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Research Article

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Prevalence and Characteristic of Diabetic Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus at National Diabetes Hospital in Tripoli- Libya 2016

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ABSTRACT

DPN is the most common form of the diabetic neuropathies. The current study aimed to determine the prevalence of DPN and the clinical feature in patients with DMII. The case serious study had been conducted in Tripoli Diabetic Hospital from June 2015 until Jan 2016, total number of admitted patients with DM II were 712, one hundred patients who were diagnosed as type 2 DM with DPN were selected for the study. Verbal consent taken, a special Performa was completed for every patient, that included detailsabout patient's demographics, some important points in clinical history, relevant investigations and clinical examination were recorded.

The study reported 100 patients, 76% of them was female, their age range was between 40-87years with mean age 62.45±11.34years, the duration of diabetes ranged from newly diagnosed to 40 years with mean 12.7±9.5years,17% of them have morbid obesity (BMI>40), 76% have neuropathy symptoms, 84% were non-smoker,40%are hypertensive, 34%are on treatment of lipid lowering drugs, 2%have RT foot ulcer, 8%have absent foot pulse (RT or LT or both), only 2(2%) are amputated ,this study shown a prevalence of neuropathy was14% and DPN were commoner at age group between (51-61) about 32%, in taller patients (>1.5 m),obese 44%,with duration >11 years ,non-hypertensive ,symptomatic (> 76%), on insulin treatment (59%), on dys-lipidemia therapy 66%, with feet pulses felt in 92%, poorly controlled DM (HBA1C >9%) were 54%. DPN were not related with TGA level, and presence of protein-urea, or feet ulcer.

Many character feature with development of DPN, there are strong association between development of peripheral neuropathy and age of the patients and duration of diabetes.

Keywords- *Diabetes mellitus; Diabetic Peripheral Neuropathy; Body Mass Index; Tripoli; Libya .*

INTRODUCTION

Diabetes mellitus (DM) is a common disorder, serious, and progressive in nature, the complications of Diabetes are due to chronic hyperglycemia which associated with long term dysfunction of various organs especially the eye, kidney, nerves, heart and blood vessels.[1] The complications of type 2 DM can be present even before formal diagnosis is made.[2]

Neuropathy can affect the sensory, motor and autonomic nervous systems, and can be acute or chronic. Chronic, symmetrical, sensory poly-neuropathy is the most common peripheral nerve syndrome in diabetes, and is usually irreversible.[3] Diabetic neuropathy (DN) is the most common form of neuropathy in developed countries and may affect about half of all patients with diabetes (DM), contributing to substantial morbidity and mortality and resulting in a huge economic burden. DN encompasses multiple different disorders involving proximal, distal, somatic, and autonomic nerves. It may be acute and self-limiting or a chronic, indolent condition. DN may be silent and go undetected while exercising its ravages, or it may present with clinical symptoms and signs that may mimic those seen in many other diseases. The proper diagnosis therefore requires a thorough history, clinical and neurological examinations, and exclusion of secondary causes. The distal neuropathies are characteristically symmetric, glove and stocking distribution, length-dependent sensorimotor polyneuropathies that develop on a background of long-standing chronic hyperglycemia superimposed upon cardiovascular risk factors. Diagnosis is based on a combination of signs, symptoms, and abnormal neurophysiological test results. No treatment has been approved for the prevention or reversal of DN. It has been estimated that between 3 and 25% of persons with DM might experience neuropathic pain. Painful DN can be difficult to treat, and is associated with reduced quality of life, poor sleep, depression and anxiety. Treatment guidelines suggest that pregabalin, gabapentin, venlafaxine, duloxetine, tricyclic antidepressants, and opioids are the drugs with the best evidence to support their use for painful DN. Tapentadol has also received FDA approval for the treatment of painful DN.[4,5] DPN

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is probably the most common form of the diabetic neuropathies.[6,7]

