International Journal of Diabetes and Endocrinology
2023; 8(1): 6-11
http://www.sciencepublishinggroup.com/j/ijde
doi: 10.11648/j.ijde.20230801.12
ISSN: 2640-1363 (Print); ISSN: 2640-1371 (Online)

Biothesiometric Assessment of Persons Living with Diabetes Mellitus in a Tertiary Hospital in Uyo, Southern Nigeria

Onung Samuel[1, *], Akhimienho Kingsley[2], Amadi Collins[3], Anyiekere Ekanem[4], Umoren Ubong[1], Ekuma Ikwo[1], Asukpong Eso[1]

[1]Endocrinology, Diabetes and Metabolism Unit, Department of Internal Medicine, University of Uyo Teaching Hospital, Uyo, Nigeria

[2]Department of Paediatrics, Edo State University, Uzairue, Nigeria

[3]Department of Chemical Pathology, University of Uyo Teaching Hospital, Uyo, Nigeria

[4]Department of Community Medicine, University of Uyo Teaching Hospital, Uyo, Nigeria

Email address:

dronungson@yahoo.com (Onung Samuel), irelosenkingsley@yahoo.com (Akhimienho Kingsley), collins338@yahoo.com (Amadi Collins), dramekanem@yahoo.com (Anyiekere Ekanem), acceptedindbeloved@ymail.com (Umoren Ubong), ikwoekuma@gmail.com (Ekuma Ikwo), asukpong@yahoo.com (Asukpong Eso)

[*]Corresponding author

To cite this article:

Onung Samuel, Akhimienho Kingsley, Amadi Collins, Anyiekere Ekanem, Umoren Ubong, Ekuma Ikwo, Asukpong Eso. Biothesiometric Assessment of Persons Living with Diabetes Mellitus in a Tertiary Hospital in Uyo, Southern Nigeria. *International Journal of Diabetes and Endocrinology*. Vol. 8, No. 1, 2023, pp. 6-11. doi: 10.11648/j.ijde.20230801.12

Received: January 10, 2023; **Accepted**: February 2, 2023; **Published**: February 16, 2023

Abstract: *Background*: The burden of foot ulceration and amputation among persons living with diabetes mellitus is quite huge and peripheral neuropathy is a well known risk factor for this. The prevalence of peripheral neuropathy and associated factors among persons living with diabetes, using an objective assessment (biothesiometer), is unknown in our study environment. *Method*: This was a cross-sectional study involving 108 age matched diabetes mellitus patients and controls. The study was conducted in the Diabetes Clinic of the University of Uyo Teaching Hospital, in Southern Nigeria. Basic demographics and other parameters such as duration of diabetes and glycated haemoglobin were recorded. All participants were recruited consecutively and screened for vibration perception threshold (VPT) using a biothesiometer. Participants with VPT $\geq$ 25 were considered to have significant neuropathy. *Results*: Significant neuropathy was recorded in 18 (33.3%) of the 54 diabetes patients. Only 3 (5.5%) of the 54 controls had significant neuropathy ($p<0.01$). The diabetes patients with significant neuropathy had a mean HbA1c of 8.9% compared to 7.3% for diabetes patients without significant neuropathy ($p=0.02$). The mean age of the diabetes patients with peripheral neuropathy was 54.0±2.3 years compared to 48.3±1.9 years for the diabetes patients without peripheral neuropathy ($p<0.01$). The mean duration of diabetes among diabetes patients with significant neuropathy was 10.3 years compared to 6.7 years for diabetes patients without significant neuropathy ($p=0.01$). Conclusion: There is a high prevalence of significant peripheral neuropathy among diabetes patients as determined using a biothesiometer. Early detection and achieving a good glycaemic control may help in reducing this burden which exposes the patients to the risk of possible amputation, depression and even death.

Keywords: Biothesiometer, Assessment, Diabetes Mellitus, Uyo, Nigeria

1. Introduction

Over the years, the prevalence of Diabetes mellitus (DM) has greatly increased globally. Sub-saharan Africa and Nigeria in particular is not spared by the sporadic rise in the prevalence of this chronic metabolic disorder. About 537 million adults are currently living with DM while an additional 374 million people have prediabetes and are at risk of developing T2DM [1]. It is projected that by the year 2045, the global prevalence of DM would have risen to 783 million

with sub-saharan Africa accounting for a significant number of those affected [1].

