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Risk Factors Associated with Peripheral Neuropathy in Type 2 Diabetic Patients at Tertiary Care Hospital-A Cross Sectional Study

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ABSTRACT

Objectives: This study was aimed to determine the prevalence of DPN among patients visiting a tertiary care hospital and the associated risk factors. Methods: A cross-sectional study was conducted among 273 type-II diabetics attending a General Medicine OPD of tertiary care hospital. Toronto clinical scoring system was used for detecting peripheral neuropathy. Data analysis was done using SPSS version 16.0. The association of risk factors with the presence of DPN was analysed by using Pearsons chisquare test. The accepted level of significance was set below 0.05 ($P<0.05$).Results: The Prevalence of peripheral neuropathy in our study was found to be 45.4%. Prevalence of DPN increased in the participants with increased age, increased duration of diabetes, increased HbA1c and increased BMI, with Hypertension & dyslipidimea and it is statistically significant with $p<0.001$. Prevalence of DPN was found higher among the male participants & smokers and it is statistically significant with $p<0.05$ & $p<0.001$ respectively. Conclusion: As there is a high prevalence of peripheral neuropathy among type-II diabetic patients, early detection through routine screening and regular follow up examinations will be helpful in preventing the progression of Neuropathy.

Key words:
Diabetic peripheral neuropathy (DPN); Risk factors; Toronto clinical scoring system (TCSS)

Introduction:

International Diabetes Federation (IDF) has estimated that there were 463 million people with diabetes worldwide in 2019 and is predicted to increase by 2045 to 700 million [1]. India is one of the 7 countries of the IDF South East Asia (SEA) region and 88 million people of South East Asia (SEA) region have diabetes and is predicted to increase by 2045 to 153 million and there were over 77 million DM patients in India which is one of the 7 countries of the IDF SEA in 2019. [2]. Diabetes mellitus is well known to cause both vascular (micro and macrovascular) and non-vascular complications. Neuropathy is one of the most frequently encountered microvascular complications and it is one of the leading causes of non-traumatic lower limb amputation [3].

Diabetic Peripheral Neuropathy (DPN) is defined as the presence of peripheral nerve dysfunction in people with diabetics after exclusion of other causes [4]. Diabetic Peripheral neuropathy involving sensory nerves may don't have symptoms or may have symptoms like numbness, paraesthesia or burning pain in the hands and/or feet [5]. As a result of peripheral neuropathy, when a foot becomes

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insensate, it is predisposed to the occurrence of neuropathic ulcers which are a leading cause of limb amputation [6]. Therefore, early recognition of high-risk population is enormously important so that rigorous modification of risk factors, accompanying foot care, could be implemented before or at early stage of neuropathic process, to reduce further complication and to initiate appropriate intervention.

Nerve conduction study (NCS) is the gold standard test for the diagnosis of Peripheral Neuropathy. But it is cumbersome and expensive and not widely available [7]. So, a clinical scoring system which can be easily performed and that correlates well with NCS, is required. The TCSS is a clinical scoring system introduced by Bril and Perkins, and has been found to have a significant correlation with sural nerve myelinated fiber density in patients with diabetic neuropathy [8]. In India it has been validated by uday Shankar et al. [9].

The present study assessed the prevalence of diabetic peripheral neuropathy (DPN) based on TCNS score and its associated risk factors.

Methods:

Study design: The study was cross sectional hospital based observational study

Ethics approval: The study was approved by the Institutional ethics committee and informed consent was obtained from the study participants.

Locus of study: General medicine OPD, Viswabharathi Medical College and General Hospital, Kurnool.

Study period: December 2019 to November 2020.

Inclusion criteria: Type-II DM patients with ≥ 3 years of duration of both the sexes aged between 35-80 years were included in the study

Exclusion criteria: Patients with history of Type-I diabetics & taking lipid lowering drugs, Pregnant women/ women who had gestational diabetes, presence of foot ulcers and amputations, and participants with other known causes of peripheral neuropathy

Sampling technique: Purposive sampling technique

Sample size estimation: A sample size of 273 was calculated based on the prevalence of diabetic neuropathy to be 19% from a study done by Ashok S et al. [10] in South India with an absolute precision of 5% and 10% non-response rate using the formula $4pq/d^2$.

