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Review Article

Diabetic Peripheral Neuropathy: A Systematic Review of Nigerian Patients

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Abstract

Diabetes mellitus is associated with microvascular and macrovascular complications. Diabetic neuropathy is the most common long-term complication of diabetes. The study was aimed at determining the prevalence of diabetic peripheral neuropathy and identifying its associated factors. Medical databases, including PubMed, Google Scholar, African Journal Online, and SCOPUS were searched and eligible studies were selected using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses algorithm. The prevalence of diabetic peripheral neuropathy in Nigeria was dependent on the modality used in diagnosing peripheral neuropathy. The overall prevalence of diabetic peripheral neuropathy in Nigeria was 31.2%–97.5%. The modality-dependent prevalences were 37%–97.5% (by biothesiometry), 41.7%–75% (by Michigan Neuropathy Screening Instrument), 31.2%–43.3% (by United Kingdom screening test), and 43.3%–69.9% (by diabetic neuropathic examination score). The associated factors were duration and control of diabetes, the age of the patient, presence of cardiovascular risk factors such as hypertension and dyslipidemia and other microvascular complications (e.g., diabetic retinopathy and nephropathy). The prevalence of diabetic peripheral neuropathy was found to be high in Nigeria and the associated risk factors were age, glycemic control, and cardiovascular risk factors.

Keywords: Diabetic neuropathy, diagnosis, Nigeria, prevalence, risk factors

Introduction and General Definitions

Diabetes mellitus comprises a group of heterogeneous metabolic disorders in which the common denominator is hyperglycemia resulting from a defect in insulin secretion, action, or both.[1] The prevalence is rising rapidly across the various continents of the world.[2] The estimated prevalence of diabetes mellitus in Africa is 3.1%.[3] In Sub-Saharan Africa, Nigeria has the highest number of persons living with diabetes mellitus.[4] According to the International Diabetes Federation, as of 2020, about 2.7 million adults had diabetes in Nigeria.[5] Figure 1 shows the regional distribution of diabetes mellitus prevalence rates across the various geopolitical zones of Nigeria.[6]

Diabetic Microangiopathy

Chronic hyperglycemia induces pathological changes in the microvasculature of nerves, retina, and glomeruli resulting in the development of diabetic microangiopathy.[7] These are the underlying mechanisms for the development of diabetic neuropathy, retinopathy, and nephropathy. There are various pathways involved in the development of diabetic microangiopathy. Hyperglycemia, through the advanced glycation end products, polyol and hexosamine pathways, triggers an injurious cascade to the basement membrane of the microvasculature.[8] Hyperosmotic stress can induce inflammation by stimulating the release of pro-inflammatory cytokines, which has been found to contribute to diabetic microangiopathy.[9] The role of oxidative stress in the development and progression of microangiopathy has been extensively described in the literature.[10] Endothelial dysfunction, through deranged nitric oxide synthase function, has also been documented to contribute to diabetic microangiopathy.[11] The mechanisms underlying diabetic microangiopathy are summarized in Figure 2.

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Diabetic Neuropathy

Diabetic neuropathy refers to symptoms and/or signs of nerve dysfunction in a patient with diabetes when other causes of nerve dysfunction have been excluded from the study.[12] Diabetic neuropathy is the most common long-term complication of diabetes with a huge contribution to the morbidity and mortality of patients with diabetes.[13] It is also the most common cause of neuropathy, especially in the advanced economies.[14] In Northern America and Europe, the estimated prevalence of diabetic neuropathy is 6%–51% depending on the population that was studied.[15] In a meta-analysis involving 23 studies done across Africa, the estimated prevalence of diabetic neuropathy in Africa was 46%.[16] In another meta-analysis, the identified factors associated with diabetic neuropathy were duration of diabetes, age, glycated hemoglobin, and diabetic retinopathy.[17] Table 1 shows the classification of diabetic neuropathy, as published by the American Diabetes Association.[18] Diabetic symmetric polyneuropathy is the most common form of diabetic neuropathy.[19]

