International Journal of Medicine Research
ISSN: 2455-7404
www.medicinesjournal.com
Volume 3; Issue 4; October 2018; Page No. 09-13

Study of clinical profile of diabetic peripheral neuropathy in type 2 diabetes mellitus

Dr. Abhishek Y Kadam[1], Dr. Krupa Pathak[2*], Dr. Smita K Trivedi
[1] Senior Resident, Department of Medicine, Medical College Baroda and SSG Hospital, Vadodara, Gujarat, India
[2] Assistant Professor, Department of Medicine, Medical College Baroda and SSG Hospital, Vadodara, Gujarat, India
[3] Professor, Department of Medicine, Medical College Baroda and SSG Hospital, Vadodara, Gujarat, India
Corresponding Author: Dr. Krupa Pathak

Abstract
Diabetic neuropathies are common chronic complications in type 2 diabetes mellitus (T2DM) and on long term it carries poor prognosis. Diabetic neuropathy may present with various sensory, motor or autonomic symptoms. The aims of study were, to assess clinical profile and severity of diabetic peripheral neuropathy & its association to glycemic status and with other modifiable and non-modifiable risk factors. The study included 45 patients with diabetic peripheral neuropathy. Detailed clinical examination including sensory and motor system examination was done and different clinical parameters were studied. Most common symptom of distal symmetrical peripheral neuropathy (DSPN) was tingling and numbness in foot and most common sign was absent ankle reflex followed by loss of vibration perception. Prevalence of peripheral neuropathy increases with increase in age of patients, duration of diabetic mellitus and poor glycemic control. Development of diabetic peripheral neuropathy is associated with other modifiable risk factors; hypertension, high body mass index (BMI), hyperlipidaemia, smoking, etc. Diabetic neuropathy is associated with development of other microvascular complications like diabetic retinopathy and diabetic nephropathy, owing to common pathway of pathogenesis.

Keywords: type 2 diabetes mellitus, distal symmetrical peripheral neuropathy, microvascular complications, neuropathy symptom score, neuropathy deficit score

1. Introduction

Diabetes is one of the major health problems all over the world. Mortality and morbidities associated with diabetes are related to microvascular and macrovascular complications of diabetes mellitus. Vascular complications both micro and macrovascular predominate the features of Indian diabetic patients due to delayed diagnosis [1]. Indians are at increased risk of T2DM and its complication, at a relatively lower BMI, because of Asians-Indians phenotype [2, 3]. In T2DM, distal symmetrical peripheral neuropathy (DSPN) may present at the time of detection or may develop only within few years of poor glycemic control. Diabetic neuropathies are troublesome and chronic complications, common to occur and on long term basis it carries poor prognosis in diabetics. Also, treatment of DSPN is symptomatic only and usually less satisfactory. If neuropathy remain undetected may progress to secondary complications like cellulitis and diabetic foot among many others, so early diagnosis of DSPN is important. The duration and level of hyperglycaemia are important determinants of microvascular complications of diabetes, including neuropathy [4]. By the time a diabetic patient has severe neuropathy, retinopathy and albuminuria are also usually present. Diabetic neuropathy is clinically present in 30-50% of all diabetes patients [2]. Diabetic Peripheral neuropathy has been associated with a number of modifiable and non-modifiable risk factors. Significant correlations were observed with BMI, duration of diabetes, quality of metabolic control, the presence of background or proliferative diabetic retinopathy, cigarette smoking, high-density lipoprotein cholesterol, presence of cardiovascular disease, elevated diastolic blood pressure, the presence of severe ketoacidosis, high fasting triglyceride, and the presence of micro albuminuria [5]. Distal symmetrical peripheral neuropathy is commonest form of diabetic peripheral neuropathy. It presents with paraesthesia and numbness in toes, in proximal ascending pattern with duration over months to years. It may lead to secondary complications like foot ulcer, gangrene, Charcot's joint and cellulitis. When sensory symptoms ascend above knee, same symptoms may develop in hands and progress in gloves distribution. Various degrees of motor involvement is also seen.

There is no definitive treatment for diabetic neuropathy and identifying potentially modifiable risk factors at an early stage leads to favourable treatment outcomes. The present study aims to evaluate DSPN in Type 2 DM patients by clinical examination and to correlate it with the other microvascular complications and various risk factor.

