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Original Research Article

Relationship between the duration of diabetes and severity of neuropathy in patients of peripheral neuropathic diabetic foot ulcers

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ABSTRACT

Background: Diabetic foot ulcer (DFU) has devastating impact on the social, personal as well as economic life of a diabetic patient. In US, prevalence of peripheral neuropathy in adult diabetics is approximately 28%. The aim of this study is to establish relationship between the duration of diabetes and severity of neuropathy in patients with peripheral neuropathic DFU.
Methods: This is a prospective observational study, including 30 patients, who underwent history, examination and Toronto clinical scoring system (TCSS) was used for diagnosing severity of diabetic peripheral neuropathy (mild, moderate, severe) from a period of October 2015 to June 2017.
Results: In this study, we observed that the mean age of the diabetic foot patients was 53.50±12.03 years ranging from 30 to 75 years. Male-to-female ratio was 1.5:1. The mean duration of diabetes was 6.38±4.57 years. The patients with mild neuropathy had a mean duration of diabetes of 4.77±2.61 years, while, those with moderate and severe neuropathy had mean duration of 7.17±1.48years and 8.48±4.59 years, respectively.
Conclusions: The study concluded that there is a significant association between duration of diabetes and severity of neuropathy, i.e., patients with longer duration of diabetes had severe peripheral neuropathy.

Keywords: Peripheral neuropathy, DFU, Semmes-Weinstein monofilament testing (10-g monofilament), TCSS

INTRODUCTION

Diabetic foot ulcer (DFU) is a debilitating complication of diabetes mellitus, not only in resource limiting countries like India but also in developed countries. Despite of multifactorial aetiology of DFUs, neuropathy plays an important role in developing these ulcers. Inappropriate footwear is the leading cause of trauma in neuropathic foot that leads to ulceration.[1] In US, prevalence of peripheral neuropathy in adult diabetics is approximately 28%.[2] Oxidative stress and inflammation lead to nerve dysfunction and cell death that cause the diabetic peripheral neuropathy. American diabetes association recommends annual screening for diabetic peripheral neuropathy, glycaemic control and foot care.[3]

The objective of this study is to access the severity of neuropathy (mild, moderate and severe) using TCSS and its relationship with duration of diabetes in patients of peripheral neuropathic DFUs.

METHOD

Study type

It is a prospective, observational study.

Study place

It was carried out in institute of medical sciences, Banaras Hindu University, Varanasi.

Study period

The study carried out from October 2015 to the June 2017.

The 30 patients of peripheral neuropathic DFU included and informed written consent were taken. Inclusion criteria of this study is patients with DFU with peripheral neuropathy and the patients with DFU for >6 weeks and exclusion criteria are DFU patients without glycemic control, diabetic Patients with the ischemic foot ulcers, pregnancy as well as patients with the concomitant malignancy.

Detailed history and examination of patients carried out and wound details were recorded. Vibration perception testing evaluated with 128Hz tuning fork. Semmes-Weinstein monofilament testing (10-g monofilament) was done to measure pressure sensation. To calculate wound area, a sterile transparent graph paper was placed on wound to mark its borders. The two largest perpendicular diameters were measured using a ruler (in millimeters) and these two diameters were multiplied to obtain wound area in mm^2. TCSS was used for diagnosing severity of the diabetic peripheral neuropathy (Table 1).[4]

Table 1: TCSS.

TCSS	Right	Left
A-Symptom score	Present=1, Absent=0	Present=1, Absent=0
1-Pain		
2-Numbness		
3-Tingling		
4-Weakness		
5-Ataxia		
6-Upper limb symptoms		
B-Reflex score	Absent=2, Reduced=1, Normal=0	Absent=2, Reduced=1, Normal=0
1-Knee reflex		
2-Ankle reflex		
C-Sensory test score	Abnormal=1, Normal=0	Abnormal=1, Normal=0
1-Pinprick		
2-Temperature		
3-Light touch		
4-Vibration		
5-Position		
Total		

Final scoring

Number of neuropathy=0-5 points, mild neuropathy=6-8 points, moderate neuropathy=9-11 points, severe neuropathy≥12 points.

Ethical approval

This study was carried out after the approval from institute ethical committee.

Statistical analysis

All the parameters studied during observation period were compared using chi-square test for parametric variables and paired T test. The critical value of 'p' indicating the probability of significant difference was taken as<0.05 for comparison. Statistical analysis was performed using SPSS 16.0 software Windows version (Inc., Chicago, USA).

RESULTS

In the study, the mean age of the diabetic foot patients was 53.50±12.03 years ranging from 30 to 75 years. Male-to-female ratio was 1.5:1. The mean duration of diabetes was 6.38±4.57 years. Out of 30 patients, 20 were anaemic (60%) with Hb<10 gm% and most of patients (40%) had HbA1c levels from 8%-10%. Our study showed that most of the patients with DFU had poor glycaemic control with a mean HbA1c of 9.93±1.01.

Table 2: Demographic characteristics.

