

Clinically Diagnosed Diabetic Neuropathy: Frequency, Types and Severity

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Objective: Studies of frequency of occurrence of diabetic neuropathy are few, and available studies were limited to the southern part of Nigeria. The objectives of the study were to determine the frequency of occurrence and grades of diabetes peripheral neuropathy using clinical measures.

Patients and Methods: Consecutive patients with diabetes mellitus attending the Jos University Teaching Hospital were recruited as the study population, including 120 diabetics and 60 age-matched, nondiabetic controls. A standard proforma based on the Michigan Neuropathy Screening Instrument (MNSI) was employed to screen for diabetic neuropathy.

Results: The frequency of occurrence of diabetic peripheral neuropathy was 75%. For the specific types of peripheral neuropathy, sensorimotor neuropathy was the commonest (40.4%, $\chi^2=29.1$; $p<0.001$). There was no significant difference, with severity of peripheral neuropathy among diabetics, when compared by gender. (Chi square=3.03, P value=0.081).

Conclusion: The frequency of occurrence of peripheral neuropathy among diabetics in Jos University Teaching Hospital from this study is rather high.

Key words: diabetes mellitus ■ peripheral neuropathy ■ Nigeria

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INTRODUCTION

Currently, there is a pandemic of diabetes mellitus (DM), with an estimated doubling of the world diabetic population from 110 million in 1994 to 221 million by 2010.¹ This increase makes diabetic complications an obvious public health problem. Estimates of the prevalence of diabetic neuropathy vary widely from 5%² to nearly 60%² and sometimes 100% if patients with asymptomatic abnormalities of nerve con-

duction are included.² In a study of 4,400 patients with type-2 DM, Pirart³ found a prevalence of 7.5% at diagnosis, which rose linearly to 50% after 25 years. In a similar study among newly diagnosed diabetics, a prevalence rate of 11.6% was reported.⁴ Another population-based study of type-1 and type-2 diabetics in the United States yielded a cumulative incidence of distal symmetrical polyneuropathy of 4% after five years and 15% after 20 years of the diagnosis of DM.⁴

It has been reported that approximately 2.2% of Nigerians are diabetics.^{5,6} An earlier documented incidence of neurological complications among diabetic Nigerians is 48%.⁷ The Nigerian Non-Communicable Diseases surveys of 1992 estimated that 25–50% of patients with DM of 10 years' duration or longer have diabetic neuropathy.⁵ Appropriate and prompt treatments of acute metabolic complications of DM and better control of hyperglycemia have led to increased longevity of patients, thus resulting in the development of long-term complications.

In this study, we report the frequency of occurrence and severity of diabetic neuropathy in Jos University Teaching Hospital (JUTH), Jos, Nigeria.

MATERIALS AND METHODS

Setting and Study Design

This is a cross-sectional study to determine the frequency of occurrence and severity of peripheral neuropathy (PN) seen in JUTH, a tertiary care center in Nigeria. The study period was December 2002 to July 2003.

SUBJECTS

Consecutive patients with DM attending the medical outpatient departments or admitted to the medical wards of JUTH were screened and examined for neurological complications. DM was diagnosed according to the American Diabetes Association, ADA/World Health Organization (WHO) consultation criteria.⁸ A similar population of age- and sex-matched, nondiabetic patients attending the General Out Patients Department of the hospital served as controls.

The study was approved by the Research and Ethical Committee of JUTH. Informed consent was obtained from the subjects and controls before enlistment for the study. Excluded from the study were pregnant women; patients with DM of specific etiology; patients with diabetic emergencies, medications known to cause PN and positive HIV or VDRL serology.

Study Procedure

A screening questionnaire was developed according to the the Michigan Neuropathy Screening Instrument (MNSI) for diabetic neuropathy.⁹ This instrument, consisting of inspection of the feet and assessments of vibratory sensation and ankle reflexes, has been previously validated against the San Antonio consensus criteria and found to be both highly specific (95%) and sensitive (80%).⁹

Demographic data, clinical history and physical findings of each subject were documented using a proforma. Nervous system examination included full assessment of cranial nerves, deep tendon reflexes, and motor and sensory functions. A tuning fork of 128 Hz was used to assess vibration sense and a 10-g filament tensiometer to assess light touch perception.

