DIABETIC FOOT DISEASE: THE ASSOCIATION OF FOOT DEFORMITIES, SENSORY TESTING AND SUGAR CONTROL IN TYPE 2 DIABETIC PATIENTS IN KENYATTA NATIONAL HOSPITAL

BY

DR MACHARIA PETER WOKABI

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A thesis to be submitted in partial fulfillment for the award of a degree in Masters in Medicine (Mmed) in Orthopaedic Surgery in the Department of Orthopaedics of the University of Nairobi

2021

DECLARATION

I hereby declare this thesis is my original work and has not been presented for a degree in any other University. Where other peoples work has been used, this has been properly acknowledged and referenced in accordance to the universities plagiarism policy

Signed..... Date...01/09/2021.....

DR MACHARIA PETER WOKABI

PRINCIPAL INVESTIGATOR

H58/87523/2016

Department of Orthopaedic Surgery, School of Medicine, University of Nairobi

Date ...01/09/2021...

Sign.....

APPROVAL BY THE UNIVERSITY SUPERVISORS

This dissertation has been submitted for examination with our approval as university supervisors.

I, DR FRED SITATI, senior lecturer, department of orthopaedic surgery University of Nairobi, orthopaedic surgeon, Division of Orthopaedic Surgery, Kenyatta National Hospital

Signature ..... Date.....01/09/2021.....

P. O Box, 19076-00202,

NAIROBI

I, DR EZEKIEL OBURU, lecturer, department of orthopaedic surgery University of Nairobi, orthopaedic surgeon, Division of Orthopaedic Surgery, Kenyatta National Hospital

Signature .....Ezekiel Oburu..... Date 01/09/2021

P. O Box, 19076-00202,

NAIROBI

DEPARTMENTAL APPROVAL

This is to certify that this thesis is the original work of Dr. Peter Macharia, Master of Medicine in Orthopaedic surgery at the University of Nairobi. This research was carried out at Kenyatta National Hospital.

SIGNATURE.....

DATE.....02/09/2021

DR VINCENT MUOKI MUTISO

SENIOR LECTURER AND CHAIRMAN,

DEPARTMENT OF OTHOPAEDIC SURGERY

UNIVERSITY OF NAIROBI

POBOX19681-00202

NAIROBI,

KENYA.

Email:mutiso@uonbi.ac.ke

DEDICATION

I dedicate this work to my dad who inspired me to do this study. And to my family, who supports me in more ways than I can express.

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May the Almighty God bless you all abundantly.

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LIST OF ABBREVIATIONS

ADA: American Diabetic Association

COVID-19: Coronavirus-2019

CTS: Carpal tunnel syndrome

DM: Diabetes Miletus

DCCP: Diabetic control and complications trial

DFU: diabetic foot ulcers

DIPJ: distal interphalangeal joint

DPN: diabetic peripheral neuropathy

DSPN: diabetic sensory polyneuropathy

GIT: Gastrointestinal tract

GUT: Genitourinary tract

HAART: Highly active anti-retroviral therapy

HbA1c: glycosylated hemoglobin

IMW: intrinsic muscle wasting

IGT: impaired glucose tolerance

KNH: Kenyatta National Hospital

KNH/UoN-ERC: Kenyatta Nationa Hospital/University of Nairobi –Ethics and Research Committee

LEA: lower extremity amputation

MNSI: Michigan Neuropathy Screening Instrument

MTJ: Metatarsal phalangeal joint

MoH- Ministry of Health

NCS: Nerve conduction studies

NIC: Neuropathy Impairment and Change

NSC: Neuropathy Symptoms and Change

PIPJ: Proximal interphalangeal joint

PPE- Personal Protective Equipment

SARS/COV2: Severe Acute Respiratory Syndrome- Coronavirus2

SPSS: Statistical Package for the Social Sciences

T2DM: Type II diabetes mellitus

UKST: United Kingdom Screening Tool

VPT: Vibration Perception Threshold

WHO: World Health Organization

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DEFINITION OF TERMS AND VARIABLES

Type 2 diabetes patients refers to any patient with persistent hyperglycemia and a degree of insulin resistance, as defined by the American Diabetes Association

Glycated hemoglobin refers to the percentage of hemoglobin in erythrocytes enzymatically linked to glucose

Clinical neuropathy refers to sensory , motor and autonomic disturbances as outlined in the Michigan Neuropathy Screening Instrument(MNSI).

ABSTRACT

Background: The 21st century has seen a rapid surge of diabetes in low and middle income countries. Sub-optimally controlled DM has been associated with a myriad of complications. Diabetic peripheral neuropathy(DPN) affects approximately 50% of Type II DM(T2DM) patients. DPN involves loss of protective sensation in the extremities, a primary risk factor to development of diabetic foot ulcers (DFU). DFU is considered the most likely forecaster of eventual limb loss/lower extremity amputation(LEA) in patients with type 2 diabetes.

LEA associated disability causes decline in the quality of life. The World Health Organization (WHO) states up to 80% of the LEA can be averted with early detection and appropriate foot care. Measurement of vibration perception threshold(VPT) by Biothesiometer has emerged as a potent screening tool for sensation impairments with a high sensitivity (80%) and specificity (98%).

Study objectives. This study evaluates foot deformities, sensory peripheral neuropathy and glycemic control amongst T2DM patients in Kenyatta National Hospital(KNH)

Study design and site: Analytical cross-sectional study on known T2DM patients in KNH wards and outpatient clinics.

Participants and Methods: The study highlighted the prevalence of foot deformities, assessed sensory neuropathy and correlated the same to glycemic control in T2DM patients with a broader goal to outline the risk of evolution of DFU in this cohort. Inclusion criteria: T2DM patients on hypoglycemic treatment. Patients with acute complications, concurrent use of drugs that affect glycemic metabolism/cause peripheral neuropathy were excluded. A clinical proforma including biodata, history and physical examination with comprehensive foot examination was administered. HbA1c levels was then analyzed. Michigan Neuropathy Screening Instrument (MNSI) was used to divide participants into those with

clinical neuropathy and those without. Peripheral sensation was then evaluated and graded for both groups using biothesiometry.

Ethical approval was obtained from the Department of Orthopaedics, KNH/UoN Ethics committee

Data management: Data was coded, entered and managed in a Microsoft Access Windows 10 database and at the end of data collection exported to Statistical Package for the Social Sciences (SPSS) V27 2020 version for analysis. To compare proportions of patients with DPN using MNSI and biothesiometry Chi square test was used

To determine and describe the correlation between glycated hemoglobin, diabetic foot deformities and sensory neuropathy Spearman Correlation Coefficient was utilized. Ordinal logistic regression model was then used to establish linear relationship of the variables.

Results: 255 patients with type 2 DM met the inclusion criteria. The age ranged from 20 to 82 years mean age was 50.44 years (95% CI; 48.62 to 52.26). Majority were female with the male: female ratio being 2:3. The incidence of foot deformities was found to be 48% with hallux claw toes valgus (7.5%) hammer toes (5.5%), claw toes (3.1%) and amputations at various level (2%) being the commonest deformities. The prevalence of ulceration was 12% with Wagner grades 2 and 3 accounting for the majority of the foot ulcer grade. The prevalence of peripheral neuropathy using clinical symptoms as outline by MNSI and biothesiometry was found to be 45% (n=115) and 64.3% (n=164) respectively. There was a statistically significant difference in diagnostic yield between MNSI and Biothesiometry (Chi-square Value 36.448, D.F. 3, P-Value <0.001). There was a weak positive correlation between HbA1c and the grade of peripheral neuropathy (Spearman rho 0.356; P-value <0.001). The coefficient of determination was 0.127

Conclusion: Foot deformities are frequent in the diabetic population and they result in alteration of gait biomechanics. The etiology of foot deformities and their exact role in foot ulcerations remains a subject of investigation. Biothesiometry is a simple, reliable, convenient and non-invasive tool for screening and

grading peripheral neuropathy. There is a correlation between the level of glycemic control and degree of peripheral neuropathy as measured using biothesiometry.

CHAPTER 1

INTRODUCTION

Diabetes mellitus has become the epidemic of the 21st century[1].According to the global body WHO, people living with diabetes increased from 108 million in 1980 to 422 million in 2014. The same duration witnessed the global prevalence among adults over 18 years old rising from 4.7% to 8.5%[2]. Perhaps, more disconcerting is the fact that almost 80% of the adult diabetics are in low and middle income countries. In Kenya, the prevalence of DM is estimated to be 3.9%, among the highest in Sub-Saharan Africa.[3]

Type II DM is part of the metabolic syndrome characterized by insulin resistance, hyperglycemia and excess body weight[1].The American Diabetes Association define type 2 DM as persistent hyperglycemia in individuals with insulin resistance. The degree of insulin resistance ranges from relative insulin deficiency to insulin secretory defects.

Sub-optimally or poorly controlled DM is associated with a wide range of complications some of which require surgical interventions. DFU is the common complication and affects an estimated 12% of DM

patients[4]. Diabetic neuropathy has the greatest effect in the development of DFU: sensory neuropathy leads to loss of the protective modality needed to prevent ulceration[5]

Diabetic foot ulceration is regarded the most onerous precursor for infections and of eventual lower extremity amputation(LEA)[5]. Poor glycemic control is almost always a predecessor to the development of neuropathy and DFU. Amputation due to diabetes leads to disability unnecessary decline in the quality of life. The WHO and International Diabetes Federation (IDF)state up to 80% of the LEA can be prevented with adequate detection and care.

The high economic and social cost for managing the complications of sub-optimally controlled DM make a compelling case for its prevention[1].

Diabetic neuropathy is the commonest complication of diabetes[1]. It affects up to 70% of the patients with longstanding diabetes[6]. The complication like other diabetic complications happens in a time-dependent manner. There exists a strong causal link between sensorimotor and autonomic neural disturbances and a range of foot deformities and pathology, including detrimental changes to peripheral bone, joints and soft tissue[6,7].

Sensory neuropathy accounts for 75% of all diabetic neuropathy[6]. As the greatest risk factor to development of DFU, routine assessment of this parameter is of paramount importance in the goal to avert diabetic foot and eventual LEA.VPT is regarded as gold standard for the screening and grading of sensory

neuropathy[7]. The biothesiometer is an instrument which measures the threshold of appreciation of vibration sense. Biothesiometer has been shown to have a sensitivity (80%) and specificity (98%) for sensory neuropathy[8]. Biothesiometry has now come to be regarded as a gold standard in assessment and early detection of sensory neuropathy[9].

Glycated hemoglobin, HbA1C, is an indispensable reflection of glycemic control. A single reading of HbA1c offers a window into the overall glycemic status of the preceding 2- 3months. This, not only provides a picture of sustained sugar levels but also correlates well with the risk of chronic and long-range adversities of sugar metabolism derangements such as diabetic foot[10].

This study seeks to investigate and outline the common foot deformities and sensory impairments in T2DM patients seen in the national referral hospital. By using both clinical signs and symptoms and vibration perception to detect neuropathy, we hope to show some shortcomings of the former in the diagnosis of neuropathy. To underscore the multifactorial etiology for DPN and diabetic foot at large, the study correlated the degree of neuropathy to glycemic control as determined by glycosylated haemoglobin levels. Subsequently, the findings and conclusions were made which can be used to determine the risk to foot ulcerations and hopefully in future efforts to mitigate the risk.

STUDY QUESTION

What is the prevalence and relationship between foot deformities, diabetic peripheral neuropathy and glycemic control?

STUDY JUSTIFICATION

In understanding that the prevalence of diabetes and other non-communicable disease are on the rise in Kenya and other developing countries and are putting a strain on the already limited resources

That as stated by World Health Organization/ International Diabetes Federation joint news release: too many people are losing lower limbs unnecessarily to diabetes; Up to 80% of LEA can be prevented by proper podiatric care protocol; that expenditure due to diabetes and its complications exert a strain on the already scarce health resources with diabetic foot ulcers accounting for to up to 25% of this expenditure.

Recognizing that studies on diabetic neuropathy in Sub-Saharan Africa are scarce; there is need to incorporate newer techniques in screening for diabetic neuropathy: there is a paucity of local data on assessment of diabetic peripheral neuropathy by vibratory perception threshold using biothesiometry. Still the clinical utility of biothesiometry rival and perhaps exceed those of nerve conduction studies. Not only can it be administered as a bed-side procedure, it can detect sub-clinical sensory deficits which would have a bearing in the management of diabetic patients.