Characteristics	Results
Mean age (Years)	53.50±12.03
Male: female	1.5:1
Mean BMI	23.5±3.8 kg/m^2 (range 17-36 kg/m^2).
Mean duration of ulcer (Months)	4.17±3.45
Mean duration of diabetes (Years)	6.38±4.57
Painful neuropathy	70%
mean wound area on day1	32.43±24.7 cm^2
mean wound area at 6 weeks	13.00±9.7 cm^2
Mean HbA1c	9.93±1.01.

The 36.67% cases had right foot ulcer, 50.0% cases had left foot ulcer and 13.3% cases had bilateral limb involvement.

Table 3: Foot involved, (n=30).

Side involved	N	Percentage (%)
Right foot	11	36.67
Left foot	15	50
Bilateral foot	4	13.33

Wound area at presentation (i.e., before glycaemic control) was 32.43±24.7, whereas, mean wound area at 6 weeks (i.e., after glycaemic control) was reduced to

13.00±9.7. This difference was statistically significant (p<0.001). Early presentation of patients with DFU and getting proper treatment (glycaemic control, regular debridement and dressing) helped in decreasing the wound size of ulcer and also prevented the progression of DFU to higher grade.

In the study, we found that painful neuropathy was seen in 70% of patients with DFU. The 50% (n=15) patients had mild peripheral neuropathy (according to TCSS). More severe neuropathy was seen in patients with longer duration of diabetes. Mean duration of diabetes in patients with mild, moderate and severe neuropathy was found to be 4.77±2.61 years, 7.17±1.48 years and 8.48±4.59 years, respectively. The relationship was statistically significant (Table 4), thereby, indicating that severity of neuropathy progresses gradually with duration of diabetes.

Table 4: Relationship between duration of diabetes and severity of neuropathy, (n=30).

Neuropathy	N	Mean duration of diabetes
Mild	15	4.77±1.61
Moderate	7	7.31±2.33
Severe	8	8.78±2.87

Anova f=9.70, p≤0.001

DISCUSSION

Poor glycaemic control and chronic hyperglycaemia activates various pathological pathways and accumulation of intracellular advanced glycated end products, thus, causing hyperglycaemic nerve damage (neuropathy). Pscherer et al found that patients with a mean HbA1c above 7.5% had 20% higher risk of amputation compared to patients with HbA1cbelow 7.5%. Contribution of several risk factors in DFU have been reported by various researchers in previous studies. There is a strong association between the presence of neuropathy in a patient with diabetes and foot ulceration. A large number of studies have identified neuropathy as a risk factor for ulceration.[5] Intact innervation is important for efficient healing of skin and epithelium. Axonal atrophy is a hallmark of diabetic peripheral neuropathy. There is an impaired peripheral nerve regeneration in diabetes mellitus.[6] Diabetic neuropathy is characterized by slower conduction velocity, impairment of axonal transport, axonal atrophy, and reduced capacity for nerve regeneration. All these features of nerve function depend on the integrity of the axonal cytoskeleton and particularly on neurofilaments. Of all available treatment options, strict glycemic control is the only method that can provide symptomatic relief by slowing the relentless progression of neuropathy. Probably, its sudden blood glucose flux that induces neuropathic pain, so, stability rather than the actual level of glycemic control is most important in pain relief. Oral hypoglycemics or insulin can be used for controlling blood sugar level; no evidence suggests that insulin is superior if blood glucose is well controlled by oral hypoglycemic agents. Thus, it can be postulated that the stable glycaemic control alone can provide symptomatic relief and decrease the progression of neuropathy. Çakici et al done a systematic review in 2016 and found that α-lipoic acid, opioids, botulinum toxin A, mexidol, reflexology and Thai foot massage had significant beneficial results in treatment of peripheral diabetic neuropathy.[7] Neurofilament (NF) expression is closely associated with axonal growth and maintenance of neuronal homeostasis. Current evidence indicates that NF plays a key role in axonal regeneration and is dependent on post-transcriptional mRNA transport, translation, and stability.[8] large myelinated sensory fibers appear to be most sensitive to functional impairment in diabetes and it is this population of neurons that exhibits the highest level of aberrant NF phosphorylation.[9] Nisar et al published the similar results that the presence of diabetic neuropathy was significantly associated with HbA1c levels and the duration of diabetes.[10] Oguejiofor et al found a lower prevalence of polyneuropathy in those with duration of DM < 5 years and highest in those with a duration of DM > 15 years.[11]

The association between the duration of diabetes mellitus and neuropathy was also evident in a research study on the epidemiology of diabetic complications.[12]

The limitation of this study is of small sample size and every patient undergoes colour Doppler to rule out ischemic foot ulcers.

CONCLUSION

The study concludes that severity of peripheral neuropathy is significantly associated with the duration of diabetes. Thus, strict glycemic control, foot care and annual screening of peripheral neuropathy in diabetic patients is strongly recommended by American Diabetes Association in order to avoid further complications like DFU.

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