The pathophysiology of diabetic peripheral neuropathy involves both metabolic and vascular mechanisms.[20] As evidenced by nerve biopsy studies, the nerve microvasculature showed thickening of the basement membrane as well as hyperplasia and hypertrophy of endothelial cells.[21] The metabolic pathways usually involve reduction-oxidation stress.[22] Diabetic peripheral neuropathy often starts from the toes until it involves both the lower and upper limbs in the gloves and stockings distribution pattern.[23] A significant proportion of patients with diabetic peripheral neuropathy present with painful symptoms such as dysaesthesia, allodynia, and hyperaesthesia.[24] Sometimes, the patient presents with numbness and it is not uncommon for patients with diabetes to be asymptomatic of diabetic peripheral neuropathy.[25] The various modalities for diagnosing diabetic peripheral neuropathy include nerve conduction studies (the gold standard), nerve biopsy, various scoring methods using signs and symptoms of peripheral neuropathy (such as Michigan Neuropathy Screening Instrument, Diabetic Neuropathy Symptoms Score, and Toronto Clinical Scoring System), vibration threshold potential using a biothesiometer, and using a monofilament.[25] Based on the reports of previous studies, the sensitivity of the various modalities of diagnosing diabetes ranged from 63% to 98%.[26-28]

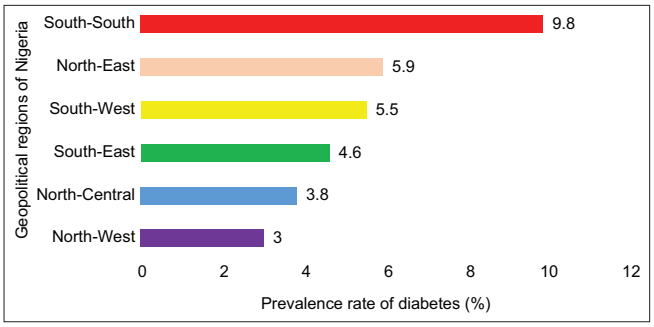

Figure 1: Prevalence of diabetes mellitus across the geopolitical zones in Nigeria

Objectives

1. To determine the prevalence of diabetic peripheral neuropathy in Nigeria
2. To identify the factors associated with the development of prevalence of diabetic peripheral neuropathy in Nigeria.

Methods

Medical databases including African Journals online, Google Scholar, Medline, and SCOPUS were used to retrieve studies on diabetic peripheral neuropathy in Nigeria. The search terms used were "diabetic neuropathy," "diabetic peripheral neuropathy," "peripheral neuropathy," and "diabetic symmetrical polyneuropathy." Other terms used in the data search included "diabetic neuropathy in Nigeria," "diabetic microangiopathy," "complications of diabetes" and "diabetic peripheral neuropathy in Nigeria." In order to improve the quantity and quality of retrieved articles, Boolean operators such as "AND" as well as "OR" were used. The gray literature was also searched to enhance the depth of the retrieved studies. The literature search was done by strictly following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The PRISMA flow diagram is shown in Figure 3.

Inclusion criteria

1. Studies done/published between January 1, 2000, and December 31, 2020, to determine the prevalence of diabetic peripheral neuropathy and its associated factors in Nigeria

Table 1: Classification of diabetic neuropathy

Types of diabetic neuropathy
Generalized
Distal symmetric polyneuropathy (typical and atypical)
Focal/multifocal
Mononeuropathy
Multiple mononeuropathies
Lumbosacral, thoracic, and cervical radiculoplexus neuropathies
Autonomic neuropathy

