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We, the undersigned, are the principal investigator and advisor for this study. We declare that this thesis is our original work.

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ABBREVIATIONS

BMI- Body mass index

BP-Blood pressure

DCCT- Diabetic control and complication trial

DFU -Diabetic foot ulcer

DM Diabetes mellitus

DN4 Douler neuropatic questioner

DSPN Distal symmetrical poly neuropathy

ETB -Ethiopian Birr

FBS - Fasting blood sugar

HbA1c - Hemoglobin A1c

HDL- High density lipoproteins

IRB- Institutional Review Board

LDL-low density lipoprotein

MNSI-Michigan neuropathy screening instrument

MNDS Michigan neuropathy diagnostic score

NSS- Neuropathy symptom score

NDS –Neuropathy disability score

TASH: Tikur Anbessa Specialized Hospital

TC- Total cholesterol

TG-Triglyceride TCSS Toronto clinical scoring system

WC-Waist circumference

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Abstract

Background

Diabetic neuropathy is most common complication in diabetic patients affecting 50-75 % of diabetic patient. In around 50% of patient distal symmetrical polyneuropathy is asymptomatic and result in increased risk of limb loss and hospitalization, which affect the quality of life of patient. Once it occur there is no reversibility, hence early picking of the problem will help in management of diabetic patient .The finding from this Study will help ,in our set up ,which tool to use to detect early distal symmetrical polyneuropathy.

Objective

The study is designed to assess Magnitude of distal symmetrical polyneuropathy using Michigan neuropathy scoring instrument and Biothesiometer among Diabetic patient attending Tikur Anbessa Specialized Hospital.

Method

An institution-based cross-sectional study was conducted at Tikur Anbessa Hospital on 290 diabetic and pre-diabetic individuals. Study subjects were recruited from the diabetic clinic using systematic random sampling methods, every other clinic schedule. Data were collected using Kobotoolbox which was fed with a well-structured questionnaire, which was then cleaned exported to Stata version 19 for Analysis. Both bivariate and multivariate binary logistic regressions were employed to identify factors associated with DSPN. A variable having a p value of <0.25 in the bivariate model was subjected to avoid confounding variable's effect. After checking for model-fitting information (Hosmer and Lemeshow test p=0.523) the adjusted odds ratio with a 95% confidence interval and a p-value <0.05 was used to determine statistical significance

Result

This study showed DSPN prevalence of 43.8% using MNSI and 85.2 % using biothesiometer. After multivariate analysis Smoking history, duration of diabetes, LDL value above 70 mg /dl and obesity have significant association with the occurrence of DSPN. Patient with smoking history had 2.5 times likely to develop DSPN as compared to non-smoke (AOR =2.5 95 % CI (1.16, 5.63),P-value of 0.02). Duration of diabetes longer than 10 years was 2 times associated with DSPN as compared to duration of below five year (AOR=2.03 95 CI(1.01,4.09) ,P-value 0.047).Patients who had LDL value above 70 mg /dl were likely to have DSPN 1.9 times DSPN (AOR=1.9 95% CI (1.05,3.45) ,P – value =0.035.Obese individuals were 2.7 times likely to have DSPN as compared to normal weight (AOR= 2.7, CI95% (1.28-5.72),P-value =0.009

Conclusion

Most of the study participant had DSPN using biothesiometer DSPN. Long duration of diabetes, smoking history, obesity and high low density lipoprotein were independent risk factor for DSPN .Biothesiometer peak 79.1% of participant with no clinical symptom based on MNSI symptom .Symptomatic participant has sever DSPN biothesiometer .Thus our finding suggest prevalence of DSPN is high and can use biothesiometer for early detection of DSPN.

1. Introduction

1.1 Back ground

Diabetes is serous, long term condition that occurs due to persistently raised blood glucose. Globally ,the prevalence of diabetes is increasing according to IDF projection 537 million adults between 20-79 have diabetes in 2021.Most of the increment occur in low and middle income countries ,where there economy is transitioning (1) The 2015 national survey revealed that 3.2 % had diabetes In Ethiopia (2) Diabetes mellitus can cause significant damage to many of the body's organs over the long term, leading to disabling and life-threatening health complications such as cardiovascular diseases (CVD), nerve damage (neuropathy), kidney damage (nephropathy), lower-limb amputation, and eye disease (which mainly affects the retina), resulting in visual loss and even blindness. However, with appropriate management of diabetes through lifestyle modifications, medication, and regular monitoring, these serious complications can be delayed or prevented altogether.(1)

As described earlier Diabetic neuropathy (DN) is the most common and troublesome complication of diabetes mellitus (DM), leading to the greatest morbidity and mortality and resulting in a huge economic burden, it is also the most common form of neuropathy in the developed countries of the world which accounts for more hospitalization (3). Neuropathy in diabetes manifests in different forms. It may occur in proximal or distal nerve fibers, may take the form of mononeuritis or entrapments involving small or large fibers, and may affect the somatic or autonomic nervous system. Off all the mentioned ,distal symmetric polyneuropathy (DSPN), the most common form of diabetic neuropathy.(4) Diabetic distal symmetric sensorimotor polyneuropathy (DSPN) represents a major health problem, associated with excruciating neuropathic pain, increased morbidity and impaired quality of life.(5) DSPN is a chronic, nerve-length–dependent, sensorimotor polyneuropathy that affects at least one third of persons with type 1 or type 2 diabetes and up to one quarter of persons with impaired glucose tolerance. (4)

Diabetic neuropathies have been classified into generalized and focal/multifocal varieties by Thomas (6) and Boulton et al. (7), which may include multiple mononeuropathy, lumbosacral, thoracic, and cervical radiculoplexus neuropathies. These patterns of neuropathy can also occur in individuals without diabetes (5). In addition, diabetic patients may develop chronic inflammatory demyelinating polyradiculopathy.

The first sign of diabetic sensory polyneuropathy (DSPN) appears to be a nerve conduction test abnormality, which is often subclinical. While the presence of diabetic retinopathy and nephropathy in a patient may support that diabetes is the cause of the polyneuropathy, it is important to exclude other potential causes of sensory motor polyneuropathy. A confirmatory diagnosis of DSPN cannot be made without evaluating nerve conduction values, and only a possible or probable diagnosis can be made in the absence of such testing. (8)

1.2 Statement of the problem

Globally prevalence of diabetes mellitus is increasing which also increase the chronic complication (1). The exact prevalence of diabetic neuropathy is variable since it is affected by the method used for screening.

Chronic painful DSPN is present in 13–26% of diabetic patients. Between 25% and 62% of patients with idiopathic peripheral neuropathy have pre-diabetes. Among pre-diabetic subjects, 11–25% exhibit peripheral neuropathy and 13–26% neuropathic pain. (5) In other study in Minnesota the prevalence of DSPN was 54% (9) and in other mulit-center study in united Kingdom , overall prevalence of neuropathy was 28.5%, the prevalence in Type 1 diabetic patients was 22.7% and in Type 2 diabetic patients it was 32.1% (10). In Africa in one met analysis which included 23 study the prevalence of diabetic peripheral neuropathy was 46% and highest report was from west Africa 44.6 %(11). In meta-analysis done in Ethiopia the overall prevalence of Diabetic peripheral neuropathy is 22.1 %(12).

1.3 Significance of the study

Diabetic neuropathy is global health care problem which impose high economic burden (3). Although different studies are done locally using different clinical tool, none of them conducted study which include biothesiometer. As previously stated, the first to be affected in DSPN is NCT which is invasive. However biothesiometer is non- invasive method that can quantify and assess vibration and detect early DSPN(8). This study will have significance in assessment of this tool with other clinical tools for early detection of diabetic neuropathy since , established symptomatic diabetic neuropathy is generally not reversible, and management aims to slow further progression and prevent complications, including diabetic foot ulcers, arthropathy, and falls(13)

2. LITERATURE REVIEW

2.1 Historical back ground

The peripheral neuropathy of diabetes has been recognized over a thousand years ago. However the first description of diabetic neuropathy was by Rollo in1798 when he described pain and paresthesia in the legs of a diabetic patient(14). Before 1850 the frequency of occurrence of nervous system abnormality led writer attributing diabetes mellitus as nervous system problem. March Decavi (1864) first recognized that diabetes mellitus is cause rather than the result of nervous system disturbance (15). Pavy described a pain of diabetic neuropathy as burning and unremitting nature' in 1887(16). Diabetic neuropathy is cause of significant morbidity in terms of amputation and prolonged hospitalization (17).

In addition to diabetes other causes of neuropathy may contribute to cause of neuropathy in diabetes. In laranzeo study CIDP was second most common cause of peripheral neuropathy for which there were no antecedent viral infection. The Other contributors to non-diabetic neuropathy among their diabetic patients include alcoholic neuropathy, nerve entrapment syndrome, polyathritis nodosa, hereditary neuropathy, inflammatory neuropathy due to human immune deficiency syndrome (18). Gorson and Ropper, found in 2005 Fifty five patients (53%) had potential additional causes for DSP. These included: neurotoxic medications, alcohol abuse, B12 deficiency and renal disease. The most common laboratory abnormalities were: abnormally low levels of vitamin B6 or B1, monoclonal gammopathy, and hyper-triglyceridaemia (19)

2.2 Classification of diabetic neuropathy

Diabetic neuropathy is a term used to describe a disorder that can be clinically evident or subclinical and occurs in individuals with diabetes mellitus, without any other apparent causes for peripheral neuropathy. The disorder affects both the somatic and autonomic parts of the peripheral nervous system (20).

