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Original Research

Peripheral sensory neuropathy in type 2 diabetes patients: A case control study in Accra, Ghana

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ABSTRACT

Objective: Peripheral sensory neuropathy (PSN) is a common cause of ulceration and amputation in diabetes (DM) patients. The prevalence of PSN in DM patients is largely undetermined in sub-Saharan African population. We studied the burden of PSN in DM patients using a validated questionnaire and quantitative sensory test.

Methods: In a case-control design, PSN was measured in 491 DM patients and 330 non-DM controls using Michigan neuropathy screening instrument (MNSI) and vibration perception threshold (VPT). PSN was defined as MNSI symptom score ≥7, MNSI examination score ≥2 or VPT ≥25V.

Results: The prevalence of PSN screened by MNSI symptom score, MNSI examination score and VPT was 7.1%, 51.5% and 24.5% in DM patients; and 1.5%, 24.5% and 8.5% in non-DM participants respectively. The major determinants of PSN screened by MNSI examination score were diabetes status [OR (95% CI): 4.31 (2.94–6.31), $p < 0.001$], age [1.03 (1.01–1.05), $p < 0.001$], previous [4.55 (2.11–9.82), $p < 0.001$] and current [8.16 (3.77–17.68), $p < 0.001$] smoking status. The major determinants of PSN screened by VPT were diabetes status [1.04 (1.02–1.06), $p < 0.001$], age [1.02 (1.01–1.03), $p = 0.047$], heart rate [1.78 (1.08–2.92), $p = 0.023$], second-hand smoking [3.66 (2.26–5.95), $p < 0.001$] and body height [3.28 (1.65–8.42), $p = 0.015$].

Conclusion: Our study has shown high burden of PSN in DM patients in Ghana using simple, accurate, and non-invasive screening tools like MNSI and neurothesiometer.

Introduction

Epidemiological transition has been under way in sub-Saharan Africa and this is in association with the dramatic increase in diabetes (DM) and accompanying vascular and neurological complications [1,2]. Peripheral sensory neuropathy (PSN) is a common microvascular complication of both type 1 and type 2 DM, and a major cause of morbidity and mortality [3,4]. PSN plays a major contributing role in the initiation of foot ulceration and non-traumatic lower-extremity amputation, resulting in severe disability, reduced quality of life, and significant economic burden to the health care system [5]. From the theatre records at the Department of Surgery, Korle-Bu Teaching Hospital, the main referral hospital in Ghana, out of 518 non-traumatic limb amputations performed within the period of January, 2014 through May, 2016, 467 (90.1%) were DM-related cases, with 318 (68.1%) below the knee amputations performed in DM patients.

Diagnosis of PSN is often made in clinical practice based on the presence of signs and symptoms of peripheral nervous system after other causes of neuropathy are excluded [3,6]. However, in up to 50% of DM patients, PSN may have no symptoms consistent with neuropathy, and hence, further neurological examination may be required for definite diagnosis [7,8]. Screening of PSN requires an appropriate tool that can detect mild form of the disease in high risk patients such as DM patients, and also, in low risk population with high sensitivity. Hence, the Michigan neuropathy screening instrument (MNSI), which is widely used for the evaluation of PSN in diabetes, was designed for such purpose [9]. Also, quantitative vibration testing is recommended in the screening and diagnosis of PSN [7]. However, this form of assessment is rarely performed in studies reporting the burden of PSN in sub-Saharan Africa.

A recent review of literature on PSN concluded that there is paucity of up-to-date epidemiological data on PSN worldwide [10], with only one outdated study reported in African population [11].

Abbreviations: DM, diabetes mellitus; MNSI, Michigan neuropathy screening instrument; PSN, peripheral sensory neuropathy; VPT, vibration perception threshold.

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From our own literature search, we found a few current studies that reported the burden of PSN in DM patients in African population to be 27.3–48.2% [4,12,13]. In this study, we investigated into the burden and determinants of PSN in DM patients and non-DM participants using MNSI and vibration perception threshold (VPT).

Methods

The study was case control design conducted at National Diabetes Management and Research Centre, Korle-Bu Teaching Hospital in Accra, Ghana, from June 2009 to May 2010. The centre is Ghana's main referral clinic and operates ambulatory DM services and research. DM patients were recruited by systematic sampling, as every 3rd consenting patient visiting the clinic. The controls were recruited afterwards and matched with the DM patients by gender and age-decade. The controls were non-DM with normal fasting glucose (<6.9 mmol/l) and post-glucose load plasma glucose (<7.2 mmol/l), recruited randomly from the communities around the hospitals. Out of 1000 volunteers (600 DM and 400 non-diabetes) invited, 866 (516 DM and 350 non-diabetes) consented to participate in the study. In the final analysis, 31 diabetes (11 did not complete the questionnaire and 20 had conflicting VPT results) and 20 non-diabetes participants (9 had impaired glucose metabolism and 11 had conflicting VPT results) were excluded. Ethical approval for this study was obtained from the University of Ghana Medical School Ethical and Protocol Review Committee (Protocol ID number: MS-Et/M.2 – P.4.10/2009–2010) and all participants gave written informed consent after the procedures involved in the study were thoroughly explained to them. A structured questionnaire was administered to all the participants to collect information on age, gender, education, employment status, duration of DM, DM medication, pre-existing hypertension, smoking and alcohol status. Second-hand smoking was assessed as living with a smoking relative or co-worker. Hypertension was defined as subjects with BP ≥140/90 mmHg and/or on antihypertensive medication.

