ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCE

SCHOOL OF BIOMEDICINE AND LABORATORY SCIENCES

DEPARTMENT OF ANATOMY

Prevalence and Associated Factors of Diabetic Neuropathy among Ethiopian Long-Term Metformin Users in Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital, Addis Ababa, Ethiopia

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LIST OF ACRONYMS AND ABBREVATIONS

WHO	World Health Organization
DN	Diabetic Neuropathy
DM	Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
VB12	Vitamin B12
IDF	International Diabetes Federation
DPN	Diabetic Peripheral Neuropathy
DSP	Distal Symmetric Polyneuropathy
DAN	Diabetic Autonomic Neuropathy
NIDDM	Non-insulin dependent diabetes mellitus
IDDM	Insulin-dependent diabetes mellitus
BUN	Blood Urea Nitrogen
BMI	Body Mass Index
DBP	Diastolic Blood Pressure
HDL	High-density Lipoprotein
DPPOS	Diabetes Prevention Program Outcomes Study

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ABSTRACT

Background: Diabetic Neuropathy (DN) is a common and serious complication of diabetes mellitus (DM), affecting up to 50% of diabetic patients globally. It leads to significant morbidity including chronic pain, loss of sensation, and increased risk of foot ulcers and amputations. Among Ethiopian Diabetic patients, studies indicate varying prevalence rates, yet limited research has focused specifically on the impact of long-term metformin use. Metformin, the first-line drug treatment for type 2 diabetes mellitus (T2DM), has been associated with Vitamin B 12 deficiency, a known risk factor for neuropathy.

Objective: The aim of the study was to determine the prevalence and associated factors of diabetic neuropathy among Ethiopian long-term metformin users attending the diabetes clinic of the Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital, Addis Ababa, Ethiopia.

Methods: The study employed a descriptive cross-sectional design that utilized quantitative methods for data collection and analysis. Data were collected using a pretested and standardized questionnaire, laboratory tests and also physical examinations. The questionnaires were originally prepared in English and then translated into Amharic to facilitate effective communication with the study participants.

Results: Of the total 390 study participants 246 (63.1%) were found to have diabetic neuropathy, while 144 (36.9%) showed no evidence of neuropathy. The factors found to be significantly associated with diabetic neuropathy include age, duration of metformin use, and fasting blood sugar level.

Conclusion and Recommendations: Among the total 390 participants, more than half were affected, highlighting the substantial burden of neuropathic complications among long-term metformin users. The study found a significant association between prolonged metformin use and the occurrence of diabetic neuropathy. This calls for a national guideline endorsement necessitating screening long-term metformin users for vitamin B 12 deficiency and early replacement to avoid this debilitating complication.

Keywords: Diabetes Mellitus, Diabetic Neuropathy, Metformin, Vitamin B 12 Deficiency

1. INTRODUCTION

1.1. Background

Diabetes mellitus (DM) is a chronic metabolic disorder marked by persistent hyperglycemia and disruptions in carbohydrate, fat, and protein metabolism. It arises from either an absolute or relative deficiency in insulin secretion and/or insulin action (1). Globally, diabetes directly contributes to approximately 1.5 million deaths annually (2). The International Diabetes Federation (IDF) estimated that in 2019, around 19.4 million adults aged 20-79 years in the African region were living with diabetes, representing a regional prevalence of 3.9% (3). In Ethiopia, the 2015 WHO STEPS survey reported a national DM prevalence of 3.2% (4). Over the past 30 years, the global prevalence of diabetes has more than doubled, underscoring its status as a growing public health crisis (5).

Diabetes is generally categorized into two main types. Type 1 diabetes (T1DM) results from an absolute insulin deficiency, often due to autoimmune destruction of pancreatic beta cells and related genetic markers. Conversely, type 2 diabetes mellitus (T2DM), the most prevalent form develops from a combination of insulin resistance and inadequate compensatory insulin secretion(6). T2DM is characterized by dysregulated metabolism of carbohydrates, fats, and proteins, due to impaired insulin function. It accounts for over 90% of all diabetes cases, surpassing both T1DM and gestational diabetes (7).

The incidence of T2DM has been increasing steadily worldwide (8). As of 2017, an estimated 462 million people were living with T2DM, equivalent to 6.28% of the global population. Prevalence varied by age group 4.4% among those aged 15–49, 15% among those 50–69, and 22% among those aged 70 and older, amounting to approximately 6,059 cases per 100,000 people (9). In Africa, the IDF projected that diabetes cases would increase from 7.1 million in 2003 to 15 million by 2025 (10). In Ethiopia, pooled estimates place the national DM prevalence at 6.5% (4). The development of T2DM is primarily driven by a combination of genetic predisposition and modifiable lifestyle factors such as obesity, abdominal fat accumulation, and physical inactivity (11).

Metformin is the most widely prescribed oral hypoglycemic agent for T2DM and has also shown analgesic effects (12). It is typically the first-line treatment for T2DM in patients with adequate renal function, with nearly 70% of U.S. Veterans using metformin as part of their diabetes management. However, prolonged use of metformin has been associated with vitamin B12 (VB12) deficiency, which may contribute to an increased risk of peripheral neuropathy among T2DM patients (13). Numerous studies have documented reduced serum VB12 levels in metformin users (14), establishing the drug as a pharmacologic cause of VB12 deficiency in diabetic patients. This deficiency can lead to significant hematologic and neurological complications. Reported prevalence rates of VB12 deficiency among long-term metformin users range from 5% to 40%, depending on the population studied (15). The risk is further increased with higher dosages and extended durations of metformin therapy (14).

The complications of chronic hyperglycemia are generally categorized as macrovascular (e.g., coronary artery disease, peripheral arterial disease, stroke) and microvascular (e.g., nephropathy, retinopathy, and neuropathy) (16). Diabetic neuropathy (DN), a microvascular complication, is defined as peripheral nerve dysfunction in individuals with diabetes after excluding other potential causes (17). DN affects approximately 30-50% of diabetic patients globally (18). It encompasses a broad spectrum of disorders, including focal and diffuse neuropathies, and may affect both peripheral and autonomic nervous systems (19). DN significantly diminishes quality of life and is associated with chronic pain, mobility impairment, foot ulcers, and an elevated risk of lower-limb amputation (20).

1.2 **Statements of the problem**

T2DM has become one of the most widespread chronic diseases globally, posing a significant challenges to public health systems (21). It accounts for approximately 90–95% of all diabetes cases and is characterized by relative insulin deficiency, peripheral insulin resistance, and sustained hyperglycemia (22). As of 2021, an estimated 537 million adults aged 20-79 years were living with diabetes worldwide, with projections indicating this number will increase to 783 million by 2045 (23). The escalating prevalence of T2DM is closely linked to the global rise in obesity, driven by energy-dense diets and sedentary lifestyles, which together constitute a growing metabolic health crisis (24). T2DM is associated with a wide range of chronic complications including cardiovascular disease, renal failure, retinopathy, and diabetic neuropathy, all of which contribute to increased morbidity and mortality (21).

In the African region, approximately 19.4 million adults were living with diabetes in 2019, corresponding to a regional prevalence of 3.9% (25). The economic impact of diabetes is substantial, with global losses in gross domestic product due to both direct and indirect costs estimated at US $1.7 trillion. Of this, US $800 billion is projected to affect low- and middle-income countries (26). A systematic review and meta-analysis of studies primarily conducted in East Africa revealed a high burden of diabetes-related complications, with diabetic peripheral neuropathy and diabetic retinopathy affecting 38% and 32% of patients, respectively (27). Furthermore, the rate of undiagnosed diabetes in Africa remains alarmingly high at 66.7%, exacerbating the region's diabetes-related health burden (4).

In Ethiopia, an estimated 2.57 million people approximately 5.2% of the population are living with diabetes, placing the country among those with the highest diabetes prevalence rates in Sub-Saharan Africa (25). Diabetes has emerged as a major public health concern in Ethiopia, alongside other non-communicable diseases. The prevalence of diabetes varies widely across regions, ranging from 0.3% to 7.0% (28). Among the complications associated with T2DM, diabetic neuropathy (DN) is particularly common. DN is defined as the presence of signs and symptoms of peripheral nerve dysfunction in individuals with diabetes, in the absence of other identifiable causes (29). Poorly managed diabetes often leads to such complications, which contribute significantly to disability, premature mortality, and a reduced quality of life (28).

Metformin remains the cornerstone of pharmacologic management for T2DM and has demonstrated additional analgesic and neuroprotective properties (12). However, prolonged metformin use has been linked to an elevated risk of vitamin B12 deficiency, which may contribute to the development or progression of diabetic peripheral neuropathy (DPN). While some studies have identified an association between metformin use and DPN, findings across the literature remain inconsistent. This inconsistency highlights the need for further investigation to clarify the relationship. Moreover, it supports the recommendation for routine monitoring of vitamin B12 levels in patients undergoing long-term metformin therapy.

1.3 Significance of the Study

The investigation of the prevalence and associated factors of diabetic neuropathy among Ethiopian long-term metformin users holds significant implications for public health, clinical practice, and healthcare policy. DN is one of the most debilitating and common complications of DM, contributing to considerable morbidity, disability, and diminished quality of life. Understanding its prevalence, particularly among long-term metformin users, is crucial for the development of targeted interventions aimed at prevention, early diagnosis, and effective management.

Given the rising burden of diabetes in Ethiopia, it is imperative to generate localized evidence to inform public health strategies. While metformin remains the primary first-line treatment for T2DM, studies have established its association with vitamin B12 deficiency-a potential contributor to the development and progression of diabetic neuropathy. In this context, investigation of the role of long-term metformin use in the pathogenesis of DN is essential, especially in Ethiopia where routine vitamin B12 screening is not standard practice.

This study is expected to provide valuable insights into the link between chronic metformin use and diabetic neuropathy, with an emphasis on identifying modifiable risk factors such as vitamin B12 deficiency. The results could inform clinical guidelines, advocating for regular vitamin B12 monitoring and potential supplementation among patients at risk. Additionally, the study may influence national diabetes management protocols by supporting the integration of neuropathy screening tools in routine care, particularly in resource-limited settings.

Given the limited existing research on metformin-induced neuropathy in Ethiopia, this study will address a critical knowledge gap and contribute to the global literature on diabetes complications. Most importantly, by raising awareness among healthcare providers and patients, the findings can improve treatment outcomes, reduce the incidence of severe complications, and enhance the overall quality of life for individuals living with diabetes in Ethiopia.

2. LITERATURE REVIEW

2.1 History and Definition of Diabetic Neuropathy

The relationship between diabetes mellitus and peripheral nerve dysfunction has been recognized for centuries. However, it was not until Marchal de Calvi's work in 1864 that DN began to be understood as a complication of diabetes rather than a primary cause (30). Most clinical manifestations of DN were described in the latter half of the 19th century. Recent advances in pathology have provided new insights into the diverse patterns of DN, revealing findings such as inflammatory lesions in focal forms of the condition (31). Despite these developments, the natural history of diabetic neuropathy remains poorly understood, partly due to inconsistent diagnostic criteria and patient selection in earlier studies (32).

DN refers to the presence of symptoms and/or signs of peripheral nerve dysfunction in individuals with diabetes after excluding other causes (29). DN encompasses a spectrum of neuropathic disorders, including focal, diffuse, proximal, and distal forms, affecting both the peripheral and autonomic nervous systems. As one of the most common chronic complications of diabetes, DN significantly contributes to both morbidity and mortality (33). It is the leading cause of peripheral neuropathy and accounts for more hospitalizations than other diabetic complications. Moreover, it is the primary cause of non-traumatic lower-limb amputations (29).