It is seen in both type 1 and type 2 DM with similar frequency and it may be already present at the time of diagnosis of type 2 DM.[8] A population survey reported that 30% of type 1 and 36 to 40% of type 2 diabetic patients experienced neuropathic symptoms.[9] Sensory symptoms are more prominent than motor symptoms and usually involve the lower limbs. These include pain, paresthesiae, hyperesthesiae, deep aching, burning and sharp stabbing sensations similar to but less severe than those described in acute sensory neuropathy. In addition, patients may experience negative symptoms such as numbness in the feet and legs, leading in time to painless foot ulcers and subsequent amputations if the neuropathy is not promptly recognized and treated. Unsteadiness is also frequently seen due to abnormal proprioception and muscle sensory function.[10,11] Alternatively, some patients may be completely asymptomatic and signs may be only discovered by a detailed neurological examination.[11]

Poor glycaemic control and duration of diabetes have consistently been shown to be associated with neuropathy. Other risk factors are age, height, male sex, and alcohol consumption although for these the evidence is less consistent. Systemic hypertension, cigarette smoking, and raised concentrations of plasma lipids are associated with increased risk of neuropathy in type1DM but not in type2 DM.[12] The central role of hyperglycaemia in the pathogenesis of diabetic peripheral neuropathy was confirmed in the large prospective Diabetes Control and Complications Trial. Intensive treatment of diabetes lowered the risk of developing clinical neuropathy by more than 60%.[13]

MATERIALS AND METHODS

This study was case serious descriptive study, it was conducted in the Diabetic hospital Tripoli from June 2015 until January 2016, total number of admitted patients with DM II were 712. One hundred patients who were diagnosed as type 2 DM with DPN were selected for the study. A special performa was completed for every patient after verbal consent taken, which included details on gender, BMI, age, duration of diabetes, history of hypertension, smoker, mode of anti-hyperglycaemic treatment, history of dyslipidema, presence of symptoms of peripheral neuropathy, examination for presence of foot ulcer, pulses of both feet (Dorsalis pedis artery) vibratory sense in the feet is tested with a 128-Hz tuning fork placed at the base of the great toenail, application of the 10g Semmes-Weinstein monofilament, deep tendon reflexes tested with tendon hummer and investigation results of HB_{A1C},LDL HDL, TGA , S. creatine level, Spot urine sample for protein urea were included. Selection of participants patients of either sex diagnosed with type 2 diabetes mellitus of any duration, established as per American Diabetes Association (ADA) guidelines (random blood sugar >200 mg/dL or fasting blood sugar >126 mg/dL) and willing to participate were included in the study. They were further classified into known diabetes mellitus (KDM) and newly detected diabetes mellitus (NDDM) based on the duration of diabetes. Patients with the diagnosis of type 2 DM of less than 6 months' duration were considered to be NDDM and KDM otherwise. Patients having type 1 diabetes, gestational diabetes and maturity onset diabetes of the young were excluded from the study.

Data collection

The information regarding demographics (age, sex), lifestyle characteristics (smoking) drug intake for DM, hypertension and dyslipidemia were collected by interviewing the participant.

Clinical and biochemical measurements

Anthropometric measurements including weight, height, body mass index (BMI; kg/m2) were carried out at the time of recruitment. Fasting lipid profile, glycated hemoglobin (HbA1c) measured using the Variant machine (Bio-Rad Laboratories, Hercules, CA, USA)., and urine analysis (for presence of protein), that assumed due to Diabetes nephro-pathy after exclude other causes as infection (UTI), uncontrolled hypertension, and heart failure, proteinurea according to spot urine testing by sulfo-salicylic acid technique.

Assessment of nuropathy

Neuropathy was assessed using 10-g monofilament, pinprick sensations, ankle reflexes and vibration perception threshold (VPT) test. The 10-g Vonfrey monofilament was placed perpendicular to the skin and pressure was applied until the filament just buckled with a contact time of 2 s. Inability to perceive the sensation at any one site was considered abnormal. In addition, ankle reflexes were also assessed with a percussion hammer, and recorded as either present or absent. So, according to A panel of clinicians under the direction of the American Diabetes Association Interest Group on Foot Care patient with DM was confirmed to have DPN if diagnosed with abnormal finding of 10-g monofilament test plus any abnormal test with, pinprick sensations or ankle reflexes or vibration perception threshold (VPT) test.[14]

Statistical analysis

Data are presented as the mean with standard deviation (SD) and numbers with percentages The data were statistically analyzed using the Statistical Package for the Social Sciences (Windows version 16.0; SPSS Inc., Chicago [IL], US).