2. Aims of study

1. To study clinical profile and severity of diabetic, Distal Symmetrical Peripheral Neuropathy (DSPN) in patients of type 2 diabetes mellitus
2. To study association of DSPN in relation to glycaemic status, and
3. To study association of DSPN with various other modifiable and non-modifiable risk factors.

3. Material and Methods

This is an observational cross-sectional study. The data was

collected from patients fulfilling the inclusion and exclusion criteria attending either out-patient or in-patient department of S.S.G Hospital, Vadodara. The duration of data collection was one year. Informed written consent was obtained from patient or a responsible attendant before inclusion in the study.The ethics committee of the institution gave the permission for the study. 45 patient with diagnosis of DSPN were included in study.

Inclusion criteria: Type 2 diabetic patients, more than 18 years of age having clinical signs and symptoms of DSPN were included in study.

Exclusion criteria: Patients with documented end stage renal disease, leprosy, current intake or previous history of drugs causing neuropathy and other secondary causes of neuropathy (alcoholism, metallic poisoning, Hansen's disease, deficiency conditions, syphilis and malignancy) excluded from study.

For data collection, detailed history was taken in each case. The patients with secondary causes of neuropathy were excluded from study. Detailed clinical examination including sensory and motor system examination was carried out. Sensory examination was done by 128 Hz tuning fork, whip of cotton and pin prick. Temperature sensation was checked by cold tuning fork. Motor examination was done and tendon hammer was used to examine deep tendon reflexes. The peripheral neuropathy disability was determined by clinical signs and using clinical scoring system, Neuropathy deficit score (NDS) and NSS (Neuropathy Symptoms Score) [6]. The parameters included in NDS are vibration perception on foot, ankle reflex, temperature sensation and touch sensation. The parameters included in NSS are sensory symptoms (tingling and numbness), site of involvement, diurnal variation, and aggravating and relieving factors. Patients were evaluated for presence of diabetic retinopathy and diabetic nephropathy related albuminuria. Statistical analysis was carried out for 45patients. They were categorized according to age, gender, duration of diabetes, NDS, NSS, examination findings and investigation profile.

4. Results

Following are the results of the study:

In our study of 45 patients, all 45 pts had features of DSPN.

- Out of 45 patients 36 patients (80%) had age more than or equal to 50 years. Maximum patients were from age group 60 to 69 years- 18 (40%); Mean age of our study group was 58.8±11.8 years (figure 1).

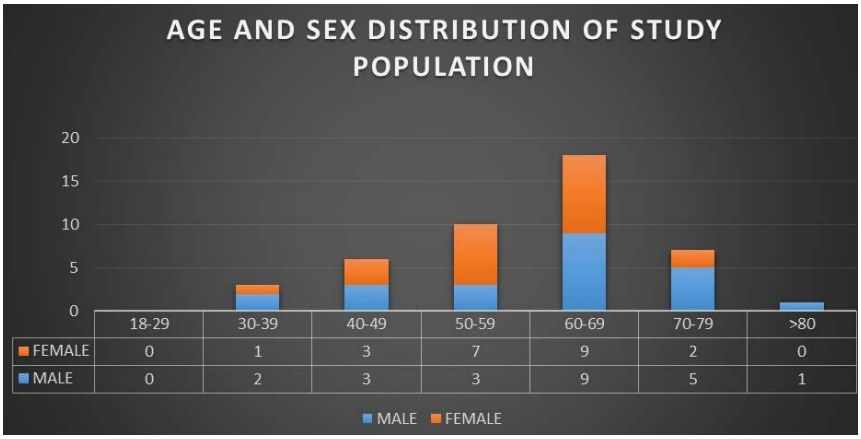

Fig 1: age and sex distribution of study population

- Most common symptom of DSPN was tingling and numbness of extremities(leg). Other symptoms were burning pain with paresthesia, limb pain with cramps and unsteadiness of gait (table 1).
- Most common sign of DSPN was absent ankle reflex followed by loss of vibration perception. Other signs were impaired joint position, impaired temperature and touch sensation, skin changes, foot trophic ulcers and thickened nerves (table 2).
- In our study population, according to Neuropathy Symptoms Score (NSS) prevalence of severe, moderate and mild neuropathy was 58%, 36% and 6% respectively. According to Neuropathy Deficit Score (NDS), prevalence of severe, moderate and mild neuropathy was 2%, 80% and 18% respectively (table 3).