Diabetic neuropathies are heterogeneous, affecting different parts of the nervous system that present with diverse clinical manifestations. They may be focal or diffuse. Most common among the neuropathies are chronic sensorimotor distal symmetric poly-neuropathy (DPN) and the autonomic neuropathies. DPN is a diagnosis of exclusion. The early recognition and appropriate management of neuropathy in the patient with diabetes is important (7)

The two most popular classification methods are those of Boulton (7) et al and Thomas (6)et al , of which that of Thomas et al is the most widely accepted, with some modifications over time. While the classification by Boulton is clinically based, that by Thomas is based on the premise that diabetic neuropathy is not a unitary condition, but is the result of a number of disturbances in the peripheral nervous system as a consequence of hyperglycemia.

Thomas et al classification of diabetic neuropathy

Rapidly reversible

-Hyperglycemic neuropathy

Generalized symmetirical polyneuropathy

-Sensomotor

-Acute sensory

-Autonomic

Focal and Multifocal

-Caranial

-Thoracolumbar radiculopathy

-Focal limbs

- Proximal motor(amyotrophy)

2.2.1 Rapidly reversible hyperglycemic neuropathy

This condition has been identified as a rapidly reversible abnormality of nerve conduction that can occur in patients with recently diagnosed or transiently poorly controlled diabetes. Along with this abnormality, patients may experience uncomfortable sensory symptoms in the distal extremities, such as severe pain, burning, aching, electrical or stabbing sensations, and paresthesia(6,7),these abnormalities of conduction are unlikely to be caused by structural abnormalities, as recovery soon follows restoration of euglycemia (7)

2.2.2 Distal symmetrical polyneuropathy

Distal symmetric polyneuropathy, the most common form of diabetic neuropathy, usually involves small and large nerve fibers. Small-nerve-fiber neuropathy often presents with pain but without objective signs or electro-physiologic evidence of nerve damage, and is recognized as a component of the impaired glucose tolerance and metabolic syndromes. The greatest risk resulting from small-fiber neuropathy is foot ulceration and subsequent gangrene and amputation. (21)

Large-nerve-fiber neuropathies produce numbness, ataxia and un-coordination, impairing activities of daily living and causing falls and fractures (21). Up to 50% of patients with diabetic neuropathy may experience symptoms, with burning pain, electrical or stabbing sensations, paresthesia, hyperesthesia, and deep aching pain being the most common. Neuropathic pain is typically worse at night, and symptoms are most frequently felt in the feet and lower limbs, although the hands may also be affected in some cases. As many as 50% of patients may be asymptomatic, and a diagnosis may only be made during an examination or when a patient presents with a painless foot ulcer(6). An abnormality of nerve conduction tests, which is frequently subclinical, appears to be the first objective quantitative indication of the condition (8)

2.2.3Acute sensory neuropathy

Acute sensory neuropathy is a distinct syndrome characterized by severe, unremitting burning pain in the lower limbs, particularly at night, and unpleasant contact cutaneous hyperesthesia in the legs. This condition typically develops following a profound and rapid weight loss. While sensory loss is often minimal, motor function and tendon reflexes are typically preserved, with the exception of loss of the ankle jerks in some patients. Autonomic dysfunction is generally not a prominent feature of acute sensory neuropathy, except for impotence in some cases (6). Acute sensory neuropathy tends to occur following periods of poor metabolic control or a sudden change in glycemic status, including an improvement in glycemic control induced by oral hypoglycemic agents. Symptoms tend to improve gradually with stabilization of glycemic control, and the condition typically resolves in less than one year(22)

2.2.4 Autonomic neuropathy

Diabetic autonomic neuropathy (DAN) results in significant morbidity and may lead to mortality in some patients with diabetes. The symptoms of autonomic dysfunction should be elicited carefully during the history, particularly since many of these symptoms are potentially treatable. Major clinical manifestations of DAN include resting tachycardia, exercise intolerance, orthostatic hypotension constipation, gastro paresis, erectile dysfunction, sudomotor dysfunction, impaired neurovascular function, “brittle diabetes,” and hypoglycemic autonomic failure (7).

CAN is the most prominent focus of autonomic dysfunction because of the life-threatening consequences of this complication and the availability of direct tests of cardiovascular autonomic function(8).Loss of sympathetic tone in the blood vessels results in vasodilatation leading to arterio-venous shunting. The “warm” neuropathic feet due to arterio-venous shunting can be associated with distension of foot veins that fail to collapse even when the foot is elevated. Peripheral sudomotor neuropathy can affect the feet with loss of sweating, resulting in dry skin with fissures predisposing to the risk of infection (23).

2.2.5 Focal and multi focal neuropathy

Different mechanisms such as mild, repeated mechanical trauma, compression and entrapment, ischemia, and inflammatory process have been invoked in the development of focal and multifocal neuropathies, which differ from typical DSPN in that they may occur early as well as later in the course of diabetes mellitus (23).

This neuropathic pattern tends to occur after 50 years of age, mostly in patients with longstanding diabetes mellitus. The DSPN does not show any trend to improvement and either relentlessly progresses or remain relatively stable over years (24). Conversely the focal diabetic neuropathies, which are often associated with inflammatory vasculopathy on nerve biopsies, remain self-limited, sometimes after a relapsing course (24).

Common nerves involved are the ulnar, median, peroneal, and medial and plantar nerves. Cranial neuropathies are extremely rare (0.05%); involve primarily cranial nerves III, IV, VI, and VII; and are thought to occur due to a micro-vascular “infarct,” which, in the majority, resolves spontaneously over several months (7).

2.2.6 Diabetic amyotrophy

Typically occurs in older patients with type 2 diabetes, and in some cases, an immune-mediated epineurial micro-vasculitis has been demonstrated in nerve biopsies(7) . The main features of diabetic amyotrophy are weakness, wasting and pain, most commonly in the quadriceps muscle. Though the weakness starts on one side, it almost always spreads to the other side in an asymmetrical manner. Patients also complain of sensory symptoms in the thigh such as severe pain, dysaesthesiae and paresthesia.

The course of the disease is variable but good functional improvement can be expected in most patients though weakness, sensory symptoms and absent tendon jerks may persist. Some patients experience multiple episodes of the condition commencing mostly on the opposite side. Conservative treatment constitutes optimizing diabetic control along with active physiotherapy and analgesia (25).

2.3. Prevalence and Burden

Diabetic polyneuropathy is one of the most common long-term complications of diabetes affecting 50% of all diabetic people (11). Early recognition and appropriate management of neuropathy in the patient with diabetes is important since 50 % of patient are asymptomatic and more than 80 % of amputation follow neuropathy or injury (8)

The prevalence of DPN varies widely in the literature. This is due to differences in the diagnostic criteria employed, types of diabetes, the different methods of patient selection, and the sample size. However, study done in Minnesota showed prevalence of diabetic poly neuropathy 54 % (9) and in other study done at multicenter in United Kingdom the overall prevalence of diabetic neuropathy was 28.5 % (10). It was also estimated that the prevalence of DPN is 8.4% in China(26), 48.1% in Sri Lanka(27), 29.2% in India (28) , 56.2% in Yemen(29) , 39.5% in Jordan(30) , 46% in Africa (11),71.1% in Nigeria (31), and 16.6% in Ghana (32) .

Studies conducted in Ethiopia have reported varying prevalence rates of diabetic neuropathy. For instance, a study conducted in 2010 at Jimma University found a prevalence rate of 29.5 %(33), while a more recent study in the same location reported a prevalence rate of 53.6% (34). Additionally, a study conducted at Addis Ababa Tikur Anbesa Hospital in 2011 reported a prevalence rate of 48.2% (35), and another study conducted at Bahardar Felegehiwot Hospital found a prevalence rate of 52.2% (36). However, a meta-analysis of 23 studies conducted in 2021 reported an overall prevalence rate of 22% (12).

2.4. Risk Factor

Diabetic neuropathy is a serious complication that can develop in patients with type 1 and type2 diabetes. There are several risk factors that contribute to the development of this condition.

One of the major risk factors is advanced age. As patients with diabetes get older, they become more susceptible to developing diabetic neuropathy. Additionally, the length and severity of hyperglycemia can also increase the risk of this condition (37,38)

Recent research has also identified other risk factors for diabetic neuropathy, including the metabolic syndrome, glycemic variability, dyslipidemia, and smoking (39,40).