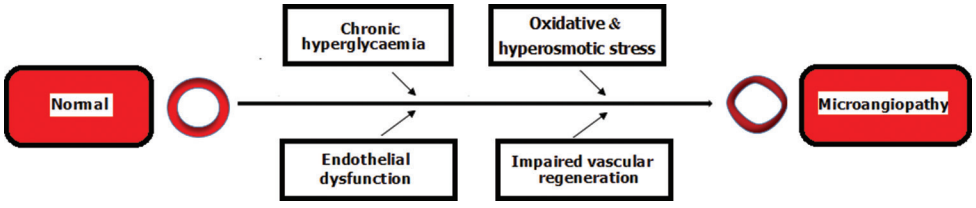

Figure 2: Pathophysiology of diabetic microangiopathy

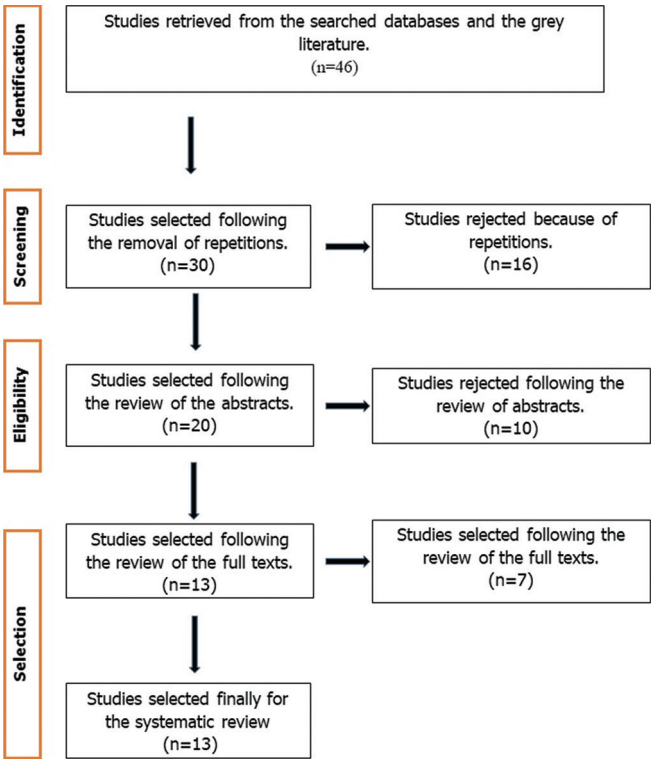

Figure 3: The PRISMA flow diagram of the literature search and selection

2. Studies whose abstracts and or full text were available at the searched databases or from the gray literature.

Exclusion criteria

1. Studies on diabetic peripheral neuropathy outside Nigeria
2. Studies on diabetic peripheral neuropathy inside Nigeria but not focusing on the prevalence of diabetic peripheral neuropathy or its associated risk factors in Nigeria.

The studies were identified and screened independently by the authors. The ones selected were agreed upon by at least two out of the three authors. Data extraction was done on a spreadsheet and the results were presented as tables and charts.

Results

Thirteen studies were selected for the systematic review. The range of the average age in the systematic review was 42–60 years. The various studies and the geopolitical zones are shown in Table 2. All the selected studies were cross-sectional studies. The sample size in each study is shown in Table 3. The total sample size was 2848.

The various modalities used in diagnosing diabetic peripheral neuropathy are shown in Table 4. Some studies used two different modalities in diagnosing diabetic peripheral neuropathy. The four modalities of diagnosing diabetic peripheral neuropathy employed in the various studies include biothesiometry, Michigan Neuropathy Screening Instrument, United Kingdom Screening Test, and diabetic neuropathy examination score. The most commonly used modality was biothesiometry.

The prevalence of diabetic peripheral neuropathy in each study is shown in Table 5. The prevalence of diabetic peripheral neuropathy in this systematic review was 31.2%–97.5%. The prevalence of diabetic peripheral neuropathy with respect to the modality of diagnosis is shown in Table 6. Averagely, the prevalence of diabetic peripheral neuropathy in Nigeria is lowest using the United Kingdom screening test and highest using the biothesiometry modality.

The associated risk factors for diabetic peripheral neuropathy according to the different studies are shown in As shown in Figure 4, the most commonly reported risk factors for diabetic peripheral neuropathy in Nigeria were the duration of diabetes and the current age of the patient as of the time of performing each study.