Data collection:

A questionnaire which included socio-demographic details such as age, sex, anthropometric details such as height, weight & BMI; smoking & Hypertension history; clinical and laboratory parameters such as Blood pressure, HbA1c, serum cholesterol, serum triglycerides, and Toronto clinical scoring system (TCSS) [8] score for detecting peripheral neuropathy were administered to each participant.

BMI: Participants weight and height readings were taken by using SECA height & weight measuring instrument and Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

Hypertension: Participants was measured on the right arm in the sitting position using mercury sphygmomanometer and considered to be hypertensive if SBP ≥140 mm Hg or DBP ≥ 90mm Hg or taking anti hypertensive treatment. [11]

Bio-chemical analysis: 5 ml of venous blood sample was collected after 8-12 hours overnight fasting. HbA1c, serum triglycerides and serum cholesterol measured. Analysis for serum total cholesterol and triglycerides was done on Stat Fax 3300 semi auto analyzer by enzymatic (CHOD-PAP) colorimetric method [12] and triglyceride by enzymatic (GPO-PAP) method. [13] Dyslipidemia was considered if total

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cholesterol was ≥ 200 mg/dl and total triglycerides ≥ 150mg/dl. [14]. Analysis for HbA1c was done on Robonik Prietest semi analyser by Immunoturbidimetric latex method. [15]

Diabetic peripheral neuropathy:Participants were screened for DPN using TCSS scale. Scoring was based on symptoms, sensory tests & reflexes. Depending upon the abnormalities, a point of 0 or 1 was given for symptoms and sensory tests and a point of 0, 1 or 2 was given for reflexes. Total score ranges from 0 to 19. Six points are derived from symptoms, eight from lower limb reflexes, and five from sensory examination distally at the toes. Components of the scale are Foot symptoms scores-Pain, Numbness, Tingling, Weakness and Ataxia. Upper-limb symptoms, reflexes-Knee reflexes and Ankle reflexes and sensory testing-Pinprick, Temperature, Light touch, Vibration and Position.
Severity of neuropathy was classified based on the score as: Score of 0-5= no peripheral neuropathy; 6-8= mild PN; 9-11= moderate PN; 12-19= severe. [8]

Statistics:
Data analysis was done by using Software Package of Social Sciences (SPSS) trial version 16.
Data were expressed as mean ± standard deviation for continuous variables and as percentages for categorical variables. Continuous data were analysed by using student unpaired t test. The association of risk factors with DPN was analysed by using Pearsons chi square test. The accepted level of significance was set below 0.05 ($P<0.05$)

Results:
A total of 273 type-II diabetes mellitus participants were included in the study;142 (52%) were male and 131(48%) were female.

The characteristics of participants was described in Table 1

TABLE 1 : Characteristics of participants

variable	Mean ± SD	category	n	(%)
Sex	-	Male	142	52
		Female	131	48
Age (Years)	54.75±9.65	<40	16	6
		40-49	69	25
		50-59	101	37
		60-69	70	26
		≥70	17	6
Hypertension	-	Present	111	41
		Absent	162	59
BMI (kg/m^2)	25.42±4.05	<18.5	6	2
		18.5-24.9	130	48
		25-29.9	98	36
		≥30	39	14
HbA1c (%)	6.12±0.57	≤6.5	212	78
		>6.5	61	22
	7.41±3.38	<6	101	37

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Duration of diabetes (years)		6-10	128	47
		>10	44	16
Serum cholesterol (mg/dl)	186.71±38.85	<200	191	70
		≥200	82	30
Serum triglycerides (mg/dl)	136.68±22.58	<150	221	84
		≥150	52	16
Dyslipidemia	-	Absent	179	65
		Present	94	34
Smoking	-	Present	76	28
		Absent	197	72

Overall, 124 patients were found to have DPN accounting for 45.4%. Prevalence of mild neuropathy was found to be 60%. Moderate neuropathy was found to be 27%, severe neuropathy was found to be 13%.