Not only Type 2 diabetes and metabolic syndrome is associated with diabetic neuropathy (41,42) but also Type 1 diabetes in EURODIAB study with no initial neuropathy developed neuropathy after 7.3 year follow up in 24. %.The risk factor for neuropathy in these type 1 patients was significantly correlated with elevated triglyceride levels, body mass index, and the presence of baseline hypertension, all indicators of the metabolic syndrome, in addition to duration of diabetes and glycosylated hemoglobin values(43)

2.5. Assessment of diabetic polyneuropathy

Though diabetic peripheral neuropathy has long been recognized, no universally accepted standard exists for the diagnosis. Thus the process of diagnosis has undergone quite some evolution from the traditional methods of symptomatology, and the use of hand held instrument, to direct morphological evaluation of whole nerve biopsies (44). The 1999 consensus recommend for the assessment of diabetic neuropathy clinical symptom, sign, quantitative sensory testing ,electrophysiology test and rarely nerve biopsy (20)

2.5.1 Clinical history

Neuropathic symptoms include pain, characteristically described as burning, painful cold, lancinating, tingling, stabbing or shooting (electric shock–like), as well as non-painful neuropathic symptoms like paresthesia (tingling, prickling or ant-like sensations), dysesthesias (unpleasant abnormal sensation whether spontaneous or evoked), sensory ataxia (ataxic gait) or numbness (often described as "wrapped in wool" or like "walking on thick socks") Neuropathic pain may be accompanied by hyperalgesia (exaggerated response to painful stimuli) and allodynia (pain triggered by normally non-painful stimuli such as the contact of socks, shoes, or bedclothes). Neuropathic pain typically worsens at night and may interfere with daily activities and reduce the quality of life and sleep (44)

2.5.2 Clinical examination

Clinical examination for detection of DPN involves simple bed side test like ankle reflex detection. Since it is early to occur best to assess if it is decreased, present or absence .The other test to assess is pain sensation using sterile pin, the site assessed on the foot depend on the algorithm used but mostly assed site are the dorsum of the great toe or plantar side of first, third and fifth toe .Light touch perception which mostly assed by 10 gm monofilament is other simple bed side test which asses proprioception (45). Monofilament test can assess also the risk of developing foot ulcer if assessed in plantar side of the foot (13). Vibration test which uses 128Hz tuning fork which is traditional way or graduated tuning fork is also another method which asses the presence of DPN. The 128 Hz tuning fork vibration test is affected by age and the technician so during interpretation need to give attention for the limitation(45).

2.5.3 Quantitative sensory testing

Quantitative sensory testing (QST) is a technique for evaluating sensory neuropathy. It detects small fiber and large fiber neuropathy through standardized and quantified sensory differences such as stimulation, vibration, and temperature. Compared with NCS, this method is noninvasive and easy to operate. In people with diabetes, sensory dysfunction precedes symptoms such as painful neuropathy and foot ulcers (46). Relevant studies have shown that according to the severity of neuropathy, the sensitivity of the heat test is variable, with cold damage being 27%–98%, heat damage being 22%–98% (47), vibration testing sensitivity being 58%–84%, and the specificity

being 51%–86% (48). In one study QST-based neural test is used to evaluate vibration perception threshold (VPT), cold perception threshold (CPT), warming perception threshold (WPT), and heat pain perception threshold (HPT). Its sensitivity to vibration test is as high as 84%, and its specificity is as high as 81%. Its sensitivity to heat test is high, and its specificity is medium, and has good repeatability and diagnostic accuracy in evaluating sensory loss (49). In China, Sun Yukai et al. believe that the sensitivity and specificity of VPT for DPN were 85.19% and 88.68%, respectively, and can be used for early screening of DPN lesions (50).

2.5.4. Clinical scoring system

Commonly used neurological scoring scales include Michigan neuropathy screening instrument (MNSI), Toronto clinical scoring system (TCSS), neuropathy symptom score (NSS), and neuropathy disability score (NDS)(51)

MNSI was first proposed in 1994 (52), including patient questionnaire and physical examination. The total score is 10 points, and more than 2 points are considered abnormal. It is widely used in clinical practice and large-scale clinical trials to evaluate distal symmetrical peripheral neuropathy, including action to control cardiovascular risk in diabetes (ACCORD) (53) and bypass angioplasty revascularization investigation 2 diabetes (BARI 2D) (54). MDNS which include NCT includes three parts: toe sensation, distal muscle strength of limbs, and tendon reflex score. The total score is 46 points, and >6 points are considered abnormal.

TCSS can be used for DPN classification, and its combined application can increase the detection rate of DPN (55). NSS is scored according to the symptoms, location, and pain relief methods of lower limbs; NDS is scored according to ankle reflex, dorsalis pedis acupuncturing sensation, toe vibration sensation, and temperature sensation (56).

Research has found that the abnormal detection rate of MDNS is 84.5%, the abnormal detection rate of TCSS is 62.0%, the abnormal detection rate of NCV is 76.0%, and the abnormal detection rate of the combination of the three is 91.5%(57). Other study which used NSS and NDS showed sensitivity and specificity of 68.0% and 77.2%, respectively, and the positive predictive value, negative predictive value, and Youden index were 86.5%, 53.5%, and 45.2% respectively, suggesting that NSS/NDS has good application value for early screening of DPN patients (51).

2.5.5 Nerve conduction test

At present, the diagnosis of diabetic peripheral neuropathy (DPN) relies primarily on identifying characteristic symptoms and signs. One of the gold standard techniques for diagnosis is nerve conduction studies (NCS)(58), which assess the ability of peripheral nerves to transmit electrical signals in patients with DN. While NCS is quantifiable, objective, and sensitive, it has several drawbacks, including being time-consuming, expensive, requiring skilled operators, and being difficult to implement in large-scale screening (59). Furthermore, NCS only evaluates large nerve fibers, whereas small nerve fibers are often affected first in DPN patients, and these small fiber neuropathies cannot be assessed by standard electrophysiological tests (48). Electrophysiology should only be used when the clinical presentation is atypical or the diagnosis is uncertain (13).

3. OBJECTIVES OF THE STUDY

3.1 General Objectives:

To determine the magnitude of DSPN using Michigan neuropathy scoring instrument and biothesiometer at TASH diabetic clinic in the Study period from July 1to September 30, 2023

3.2 Specific Objectives

3.2.1 To describe the risk factors associated with DSPN in the study participants attending at TASH diabetic clinic in the period from July1 to September, 2023

3.2.2 To compare Michigan neuropathy scoring instrument with biothesiometer for screening of in the study participants attending at TASH diabetic clinic in the period from July1 to September, 2023

4. METHODOLOGY

4.1 Study setting

Tikur Anbessa Specialized Teaching Hospital: It is the largest tertiary, teaching referral hospital in Ethiopia. It is the pioneer teaching hospital in the capital Addis Ababa, under AAU-CHS. Their Endocrine centers which house the Diabetic clinic provide service for diabetic patient in days of the week. The service is led by endocrinologist. About 70 to 100 clients are seen in each day of the clinic day. The Hospital launched digital system starting from 2018

4.2 Study period:

The study was conducted in the period from July1to September30,2023 at Tikur Anbessa specialized hospital in Diabetic center.

4.3 Study design:

An institution-based cross-sectional study was conducted on diabetic patient on follow up at the diabetic clinic in Tikur Anbessa Specialized Teaching Hospital

4.4 Study Population:

All DM patients who fulfill the eligibility criteria was included in the study

4.5. Eligibility

4.5.1. Inclusion criteria:

- All DM patients, Type 1 after 5 years of diagnosis or Type 2;
- Age 18 years and above
- Those with impaired fasting

4.5.2. Exclusion criteria:

- Age groups below 18 years of age
- Those who are admitted to the ward
- Those patient who are not willing to participate on the study
- Those patient already diagnosed with other causes of peripheral neuropathy

4.6 Sample size determination

For sample size determination, the single population formula was used, considering the prevalence of DSPN in DM subjects in a similar setup is 22%. (12)

$$n = \frac{[z]^2 \times p(1-p)}{d^2}$$

Where:

n =minimum sample size for a statistically significant study

z = normal deviant at a apportion of 95 % confidence and, which is 1.96

d = marginal Error taken as 5%

p =expected proportion of the population with DPN in DM patients in a similar setup is22 %.(12)

q = 1-p

- ✓ With this this formula sample size was 264
- ✓ Correction of sample size is required, giving the population size is < 10,000 and corrected with the following formula

$$n = \frac{n0}{1 + \frac{n0}{N}}$$

n = Final sample size

n0 = Initial sample size

N = Source population size

Based on the above procedure the sample size will be 264 and a 10 % non-respondent rate was added to give a final sample size of 290.

4.7 Sampling Procedure

Subjects were recruited from the diabetic clinic using systematic random sampling methods, every other day of clinic schedule

4.8 Data collection Methods

Kobotoolbox was used to collect all the necessary data. It was coded with relevant questions regarding the socio-demographic data (age, sex, area of residence, marital status, level of education and monthly income), behavioral assessment (previous and current smoking and alcohol history), their diabetes (type, duration, control, type of medication they use) and comorbidities (hypertension, dyslipidemia, DM related complications). It also addressed all the MNSI history version questions (both positive and negative symptoms) and examination findings (foot examination, vibration perception, mono-filament test and ankle reflex). It had apart that assessed the vibration perception using biothesiometer. Data was collected by the PI and 2 other trained general practitioner rained data collectors with a printed questionnaire with all the necessary variables included. Relevant history, including, socio-demographic data, symptoms of neuropathy, smoking history and alcohol consumption will be taken. BP, weight and height measurements, foot examination including microfilament test and vibration sensation test in addition to waist circumference will be obtained on the spot during focused physical examination. Laboratory investigations targeting metabolic profile (FBS/ A1C level, and Lipid profile) w retrieved from the

patients electronic based documentations, if they have been evaluated recently (in the past 6 months) in accordance with the standard of care

4.9 DSPN Screening tools

There are several scoring systems established to aid in reaching into the diagnosis of DSPN. The Michigan Neurology Screening Instrument, Utah Early neuropathy Scale (UENS), Toronto Clinical Neurology Score,United Kigdom Screening Test and Douleur neuropathic questionnaire (DN_4) tool are among the proposed simple clinical screening tests. For this study we used the MNSI history version and foot examination version scores for its technical simplicity. Additionally biothesiometer which will assess the vibration perception test also will be done.

