቸውን መረጃ መሰብሰብ እንዲችሉ አስፈላጊውን ትብብር እንዲደረግላቸው በትህትና እንጠይቃለን፡፡

ከሰላምታ ጋር

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Assurance of Principal of Principal Investigator

The undersigned agrees to accept responsibility for the scientific ethical and technical conduct of the research project and for the provision of the required progress reports as per the terms and conditions of the faculty of medical science in effect at the time of grant is forwarded as the result of this application.

Full Name of the student_____

Date _____

Signature _____

Approval of the First Advisor

Full Name of the first advisor_____

Date _____

Signature_____

Approval of the Second Advisor

Full Name of Advisor: _____

Date_____

Signature_____