Diabetes mellitus is known to cause several complications which places a huge burden on the patient and their caregivers. One of such complications which could eventually lead to diabetes mellitus foot syndrome (DMFS), amputation and possible death, is diabetic peripheral neuropathy (DPN) [2]. Diabetes mellitus is among the commonest causes of lower extremity amputation. In one study, diabetes was found to cause a higher incidence of amputation than road traffic accident [3]. Peripheral neuropathy, which is the commonest reported chronic complication of DM, is an important risk factor for DMFS and lower extremity amputation. It most commonly presents with a reduction or absence of vibration sense in the toes. It can be assessed using different methods including the use of 10g Semmes -Weinstein monofilament testing, 128 HZ tuning fork or via the use of a biothesiometer [4].

Biothesiometer is a sophisticated handheld device that quantitatively assesses the vibration sense by measuring the vibration perception threshold (VPT), which is considered the gold standard for the diagnosis of diabetic peripheral neuropathy [4]. The biothesiometer can easily be used in the outpatient setting to assess persons living with diabetes for early and subclinical DPN. Early identification of those with DPN using this instrument, has been shown to greatly reduce the risk of DMFS and consequent amputation and deaths among diabetes patients [5]. Unfortunately, most patients with DPN, often present late with irreversible nerve damage. There is no documented evidence of a study on DPN using a biothesiometer as the benchmark for assessment in our study environment, hence the need for this study.

2. Methodology

This was a cross-sectional descriptive study conducted in the Endocrinology, Diabetes and Metabolism Clinic of the University of Uyo Teaching Hospital (UUTH). The University of Uyo Teaching Hospital is located in Akwa-Ibom state, Southern Nigeria and is one of two tertiary healthcare centres in the state. It basically offers specialist care to inhabitants of Uyo, an urban settlement and capital of Akwa-Ibom state. It also receives referral from surrounding cities in Nigeria and neighboring Cameroon. The Endocrine clinic of UUTH is run twice weekly by a team of Consultants and a number of Specialist Senior registrars and registrars in training. The first clinic is a Specialist clinic that caters strictly for persons living with diabetes mellitus while the other clinic focuses on other endocrine cases as well as general medical cases. An average of seventy patients are seen weekly in the diabetes clinic of UUTH. Patients from virtually all tribes in Nigeria are seen in UUTH, Uyo.

The study was conducted over a three months period, starting from September and terminating in November of 2018. A total of one hundred and eight participants were recruited for the study. Fifty four of the participants were persons living with diabetes mellitus while the remaining fifty four were recruited as controls for the study. Recruitment of diabetes patients was done consecutively on every Diabetes clinic day. The first twenty patients in the clinic register were contacted and those who consented were enrolled for the study. The consenting patients were given appointment to visit the diabetes clinic for the study proper. An average of ten diabetes patients were enrolled into the study weekly. On the day of the study, while in the diabetes clinic, the patients biodata including duration of diabetes were recorded. They were examined and blood samples taken for fasting plasma glucose and glycated haemoglobin after taking the necessary precautions. Glycosylated haemoglobin (HbA1c) was assayed using a fully automated Boronate Affinity assay for the determination of the percentage of hemoglobin A1C (HbA1c %) in whole blood. Poor glycaemic control consisted of glycosylated hemoglobin (HbA1c) levels of ≥7%. The feet of the participants were then assessed in a standardized fashion by a single observer, to determine the VPT using a biothesiometer (see Figure 6). The VPT was measured at the distal plantar surface of the great toe of both feet. The voltage was slowly increased at the rate of 1MV/sec. The VPT score was defined as the voltage when the subject first indicated that he or she can feel the vibration. The mean of three records were taken and neuropathy was diagnosed if the VPT was ≥25mV. The evaluation of the DM patients was done over a six weeks period. The controls were recruited from members of staff of the hospital, relatives and caregivers of patients, who were non-diabetic. They were assessed like their diabetes counterparts as described above.

Data obtained was arranged into tables and charts and analyzed using the statistical package for the social sciences version 20 (SPSS version 20). Data distribution for normality was done using the Pearson's test. Summary description of data was listed as mean, median, standard deviations, confidence intervals, proportions and tables. The comparison of categorical variables was determined using Chi square with the level of significance set at p values <0.05.

