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"UNCOVERING THE BURDEN OF DIABETIC PERIPHERAL NEUROPATHY: A HOSPITAL-BASED STUDY ON PREVALENCE AND RISK FACTORS

Sanjay Dattatraya Bhalerao[1*], Manila Jain[2], Avinash Prabhakar Kulkarni[3]

[1*]Department of Physiology, Index Medical College & Hospital, Indore, MP
[2]Prof & HOD, Department of Physiology, Index Medical College & Hospital, Indore, MP
[3]Department of Physiology, BGS Medical College & Hospital, Bangalore

Corresponding Author: Sanjay D.Bhalerao
*Department of Physiology, Index Medical College & Hospital, Indore, MP, Mobile: 9844491356, email Id : drsanjaydbhalerao@yahoo.com

ABSTRACT

Introduction: Diabetes Mellitus (DM) is becoming a significant health concern due to its severe complications. In India, the prevalence of type 2 diabetes mellitus (T2DM) is likely to vary across regions due to differences in lifestyles and demographic factors. DM is also well known for its chronic complications, collectively referred to as "tripathy," which includes neuropathy, retinopathy, and nephropathy. Among these, diabetic neuropathy, particularly Diabetic Peripheral Neuropathy (DPN), is the most common clinical complication. The presence of DPN is linked to a worsened prognosis and a reduced quality of life. The likelihood of developing peripheral neuropathy in DM depends on various factors. It is crucial to evaluate the prevalence and risk factors in order to develop strategies that can slow or halt the disease's progression. Since there is no definitive data on the prevalence and risk factors for diabetic peripheral neuropathy, this study aims to assess them within a hospital setting.

Material and Methods: A cross sectional study was conducted to find out the prevalence and risk factors for diabetic peripheral neuropathy in T2DM individuals of age above 30 years visiting Index Medical College and Hospital, Indore, Madhya Pradesh. 400 participants having type 2 diabetes participants were enrolled in the study. Participants identified as T2DM were screened and assessed by using diabetic Neuropathy Examination Score (DNE) to identify the presence of diabetic peripheral neuropathy.

Results: - Overall prevalence of DPN was found to be 49.35%. Prevalence was increase with advancement of age, more than 60 years of age (90.32%). Male's had higher prevalence (79.98%) as compare to female participants (60.53%). Age, diet, BMI, truncal obesity, smoking, alcohol consumption and family history of diabetes appear to increase the risk for developing DPN. Furthermore, advance age and duration of diabetes appear to be risk factors fordeveloping DPN in the T2DM participants.

Conclusion: - The high prevalence of DPN in the study area indicates the influence of socioeconomic changes on the occurrence of the disease. The Diabetic Neuropathy Examination score can serve as effective screening tools for assessing DPN in community settings. It is essential to implement screening and awareness programs for the early detection of diabetic complications to prevent long-term consequences. The study's findings highlight the importance of promoting preventive measures to avoid or delay the onset of chronic diabetes complications. This can be achieved through proper glycemic control, regular monitoring, lifestyle changes, and the practice of exercise and yoga to

maintain a healthy balance between sympathetic and parasympathetic tone.

Key words: autonomic function tests; type 2 diabetes mellitus; diabetic peripheral neuropathy; autonomic dysfunction; diabetic symptom score; diabeticneuropathy examination score.

INTRODUCTION:

Diabetes Mellitus (DM) is widely recognized for its microvascular complications, often referred to as "tripathy," which includes diabetic neuropathy, retinopathy, and nephropathy. Diabetic retinopathy can lead to visual impairments, including reduced vision and potential blindness. Diabetic nephropathy, caused by the impact of diabetes on the kidneys, results in the loss of small or progressively larger amounts of protein in the urine, leading to chronic kidney disease that may eventually require dialysis. Another prevalent and significant complication of diabetes is diabetic neuropathy (DN),[1-5] which is a diverse condition affecting both sensory and motor nerves, as well as the autonomic nervous system. Symptoms of DN typically include numbness, tingling, and pain in the feet, and can also increase the risk of skin damage due to altered sensation. DN can affect various organ systems, including the gastrointestinal, urogenital, and cardiovascular systems. When combined with vascular disease in the legs, neuropathy increases the risk of diabetes-related foot issues, such as diabetic foot ulcers, which are difficult to treat and may sometimes require amputation. The pathogenesis of DN involves several factors, including altered metabolism, vascular insufficiency, loss of growth factors, and autoimmune nerve destruction in both visceral and cutaneous areas.[6-10] Despite its significant impact on survival and quality of life, DN remains one of the least recognized and understood complications of diabetes. The most common forms of DN are diabetic autonomic neuropathy (DAN) and diabetic peripheral neuropathy (DPN). DAN affects the nerves controlling heart rate, blood pressure, blood glucose regulation, and other internal organs, leading to issues such as digestive problems, respiratory dysfunction, urinary difficulties, sexual dysfunction, and vision issues. It also affects the system responsible for restoring normal blood glucose levels after a hypoglycemic episode, causing the loss of warning signs like sweating and palpitations.[11-17]