OBJECTIVES

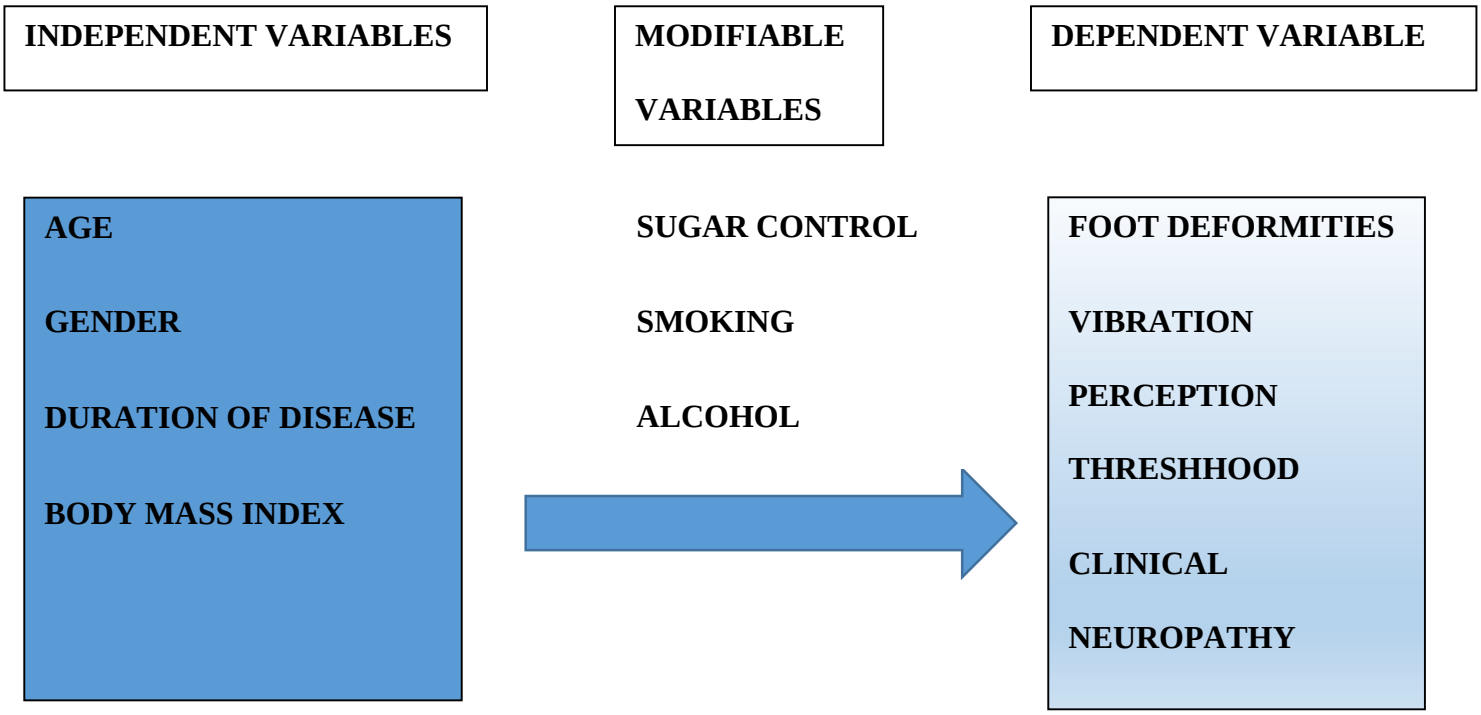
MAIN OBJECTIVE

To describe foot deformities, grade diabetic sensory neuropathy and describe its correlation to HbA1c among diabetic patients in Kenyatta National Hospital

SPECIFIC OBJECTIVES

1. To describe foot deformities amongst type 2 diabetic patients in Kenyatta National Hospital
2. To determine the prevalence of clinical neuropathy among the diabetic population of KNH using the Michigan Neuropathy Screening Instrument(MNSI)
3. To determine the prevalence of peripheral neuropathy in diabetic population in Kenyatta National Hospital using biothesiometry
4. To compare the prevalence of peripheral neuropathy using MNSI and biothesiometry in diabetic population of KNH
5. To determine HbA1c levels and describe its correlation with the grade of peripheral neuropathy

CONCEPTUAL FRAMEWORK



CHAPTER 2.

LITERATURE REVIEW

2.1 THE BURDEN OF DIABETES

Diabetes is a leading public health problem which in the 21st century has approached epidemic proportions globally[1]. 8.5% of the global citizenry have been diagnosed. This proportion is obviously a conservative estimate, when you put into consideration that much of the emerging cases of diabetes are in the developing world, where health- seeking morale remains low. Yes, the prevalence of diabetes is rising steadily and this rise is skewed to the developing world. This trend is worsened by the fact that most frequently affected are in the middle productive years of their lives,35-64 years[1,2].

In Kenya, the estimated population of diabetes is about 4% of the adult population, the 3rd highest proportion in the continent[11].Diabetes has become a leading cause of blindness, renal disease, coronary, cerebral vascular events and limb amputations[1,2]. Managing diabetes and its complications is a tall order exerting a heavy strain on the already scarce resources. The WHO estimates that 15% of the health budget goes to the management of DM and its complications[2].

Peripheral neuropathy is by far the commonest adverse outcomes of diabetes. It usually affects motor, sensory and autonomic parts of the nervous system. 75% of peripheral neuropathy in diabetics is sensory neuropathy[7,12].DPN has been associated with insensate lower extremities that are prone to DFU[12]. The latter have been implicated in 85% of non-traumatic LEA which leads to decline in quality of life.

Nyamu found a prevalence of DFU at 4.6% in a 2003 cross-sectional study done in KNH[13].The lifetime risk of getting DFU has been variously estimated to be between 12 -24 %. The annual risk of developing DFU is estimated at 2.8%,[14]

Diabetic foot has been cited as the commonest reason for hospital admission[14,15]and confinement among diabetics. Upon hospitalization, prolonged hospital stays and the lingering threat of limb loss haunts these patients.

Diabetic foot is largely a preventable complication[16] with simple measure such as proper foot wear, regular foot examination and tight glycemic control. The key to successful treatment of DFU is early presentation, early diagnosis and early treatment[16]. Unfortunately, patients' knowledge on diabetes self-care remains perilously inadequate. Ndirangu found that knowledge level corresponded with clinical outcome and patients with low levels of knowledge frequently ended having diabetic complications[17].

Diabetes and its complications are extremely burdensome on the health and economies worldwide. An estimated 15- 25% of the cost goes to management of diabetic foot and its complications [16]. The latter are largely preventable so the huge expenditure would be averted with proper screening and foot care practices. WHO estimated a lower extremity is lost to diabetes every 30 seconds[18]. It would seem unacceptable that such enormous reduction in quality of life/ disability, not to mention huge public resources are lost to LEA while this remains preventable and the solutions clear and affordable[16].

The Kenyan government has rolled out Universal Health Coverage. There is need for an integrated framework for the prevention, control and treatment of DFU among other chronic diseases. This is especially in view of limited resources.

2.2 DIABETIC PERIPHERAL NEUROPATHY

Diabetic peripheral neuropathy, can be described as somatic nerve disturbance in diabetics that attributable to no other causes. DPN, the commonest complication in diabetes, occurs in up to 67% of people with diabetes and affects both the sensorimotor and autonomic divisions.

Sensory peripheral neuropathy account for 75% of diabetic peripheral neuropathy. Clinically it presents as numbness and paraesthesias in a length-dependent 'stocking glove' distribution[20].

Chege performed a descriptive cross-sectional study to determine the period-prevalence of DPN among diabetic patients attending KNH. Using patients' history and physical examination she found a prevalence of 41%. The study recommended early diagnosis and management of DM to reduce DPN[31].The prevalence of peripheral neuropathy was much higher at 71% in a similar study done in North-Eastern Tanzania[32].

A study on Saudi patients using more objective nerve conduction studies found a prevalence of 89% for sub-clinical and symptomatic neuropathies. The same study found that using traditional methods of checking DPN placed the prevalence at only 9.1% an enormous discrepancy[33].

2.2.1. Pathogenesis of diabetic peripheral neuropathy

Sensory neuropathy in diabetes mellitus appears to be complex and multifactorial. While the exact pathogenesis of diabetic peripheral neuropathy (PN) remains a matter of postulation, various aetiologic factors have been proffered. Plausible causative actors for neuronal damage include, hyperglycemia, protein glycation, free radicals and oxidative stress[18].

Diabetes Control and Complications Trial (DCCT) hypothesized that the persistent hyperglycaemia is the chief culprit in the evolution and progress of

diabetic neuropathy[18.19]. Early lesions of diabetic neuropathy may arise from exposure of peripheral nerves to hyperglycaemia. The uptake of simple sugars into

neurons are insulin independent; and as such, directly proportional to circulating blood sugars levels. Reduction in biomolecules that support growth and survival of nerves such as Nerve Growth Factors and Insulin-like Growth Factor also a contribute to nerve damage[7].

Cashman and Hoke proffer that neuropathy in diabetes is convergence of six elementary pathos-mechanisms: dysfunctional sugar metabolism, non-enzymatic protein modification, organelle malfunction, disrupted intracellular signaling, dampened neuronal transport, and maladaptive ion channel dynamics. The different mechanisms all contribute to axonal dysfunction and symptoms of neuropathy[20].

2.2.2 Types of diabetic peripheral neuropathy

Rapidly reversible hyperglycaemic neuropathy:

This form, the mildest of DPN, manifests by transient sensory disturbances in patients with recent onset hyperglycemic state. The symptoms promptly stop upon attainment of euglecemia[21]**.**

Diabetic Sensorimotor Polyneuropathy:

The commonest type of DPN (80%)[21].Usually occur in a length and time dependent, stocking and glove distribution. Sensory neural damage alone accounts for 75% of DSPN. The neural damage is progressive and often symmetrical, starting from the distal appendages and moving centrally to the trunks

Diabetic Autonomic Neuropathy:

This debilitating form of diabetic neuropathy has profound debilitating effect on longevity [22]. It manifests mainly with GIT, GUT malfunction. Sudomotor denervation causes dry cracked skin can lead to ulceration and subsequent infection.

Focal and Multifocal Neuropathies:

Rarer than sensorimotor and autonomic neuropathy. They form a broad category of the less common nerve disturbances in diabetic neuropathy. They encompass the entrapment syndromes, mononeuropathies, neuropathy of the cranial and truncal nerves.

Mononeuropathies tend to be rapid in onset, involve the median nerve (5.8%), ulnar nerve (2.1%), radial nerve (0.6%) [23]. They resolve spontaneously more often than not.

Carpel tunnel syndrome is the commonest nerve entrapment in diabetic patients. Perkins et al[24] found that the overall prevalence CTS was 2% in the non-diabetic patients and in the excess of 30% in the patient population with diabetic polyneuropathy[24].

Diabetic Amyotrophy:

A rare form of diabetic neuropathy, mainly seen in the elderly diabetic patients. It usually manifests with pain and unilateral or bilateral atrophy of the thigh muscles. The exact etiopathogenesis is elusive**[25].**

Acute Sensory Neuropathy

This distinct form of DPN is debilitating but gratefully rare manifestation of nerve dysfunction in diabetics. Its referred to as diabetic cachexia and manifests with severe pain, weight loss, depression in the absence of clinical signs of DPN[22]. Normally resolves within a year.

Insulin Neuritis:

There is a hypothesis that insulin causes a disturbance in endoneural oxygen tension in peripheral nerves. This effect is dampened or abolished altogether in prolonged hyperglycemia. Restoring normoglycemic states re-sensitizes the nerves creating a hyper excitable state[26].

2.3 Evaluation for Diabetic Peripheral Neuropathy

A variety of modalities are available to evaluate both subjective and objective measures of peripheral nerve functions. Sensory neuropathy can manifest clinically as wide variety of sensory modality disturbances[23]. A structured list of signs and symptoms can therefore be useful for screening any at-risk patient for possible neural dysfunction

Sensory neuropathy, the most common of DPN is usually gradual in onset, showing a characteristic stocking-and- glove distribution which typically starts at the tip of the extremities. These symptoms may be positive or negative, diffuse or focal[24]. Numbness, loss of balance, painless injuries are common 'negative' symptoms. Burning pain sensation, tingling, electric shock like feeling and hypersensitivity to touch are some 'positive' symptoms.

The earliest clinical sign in diabetic sensory neuropathy is the decrease or loss of vibratory and pin prick sensation over the toes. Vibratory sense in the feet has traditionally been assessed using a 128Hz tuning

fork while protective sensation has always been assessed with a 10g 5.07 Semmes-Weinstein monofilament[24,25]. Dyck et al. have proposed ta criteria for diagnosis of peripheral neuropathy:

1. Signs of peripheral neuropathy,
2. abnormalities of quantitative sensory testing and
3. abnormal electrophysiological tests[34,39].

Diagnosis for sensory peripheral neuropathy require any two of three in the criteria

According to Perkins et al annual screening for diabetic peripheral neuropathy using pain sensation (pin prick), the Semmes Weinstein monofilament or vibration testing[24] should be performed on all patients with diabetes.