DN typically begins with sensory loss in the lower extremities and is often associated with pain and functional limitations. At least half of all individuals with diabetes will eventually develop some form of neuropathy (34). DN is the most frequently occurring neuropathy in developed countries, characterized by a wide range of clinical presentations (35). Diabetic neuropathies are the most prevalent chronic complications of diabetes. This heterogeneous group of conditions affects different parts of the nervous system and presents with diverse clinical manifestations (36). Diabetic neuropathy is not a single entity but rather a number of different syndromes, each with a range of clinical and subclinical manifestations (37). Diabetic neuropathy is one of the most common long-term complications of diabetes and is the main initiating factor for foot ulceration, Charcot neuroarthropathy, and lower-extremity amputation (38).

2.2 Prevalence of Diabetic Neuropathy

The global prevalence of diabetic peripheral neuropathy (DPN) varies considerably, with estimates ranging from 22.7% to 54%, depending on diagnostic methods, patient demographics, and study design. In Iran, studies have reported DPN prevalence rates ranging from 32% to 75.1%. Diabetic autonomic neuropathy, a particularly severe form, has been linked to silent myocardial infarctions and reduced life expectancy, with mortality rates between 25% and 50% within 5 to 10 years. Up to two-thirds of diabetic individuals may exhibit clinical or subclinical neuropathic signs. One study documented an increase in DPN incidence from 7.5% at diabetes diagnosis to 50% after 25 years (29).

Painful diabetic neuropathy (PDN), defined by a neuropathic symptom score (NSS) ≥5 and a neuropathic disability score (NDS) ≥3, has a prevalence of 21%. Among those with severe neuropathy (NDS >8), painful symptoms were reported in 60% of cases. Interestingly, 26% of individuals without neuropathy (NDS ≤2) also reported painful symptoms. The adjusted odds of painful symptoms were twice as high in individuals with T2DM compared to T1DM (OR = 2.1, 95% CI: 1.7–2.4, $P < 0.001$) and were independent of other factors such as insulin use, foot deformities, smoking, or alcohol consumption. Women had a 50% higher risk of painful symptoms than men (OR = 1.5, 95% CI: 1.4–1.6, $P < 0.0001$). Although the overall prevalence of neuropathy was lower among South Asians (14%) than Europeans (22%) and African Caribbeans (21%), painful symptoms were more common among South Asians (38% vs. 34% vs. 32%, respectively, $P < 0.0001$) (39).

In a large population-based study from Augsburg, Germany, the prevalence of DPN was 28% among individuals with diabetes, 13% in those with impaired glucose tolerance, 11% in those with impaired fasting glucose, and 7% in those with normal glucose levels (40). Another study in Oxford, England, found that 16.7% of patients had autonomic neuropathy based on abnormal heart rate variability tests. A multicenter study by Ziegler et al. involving 1,171 diabetic patients reported cardiac autonomic neuropathy (CAN) in 25.3% of individuals with T1DM and 34.3% with T2DM, based on abnormalities in more than two out of six autonomic function tests. Under stricter criteria (abnormalities in at least three tests), prevalence dropped to 16.8% in T1DM and 22.1% in T2DM (41).

The Rochester Diabetic Neuropathy Study, which examined a cohort of 870 diabetes patients, reported that 66% of individuals with insulin-dependent diabetes mellitus (IDDM) and 59% of those with non-insulin-dependent diabetes mellitus (NIDDM) had some form of neuropathy. Within the IDDM group, polyneuropathy was observed in 54%, asymptomatic carpal tunnel syndrome in 22%, and symptomatic carpal tunnel syndrome in 11%. Among NIDDM patients, 45% had polyneuropathy, and 29% had carpal tunnel syndrome. Only 6% of IDDM and 1% of NIDDM patients exhibited severe polyneuropathy (stage 2b), and none reached stage 3 (42).

2.3 Factors of Diabetic Neuropathy

Neuropathy is one of the most disabling complications of diabetes, with prevalence estimates ranging from 50% to 90%, depending on the diagnostic tools used (43). Some studies have identified age and duration of diabetes as significant risk factors, while others have also highlighted poor metabolic control, smoking, low HDL cholesterol levels, and the presence of retinopathy (44). Older adults are particularly vulnerable to both acute and chronic microvascular complications, including DN. Reported prevalence rates vary widely from 5% to 100% largely due to differences in diagnostic criteria (45). A meta-analysis identified several consistent risk factors for DPN, including diabetes duration, age, HbA1c levels, smoking, body mass index (BMI), fasting plasma glucose, blood urea nitrogen (BUN), and diastolic blood pressure (DBP) (46).

2.4 Relationship Between Diabetic Neuropathy and Long-Term Metformin Use

Metformin remains the preferred first-line therapy for individuals with T2DM and normal renal function, with approximately 70% of U.S. Veterans prescribed this medication. Despite widespread use, its role in vitamin B12 deficiency is a growing concern, particularly given the prevalence of B12 deficiency in metformin-treated patients, which ranges from 5.8% to 52% (47).

Older adults, especially those with T2DM, are at greater risk of B12 deficiency, which can exacerbate or mimic neuropathic symptoms. Several studies have reported that long-term metformin use is associated with reduced serum vitamin B12 concentrations (48). Although the clinical implications of low B12 levels remain debated, prolonged deficiency may lead to irreversible nerve damage (49). Early studies suggested that up to 30% of patients on long-term metformin therapy experience B12 malabsorption, with average reductions in serum B12 levels

ranging from 14% to 30% (50). Cobalamin (B12) deficiency, particularly when it involves reduced methyl cobalamin, has been strongly linked to neurological symptoms, including peripheral neuropathy. This deficiency may be exacerbated in patients already suffering from DPN and could be further aggravated by continued metformin use (51).

2.5 **Conceptual Framework**

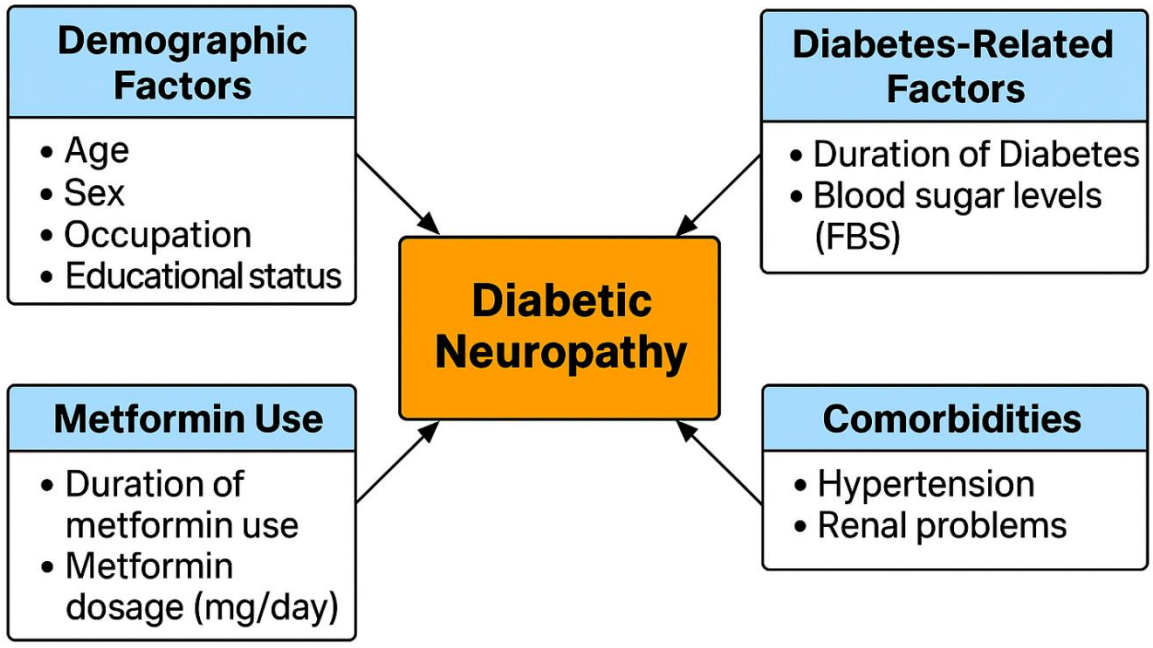

Figure 1: Conceptual Framework for the Study

This conceptual framework was developed based on a review of relevant literature from various sources.

3. OBJECTIVES

3.1. General Objective

- To determine the prevalence and associated factors of diabetic neuropathy among Ethiopian long-term metformin users in Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital, Addis Ababa, Ethiopia, 2025

3.2 Specific Objectives

- To estimate the prevalence of diabetic neuropathy in Ethiopian diabetic patients on long-term metformin treatment.
- To identify factors associated with diabetic neuropathy in Ethiopian population.

4. METHODOLOGY

4.1. Study Area

The study was conducted in Addis Ababa, in two tertiary hospitals of Ethiopia Tikur Anbessa Specialized Hospital (TASH) and Yekatit 12 Hospital. Tikur Anbessa Specialized Hospital is Ethiopia's largest general public hospital and one of the University Hospitals in the country. It was established in 1964. In 1998 Tikur Anbessa Specialized Hospital, which is also the largest and oldest referral teaching hospital in the country, was given to AAU by the Ministry of Health as a main teaching hospital. It has nearly 200 doctors, 700 beds, 379 nurses and 115 other health professionals offering health care services. The hospital consists of 950 permanent contract administrative staffs that supports the hospital activities. The faculty is the oldest and the largest among the health training institutions in the country, staffed with the most senior specialists. The hospital provides a tertiary level health care service and it is administered by Addis Ababa University.

Yekatit 12 Hospital was established in 1923 and is among the well-recognized hospitals in Addis Ababa. The hospital offers many preventive, curative, and rehabilitative health services for approximately 4 million people, and is also a teaching hospital.

4.2. Study Period

- The study was conducted from February to October, 2025

4.3. Study design

- A Hospital-Based Cross-sectional study was conducted in Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital, Ethiopia

4.4. Population

4.4.1. Source Population

- All patients who attended Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital for diabetes follow-up

4.4.2. Study Population

- All patients who presented to Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital for T2DM follow-up and also who are long-term metformin users.

4.4.3. Study Unit

- All patients who attended Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital for T2DM follow-up and also who are long-term metformin users presented during the study period.

4.5. Eligibility Criteria

4.5.1. Inclusion criteria:

- Ethiopian patients diagnosed with T2DM.
- On metformin treatment for at least 5 years.
- Aged 30 years and above.

4.5.2. Exclusion criteria:

- Patients with pre-existing neurological conditions unrelated to diabetes.
- Patients on other medications known to cause neuropathy (e.g., chemotherapy drugs).

4.6. Sample Size and Sampling Procedure

The sample size was determined using Cochran's formula, which is appropriate for estimating proportions in large populations.

The formula is given as:

$$n = \frac{\left(\frac{z\alpha}{2}\right)^2 * p_* (1-p)}{d^2}$$

Where:

- n: required sample size for the study
- z: standard normal deviate corresponding to the desired confidence level (Z=1.96), CI of 95% = 0.05
- z: estimated prevalence of diabetic neuropathy (38%, based on previous studies conducted in East Africa (51)
- d: margin of error= set as 5% (0.05)

Substituting the values into the formula:

$$n = \frac{\left(\frac{z\alpha}{2}\right)^2 * p_* (1-p)}{d^2}$$

Therefore, the minimum required sample size was 362 participants. To account for potential non-response and ensure adequate power, an additional 10% was added resulting in a final sample size of **398 participants**.