3. Results

3.1. Anthropometric and Clinical Indices of Participants

The anthropometric and clinical indices of the study Participants is shown in table 1. The diabetes patients and controls are equally matched by age with mean ages of 51.9±5.9 and 50.9±4.6 respectively for the DM and controls (p=0.35). The diabetes patients had a higher mean blood pressure compared to the controls and the difference was significant (p=0.01). The glycaemic control of the diabetes patients was suboptimal with a mean HbA1c of 8.1±1.3%. The diabetes patients had a statistically significantly higher vibration perception threshold compared to the controls, 32.5±2.3 vs 23.8±1.9 (p<0.01).

Table 1. *Anthropometric and clinical indices of participants.*

VARIABLES	MEAN ±SD (DM)	MEAN±SD (CONTROLS)	STUDENT T-TEST	P-VALUE
AGE (YRS)	51.9±5.9	50.9±4.6	0.64	0.35
DM DURATION	8.5±1.3			
Systolic BP (mmHg)	148.7±20.8	131.4±12.5	3.15	0.01
Diastolic BP (mmHg)	88.9±8.4	73.8±9.0	3.98	0.01
HbA1c (%)	8.1±1.3	5.2±0.9	6.51	<0.01
WC (cm)	90.3±11.5	87.7±10.5	0.83	0.17
BMI (kg/m^2)	26.3±3.6	26.9±4.6	0.45	0.51
VPT	32.5±2.3	23.8±1.9	7.95	<0.01

WC=Waist Circumference, VPT=Vibration Perception Threshold

3.2. Comparison of Diabetes Patients Using Peripheral Neuropathy.

The diabetes patients who had peripheral neuropathy were compared with their counterparts without peripheral neuropathy using some criteria as shown in table 2. The DM patients with peripheral neuropathy were older than their counterparts without peripheral neuropathy (54.0±2.3 vs 48.3.±1.9) and this difference was statistically significant (p<0.01). Also, the duration of diabetes was longer among diabetes patients with peripheral neuropathy compared to diabetes patients without peripheral neuropathy, 10.3±1.2 vs 6.7±0.3 (p<0.01). The mean systolic and diastolic blood pressure of the DM patients with peripheral neuropathy was higher compared to their counterparts without peripheral neuropathy (p=0.01, p=0.02 respectively). The DM patients with peripheral neuropathy had a higher mean HbA1c compared to DM patients without peripheral neuropathy, 8.9±1.4 vs 7.3±1.3 (p=0.01).

Also, obesity, using waist circumference and body mass index (BMI) was used to compare these two groups of DM patients. The mean waist circumference of DM patients with peripheral neuropathy was 94.5±4.6, compared to 88.3±3.9 for those without peripheral neuropathy (p=0.01). For BMI, the mean for the DM patients with peripheral neuropathy was 27.5±1.9 and 25.8±2.1, for those without peripheral neuropathy (p=0.03).

Table 2. *Comparison of diabetes patients with and without peripheral neuropathy.*

VARIABLES	DM PTS WITH PN. MEAN ±SD	DM PTS WITHOUT PN. MEAN±SD	STUDENT T-TEST	P-VALUE
AGE (YRS)	54.0±2.3	48.3.±1.9	4.13	<0.01
DM DURATION (YRS)	10.3±1.2	6.7±0.3	4.59	<0.01
Systolic BP (mmHg)	153.0±9.4	145.0±8.3	3.66	0.01
Diastolic BP (mmHg)	90.3±3.8	86.2±4.9	2.98	0.02
HbA1c (%)	8.9±1.4	7.3±1.3	3.55	0.01
WC (cm)	94.5±4.6	88.3±3.9	3.25	0.01
BMI (kg/m^2)	27.5±1.9	25.8±2.1	2.39	0.03

PN=Peripheral Neuropathy, WC=Waist Circumference

3.3 Prevalence of Peripheral Neuropathy Among Participants

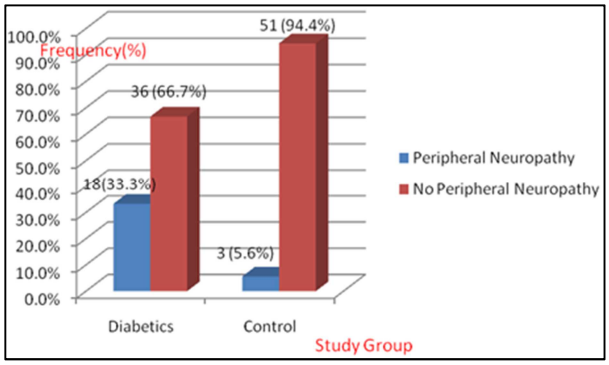

Figure 1. *Prevalence of peripheral neuropathy in all participants.*

The prevalence of peripheral neuropathy among the study.