Locally, the assessment and diagnosis of DPN nearly always dependent on clinical signs and symptoms. While this is an inexpensive and convenient modality, peripheral neuropathy can exist in the absence of symptoms and signs. This 'subclinical 'neuropathy is no less detrimental and still exposes the patient to risk for ulcerations. Sheshah et al[33] found a prevalence of 91% of neuropathy in a cohort of T2DM patient, when DPN was screened using vibration perception threshold. In the same cohort, the prevalence dropped to 9.1% when screening was done using just signs and symptoms. This suggests that an overwhelming majority of patients with peripheral neuropathy are symptoms free and that clinical clerkship alone is insufficient to rule out neuropathy.

The tuning fork is a time honored modality for assessing vibrotactile perception. It provides a cheap convenient way to assess the large nerve fibers. The tuning fork however, remains awfully unobjective and lacks in both specificity and sensitivity in early cases of DPN.

Electrodiagnostic tests such as Nerve Conduction Studies (NCS) and Electromyography (EMG) have been regarded as gold standard in the assessment of peripheral neuropathy. However, their cost remains prohibitive especially in resource strained settings. Moreover, these tests require specially trained

personnel, usually a neurologist to perform and interpret making their utilization expensive and time consuming.

Biothesiometry provides a suitable, inexpensive and valuable alternative in the assessment of DPN. To the best of my knowledge we have no local studies on diabetic neuropathy assessment using biothesiometry.

2.3.1 ***Role of Michigan Neuropathy Screening Instrument:***

MNSI is a clinically validated tool for assessing diabetic peripheral neuropathy. First published in 1994. MNSI has proven a valuable tool first for the ease of its use and second for its reliability. The tool comprises of two parts, a self-administered set of targeted questions and A clinical evaluation part. The latter is usually performed and interpreted by the clinician[42].

As a clinical tool, MNSI have a degree of reproducibility that rivals that of time tested Nerve Conduction studies and therefore serves as a fairly objective assessment for peripheral neuropathy[42]

MNSI was primarily designed as a screening tool for diabetic neuropathy in an outpatient setting. Its use, however, expands beyond outpatients' settings and to peripheral neuropathy due to causes other than diabetes.

Part A of MNSI is a self-administered questionnaire with a set of 15 closed ended questions that are awarded a score based on a yes/no response. A higher score indicates more neuropathic symptoms. A cut off score of 4 is considered significant

A study done by Moghataderi et al comparing MNSI with NCS determined sensitivities and specificities for different scores on MNSI They recorded that 79% sensitivity at a cut off value of >/= 1.5 which

decreases to 35% when the same was increased to 3. The specificity, however, rise with corresponding rise in the cut off value of MNSI[27]

Fateh et al described the effectiveness of MNSI and United Kingdom Screening Tool (UKST) in the diagnosis of DPN. They found that the percentage of neuropathy picked by the two questionnaires ranged between 69 to 73% and concluded that MNSI is a sensitive screening tool for routine evaluation of DPN[43]

A recent study in Romania by Muntean et al found there was no consensus in the evaluation and diagnosis of DPN. The study found a strong relation between MNSI and sensory and motor parameters tested by NCS and concluded that while MNSI is less sensitive than electrophysiological tests such as NCS, its clinical utility remains invaluable. They concluded there was need to implement a standardized protocol with validated scales such as MNSI for objective evaluation and follow-up for patients with DPN[44]

Regarding the diagnostic capability of MNSI, Xiong et al found a score greater than 1.5 yielded a sensitivity of 80%when compared to electromyography (EMG) and NCS. They also found that as a diagnostic tool, MNSI was superior to other validated scales namely the Neuropathy Impairment Score (NIS) and the Neuropathy Symptoms and Change (NSC). However, advantageous though it is, the utility MNSI was found to be limited in diagnosis of autonomic Neuropathy.[45]

Vibration Perception Threshold

Vibration perception threshold(VPT) has long been considered the gold standard in assessment of peripheral neuropathies such as DPN[8,24]. Assessing the (VPT) is an easy and reliable way of delineating Type A nerve fiber dysfunction. VPT, in the range of 50 -300Hz induces a signal through the Pacinian and Meissner corpuscles. The two mechanoreceptors then transduce the mechanical signal to a neural signal through in large-diameter fibers to the CNS through the posterior columns. A strong relationship exists between loss of vibratory sensory modality and the progression of multiple indicators of DPN[14].

Its stipulated that sensory neuropathy precedes the loss of protective sensation and is the ulceration that ultimately ensues. Since DPN is overwhelmingly a sensory neuropathy[20] which turns out to be a pivotal element in the cascade from foot ulceration to limb loss, selecting a quick, affordable and accurate clinical tool to evaluate at-risk patients is of paramount importance.

Bloom et al performed a preliminary study suggesting biothesiometry offers a more predictable assessment for neuropathy than the time honored tuning fork. They affirmed that the biothesiometer when used to assess VPT gives a quick and reliable scale that can give an objective measure, not just for the status but also the progress of DPN.[46]

Literature is abounding with evidence to suggest that VPT measures can be used to accurately and easily identify at-risk diabetic patients, especially those with early and subtle neuropathic symptoms. The ideal screening tool for DPN should be inexpensive and easy to administer yet possessing high sensitivity, specificity and positive predictive power. While tissue biopsy and NCS are still regarded as gold standard, the two are clearly impractical for routine screening. On the other hand, VPT assessment is cheap, non-invasive and easy to perform and interpret. Abnormal VPT values have been reported as an independent risk factor for foot ulceration[47,48]

Neurological testing such as VPT consistently yield a higher prevalence of DPN compared to history and physical examination alone. In the same population of diabetic patients Mete et al found a prevalence for DPN of 32.1% and 74.5% using MNSI questionnaire and neurothesiometer respectively. They recommend that in evaluation of neurological impairment due to diabetes, neurological tests such as VPT be used for more accurate results and therefore early targeted preventive therapy to avert complications[49]

BIOTHESIOMETRY -an objective way of assessing vibration perception threshold

Biothesiometer is a clinical device capable of measuring with precision the threshold of vibration perception. The time honored tuning fork (128 Hz) has a long history of clinical use as a screening tool for sensory dysfunctions, diabetic or otherwise. Biothesiometer can be viewed as an upgraded tuning fork that uses electrical energy rather than mechanical vibrations. Assessing VPT helps detect large myelinated nerve fibers and detect sensory neuropathy earlier, even prior to clinical onset of signs and symptoms.

The device has a single vibrating probe which is place on the skin of the person being assessed. The vibration signal is then introduced through the probe; the amplitude being changed by adjusting the voltage gradually by turning a dial. The subject has to report the moment vibration is first felt. The corresponding voltage value is then noted and with it the grade of sensory neuropathy.

A study by Bloom et al showed that biothesiometry offers more predictable results in assessment of neuropathy compared to the tuning fork[46]

Pourhamidi et al compared the diagnostic utility of the tuning fork, monofilament, biothesiometer and biopsy in diabetic peripheral neuropathy. From the study, they concluded routine use of biothesiometry in screening DPN is a sensitive test for detecting neurological defects in large nerve fibers but not small nerve fibers. Combining biothesiometry and skin biopsy increased sensitivity of finding small nerve fibers neuropathy to 81%[(50)]

The limitation in biothesiometry, lies in the amount of pressure applied on its probe as this can induce a signal to the mechanoreceptors. Local limb temperature, assessment site, presence of foot deformities and patients' psychological factors are potential confounders. These drawbacks notwithstanding, biothesiometry remains solid as a screening tool of choice for diabetic neuropathy.

Young et al[8] has demonstrated that with biothesiometry the sensitivity stands at 80% and specificity stands at an all-time high of 98% when compared to NCS. These conclusions followed a prospective study

to screen for spontaneous development DFU based on the VPT values. In the utility of VPT as a tool for screening and diagnosis of peripheral neuropathy, there lacks a consensus in the cut off value that signals neural dysfunction. Figures ranging from 15 volts to 25 volts have been used as the cutoff [8,28,27]. Because the voltage is measure in a numerical scale, grading can then be done based on the amount of voltage needed to elicit a perceptible vibration.

In the above prospective study Young et al[8] were able to demonstrate a measurable effect of reduced VPT and development of foot ulcers. The cumulative incidence of DFU when VPT was <15V and > 25V is 2.9% and 19.8% respectively. This indicates a X7 increase in relative risk of ulceration: when the VPT is more than 25V as opposed to a VPT of less than 15V. Correspondingly, diabetic patients with a VPT reading of > 25V need a more intensive and vigilant foot care program to match the high risk of ulceration. This doesn't mean that patient with lower risks for ulceration need not be vigilant. The pathway to diabetic foot is in no way dependent on the neural dysfunction alone, significant though the latter might be. By grading VPT and therefore the degree of sensory neuropathy, biothesiometry aids in structuring a foot care package based on the relative risk for evolution of DFU.

Saha et al[29] did a study to establish the utility of VPT testing in the early detection of DPN. In a population sample 60 diabetic patients, 50% had clinical evidence of sensory neuropathy the remaining population exhibited no clinical evidence of neuropathy based on MNSI. In the former group, 26.6% showed no neuropathy based on VPT assessment using biothesiometry. An overwhelming majority of the patients with clinical neuropathy based on MNSI had grade 2 severity when assessed via biothesiometry. Interestingly,60% of the patients with no clinical evidence of neuropathy recorded grade 1 severity of neuropathy on biothesiometry. This demonstrates that VPT using biothesiometry can detect even subtle sub-clinical cases of sensory dysfunction which proves it invaluable as a screening tool, essential in early

commencement of targeted foot practices and perhaps need for enhanced normoglycemia for prevention or slowing progression of DPN

2.4 GLYCATED HEMOGLOBIN- THE BIOMARKER FOR DIABETES CONTROL

Diabetes is metabolic and endocrine dysfunction disorder characterized by persistent hyperglycemia. Glycemic control, therefore, is the cornerstone of managing diabetes and ameliorating or averting its complications. Glycated hemoglobin is the most widely utilized biomarker in the assessment of glycemic control. It has also been widely endorsed as a screening tool in diabetes as it measures long term glycemic exposure[30]. Hemoglobin, the most abundant protein in blood, spontaneously combine with sugars present in the bloodstream forming glycated haemoglobin HbA1c. Consequently, the amount of HbA1c tends to be proportional to long term glycemic levels in bloodstream. Diabetic complications are associated with impaired glycemic control which happens in a time-dependent manner. Time dependent glycemic control can, therefore, be used to assess the potential risk for complications such a DPN[38].

Diabetic peripheral neuropathy is a multifaceted entity that presents in various forms[39]. Jian et al found that long term hyperglycemia as assessed by cumulative HbA1c is independently associated with DPN in patients with T2DM[38].

Ishibashi et al investigated the impact of normalizing HbA1c on microvascular complications of diabetes like neuropathy. They found that normalizing HbA1c T2DM of even over a short duration improves in overall microvascular complications including neuropathy and nephropathy effectively and significantly more than standard glycemic control[51]. They also found that normalizing HbA1c levels for 2 years

improved most neural and physiological dysfunctions to levels comparable to those of subjects with impaired glucose tolerance (IGT).

HbA1c and diabetic peripheral neuropathy

Peterson et al explored the association between HbA1c and peripheral neuropathy in a 10-year follow-up study on patient with normal glucose tolerance, impaired glucose tolerance and T2DM by measuring sural nerve function. They found that increase in HbA1c was varies inversely with amplitude of the sural nerve in all patients regardless of metabolic status. They recommended early detection for prevention of neuropathy in patients with IGT and T2DM.[52]

In evaluation of different HbA1c levels to determine the risk for DPN, Hoque et al found increased risk for neuropathy with HbA1c >8%[53]. In a 3-year retrospective study, Lai et al found that HbA1c variability correlates strongly with severity of diabetic neuropathy on T2DM patients[54]. The results were replicated in a study on type 1 diabetic patients by Pinto et al[55] in a different study, Maiya et al found a linear correlation between HbA1c levels and VPT in 534 T2DM patients[56]. The studies concluded that the strong association between HbA1c can be exploited to predict and possibly avert foot complications in diabetic patients.

Poor glycemic control has been shown to predispose to microvascular complications in diabetics. Specific to neuropathy suboptimal control of blood sugar was linked to progressive neuronal deterioration and accelerated loss of protective sensation[57,58]

2.4 DIABETIC FOOT

2.4.1 Foot Deformities

While the musculoskeletal disorders in DM are not specific, they occur with a higher frequency in diabetic patients and are considered as one of the most common and devastating complications of DM. The exact cause of foot deformities in diabetes remains a subject of debate. There is consensus, however, that foot deformities play a significant role in development of DFU. It has been postulated that foot deformities within DM occur as a result of motor neuropathy causing atrophy and muscle imbalance. The structural foot deformities that are commonly reported are claw and hammer toes, prominent metatarsal heads, pes cavus[64]. Intrinsic muscle wasting has been further attributed to clawing and subsequent evolution of dorsal and plantar ulcers (DFU).