DPN, a prevalent complication, is estimated to affect 30% to 50% of individuals with diabetes. The most common form of DPN is chronic sensorimotor distal symmetric polyneuropathy. Epidemiological data shows that the prevalence of DPN is higher in type 2 diabetes compared to type 1. Studies have observed peripheral neuropathy in about one-third of patients with type 1 diabetes (T1DM) and more than half of those with type 2 diabetes (T2DM). However, other cohort studies have found that 66% of T1DM and 59% of T2DM patients had objective evidence of DPN. Despite being one of the most common long-term complications of diabetes, the prevalence of DPN remains largely unknown, as studies vary significantly in their definitions, methods of assessment, and patient selection.[17-26] The slow and insidious onset of DPN may contribute to a lack of awareness among patients, leading to prolonged undiagnosed suffering. Early diagnosis and intervention are crucial in preventing the severe consequences of diabetic complications. Due to the limited number of studies on the prevalence and risk factors of DPN, this study aims to assess these factors among individuals with type 2 diabetes (T2DM).

METHODOLOGY

A cross-sectional study was carried out at Index Medical College and Hospital from Dec.2022 to. Dec.2023 The study was approved by the Index Medical College and Hospital Institutional Ethics Committee and voluntary Informed consent was taken from all participants before enrolling into the study. Participants of age 30 years and above, with symptoms of T2DM and known cases of type 2 diabetes mellitus were included in the study. Exclusion criteria for the study included individuals who refused to provide informed consent, pregnant women or those who had delivered a baby weighing 4.5 kg or more, as well as women with a history of gestational diabetes. Additionally, individuals with Type 1 Diabetes Mellitus (T1DM), cognitive, neurological, psychological, or endocrinal disorders, and those with congenital heart diseases were excluded. The sample size was calculated

based on a reported prevalence of 39.3%, similar to the study area, with an absolute error of 5% and a 95% confidence level, resulting in an estimated sample size of 382. Participants' personal details and history were collected through a pre-designed questionnaire covering demographic, behavioral, social, and biological variables. Education level was classified according to the International Standard Classification of Education, and literacy was categorized as illiterate, primary, secondary, or graduate and above. Occupation was classified into workers (skilled, unskilled, or professional) and non-workers (homemakers or elderly persons). Smoking and alcohol consumption patterns were also recorded. A detailed family history of Type 2 Diabetes Mellitus (T2DM) was documented, with family history verified through blood glucose measurements or physician reports. Known T2DM cases were included, with details on the duration of diabetes and medication. Anthropometric measurements included weight, height, BMI (using Quetelet's equation), waist and hip circumference, waist-to-hip ratio, and classifications for central and truncal obesity. Blood pressure was measured in the sitting position, and participants were classified as hypertensive if diagnosed previously or if their systolic blood pressure (SBP) was >140 mmHg or diastolic blood pressure (DBP) was >90 mmHg.[26-41] The assessment of Diabetic Peripheral Neuropathy (DPN) was conducted using the Diabetic Neuropathy Examination (DNE) scores. Participants were provided instructions on the procedure, which involved a comprehensive neurological examination similar to the earlier Neuropathy Disability Score (NDS). The DNE score comprises eight components: two assessing muscle strength, one for tendon reflex, and five for sensory tests. The total score ranges from 0 to 16, with a score greater than 3 points indicating abnormal findings. Muscle strength was evaluated in the quadriceps femoris and tibialis anterior, reflexes were assessed by the ankle reflex, and sensations including pinprick sensitivity, touch sensitivity, vibration perception, and joint position sense were tested, all on the right leg and foot. For each test, scores were assigned as 0 (normal), 1 (mild/moderate deficit), or 2 (severely disturbed/absent). The MRC scale (3-4) was used for muscle strength, with reflexes and sensations categorized as decreased but present (score of 1) or absent (score of 2). A score greater than 3 points indicated the presence of polyneuropathy.[42] Statistical analysis was performed using the SPSS software (trial version 16). A significance level of $P \leq 0.05$ with a 95% confidence interval (CI) was used to determine statistical significance. The study employed descriptive statistics, chi-square tests for associations, and regression analysis to estimate risk factors.