Participants was assessed and the result is as shown in Figure 1. Among the 54 DM Patients, 18 (33.3%) had significant peripheral neuropathy. Among the 54 Controls, 3 (5.6%) had significant peripheral neuropathy (p<0.01).

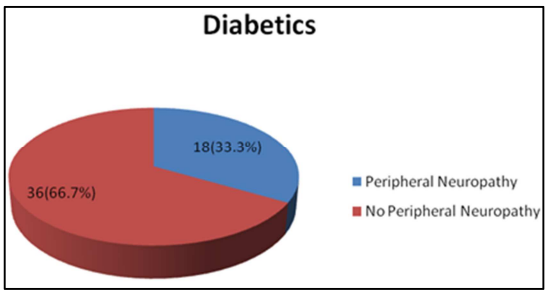

Figure 2. *Prevalence of peripheral neuropathy among diabetics.*

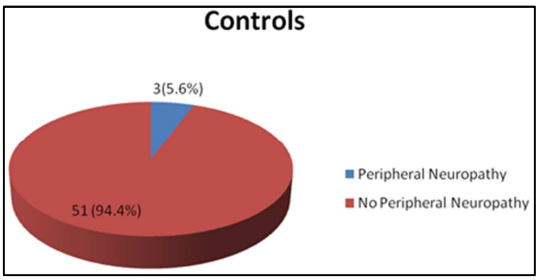

Figure 3. *Prevalence of peripheral neuropathy among controls.*

This finding is further represented as shown in figures 2 and 3 for the DM Patients and Controls respectively.

3.4. Footcare Awareness Among Diabetes Participants

The study participants living with diabetes were assessed to know their level of awareness concerning footcare as a preventive measure for foot ulceration and amputation. As shown in Figure 4, 40 out of the 54 patients representing 74% said that they had never received any formal education on footcare. Out of the 40 DM patients with poor knowledge of footcare, 30 (75%) had significant peripheral neuropathy ($p<0.01$). This is shown in Figure 5.

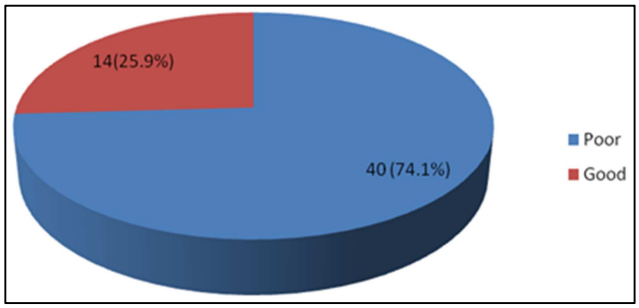

Figure 4. *Footcare awareness among diabetics.*

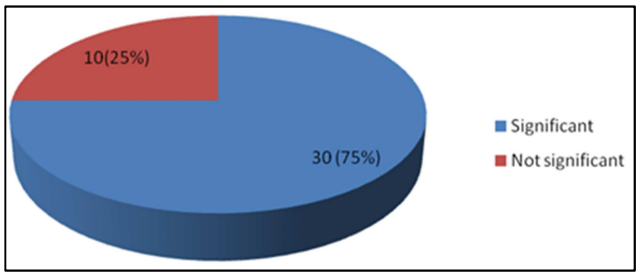

Figure 5. *Peripheral neuropathy among diabetics with poor footcare knowledge.*

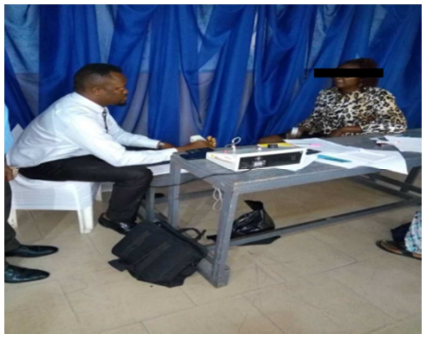

Figure 6. *Pic. showing exam. of one of the participants using a biothesiometer.*

4. Discussion

Healthcare professionals are increasingly becoming aware of the need for early detection of the main risk factors for DM foot ulcerations since this particular complication has been linked with high disease morbidity and mortality especially in resource-constrained settings like ours. Aside from foot ulceration, other common sequelae of DPN include leg amputation and painful DPN, often leading to anxiety, depression, sleep disorders, reduced quality of life and death in extreme cases [6].