Discussion

The frequency of diabetic peripheral neuropathy in Nigeria,

Table 2: List of selected studies across the geopolitical zones

Geopolitical zone	Studies	Year of publication
South-West	Owolabi and Ipadeola[29]	2012
	Olamoyegun *et al*.[30]	2015
	Ogbera *et al*.[31]	2015
	Adesina *et al*.[32]	2016
North-Central	Ugoya *et al*.[33]	2006
	Uwakwe *et al*.[34]	2017
	Bello *et al*.[35]	2019
South-East	Asomugha[36]	2012
	Ede *et al*.[37]	2018
North-West	Ibrahim *et al*.[38]	2015
	Kaoje *et al*.[39]	2020
North-East	Salawu *et al*.[40]	2018
Multicentric, involving many zones	Chinenye *et al*.[41]	2012

Table 3: Sample size and prevalence rates in the selected studies

Study	Sample size	Prevalence (%)
Adesina *et al*.[32]	50	50.0
Olamoyegun *et al*.[30]	90	69.6
Uwakwe *et al*.[34]	100	75
Ede *et al*.[37]	100	73.3
Ugoya *et al*.[33]	120	75
Bello *et al*.[35]	175	41.7
Asomugha[36]	200	97.5
Ogbera *et al*.[31]	225	37
Salawu *et al*.[40]	250	86.8
Owolabi and Ipadeola[29]	277	71.1
Kaoje *et al*.[39]	330	39.7
Ibrahim *et al*.[38]	400	31.2
Chinenye *et al*.[41]	531	59.2
Total	2848	

Table 4: Modalities for diagnosing diabetic peripheral neuropathy in various studies

Modality of diagnosis	Studies
Biothesiometry using VPT	Salawu *et al*.[40] Asomugha[36] Kaoje *et al*.[39] Uwakwe *et al*.[34] Olamoyegun *et al*.[30] Adesina *et al*.[32] Ogbera *et al*.[31]
United Kingdom screening test	Ibrahim *et al*.[38] Kaoje *et al*.[39]
Diabetic neuropathic examination score	Asomugha[36] Olamoyegun *et al*.[30]
Michigan neuropathy screening instrument	Bello *et al*.[35] Ede *et al*.[37] Ugoya *et al*.[33] Owolabi and Ipadeola[29]

VPT: Vibration perception threshold

according to this systematic review, was 37.2%–97.5%. This is a wide range largely due to differences in sociodemographics and methodology. In a systematic review and meta-analysis, involving studies across the African continent, the prevalence rate of diabetic peripheral neuropathy ranged between 16.6% and 83.4%.[29] The range was also wide and the rate is comparable with the present study. The main reasons put forward for the wide range were differences in sociodemographics, type of diabetes and the methods employed in diagnosing diabetic peripheral neuropathy, just as was found in this systematic review. In another systematic review done in China, the prevalence rate of diabetic peripheral neuropathy was also found to be very wide and variations in demographics and methods of diagnosing the disease were reported as being responsible for this wide range.[42]

Similarly, in a systematic review done in Iran, the prevalence of diabetic peripheral neuropathy in the various studies ranged from 27.4% to 87.3%. Just as it was stated for the African and Chinese systematic reviews, the authors in the Iranian study also acknowledged a wide range in the prevalence of diabetic peripheral neuropathy and ascribed this wide variation to the differences in sociodemographics and research methods.[12] The sensitivity and specificity of the various diagnostic modalities for diabetic peripheral neuropathy vary, so it is expected that the different methods will yield different prevalence rates.[12]

The most prominent associated risk factor for diabetic peripheral neuropathy in this study was the duration of diabetes. A similar finding has been reported from other previous systematic reviews in Africa and Asia.[16,42,43] This is important because the prevalence of early-onset diabetes is increasing in Nigeria due to the adoption of Western lifestyles and the risk of developing peripheral neuropathy with its attendant complication of diabetic foot ulcer will also increase in this population.[44] It is therefore of crucial importance to prevent or delay the onset of diabetes.