Intrinsic foot muscles atrophy and imbalance and the resulting limitation of joint mobility ultimately manifest with foot deformities and altered gait biomechanics. This results in abnormal loading of the foot an established risk factor to ulceration.

DFU is one of the commonest and dreadful diabetic complications, with a lifetime risk close to 20% of all patients with diabetes. Even in the developed world and with all the advances in diagnostic technology, foot complications continue to be the commonest reason for hospitalization in this particular population[40].

2.4.2 Diabetic foot syndrome

Diabetic foot is a spectrum of disease ranging from the symptom free patient, who may require only preventive measures for foot care health, to the full blown and critically ill patient in whom both loss of life and limb are lingering threats. In fact, the magnitude of the burden of this complication alone is such that WHO has issued an international alert that all health agencies need to shift their strategies to prevention.[2,15]

The principal pathogenic mechanisms involved in diabetic foot disease include ischemia, neuropathy, and infection. Acting synergistically, they contribute to the sequence of skin and soft tissue ulceration, infection, necrosis and eventually gangrene. Prevention and treatment of diabetic foot should be tailored to these pathogenic factors, approached solely or in combination[41].

Farooque et al performed a study to correlate glycemic control and Wagner classification in patients with diabetic foot. They found a linear relationship between HbA1c and Wagner grade of diabetic foot further establishing the diagnostic and prognostic utility of HbA1c, not just in peripheral neuropathy but in diabetic foot as a whole[59]

There is no doubt that poor glycemic control portends a poor prognosis in patients who develop neuropathic ulcers[60]. As a validated measure of glucose levels in blood, HbA1c gives a precious insight of long term glycemic states as opposed to single measure of blood sugar levels. Its therefore needless to overemphasize the value of HbA1c in identification of the high-risk patient and tailoring a total foot care prevention program accordingly, to reduce the incidence of ulceration and eventual amputation.

In a diabetic population cohort in the UK, Walsh et al noted a strong association between DFU and mortality that couldn't be explained by other complications. Among the over 400,000 patients, 20 737 developed DFU; 5.0% of participants who developed foot ulceration died within 12 months of their first foot ulcer consultative visit. in overall, a shocking 42.2% of people with foot ulcers died within 5 years[61]. Whereas diabetic foot ulcers can lead to limb loss, it's inconceivable that DFU becomes life-threatening as its amenable to lower extremity amputation. They concluded that development of DFU in a diabetic patient should be regarded as a major warning beacon for serious and life-threatening occult complications

CHAPTER 3

PATIENTS AND METHODS

STUDY DESIGN

Analytical cross-sectional study

STUDY SETTINGS

Kenyatta National Hospital: outpatient department, diabetic clinic and wards.

KNH is located in Kenya's main city Nairobi and serves as the national referral and teaching hospital. As the biggest public hospital in the East African region and a bed capacity of 1800, the hospital sees a steady daily flow of patients with diabetic foot complications accounting for approximately 11.4% of all admissions[15].

The hospital runs a specialized diabetics clinic managed by a team of diabetologists, internists, graduate resident doctors, nutritional counsellors, educators, medical assistants, and qualified and trainee nurses. The clinic serves approximately 400 diabetes mellitus patients each week Monday through Friday.

STUDY DURATION

October- April 2021

STUDY POPULATION

Type II DM patients presenting to KNH within the duration of the study

INCLUSION CRICTERIA

1. Patients with type 2 diabetes
2. Patients who have had at least 3 months since diagnosis
3. Patients above 18 years of age

EXCLUSION CRICTERIA

1) Patients with acute complications such as Diabetic Ketoacidosis
2) Patients on treatment regimen known to cause neuropathy such as Anti-Retroviral Therapy (HAART)
3) Patients with other metabolic / endocrine conditions known to cause neuropathy such as hyperthyroidism, Rheumatoid Arthritis
4) Patients on therapy with drugs known to interfere with glucose metabolism e.g. steroids
5) Patients with bilateral amputation of the lower limbs
6) Patients who decline to give consent

SAMPLE SIZE

The Cochrane formula will be used to estimate the sample size

$$n0 = \frac{Z^2(1-\infty/2) \times P(1-P)}{d^2}$$

The d value is considered to be significant below 0.05(absolute error of 5%) giving us a standard normal variant (Z) of 1.96

Where;

n0 = sample size to be determined

Z^2 (1-∞/2) =is the standard error of the mean corresponding to a 95% confidence interval and the corresponding value from a t-table is 1.96.

P = is the expected prevalence of DPN. In this case, the value of P was 0.5, the best average estimate for predetermined outcomes

d = is the target margin of error, which is set at 5 %(0.05) to increase precision.

Dykes et al found a 70% prevalence of diabetic peripheral neuropathy in a cohort of T2DM patients

$$n0 = \frac{1.96^2 x\ 0.7(1 - 0.7)}{0.05^2}$$

=322.69 ==323

Mugambi's study found the total number of diabetic patients in KNH is 1788. Given the population of interest is <10,000, we modify Fischer's formula by including the finite population correction factor (FPC) as;

$$\mathbf{n} = \frac{n_0}{1 + \frac{n_0 - 1}{N}}$$

Where;

n= the sample from the finite population

N= Total population of diabetic patients in KNH inpatient and outpatient clinics: Eric Mugambi: the classification of diabetic patients into risk strata for foot ulcer development

East Afr Med j. 2009; 86(5)23- 39

n= 254.49 ==255

SAMPLING

Patients was recruited through random sampling with participants picked at regular intervals by the principal researcher. Written informed consent with was obtained prior to the sampling process.

Sampling procedure

A sampling frame was made using the patients register. Simple random sampling was then used to pick the first participant. Subsequent participants will be recruited at regular intervals to minimize selection bias. Participants will be selected from the sampling frame at steady intervals i.e. every K^{th} patient

where K = S/N

S is the total number of patients in the sampling frame

N is the sample size

DATA COLLECTION TOOLS

Data was coded, entered and managed in a Microsoft Access Windows 10 database and at the end of data collection exported to SPSS V27 2020 version for analysis.

The baseline characteristics were summarized and presented as means, medians and proportions.

GLYCATED HEMOGLOBIN

The tests were done in the KNH biochemistry lab which is ISO:9001 certified.

HbA1c is routinely used to monitor long term glycemic control in diabetic patients. 1 ml of venous whole blood specimen was collected in EDTA, by a trained phlebotomist. Whole blood specimens are stable for up to 8 hours at room temperature. Prior to analysis each patients sample was mixed by gentle inversion to ensure homogeneity.

Immunoassay method of HbA1c analysis was used. This method utilizes specific antibodies against N-terminal glycated amino acids of the beta chain of glycated hemoglobin. HbA1c concentration is measured based on a specific chemical reaction to the glycated N-terminal valine of the β-chain. An excess of anti-HbA1c antibodies added to a hemolyzed sample binds to HbA1c. The excess antibodies agglutinate. The turbidity of the resulting immunocomplexes is measured photometrically using a turbidimeter. Bioris Superior S01 model of machine was used to analyze glycated hemoglobin concentration.

VALIDITY AND RELIABILITY OF DATA COLLECTION TOOLS

The Michigan Neuropathy Screening Instrument has high specificity and likelihood ratios (>5) and moderate to good post-test probability and thus a high diagnostic impact for DPN.[27]

Biothesiometry has a demonstrable high sensitivity and specificity for sensory neuropathy. Compared to nerve conduction studies, its inexpensive and easily performed as a bedside procedure.[7]

Glycosylated hemoglobin is a reliable biomarker for sugar control with potential to predict both microvascular and macrovascular diabetic complications.

INVESTIGATOR CALIBRATION PROTOCOL

Superior as it is to the other methods of assessing VPT, biothesiometry grading of the sensory modality relies on the patient's word of confirmation and is still much subjective. To mitigate this attempts has to be made to ensure the patients reports a sensation only when a genuine stimulus is perceived. Patient education prior to testing has been shown to lead to a more reliable and reproducible reading. Testing the vibratory probe on a part of the body different from the area of interest (i.e. the foot), is just one of the ways to minimize the risk. Asking the patient to close their eyes during the test helps remove what is possibly a conflating visual signal. At least 3 tests were performed on each foot at different anatomical points. Regions with obvious deformities such as callus and fissures was avoided altogether.

Being a single center study, ensured similar standard operating procedure are used. Identification and recruitment of participants was randomized to reduce bias. Quality assurance and tools calibration was ensured prior to commencement of the study.

The glycated hemoglobin measurement was done KNH Lab 16 which is ISO 9001 certified.

DATA ANALYSIS

The period prevalence of DPN was expressed as a proportion

$n/N * 100\%$

where n= number of patients with DPN

N = total population sampled

To compare proportions of patients with DPN using MNSI and biothesiometry Chi square test was used

To determine and describe the correlation between glycated hemoglobin, diabetic foot deformities and sensory neuropathy Spearman Correlation Coefficient (Spearman's rho) was utilized. Ordinal logistic regression model was then then employed to establish linear relationship of the variables.

The Chi-square test was used for inferential statistics, analyzing categorical data. All statistics, descriptive or inferential were performed to within 5% level of significance (95% confidence interval). The results of the study are presented in forms of tables, histograms and pie charts.

ETHICAL APPROVAL

All appropriate legal and ethical regulations concerning use of human volunteers in a study were adhered to the whole duration of the study. Ethical approval was procured from the Department of Orthopaedic Surgery, in the University of Nairobi, after which, permission was sought from Kenyatta National Hospital, Ethics and Research Committee (KNH/UON-ERC). Data collection was initiated only after ethical approval had been obtained. Participants or their next of kin were requested to give written informed consent during recruitment. Participants were informed on the theoretical framework of the research and unwilling participants were informed of the freedom to opt out even after consent is given.

Participants were informed that such withdrawal will have not in any way impact the care due to them. All information obtained was treated as confidential. All these voluntary participants were accorded a coded study identification number linking them to their bio-data to avoid using actual names. The database access is limited to the principal investigator.

STUDY LIMITATIONS AND DELIMITATIONS

Corona virus disease (COVID-19) was declared a global pandemic by World Health Organization on 30th December 2019. The Kenyan government reported the first case of COVID-19 in March 2020. Subsequently the Ministry of Health instituted several protective measures to curb the disease spread. These measures require in part that all suspected patients be screened for COV/SARS II and all health workers wear appropriate protective gear.

The Ministry of Health guidelines were adhered to during this study with all participants being required to wear a face mask. The principal investigator and his assistants wore protective gear during the process of data collection. Accordingly, patients with symptoms akin to those of COVID-19 were referred for screening.

Biothesiometry assesses vibratory perceptions which is transmitted type A large nerve fiber, through the posterior column: cuneatus and gracilis. Diabetic peripheral neuropathy affects both small and large diameter fibers.

Age has been shown to be an independent factor in conduction of impulses in peripheral nerves. Diabetic peripheral neuropathy has been shown to affect the nervous system in a time dependent manner. The duration of diabetes in the participants is highlighted and compared to both the severity of DPN and the glycemic control.

DISSEMINATION OF THE STUDY FINDINGS

Findings of the study will be disseminated in a three-tier fashion. One copy of the published dissertation will be kept at the Department of Orthopaedics, University of Nairobi. A copy will be placed at the

university library. The highest level of sharing of the findings will be through publication in a peer-reviewed journal

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter gives the results of the study findings. The results are presented in sections that include: response rate, demographic information, descriptive statistics, foot deformities, prevalence of peripheral neuropathy, comparison of peripheral neuropathy as determined using MNSI and biothesiometry in diabetic population of KNH, levels of HbA1c and its correlation with the grade of peripheral neuropathy.

4.2 Response Rate

A total of 255 diabetic patients participated in the study giving a response rate of 100%.

4.3. Demographic information

4.3.1 Numerical data (Age, Duration since diagnosis, and BMI) of the patient population

The youngest patient was 20 years, the oldest was 82 years and the mean age was 50.44 years (95% CI; 48.62 to 52.26). The minimum duration since diagnosis was six months, the longest duration was 46 years and the mean duration was 10.4 years (CI: 9.4 to 11.4). The mean BMI was 25.9 (95%CI: 25.33 to 26.47). The minimum BMI was 17.8, while the maximum was 42.9.

Table1 below displays the results.