Table 1: Frequency distribution of symptoms of diabetic neuropathy

Symptoms Frequency	Frequency
Numbness and tingling of extremities(leg)	91%
Burning or electric pain	45%
Paraesthesia	6%
Limb pain and cramps	27%
Unsteadiness of gait	6%

Table 2: Frequency distribution of signs of Distal Symmetrical Polyneuropathy

Signs	Number of Patients	Frequency in Percentage
Absent Ankle reflex	43	97%
Impaired Vibration	35	78%
Impaired Joint position	14	31%
Impaired Temperature sense	10	22%
Impaired Touch	08	18%
Limb Skin changes	10	22%
Foot trophic changes	10	22%
Thickened nerves	05	12%

Table 3: Severity of diabetic neuropathy with clinical scoring system

Neuropathy Severity	NSS scoring system		NDS scoring system	
	No. of patients	%	No. of patients	%
Mild	3	6%	8	18%
Moderate	16	36%	36	80%
Severe	26	58%	1	2%
Total	45		45	

- 58% of patients had duration of diabetes more than 5 years.
- 74% patients had FBS > 200 mg/dl, 98% had PP2BS > 200 mg/dl and 87% of patients had HbA1c > 9 %.
- Prevalence of diabetic retinopathy and albuminuria was 52% and 56% respectively in study group
- Among 45 patients with diabetic peripheral neuropathy, 69% of patients were overweight to obese with BMI >23 kg/m2. With mean BMI of study population was 24.5±3.33 kg/m2.
- In our study 69% of patients had hypertriglyceridemia. With mean value of 182±76.2 mg/dl.
- In study 27% of patients had hypercholesterolemia with mean value of 175+45 mg//dl.
- In study 57% patients had hypertension.(table 4-5)

Table 4: Mean value of various modifiable and non-modifiable risk factors

Parameter	Mean Value (mean + SD)
BMI	24.5 +3.33 kg/m^2
FBS	248 + 82 mg/dl
PP2BS	332 + 80 mg/dl
HbA1C	12 + 2.7 %
Duration of Diabetes Mellitus	7.2 + 6.6 years
Waist circumference	91.5 + 12.5 cm
Total cholesterol	175 + 45 mg/dl
Triglycerides	182 + 76.2 mg/dl

Table 5: other modifiable risk factors of diabetic neuropathy

Modifiable Risk Factors	Number of Patients	Percentage
Hypertension	26	57%
BMI >23	31	69%
Hypercholesterolemia (>200 mg/dl)	12	27%
Hypertriglyceridemia (>150 mg/dl)	31	69%

5. Discussion

1. In our study of 45 patients, all patients had distal symmetrical peripheral neuropathy. Chronic sensorimotor distal symmetric polyneuropathy is the most common form of neuropathy in diabetic Neuropathies [7, 8].
2. Age group in our study ranged from 18-82 years. Among this, prevalence of diabetic peripheral neuropathy was more in 60-69 years (40%) and 50-59 years (22%) age group which suggest that prevalence of neuropathy increase as age advanced.
   Behl *et al.* [9] demonstrated that middle age/elderly diabetic were generally more affected. Shaw *et al.* [10] showed incidence of peripheral neuropathy was 17.6% between age group of 20-40 years and 56.8% between 40-70 years. Kasturi *et al.* [11] successfully done study on 100 patients and found incidence of peripheral neuropathy as 24% in age group 21-40 years & 58% in 40 to 70 years age group. Mean age of our study group was 58.8±11.8 years. Jain *et al.* [12] (2016) reported the same result (56±12.3 years) of mean age group. Jayprakash *et al.* [13] reported 53.3±11.8 years as a mean age for diabetic peripheral neuropathy.
3. Most common symptom was numbness and tingling of extremities (91%) in our study group. In study of Adgaonkar *et al.* [14], most common symptom of DSPN was tingling and numbness, present in 100% of patients.As per discussion in Diabetes care 2017 [15] the most common early symptoms are induced by the involvement of small fibers and include pain and dysesthesias (unpleasant sensations of burning and tingling).
4. Most common sign of DSPN was absent ankle reflex in study population, in 97% patients with DSPN ankle reflex was absent. As per study published by Jayprakash et al. [13], Loss of ankle reflex had sensitivity of 90.7 %, specificity of 37.3 %, PPV (positive predictive value) 56.1%, NPV(negative predictive value) 81.7%, accuracy of 69.6%. In study by Tres *et al.* [16] sensitivity and specificity for absent ankle reflex was 75 and 89 percent. The disadvantage of relying purely on absent ankle reflex for peripheral neuropathy diagnosis is the high prevalence of absent ankle reflex even in normal population [17]. Second most common sign was impaired vibration on dorsum of foot, present in 78% of patients. As per study published by Jayprakash *et al.* [13], Vibration sensation with tuning fork 128 Hz had 62.5 % sensitivity, 95.3 % specificity, PPV of 93%, NPV of 71.3%, accuracy of 78.9%. The sensitivity and specificity of vibration testing for peripheral neuropathy has been estimated to be 53 and 99 per cent, respectively in study by Singh N *et al.* [18] In study of Adgaonkar *et al.* [14], Most common sign was impaired vibration present in 86% of the patients, followed by absent ankle jerk, present in 80% of the patients. The