RESULTS

Of the 385 screened participants (mean age of 52.26±8.84 years), majoritybelonged to age group of 40-49 year (31.94%), ≥ 60 years (40.25%) and 50-59 years (20.77%) whereas the participants with age group of 30-39 years constituted a very less portion (7.2 %). There were more females (57.92%) than males. Nearly half (42.85%)of the participants were illiterate and around one thirds of them (22%) had Primary school education while very few had completed primary school education (17%) and graduation (23%). Majority of participants were farmers (Skilled I –46.75%) and not involved in active work (Housewives and older people – 23.37%). Majority were consuming mixed diet (79.22%). Nearly two-thirds of the participants were overweight (35%) and nearly half of them had both central and truncal obesity (63.63.2%). Among the males, approximately half of the participants were smokers (44.9%) and alcoholics (69.13%). Nearby, three fourth of the participants had family history of diabetes (63.09.4%). (Table 1,2)

The mean Age (P =0.002), Weight (P<0.001), BMI (P <0.001), SBP (P<0.001) and Fasting blood sugar (P <0.001) were significantly higher in T2DM participants as compared to non-diabetics. (Table 2)

Majority of the T2DM participants (60.28%) showed severe deficit in sensation which includes burning foot sensation, numbness of the foot, almost nearly 1/3rd of them were had pricking sensation in the foot (39.79%). Nearly 2/4th of them showed abnormal tactile localization (62.43%) and tactile discrimination (65.17%). 3/4th T2DM participants (63.13%) had neuropathy on vibration perception. Almost 60.77% of the T2DM participants had diminished ankle reflex and muscle strength (59.74%). (Table 3).

Overall prevalence of the diabetic peripheral neuropathy in the study area was 49.35%. (Figure 1).

The age of the participants showed significant association with the prevalence of DPN (P < 0.001). (Figure 2) In comparison with the age group of 30-39 years and 40-49 years, the age group of 50-59 years (85%) and ≥ 60 years (90.32%) had higher prevalence of DPN. The relationship between gender (P = 0.002) and prevalence of DPN was found to be significant. Males had slightly higher prevalence of DPN (70.98 Vs 60.53%) than females. There was no significant differences in the prevalence of DPN within smokers, alcoholics, family history of diabetes, consuming mixed diet, and overweight, obese and with truncal obesity. Longer duration of diabetes (P < 0.001) and presence of DPN were found to be significantly associated. Prevalence of DPN was higher in the participants with duration of diabetes >11 years (97.61%) and 6-10 years (95.91%) as compared to the newly diagnosed. There was significant increase in the prevalence of DPN with increase in the age. (P < 0.001) In comparison with age group of 30-39 years,40-49 years and ≥ 60 years, agegroup of 50-49 years (OR 235.25 CI 5.541-865.9, P = 0.004) had highest risk for development of DPN. (Figure 4.15.2.1) Longer duration of diabetes (P < 0.001) showed significant association with prevalence of DPN. (Figure 4.15.2.2) Participants with duration of diabetes ≥ 11 years, 6-10 years and ≤ 5 years had 565.5-fold, 175.5-fold of higher risk of having DPN respectively as compared to newly diagnosed. Out of 11 factors analyzed, only 3 potential risk factors (age, gender and duration of diabetes) had significant association with prevalence of DPN in Multivariate analysis.(Table 4,5, 6)