RESULTS

The total number of admitted patients within the study period (June 2015 to Jan 2016) were 712 patients, 100 patients have DPN that included in the study, the prevalence was 14%.

The study reported 100 patients, 76% of them were female their age range between 40-87 years with mean age of 62.45±11.34 year, the duration of diabetes ranged from newly diagnosed to 40 years with mean duration 12.7±9.5 years,17% of patients have morbid obesity (BMI>40), 76% have neuropathy symptoms, 84% were non-smoker, 40% were hypertensive, 34% were on treatment of lipid lowering drugs, 2% had RT foot ulcer, 8% with absent foot pulse (RT or LT or both), only 2(2%) were amputated lower limb. This study shows a significant relation for age and duration of diabetes with the development of diabetic neuropathy that subjecting them to high risk of lower limb amputation

Table 1: Distribution of the patients character (clinical presentation: history, examination) at National Diabetes Hospital Tripoli-Libya 2016

Character	Frequency No(%)
Sex Female Male	76 (76%) 24 (24%)
Age in years 40-50 51-61 62-72 >73 Mean age 11.34±62	18%))18 32 (32%) 28 (28%) 3(3%)
Height m 1.5- 1.3 1.5> Mean height 0.1±1.56 m	49%))49 51(51%)
Body Mass Index 18 (Normal- 24.5%) (Over weight 29.5 -25 %) (Obese 30 -39.5 %) (Morbid obesity < 40 %) Mean BMI 32.29±7.5	13 (13%) 24%))24 44%))44 17(17%)
DM of Duration Newly - years10 20-11 30-21 40-31 Mean Duration 12.7±9.5	36%))36 38%))38 20%))20 6(6%)
nsion Hyperte present tAbsen	(40%)40 60(60%)
Symptom of neuropathy Present Absent	76%))67 24%))24
Smoker	16(16%)
DM for Treatment agentOr hypoglycemic al Insulin Combined	19%))19 59%))59 22(22%)
Dyslipidemia for Treatment	66(66%)
foot of Amputation	2(2%)
Presence of feet ulcer	11(11%)
pulse foot of Palpable	92(92%)

Table 2: Distribution of the patient's character (investigations) at National Diabetes Hospital Tripoli-Libya 2016

Investigation	No%) Frequency)
$_{c1A}$**HB** 7%-6.5 9%-7< 9%< Mean HB_{A1C} 2.79±9.79 gm%	11%))**11** 35%))**35** **54**(54%)
cholesterol LDL 100≥ mg/dl Mean 42.63±114 mg/dl	**70**(70%)
Triglycaeridemia TGA 150≥ mg/dl Mean 145.2±156.6 mg/dl	**42**(42%)
proteinurea Present	**16**(16%)

DISCUSSION

In this study DPN prevalence as well as the associated factors observed were very similar to that obtained by studies developed among patients with DMII in other countries.

The global estimates of DPN prevalence vary widely from 9.6 to 88.7% in different populations. This may be attributed to different types of diabetes, existing health care facilities, sample selection, different diagnostic criteria used, variable methods etc.[15-17]

A higher prevalence of DPN was observed in Saudi population with diabetes was19.9%, compared to the worldwide average estimate among diabetics (8.1% – 12.2%).[18] In Saudi Arabia, an earlier study the prevalence of 65.3% has been previously reported for painful DPN in a nationally representative diabetic population. In other Middle East countries, the prevalence rates of painful DPN were 61.3%, 57.5%, 53.9% and 37.1% for Egyptian, Jordanian, Lebanese, and Gulf States population, respectively. However, DPN cases in these studies was ascertained by questionnaire (Douleur Neuropathique 4, DN4) other than objective measurement that might explain the difference between the presenting study results and those from the previous studies in Middle East countries.[18]

In Brazil data have shown the prevalence was 16.7% of patients with DMII attending a teaching medical outpatient setting, as well as its association with disease duration.[19]