4.9.1 MNSI History Version

It contains 15 items which was administered by the interviewer, of which 13 items assess symptoms of DPN while item #4 is a measure of impaired circulation and item #10 is a measure of general asthenia, hence were not included in scoring. 'Yes' responses to questions 1–3, 5, 6, 8, 9, 11, 12, 14, and15 were each counted as one point and 'No' responses to questions 7 and 13 likewise counted as one point. The total score ranges from 0 to 13 points and a score of ≥7 indicated the presence of DPN (Se 13%, Sp 99%). When a score ≥4 is used, Se becomes 40% and Sp becomes 92%.[30]

4.9.2 MNSI Examination Version: Procedure and Scoring

It assesseS the following five variables on each foot which was performed by data collectors:

1. Each foot was inspected for deformities, dry skin, and calluses or infections, and each foot with any abnormality received a score of one and if not 0
2. Each foot was inspected for ulcer, and each foot with an ulcer received a score of 1 and if not 0
3. Examination of vibration sense by tuning fork: 128 hertzA/128-hertz (HZ) cycle tuning fork made in China was used to detect loss of vibration. Vibration sensation was tested in the great toe and the score was designated as follows for each foot. Vibration was present and scored 0 if the examiner senses the vibration on his finger for <10 seconds, 0.5 score when the examiner felt the vibration for ≥10 seconds after the patient stopped to feel it at the great toe, and 1 point for absent vibration.
4. Detection of the ankle reflex: Ankle reflex function was detected using standard triangular rubber-headed hummer made in China. If ankle reflex was present, it was scored as 0, If ankle reflex was present using reinforcement it is scored 0.and if the reflex was absent it is scored 1.
5. Monofilament test: A 10 g monofilament made in China was used to detect loss of pressure sensation on the feet. It is an objective instrument used in screening the diabetic foot for loss of protective sensation. Each monofilament was used to test 30 patients, unless it is physically bent, to avoid diagnosing error. The participant, whose eyes were closed, was asked to respond yes if he/she felt the filament. Ten site were assessed , nine on plantar side of the foot and one on dorsum side of the foot. If the sensation was present at eight or more site it was scored 0,if it sensation was present at seven or below site it was scored 0.5 and if sensation was absent it was scored 1.

Both feet were independently assessed and the scores for both feet were added together. After summing up all the components, the patient was considered to have DPN if the score was ≥2 out of the maximum 10-point scale on examination version of MNSI

4.9.3 Biothesiometer

A biothesiometer is an instrument that can detect and quantify diabetic peripheral neuropathy in its early stages. It functions similarly to an electronic tuning fork. It carries a vibrating probe that detects neuropathy when connected to the bottom of the foot. The amplitude of vibrations is measured (volts) from 0-to maximum of 50 volts and can be adjusted by rotating the dial. Once the vibration has been detected, the individual being tested indicates.(60)

Biothesiometer with model name vibrotest which had frequency of 50 Hz and had volt 0-50 volts which was applied at six sites on six areas on each foot's plantar area. These areas were tested, the plantar aspect of the big toe, three metatarsal heads, the instep, and the heel. Average for each foot was taken and average of the two feet was taken. Results was normal less than 15 ,grade 1 neuropathy (15-20 volts),grade 2 neuropathy (20-24))volts and grade 3 neuropathy was above 25 volts , which indicate higher correlation with complication (61,62).

Weight was measured using a standard weight scale in kg approximated to the nearest whole number for each subject. Height was measured using a standard height measurement scale in meters with upright standing position and was approximated to the nearest whole number. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Patient records (charts) were used to take clinical variables, including laboratory data. Data collection was carried out by two general practitioner and the PI with the supervision of a principal investigator.

4.10 Study variables

4.10.1 Dependent variable

- ✓ DSPN

4.10.2 Independent variables

- ✓ Socio-demographic characteristics
- ✓ BP measurements
- ✓ Weight, height and BMI
- ✓ Waist circumference
- ✓ Alcohol intake
- ✓ Smoking
- ✓ Duration of DM
- ✓ Comorbidities (Hypertension, Dyslipidemia, CVD)
- ✓ Metabolic work-ups

4.11 Operational Definitions

DSPN: is present if the patient's history version of MNSI questionnaire score was ≥4 abnormal responses in the legs and/or if the lower extremity examination version of MNSI score was ≥2.(52)
DSPN; On biothesiometer above 15 volts on average of the six sites on plantar side of each foot(62)

Positive vibration perception: using a 128 cycle tuning fork placed at the distal interphalangeal joint of the big toe, and if the patient is not able to note the end of vibration sensation while the examiner's hand feel it.

Positive Monofilament test: Using Semmes-Weinstein 10g monofilament the patient is asked about the pressure sensation feeling. If patient couldn't be able to feel the pressure sensation on 4 or more site it is decreases and if patient doesn't feel at all it is absent

Hypertension; Bp recorded and if above 130/80 according to ADA 2022 guideline

Uncontrolled hypertension: any BP record, sitting/ standing ≥130/80

Orthostatic hypotension: whenever the difference between SBP records in standing and sitting position exceeds 20mmHg and between the DBP exceeds 10mmHg

Poor glycemic control: when HgA1C level is above 7.0% and FBS above 130

Dyslipidemia: any one of the following parameters met (Total Cholestrol ≥200mg/dl, Triglyceride ≥150mg/dl, LDL ≥130mg/dl, HDL >40mg/dl)

BMI: is a measure of body fat based on weight (in kg) and height (in m). BMI groups of underweight (< 18.5 kg/m2), normal (≥18.5 kg/m2, < 23.0 kg/m2), overweight (≥23.0kg/m2, <25.0 kg/m2) and obese (≥25.0 kg/m2) were categorized based on the BMI criteria made by the WHO

Visceral Obesity: is there when the WC measurement is ≥94cms for men and ≥80cms for female participants

Amputation: is the surgical removal of the whole or a part of the limb including its distal end.

DM Duration: *The duration of DM was calculated as age at data collection minus age at onset of DM.*

4.12. Data Quality control

Data was collected using an electronic based pretested structured questionnaire by a well-trained data collectors (two GPS and PI) after patients were selected by a systematic randomized sampling method. The data collectors were trained prior to data collection about the objectives of the study, methods of data collection, its importance, and confidentiality. Collected data was evaluated regularly for completeness and consistency by the PI.

4.13 Data entry

Data entry was made using a Kobo Toolbox online-offline data collection form; data was exported automatically for analysis to the SPSS Software.

4.14 Ethical consideration

Data collection was started after the research proposal was reviewed and approved by the research committee of the internal medicine department and IRB of the internal medicine department. During the data collection, the name and personal identification of a patient was not be asked. All information collected during this research was coded, data collection tools were locked, and will not be accessed by any individual except the PI. All data and information were confidential. An adequate explanation were given to the participants about the objective of the study, its importance and benefit, confidentiality, their right not to be involved, and the right to withdraw from the study, and they were reassured that their withdrawal will not affect their treatment. Verbal informed consent was taken from all study participants.

5. Statistical analysis.

Kobo tool box was used to collect the data, which was then cleaned and exported Stata Version 19 for analysis. For normally distributed data, continuous variables were reported as the mean with standard deviation, and for those not normally distributed, the median with interquartile range (IQR), whereas categorical variables were presented as frequency and percentages. To compare groups for categorical variables in bivariate analysis was used. To see if there is a statistically significant difference in the means of two unrelated groups, independent t-tests or the Mann-Whitney U test, as appropriate, were used to determine whether there is a statistically significant difference in the means of two unrelated groups. To identify potential significant factors for the final models, in the bivariate analysis, variables with a p-value of less than 0.25 were used to determine independent factors associated with the prevalence of DSPN. In the final multivariable binary logistic regression model, after checking for model-fitting information (Hosmer and Lemeshow test p=0.523) the adjusted odds ratio with a 95% confidence interval and a p-value <0.05 was used to determine statistical significance

6. Result

6.1 Socio-demographic result

In the study, a total of 290 patients with diabetes mellitus (DM) were included. The prevalence of diabetic sensorimotor polyneuropathy (DSPN) was assessed using a biothesiometer, and it was found to be 247 patients, which corresponds to 85.2% of the study population. Among the participants, severe diabetic sensorimotor polyneuropathy (DSPN) was detected by the biothesiometer 152 (52.07%).The mean average biothesiometer value was 28.8 volt , with a standard deviation (SD) 12.45. The minimum value recorded by the biothesiometer was 8. Additionally, the prevalence of DSPN was calculated by combining the neuropathic ,MNSI symptom DSPN prevalence of 64 patients (22.1%) and the foot appearance DSPN using MNSI, prevalence of 99 patients (34.14%), resulting in a total of 127 patients (43.79%).