Table 1: Socio-Demographic Details of study participants in the study area

Characteristics	Category	Number (N)	Percentage
Age	30-39	50	13.08
	40-49	177	46.33
	50-59	65	17.01
	≥60	90	23.56
Gender	Male	138	36.12
	Female	244	63.87
Education	Illiterate	165	42.85
	Primary school	85	22
	Secondary school	75	19.48
	Graduation and above	60	15.58
Occupation	Skilled I	180	46.75
	Skilled II	40	10.3
	Skilled III	25	6.49
	Skilled IV	50	12.98
	Non workers	90	23.37
Diet	Veg	80	20.77
	Mixed diet	305	79.22
BMI	≤18.5-18.9	6	1.5
	19-24.9	80	20.77
	25-29.9	145	37.66
	≥30	154	40
Central Obesity	Yes	198	51.42
	No	187	48.57
Truncal Obesity	Yes	178	46.23
	No	207	53.7
Smoking	Yes	212	55
	No	123	44.9

Alcohol consumption	Yes	223	57.92
	No	162	42.07
Family History of DM	Yes	133	34
	No	252	65.65
Total		**385**	**100**

Table 2: Comparison of anthropometric & biochemical variables betweendiabetic and non-diabetic participantse

Variable	Category	Mean ± SD	P value
Age*	Non-diabetic	53.02±8.5	0.001*
	T2DM	55 .43±8.5	
Height	Non-diabetic	157.4±8.1	< 0.001*
	T2DM	153.8±8.2	
Weight*	Non-diabetic	57.6±7.8	< 0.001*
	T2DM	68.27±8.4	
BMI*	Non-diabetic	25.43±3.2	< 0.001*
	T2DM	29.25±4.5	
Waist-Hip Ratio	Non-diabetic	0.87±0.06	0.075
	T2DM	0.98±0.07	
FBS*	Non-diabetic	99.2±11.4	< 0.001*
	T2DM	135.2±37.1	
SBP*	Non-diabetic	120.4±10.5	< 0.001*
	T2DM	130.0±13.2	
DBP	Non-diabetic	85.7±5.5	0.390
	T2DM	86.5±8.4	

***Significantly higher among T2DM participants (P < 0.05)**

Table 3: Distribution of type-2 diabetes mellitus participants according to the Sensory test, Joint position, ankle reflex, vibration perception test and Muscle strength

Category	N (%)
Sensitisation (Fine and Crude Touch)	
Normal	189(49.09)
Mild / Moderate deficit	78(39.79)
Severely deficit/Absent	118(60.20)
Tactile localization	
Normal	180(46.75)
Mild / Moderate deficit	77(37.56)
Severely deficit/Absent	128(62.43)
Tactile discrimination	
Normal	180(46.75)
Mild / Moderate deficit	70(34.82)
Severely deficit/Absent	133(65.17)
Vibration Perception Test	
Normal	168(43.63)
Mild / Moderate deficit	80(36.86)
Severely deficit/Absent	137(63.13)
Joint Position	
Normal	182(47.27)
Mild / Moderate deficit	70(34.48)
Severely deficit/Absent	133(65.51)
Ankle reflex	
Present	151(39.22)
Absent	234(60.77)
Muscle strength	
Present	155(40.25)
Absent	230(59.74)