Systematic random sampling was employed to include study participants who met the inclusion criteria during the study period. Out of 398 patients, **390 participants** were included with a response rate of **98%.**

4.7. Study Variables

4.7.1. Dependent Variables

- Diabetic neuropathy

4.7.2. Independent Variables

- Demographic- Age, Sex, Occupation
- Diabetes related- Duration of Diabetes, Blood sugar control (HbA1c)
- Metformin use- Duration of metformin, Metformin dosage (mg/day)
- Nutritional/Biochemical status- Serum Vitamin B12 level (pg/mL)
- Comorbidities- Hypertension, Renal function (eGFR or serum creatinine)

4.8 Operational and Term Definitions

Prevalence- The proportion of study participants diagnosed with diabetic neuropathy among the total number eligible long-term metformin users enrolled in the study at the time of assessment.

Associated Factors- Demographic (e.g. age, gender), clinical (e.g. duration of diabetes and glycemic control), and biochemical (e.g. Vitamin B12 levels) variables that demonstrate a statistically significant association with presence of diabetic neuropathy.

Diabetic Neuropathy (DN)- A clinical or subclinical condition characterized by signs and/or symptoms of peripheral nerve dysfunction in a patient with diabetes mellitus, diagnosed using the Michigan Neuropathy Screening Instrument (MNSI) and 10g monofilament test, after ruling out other causes of neuropathy.

Type 2 Diabetes Mellitus(T2DM)- A metabolic disorder diagnosed in accordance with established clinical guidelines (e.g. fasting blood glucose ≥126 mg/dl, HbA1c ≥6.5%), and characterized by insulin resistance with relative insulin deficiency.

Ethiopian Diabetic Patients- Individuals of Ethiopian nationality or residence who have been formally diagnosed with T2DM and meet the study's inclusion criteria.

Age ≥30 Years- Participants eligible inclusion must be 30 years or older, as specified in the inclusion criteria.

Long-term metformin use- continuous administration of metformin for duration of five years or more in patients diagnosed with type 2 diabetes mellitus (T2DM)

Vitamin B12 Deficiency- A serum vitamin B12 concentration of <200 pg/ml, which may be associated with hematological or neurological manifestations.

Neuropathy Symptoms- Subjective sensory disturbances (e.g. numbness, tingling, burning pain) reported by participants in response to the standardized questionnaire tools used in the study.

Clinical Assessment Tools: Michigan Neuropathy Screening Instrument (MNSI)- A validated clinical tool used to assess the presence and severity of diabetic neuropathy through symptom scoring and physical examination findings. For the prevalence of diabetic neuropathy a total score of 9 and above is considered to have diabetic neuropathy. Whereas, for the severity of diabetic neuropathy a total score of 0-5 is considered as no neuropathy, 6-10 as mild neuropathy, 11-15 as moderate neuropathy and >15 as severe neuropathy.

10g Monofilament Test- A standard method used to assess peripheral sensory loss by applying a 10-gram pressure filament to predefined points on the foot.

4.9 Data Collection

Clinical Assessment:

- Neuropathy was diagnosed using the Michigan Neuropathy Screening Instrument (MNSI) and the 10g monofilament test.

Questionnaires

- Socio-demographic data
- Diabetes history (duration, glycemic control)
- Metformin use (duration, dosage)
- Neuropathy symptoms and quality of life impact (using validated scales)

Laboratory Tests

- Fasting blood glucose
- HbA1c levels

4.10 Data Quality Control

Training was given to the data collectors and supervisors on techniques of data collection, data collection material and purpose of research and a pilot test of the data collection tool on a small sample was conducted before full data extraction.

Data Validation and Cross-Checking were also conducted by comparing extracted data with hospital logbooks, HMIS (Health Management Information System), and patient records to ensure completeness and Data Cleaning was performed by identifying and correcting duplicate records, missing values, and outliers before analysis. Supervision was carried out daily to check completeness and consistency by both the supervisor and the principal Investigator (PI) to assure the quality of data.

4.11 Data Analysis and Interpretation

Researchers checked the data for completeness after each collection and the data were entered into Epi-Data version 4.7 and then it was exported to SPSS Version 27 for analysis.

For categorical data, descriptive statistics like frequency and percentage were computed and presented by the use of tables, bar graphs and pie chart. Continuous variables were summarized using means, median, mode and standard deviation. Associations between diabetic neuropathy and variables such as metformin use, vitamin B12 levels, and other risk factors were analyzed using Binomial regression model by running bivariate and multivariate logistic regression models. Whereas, Association between the independent variables and the severity of diabetic neuropathy were analyzed using the multinomial regression model.

4.12 Ethical consideration

Ethical clearance was obtained from Department of Research Ethics Review Committee (DRERC) of Addis Ababa University in Anatomy department (DRERC/13/20). Then this ethical clearance and cooperation letter was sent for Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital outpatient department director to obtain consent to perform data collection. Confidentiality of patient information was maintained through taking the data anonymously. After data collection, the raw data was secured and wasn't accessed by anyone except the principal investigator and no personal identifiers used to keep confidentially.

5. RESULT

5.1. Socio-demographic Characteristics of Participants

A total of 390 adult patients with Type 2 Diabetes Mellitus who were on follow-up at Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital were included in the study. Of these, 193 (49.5%) were male and 197 (50.5%) were female. Regarding age distribution, the majority of participants were aged 51-70 years, accounting for over 60% of the sample. In terms of residence, 358 (91.8%) lived in urban areas, while 32 (8.2%) resided in rural settings. Regarding educational status, 116 (29.7%) of respondents had attained higher education. Occupational status was distributed as follows 149 (38.2%) employed, 128 (32.8) unemployed, and 113 (29.0%) retired.

Table 1 Socio-demographic characteristics of participants

Variable	Category	N	%
Age (years)	31-40	19	4.9
	41-50	58	14.9
	51-60	118	30.3
	61-70	123	31.5
	>70	72	18.5
Sex	Male	193	49.5
	Female	197	50.5
Residence	Urban	358	91.8
	Rural	32	8.2
Education level	No formal	99	25.4
	Primary	96	24.6
	Secondary	79	20.3
	Higher	116	29.7
Occupation	Employed	149	38.2
	Unemployed	128	32.8
	Retired	113	29.0

5.2 Clinical and laboratory characteristics of participants

Our findings indicated that, 145 (37.2%) had been living with diabetes for 5-10 years, while the majority, 245 (62.8%), had been diagnosed for more than 10 years. Similarly, most participants had used metformin for over a decade, with 249 (63.8%) reporting more than 10 years of use compared to 141 (36.2%) who had taken it for 5–10 years. Notably, daily dosage analysis showed that most patients, 215 (55.1%) were prescribed more than 1,000 mg/day, while 134 (34.4%) took 1,000 mg/day and only 41 (10.5%) were on 500 mg regimens, indicating a predominant use of higher metformin doses in this population. The mean ± SD for HbA1c level among participants was 8.87 ± 1.45%, while the mean ± SD for fasting blood sugar was 153.65 ± 44.39 mg/dL.

Table 2 Clinical and laboratory Characteristics of participants

Variable	Category	N	%
Duration of diabetes (years)	5-10 Years	145	37.2
	>10 Years	245	62.8
Regular Monitoring of Blood Sugar	Yes	287	73.6
	No	103	26.4
Diabetes Related Complications	Yes	239	61.3
	No	151	38.7
Duration of metformin use (years)	5-10 Years	141	36.2
	>10 Years	249	63.8
Daily metformin dose (mg)	500 mg/day	41	10.5
	1000 mg/day	134	34.4
	>1000 mg/day	215	55.1
Side Effects of Metformin	Yes	77	19.7
	No	313	80.3
Insulin Use	Yes	90	23.1
	No	300	76.9
Any Comorbidities	Yes	285	73.1
	No	105	26.9
Any Medication used for nerve Health	Yes	83	21.3
	No	307	78.7

5.3 Prevalence of diabetic neuropathy

This finding revealed that, 246 (63.1%) was found to have diabetic neuropathy, while 144 (36.9%) did not show evidence of neuropathy. This indicates that more than half of the study population is affected, highlighting the substantial burden of neuropathic complications in long-term metformin users.

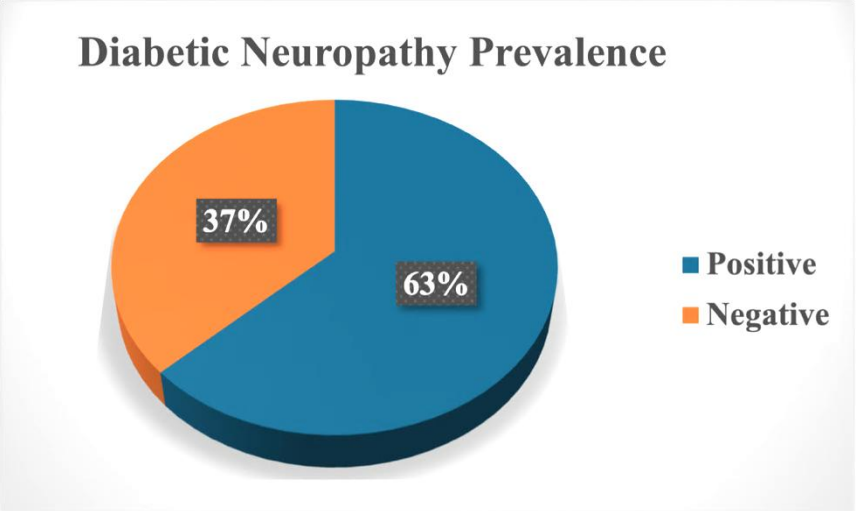

Figure 2: Prevalence of diabetic neuropathy among the study participants.

The prevalence of diabetic neuropathy among the study participants was high, with 63% presenting with neuropathy (positive) and 37% showing no evidence of neuropathy (negative).

5.4 Distribution of Diabetic Neuropathy across Duration of Metformin Use

Among participants who had taken metformin for 5-10 years, 42.6% developed neuropathy while 74.7% of those who had used metformin for more than 10 years experienced neuropathy. This suggests that longer duration of metformin is greatly associated with higher prevalence of diabetic neuropathy.

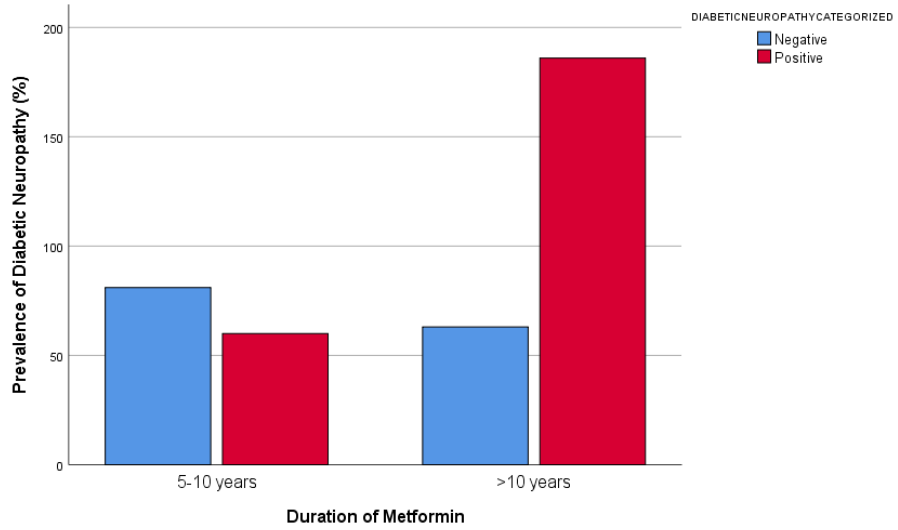

Figure 3: Prevalence of diabetic neuropathy by Duration of metformin use among study participants

5.5 Associated factors for Prevalence of Diabetic Neuropathy

Each independent variable was assessed to evaluate for their association with diabetic neuropathy. Variables including age, educational status, occupational status, duration of diabetes, duration of metformin use, any side-effects of metformin, HbA1c, FBS and insulin use and any co morbidities showed significant crude associations. They were then included as candidate for the binomial multivariate logistic regression to evaluate their independent effect.