Table 1: Demographic Information (Numerical data) of the patient population

Variable	N	Mean	95% Confidence Interval	
			Lower	Upper
Age	255	50.44	48.62	52.26
Duration Since Diagnosis	255	10.4	9.4	11.4
Body Mass Index	255	25.9	25.33	26.47

The majority (59.2%) of the patients were of female gender.

The minimum duration since diagnosis was six months, while the longest was 46 years and the mean duration was 10.4 years (CI: 9.4 to 11.4).

Majority of the population (94.9%, n=242) were non-smokers. Seven patients (2.7%) smoked one pack per year, five patients smoked two packs per year while one patient smoked 15 packs.

Majority of the patients (88.6% n=226) said they were not taking alcohol. Twenty-nine patients (11.4%) consumed alcohol.

4.3.2Ulcerations

Majority (n=238; 93.3%) of the patients had no visible ulcerations on the right lower limb. These were classified as 'foot at risk' group (Wagner 0). Wagner 1 and Wagner 2 grades were present in seven patients each (2.7%). Three patients (1.2%) had Wagner 3 grade of ulceration on the right limb.

Table 2 below displays the distribution.

Table 2: Stratification of the right feet: Wagner's scale

	Frequency	Percent
Wagner 0	238	93.3
Wagner 1	7	2.7
Wagner 2	7	2.7
Wagner 3	3	1.2
Total	255	100

Ulcerations: Left lower limb

Majority (n=235; 92.2%) of the patients had no ulcerations on the left limb. Patients with Wagner 1 grade were six (2.4%), those with Wagner 2 grades were eleven (4.3%). Two patients (0.8%) had Wagner 3 grade of ulceration on the left limb while one patient (0.4%) presented with Wagner 4.

Table 3 below displays the distribution.

Table 3: Stratification of the left feet: Wagner's scale

	Frequency	Percent
Wagner 0	235	92.2
Wagner 1	6	2.4
Wagner 2	11	4.3
Wagner 3	2	0.8
Wagner 4	1	0.4
Total	255	100

4.3.9 VIBRATIONS RIGHT AND LEFT BIG TOES

Majority (n=203; 79.6%) had normal vibrations. Thirty-six (n=36; 14.1%) patients presented with moderate VPT impairment. Those with severely impaired vibration perception on the right were eleven (n=11; 4.3%) while those with mild on the left limb were four (n=4; 1.6%).

Table 4 below illustrates the results

Table 4: Vibration Perception Right and Left Big toes

	Frequency	**Percent**
Normal	203	79.6
Severe	1	0.4
Moderate	36	14.1
Mild Right	11	4.3
Mild Left	4	1.6
Total	255	100

4.4 Foot Deformities amongst Type 2 Diabetic Patients in Kenyatta National Hospital

For stratification we divided foot deformities into cutaneous and structural deformities. Each limb was assessed separately as outlined in the screening tool.

4.4.1 Left Foot deformities

Patients who presented with structural deformities of the left foot were eighty-five (n=85; 33.3%). Those with cutaneous deformities were twenty-nine (n=29; 11.4%). Approximately fifty-five percent of the patients had no abnormalities of the left foot (n=141; 55.5%). Figure 1 presents the results.

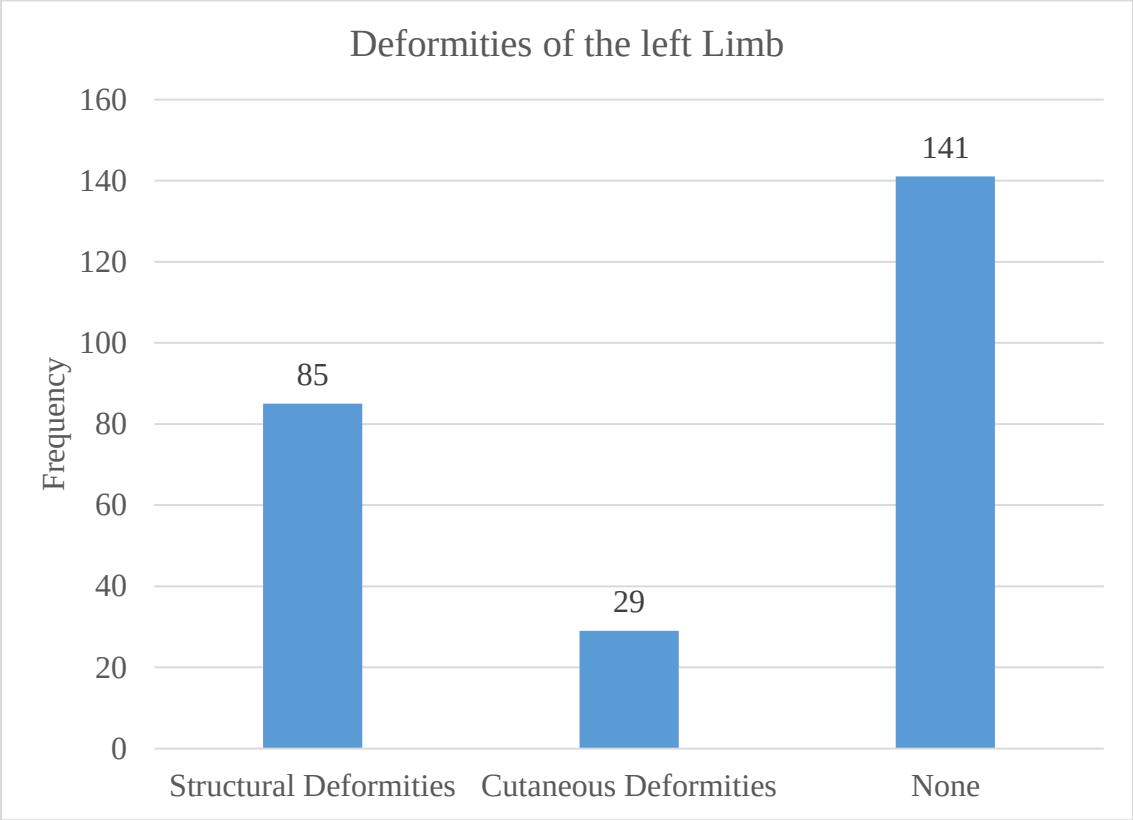


Fig 1: Left foot deformities in the sample population

4.4.2 Right Foot Deformities

Approximately thirty-four percent (n=86; 33.7%) of the patients presented with Structural deformities. Thirty-five (n=35; 13.7%) patients were diagnosed with cutaneous deformities. Majority (52.5%; n=134) of the patients had no deformities of the right foot. Figure 2 below displays the results

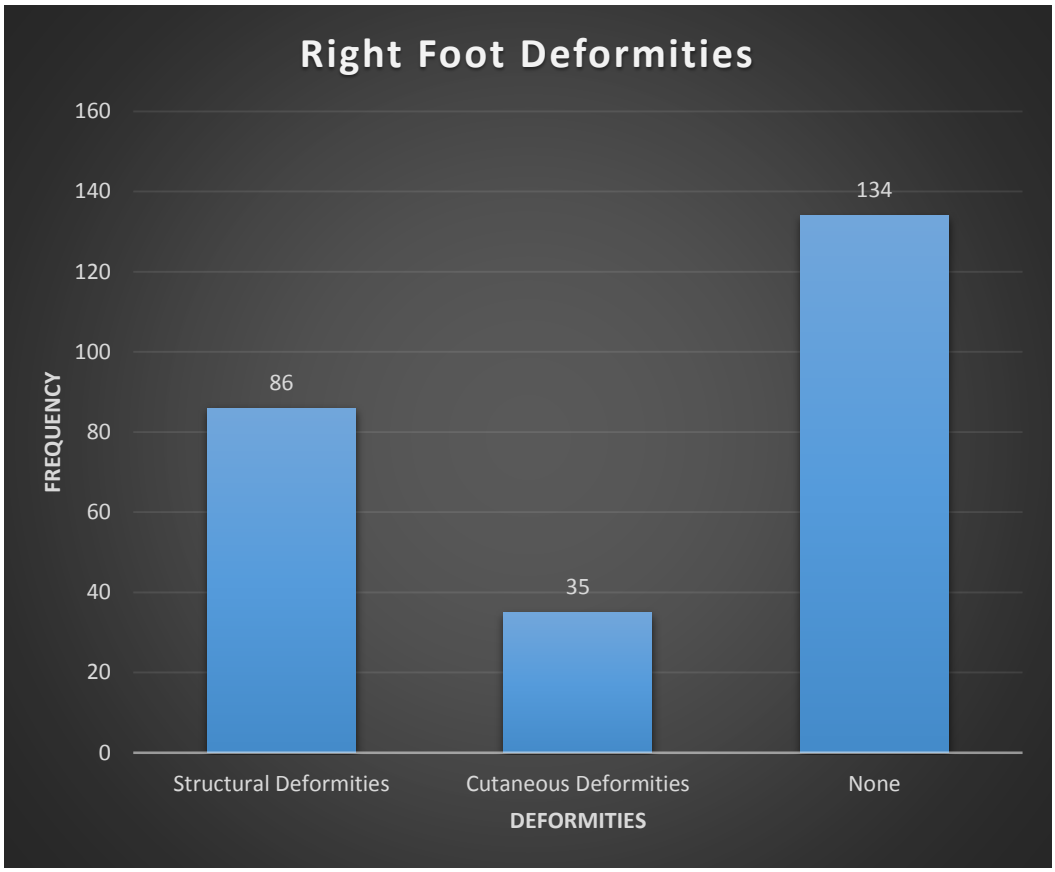


Fig.2: Foot Deformities of the Right Foot

The types and definitions of structural foot deformities		Right	Left
Hallux valgus	Lateral deviation of the great toe at the metatarsophalangeal joint (MTPJ)	19(7.5%)	12(4.7%)
Hallux rigidus	Little or no movement in either flexion or extension at the MTPJ	2(<1%)	1(<1%)
Hammer toes	Fixed flexion deformity of the proximal inter-phalangeal (PIP	14(5.5%)	14(5.5%)
Charcot joint	Gross deformity of the foot with loss of pain sensation clinically	2(<1%)	2(<1%)
Pes Cavus	High longitudinal arch with an angle between the forefoot and hind foot approaching a right angle. The fore foot is splayed with clawing of the toes	10(3.9%)	10(3.9%)
Pes Planus	Reduced longitudinal arch so that on standing its medial border is in contact with the ground	12(4.7%)	17(6.7%)
Claw toes	Fixed flexion deformity of the proximal inter-phalangeal joint with similar fixed deformity of the DIPJ. The MTPJ is hyperextended	8(3.1%)	8(3.1%)
Bunionette deformity	Prominence of the lateral aspect of the fifth metatarsal head	9(3.5%)	9(3.5%)

Cutaneous Foot deformities		Right	Left
Fissures	A linear cleavage /split of the skin	4(1.6%)	4(1.6%)
Callus	A localized and firm thickening of the skin	23(9%)	23(9%)
Dry skin (xerosis cutis)	Abnormal dryness of the skin)	20(7.8%)	20(7.8%)
Onychocryptosis	growth of nail fold inwards into the nail bed	8(3.2%)	8(3.2%)

Table 5: summary of the foot deformities in the diabetic population in KNH

4.5: Prevalence of Clinical Neuropathy

4.5.1Prevalence of peripheral neuropathy among the Diabetic Population of KNH using the Michigan Neuropathy Screening Instrument (MNSI)

The prevalence of Neuropathy among diabetic population of Kenyatta National Hospital using MNSI was 45% (n=115).