Impaired vibration sense is an early sign of neuropathy, hence its assessment is an important element in the neurological examination of the patient with diabetes mellitus. In a Study that compared the efficacy of the use of a biothesiometer with that of the tuning fork, the biothesiometer was found not only to have comparable efficacy to the tuning fork but was more useful in large outpatient clinics [7]. In this study, significant peripheral neuropathy (SPN) was present in one-third of the diabetes population. Also, demonstrated in this study is a positive relationship between increasing age, duration of DM, glycated haemoglobin levels and the presence of SPN. A similar Nigerian study by Ogbera et al [8], screened DM patients for peripheral neuropathy (PN) using a biothesiometer and reported a higher prevalence of 56%. Another Nigerian study reported that biothesiometry detected PN in 47.8% of those with duration of DM < 5 yrs and in 100% of those with DM duration > 15 years [9]. In India, a crossectional comparative study evaluated the role of biothesiometry in the diagnosis of diabetes peripheral neuropathy in newly diagnosed patients. The study reported a prevalence of 43.3% [10]. The higher prevalence of SPN in some of these studies can be explained by a lower VPT cut off (>15 volts) used especially in the Indian and Ogbera studies as opposed to 25 volt used in this study. The use of biothesiometry with a cut of of 25 volt is considered the gold standard method of evaluating for peripheral neuropathy [11].

The pathogenesis of diabetic peripheral neuropathy is complex and is marked by both metabolic and vascular factors [12]. Chronic hyperglycemia is only one of the many key metabolic factors known to cause axonal and microvascular injury leading to SPN. A comprehensive, but by no means exhaustive list of key players include hyperglycemia, toxic adiposity, oxidative stress, mitochondrial dysfunction, activation of the polyol pathway, accumulation of advanced glycation end products (AGEs), and elevation of inflammatory markers [13]. Glucose uptake in peripheral nerves is independent of insulin and high blood glucose levels in DM thus leading to high nerve glucose concentrations which stimulate the polyol pathway. The result is the increased production of sorbitol and fructose in the nerve tissue, which cause nerve fiber swelling through their osmotic action, with resultant peripheral nerve damage and dysfunction [14].

The role of increasing age as a contributor to the rising incidence of diabetes peripheral neuropathy has been highlighted as one of the findings from this study. A cross-sectional descriptive study conducted in Lagos, Nigeria, reported a similar finding and even concluded that being elderly was a predictor of PN [8]. A systematic review and meta analysis of risk factors for DPN by Liu et al [15], documented a significant association between increasing age and the risk of developing SPN among diabetes patients.

Also, shown from this study is a statistically significant

association between the duration of DM and SPN. Several local and international studies corroborate this finding which is not unusual. A study in Jordan by Khawaja et al [16], noted that the duration of DM was the strongest predictor of DPN. Duration of diabetes is one factor that has been implicated in virtually all the chronic complications of DM including DPN. Oguejiofor et al also noted in a study in Nnewi, Nigeria, that, as the duration of DM increased, the risk of developing PN and subsequently diabetic foot disease increased even in those without symptoms of PN [17]. This is so because DM is known to be a progressive metabolic condition with complications including peripheral neuropathy, setting in as the duration of the condition increased [6].

The association of a longer duration of DM with PN is probably due to increased production of advanced glycosylation end products (AGEs) resulting in damage to endothelial cells of the vasa nervorum that supplies the nerves with the consequent damage to the nerves. This is known to occur over time in the course of the DM history [18].

A positive association between long term glycaemic control using glycated Haemoglobin (HbA1c) and SPN, is shown in this study. Poor glycaemic control as defined by a higher than normal HbA1c (>7%) was associated with a higher prevalence of SPN. Similar findings have been reported by several researchers both local and international. A possible relationship between glycaemia and PN was pointed out by findings from the UKPDS [19]. Ogbera et al [8] went further to report that poor long-term glycaemic control i.e HbA1c > 7% is an important predictor of PN. A more intensive approach to glycaemic control has been known to slow the progression of DM including the onset of complications like peripheral neuropathy [20]. A better glycaemic control has been shown to improve clinical outcome in diabetes peripheral neuropathy [21, 22]. Intensively controlling glycaemia as a preventive measure is necessary because the response to the various treatment options for peripheral neuropathy so far has not been encouraging [23].