Table 3: Binomial Bivariate Logistic Regression Analysis of Factors Associated with Diabetic Neuropathy Prevalence

Variable	Category	Crude OR (Exp(B))	95% Confidence Interval	p-value
Age	31-40	0.11	0.04-0.35	0.00*
	41-50	0.17	0.08-0.37	0.00*
	51-60	0.45	0.23-0.91	0.27*
	61-70	0.47	0.23-0.93	0.03*
	>70	1.00	-	-
Sex	Male	1.21	0.80-1.82	0.37
	Female	1.00	-	-
Residence	Urban	1.19	0.57-2.48	0.65
	Rural	1.00	-	-
Educational Status	No formal education	1.76	1.01-3.08	0.05*
	Primary	1.94	1.10-3.43	0.02*
	Secondary	1.37	0.77-2.46	0.29
	Higher	1.00	-	-
Occupation	Employed	0.36	0.21-0.61	0.00*
	Unemployed	0.46	0.26-0.82	0.0*
	Retired	1.00	-	-
Duration of Diabetes	5-10 Years	0.25	0.16-0.38	0.00*
	>10 Years	1.00	-	-
Diabetes Related Complication	Yes	1.27	0.84-1.94	0.26
	No	1.00	-	-
Regular Monitoring of Blood Sugar	Yes	0.89	0.57-1.43	0.63
	No	1.00	-	-
Duration of Metformin	5-10 Years	0.25	0.16-0.39	0.00*
	>10 Years	1.00	-	-
Daily metformin dosage	500 mg/day	0.48	0.31-0.75	0.00*
	1000 mg/day	0.48	0.24-0.95	0.03*
	>1000 mg/day	1.00	-	-
Any Side effects of Metformin	Yes	1.37	0.81-2.34	0.24*
	No	1.00	-	-
Last Recorded HbA1C level	Continuous	1.17	1.01-1.36	0.04*
Fasting Blood Sugar	Continuous	1.00	1.00-1.01	0.01*
Insulin Use	Yes	1.37	0.84-2.31	0.19*
	No	1.00	-	-
Any Co-morbidities	Yes	1.75	1.11-2.76	0.02*
	No	1.00	-	-

Age, Duration of metformin, and Fasting blood sugar were found to be significant predictors of diabetic neuropathy after adjustment.

Patients aged 31-40 (AOR = 0.26, 95% CI: 0.07–0.90, p = 0.03) and 41-50 years (AOR = 0.36, 95% CI: 0.15–0.88, p = 0.02) had lower odds of developing neuropathy compared with those over 70 years. Duration of Metformin was also significantly associated with neuropathy. Participants who had used metformin for 5-10 years were less likely to develop neuropathy compared with those who had used if for more than 10 years. Additionally, for every 1mg/dL increase in fasting blood sugar the odds of developing diabetic neuropathy slightly increased by 1%.

Table 4: Binomial Multivariate Logistic Regression Analysis of Associated Factors Related with Diabetic Neuropathy Prevalence

Variable	Category	Adjusted OR (Exp(B))	95% Confidence Interval	p-value
Age	31-40	0.26	0.07 – 0.90	0.03*
	41-50	0.36	0.15 – 0.88	0.02*
	51-60	0.67	0.31 – 1.46	0.31
	61-70	0.56	0.27 – 1.15	0.12
	>70	1.00	-	-
Educational Status	No Formal Education	1.80	0.87 – 3.73	0.11
	Primary	1.86	0.97 – 3.57	0.06
	Secondary	1.58	0.81 – 3.09	0.18
	Higher	1.00	-	-
Occupation	Employed	0.72	0.37 – 1.37	0.31
	Unemployed	0.59	0.30 – 1.57	0.12
	Retired	1.00	-	-
Duration of Metformin	5-10 Years	0.40	0.24 – 0.67	0.00*
	>10 Years	1.00	-	-
Any Side effects Of Metformin	Yes	1.44	0.80 – 2.61	0.23

	No	1.00	-	-
Any Comorbidity	Yes	1.17	0.70 – 1.95	0.56
	No	1.00	-	-
Fasting Blood Sugar	Continuous	1.01	1.00 – 1.01	0.04*

5.6 Severity of Diabetic Neuropathy

This finding suggested that, 16 (4.1%) had no neuropathy, 174 (44.6%) had mild neuropathy, 134 (34.4%) had moderate neuropathy, and 66 (16.9%) had severe neuropathy. The largest proportion of participants fell into the mild and moderate categories, indicating that the majority of long-term metformin users experience some degree of neuropathic complications.

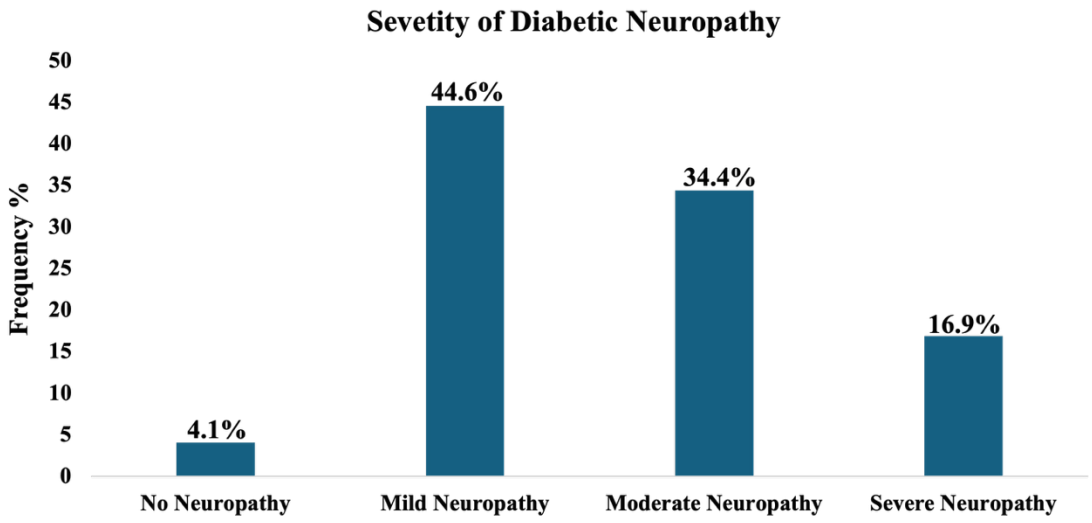

Figure 4: Severity of Diabetic Neuropathy among participants.

The graph indicates that among all participants, the majority experience mild to moderate complications.

5.7 Associated factors for Severity of Diabetic Neuropathy

Independent variables were assessed to evaluate for their association with the severity of diabetic neuropathy. Variables including age, residence, occupational status, duration of diabetes, duration of metformin use, any side-effects of metformin, HbA1c, FBS and insulin use and any co morbidities showed significant crude associations. They were then included as candidate for the multinomial multivariate logistic regression to evaluate their independent effect.

Table 5: Multinomial Bivariate Logistic Regression Analysis of Diabetes Related Factors Associated with Diabetic Neuropathy Severity

Variable	Category	No Neuropathy OR (95% CI, p)	Mild Neuropathy OR (95% CI, p)	Moderate Neuropathy OR (95% CI, p)
Age Category	31-40	19.00 (2.21–163.57, 0.007) *	9.50 (0.42–217.61, 0.159) *	2.00 (0.21–19.16, 0.548)
	41-50	9.35 (2.88–30.36, 0.000) *	3.80 (0.42–34.08, 0.233) *	1.90 (0.62–5.87, 0.265) *
	51-60	3.70 (1.47–9.33, 0.006) *	2.53 (0.41–15.75, 0.319)	2.03 (0.92–4.48, 0.078) *
	61-70	2.14 (0.90–5.07, 0.085) *	2.56 (0.48–13.71, 0.273)	1.00 (0.49–2.06, 1.000)
	>70	-	-	-
Sex	Male	0.91 (0.51–1.65, 0.764)	0.31 (0.09–1.07, 0.065) *	0.99 (0.56–1.74, 0.960)
	Female	-	-	-
Residence	Urban	1.61 (0.64–4.03, 0.313)	2.37 (0.28–20.19, 0.430)	2.59 (1.00–6.69, 0.050) *
	Rural	-	-	-
Educational status	No formal Education	0.45 (0.20–1.03, 0.059) *	1.56 (0.38–6.31, 0.536)	0.95 (0.43–2.08, 0.894)
	Primary	0.49 (0.22–1.10, 0.085) *	0.44 (0.07–2.76, 0.384)	0.95 (0.43–2.08, 0.894)
	Secondary	0.65 (0.28–1.52, 0.320)	0.86 (0.16–4.51, 0.856)	0.84 (0.36–1.95, 0.683)
	Higher	-	-	-
Occupation	Employed	3.54 (1.69–7.39, 0.01) *	1.29 (0.29–5.75, 0.74)	1.29 (0.65–2.53, 0.48)
	Unemployed	2.75 (1.27–5.98, 0.01) *	3.00 (0.79–11.46, 0.11)	1.50 (0.75–3.02, 0.26)
	Retired	-	-	-
Duration of Diabetes	5-10 Years	4.74 (2.42–9.26, 0.01) *	2.64 (0.84–8.30, 0.09) *	1.19 (0.61–2.31, 0.62)
	>10 Years	-	-	-
Diabetes Related Complication	Yes	0.97 (0.53–1.75, 0.91)	1.23 (0.40–3.78, 0.72)	1.44 (0.80–2.57, 0.22) *
	No	-	-	-

Regular Monitoring of Blood Sugar	Yes	0.86 (0.42–1.75, 0.67)	0.59 (0.18–1.99, 0.39)	0.63 (0.32–1.24, 0.18) *
	No	-	-	-
Duration of Metformin	5-10 Years	5.90 (2.89–12.03, 0.01) *	3.50 (1.09–11.27, 0.04) *	1.62 (0.80–3.29, 0.19) *
	>10 Years	-	-	-
Daily metformin dosage	500 mg/day	1.66 (0.63–4.38, 0.31)	1.01 (0.18–5.59, 0.99)	0.77 (0.29–2.04, 0.61)
	1000 mg/day	2.06 (1.07–3.93, .030) *	0.53 (0.13–2.12, 0.37)	0.92 (0.49–1.74, 0.799)
	>1000 mg/day	-	-	-
Any Side effects of Metformin	Yes	2.05 (1.07–3.93, 0.03) *	0.53 (0.13–2.13, 0.37)	0.92 (0.49–1.74, 0.79)
	No	-	-	-
Last Recorded HbA1C level		0.83 (0.67–1.03, 0.08) *	1.38 (0.99–1.91, 0.05) *	1.02 (0.84–1.24, 0.86)
Insulin Use	Yes	0.69 (0.35–1.40, 0.31)	1.31 (0.40–4.32, 0.66)	0.92 (0.48–1.76, 0.79)
	No	-	-	-
Any Co-morbidities	Yes	0.53 (0.27–1.04, 0.06) *	1.28 (0.32–5.07, 0.73)	1.02 (0.52–2.00, 0.96)
	No	-	-	-

Age, Residence, Duration of Metformin and Fasting blood sugar became significant factors after their adjustment for the severity of diabetic neuropathy.