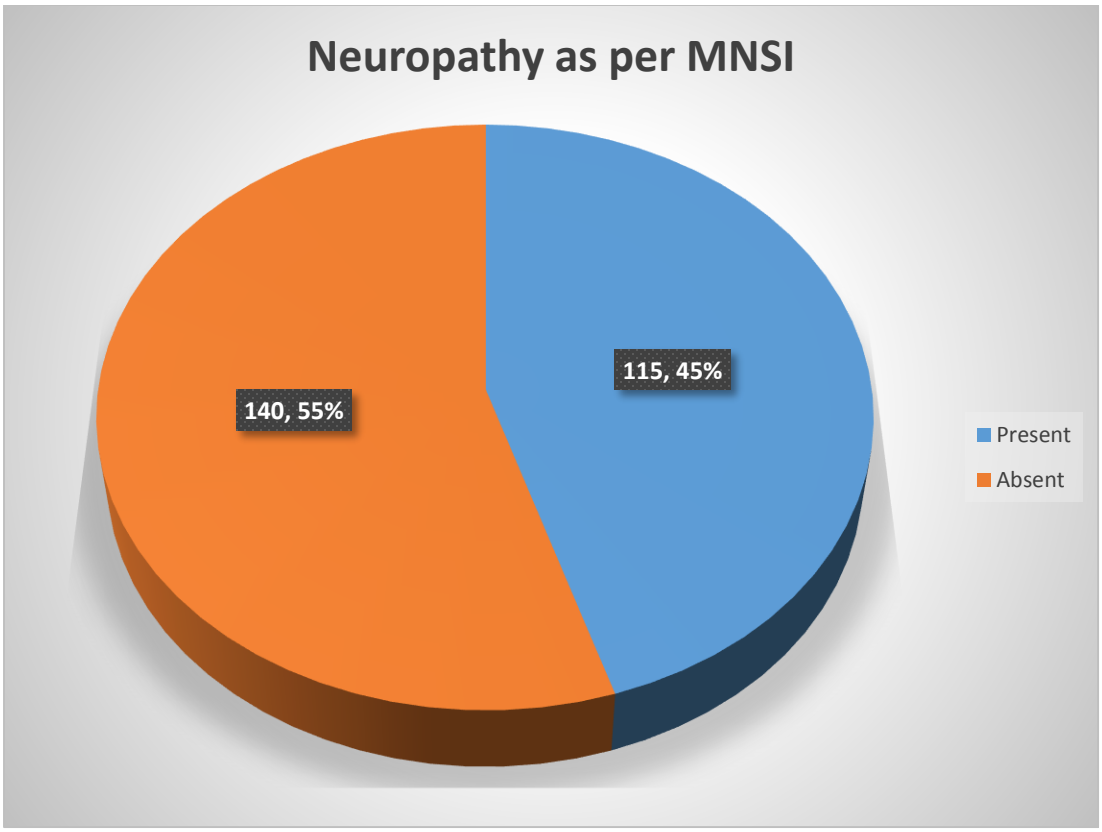


Fig. 3: Neuropathy prevalence per MNSI

4.5.2: Prevalence of Peripheral Neuropathy in Diabetic Population in Kenyatta National Hospital Using Biothesiometry

The prevalence of periphery Neuropathy in the diabetic population in KNH using biothesiometry was 64.3% (n=164). Those with grade one was 46% (n-=116), Grade two was seventeen (17%, n=44) percent and Grade three was two (2%, n=4).

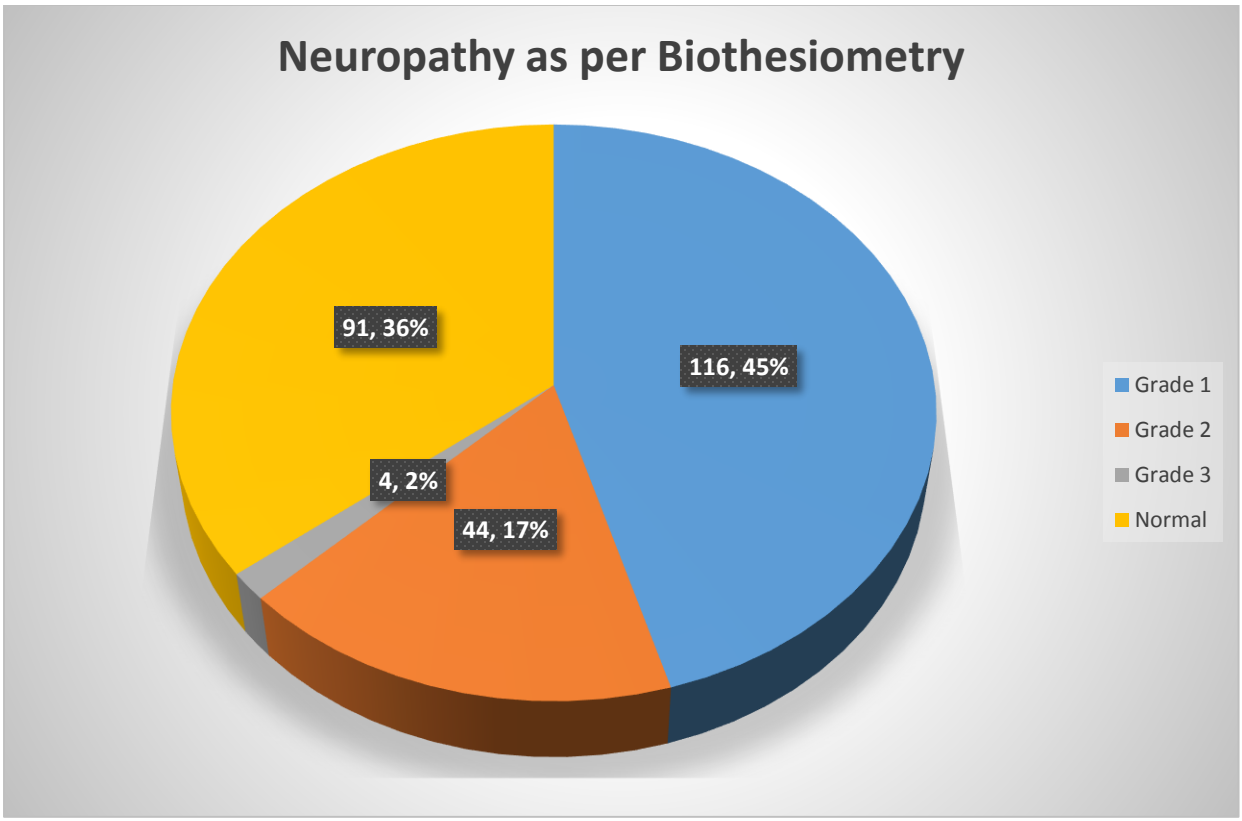


Fig. 4: Neuropathy as per the Biothesiometry

4.6: Comparison between the Prevalence of Peripheral Neuropathy using MNSI and Biothesiometry in Diabetic Population of KNH

There was a statistically significant difference between MNSI measurement and Biothesiometry (Chi-square Value 36.448, D.F. 3, P-Value <0.001).

		Biothesiometry				**Total**	**Chi-Square**	**df**	**P-value**
		Grade 1	Grade 2	Grade 3	Normal				
Neuropathy as per MNSI	Present	63	30	3	19	115			
	Absent	53	14	1	72	140	36.448	3	<0.001
Total		116	44	4	91	255			

Patients with grade one were 78% (OR=0.222, P-value <0.001) less likely to be diagnosed to have no neuropathy using MNSIA as compared to those with normal biothesiometry. Patients with Grade 2 were 88% less likely to be diagnosed to have no neuropathy using MNSIA as compared to those with normal biothesiometry (OR=0.123; P-Value <0.001). Patients with Grade three were 91% less likely to be diagnosed to have no neuropathy using MNSIA as compared to those with normal biothesiometry (OR=0.088; P-Value 0.04).

Table 6: Binary Logistic Regression.

		B	S.E.	Wald	df	Sig.	OR
Step 1a	**BIOTHESIOMETRY**			**33.097**	**3**	**<0.001**	
	Grade 1 (<16 -25mV)	**-1.505**	**0.318**	**22.37**	**1**	**<0.001**	**0.222**
	Grade 2 (25-40mV)	**-2.094**	**0.414**	**25.609**	**1**	**<0.001**	**0.123**
	Grade 3 (>40mv)	**-2.431**	**1.183**	**4.221**	**1**	**0.04**	**0.088**
	Constant	**1.332**	**0.258**	**26.681**	**1**	**<0.001**	**3.789**
a Variable(s) entered on step 1: BIOTHESIOMETRY.							

4.7 HbA1c levels and its correlation with the grade of peripheral neuropathy

4.7.1 HbA1c levels

Majority of the patients (46%, n=117) had normal HbA1c (<7%). Eighty-seven patients (34%) had fair HbA1c levels (7-9%). Fifty-one patients (20%) had poor HbA1c levels (>9%).

	Frequency	Percent	Valid Percent	Cumulative Percent
POOR	**51**	**20**	**20**	**20**
FAIR	**87**	**34.1**	**34.1**	**54.1**
GOOD	**117**	**45.9**	**45.9**	**100**
Total	**255**	**100**	**100**	

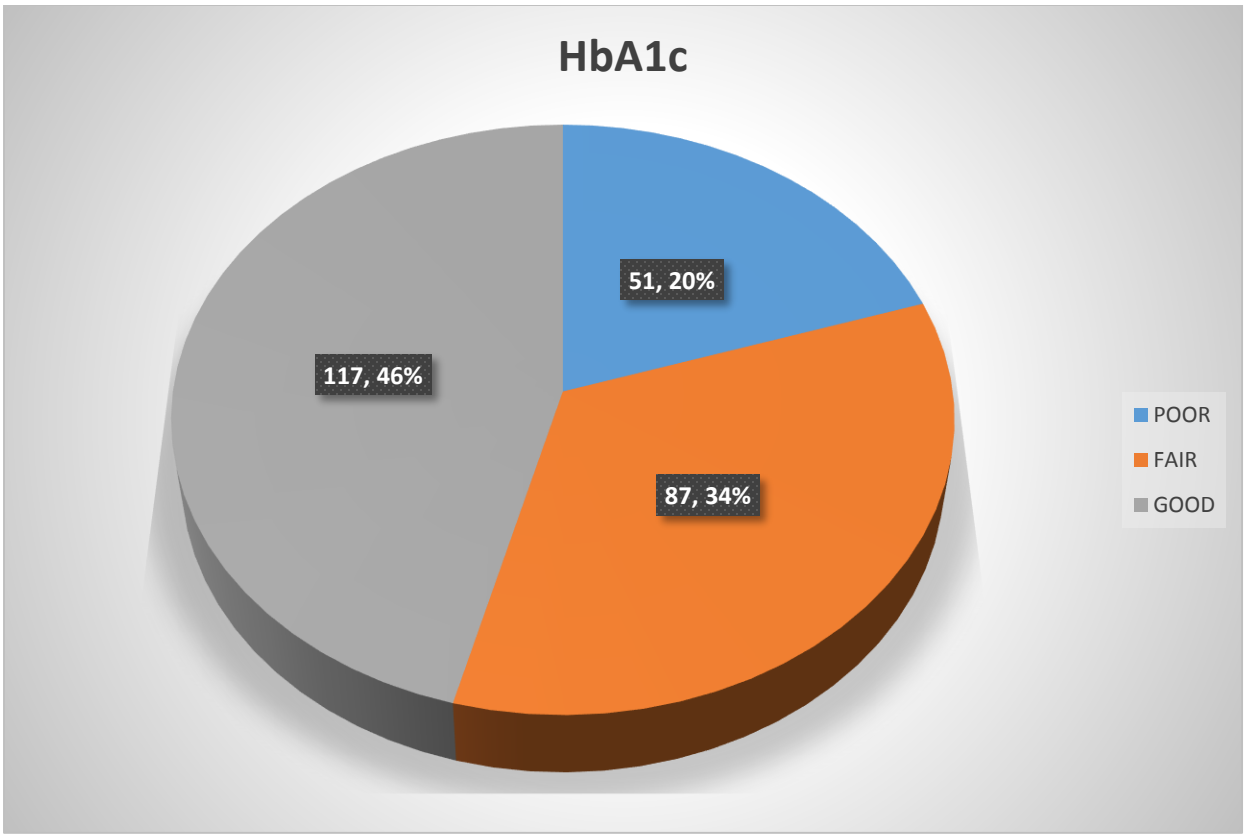


Fig. 5: HbA1c Levels in the sample population

4.8.2 Correlation HbA1c Levels with the Grade of Peripheral Neuropathy

There was a weak positive correlation between HbA1c and the grade of peripheral neuropathy (Spearman rho 0.356; P-value <0.001). The coefficient of determination was 0.127.

Table 7: Spearman correlation Between HbA1c Levels with the Grade of Peripheral Neuropathy

			Biothesiometry	**Blood sugar (HBA1C)**
Spearman's rho	Biothesiometry	Correlation Coefficient	1	.356**
		Sig. (2-tailed)	.	<0.001
		N	255	255
	Blood sugar (HBA1C)	Correlation Coefficient	.356**	1
		Sig. (2-tailed)	<0.001	.
		N	255	255
**** Correlation is significant at the 0.01 level (2-tailed).**				

Demographic parameters and clinical neuropathy as assessed by MNSI

There was no statistically significant association between Gender and Neuropathy (chi-square 0.237; df 1; P-value 0.626)

There was no statistically significant association between Smoking and Neuropathy

There was a statistically significant association between alcohol consumption and development of neuropathy (Chi-square 3.806, df 1, P-value 0.05). A patient taking alcohol was 2.18 (95%CI: 1.009 to 4.006) times more likely to develop neuropathy as compared to a patient not taking alcohol.