The level of foot care awareness among the diabetes participants from this study is poor. Majority of the diabetes participants with significant peripheral neuropathy admitted to having a poor knowledge of foot care. The finding of poor foot care knowledge in persons with background DPN further increases the risk of foot ulceration. A similar finding has been reported by other researchers [24, 25]. Also, known to be associated with poor knowledge and practice of foot care is an increased incidence of diabetic foot ulceration, often a precursor to amputation and possible death [26].

5. Conclusion

There is a high prevalence of significant peripheral neuropathy among diabetes mellitus patients as determined using a biothesiometer, considered the gold standard for diagnosing peripheral neuropathy. Participants with poor glycaemic control and long duration of diabetes were more affected. Early detection and achieving a good glycaemic control may help in reducing this burden which exposes the patients to the risk of possible amputation and death.

6. Recommendations

This study has shown that peripheral neuropathy is common among diabetes patients with poor glycaemic control. A follow up study to determine the effect of improved glycaemia on the prevalence and severity of peripheral neuropathy is recommended. Also, a study to further elucidate the knowledge and practice of footcare among participants is recommended.

Conflict of Interests

The authors declare that they have no competing interests.

Author Contribution

The authors played the roles assigned to their names below:

Dr Samuel Onung – Study design, conceptualization, initial write up and review of final draft

Dr Kingsley Akhimienho – Initial write up and review of final draft

Dr Ubong Umoren-–– Initial write up and review of final draft

Dr Ekuma Ikwo –Recruitment and review of final draft

Dr Asukpong Eso – Recruitment and review of final draft

Dr Collins Amadi – Adequate laboratory sampling and precision, review of final draft

Dr Ekanem Anyiekere – Data analysis and interpretation, review of final draft

References

[1] Sun H, Saeedi P, Karuranga S, Pinkepork M, Ogurtsova K, Duncan BB et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Prat 2022.

[2] Kelkar P. Diabetic neuropathy. Semin Neurol. 2005; 25 (2): 168–173. doi: 10.1055/s-2005-871325.

[3] Zanni GR, Wick JY. Understanding amputation. Consult Pharm 2008; 23 (12): 944-8.

[4] Iqbal Z, Azmi S, Yadav R, Ferdousi M, Kumar M, Cuthbertson DJ, et al. Diabetic peripheral neuropathy: epidemiology, diagnosis, and pharmacotherapy. Clin Ther. (2018) 40: 828–49. doi: 10.1016

[5] BMK Aruna et al. Role of Biothesiometry in the diagnosis of diabetic neuropathy. Indian Journal of Clinical Anatomy and Physiology, July-September, 2017; 4 (3): 329-331.

[6] Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Phys Ther. 2008 Nov; 88 (11): 1254-64. doi: 10.2522/ptj.20080020. Epub 2008 Sep 18. PMID: 18801858; PMCID: PMC3870323.

[7] Oguejiofor OC, Onwukwe CH, Ezeude CM, Okonkwo EK, Nwalozie JC, Odenigbo CU, Oguejiofor CB. Peripheral neuropathy and its clinical correlates in Type 2 diabetic subjects without neuropathic symptoms in Nnewi, South-Eastern Nigeria. J Diabetol 2019; 10: 21-4.

[8] Ogbera AO, Adeleye O, Solagberu B, Azenabor A. Screening for peripheral neuropathy and peripheral arterial disease in persons with diabetes mellitus in a Nigerian University Teaching Hospital. BMC Res Notes. 2015 Oct 4; 8: 533. doi: 10.1186/s13104-015-1423-2. PMID: 26435536; PMCID: PMC4592746.

[9] Ugoya SO, Ugoya TA, Puepet F, Agaba EI, Ogunniyi AO. Risk determinants of diabetic peripheral neuropathy in Jos, North central Nigeria J Chin Clin Med. 2008; 3: 285–91.

[10] Gill HK, Yadav SB, Ramesh V, Bhatia E. A prospective study of prevalence and association of peripheral neuropathy in Indian patients with newly diagnosed type 2 diabetes mellitus. J Postgrad Med. 2014 Jul-Sep; 60 (3): 270-5. doi: 10.4103/0022-3859.138750. PMID: 25121366.