Definitions

PN was defined as: a) failure to elicit the knee and/or ankle reflexes after reinforcement with or without symptoms of neuropathy or gross sensory disturbance in both feet, b) typical loss of sensation to pin prick and deep pain distally, c) loss of proprioception with sensory ataxia and a positive Romberg sign, or d) symptoms of burning sensation in the feet at night and day.¹⁰

Grades of PN. Grade 0 denotes no symptoms but a sign of neuropathy, grade 1 is ≥ 2 abnormal neurological tests, grade 2 for ≥ 2 abnormal tests plus symptoms, while grade 3 is ≥ 2 abnormal tests plus debilitating symptoms.¹⁰

Autonomic neuropathy (AN). Classic histories of chronic diarrhea (especially at night), gustatory sweating and dizziness on standing, presence of erectile dysfunction and a fall of ≥ 30 mmHg in systolic blood pressure on standing were significant for AN.¹¹

STATISTICAL ANALYSIS

Data obtained was analyzed using the EPI Info™ 2000 statistical software. Results were expressed as means (SD) or with ranges for continuous variables and proportions for categorical variables. Chi square was used to determine significance of association between groups or proportions. Student's t test and/or ANOVA were used to compare means of results where indicated. Ordinal category results were analyzed using contingency table analysis (<http://members.aol.com/johnp71/ordinal.html>). A p-value of <0.05 was considered significant. Fisher's test results were used where number in cells was <5 .

RESULTS

Clinical Characteristics of Study Subjects

Table 1 shows the clinical characteristics of the study subjects. The mean age of the diabetics was 53.0 ± 12.4 years, while that of the controls was 54.5 ± 13.9 , ($p>0.05$). Their ages ranged from 22–87 years. The mean duration of DM was 8.4 ± 6.9 years. Sixty-five percent had been diabetic for five years.

Ninety (75%) diabetic subjects had clinical evidence of neuropathy, compared with 20 (33.3%) of controls [odds ratio (OR) 6.00, 95% CI=3.05–11.81; $P<0.0001$], as shown in Table 1. The mean age of subjects with diabetic PN was higher than those without PN (54.8 ± 12.1 vs. 47.7 ± 12.2 years, $p=0.005$). Forty-three male diabetics (47.8%) and 47 female diabetics (52.2%) had PN respectively, OR=0.91, 95% CI=0.40–2.09, $p=0.83$. The largest number of subjects with diabetic PN was in the age group of 40–49 years, totaling 21 (33.9%). This middle-age affection is shown in Figure 1.

The mean duration of DM in subjects with PN was 9.4 ± 7.4 years. This was higher when compared with a figure of 5.3 ± 3.6 years in those without ($p=0.003$). The glycemic control using glycated hemoglobin among diabetics with PN was significant when compared to diabetics without. The mean HBA₁C of diabetics with PN was $8.5 \pm 3.5\%$, while those without is $5.9 \pm 2.5\%$ ($P=0.0001$).

Table 1. Characteristics of study subjects

Characteristics	Diabetics (N=120)	Controls (N=60)
Number (male/female)	58/62	29/31
Age (years) (mean, SD)	53.0 ± 12.4	54.5 ± 13.9
Duration of diabetes mellitus (years)	8.4 ± 6.9	—
Mode of treatment (%)		
OHA	82.5	—
Insulin	12.5	—
Diet alone	5	—
Frequency of peripheral neuropathy (%)	90 (75)	20 (33.3)
Diabetics with peripheral neuropathy; N=90 (HBA ₁ C) (%)	8.9 ± 3.5	
Diabetics without peripheral neuropathy; N=30 (HBA ₁ C) (%)	5.9 ± 2.5	

Types of Diabetic Peripheral Neuropathy

Sensorimotor polyneuropathy was the most common form of PN, with a frequency of 40.4%, followed by mixed type PN (26.7%) and AN (15.6%), as shown in Figure 1. The highest proportion among the diabetics was in the age group of 60–69 years with a frequency of 34.2%, while in the control group, the highest proportion was found in the 50–59-year age group with a total of 27.3%.

Grades of Peripheral Neuropathy

The different grades of neuropathy using the Dyck grading system are shown in Table 2. The different groups were subjected to analysis using Chi square for trend for ordinal categories. This was analyzed based on gender among the diabetics. Thirty-eight subjects—14 male diabetics and 24 female diabetics (42.2%)—had stage-0 neuropathy, while 23—12 male and 11 female—diabetics (25.5%) had stage 1. There was no significant difference between males and females with severity of PN. The following was obtained when compared by gender. ($\chi^2=3.03$, $P=0.081$). Further analysis using contingency table analysis for ordinal categorical values showed trends toward male predominance, as severity of neuropathy worsened—though not included in Table 2 (concordant pairs=450, discordant pairs=849, tied on X=1106, tied on Y=1810, SE=216.6, Z score=-1.8414 and $P=0.06$).