Patients aged 31–40 years (AOR = 7.45, 95% CI: 0.73–75.71, p = 0.04) had significantly higher odds of having no neuropathy compared with those over 70 years. Similarly, urban residents (AOR = 2.73, 95% CI: 1.02–7.30, p = 0.05) are more likely to have moderate neuropathy compared with rural residents.

Duration of Metformin was also a significant predictor in which participants using metformin for 5-10 years (AOR = 3.29, 95% CI: 1.47–7.36, p = 0.01) had higher odds of having no neuropathy compared with those using it for more than 10 years. Additionally, fasting blood sugar (AOR = 0.99, 95% CI: 0.99–7.36, p = 0.02) was inversely associated with having no neuropathy, indicating that having high blood sugar reduces the likelihood of being free from neuropathy.

Table 6: Multinomial Multivariate Logistic Regression Analysis of Factors Associated with Diabetic Neuropathy Severity

Variable	Category	No Neuropathy Adjusted OR (95% CI, p)	Mild Neuropathy Adjusted OR (95% CI, p)	Moderate Neuropathy Adjusted OR (95% CI, p)
Age Category	31-40	7.45 (0.73–75.71, 0.04) *	4.22 (0.13–141.91, 0.42)	1.84 (0.17–20.24, 0.62)
	41-50	3.83 (0.99–14.77, 0.05)	2.13 (0.18–25.79, 0.56)	1.69 (0.48–5.99, 0.41)
	51-60	2.50 (0.88–7.13, 0.09)	2.09 (0.29–15.27, 0.47)	2.15 (0.88–5.29, 0.09)
	61-70	1.92 (0.76–4.84, 0.17)	2.63 (0.45–15.30, 0.28)	1.17 (0.54–2.52, 0.69)
	>70	-	-	-
Sex	Male	1.31 (0.65–2.61, 0.45)	0.53 (0.14–2.11, 0.37)	1.19 (0.63–2.27, 0.58)
	Female	-	-	-
Residence	Urban	1.59 (0.56–4.30, 0.40)	2.83 (0.29–27.08, 0.37)	2.73 (1.02–7.30, 0.05) *
	Rural	-	-	-
Educational status	No formal education	0.57 (0.20–1.61, 0.29)	1.69 (0.28–10.15, 0.56)	1.28 (0.51–3.23, 0.59)
	Primary	0.59 (0.23–1.49, 0.26)	0.45 (0.06–3.29, 0.43)	1.15 (0.49–2.71, 0.75)
	Secondary	0.65 (0.25–1.69, 0.38)	0.97 (0.17–5.58, 0.97)	0.96 (0.39 –2.32, 0.92)
	Higher	1.00	-	-
Occupation	Employed	2.38 (0.69–8.19, 0.17)	4.92 (0.34–69.77, 0.24)	3.26 (0.98–10.87, 0.06)
	Unemployed	2.09 (0.81–5.41, 0.13)	1.79 (0.35–9.10, 0.48)	1.21 (0.53–2.74, 0.65)
	Retired	1.00	-	-
Duration of Metformin	5-10 Years	3.29 (1.47–7.36, 0.01) *	3.08 (0.76–12.48, 0.12)	1.35 (0.61–2.97, 0.46)

	>10 Years	-	-	-
Daily metformin dosage	500mg/day	0.70 (0.23–2.14, 0.53)	0.73 (0.12–4.49, 0.74)	0.57 (0.20–1.56, 0.29)
	1000mg/day	1.33 (0.65–2.72, 0.44)	0.48 (0.11–2.05, 0.32)	0.81 (0.41–1.58, 0.54)
	>1000mg/day	-	-	-
Any Comorbidities	Yes	0.72 (0.16–6.19, 0.66)	0.72 (0.16–6.19, 0.66)	0.85 (0.39–2.43, 0.67)
	No	1.00	-	-
FBS	Continuous	0.99 (0.98–0.99, 0.02) *	1.00 (0.99–1.02, 0.18)	0.99 (0.99–1.00, 0.40)
Insulin use	Continuous	1.06 (0.49–2.28, 0.87)	1.74 (0.48–6.38, 0.40)	0.93 (0.47–1.85, 0.84)

6 DISSCUSSIONS

This study assessed the prevalence and determinants of diabetic neuropathy among adults with T2DM on long-term metformin therapy at two major referral hospitals in Addis Ababa. The finding revealed a high prevalence (63.1%), with most patients presenting with mild to moderate forms of severity. Longer metformin exposure (>10 years) and elevated fasting blood glucose were independently associated with diabetic neuropathy, while younger adults (31-50 years) had significantly lower odds compared with those older than 70 years. These findings highlight the combined impact of long-term metformin therapy and poor glycemic control on diabetic neuropathy risk.

6.1 Prevalence of Diabetic Neuropathy

The observed prevalence of 63.1% exceeds global pooled estimates of 25–35% (36,52,53), but remains within the upper range when sensitive diagnostic tools are employed. Sub-Saharan Africa studies report similarly high burdens, ranging from 45% in Kenya to 68% in Nigeria (54-56). A recent African meta-analysis estimated a pooled prevalence of 53%, with considerable heterogeneity (57). Regional studies in Ethiopia have reported similar high burdens of diabetic neuropathy, corroborating our findings (58-60).

6.2 Associated Factors of Diabetic Neuropathy

Long-term Metformin exposure

Neuropathy was significantly more common in patients using metformin for over 10 years, supporting evidence that prolonged therapy predisposes to vitamin B12 deficiency—a well-established cause of sensory neuropathy (61–64). Randomized and longitudinal studies, including the Diabetes Prevention Program Outcomes Study (DPPOS), have shown progressive declines in vitamin B12 levels with metformin use and higher neuropathy prevalence in those deficient (61,62). Systematic reviews reinforce this association (63,64), and the American Diabetes Association (ADA) Standards of Care (2025) recommend periodic assessment of vitamin B12 in individuals on long- term metformin, particularly when anemia or neuropathy is suspected (65).

Age

Patients aged 31–50 years had lower odds of neuropathy than those over 70. This may reflect shorter duration of diabetes and metformin reduces the risk of developing the complication. Similar findings have been reported in USA and Iran, where younger patients has lower risk of neuropathy when compared with older aged patients (44,48).

Glycemic exposure

Elevated fasting blood glucose was independently associated with DN, consistent with the established role of hyperglycemia in promoting oxidative stress, mitochondrial injury, and microvascular ischemia (44). This reinforces the central role of durable glycemic control in preventing progression (52,53).

Socioeconomic determinants

Lower educational attainment was linked with greater neuropathy risk, reflecting the influence of health literacy, adherence, and self-management. Comparable associations have been reported in Ghana and the U.S (48). Occupational status also mattered: unemployed participants were more likely to have neuropathy than retired individuals, suggesting barriers to healthcare access and lifestyle differences.

Duration and treatment

Longer diabetes duration (>10 years) strongly predicted neuropathy, in line with established evidence linking chronicity to microvascular complications (36). Although most patients received >1000 mg/day metformin, dosage was not independently predictive after adjustment. The wide variation in reported vitamin B12 deficiency prevalence among metformin users from 7.8% in Saudi Arabia to >40% in Ghana—supports the biological plausibility of our findings (66).

Protective factors

Only 21.3% of patients reported taking nerve health supplements, yet supplementation was strongly protective. Comparable evidence from India demonstrates that vitamin replacement can significantly reduce deficiency and neuropathy prevalence in long-term metformin users (67).

6.3 Severity of Neuropathy

Most participants had mild (44.6%) or moderate (34.4%) neuropathy, with 16.9% classified as severe. This distribution aligns with staging patterns observed in longitudinal cohorts, where early sensory deficits precede disabling complications (7,68). Patients taking supplements were less likely to experience severe neuropathy, reinforcing the value of preventive intervention.

6.4 Relationship between Long-term Metformin Use and Vitamin B12 Levels

Although the present study did not directly assess the relationship between long-term metformin use and serum Vitamin B12 levels, numerous International and Ethiopian studies have demonstrated as significant association between chronic metformin theraphy and vitamin B12 deficiency.

Evidence from international research consistently supports this relationship. For instance, a study conducted in United States found that approximately 7% of individuals with diabetes receiving metformin were vitamin B12 deficient (<170 pg/dL) compared to 3% of persons among non-diabetic individuals or those not using metformin (P = .0001) (48). Similarly, another study reported that patients using metformin for 3 years or longer had an adjusted odds ratios of 2.39 (95% confidence interval, 1.46-3.91) (P = 0.001) for vitamin B12 deficiency compared with those using it for less than 3 years. The authors concluded that metformin dose and duration of use were the strongest independent predictor of vitamin B12 deficiency, supporting a dose-dependent effect (50).

Ethiopian data further strengthen these findings. A study conducted at Tikur Anbessa Specialized Hospital in Addis Ababa revealed that 21.1% of patients with T2DM on metformin therapy exhibited low serum vitamin B12 levels, compared to 4.0% among those not receiving metformin. The study demonstrated a significant negative correlation between metformin dose and treatment duration with serum vitamin B12 concentration, indicating that prolonged and higher-dose metformin use is associated with greater risk of deficiency(71).

Taken together, these findings suggest that long-term metformin therapy adversely affects vitamin B12 status, likely through reduced intestinal absorption. While our study did not include a direct assessment of serum vitamin B12 levels, these consistent findings from both international and Ethiopian research highlight the importance of monitoring vitamin B12 status in patients on long-term metformin therapy to prevent potential neurological and hematological complications.

7. STRENGTH AND LIMITATION OF THE STUDY

7.1 Strength of the study

- ✓ Large sample size, which increases the statistical power and reliability of the findings
- ✓ Use of robust regression analyses, enhancing the validity of the results by accounting for potential confounding variables and outliers.

7.2 Limitation of the study

- ✓ Cross-sectional design, which limits causal inference
- ✓ Absence of direct VB12 measurements

8. CONCLUSION

This study demonstrates that diabetic neuropathy is highly prevalent among patients with type 2 diabetes on long-term metformin treatment in Ethiopia, with most patients presenting with mild to moderate form of severity. Prolonged metformin use (>10 years), poor glycemic control, longer diabetes duration, and lower educational status were significant risk factors, while vitamin supplementation emerged as a strong protective factor. These findings underscore the dual contribution of hyperglycemia and metformin-associated vitamin B12 deficiency to neuropathy development. Routine screening for neuropathy, regular monitoring of vitamin B12 levels, and timely supplementation, alongside sustained glycemic management and patient education, should be prioritized to reduce neuropathy burden and improve quality of life in this high-risk population.

Mechanistic and Clinical Considerations

These findings underscore two converging mechanisms: (A) vitamin B12 deficiency due to prolonged metformin use and (B) hyperglycemia-driven metabolic and vascular damage. Acting synergistically, they accelerate nerve injury in long-standing diabetes (61–63,69). Clinically, three priorities emerge: (a) routine screening and correction of vitamin B12 deficiency in chronic metformin users, (b) optimization of glycemic control, and (c) targeted monitoring of high-risk groups, including older adults and those with longer disease duration.