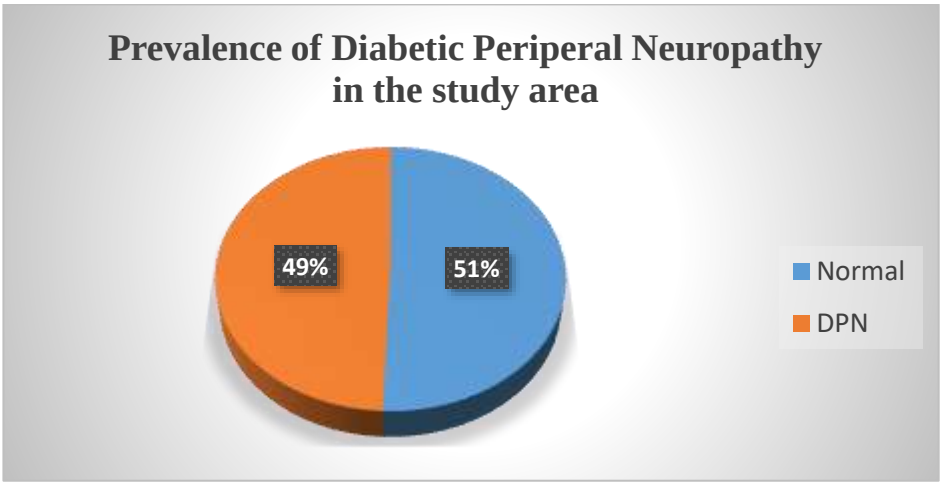

Figure 1: Prevalence of Diabetic peripheral Neuropathy in the study area

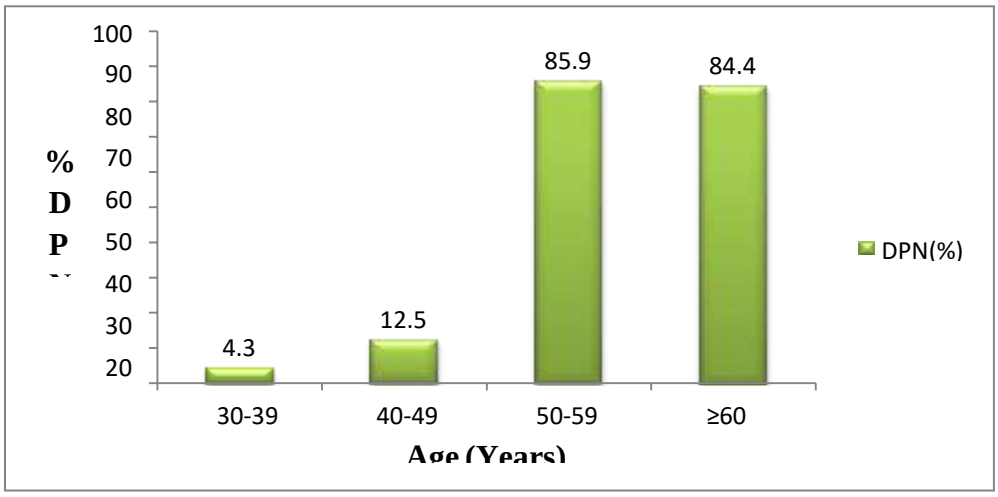

Figure 2: Association between age groups and prevalence of DPN-DNEscoring method

Figure 3: Association between duration of diabetes and prevalence of DPN –DNE scoring method

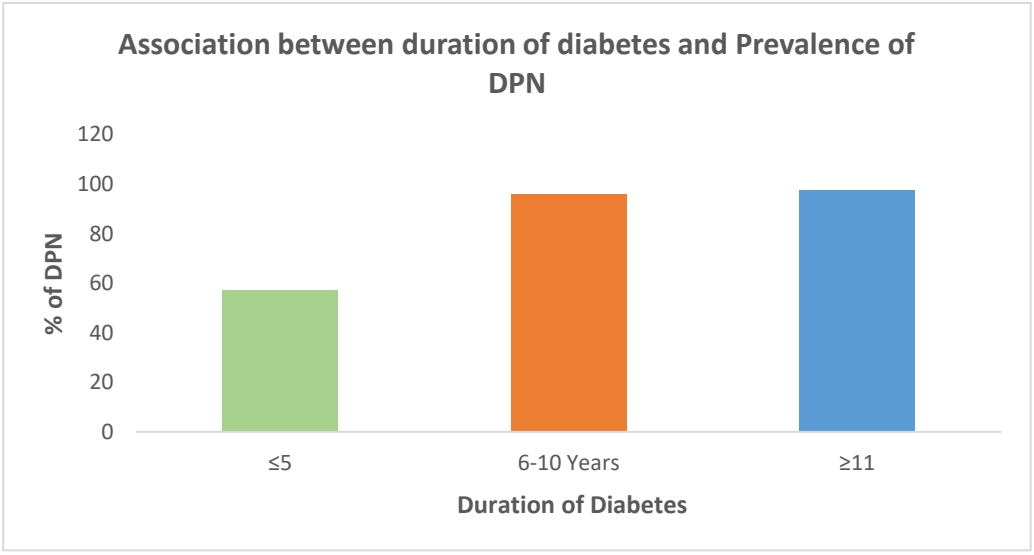

Table 4: - Association between age, gender, smoking, alcohol consumptionand prevalence of DPN – DNE method