DISCUSSION

Studies on the epidemiology of diabetic neuropathy have been hampered by lack of

standard definition, intra/interobserver differences in eliciting symptoms and signs, and the lack of reliable and reproducible tests. Although methods of assessing peripheral nerve function are improving, no single test is indicative of nerve disease.¹¹ The San Antonio conference on diabetic neuropathy¹⁸ recommended obtaining ≥ 1 measure from each of the following categories to better define and classify diabetic neuropathy: clinical symptoms, clinical examination, electrodiagnostic studies, quantitative sensory testing and autonomic function testing. The MNSI⁹ used in this study has been previously validated against the San Antonio consensus criteria and found to be both highly specific (95%) and sensitive (80%).⁹

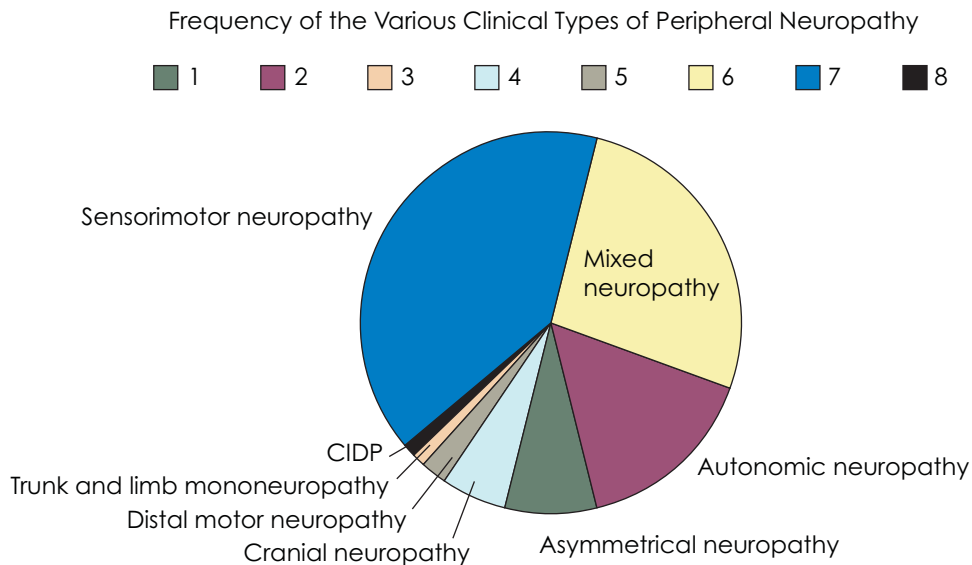
The frequency of diabetic neuropathy in the cohort studied at JUTH was 75%, with stage-0 PN accounting for 44.2% and stage 1 (26.7%). This frequency of occurrence compares well with the rate of 60–100% estimated in the western world.² The various clinical types of PN in this study correlate well with most studies all over the world, as sensorimotor polyneuropathy—diagnosed in 40.4%—is the most common.¹² These clinical types were not statistically significant when assessed individually, which may be attributed to the diagnostic criteria of the instrument. However, the overall prevalence is

Table 2. Grades of diabetic-peripheral neuropathy by gender

Grades	Male Diabetics	Female Diabetics	Odds Ratio
0	14	24	1.00
1	12	11	1.87
2	9	6	2.57
3	6	4	2.57

Chi square for trend=3.03, p=0.081

Figure 1. Various clinical types of peripheral neuropathy



higher than that reported from the United Kingdom, where the prevalence of PN among diabetics was 28.5%.¹² It is also higher than the 35.9% reported from Saudi Arabia.¹³ In a previous study in Nigeria, Osuntokun and colleagues⁷ reported a lower prevalence of 48%. These conflicting figures are due to differences in the minimum criteria for making a diagnosis, sample size and exclusion criteria.

PN was manifested at a significantly middle age in our study. This is in agreement with Vondrova and coworkers in Czech, who found that diabetic polyneuropathy was manifested at a younger age.¹⁹

The overall frequency of occurrence of diabetic AN in this study (31.7%) showed that objective evidence of AN occurs commonly in diabetics. Although Canal and coworkers¹⁴ found that 4% of type-1 DM patients had autonomic symptoms within the first year of diagnosis rising to 28% after five years, the high prevalence rate in our study is in keeping with the findings of previous studies. Fernandez-Castaner and colleagues¹⁵ reported that 53% of an unselected series of diabetics had symptoms suggestive of autonomic dysfunction, while Thi and coworkers¹⁶ documented that 67.6% of Vietnamese diabetics have cardiac AN. Most studies suggest a fairly close association between AN and sensory neuropathy. Nearly all diabetics with AN have an associated somatic neuropathy that precedes abnormalities of autonomic function.¹⁷

Our study was not without limitations. We were unable to carry out nerve conduction studies and biopsy on our subjects, although clinical examination has been found to have substantial correlation with nerve pathology.¹⁰ Further studies utilizing electrophysiologic evaluation would further elucidate the enormity of this problem.

In conclusion, the prevalence of PN among diabetics in JUTH from this study is high (75%). This means that PN among diabetics is still a major diagnostic and management problem that is not properly attended to in our clinics. Among the different types of neuropathy, sensorimotor neuropathy was the commonest, with a prevalence of 40.4%. Pure AN had a prevalence of (15.6%).

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