Implications for Practice and Policy

Routine neuropathy screening and B12 monitoring should be incorporated into diabetes care in Ethiopia. Expanding access to cost-effective supplementation and patient education programs may reduce neuropathy burden and improve long-term outcomes.

9. RECOMMENDATION

Routine neuropathy screening and Vitamin B12 monitoring should be incorporated into diabetes care in Ethiopia. Expanding access to cost-effective supplementations and patient education programs may help reduce the burden of neuropathy and improve long-term health outcomes for patients.

Future research should include prospective studies that incorporate biochemical assessments and intervention trials. Conducting such prospective studies will allow for more direct evaluation of relationships between risk factors, interventions, and the development or progression of diabetic neuropathy. This approach will strengthen the evidence based and guide more effective strategies for prevention and management.

REFERENCES

1. Barceló A, Rajpathak S. Incidence and prevalence of diabetes mellitus in the Americas. Rev Panam Salud Pública. 2001 Nov;10(5):300–8.

2. Mekuria Negussie Y, Tilahun Bekele N. Diabetic peripheral neuropathy among adult type 2 diabetes patients in Adama, Ethiopia: health facility-based study. Sci Rep. 2024 Feb 15;14(1):3844.

3. Health-related quality of life of patients with type 2 diabetes mellitus at a tertiary care hospital in Ethiopia | PLOS One [Internet]. [cited 2025 Mar 27]. Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0264199

4. Zeru MA, Tesfa E, Mitiku AA, Seyoum A, Bokoro TA. Prevalence and risk factors of type-2 diabetes mellitus in Ethiopia: systematic review and meta-analysis. Sci Rep. 2021 Nov 5;11(1):21733.

5. The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives | Nature Reviews Endocrinology [Internet]. [cited 2025 Mar 25]. Available from: https://www.nature.com/articles/nrendo.2011.183

6. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2014 Jan 1;37(Supplement_1):S81–90.

7. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, et al. Type 2 diabetes mellitus. Nat Rev Dis Primer. 2015 Jul 23;1:15019.

8. Olokoba AB, Obateru OA, Olokoba LB. Type 2 Diabetes Mellitus: A Review of Current Trends. Oman Med J. 2012 Jul;27(4):269–73.

9. Abdul Basith Khan M, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes — Global Burden of Disease and Forecasted Trends. J Epidemiol Glob Health. 2020 Mar 1;10(1):107–11.

10. Medscape [Internet]. [cited 2025 Mar 27]. Diabetes in the African Diaspora - Page 2. Available from: https://www.medscape.com/viewarticle/560718

11. Alberti KGMM, Zimmet P, Shaw J. International Diabetes Federation: a consensus on Type 2 diabetes prevention. Diabet Med. 2007;24(5):451–63.

12. Is metformin a possible treatment for diabetic neuropathy? - Wei - 2022 - Journal of Diabetes - Wiley Online Library [Internet]. [cited 2025 Mar 25]. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/1753-0407.13310

13. Vitamin B12 deficiency in metformin-treated type-2 diabetes patients, prevalence and association with peripheral neuropathy | BMC Pharmacology and Toxicology [Internet]. [cited 2025 Mar 25]. Available from: https://link.springer.com/article/10.1186/s40360-016-0088-3

14. The role of metformin on vitamin B12 deficiency: a meta-analysis review | Internal and Emergency Medicine [Internet]. [cited 2025 Mar 25]. Available from: https://link.springer.com/article/10.1007/s11739-014-1157-5

15. Alvarez M, Sierra OR, Saavedra G, Moreno S. Vitamin B12 deficiency and diabetic neuropathy in patients taking metformin: a cross-sectional study. 2019 Oct 1 [cited 2025 Mar 20]; Available from: https://ec.bioscientifica.com/view/journals/ec/8/10/EC-19-0382.xml

16. Fowler MJ. Microvascular and Macrovascular Complications of Diabetes.

17. Diabetic neuropathy | Postgraduate Medical Journal | Oxford Academic [Internet]. [cited 2025 Mar 11]. Available from: https://academic.oup.com/pmj/article/82/964/95/7045246

18. Geerts M, Bours G, Wit R de, Landewé S, van Haarlem A, Schaper N. Prevalence and impact of pain in diabetic neuropathy. Eur Diabetes Nurs. 2009 Sep 1;6(2):58–64.

19. Vinik A, Ullal J, Parson HK, Casellini CM. Diabetic neuropathies: clinical manifestations and current treatment options. Nat Clin Pract Endocrinol Metab. 2006 May;2(5):269–81.

20. Booya F, Bandarian F, Larijani B, Pajouhi M, Nooraei M, Lotfi J. Potential risk factors for diabetic neuropathy: a case control study. BMC Neurol. 2005 Dec;5(1):24.

21. He KJ, Wang H, Xu J, Gong G, Liu X, Guan H. Global burden of type 2 diabetes mellitus from 1990 to 2021, with projections of prevalence to 2044: a systematic analysis across SDI levels for the global burden of disease study 2021. Front Endocrinol [Internet]. 2024 Nov 8 [cited 2025 Mar 26];15. Available from: https://www.frontiersin.org https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2024.1501690/full

22. Cannon A, Handelsman Y, Heile M, Shannon M. Burden of Illness in Type 2 Diabetes Mellitus. J Manag Care Spec Pharm. 2018 Sep;24(9-a Suppl):S5–13.

23. Home, Resources, diabetes L with, Acknowledgement, FAQs, Contact, et al. IDF Diabetes Atlas [Internet]. [cited 2025 Mar 26]. Available from: https://diabetesatlas.org/

24. Zimmet P. The burden of type 2 diabetes: are we doing enough? Diabetes Metab. 2003 Sep 1;29(4, Part 2):6S9–18.

25. Gebremariam GT, Biratu S, Alemayehu M, Welie AG, Beyene K, Sander B, et al. Health-related quality of life of patients with type 2 diabetes mellitus at a tertiary care hospital in Ethiopia. PLOS ONE. 2022 Feb 18;17(2):e0264199.

26. Roglic G. WHO Global report on diabetes: A summary. Int J Noncommunicable Dis. 2016 Jun;1(1):3.

27. Solela G, Gessesse HA, Zegeye H, Worku A, Leulseged B. Prevalence, patterns, and determinants of vascular complications of type 2 diabetes in a teaching hospital in Addis Ababa, Ethiopia: a retrospective study. BMC Endocr Disord. 2024 Sep 18;24(1):190.

28. Dimore AL, Edosa ZK, Mitiku AA. Glycemic control and diabetes complications among adult type 2 diabetic patients at public hospitals in Hadiya zone, Southern Ethiopia. PLOS ONE. 2023 Mar 23;18(3):e0282962.

29. Bansal V, Kalita J, Misra UK. Diabetic neuropathy. Postgrad Med J. 2006 Feb 1;82(964):95–100.

30. Boulton AJM, Malik RA. DIABETIC NEUROPATHY. Med Clin North Am. 1998 Jul 1;82(4):909–29.

31. Said G. Chapter 33 - Diabetic neuropathy. In: Said G, Krarup C, editors. Handbook of Clinical Neurology [Internet]. Elsevier; 2013 [cited 2025 Mar 19]. p. 579–89. (Peripheral Nerve Disorders; vol. 115). Available from: https://www.sciencedirect.com/ science/ article/pii/B9780444529022000333

32. Boulton AJM, Malik RA. DIABETIC NEUROPATHY. Med Clin North Am. 1998 Jul 1;82(4):909–29.

33. Vinik AI, Mehrabyan A. Diabetic neuropathies. Med Clin. 2004 Jul 1;88(4):947–99.

34. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. Nat Rev Dis Primer. 2019 Jun 13;5(1):1–18.

35. Said G. Diabetic neuropathy—a review. Nat Clin Pract Neurol. 2007 Jun;3(6):331–40.

36. Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care. 2017 Jan;40(1):136–54.

37. Vinik AI. Diabetic Neuropathies. In: Skyler J, editor. Atlas of Diabetes: Fourth Edition [Internet]. Boston, MA: Springer US; 2012 [cited 2025 Mar 19]. p. 295–312. Available from: https://doi.org/10.1007/978-1-4614-1028-7_14

38. Ziegler D, Gries F a., Spüler M, Lessmann F, Group DMS. The Epidemiology of Diabetic Neuropathy. Diabet Med. 1993;10(S2):82S-86S.

39. Abbott CA, Malik RA, van Ross ERE, Kulkarni J, Boulton AJM. Prevalence and Characteristics of Painful Diabetic Neuropathy in a Large Community-Based Diabetic Population in the U.K. Diabetes Care. 2011 Sep 15;34(10):2220–4.

40. Anandhanarayanan A, Teh K, Goonoo M, Tesfaye S, Selvarajah D. Diabetic Neuropathies. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chrousos G, Corpas E, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000 [cited 2025 Mar 19]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK279175/

41. Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic Autonomic Neuropathy. Diabetes Care. 2003 May 1;26(5):1553–79.

42. Tadesse DB, Gebrewahd GT, Hailay A, Aberhe W, Mebrahtom G, Zereabruk K, et al. Diabetic Peripheral Neuropathy in Ethiopia: A Systematic Review and Meta-Analysis. J Diabetes Res. 2021;2021(1):5304124.

43. Pittenger G, Vinik A. Nerve Growth Factor and Diabetic Neuropathy. J Diabetes Res. 2003;4(4):153048.

44. Booya F, Bandarian F, Larijani B, Pajouhi M, Nooraei M, Lotfi J. Potential risk factors for diabetic neuropathy: a case control study. BMC Neurol. 2005 Dec 10;5:24.

45. Popescu S, Timar ,Bogdan, Baderca ,Flavia, Simu ,Mihaela, Diaconu ,Laura, Velea ,Iulian, et al. Age as an independent factor for the development of neuropathy in diabetic patients. Clin Interv Aging. 2016 Mar 15;11:313–8.

46. Liu X, Xu Y, An M, Zeng Q. The risk factors for diabetic peripheral neuropathy: A meta-analysis. PLOS ONE. 2019 Feb 20;14(2):e0212574.

47. Ahmed MA, Muntingh G, Rheeder P. Vitamin B12 deficiency in metformin-treated type-2 diabetes patients, prevalence and association with peripheral neuropathy. BMC Pharmacol Toxicol. 2016 Oct 7;17(1):44.

48. Serra MC, Kancherla V, Khakharia A, Allen LL, Phillips LS, Rhee MK, et al. Long-term metformin treatment and risk of peripheral neuropathy in older Veterans. Diabetes Res Clin Pract. 2020 Dec;170:108486.

49. Singh AK, Kumar A, Karmakar D, Jha RK. Association of B12 deficiency and clinical neuropathy with metformin use in type 2 diabetes patients. J Postgrad Med. 2013 Dec;59(4):253.

50. Ting RZW, Szeto CC, Chan MHM, Ma KK, Chow KM. Risk Factors of Vitamin B12 Deficiency in Patients Receiving Metformin. Arch Intern Med. 2006 Oct 9;166(18):1975–9.

51. Solela G, Gessesse HA, Zegeye H, Worku A, Leulseged B. Prevalence, patterns, and determinants of vascular complications of type 2 diabetes in a teaching hospital in Addis Ababa, Ethiopia: a retrospective study. BMC Endocr Disord. 2024 Sep 18;24(1):190.

52. Tesfaye S, Selvarajah D. Advances in the epidemiology, pathogenesis and management of diabetic peripheral neuropathy. Diabetes Metab Res Rev. 2012 Feb;28 Suppl 1:8–14.