good correlation between VPT(Vibration Perception Threshold) score with tuning fork, monofilament and ankle reflex shows that simple bed side tests are useful in clinical practice, even in those subjects in whom foot care practices are not followed. Also Combinations of more than one test have >87% sensitivity in detecting DSPN (ADA2017) [3], So this simple bed side tests- vibration perception by 128 Hz tunning fork and ankle reflex provide good bed side practice value in diagnosis of diabetic neuropathy

5. In study population 26 patients (58%) patients were known case of diabetes mellitus since more than 5 years. Most patients were from group 5 to 10 years duration of diabetes. Only 15% patients were known case of diabetes since less than 1 year of duration. In study of Adgaonkar *et al.* [14], maximum incidence was noted where duration of diabetes was >6 years. Kasturi *et al.* [11] also found the positive correlation between duration of diabetes mellitus and incidence of peripheral neuropathy. In our study, mean duration of diabetes mellitus in study population was 7.2± 6.6 years; that is similar to the mean duration of 7.18± 6.92 years in study by Jayprakash *et al.* [13].
6. 74% patients had FBS > 200 mg/dl, 98% had PP2BS > 200 mg/dl and 87% of patients had HbA1c > 9 %. In study of Adgaonkar *et al.* [14[, maximum patients of peripheral blood sugar levels of fasting 200 to 220 mg/dl & post meal more than of 260 mg/dl showed the presence of peripheral neuropathy. Behl *et al.* [9] in a study of 539 diabetic patients found direct correlation of severity of hyperglycemia with incidence of peripheral neuropathy. Mean FBS in our study group was 248 ± 82 mg/dl. That correlate well with study by Jain *et al.* [12] which is 223+71mg/dl. In study by Jayprakash *et al.* [13] mean FBS was 149 ± 57.56 mg/dl. In study of Adgaonkar *et al.* [14], Maximum patients of PP2BS more than of 260 mg/dl showed the presence of peripheral neuropathy. In our study group majority (87%) of the patients had HbA1C level >9 %, suggestive of poor glycemic control, with mean HbA1C of 12±2.7% in study population. In study carried out by Jain *et al.* [12] 60% of patients with diabetic neuropathy had HbA1C level > 9%, with mean HbA1C of 9.2±2.3.
7. Among 45 patients with diabetic peripheral neuropathy, 69% of patients were overweight to obese with BMI >23 kg/m2. With mean BMI of study population was 24.5±3.33 kg/m2. In study of Jain *et al.* [12] and Jayprakash *et al.* [13] it was 28.1+12.2 and 25.2±4.96 respectively. In our study 69% of patients had hypertriglyceridemia, with mean value of 182±76.2 mg/dl. Comparable with value of study by Jayprakash *et al.* [13] 163.10 ± 76.89 mg/dl. In study 57% patients had hypertension. Aggressive treatment of hypertension is now standard practice in the management of nephropathy and retinopathy, and the result of present study make a case for clinical trials to confirm the efficacy of antihypertensive agents and other strategies to reduce cardiovascular risk reduction in slowing the progression of neuropathy [19]. As per data published cardiovascular risk factors, such as hypertension, obesity, and elevated triglyceride levels, and the presence of cardiovascular disease at baseline appear to be related to newly diagnosed neuropathy [19].
8. In study population 52 % of patients with diabetic peripheral neuropathy had presence of diabetic retinopathy changes on dilated fundus examination. 56% of patients among patients with diabetic neuropathy and normal serum creatinine had presence of albuminuria in urine examination suggestive of nephropathy changes. Peripheral neuropathy, a common microvascular complication of diabetes, is often associated with concomitant retinopathy and albuminuria [3]. Individuals with diabetes with early retinal arteriolar abnormalities are more likely to have diabetic peripheral neuropathy, independent of hyperglycemia and major vascular risk factors [3].