Table 1 socio-demographic characteristics of the participant

Age	Mean 55.7 SD 12.4 Min 18 max 80	number	percent
Age	<30	10	3.45
	30-49	71	24.48
	>50	209	72.07
Sex	female	163	56.21
	male	127	43.79
Residency	urban	252	86.9
	Semi-urban	23	7.93
	rural	15	5.17
marital status	single	29	10
	married	215	74.14
	divorced	25	8.62
	widowed	21	7.24
Level of education	No formal education	24	8.28
	Primary	97	33.45
	High school	74	25.52
	College and above	95	32.76
occupation	Gov't employee	39	13.45
	Housewife	82	28.28
	Retired	74	25.52
	Self-employed	95	32.76
MNSI symptom	DSPN	64	22.07
	no DSPN	226	77.93
MNSI Exam	DSPN	99	34.14
	No DSPN	191	65.86
Over All MNSI	DSPN	127	43.79

	No DSPN	163	56.21
Biothesiometer	DSPN	247	85.17
	No DSPN	43	14.83

The participants in the study had a mean age of 55.7 years, with more than half of them being 50 years or older. Among the participants, 163 patients (56.2%) were female, and the majority of them, 252 patients (92.1%), lived in urban areas. In terms of marital status, 215 patients (74.1%) were married. Regarding education, 75 patients (32.8%) had attended college or universities. In relation to income, 191 patients (65.9%) were earning less than 5,000 Ethiopian Birr (ETB) per month (table 1).

6.3 Habit and clinical characteristics result

Among the participants in the study, 44 patients (15.2%) had a history of smoking, while 6 patients (2.2%) were identified as current smokers. Additionally, a majority of 154 patients (53.1%) had a previous history of alcohol intake, while 10 patients (3.4%) reported current alcohol intake.

Table 2 .Clinical parameter of the participant

variable	variable	Frequency	Percent
Type of DM	Pre-diabetes	5	1.72
	Type 1 DM	33	11.38
	Type 2 DM	252	86.9
	<10yr	148	51.03
Duration of DM	11-20yr	85	29.31
	>20yr	57	19.66
Type of medication	yes	283	97.59
	no	7	2.41
Lipid lowering drug	yes	231	79.66
	no	59	20.34
vitaminB12 checked	yes	11	3.79
	no	279	96.21
Microvascular complication	No complication	208	71.72
	DKD	32	11.03
	DR	30	10.34
	DKD and DR	20	6.9
Comorbidity			
Hypertension	yes	175	60.34
	no	115	39.66
Dyslipidemia	yes	169	58.28
	no	121	41.72
RVI	yes	15	5.17
	no	275	94.83
cardiac	yes	70	24.14
	no	220	75.86

Among the participants in the study, 252 patients (86.9%) were known to have type 2 diabetes mellitus (DM). The majority of these patients, 283 (97.6%), had already initiated anti-DM medications. Insulin therapy was being used by 183 patients (64.7%) figure 1 .In terms of diabetic duration, 142 participants had a duration of more than 10 years. Among the participant, 72 (24.82%) had microvascular complications, with the most common being diabetic nephropathy, affecting 32 patients (11.03%).The most prevalent comorbidity among the participants was hypertension, which was present in 60.3% of the patients. Dyslipidemia was the second most common comorbidity, affecting 58.3% of the participants. Cardiac disease was reported in 24.1% of the patients (table 2).

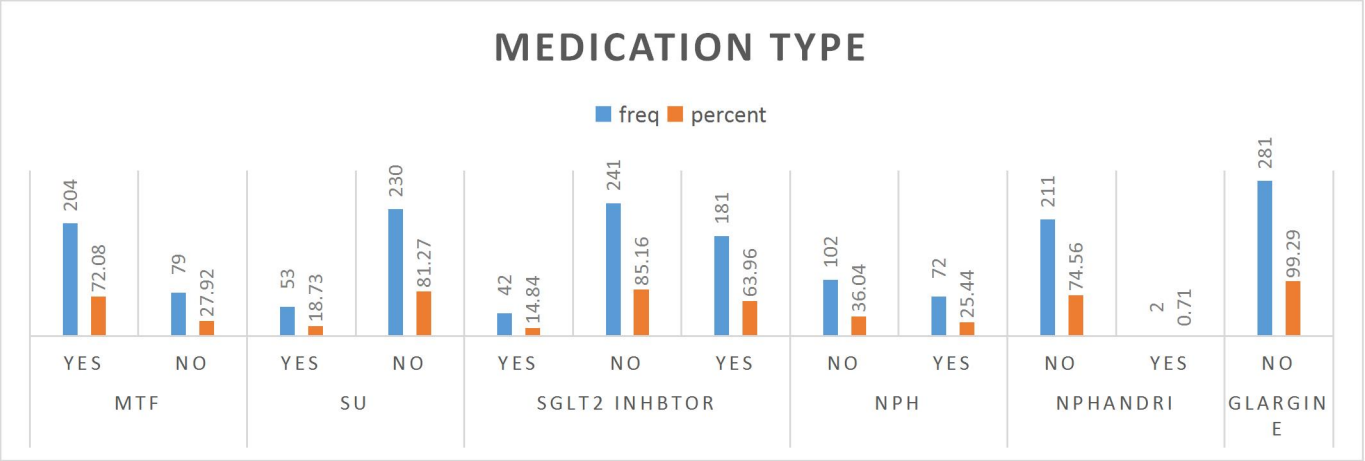


Figure 1 Type of diabetic medication participant taking

6.3 Michigan neuropathic screening instrument result

The most common neuropathic symptoms reported by the participants were numbness, reported by 181 patients (62.4%), and burning sensation, reported by 128 patients (44.1%) figure 2. The most common abnormal physical findings associated with neuropathy were, reduced and vibration sensation, observed in 153 patients (53.79%), and, diminished and absent ankle reflex, found in 67 patients (23.1%) Figure 3.

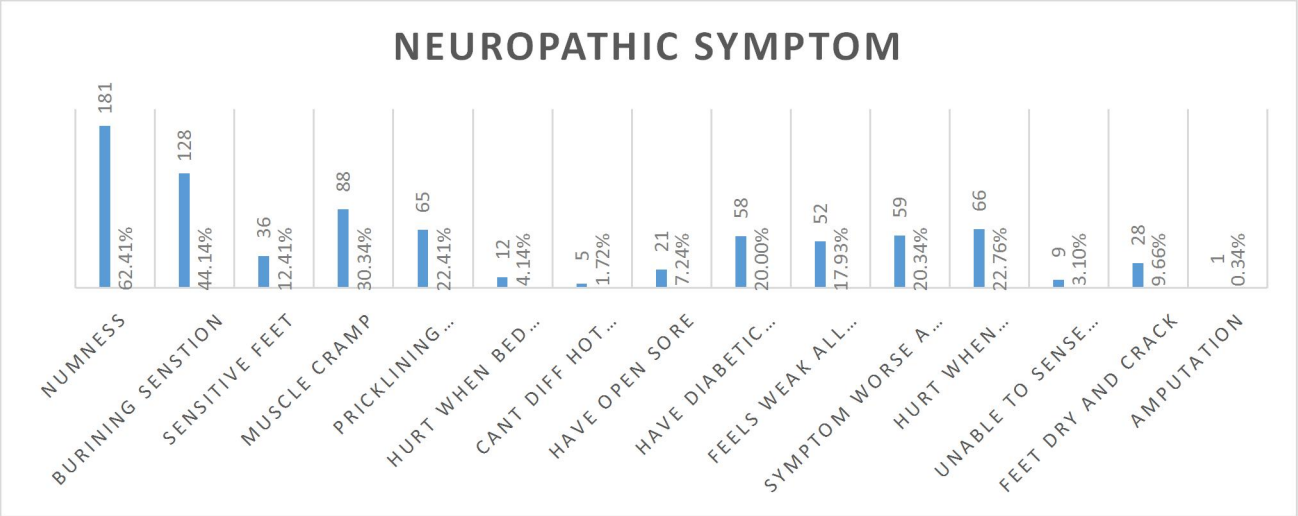
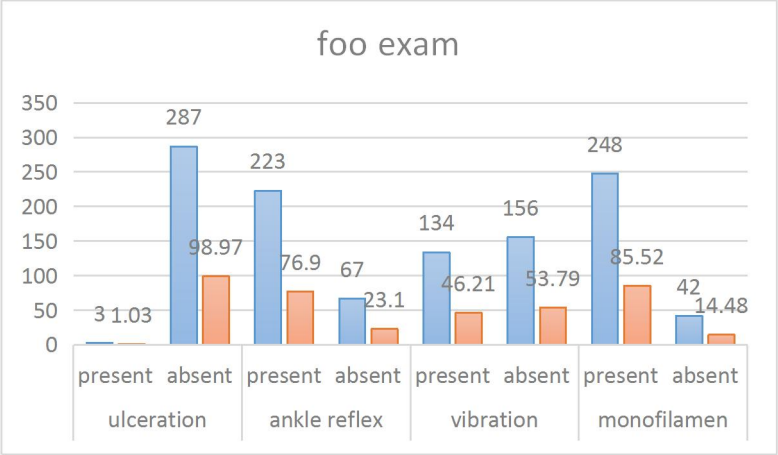


Figure 2 Neuropathic symptom frequency of participant



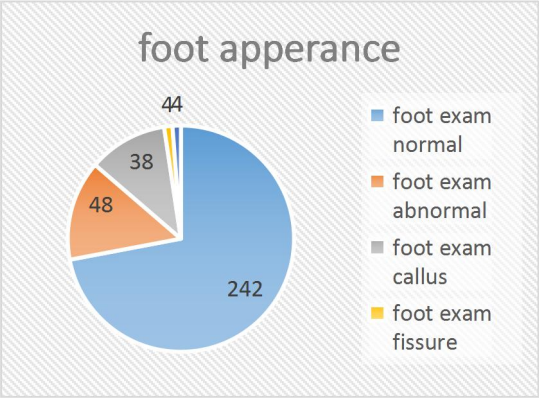


Figure 3 Foot exam frequency of participant

The majority of the participants, 241 patients (83.1%), were classified as obese, with 155 of them being female (53.45%). Hypertension was uncontrolled in 163 participants (56.2%), and orthostatic hypotension was detected in 6 participants (2.07%).There were missing data on HbA1c, which was done in 182 participants. Among those with available data, 132 patients (72.5%) had suboptimal glycemic control. Fasting blood sugar was sub-optimally controlled in 189 participants (65.17%).When assessing LDL levels, the majority of participants, 195 patients (67.2%), had LDL levels that were off target.