The comparison of continuous variables between DPN & Non DPN participants was mentioned in table 2

Table 2: Comparison of continuous variables between DPN & NON DPN participants

Demographic variable		Participants presenting DPN (n=124)	Participants not presenting DPN (n=149)	Student unpaired t test & P value
Age (Years)	Mean ± SD	57.47±9.6	52.50±9.06	p< 0.001**
BMI (kg/m^2)	Mean ± SD	27.81±3.42	23.43±3.42	P< 0.001**
Duration of Diabetes	Mean ± SD	8.63±3.70	6.52±3.02	P< 0.001**
HbA1c (%)	Mean ± SD	6.48±.51	5.79±.44	P< 0.001**
SBP (mmHg)	Mean ± SD	148.47±7.42	119.01±9.75	P< 0.001**
DBP (mmHg)	Mean ± SD	91.53±5.28	76.20±6.49	P< 0.001**
Serum triglycerides (mg/dl)	Mean ± SD	141.3±25.55	132.85±19.03	P< 0.001**
Serum cholesterol (mg/dl)	Mean ± SD	201.32±41.6	174.56±31.6	P< 0.001**

* Significance ** Highly significance

Association between various risk factors and prevalence of DPN was described in Table 3

Table 3: Association between various risk factors and prevalence of DPN

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Demographic variable		Participants presenting DPN (n=124)	Participants not presenting DPN (n=149)	Chisquare test & P value
Age (Years)	<40	0	16	P<0.001**
	40-49	29	40	
	50-59	44	57	
	60-69	37	33	
	≥70	14	3	
Gender	Male	74	68	P<0.05*
	Female	50	81	
BMI (kg/m^2)	<18.5	0	6	P< 0.001**
	18.5-24.9	28	102	
	25-29.9	65	33	
	≥30	31	8	
Duration of Diabetes (years)	<6	33	71	P< 0.001**
	6-10	56	63	
	>10	35	15	
HbA1c (%)	<6.5	54	140	P< 0.001**
	≥6.5	70	9	
Hypertension	Hypertensives	70	41	P< 0.001**
	Non-hypertensives	54	108	
dyslipidemia	Present	72	22	P< 0.001**
	Absent	52	127	
smoking	Smokers	63	13	P< 0.001**
	Non-smokers	61	136	

DISCUSSION:

Very few studies have reported the usage of TCSS in diagnosing DPN. In this study we evaluated the presence of DPN in type-II diabetic patients using TCSS and determined the association of risk factors with DPN. The prevalence of DPN in our study was found to be 45.6%. this prevalence was lower than the prevalence of 60% reported at Kurnool by pradeep Battula et al.. [16]This could be due to different types of diabetes (e.g., type 1 and type 2 diabetes), sample selection, different diagnostic criteria used

In the present study, we found that males are having the DPN more than the females and it is statistically significant with similar study [17] showing that males being at higher risk in the Diabetes Control and Complications Trial. This was also consistent with the Byron M. Perrin et al. study, [3618] which showed Males are more associated with higher risk. Men tend to seek access to health services less than females, perceive that they have less time for their own health and will engage in fewer health-promoting activities [19]

In the present study, BMI was found to be associated with DPN. This was similar to the Braffett BH et al.[20] study which found that great weight and BMI are significantly associated with DPN. Proposed mechanisms for this nerve damage include fat deposition, extracellular protein glycation, mitochondrial dysfunction, oxidative stress and activation of counter-regulatory signaling pathways leading to chronic metabolic inflammation [21-23]

HbA1c was found to be associated with DPN in this study, which was also proved by. Muhammed Umer Nisar etal study [24] which found that Patients with an HbA1c > 6.5% were 16.9 times more likely to develop neuropathy.

Duration of diabetes was found to be associated with DPN in this study, which was also proved by. bansal etal study [25] which found that chronic exposure to Hyperglycemia is a risk factor in the development of DPN.

In our study Dyslipidemia along with higher triglyceride level & higher LDL-Cholesterol were found to be associated with DPN. Similarly Katulanda P et al. [26] in their study found higher levels of triglycerides as the predictor of DPN and Shiro Tanaka et al [27] in their study predicted that higher LDL Cholesterol is associated with DPN.

In our study Hypertension was found to be associated with DPN. Similarly Sendi RA etal. [28] in their study found a strong association between DNP and Hypertension. Hypertension may reduce density of myelination of peripheral nerves that shows that hypertension may cause peripheral diabetic neuropathy or may exaggerate the complications of peripheral diabetes neuropathy [29]

In our study Smoking was found to be associated with DPN. Similarly van der Velde JHPM et al. [30] in their study found that smoking independently contribute to worse nerve function.

Conclusions:

In our study the prevalence of diabetic peripheral neuropathy using TCSS was found to be high among T2DM patients and the Peripheral neuropathy cases were found to be mild to moderate severity. Early identification and proper intervention are compulsory in patients with type-II diabetes in preventing the progression of diabetic peripheral neuropathy.

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