6. Conclusion

1. Distal symmetrical Sensory motor polyneuropathy is the most common in diabetic peripheral neuropathy.
2. Prevalence of peripheral neuropathy increases with increase in age of patients, duration of diabetic mellitus and poor glycemic control.
3. Most common symptom of DSPN is tingling and numbness of extremities.
4. Most common sign of DSPN is absent ankle reflex and impaired vibration sensation. Combination of 2 or more parameters of DSPN provide high sensitivity and specificity of diagnosis. It can predict neuropathy before development of DSPN related complications like foot ulcers.
5. Development of diabetic peripheral neuropathy is associated with other modifiable risk factors namely, hypertension, high BMI, hypertriglyceridemias etc.
6. Diabetic neuropathy is associated with development of other microvascular complications namely diabetic retinopathy and diabetic nephropathy, owing to common pathway of pathogenesis.

7. References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27:1047-53.
2. McCance Dr, hadden Dr, Atkinson AB, *et al.* The relationship between long-term glycemic control and diabetic nephropathy. QJ Med. 1992; 82:53-61
3. Mengistu M. The pattern of chronic complications in adult Ethiopian Diabetics: Ethiop. Med J. 1987; 25:167-176
4. Michael J. Fowler, MD, Microvascular and Macrovascular Complications of Diabetes; Clinical Diabetes. 2008; 3(2).
5. Vascular Risk Factors and Diabetic Neuropathy: Nengl j med. 2005; 352:1925-1927. www.nejm.org
6. Michael J. Fowler, MD, Microvascular and Macrovascular Complications of Diabetes; Clinical Diabetes. 2008; 26(2).
7. Melton LJ, Dyck PJ. Epidemiology: In: Diabetic Neuropathy. 2nd ed. Philadelphia: W.B. Saunders; 1999
8. Diabetes Care. 2003; 26:697-701.

9. BehlA, Khosla HL, Caroli RK. A study of the involvement of the nervous system with special reference to neuropathy in diabetes mellitus. Indian Med Gaz. 1967; 24:53.
10. Shaw JE, Hodge AM, deCoruten M, Dowse GK, Gareeboo H, Tuomilehto J *et al*. Diabetic peripheral neuropathy in Mauritius: Prevalence and risk factors. Diabetes Res ClinPract., 1998; 43(2):131-139
11. Kasthuri AS, Sofat MS, Kumar N. Somatic peripheral neuropathy in diabetes mellitus. MJAFI. 2000; 56:33-3.
12. Sandeep Kumar Jain, M.S. Johri. Study to know the prevalence of microvascular complications in type 2 diabetes mellitus patients. International Journal of Contemporary Medical Research. 2016; 3(7):1992-1994.
13. Jayaprakash. Indian J Med Res 133. 2011; pp. 645-64949.
14. Adgaonkar, *et al.* Sch. J App. Med. Sci. 2014; 2(4C):1347-1350.
15. Microvascular Complications and Foot Care; Diabetes Care. 2017; 40(1).
16. Tres GS, Lisbôa HR, Syllos R, Canani LH, Gross JL. Prevalence and characteristics of diabetic polyneuropathy in Passo Fundo, South of Brazil. Arq Bras Endocrinol Metabol. 2007; 51:987-92.
17. Meijer JW, Sonderen EV, Blaauwwiekel EE, Links TP. Groothoff JW, Eisma WH, *et al.* Diabetic Neuropathy Examination: a hierarchical scoring system to diagnose distal polyneuropathy in diabetes. Diabetes Care. 2000; 23:750.
18. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in 1. Patients with diabetes. JAMA. 2005; 293(28).
19. Vascular Risk Factors and Diabetic Neuropathy: Nengl j med. 2005; 352:1925-1927. www.nejm.org