The age of the patients was also another strong predictor of the occurrence of diabetic peripheral neuropathy, according to the findings of this study. Other studies have also documented age as a prominent factor associated with the development of diabetic peripheral neuropathy.[17,45,46] It has been reported that nerve conduction velocity declines with age and this may be responsible for the effect of age on the incidence of peripheral neuropathy in individuals with diabetes.[47]

Table 5: Prevalence of diabetic peripheral neuropathy using different modalities of diagnosis

Diagnostic modality	Prevalence (%)
Biothesiometry using VPT	37-97.5
Michigan neuropathy screening instrument	41.7-75
United Kingdom screening test	31.2-43.3
Diabetic neuropathic examination score	43.3-69.6

VPT: Vibration perception threshold

The present systematic review also showed that poor glycemic control was associated with diabetic peripheral neuropathy. Similarly, Aleidan *et al*.[48] in Saudi Arabia, Awadalla *et al*.[49] in Sudan and Gill *et al*.[50] in Ethiopia independently reported that poor glycemic control was associated with diabetic peripheral neuropathy. Studies have shown that prolonged exposure of nerves to hyperglycemia is critically important for the development of diabetic peripheral neuropathy.[51,52]

This study also found the universal cardiovascular risk factors such as hypertension, obesity, dyslipidaemia, smoking, and alcohol ingestion to be associated with diabetic neuropathy. Smith *et al*., also reported an association between dyslipidemia as well as obesity and diabetic peripheral neuropathy.[53] Papanas and Ziegler, also reported a strong association between

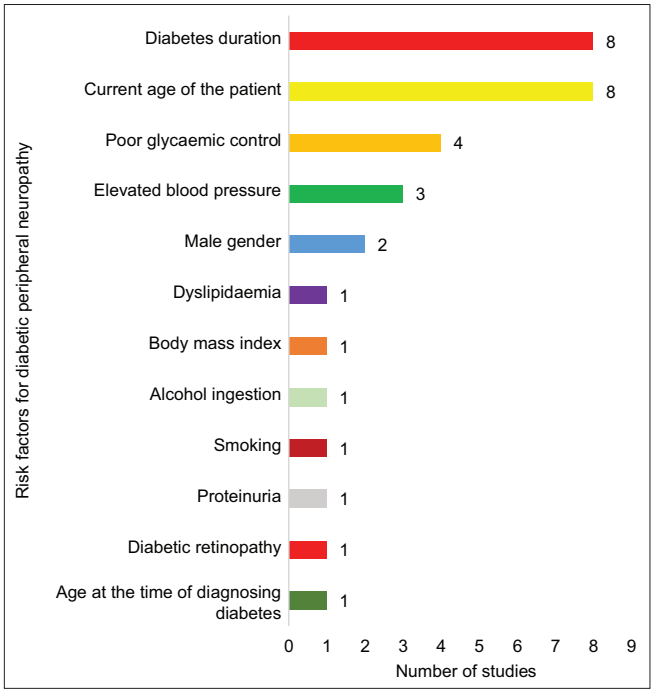

Figure 4: Risk factors for diabetic peripheral neuropathy and the number of studies reporting each

Table 6: Risk factors for diabetic peripheral neuropathy

Risk factors	Studies
Current age of the patient	Salawu *et al*.[40] Asomugha[36] Bello *et al*.[35] Ede *et al*.[37] Uwakwe *et al*.[34] Olamoyegun *et al*.[30] Ogbera *et al*.[31] Owolabi and Ipadeola[29]
Diabetes duration	Salawu *et al*.[40] Ibrahim *et al*.[38] Asomugha[36] Bello *et al*.[35], Ede *et al*.[37] Uwakwe *et al*.[34] Olamoyegun *et al*.[30] Adesina *et al*.[32]
Male gender	Asomugha[36] Olamoyegun *et al*.[30]
Poor glycemic control	Bello *et al*.[35] Ede *et al*.[37] Olamoyegun *et al*.[30] Ogbera *et al*.[31]
Elevated blood pressure	Salawu *et al*.[40] Bello *et al*.[35] Olamoyegun *et al*.[30]
Age at the time of diagnosing diabetes	Ibrahim *et al*.[38]
Diabetic retinopathy	Ibrahim *et al*.[38]
Proteinuria	Ibrahim *et al*.[38]
Smoking	Ede *et al*.[37]
Alcohol ingestion	Ede *et al*.[37]
Body mass index	Olamoyegun *et al*.[30]
Dyslipidemia	Owolabi and Ipadeola[29]

traditional cardiovascular risk factors such as hypertension, obesity, dyslipidaemia, smoking and alcohol ingestion, and diabetic peripheral neuropathy.[54]