In Turkey, the prevalence was recorded for 16.0% of diabetic patients attending a teaching center[19] and in Belgium was 14.0% of patients with DM attending clinics.[20]

Differences in neuropathic pain frequency may also significantly differ among patients with DM with different glycemic control; factors such as weight, peripheral arterial disease and age are more associated to DPN.[21] With regard to the latter, notwithstanding other authors also reinforcing the idea that the number of individuals with neuropathic pain is higher among older people, that was similar in this study.[22]

Our results show that time after DM2 diagnosis was associated to neuropathic pain; this finding is in line with

those recently observed by other authors, that diabetes duration affects other disease co-morbidities.

An early study of diabetic peripheral neuropathy in a population used retrospective review of case records to ascertain symptoms or signs of neuropathy. Four per cent of diabetic patients developed peripheral neuropathy within five years of diagnosis. By 20 years after diagnosis, the prevalence had risen to 15%. Distal symmetric sensory neuropathy predominated. Many surveys since, both population based and of clinical case series, have shown that these rates are probably under-estimates.[23]

A recently published investigation in which a cohort of incident cases of type 2 DM was followed up for 10 years found that 8% fulfilled criteria for definite or probable neuropathy at the time of diagnosis compared with 2% in the control group. After 10 years of follow up, the prevalence of neuropathy had increased to 42% among diabetic patients and to 6% in controls.[24]

A study, was done at the Shariati Hospital diabetes clinic ,shown statistically significant relationships between neuropathy and age, gender, glycemic control and duration of disease. No correlation was found with any atherosclerosis risk factor (high BP, hyperlipidemia, cigarette smoking).[25]

Tesfye *et al*. studied 3,250 diabetic patients and reported an overall prevalence of peripheral neuropathy in 28% of them. The condition was significantly associated with age, duration of disease, height, diastolic blood pressure, smoking status, low HDL cholesterol level, high triglyceride level and HbA_{1C}.[26]

The Ashok study showed significant relationships only with age and duration of disease.[27] No other association was detected. Other studies have shown associations of neuropathy with age[27-31], duration of disease,[18,31,33] metabolic control,[14,31-34] height,[29,35,36] cigarette smoking,[14,32,37] retinopathy[14,34] and reduced HDL level.[34]

The DCCT (Diabetes Control and Complications Trial)[38] and UKPDS (United Kingdom Prospective Diabetes Study) results,[39] confirm the association of neuropathy with male gender, age, glycemic control (HbA_{1C}) and duration of disease. The United Kingdom Prospective Diabetes Study Group showed a significant increase in the incidence of DPN in older patients. Neuropathy increases with age and duration of diabetes, and is present in more than 50% of patients with type 2 diabetes aged over 60 years.[39]

A cross sectional study in 2014 in a tertiary center in North India showed a prevalence of 29.2%[40], also showed the following factors were associated with DN: Age, Duration of diabetes, Dyslipidemia, Glycated hemoglobin. The presence of other microvascular complications, Macrovascular complications, Alcoholic status.

A cross-sectional study was carried out on T2DM patients with overweight/obese in 60 hospitals in Guangdong province, shown DPN is prevalent (33.1%), and is significantly associated with age, HbA1c and duration of diabetes.[41]

The most common factors that may influence the DPN are age, duration of diabetes since diagnosis, poor glycemic control; history of ulcer; education level, smoking habit, drinking alcohol and body mass index directly increases the incidence of DPN.[42-43]

The study shown that age above 50 years were found to be significantly associated with the development of DPN. Which is similar to findings reported in studies conducted in University of Alfenas, Brazil, Fasa University, Hamedan province, Iran, Ethiopia, Benin, USA, Nigeria respectively.[41,44,45-49]

A cross-sectional study done by Tesfaye S *et al* shown the prevalence of DPN was 37.9%. Severe neuropathy prevalence was found to be 8.6% who were at the risk of foot ulceration or lower limb amputation. DPN was associated significantly with increasing age, early onset of diabetes, female gender and dyslipidemia.[50]

According to the EURODIAB Study, the main factors related to DN are: Duration of diabetes, Glycaemic control. The other risk factors were: Hypertension, Smoking, Obesity, Elevated triglyceride levels, and Presence of cardiovascular disease at baseline.[38]