6.4 Result of Biothesiometer

Among participant who had DSPN based on biothesiometer 247 (85.2%), sever DSPN was detected in 151 (52.07%) of the participant .The mean average biothesiometer was 28.8 with SD minimum value was 8 volt. Those who had no clinical diagnosis of DSPN using MNSI but was found to have DSPN on biothesiometer are 130 (79.75%), among this 63 (38.65) has sever DSPN on biothesiometer. Among those who had sever DSPN on biothesiometer one or more neuropathic symptom was there in 140 (92.7) of the participant, Likewise one or more physical sign of neuropathy was found in 123 (81.4%) of the participant who has sever DSPN on biothesiometer

Table 3. Biothesiometer result of participant

biothesiometer severity	Freq.	Percent
<15	43	14.83
15-20	55	18.97
20-25	41	14.14
>25	151	52.07

Table 4. Physical exam finding and laboratory parameter of the participants

Variables		Frequency	percent
BP	controlled	127	43.79
	uncontrolled	163	56.21
orthostatic hypotension	NO	284	97.93
	Yes	6	2.07
WC	Male normal	41	14.13
	male obese	86	29.66
	female normal	8	2.76
	female obese	155	53.45
BMI	normal	82	28.2
	over weight	126	43.45
	class I obesity	61	21.03
	class II obesity	15	5.17
	class III obesity	6	2.07
FBS	controlled	101	34.83
	uncontrolled	189	65.17
HbA1C	controlled	50	27.47
	uncontrolled	132	72.53
Total cholesterol	controlled	257	88.62
	uncontrolled	33	11.38
TG	controlled	206	71.03
	uncontrolled	84	28.97
HDL	controlled	144	49.66
	uncontrolled	146	50.34
LDL	controlled	95	32.76
	uncontrolled	195	67.24

	Mean	**SD**
BMI	27.7kg/m2	4.6kg/m2
FBS	162 mg/dl	61.1mg/dl
HbA1c (n=182)	8.5 %	2.2%
TC	146 mg/ dl	41.3mg/dl
TG	133 mg /dl	71.5mg/dl
LDL	90 mg /dl	34.9mg/dl
HDL	43.7 mg /dl	32.5mg/dl
Waist circumference	99.9 cm	11.8 cm
SBP	134 mmHg	17mmHg
DBP	77 mmHg	11mmHg

There was significant association of biothesiometer with MNSI symptom like numbness, burning ,prickling sensation (table 5).Likewise, there is significant association of biothesiometer with ,physical exam part of MNSI ,abnormal finding foot (callus),vibration and monofilament .Over all biothesiometer had significant association with physical exam part of MNSI (table 6)

Table 5. Biothesiometer association with MNSI symptom

	Biothesiometer		
	DSPN	**NO DSPN**	**P value**
No	247	43	
numbness			0.003
No	84 (34.0%)	25 (58.1%)	
yes	163 (66.0%)	18 (41.9%)	
burning			0.047
no	132 (53.4%)	30 (69.8%)	
yes	115 (46.6%)	13 (30.2%)	
Sensitive foot			0.24
no	214 (86.6%)	40 (93.0%)	
yes	33 (13.4%)	3 (7.0%)	
Prickling sensation			0.025
no	186 (75.3%)	39 (90.7%)	
yes	61 (24.7%)	4 (9.3%)	
Cant diff hot and cold			0.74
no	243 (98.4%)	42 (97.7%)	
yes	4 (1.6%)	1 (2.3%)	
Have open sore			0.066
no	232 (93.9%)	37 (86.0%)	
yes	15 (6.1%)	6 (14.0%)	
Symptom worse at night			0.76
no	196 (79.4%)	35 (81.4%)	
yes	51 (20.6%)	8 (18.6%)	
Hurt when walking			0.48
no	189 (76.5%)	35 (81.4%)	
yes	58 (23.5%)	8 (18.6%)	
Un able to sense feet			0.75
No	239 (96.8%)	42 (97.7%)	
yes	8 (3.2%)	1 (2.3%)	
Feet dry and crack			0.64
no	224 (90.7%)	38 (88.4%)	
yes	23 (9.3%)	5 (11.6%)	

Table 6 biothesiometer association with MNSI physical exam

Foot exam	Yes	no	0.023
normal	201 (81.4%)	41 (95.3%)	
abnormal	46 (18.6%)	2 (4.7%)	

Ankle reflex			0.25
Present	187(75.71%)	36(83.72%)	
Absent	60(24.29%)	7(16.28%)	
vibration			<0.001
present	97(39.27%)	37(86.05%)	
Present	150(60.73%)	6(13.95%)	
Monofilament			0.003
Present	205(83%)	43(100%)	
absent	42(17%)	0	
MNSI symptom			0.55
DSPN	191(77.33%)	35(81.4%)	
No DSPN	56(22.67)	8(18.6%)	
MNSI physical exam			<0.001
DSPN	152(61.54%)	39(90.7%)	
NO DSPN	95(38.64%)	4(9.3%)	

6.5 Independent predictor of DSPN result

Variable from bivariate analysis with p-value of 0.25 were taken into final model. Smoking history, duration of diabetes, LDL value above 70 mg /dl and obesity have significant association with the occurrence of DSPN. Patient with smoking history had 2.5 times likely to develop DSPN as compared to non-smoke (AOR =2.5 95 % CI (1.16, 5.63),P-value of 0.02). Duration of diabetes longer than 10 years was 2 times associated with DSPN as compared to duration of below five year (AOR=2.03 95 CI(1.01,4.09) ,P-value 0.047).Patients who had LDL value above 70 mg /dl were likely to have DSPN 1.9 times DSPN (AOR=1.9 95% CI (1.05,3.45) ,P – value =0.035.Obese individuals were 2.7 times likely to have DSPN as compared to normal weight (AOR= 2.7, CI95% (1.28-5.72),P-value =0.009

DSPN	DSPN		COR (95 %CI)	AOR	P>z
	YES 127	NO=163			
age					
<30	1	9			
30-49	25	46	4.89(0.58,40.85)	2.11(0.24,18.87)	0.505
>50	101	108	8.41 (1.04,67.62)	4.06(0.46,35.68)	0.206
smoking					
no	101	145			
yes	26	18	2.07(1.07-3.98)	2.56(1.16,5.63)	0.02
currently drinking alcohol					
no	8	2			
	119	161	5.4(1.12,25.94)	5.09(0.81,32.1)	0.084
duration of DM					
<5 yr	27	53			
5-10 yr	25	43	1.14(0.58,2.24)	1.11(0.49,2.53)	0.797
>10 yr	75	67	2.19(1.24,3.88)	2.03(1.01,4.09)	0.047

Sglt2 inhibitor					
NO	98	143			
yes	25	17	2.1(1.10,4.18)	2.22(0.96,5.1)	0.061
education level					
No formal	14	10			
primary school	77	50	0.67(0.27,1.66)	0.74(0.27,2.02)	0.556
preparatory school	27	47	0.41(0.16,1.04)	0.33(0.12,0.94)	0.038
collge and above	39	56	0.49(0.2,1.23)	0.37(0.13,1.01)	0.053
DKD					
no	100	138			
yes	27	25	1.4(0.81,2.72)	0.83(0.39,1.8)	0.642
HTN					
no	44	71			
yes	83	92	1.45(0.9,2.35)	0.63(0.34,1.18)	0.151
DR					
no	96	144			
yes	31	19	2.4(1.3,4.58)	1.64(0.75,3.62)	0.216
dyslipidemia					
optimal	38	83			
suboptimal	89	80	2.4(1.40,3.91)	1.63(0.91,2.93)	0.101
cardiac Ds					
no	86	134			
yes	41	29	2.2(1.27,3.80)	1.54(0.77,3.1)	0.223
LDL interpreted					
optimal	34	61			
suboptimal	93	102	1.63(0.98,2.71)	1.9(1.05,3.45)	0.035
BMI					
normal	29	53			
over weight	46	80	1.05(0.58.1.87)	0.81(0.41,1.58)	0.531
obese	52	30		2.7(1.28,5.72)	0.009

Table7. Bi-variable and multivariable analyses of factors associated with DSPN

7. Discussion

In this study the prevalence of DSPN using MNSI is 43.79 %, which is comparable to the study done in Africa 46 %(11), 48.1 % in Sirilanka (27) and study done Addis Ababa Tikur Anbesa Hospital in 2011, 48.2% (35).The study has high prevalence compared to study done in united kingdom (28.5%), China (8.4%), India (29.9%), Ghana (16.6%) and meta-analysis in 2021 in Ethiopia (22%) ((10,12,26,28).The explanation for this is use of different scoring method for assessment of DSPN .The study has low prevalence compared to Minnesota study (54%),Nigerian (71.1%), Jimma university study (53.6%) and Bahardar Felegehiwot hospital (52.2%). ((9,31,34,36)) .The low prevalence compared to these studies may be because the Minnesota study used nerve conduction and the study population in the Nigerian study included those who had duration of Diabetes more than 5,but this study included patient with pre-diabetes also .The symptom score in this study was 22.07 % which is low compared to physical exam 34.14 % ,this finding was comparable to study done in Jimma university and Bahardar Felege Hiwot hospital (34,36). The explanation for this might be low symptom perception since we don't frequently practice MNSI symptom score to diagnose DSPN.