53. Callaghan BC, Cheng HT, Stables CL, Smith AL, Feldman EL. Diabetic neuropathy: clinical manifestations and current treatments. Lancet Neurol. 2012 Jun;11(6):521–34.

54. Nyamu PN, Otieno CF, Amayo EO, McLigeyo SO. Risk factors and prevalence of diabetic foot ulcers at Kenyatta National Hospital, Nairobi. East Afr Med J. 2003 Jan;80(1):36–43.

55. Ogbera OA, Osa E, Edo A, Chukwum E. Common clinical features of diabetic foot ulcers: perspectives from a developing nation. Int J Low Extrem Wounds. 2008 Jun;7(2):93–8.

56. Kisozi T, Mutebi E, Kisekka M, Lhatoo S, Sajatovic M, Kaddumukasa M, et al. Prevalence, severity and factors associated with peripheral neuropathy among newly diagnosed diabetic patients attending Mulago hospital: a cross-sectional study. Afr Health Sci. 2017 Jun;17(2):463–73.

57. Alam U, Riley DR, Jugdey RS, Azmi S, Rajbhandari S, D'Août K, et al. Diabetic Neuropathy and Gait: A Review. Diabetes Ther Res Treat Educ Diabetes Relat Disord. 2017 Dec;8(6):1253–64.

58. Tadesse DB, Gebrewahd GT, Hailay A, Aberhe W, Mebrahtom G, Zereabruk K, et al. Diabetic Peripheral Neuropathy in Ethiopia: A Systematic Review and Meta-Analysis. J Diabetes Res. 2021;2021:5304124.

59. Wang C, Wang H, Zhou Y, Zhang S, Huang M. Evaluation of the clinical value of shear wave elastography for early detection and diagnosis of diabetic peripheral neuropathy: a controlled preliminary prospective clinical study. BMC Musculoskelet Disord. 2022 Dec 22;23(1):1120.

60. Worku D, Hamza L, Woldemichael K. Patterns of diabetic complications at jimma university specialized hospital, southwest ethiopia. Ethiop J Health Sci. 2010 Mar;20(1):33–9.

61. de Jager J, Kooy A, Lehert P, Wulffelé MG, van der Kolk J, Bets D, et al. Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled trial. BMJ. 2010 May 20;340:c2181.

62. Aroda VR, Edelstein SL, Goldberg RB, Knowler WC, Marcovina SM, Orchard TJ, et al. Long-term Metformin Use and Vitamin B12 Deficiency in the Diabetes Prevention Program Outcomes Study. J Clin Endocrinol Metab. 2016 Apr;101(4):1754–61.

63. Liu KW, Dai LK, Jean W. Metformin-related vitamin B12 deficiency. Age Ageing. 2006 Mar;35(2):200–1.

64. Chapman LE, Darling AL, Brown JE. Association between metformin and vitamin B12 deficiency in patients with type 2 diabetes: A systematic review and meta-analysis. Diabetes Metab. 2016 Nov;42(5):316–27.

65. Volume 48 Issue Supplement_1 | Diabetes Care | American Diabetes Association [Internet]. [cited 2025 Sep 21]. Available from: https://diabetesjournals.org/care/issue/48/Supplement_1

66. Sakyi SA, Laing EF, Mantey R, Kwarteng A, Owiredu EW, Dadzie RE, et al. Profiling immuno-metabolic mediators of vitamin B12 deficiency among metformin-treated type 2 diabetic patients in Ghana. Nwosu BU, editor. PLOS ONE. 2021 Mar 30;16(3):e0249325.

67. Farooq MD, Tak FA, Ara F, Rashid S, Mir IA. Vitamin B12 Deficiency and Clinical Neuropathy with Metformin Use in Type 2 Diabetes. J Xenobiotics. 2022 May 31;12(2):122–30.

68. Saif DS, Zewain SK, Mohamed AR, Rabee RM, Afifi N, Abdel-Fattah YH, et al. The Prevalence of Peripheral Neuropathy in a Cohort of Egyptians with Prediabetes. Clinical and Electrophysiological Study. Clin Diabetol. 2025;14(4):221–8.

69. Edwards JL, Vincent AM, Cheng HT, Feldman EL. Diabetic neuropathy: mechanisms to management. Pharmacol Ther. 2008 Oct;120(1):1–34.

70. Saif DS, Zewain SK, Mohamed AR, Rabee RM, Afifi N, Abdel-Fattah YH, et al. The Prevalence of Peripheral Neuropathy in a Cohort of Egyptians with Prediabetes. Clinical and Electrophysiological Study. Clin Diabetol. 2025;14(4):221–8.

71. Tesfaye S, Hailu E, Abebe M, Fekadu S, Wolde M, Worku A, Welde M, Getachew T, Nigussie S, Berhanu G. Effect of long-term metformin therapy on vitamin B12 status among type 2 diabetic patients attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. BMC Endocrine Disorders. *2022;22(1):85. doi:10.1186/s12902-022-00957-4.*

Annexes

Annex I. Participant information sheet (English Version)

Department of Anatomy, School of Biomedicine and Laboratory Sciences, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia.

Title of the Research Project: Prevalence and Associated factors of diabetic neuropathy among Ethiopian long-term metformin users in Tikur Anbessa Specialized Hospital and Yekatit 12 Hospital, Addis Ababa, Ethiopia. First of all, we would like to thank you in advance for your cooperation and consent in participation in this study. Please read or listen when it is read for you about the general information of the study. If you have any question regarding the study please ask freely.

Background information

My name is Michael Teshale, a Master's degree (MSc) student in Biomedical Science specializing in Human Anatomy at Addis Ababa University. I am planning to conduct a medical research study, which I invite you to take part in.

Background: Diabetic Neuropathy (DN) is a common and serious complication of diabetes mellitus (DM), affecting up to 50% of diabetic patients globally. It leads to significant morbidity including chronic pain, loss of sensation, and increased risk of foot ulcers and amputations. Among Ethiopian Diabetic patients, studies indicate varying prevalence rates, yet limited research has focused specifically on the impact of long-term metformin use. Metformin, the first-line drug treatment for type 2 diabetes mellitus (T2DM), has been associated with Vitamin B 12 deficiency, a known risk factor for neuropathy.

Aim of the study

- The purpose of this study is to assess the prevalence of diabetic neuropathy and its associated risk factors in long-term metformin users at Tikur Anbessa Specialized Teaching Hospital and Yekatit 12 Hospital, Addis Ababa, Ethiopia.

Benefits for participants

Study participants will not have any financial incentives or other inducements from participating on this study. However, based on the diagnosis result you will be treated accordingly. Most importantly, the result of the study will be beneficial for planning to screen, prevent or treat neuropathy due to long-term metformin use. Hence, you are indirectly benefiting other patients and the society in this respect.

Risks and complication

There are no anticipated risks to your participation. Questions and Standardized simple physical examinations are done.

Confidentiality

On the request paper your name or your identities will not be mentioned and any information given to me will remain confidential and your privacy will be respected. Results and information given by the participants will serve only for this research not for any other purpose. Participation in this study is exclusively voluntarily. If you are not interested to participate, there will be no consequences.

Person to contact

If you have any questions about this study, you should feel free to ask now or anytime throughout the study by contacting:

PI Address: Michael Teshale: Department of Anatomy, School of Biomedicine and Laboratory Sciences, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia.

Cell phone: +251-927 697027

Email: michael-gsr-1411-16@aau.edu.et

Questionnaire: Prevalence and Associated Factors of Diabetic Neuropathy Among Ethiopian Long-Term Metformin Users

Section 1: Demographic Information

1. Age	☐ 31-40 years
	☐ 41-50 years
	☐ 51-60 years
	☐ 61-70 years
	☐ >70 years
2. Gender	☐ Male
	☐ Female
3. Residence	☐ Urban
	☐ Rural
4. Level of Education	☐ No formal Education
	☐ Primary Education
	☐ Secondary Education
	☐ Higher Education

Section 2: Diabetes History

6. How long have you been diagnosed with diabetes?	☐ 5-10 years
	☐ More than 10 years
7. Have you been diagnosed with any diabetes-related complications?	☐ Yes
	☐ No

8. Do you regularly monitor your blood sugar levels?	☐ Yes
	☐ No
9. What was your last recorded HbA1c level (if known)?	_____ %

Section 3: Metformin Use

10. How long have you been taking metformin?	☐ 5–10 years
	☐ More than 10 years
11. What is your current metformin dosage?	☐ 500 mg/day
	☐ 1000 mg/day
	☐ More than 1000 mg/day
12. Have you ever experienced any side effects from metformin?	☐ Yes
	☐ No
13. Have you been tested for vitamin B12 deficiency?	☐ Yes
	☐ No
14. If tested, was your vitamin B12 level found to be	☐ Normal
	☐ Low
15. Are you taking any additional supplements or medications for nerve health (e.g., vitamin B12, pain relievers)?	☐ Yes
	☐ No

MICHIGAN NEUROPATHY SCREENING INSTRUMENT

Patient version

A. History (To be completed by the person with diabetes)

Please take a few minutes to answer the following questions about the feeling in your legs and feet. Check yes or no based on how you usually feel. Thank you

1. Are your legs and/or feet numb?	☐ Yes
	☐ No
2. Do you ever have any burning pain in your legs and/or feet?	☐ Yes
	☐ No
3. Are your feet too sensitive to touch?	☐ Yes
	☐ No
4. Do you get muscle cramps in your legs and/or feet?	☐ Yes
	☐ No
5. Do you ever have any prickling feelings in your legs or feet?	☐ Yes
	☐ No
6. Does it hurt when the bed covers touch your skin?	☐ Yes
	☐ No
7. When you get into the tub or shower, are you able to tell the hot water from the cold water?	☐ Yes
	☐ No
8. Have you ever had an open sore on your foot?	☐ Yes
	☐ No
9. Has your doctor ever told you that you have diabetic neuropathy?	☐ Yes
	☐ No

10. Do you feel weak all over most of the time?	☐ Yes
	☐ No
11. Are your symptoms worse at night?	☐ Yes
	☐ No
12. Do your legs hurt when you walk?	☐ Yes
	☐ No
13. Are you able to sense your feet when you walk?	☐ Yes
	☐ No
14. Is the skin on your feet so dry that it cracks open?	☐ Yes
	☐ No
15. Have you ever had an amputation?	☐ Yes
	☐ No
TOTAL	_____

B. Physical Assessment

1.Appearance of foot	
Right Foot- Normal	☐ Yes
	☐ No
Left Foot- Normal	☐ Yes
	☐ No
If no, check all that apply	☐ Deformities
	☐ Dry skin, callus
	☐ Infection
	☐ Fissure

	☐ Other
2.Ulceration	
Right Foot	☐ Yes
	☐ No
Left foot	☐ Yes
	☐ No
3.Ankle Reflexes	
Right Foot	☐ Yes
	☐ No
Left Foot	☐ Present
	☐ Absent
4.Vibration	
Right Foot	☐ Present
	☐ Reduced
	☐ Absent
Left Foot	☐ Present
	☐ Reduced
	☐ Absent
5.10 gm filament (number of applications deducted out of 10 applications)	
Right Foot	☐ Present (8 and above)
	☐ Reduced (1-7)
	☐ Absent (0)
Left Foot	☐ Present (8 and above)
	☐ Reduced (1-7)
	☐ Absent (0)

Annex II. Participant information sheet (Amharic Version)