There was no statistically significant relationship between age and neuropathy (P-Value 0.4)

The relationship between the duration since diagnosis and development of neuropathy was not statistically significant

Relationships between Deformities of the left Limb and Development of Neuropathy

There was no statistically significant relationship between the deformities of the left limb and development of Neuropathy

Table 8: Relationships between Deformities of the left Limb and Development of Neuropathy

	B	S.E.	Wald	df	Sig.	OR
DEFORMITY Left			4.791	2	0.091	
Structural Deformities	-0.518	0.277	3.483	1	0.062	0.596
Cutaneous Deformities	-0.655	0.411	2.532	1	0.112	0.52
Constant	0.447	0.173	6.703	1	0.01	1.564

Relationships between Deformities of the left Limb and Development of Neuropathy

There was no statistically significant relationship between right limb deformities and development of neuropathy.

Table 9: Relationships between Deformities of the left Limb and Development of Neuropathy

	B	S.E.	Wald	df	Sig.	OR
DEFORMITY Right			4.973	2	0.083	
Structural Deformities	-0.455	0.279	2.662	1	0.103	0.634
Cutaneous Deformities	-0.743	0.385	3.729	1	0.053	0.476
Constant	0.455	0.177	6.601	1	0.01	1.577

Correlation between blood sugar control and ulceration

There was no statistically significant correlation between blood sugar control and Ulcerations

Table 10: Correlation between blood sugar control and ulceration

			Blood sugar (HBA1C)	ULCERATIONS Right, Left
Spearman's rho	Blood sugar (HBA1C)	Correlation Coefficient	1	-0.114
		Sig. (2-tailed)	.	0.07
		N	255	255
	ULCERATIONS Right, Left	Correlation Coefficient	-0.114	1
		Sig. (2-tailed)	0.07	.
		N	255	255

CHAPTER FIVE: DISCUSSION

This chapter discusses the findings of our study. As set out in our objectives, we screened 255 participants who met the inclusion criteria, for foot deformities, sensory neuropathy and sugar control levels.

Foot Deformities

While overall cause of foot deformities in diabetic patients is still a subject of debate, there is consensus on their impact in precipitating ulceration.

Our study found a prevalence of 47% of various structural and non-structural foot deformities amongst T2DM patients. This prevalence is close to the 47% found by Walter et al in a cohort of 1150 diabetic patients[64]. In terms of demographic patterns, we found no association between gender and foot deformities although Haddad et al have shown a higher prevalence of foot deformities in women. According to Walter et al, there was a highly significant difference in the male: female ratio in the prevalence of foot deformities (63.8%vs 34.7%). While the slight majority (57%) of the sampled population was female, the association of deformity and gender was not significant. We however, did observe laterality for isolated foot deformities: most deformities affected the right foot (47.8 vs 44.3%). The latter was not observed in the study by Haddad et al

The commonest structural deformities included hammer toes (5.5%), hallux valgus (7.5%). Claw toes, a deformity that has been especially linked to diabetic motor neuropathy was found in 3.1% of the patients and involved the 2nd or 3rd digits. Sarla et al found claw toes to be the commonest deformity while varus deformity and hallux valgus were the second and third commonest deformities respectively[65]. Walter et al found claw toes to be the second commonest foot deformity after hallux valgus in diabetic patients[64].

They also drew an association between claw toe deformity and peripheral neuropathy, which we were unable to establish in our sample population. One way of explaining this would be the difference of the mean age and duration of disease in the two population samples. Compared to the UK study by Walter et al, we found the mean age of our population to be relatively young (55 vs 69%).

Other deformities included Charcot foot 0.4%(1patient), hallux varus 1.6%(4 patients) and amputations 2%(5 patients). Although some studies have warned that Charcot foot is frequently underdiagnosed, Walter et al found a prevalence of 0.4 and 0.6 amongst men and women respectively. Sarla et al found a prevalence for Charcot foot at1.42% in a cohort of 70 diabetic patients[65]. While still inconclusive, a prevalence of 0.4% among our 255 patients may indicate the rareness of this devastating complication.

Approximately 2% of the sampled population had some level of amputation that ranged from loss of a single toe to below knee amputation. Curiously, all the amputations were on the right foot.

Other studies have established an association between age and foot deformities, a conclusion we were unable to draw from our data. Walter et al established an association between foot deformities and age in diabetic patients[64]. It's worth noting, however, that the mean age for our 255 patient was relatively young (55 years). This is line with disease dynamics, and the fact that T2DM in developing countries seems to more prevalent in adults, between 18 and 62 years as opposed to the elderly[1,2]. Our findings replicates those of Sarla et al in an Indian cohort of diabetic patients where the foot deformities failed to show an association with age or gender[65].

Cutaneous deformities including trophic nail changes and xerosis cutis were also common. These usually indicative of dysfunctions autonomic nervous system. We found nail trophic changes and skin fissuring to the commonest cutaneous deformities in our sample population. Cumulatively, 57.8 of the diabetic population had cutaneous deformities. Shirazi et al concluded in a meta-analysis that about 70% of diabetic patient had pathologic skin changes and 30-91% get dermatological pathologies at some point in the course of the disease[67]. The fact that this was done in north American population where patient awareness

and health accessibility may be less challenging compared to our environment, underscore the dire need for comprehensive foot examination

Peripheral neuropathy

We screened 255 diabetic patients using both MNSI and biothesiometry and established the prevalence of DPN in the 255 patients was 45% and 64% respectively.

In 2012, Chege et al found a period-prevalence of DPN at 41% among diabetic patients attending KNH using patients' history and physical examination for diagnosis[31]. By using a structured list of signs and symptoms in MNSI, we found a DPN prevalence of 45%, a statistic with insignificant difference from that earlier study for the same study setting and population. This prevalence closely reflects findings of studies in other parts of the world: Kärvestedt et al found a DPN prevalence of 43% in a Swedish diabetic population. Mete et al found a prevalence of 32% by using MNSI.

Our study sought to compare the diagnostic yield of a validated clinical tool and biothesiometry. We found a prevalence of 64% for peripheral neuropathy in the same population when VPT using biothesiometry was used. These findings mirror those of Sheesha et al[33] and Mete et al[49].

Sheesha et al reported a higher discrepancy when DPN was diagnosed clinically and using adjunct instruments like biothesiometry (9.1% Vs 89% respectively)[33]. Mete et al found a prevalence for DPN of 32.1% and 74.5% using MNSI questionnaire and VPT respectively[49.] Saha et al found that 60% of apparently asymptomatic diabetic patients exhibited grades 1 and 2 neural dysfunction when biothesiometry testing was done[29]. We did establish that 19 % of the T2DM patient in our setting had silent (subclinical) neural disturbances majority of them grade 1 based on the biothesiometric scale. Our study, therefore, confirms that measurement of vibration perception threshold using biothesiometry demonstrates superiority over clinical methods alone

By detecting subclinical neuropathies, timely interventions can be implemented to avert diabetic foot syndrome

Glycemic control and peripheral neuropathy

Only 46% of our patients met the glycemic control recommended by ADA. Majority of the sampled patient had sub-optimally controlled glycemic levels. Eighty-seven patients (34%) had fair (7.1-8.9%) HbA1c levels. Fifty-one patients (20%) had poor control (>9 %)HbA1c. Mwavua et al in a 2015 multicenter study including KNH and Thika Level 5 Hospital found the proportion (95 % CI) with good glycemic was only 17 % (12.0–22.5)[66]. Since the level of control was comparable in both institutions, periodic changes of HbA1c with the lifecycle of the red cells might explain the difference in our findings.

There was a *weak* correlation between glycemic control and sensory deficits as assessed by biothesiometry. All 51 patients with HbA1c above 9% (poor control group) showed a degree some derangement in VPT. Lai et al has established a *strong* correlation in HbA1c *variability* and the severity of DPN[55]. We were able to show a linear correlation between HbA1c and peripheral neuropathy replicating the findings of Maiya et al[56]. Our study did establish a correlation albeit weak between HbA1c and the degree of peripheral neuropathy. This weaker link might be due to the utilization of a single HbA1c reading as opposed to variability of the same.

The risk of developing DPN has been calculated to rise by approximately 10-15% for every 1% rise in HbA1c[63]. The association between HbA1c and neuropathy can by deduction therefore, be exploited to predict and possibly avert foot complications in diabetic patients.

Conclusions

Although foot deformities are prevalent in diabetic patients the precise impact in the causal pathway to foot ulcerations remains unclear. By using biothesiometry we found a prevalence of 64% higher than 41% found by Chege et al in the same population[31]. This confirms that conventional clinical evaluation is insufficient at best as pertains to neuropathy assessment. The ideal screening tool for diabetic neuropathy is one that will provide accurate and objective results in a relatively short period, is not time consuming to administer, is readily available and possesses high sensitivity, specificity and positive predictive power.

Biothesiometry is a simple, reliable, noninvasive and convenient tool proven to diagnose neuropathy even in the subclinical stage.

The ability to predict the risk to ulceration subsequent amputation and other complication can, potentially, prevent adverse outcomes and the enormous attendant costs A standardized protocol for assessment of diabetic foot at risk' is crucial if the battle to prevent eventual ulceration and limb loss is to be won.

There is a causal linkage between sustained hyperglycemic states and peripheral neuropathy. Diabetic peripheral neuropathy has been implicated as the inciting force that triggers foot deformities and impairs sensation leading to ulceration. Ishibashi et al found that normalizing HbA1c in diabetic patients, even over a short duration, improves in overall microvascular complications including neuropathy effectively and significantly more than standard glycemic control.[55] There is an association albeit weak between impaired vibration perception and the rising HbA1c levels, thus suggesting the onset of neuropathy. Other studies like that of Hoque et al found a strong correlation when HbA1c variability was used.

Recommendations

To the best of our knowledge, no one has attempted to describe foot deformities in the diabetic population in Kenya, or tried to associate how these deformities contribute to diabetic foot syndrome. A comprehensive understanding of the etiology of foot deformities in diabetes mellitus is essential for pro-active management of the foot in anticipation of the development of foot deformities and ulceration

We believe early effective assessment can reduce the severity of complications including ulceration and amputations. In view of the rising incidence of diabetes in our population and its menacing impact on the lower extremities, we recommend a preventative approach to diabetic foot disease.

The diagnostic accuracy of clinical examination in peripheral neuropathy remains low. We recommend a standardized protocol for all diabetic patients which includes validated neuropathy screening tools like MNSI. We further recommend that biothesiometry be done on all diabetic patient on a regular interval to allow for detection of subclinical neuropathy.

We recommend that orthopaedic assessment be an integral part during the identification and multidisciplinary assessment of the diabetic 'foot at risk.' The identification of foot deformities up to and including Charcot foot, pathological gait biomechanics should be promptly treated by implementing offloading measures including prophylactic surgeries as appropriate.

Since this was a cross sectional study, follow-up studies and interventional studies are required to emphasize the extent of the benefits of the VPT estimation, and the exact risk of ulceration posed by specific foot deformities.

Disclaimer

The authors have no conflict of interest to declare

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APPENDICES

1. Consent /Fomu ya Idhini
2. Data collection sheet
3. Michigan Neuropathy Screening Instrument (MNSI
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    - **Data collection approval letter**
    - **Clinical conduct certificate**
    - **Plagiarism report**

CONSENT/FOMU YA IDHINI

STUDY ON DIABETIC FOOT DISEASE: FOOT DEFORMITIES, SENSORY DEFECTS AND SUGAR CONTROL IN TYPE II DIABETIC PATIENTS IN KENYATTA NATIONAL HOSPITAL

PRINCIPAL INVESTIGATOR ……

Introduction:

Please allow me to tell you about the above cited study I am conducting. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research:

i) Your decision to participate is entirely voluntary

ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal

iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? YES / NO

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Protocol No. _____

About this study

I am conducting a study on diabetic foot disease, foot deformities and peripheral neuropathy to show its correlation with glycemic control in the diabetic population in KNH. Your participation in this study will include you giving me details on your age, and symptoms. In additional I will take biometric measures of your height weight and assess the sensation in your feet using a biothesiometer.

In total we will recruit and assess 255 willing participants chosen randomly from all patients attending this clinic. I am requesting for your consent to be a participant.

If you become a participant

You will upon signing the consent form, be interviewed by a trained interviewer about your health conditions to find out any symptoms you may be experiencing. With the help of the interviewer you will also fill a questionnaire checking symptoms and signs of peripheral neuropathy.

The interview will be in a private area and will take approximately 10 minutes after which you will be guided to another area where a sample of blood will be taken to check the status of your sugar control (HbA1c).

The turnaround time for this test is 1-2 hours. For your convenience and with your consent, we will ask for a telephone number where we can contact you. Once the results are released we will contact you to notify you of the results and inform you of the specific risk factors to ulceration and how they can be mitigated. The contact information, should it be provided, will be used only by people working for this study and will remain confidential

Are there any risks, harms discomforts associated with this study?