After performing multi -variety analysis for DSPN , smoking (AOR =2.5 95 % CI (1.16, 5.63),P-value of 0.02),duration diabetes (AOR=2.03 95 CI(1.01,4.09) ,P-value 0.047), BMI (AOR= 2.7, CI95% (1.28-5.72),P-value =0.009 and High LDL(AOR=1.9 95% CI (1.05,3.45) ,P – value =0.035 were found to have significant association . Smoking were found to be significantly associated with DSPN. This finding were similar in studies done in US, Iran, and Ethiopia. (9, 34, 63) . In our study duration of diabetes greater than 10 years was significantly associated with DSPN. This is same as various other study finding (30,31,36,43). This association is due to long duration hyperglycemia resulting in oxidative stress in the diabetic neurons (56).The other significant association was high LDL which is also finding from Chinese study((64).Obesity was significantly associated with DSPN same as finding in Iran and Ethiopia(36,63)

The prevalence of DSPN using biothesiometer is 83.9% which shows high sensitivity of the biothesiometer. The prevalence in this study is higher than the Nigerian study which in diabetic participant the prevalence was 68.1% (65).Another study also showed prevalence of DSPN using biothesiometer 34.9%(66).The explanation for the higher prevalence in these studies is different cut of points for assessing DSPN, which is higher than 25 volt and in the study with prevalence of 34.9 % the study include newly diagnosed patient with diabetes . In this study the cutoff point we used for DSPN is above 14.9 volt which was evidenced by Chinese study which compared it with nerve conduction test which is gold standard and another study which also assessed the vibroseness used cut off point of point which was used in this study (67,68).The prevalence in this study was higher to study done in India which is 74 %((49)) which us the same cut off point .This can be explained by the subjectivness of the vibration perception test .The other study done in India again showed prevalence of 96.5 % which is higher than prevalence in this study .This can be due to in the Indian study included more of known diabetic neuropathy patient (62).

Our study showed majority 151(52 %) of the patient had DSPN on biothesiometer had sever DSPN ,which also same finding Nigerian and Indian study (62,65).Majority 140 (92.7%)of

patient who had sever DSPN on biothesiometer has one or more symptom MNSI symptom . This is also comparable to the Indian finding. ((62,66)) .The explanation for this is the biothesiometer has high sensitivity. ((68)). Biothesiometer peaked 130 (79.75 %) who had no clinical symptom or Sign based on MNSI. This is almost comparable to Nigerian study which peaked 70% DSPN with no clinical symptom of DSPN(65).

8. Conclusion and recommendation

8.1 conclusion

Around 43.8% of the study participant had DSPN using MNSI and using biothesiometer DSPN was found in 85.2 % participant. Long duration of diabetes, smoking history, obesity and high low density lipoprotein were independent risk factor for DSPN .Biothesiometer peak 79.1% of participant with no clinical symptom based on MNSI symptom .Symptomatic participant has sever DSPN biothesiometer .Thus our finding suggest prevalence of DSPN is high and can use biothesiometer for early detection of DSPN

8.2 Limitation

Lack of nerve conduction test and study type makes it difficult for validity of biothesiometer and to have cut off point for biothesiometer .The participant recall bias probably has affected the MNSI history score, which is reflected by the discrepancy between the symptom and exam version of MNSI. Incomplete laboratory value for glycated hemoglobin made it difficult to assess the glycemic level association.

8.3 Recommendation

The findings highlight the necessity of including biothesiometer for diagnosis of DSPN. Long duration diabetes, smoking history, obesity and uncontrolled low density lipoprotein are risk that can be used to build tailored interventions and preventive initiatives.

More study, preferably large scale multicenter national study is needed to confirm these findings and investigate other factors that may contribute to the burden of DSPN among diabetic people in Ethiopia

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ANNEX

Information and Consent form

Dear participant

The purpose of this study is to assess magnitude of diabetic neuropathy using MNSI and biothesiomter. Since the finding of this study is important to determine future decision regarding diabetic neuropathy, I kindly request genuine participation.

You have full right to participate throughout or to discontinue at any time or never to participate in the study .The information you give will be used only for the purpose of this study confidentially.

Consent form

I, the under signed have heard the information in the information sheet and understand the purpose of and significance of the study.

I agree to participate in the research voluntarily

Signature ---------- Date

MICHIGAN NEUROPATHY SCREENING INSTRUMENT

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 you 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: _____

MICHIGAN NEUROPATHY SCREENING INSTRUMENT

B. Physical Assessment (To be completed by health professional)

1. Appearance of Feet

	Right	Left
a. Normal	☐ 0 Yes ☐ 1 No	Normal ☐ 0 Yes ☐ 1 No
b. If no, check all that apply:		If no, check all that apply:
Deformities	☐	Deformities ☐
Dry skin, callus	☐	Dry skin, callus ☐
Infection	☐	Infection ☐
Fissure	☐	Fissure ☐
Other	☐	Other ☐
specify:	_____	specify: _____

	Right			Left		
2. Ulceration	Absent ☐ 0		Present ☐ 1	Absent ☐ 0		Present ☐ 1
3. Ankle Reflexes	Present ☐ 0	Present/ Reinforcement ☐ 0.5	Absent ☐ 1	Present ☐ 0	Present/ Reinforcement ☐ 0.5	Absent ☐ 1
4. Vibration perception at great toe	Present ☐ 0	Decreased ☐ 0.5	Absent ☐ 1	Present ☐ 0	Decreased ☐ 0.5	Absent ☐ 1
5. Monofilament	Normal ☐ 0	Reduced ☐ 0.5	Absent ☐ 1	Normal ☐ 0	Reduced ☐ 0.5	Absent ☐ 1

Signature:_____ Total Score _____ /10 Points

Questionnaire

MRN ----------Date of interview ---------- Interviewer Name

Ser No	Questions	Response and coding	Skip
	Socio-demographic		
101	How old are you	---------- yrs	
102	Sex	1. Male 2 .Female	
102	Where do you reside?	1. Urban 2. Semi-rural 3. rural	
103	What is your current marital status?	1.Single 2.Married 3.Divorced 4. Widowed	
104	Which of the following best describes your main work status over past 12 months?	1. Government employee 2. Self employed 3. House wife 4. Farmer 5. Others specify ----	
105	What is your level of education?	1.No formal education 2.Primary school 3.secondary school 4. preparatory school 5.College/university completed 6.postgraduate degree	
106	What is your monthly income?	1.Less than 5000 birr 2.Between5000-10000birr 3.Above 10000 birr	
	2.Life style factors		
201	Have you ever smoked any tobacco, such as cigarettes, cigar or pipes?	1. Yes 2. NO	
202	Do you currently smoke tobacco products?	1. Yes 2. NO 3. If yes ----------pack/yr	
203	Have you ever consumed an alcoholic drink such as beer, wine, spirits, fermented cider or tejj, tella, areke?	1.Yes 2. NO	
204	Do you currently drink alcohol frequently?	1. Yes 2. No	

	3.Diabetes related question		
301	Which type of diabetes do you have a. Type 1 b. Type 2	1. Type 1 2. Type 2 3. Pre-diabtes	
302	How long ago were you diagnosed with diabetes?	----------	
303	Do you take medication for the diabetes?	1. Yes 2. No	
304	What anti diabetic medication are you taking	----------	
305	Do you take lipid lowering drugs	1. Yes 2. No	
306	Have ever checked vitamin B12 level and supplemented	1. yes 2. No	
	4.Diabetic complication related questions		
401	Which symptom of neuropathy do you have? (based on Michigan symptom score)	1.Numbness 2. Burning sensation 3. Prickng sensation 4. are your feet sensitive to touch 5.Does it hurt when the bed sheet touches your skin 6.Muscle crumps 7.Could you be able to differentiate cold and hot water 8.Do you feel week all over most of the time 9. Do your leg hurts when you walk 10. are you able to sense your feet when you walk 11.Is the skin on your feet so dry it crack opens 12.Have you ever told to have diabetic neuropathy 13.Do you have history of DFU 14.Do you have History of amputation 15.are your symptom worse at night 16. None of the above	
402	Do you walk bare footed?	1. Yes 2. NO	
403	Do you have other diabetes complication?	1. Diabetic kidney disease 2. Diabetic retinopathy 3. Other	

		Specify------	
404	Do you have other comorbidities?	1. Hypertension 2. Dyslipidemia 3. RVI 4. Cardiac disease 5. Other specify ------- 6. No comorbidity	
	5.Physical examination		
501	Blood pressure	1.Sitting 2.standing	
502	Weight	-------	
503	Height	----------	
504	Body mass index	----------	
505	Waist circumference	----------	
506	Foot examination base on Michigan examination score Appearance of both foot	1 Normal 2 No If no is there Rt Lt 1. Deformity 2.Dry skin, callus 3.Infection 4.Fissure 5. other specify ---------	
507	Ulceration of the foot?	Rt Lt 1 Absent 2.present	
508	Ankle reflex?	1 present Rt Lt 2.present with reinforcement 3. Absent	
509	Vibration perception at great toe using tuning fork?	Rt Lt 1.Present 2.Decreased 3.Absent	
510	Monofilament?	Rt Lt 1.Normal 2.Reduced 3. Absent	
511	Biothesiometer (VPT)?	Rt---------- Lt----------	
	6.Laboratory test		
601	HbA1c		
602	FBS		
603	Lipid profile		