Potential riskfactors	Sub-Category	DNS Score ≤ 0	Diabetic neuropathy Examination Score(DNE) Score ≥ 3
Age*	30-39	28((7.2)	2(4.3)
	40-49	123(31.94)	22(17.88)
	50-59	80(20.77)	68(85)
	≥60	155(40.25)	140(90.32)
		$\chi 2 = 2.442$, df = 3, P < 0.001*	
Gender*	Male	162(42.07)	115(70.98)
	Female	223(57.92)	135(60.53)
		$\chi 2 = 6.200$, df = 1, P = 0.002*	
	No	212(55.06)	135(63.67)

		))	
Smoking	Yes	173(44.93)	85(49.41)
χ^2 = 0.003, df = 1, P = 0.901			
Alcohol consumption	No Yes	227(58.96)	120(53.81)
		158(41.03)	112(66.66)
χ^2= 2.310, df = 1, P = 0.122			
Family History of DM	No	133(34.45)	68(51.12)
	Yes	252(65.45)	161(63.88)
χ^2 = 2.021, df = 1, P = 0.140			

Figures in parentheses indicate the percentage of respective frequency,χ^2 = Chi-square value and df = degree of freedom
**Potential risk factors significantly associated with prevalence of DPN*

Table: 5 - Association between diet, BMI, central, truncal obesity, duration ofdiabetes and prevalence of DPN – DNE method

Potential predictors	Sub-Category	DNS Score ≤ 0	Diabetic neuropathy Examination Score(DNE) Score ≥ 3
Diet	Veg	115(24.3)	60(52.2)
	Mixed	359(75.7)	220(61.3)
χ^2= 2.890, df = 1 , P < 0.070			
BMI	≤18.9	5(1.1)	3(60)
	19-24.9	103(21.7)	57(55.3)
	25-29.9	209(44.1)	130(62.2)
	≥30	157(33.1)	90(57.3)
χ^2= 1.540, df =3, P = 0.622			
Central obesity	No	253(53.4)	150(59.3)
	Yes	221(46.6)	130(58.8)
χ^2= 0.015, df = 1, P = 0.912			
Truncal obesity	No	230(48.5)	140(60.9)
	Yes	244(51.5)	140(57.4)
χ^2= 0.578, df = 1, P = 0.433			
Duration of	New	175(36.9)	2(1.1)

DM*			
	≤5Years	38(8)	22(57.9)
	6-10	123(25.9)	120(97.6)
	≥11	138(29.1)	136(98.6)
χ^2= 4.024, df = 3, P < 0.001*			

Figures in parentheses indicate the percentage of respective frequency,χ^2 = Chi-square value and df = degree of freedom
**Potential risk factors significantly associated with prevalence of DPN*

Table 6: - Socio-demographic and anthropometric risk factors for DPN

Risk factors	Sub-Category	Multivariate analysis		
		DNE scoring method		
		OR	95%CI	P value
Age* (Years)	30-39	1	-	-
	40-49	55.418	1.476-213.3	0.021*
	50-59	224.25	5.541-865.9	0.002*
	≥60	190.57	5.898-746.1	0.001*
χ^2= 2.432, df = 3, P < 0.001*				
Duration of DM* (Years)	≤ 5	1	-	-
	6-10	175.5	222.79-115.6	<0.001*
	≥11	566.8	420.51-675.3	<0.001*
χ^2= 4.073, df =2, P < 0.001*				
Gender	Male	1	-	-
	Female	0.565	0.175-1.689	0.267
χ^2= 6.209, df =1, P = 0.022*				

**Risk factors for DPN (P<0.05), χ^2 = Chi-square value and df = degree of freedom,OR = odds ratio*

DISCUSSION

Diabetic peripheral neuropathy (DPN) is a common complication of diabetes mellitus and can often

be the first symptom in individuals with type 2 diabetes mellitus (T2DM). The prevalence of DPN ranges from 5% to 100%. In the current study, 49.35% of participants with T2DM showed clinical signs of diabetic peripheral neuropathy, while other studies, such as one by Franklin et al., reported a prevalence of 27.8%. Additionally, Ashok S and his team found that 5.4% of T2DM patients had neuropathy at the time of diagnosis. The variation in DPN prevalence across different studies may be attributed to differences in the methods used to assess it. The present study relied on clinical examination, including the Diabetic Neuropathy Examination (DNE) score.[43-45]