In a study carried out in Iran, duration of DM II, in addition to age and education level, among other factors, was associated to complications, especially cardiovascular complications.[51] In Canada, a cohort study carried out for more than 20 years with diabetic patients in a young population has also recorded that renal system complications increase with longer DM2 duration.[52]

Using a case definition that required at least two of the following three criteria-sensory symptoms in hands or feet, sensory or motor signs on examination, or absent or diminished tendon reflexes-a large registry based study of insulin dependent diabetic patients found an overall prevalence of distal symmetric polyneuropathy of 34%, which rose to 58% in people 30 years of age and older.[53]

A study of patients with DMII, using criteria in which decreased or absent thermal sensation replaced sensory or motor signs, reported a prevalence of 26%.[54]

A higher prevalence of DPN was observed in Saudi population with diabetes, compared to the worldwide average estimate. Diabetes duration and glycemic control were strongly associated with DPN. Other correlates, including abdominal obesity and two relatively novel clinical markers (creatinine and white blood cell count) were also identified, which may contribute to the risk prediction of DPN.[18]

Elhwuegi AS *et al* study show, 41.5% of all diabetic patients suffered from at least one microvascular complication. The most common was retinopathy (16.2% of the patients), followed by peripheral neuropathy (11.2%), then peripheral neuropathy and retinopathy (6.5%). Most of the complications (87.3%) were seen in patients with type 2 DM. Microvascular complication usually relates to the duration of illness.[55]

Unlike to the present study, increased body mass index was significantly associated with the development of DPN in diabetes patients in multivariate analysis. This is comparable to the results of studies in South Africa, Ethiopia, Logos, Nigeria, Taiwan USA, UAE.[42,56-59] The authors also reported that co- morbid like hypertension, peripheral vascular diseases and increasing BMI by itself can proportionally increase the risk of DPN among patients with DMII.

Duration of diabetes mellitus for more than 10 years were found to be significantly associated with the development of DPSN in patients with DMII in multivariate analysis. Similar to the findings obtained in Iran, India and Brazil respectively.[58-60] Longer duration or chronic hyper glycaemia might result in glycosylation of nervous tissue and therefore damage, that was the same as in the present study.

Gashaw J *et al*[61] study shown that smoking was not significantly associated with DPN Which was similar to findings in the present study. Only 16% of the participants reported as smokers. But all of them were found to have DPN. that might be due to small number of smokers in the study population. Unlike the present study, most of the studies done on the developments of DPSN reported association with the cigarette smoking.[62-64]

Unlike the present study, presence of hypertension, and male gender were significantly associated with the incidence of DPSN in studies done in Iran, Benin, Bangladesh, Taiwan, and Ethiopia respectively.[47,57-59,65] The possible reason behind this might be the methodology of the study, study area, and difference in sample size of the study.

As to remaining characteristics, there have been no associations with other variables for individuals with neuropathic pain. Among patients attending National diabetes hospital, mean time of DMII diagnosis was 12.7 years, which is in line with other authors.[66] In addition, most patients were females (76%), mean age of 62 years, also in line with different studies carried out with similar population.

These results were consistent with the current study, 100 out of 712 admitted case to Diabetic hospital during study period were diagnosed with DPN after excluding other causes of peripheral neuropathy (the prevalence was 14% that lower than other country) that may be due to small number of study population within shorter duration, that deserves further researches.

Regarding associated factors were comparable similar, that indicate applying a patient education program to raise understanding of DM is the most vital measure in the avoidance of DPN, the authorities should make definite program of foot care for every patients .

CONCLUSION

DPN is a common micro-vascular complication of DM, affecting mainly old patients with DMII who had history of long standing badly controlled D M.

Most of the time nerve damage and DPN are irreversible. Hence, early screening and identifying associated factors is very crucial especially for developing countries with low resource settings.

RECOMMENDATIONS

Educate all people with diabetes about foot care. Identify those with high risk and interfere as early as possible. It important to pay attention to preventative measures like optimal glucose control with regular visits to diabetic clinic.

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