አባሪ 1: የዋናው መርማሪ ዋስትና

ስሜ ሳባ በላይ እባላለሁ ተመራማሪ ነኝ ለምርምር ፕሮጀክቱ ሳይንሳዊ፣ ስነ-ምግባር እና ቴክኒካል ምግባር እና ለሁሉም የምርምር ኘሮጀክቱ ባለድርሻ አካላት የሂደት ሪፖርቶችን ለማቅረብ ሀላፊነቴን እንደምወስድ ለማረጋገጥ ፊርማዬን ከዚህ በታች አስቀምጫለሁ።

ፊርማ ---------- ቀን ----------

አድራሻ ስልክ ቁጥር 0911340433

ኢሜል; BLYSABA4@GMAIL.COM

TASH , አዲስ አበባ, ኢትዮጵያ

አባሪ II የመረጃ እና የፍቃድ ቅጽ

የመረጃ ወረቀት

ውድ ተሳታፊ የዚህ ጥናት አላማ MNSI እና BIOTHESIOMTERን በመጠቀም የዲያቢቲክ ኒውሮፓቲ መጠንን ለመገምገም ነው። የዚህ ጥናት ግኝት የስኪር በሽታ ነርቭ በሽታን በተመለከተ የወደፊት ውሳኔን ለመወሰን አስፈላጊ ስለሆነ, እውነተኛ ተሳትፎን በአክብሮት እጠይቃለሁ::

በማንኛውም ጊዜ ለመሳተፍ ወይም ማቋረጥ ወይም በጥናቱ ላይ ላለመሳተፍ ሙሉ መብት አለዎት። የምትሰጠው መረጃ በምስጢር ለጥናት ዓላማ ብቻ ጥቅም ላይ ይውላል።

የፍቃድ ቅፅ

እኔ፣ በስሩ የተፈረመው በመረጃ ወረቀቱ ውስጥ ያለውን መረጃ ሰምቻለሁ እናም የጥናቱ ዓላማ እና አስፈላጊነት ተረድቻለሁ። በጥናቱ በፈቃደኝነት ለመሳተፍ ተስማምቻለሁ።
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አባሪ III መጠይቅ

MRN ------ የቃለ መጠይቁ ቀን ---------- የጠያቂው ስም----------

	ጥያቄዎች	ጥያቄዎች ምላሽ እና ኮድ መስጠት	ኮድ መዝለ
	1.የስነ ህዝብ አወቃቀር መረጃ		
101	ስንት አመትህ ነው	------ዓመት	
102	ጸታ	1. ወንድ 2. ሴት	
103	የት ነው የሚኖሩት?	1. ከተማ 2. ከፊል-ገጠር 3. ገጠር	
104	አሁን ያለዎት የጋብቻ ሁኔታ?	1. ነጠላ 2. ያገባ 3.የተፋታ 4. ባል የሞተባት	
105	ከሚከተሉት ውስጥ ባለፉት 12 ወራት ውስጥ የእርስዎን ዋና የስራ ሁኔታ በተሻለ ሁኔታ የሚገልጸው የትኛው ነው?	1. የመንግስት ሰራተኛ 2. በራስ ተቀጣሪ 3. የቤት ሚስት 4. ገበሬ 5. ሌሎች----------	
106	የትምህርት ደረጃዎ ስንት ነው?	1. ምንም መደበኛ ትምህርት 2. የመጀመሪያ ደረጃ ትምህርት ቤት 3.ሁለተኛ ደረጃ ትምህርት ቤት 4. የመሰናዶ ትምህርት ቤት 5.ኮሌጅ/ዩኒቨርስቲ ተጠናቀቀ 6.የድህረ ምረቃ ዲግሪ	
107	ወርሃዊ ገቢዎ ስንት ነው?	1.ከ5000 ብር በታች 2.ከ5000-10000ብር መካከል 3.ከ10000 ብር በላይ	
	2.የሕይወት ዘይቤ መጠይቆች		
201	እንደ ሲጋራ፣ ሲጋራ ወይም ቧንቧ ያሉ ትንባሆ አጨስህ ታውቃለህ?	1. አዎ 2. አይ	
202	በአሁኑ ጊዜ የትምባሆ ምርቶችን ያጨሳሉ?	1. አዎ 2. አይ 3. አዎ ከሆነ ----- እሽግ /በ ዓመት	
203	እንደ ቢራ፣ ወይን፣ ተጅ ጠላ አረቄ የመሳሰሉ የአልኮል መጠጦችን ጠጥተህ ታውቃለህ?	1. አዎ 2. አይ	
204	በአሁኑ ጊዜ አልኮል በብዛት ይጠጣሉ?	1. አዎ	

		2. አይ	
	3.ከስኪር በሽታ ጋር የተያያዘ ጥያቄ		
301	ምን ዓይነት የስኪር በሽታ አለህ	1. ዓይነት 1 2. . ዓይነት 2 3. ቅድመ ስኪር	
302	ከስንት ጊዜ በፊት በስኪር በሽታ ተይዘዋል?	------	
303	ለስኪር ህመም መድሃኒት ትወስዳለህ?	1. አዎ 2. አይ	
304	ምን ዓይነት የስኪር በሽታ መድሃኒት እየወሰዱ ነው	----------	
305	ቅባት የሚቀንሱ መድኃኒቶችን ትወስዳለህ	1. አዎ 2. አይ	
306	የቫይታሚን B12 ደረጃን ተመርመረህ ና ታክመህ ተውቃለህ	1. አዎ 2. አይ	
	4.ከስኪር በሽታ የሚያመጣቸው ጉዳት ጥያቄዎች		
401	የትኛው የነርቭ በሽታ ምልክት አለህ? (በሚቺጋን ምልክት ውጤት ላይ የተመሠረተ)	1. መደንዘዝ 2. የማቃጠል ስሜት 3. የመወጋት ስሜት 4. እግርዎ ሲነካ ህመም አለው 5.የአልጋው አንሶላ ቆዳዎን ሲነካ ያማል 6.ጡነቻ ህመም አለው 7.እርስዎ ቀዝቃዛ እና ሙቅ ውሃ መለየት ይችላሉ 8.DO YOU FEEL ሳምንት በላይ ብዙ ጊዜ 9. በእግር ሲጓዙ እግርዎ ህመም ለው 10.ስትራመዱእግሮችህን አይደነዘዙም 11.በእግርዎ ላይ ያለው ቆዳ በጣም ደረቅ ሆኖ ይሰነጠቃል 12.የስኪር በሽታ ኒዩሮፓቲ እንዳለህ ነግረህ ታውቃለህ 13. የ እግር ቁስለ አጋጠሞ ያቃል 14.እግር መቆረጥ አጋጠሞ ያቃል 15.ምልክትዎ በምሽት የከፋ	

		ነው 16. ከላይ ከተጠቀሱት ውስጥ አንዳቸውም ምልክት የለኝም	
402	በባዶ እግራችሁ ትሄዳላችሁ?	1. አዎ 2. አይ	
403	ሌላ የስኪር ህመም ያመጣው ችግር አለህሽ?	1. ክስኪር በሽታ የተያያዘ የኩላሊት በሽታ 2. የስኪር በሽታ ያመጣው ሬቲኖፓቲ 3. ሌላ ይግለጹ-----	
404	ሌሎች ተጓዳኝ በሽታዎች አሉዎት?	1. የደም ግፊት 2. ዲስሊፒዲሚያ 3. HIV በሽታ 4. የልብ በሽታ 5. ሌላ ይግለጹ ------- 6. ምንም ተጓዳኝነት የለም	
	5.የአካል ምርመራ		
501	የደም ግፊት	1. ተቀምጠው 2.ቆመው	
502	ክብደት	--------	
503	ቁመት	---------	
504	የሰውነት ብዛት መረጃ ጠቋሚ (BMI)	-----	
506	የወገብ ዙሪያ	----------	
507	ሚቺጋን የእግር ምርመራ መሠረትየሁለቱም እግሮች ገጽታ	1 ኖርማል 2 ችግር ያለው ኖርማል ካልሆነ 1. የአካል ጉድለት አለው 2.ደረቅ ቆዳ, CALLUS አለው 3. ኢንፌክሽን አለው 4 የተሰነጠቀ አለው 5. ሌላ ይግለጹ -----	
508	የእግር ቁስለት?	1. አለ 2. የለም	
509	የቁርጭምጭሚት ምላሽ?	ቀኝ ግራ 1 አለ 2.በማጠናከሪ አለ 3.የለም	
510	የንዝረት ግንዛቤ በትልቁ ጣት ?		

		ቀኝ ግራ 1.አለ 2.ቀንሶአል 3.የለም	
511	ሞኖፊላመንት ምርመራ?	ቀኝ ግራ 1. መደበኛ 2. የቀነስ 3. የለም	
512	ባዮቴሶምትር ምረመራ?	1.ቀኝ------ 2. ግራ---------	
	6.ላቦራቶሪ		
601	የሶስተ ወር የስኪር ክምችት	---------	
602	በባዶ ሆድ የስኪርመጠን	---------	
603	የቅባት መጠን	----------	