The results of the current study indicated that the prevalence of diabetic peripheral neuropathy (DPN) increases with age and the duration of diabetes, suggesting that both age and diabetes duration are risk factors for DPN. Additionally, the study found that participants aged 60 years or older and with a diabetes duration of 11 years or more had a higher risk of developing DPN. This finding aligns with a study by Fargol Booya et al., conducted on 110 patients in Iran, which also identified age and diabetes duration as key contributors to DPN development. Similarly, a study by R. Predeepa and Rema M on an urban South Indian population showed results consistent with our observations. Furthermore, the present study revealed a significant association between gender and the prevalence of DPN, while factors such as diet, BMI, truncal and central obesity, smoking, alcohol consumption, and family history of diabetes did not show significant associations. These findings are similar to those reported in a multicenter study by MJ Young et al. on the prevalence and risk factors of DPN in the United Kingdom. In conclusion, our study found a higher prevalence of DPN in the study area, with age, occupation, smoking, alcohol consumption, family history of diabetes, diet, BMI, and truncal obesity identified as relative risk factors for DPN. Moreover, advanced age and longer duration of diabetes appear to be significant risk factors for developing DPN.[46,47]

CONCLUSION:

A notably high prevalence of diabetic peripheral neuropathy (DPN), greater than initially expected, was observed in the population of Indore, Madhya Pradesh. The findings from this study could be valuable in tailoring local strategies for planning, implementing, and evaluating national health programs such as the National Programs for Control of Diabetes, Cardiovascular Diseases, and Stroke (NPDCS). The high prevalence of DPN in both urban and rural areas of Indore highlights the influence of socioeconomic changes on the occurrence of DPN.

The parameters used in this study for assessing DPN, including the DNE scoring method, align with the recommendations of the European Society of Cardiology Task Force and the ADA & AAN. The study showed a decline in DNE clinical assessment values, which not only have negative prognostic significance but also may precede the clinical onset of DPN.

Increasing age and longer diabetes duration were identified as risk factors for DPN development. The DNE scoring method can serve as an effective screening tool for assessing DPN in community settings. There is a pressing need to implement screening and awareness programs for the early detection of diabetic complications to prevent long-term effects. The results of this study emphasize the importance of promoting preventive measures, including good glycemic control, regular monitoring, lifestyle changes, exercise, and yoga, to prevent or delay the onset of chronic diabetes complications and maintain a balanced sympathetic and parasympathetic tone.

RECOMMENDATIONS

Given the high prevalence of Diabetic Peripheral Neuropathy (DPN) found in individuals with Type 2 Diabetes in this study, it is recommended to incorporate routine DPN screening into clinical practice. Early detection of DPN is essential to prevent severe complications like foot ulcers, infections, and amputations. Healthcare providers should employ simple, cost-effective screening methods such as the 10g monofilament test, vibration perception test, and thorough foot examinations during regular check-ups for diabetic patients. These screening tools can help identify neuropathy early, enabling timely interventions to slow its progression.

The study also underscores poor glycemic control as a major risk factor for the development and progression of DPN. As a result, it is crucial for healthcare professionals to prioritize maintaining

optimal blood glucose levels in individuals with Type 2 Diabetes. This can be achieved by educating patients on the importance of consistent blood glucose monitoring and adherence to prescribed treatments. Additionally, healthcare providers should aim for an HbA1c level below 7%, which has been shown to lower the risk of developing diabetic complications, including DPN. Lifestyle changes such as adopting a healthy diet, engaging in regular physical activity, and managing weight should also be promoted as part of a comprehensive diabetes management plan.

LIMITATIONS OF THE STUDY

Measuring HbA1c would have offered a more accurate evaluation of the individuals' glycemic control. Examining the dose-response relationship between smoking and alcohol consumption could have provided a more thorough understanding of their association with the development of diabetic neuropathy. Additionally, using vibration perception as a method to assess diabetic peripheral neuropathy could be considered as a straightforward screening tool for use in community settings.

CONFLICT OF INTREST: there is no conflict of interest

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