በአዲስ አበባ ዩኒቨርስቲ፤ የጤና ሳይንስ ኮሌጅ የአናቶሚ ት/ክፍል

የጥናቱ ርዕስ፡- ለረጅም ጊዜ ሜትፎርሚን በሚወስዱ የስኳር በሽተኞች ላይ የነርቭ ህመም ችግር መጠኑ ምን ይመስላል የሚል ጥናት በጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል እና በየካቲት 12 ሆስፒታል አዲስ አበባ ኢትዮጵያ በቅድሚያ በዚህ ጥናት ላይ ለመሳተፍ ፍቃደኛ በመሆንዎ እናመሰግናለን፡፡ እባክዎ ስለጥናቱ ጠቅላላ መረጃ በጥሞና ያንብቡ ወይም ሲነበብሎት ይስሙ፤ ማንኛውም፤ ግልፅ ያልሆነ ነገረ ካጋጠመዎት በነፃነት ይጠይቁ፡፡

ስለ ጥናቱ መግቢያና አላማው

እኔ ሚካኤል ተሻለ እባላለሁ፡፡ በአዲስ አበባ ዩኒቨርስቲ በባዮሚዲካል ሳይንስ (በአናቶሚ ስፔሻሊቲ) በመደበኛው ኘሮግራም የማስተርስ (የሁለተኛ) ድግሪ እየተማርኩ ሲሆን ለመመረቂያ ማሟያ የሚሆነኝን ጥናት ለረጅም ጊዜ ሜትፎርማን በሚወስዱ የስኳር በሽተኞች ላይ የነርቭ ህመም ችግር መጠኑ ምን ይመስላል የሚል ጥናት በጥቁር አንበሳ ስፔሻልይዝድ ሆስፒታል እና በየካቲት 12 ሆስፒታል ውስጥ በማጥናት ላይ እገኛለው፡፡

በዚህ ጥናት መሳተፍ የሚያስገኛቸው ጥቅምች

በዚህ ጥናት ስለተሳተፉ ምንም ዓይነት ክፍያ/ጉቦ አይከፈልዎትም፡፡ ቢሆንም በምርመራው ውጤት መሰረት ህክምና ያገኛሉ፡፡ በጣም አስፈላጊው ነገር የዚህ ጥናት ውጤት ለረጅም ጊዜ ሜትፎርሚን ሰሚ ወስዶ የስኳር በሽተኞች የነርቭ ህመም ችግራቸው ያለበት ደረጃ ማወቅ እና ካሉ አስፈላጊውን ጥንቃቄ ወይም ህክምና እንዲደረግላቸው ይረዳል፡፡ ስለዚህ በጥናቱ በመሳተፍዎ በተዘዋዋሪ መንገድ ለሌሎች ህመሙን ብሎም ለህብረተሰቡ ይጠቅማል ማለት ነው፡፡

የጥናቱ ተሳታፊ በመሆንዎ የሚገጥምት ጉዳት/ችግር

የጥናቱ ተሳታፊ በመሆንዎ ምንም አይነት ጉዳት አይደርስቦትም፡፡ ለምርምሩ የሚያስፈልጉ ጥያቄዎች እና የአካል ምርመራ እናደርጋለን፡፡ በዚህ ሂደት ውስጥ ምንም ጉዳት አይደርስበትም፡፡

ሚስጥራዊነቱ

በመጠየቂያው ወረቀት ላይ የተሳታፊዎች ስም ወይም ማንነት አይገለፅም። የሚሰጡት መረጃ ሚስጥራዊነቱ የተጠበቀ ነው። በተሳታፊዎች የሚሰጥ ናሙና ለዚህ ጥናት ብቻ የሚያገለግል ይሆናል። በዚህ ጥናት ውስጥ ላለመሳተፍ ከወሰኑ በዚህ የህክምና ቦታ ውስጥ የሚሰጥዎት አገልግሎት አይቋረጥም። በጥናቱ ለመሳተፍ የሚስማሙ ከሆነ የስምምነት ቅጹ ላይ በጽሑፍ ወይም በጣት ፊርማዎት ማስቀመጥ ይኖርቦታል።

ሚካኤል ተሻለ

የባዮሚዲካል ሳይንስ ት/ክፍል፤ የጤና ሳይንስ ኮሌጅ፤ አዲስ አበባ ዩኒቨርስቲ

ሞባይል +251-9-27697027

ኢ- ሜይል michael-gsr-1411-16@aau.edu.et

መጠይቅ፡ በስኳር በሽታ ምክንያት የሚመጣ የነርቭ ህመም ችግር እና ተያያዥ ምክንያቶች በኢትዮጵያ የረጅም ጊዜ የሜትፎርሚን ተጠቃሚዎች ላይ

ክፍል 1 የስነ ህዝብ አወቃቀር መረጃ

1. ዕድሜ	☐ 31-40 ዓመት
	☐ 41-50 ዓመት
	☐ 51-60 ዓመት
	☐ 61-70 ዓመት
	☐ >70 ዓመት
2. ፆታ	☐ ወንድ
	☐ ሴት
3. መኖሪያ	☐ ከተማ
	☐ ገጠር
4. የትምህርት ደረጃ	☐ መደበኛ ትምህርት የለም
	☐ የመጀመሪያ ደረጃ ትምህርት
	☐ የሁለተኛ ደረጃ ትምህርት
	☐ ከፍተኛ ትምህርት

ክፍል 2 የስኳር በሽታ ታሪክ

6. በስኳር በሽታ የተያዙት ለምን ያህል ጊዜ ነው?	☐ 5-10 ዓመታት
	☐ ከ 10 ዓመታት በላይ
7. ከስኳር በሽታ ጋር በተያያዘ የመጣ ተጓዳኝ ችግር/ህመም አለብዎት?	☐ አዎ
	☐ አይ

8. በደምዎ ውስጥ ያለውን የስኳር መጠን በየጊዜው ይቆጣጠራሉ ?	☐ አዎ
	☐ አይ
9. ለመጨረሻ ጊዜ የተመዘገበው የHb1 (መጠን የሚታወቅ ከሆነ ስንት ነበር? -------)	_____ %

ክፍል 3፡- የሜትፎርሚን አጠቃቀም

10. ሜትፎርሚን ለምን ያህል ጊዜ እየወዱ ነው?	☐ 5–10 ዓመታት
	☐ ከ 10 ዓመታት በላይ
11. አሁን ላይ የሚወስድት የሜትፎርሚን መጠን ምን ያህል ነው?	☐ በቀን 500 ሚ.ግ
	☐ በቀን 1000 ሚ.ግ
	☐ በቀን ከ1000 ሚ.ግ በላይ
12. በሜትፎርሚን ምክንያት የመጣ የጎንዮሽ ጉዳት አጋጥሞት ያውቃል?	☐ አዎ
	☐ አይ
13. የቫይታሚን B12 መጠን ተመርምረው ያውቃሉ?	☐ አዎ
	☐ አይ
14. ከተመረመሩ የቫይታሚን B12 መጠንዎ እንዴት ነበር?	☐ መደበኛ
	☐ ዝቅተኛ
15. ለነርቭ ጤና (ለምሳሌ ቫይታሚንB12፣ የህመም ማስታገሻዎች)ተጨማሪ ማሟያዎችን ወይም መድሃኒቶችን እየወሰዱ ነው?	☐ አዎ
	☐ አይ

ማቺጋን ኒውሮፓቲ የማጣሪያ መሳሪያ

ሀ. ታሪክ (በስኳር ሀመምተኛ የሚሞላ)

(እባክዎትን ጥቅት ደቂቃዎችን ይውሰዱ እና ስለ እግርዎ እና እግሮት ላይ ስለሚሰቱ ስሜቶችን የሚተሉትን ጥያቄዎችን ይመልሱ። በተለምዶ በሚሰማዎት ስሜት ላይ በመመስረት አዎ ወይም አይ ብለው ያረጋግጡ። አመሰግናለሁ።)

1. እግሮችዎን ይደነዝዞታል?	☐ አዎ
	☐ አይ
2. በእግሮችዎ ላይ የሚያቃጥል ስሜት/ህመም አለዎት?	☐ አዎ
	☐ አይ
3. እግሮችዎን ለንክኪ በጣም ስሜታዊ ናቸው?	☐ አዎ
	☐ አይ
4. እግሮችዎ ላይ በሚገኙ ጡንቻዎች ላይ የህመም ስሜት አለዎት?	☐ አዎ
	☐ አይ
5. እግሮችዎ ላይ የመውጋት ስሜት ይሰማዎታል?	☐ አዎ
	☐ አይ
6. የአልጋልብስ እግሮትን በሚነካ ጊዜ ያሞታል?	☐ አዎ
	☐ አይ
7. ወደ መታጠቢያ ገንዳ ወይም ገላ መታጠቢያ ሲገቡ ሙቅ ውሃን ከቀዝቃዛ ውሃ መለየት ይችላሉ?	☐ አዎ
	☐ አይ
8. በእግርዎ ላይ ክፍት የሆነ ቁስለት አጋጥሞዎት ያውቃል?	☐ አዎ
	☐ አይ

9. ዶክተርዎ በስኳር በሽታ ምክንያት የሚመጣ የነርቭ ችግር/ህመም እንዳለብዎ የሚመጣ የነርቭ ችግር/ህመም እንዳለብዎ ነግሮዎት ያውቃሉ?	☐ አዎ
	☐ አይ
10. ብዙ ጊዜ ድካም ይሰማዎታል?	☐ አዎ
	☐ አይ
11. የነርቭ ችግር/ህመም በማታ ይባባስቦታል?	☐ አዎ
	☐ አዎ
12. በእግር ሲጋዙ ህመም ይሰማዎታል?	☐ አዎ
	☐ አይ
13. በእግር ሲጋዙ እግሮችዎ እንዳሉ ይሰማዎታል?	☐ አዎ
	☐ አይ
14. የእግሮችዎ ቆዳ ከመድረቅ ብዛት ተሰንጥቆቦታል?	☐ አዎ
	☐ አይ
15. እግሮ ተቆርቦታል?	☐ አዎ
	☐ አይ

ለ. አካላዊ ግምገማ

1. የእግር ገፅታ	
የቀኝ እግር መደበኛ	☐ አዎ
	☐ አይ
የግራ እግር መደበኛ	☐ አዎ
	☐ አይ

አይደለም ከሆነ ፣ የሚከተለውን ሁሉ አረጋግጥ	☐ የአካል ጉድለት
	☐ ደረቅ ቆዳ
	☐ ኢንፌክሽን
	☐ መሰንጠቅ
	ሌላ ……..
2. ቁስለት	
የቀኝ እግር	☐ አዎ
	☐ አይ
የግራ እግር	☐ አዎ
	☐ አይ
3. የቁርጭምጭሚት ምላሽ	
የቀኝ እግር	☐ አዎ
	☐ አይ
የግራ እግር	☐ አዎ
	☐ አይ
4.ንዝረት	
የቀኝ እግር	☐ አለ
	☐ ቀንሷል
	☐ የለም
የግራ እግር	☐ አለ
	☐ ቀንሷል
	☐ የለም
5.10 ግራም ክር(ከ10 መተግበሪያዎች የተቀነሱ መተግበሪያዎች ብዛት)	
የቀኝ እግር	☐ አለ (8 እና ከዚያ በላይ)

	☐ **ቀንሷል** (1-7)
	☐ **የለም** (0)
የግራ እግር	☐ **አለ** (8 እና ከዚያ በላይ)
	☐ **ቀንሷል** (1-7)
	☐ **የለም** (0)