Michigan neuropathy screening instrument

The MNSI questionnaire was administered to all participants by a trained assistant. Responses were added to obtain a total score; 'Yes' responses to questions 1–3, 5–6, 8–9, 11–12, 14–15 were each counted as one point and 'No' responses to questions 7 and 13 likewise counted as one point. Question 4 was considered to be a measure of impaired circulation and question 10 a measure of general asthenia and were excluded in the published scoring algorithm [9]. A score of ≥7 was considered abnormal. In the MNSI examination, a physician inspected each foot for deformities, dry skin, calluses, infections and fissures, and the presence of any abnormality was scored as 1. Also, ulceration on each foot was scored as 1. The ankle reflexes were elicited and if absent, the patient was asked to perform the Jendrassik manoeuvre. If the reflex was present upon the Jendrassik, it was designated as present with reinforcement and scored as 0.5. In the absence of reflex after the Jendrassik manoeuvre, a score of 1 was assigned. Vibration sensation was then tested on the great toe using a 128-Hz tuning fork. Generally, the vibration is felt in the examiner's hand for 5 seconds longer than the a normal person can feel at the great toe. Vibration was scored as present, if the examiner sensed the vibration on his or her hand for not up to 10 s longer than the period the subject felt that vibration on the great toe (scored as null); as decreased if the vibration is sensed for ≥10 s (scored as 0.5); or absent (scored as 1) if no vibration was felt at all. The total possible score is 8 points and, in the published scoring algorithm, a score of ≥2.5 is considered abnormal [6].

Neurothesiometry

Neurothesiometry was performed using hand-held neurothesiometer (Horwell Neurothesiometer, Scientific Laboratory Supplies Ltd, Nottingham, UK) to read vibration perception threshold (VPT) from the apex of the big toe of both legs, with subject in a supine position, feet elevated with pillow support and eyes closed. The neurothesiometer is a validated battery-operated diagnostic instrument that assesses sensitivity thresholds at various sites on the body surface. On the basis of the method of limits, participants were asked to indicate when they first perceived vibration sensation after stimulus was applied to the distal pulp of the toe. The intensity of the stimulus was gradually increased at a rate of 0.5 V/s from null to a voltage at which vibration was first detected. VPT was performed on each participant about 3–5 times and, at least, three VPTs the differed ≤5 V were averaged and used for analysis. A null stimulus test was added randomly to ensure participant adherence and understanding of the test requirements. Participants who failed to provide 3 consistent values of VPT within 5 V after several measurements were excluded from the analysis as having conflicting VPTs.

Statistical analysis

The data was analysed using IBM SPSS Version 20. Differences in mean values of continuous were assessed using student's *t*-test, and distribution of categorical variables with χ^2 test. Binary logistic regression model was used to determine independent clinical factors associated with PSN. $p < 0.05$ was considered statistically significant.

Results

DM patients were older, with higher proportion of hypertension, alcohol intake, and fewer current smokers than non-DM controls. Also, DM patients had higher means of BMI, heart rate, systolic, diastolic, mean and pulse blood pressures, as well as higher level of unemployment. Majority of the DM patients were on oral hypoglycaemic medication. Compared to non-DM controls, prevalence of PSN screened by MNSI symptom score, examination scores and VPT was higher in DM patients (Table 1). Among DM and non-DM participants with PSN screened by the MNSI examination score, majority were with the age range of 40–69 years, and predominantly females (Fig. 1a,b). However, when PSN was screened by VPT, the proportion of females with neuropathy was higher in DM patients, and the proportion of males was higher in non-DM participant; majority of PSN patients were likewise within the age range of 40–69 years (Fig. 2a,b).

Multivariable backward conditional logistic regression models were constructed with PSN screened by MNSI symptoms, MNSI examination and VPT as dependent variables. In all participants, DM status, age, heart rate, second-hand smoking and body height increased the odds of abnormal VPT after multiple adjustments of risk factors. In DM patients, age, duration of DM, heart rate and body height increased the risk of prevalence of abnormal VPT; and in non-DM controls, heart rate, body height increased the odds, whereas being fully employed decreased the odds of abnormal VPT. With respect to PSN screened by MNSI examination, DM status, age, female gender, cigarette smoking and working part-time increased the odds, whereas working full-time decreased the odds of PSN in all participants. In DM patients, age and female gender increased the odds of PSN, whereas diastolic pressure decreased the odds of PSN. In non-DM controls, alcohol use, cigarette smoking and working part-time increased the odds of PSN, whereas working full-time decreased the odds of PSN (Table 2).