All medical research has the potential to inflict some psychological, social, emotional and physical risks. For this, all effort should always be put in place to minimize these anticipated risks. One such risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all the

paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

It may be embarrassing for you to have your weight and body mass index taken. We will do everything we can to ensure that this

is done in private. Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews.

You may feel some discomfort when a sample of blood is taken, and you may have a small bruise or swelling in your forearm. In case of an injury, illness or complications related to this study, contact the study

staff right away at the number provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

Participants benefits

The benefits of getting involved in this study will be the awareness thereafter of your risk for developing foot ulcers. This will help you and the care providers incorporate foot care practices that can help avert

such an eventuality. Upon completion, the final data will be used to make recommendations that will hopefully impact the future of diabetic foot care practices in KNH and the nation/region at large.

Financial implications

All costs accrued from investigations in the study will be funded by the principal investigator.

Where more clarity is required

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the

Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee

Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

What are the options now?

Your participation at every stage of the study is voluntary. You have the right to withdraw from the study at any time. Such withdrawal will in no way affect your care now or in future.

STATEMENT OF CONSENT

Participants consent

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study

I certify that the study has been fully explained to me and I am willing to participate in it.

Participant's Signature (or thumbprint) …….

Date……

I confirm that I have clearly explained to the participant the nature of the study and the contents of this consent form in detail and the participant has decided to participate voluntarily without any coercion or undue pressure.

Investigator's Signature……...

Investigators role…….

Date …….……

Witness Signature.....Date.....

For Any Enquiries, please contact:

1. Dr. Peter Macharia,

Principle investigator

Mobile number: 0721112326

E-mail: drmachariapeter@gmail.com

2. Dr. Fred Sitati,

Senior Lecturer, Department of Orthopaedic Surgery, University of Nairobi.

Mobile number: 0722607220

Email: fredsitati@yahoo.com

3. Dr. Ezekiel Oburu,

Lecturer, Department of Orthopaedic surgery, University of Nairobi.

Mobile number: 0708728060

Email: oburue@gmail.com

4. Kenyatta National Hospital/University of Nairobi Ethics and Research Committee

College of Health Sciences

P.O. Box 19676-00202

Nairobi

Telephone: 020-2726300 Ext 44355/+254202726300-9

Email: uonknh_erc@uonbi.ac.ke

FOMU YA IDHINI

SOMO: UGONJWA WA MIGUU KWA KISUKARI; KASORO ZA MIGUU, KUHISI NA HALI YA SUKARI KWA WANAOUGUA KISUKARI KATIKA HOSPITALI YA KITAIFA YA KENYATTA

Nambari ya kushiriki…….

Utangulizi

Niruhusu nikweleze kuhusu utafiti tunaokusudia kufanya. Nia ya ufafanuzi huu ni kukuelimisha wewe kuhusu utafuti kabla ya wewe kuamua kama utakubali kuwa mshiriki au la. Haki zako kama mshiriki ni kama zifuatavyo

I) Uko na haki ya kuelewa uhuru wako kukubali ama kukataa kushiriki katika utafiti huu

II) Uko na haki ya kutoka katika utafiti huu hata baada ya kukubali unapogeuza nia

III) Uko na haki ya kupewa matibabu yote bila chuki wala fitina baada ya kukataa kushiriki tena katika utafiti huu

Je umetupa kibali cha kuendelea

Ndio La

Ufafanuzi

Nafanya utafiti kuonyesha vile wagonjwa wa kisukari huenda mwishowe wakapata adhari za vidonda vya miguu na hatimaye wengine hukatwa miguu. Nia yangu ni kuona jinsi tunavyoweza kuzuia mapema hatima hii.

Katika huu utafiti tunasaka washiriki 255 watakaochuguliwa bila kwa mpangilio bila mwelekezo. Tungetaka uzingatie kuwa mshiriki pia.

Taratibu

Ukikubali kushiriki tutakuuliza maswali kama vile umri na jinsi unavyohisi miguu. Pia tutakupima uzito, urefu na tupime hali yako ya kuhisi katika miguu tukitumia kifaa mpya –Biothesiometer. Hii itachukua muda wa takriban robo saa na itafanyika kwa sehemu iliyojitenga kuhakikisha usiri wako haudhulumiwi. Baadaye tutapima damu kuona jinsi hali yako ya kisukari ilivyo yaani HbA1c.

Je kuna adhari gani kushiriki katika utafiti huu?

Utafiti wowote wa kiafya unaweza kuwa na adhari kama vile kuzambaa kimakosa kwa ujumbe wa kibinafsi na pia uchunguzi waweza kuwa na maswali ya kufedhehesha.

Mikakati tuliyoiweka ni ya kuzuia upeperushaji usio wa hiari wa ule ujumbe tutakaokusanya kama vile kutotumia majina ya washiriki. Badala yake tutatumia nambali maalum ya kuwatambulisha itakayojulikana tu ma mtafiti.

Iwapo maswali uoyote ya kuaibisha itakuwepo, mshiriki akona hiari ya kukataa kujibu na pia hiari ya kukataa kuendelea kushiriki hata baada ya kupeana saini.

Je, kuna faida gani kushiriki

Ukishiriki katika huu utafiti, tutakwelezea jinsi hali ya kuhisi ilivyo katika miguu yako. Hili ni la muhimu kwako na kwa madaktari wako inapokuja kuzuia vidonda vya miguu siku za usoni.

Na malipo je?

Matumizi yote yauchunguzi katika utafiti huu itagharamiwa kikamilifu na mtafiti mkuu

Maelezo zaidi

Ijapo una maswali, usisite kuwasiliana nasi wakati wowote kwa namna zilizotadhrishwa.

Iwapo ungetaka kujua Zaidi haki zako kama mshiriki, tafadhali wasiliana na mwenyekiti au katibu wa Kamitii ya utafiti ya Hospitali ya Kitaifa ya Kenyatta na Chuo Kikuu cha Nairobi kwa simu 2726300 Ext. 44102 au barua pepe uonknh_erc@uonbi.ac.ke.

Hati ya Ruhusa

Sahihi ya mshiriki.....Tarehe.....

Ninathibitsha yakwamba nimetoa maelezo sahihi kwa mhusika kuhusu huu utafiti na yale yote yaliyomo kwa ustadi, naye mhusika ametoa uamuzi wa kushiriki bila ya kushurutishwa.

Sahihi ya mchunguzi……Tarehe……

Sahihi ya shahidi……...Tarehe…….

1. Mshiriki mkuu

   Dr Peter Macharia

   Simu ya rununu: 0721112326

   Barua pepe: drpetermacharia@gmmail.com

2. Dr Fred Sitati

   Mhariri Mkuu, Chuo Kikuu cha Nairobi

   Simu ya rununu: 0722607220

   Barua pepe: fredsitati@yahoo.com

3. Dr Ezekiel Oburu

   Mhariri, Chuo Kikuu cha Nairobi

   Simu ya rununu: 0708728060

Barua pepe: oburue @gmail.com

4. Hospitali ya kitaifa ya Kenyatta /Chuo Kikuu cha Nairobi, Kamati ya maadili na utafiti. Chuo cha sayansi ya afya

   Sanduku la posta 19676-00202 Nairobi

   simu: +254202726300-9 Ext 44355 barua pepe: uonknh_erc@uonbi.ac.ke

MICHIGAN NEUROPATHY SCREENING INSTRUMENT

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 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

DATA COLLECTION SHEET

PATIENT'S BIODATA

AGE …….
IP NUMBER…….
GENDER *(circle one)* M F
DATE……
CONTACTS…….

HISTORY

Duration since diagnosis/ age at diagnosis
Alcohol consumption Y/N
Smoking Y/N
MNSI A Score N/15
MNSI B score N/10

OBSERVATIONS

Height (m)……
Weight (kg)…….
BMI(kg/m^2)……

INVESTIGATIONS

HbA1c

DIABETIC CONTROL	VALUE
Good control	< 7%
Fair	7-9%
Poor	>9%

BIOTHESIOMETRY

SEVERITY	VPT
Normal	Up to 15 volts
Grade 1	16- 25 volts
Grade 2	25-40 volts
Grade 3	>40 volts

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:
☐ Structural deformity (Specify) (specify)	Structural deformity
☐ ……. …….	……
☐ Cutaneous deformity	Cutaneous deformity
Fissures …….	Fissures
Dry skin	Dry Skin
Nail changes	Nail Changes
Hair loss	

2. Ulcerations (wagner)

Right	Left

3. Ankle reflex

Right	Left

4. Vibration at big toe

Right	Left

5. Monofilament

Right Left

Total score…….

TIMELINE GANTT CHART

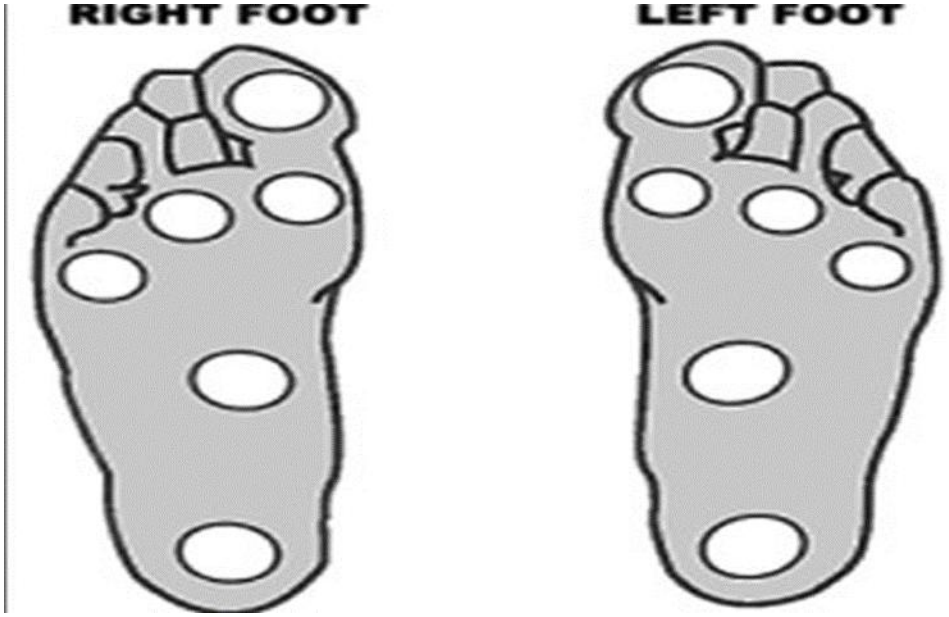
	AUG – NOV 2020	DEC 2021	FEB 2021	MAR 2021	APR 2021	MAY 2021
Proposal writing and presentation						
Ethical approval						
Data collection						
Data analysis						
Dissertation writing						
Presentation of results						

BUDGET

ITEM	QUANTITY	UNIT(Ksh)	**TOTAL (Ksh)**
❖ Pens ❖ Writing pads ❖ ❖ Printing fees ❖ Binding fees	1 box 5 9 9	400 250 500 100	400 1250 4500 900
ERC fees	1	2000	2000
Consultation Statistician	1	20000	20000
Laboratory fees	255	1000	255,000
Biothesiometer	1	35000	35,000
TOTAL			347,000

PROTOCOLS

Biothesiometer is a device which can quantify and pick early cases of diabetic peripheral neuropathy. It works on the principle of an electrical tuning fork. It has a vibrating probe which when applied to the plantar aspect of feet detects neuropathy. The vibration amplitude is measured in volts and can be changed by turning the dial. The person being tested indicates as soon as the vibration is felt.



Vibration proprioception will be measured over the first DIP joint, MTP joint and the heel. With voltage being gradually adjusted at the rate of 1 mV/sec : the vibration perception testing value being defined as the voltage level when the subject indicates that he or she first perceived the vibration sense.
The mean of three records will be taken.

Scoring:
<15mV – normal
15-25mV – mild neuropathy
25-40mV – moderate neuropathy
>40mV - Severe neuropathy

10/9/2021. 8%

Diabetic Foot Disease: The Evaluation Of Foot Deformities, Sensory Testing And Sugar Control In Type 2 Diabetic Patients In Kenyatta National Hospital

ORIGINALITY REPORT

8%	3%	6%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to University of Nairobi Student Paper	1%
2	Akbari, Cameron, and Frank Logerfo. "The acute diabetic foot", Emergency Vascular and Endovascular Surgical Practice Second Edition, 2005. Publication	1%
3	"Abstracts", Diabetologia, 2005 Publication	1%
4	hdl.handle.net Internet Source	1%
5	www.ajol.info Internet Source	<1%
6	lup.lub.lu.se Internet Source	<1%
7	Walsh, J. W., O. J. Hoffstad, M. O. Sullivan, and D. J. Margolis. "Association of diabetic foot ulcer	<1%

DR V.M. MWITSO 10th Sept 2021