In addition, the presence of other microangiopathic disorders such as diabetic retinopathy and diabetic nephropathy was found to be associated with the development of diabetic peripheral neuropathy. Other authors have documented a similar association among the microvascular complications of diabetes.[55-57]

Conclusion

Diabetic peripheral neuropathy is a common microvascular complication among patients with diabetes mellitus in Nigeria. The factors associated with the presence of diabetic peripheral neuropathy are the duration of diabetes, age of the patient, and cardiovascular risk factors such as hypertension and dyslipidemia and other microvascular complications such as diabetic retinopathy and nephropathy.

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Conflicts of interest

There are no conflicts of interest.

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ملخص المقال باللغة العربية

الاعتلال العصبي المحيطي السكري: مراجعة منهجية للمرضى النيجيريين

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يرتبط مرض السكري بمضاعفات الأوعية الدموية الدقيقة والكبيرة. يعد الاعتلال العصبي المحيطي السكري من أكثر المضاعفات شيوعاً على المدى الطويل لمرضى السكري. هدفت هذه الدراسة إلى تحديد مدى انتشار الاعتلال العصبي المحيطي السكري وتحديد العوامل المرتبطة به لمرضي نيجيريين. تم البحث في قواعد البيانات الطبية، بما في ذلك (بوب ميد، مانحة جوجل، والمجلات الأفريقية على النت، وكذلك باحث سكوباس)، وتم اختيار الدراسات المؤهلة باستخدام عناصر التقارير المفضلة للمراجعات المنهجية وخوارزمية التحليلات الوصفية (PRISMA) برزما. ولقد وجد أن نسبة تشخيص انتشار الاعتلال العصبي المحيطي السكري في نيجيريا يعتمد بشكل رئيسي على الطريقة المستخدمة في التشخيص. كان معدل انتشار الاعتلال العصبي المحيطي السكري في نيجيريا بصفة عامة يتراوح ما بين 31.2٪ إلى 97.5٪. كانت معدلات الانتشار المعتمدة على التشخيص بطريقة القياس الحيوي تتراوح ما بين 37٪ إلى 97.5٪. أما طريقة التشخيص بواسطة أداة فحص اعتلال الأعصاب لميشيغان فتراوحت ما بين 41.7٪ إلى 75٪. ومن ناحية أخري فإن طريقة التشخيص بواسطة اختبار فحص المملكة المتحدة فتراوح ما بين 31.2٪ إلى 43.3٪. وأخيراً فإن طريقة التشخيص بواسطة نتيجة فحص مرض السكري العصبي فأعطت نتائج تراوحت ما بين 43.3٪ إلى 69.9٪. كانت العوامل المرتبطة بمعدل انتشار الاعتلال العصبي المحيطي السكري في نيجيريا تشمل مدة مرض السكري والتحكم فيه، وعمر المريض، ووجود عوامل الخطر القلبية الوعائية (مثل ارتفاع ضغط الدم، وخلل الدهون في الدم، ومضاعفات الأوعية الدموية الدقيقة الأخرى مثل اعتلال الشبكية السكري واعتلال الكلية).

الاستنتاج: وجد أن معدل انتشار الاعتلال العصبي المحيطي السكري مرتفع في نيجيريا، وعوامل الخطر المرتبطة بها هي العمر والتحكم في نسبة السكر في الدم وعوامل الخطر القلبية الوعائية.

الكلمات المفتاحية: اعتلال الأعصاب السكري، الانتشار السكري، عوامل الخطر السكري، التشخيص السكري، نيجيريا.