[11] Jayaprakash P, Bhansali A, Bhansali S, Dutta P, Anantharaman R, Shanmugasundar G, Ravikiran M. Validation of bedside methods in evaluation of diabetic peripheral neuropathy. Indian J Med Res. 2011 Jun; 133 (6): 645-9. PMID: 21727664; PMCID: PMC3135993.

[12] Cameron NE, Eaton SE, Cotter MA, et al.: Vascular factors and metabolic interactions in the pathogenesis of diabetic neuropathy. Diabetologia. 2001; 44 (11): 1973–88.

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

[14] Singh R, Kishore L, Kaur N: Diabetic peripheral neuropathy: current perspective and future directions. Pharmacol Res. 2014; 80: 21–35. 10.1016/j.phrs.2013.12.005

[15] Liu X, Xu Y, An M, Zeng Q. The risk factors for diabetic peripheral neuropathy: A meta-analysis. PLoS One. 2019 Feb 20; 14 (2): e0212574. doi: 10.1371/journal.pone.0212574. PMID: 30785930; PMCID: PMC6382168.

[16] Khawaja N, Abu-Shennar J, Saleh M, Dahbour SS, Khader YS, Ajlouni KM. The prevalence and risk factors of peripheral neuropathy among patients with type 2 diabetes mellitus; the case of Jordan. Diabetol Metab Syndr. 2018 Feb 21; 10: 8. doi: 10.1186/s13098-018-0309-6. Erratum in: Diabetol Metab Syndr. 2018 May 18; 10: 43. PMID: 29483946; PMCID: PMC5822644.

[17] Oguejiofor OC, Odenigbo CU, Oguejiofor CB. Evaluation of the effect of duration of diabetes mellitus on peripheral neuropathy using the United Kingdom screening test scoring system, bio-thesiometry and aesthesiometry. Niger J Clin Pract. 2010; 13 (3): 240–247.

[18] Shun CT, Chang YC, Wu HP, Hsieh SC, Lin WM, Lin YH, et al. Skin denervation in type 2 diabetes: correlations with diabetic duration and functional impairments. Brain. (2004) 127: 1593–605. doi: 10.1093/brain/awh180

[19] Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. (1998) 352: 837–53. doi: 10.1016/S0140-6736(98)07019-

[20] Ismail-Beigi F, Craven T, Banerji MA, Basile J, Calles J, Cohen RM, et al. Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial. Lancet. (2010) 376: 419–30. doi: 10.1016/S0140-6736(10)60576-4

[21] Callaghan BC, Little AA, Feldman EL, Hughes RA. Enhanced glucose control for preventing and treating diabetic neuropathy. Cochrane Database Syst Rev. 2012: Cd007543. doi: 10.1002/14651858.CD007543.pub2

[22] Ang L, Jaiswal M, Martin C, Pop-Busui R. Glucose control and diabetic neuropathy: lessons from recent large clinical trials. Curr Diabetes Rep. (2014) 14: 528. doi: 10.1007/s11892-014-0528-7

[23] Malik RA. Why are there no good treatments for diabetic neuropathy? Lancet Diabetes.

[24] Saber, Hemin Jawad1; Daoud, Ali Shakir2. Knowledge and practice about the foot care and the prevalence of the neuropathy among a sample of type 2 diabetic patients in Erbil, Iraq. Journal of Family Medicine and Primary Care 7 (5): p 967-974, Sep–Oct 2018. | DOI: 10.4103/jfmpc.jfmpc_163_18

[25] George H, Rakesh P, Krishna M, Alex R, Abraham VJ, George K, Prasad JH. Foot care knowledge and practices and the prevalence of peripheral neuropathy among people with diabetes attending a secondary care rural hospital in southern India. J Family Med Prim Care. 2013 Jan; 2 (1): 27-32. doi: 10.4103/2249-4863.109938. PMID: 24479039; PMCID: PMC3894008.

[26] Adeyemi TM, Olatunji TL, Adetunji AE, Rehal S. Knowledge, Practice and Attitude towards Foot Ulcers and Foot Care among Adults Living with Diabetes in Tobago: A Qualitative Study. Int J Environ Res Public Health. 2021 Jul 29; 18 (15): 8021. doi: 10.3390/ijerph18158021. PMID: 34360314; PMCID: PMC8345419.