Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/ftar0k98

# A STUDY ON THE PREVALENCE OF SMALL FIBRE NEUROPATHY USING TORONTO CLINICAL NEUROPATHY SCORE IN DIABETICS

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## ABSTRACT

**Introduction**: Numerous vascular & non-vascular problems are linked to diabetes, a metabolic disease that is not communicable. Small fibre neuropathy arises from the targeted injury of the slender fibres within the peripheral nerve. the present study was conducted to study prevalence of small fibre neuropathy by using Toronto clinical neuropathy scale in diabetic population.

**Material & Methods**: The prospective, cross-sectional study was conducted among 151 patients with reports of blood sugars in diabetic range from January 2023 to June 2023 in Department of General Medicine, at Apollo Institute of Medical Sciences & Research, Hyderabad. Toronto Clinical Neuropathy score will be recorded for each patient. Results were analyzed using SPSS version 25.0.

**Results:** Maximum patients were in the age group of 51-60 years (27.8%) & least were in the group of 81-90 yeas (1.3%). Out of 151 patients 56.3% were male & 43.7% were female. The mean duration of diabetes was 7.2±2.3 years, mean FBS was 157.49±23.1 mg/dl, mean PLBS was 270.42±31.5, mean HbA1C was 8.84±1.2 % & 71.5% of patients had symptoms of disease. The mean TCNS score was 3.64±0.78. Out of 151 patients 102 (67.5%) were without DPN, 39 (25.8%) had mild DPN & 10 (6.62%) had moderate DPN. The duration of diabetes showed significant relationship (p=0.000) with the severity of diabetic neuropathy.

**Conclusion**: TCNS is a sensitive scoring system employed for the diagnosis of diabetic neuropathy & serves as a cost-effective bedside screening instrument.

**Key Words:** Diabetes, Nerve Conduction, Neuropathy, Small Fibre, TCNS.

## INTRODUCTION

Diabetes is a non-communicable metabolic disorder & worldwide prevalence has reached epidemic proportions, & is set to increase to 629 million by the end of 2045 in India.[1] It is commonly known that diabetes can result in both non-vascular & vascular (micro & macrovascular) problems. Along with peripheral vascular disease, neuropathy is one of the most common microvascular consequences & a major contributor to non-traumatic lower limb amputation.[2] The prevalence of diabetic neuropathy in the Indian population ranges from 19.1% to 29.2%.[3] Small fibre neuropathy (SFN) arises from the damage of peripheral nerve fibres characterised by a thin myelin sheath (Aδ) & the absence of myelin (C fibres). These fibres mediate temperature & pain sensations, as well as regulate autonomic activities; they constitute 80-90% of peripheral nerves.[2–4] Patients with small fibre neuropathy typically have somatic symptoms, however autonomic dysfunctions may also arise. Somatic symptoms may encompass numbness, paraesthesia, hypo- or hyperalgesia, allodynia, & neuropathic pain. Neuropathic pain is incapacitating, characterised by searing, prickling, itching, stabbing, & "lightning-like" sensations, significantly affecting quality of life.[5]

Autonomic disorders encompass xerophthalmia & xerostomia, dysregulated sweating, modified gastrointestinal motility & bladder function, irregular heart-rate variability, & orthostatic complications such as hypotension & tachycardia.[5,6] A recent proposal recommended a subclassification based on the predominant symptoms.[7] Small Fibre Neuropathy (SFN) may be idiopathic when the aetiology remains unidentified; nonetheless, other prevalent diseases could contribute to its manifestation. Consequently, individuals with SFN must undergo extensive diagnostic evaluations to discover or rule out metabolic, neoplastic, viral, or genetic disorders.[8,9] An additional challenge is that SFN may represent an initial stage of neuropathy, which might subsequently advance to include thick fibres.

The gold standard for diagnosing peripheral neuropathy has been nerve conduction studies (NCS). Nonetheless, it is unwieldy, costly, & not readily accessible.[10] Consequently, a clinical scoring system that is simply implementable & has strong correlation with NCS is essential in resource-limited environments such as India. Various scoring systems have been developed for the diagnosis & classification of diabetic peripheral neuropathy (DPN), including the Total Clinical Neuropathy Score (TCNS) & its modified version (mTCNS), the Michigan Neuropathy Screening Instrument (MNSI), & the Neuropathy Impairment Score (NIS), among others.[11,12] The TCNS, developed by Bril V & Perkins B, has been assessed in multiple studies from Canada & the United States, demonstrating a substantial association with sural nerve myelinated fibre density in patients with diabetic neuropathy.[13]

Hence the present study was conducted to study prevalence of small fibre neuropathy by using Toronto clinical neuropathy scale in diabetic population attending Apollo Institute of Medical Sciences & Research, Hyderabad, Telangana.

## MATERIAL & METHODS

The prospective, cross sectional study was conducted from January 2023 to June 2023 in Department of General Medicine, at Apollo Institute of Medical Sciences & Research, Hyderabad. Ethical clearance was taken from institutional ethics committee of the centre before commencement of study. Patients were asked to sign an informed consent form after explaining them the complete procedure.

By keeping the Prevalence of the disease -50%
Precision-10%
Significance level alpha-0.05
Drop out 10%

Final sample size estimated was 151. Patients visiting General medicine outpatient department or inpatients with blood sugars in diabetic range were selected on the basis of inclusion & exclusion criteria.

**Inclusion Criteria**

- Patients visiting General medicine OPD/IPD with reports of blood sugars in diabetic range with any duration of illness, with or without symptoms of neuropathy were included in this study after taking informed consent.

**Exclusion Criteria**

- Other causes of neuropathy are excluded by history & clinical examination & by investigations if required like vitamin B12.
- Psychiatric ailment.

The patients underwent a history & physical examination, which included the evaluation of the TCNS score. Subsequently, they underwent evaluation by NCS utilising the RMS EMG EP Mark2 recorder, alongside assessments of motor function for the median, ulnar, peroneal, & tibial nerves, as well as sensory function for the median, ulnar, radial, & sural nerves. Motor amplitudes were measured in millivolts, sensory amplitudes in microvolts, & velocities in metres per second. The demographic data of the patients was recorded using a pre-structured proforma. The clinical profile of the patient was documented, including age, gender, duration of diabetes, HbA1c values, & associated microvascular issues.

Toronto Clinical Neuropathy score will be recorded for each patient. Pressure sensation will be assessed using 10 gm monofilament at dorsum of the feet & hand after explaining to the patients & response will be documented as +/-, giving the score as 1/0 respectively. Pain sensation will be done using a pin-prick, after explaining to the patient pinprick sensation to dorsum & ventral aspect great toe & ulnar tuberosity, examined with pin prick with moderate intensity & compared with normal individual & response will be documented as +/, giving the score as 2/1/0 respectively. Vibration sense will be tested by using a 256 Hz tuning fork which was put on the first toe at bony prominent area & ulnar prominence after explaining to the patient & then then determining when the vibration stops & compared with normal individual & response will be documented in +/- giving score of 1/0. Temperatures (cold & warm) will be tested by placing hot & cold test tubes on the dorsum of the foot & hand with temperature variation of+/-10°C. Tendon reflex will be tested by striking the Achilles & quadriceps tendons with a reflex hammer & response will be documented in present /delayed /absent giving the score as 2/1/0 respectively. Weakness of small foot muscles & dorsi-flexors with clinical muscle testing is observed. Associated skin changes in affected areas may include dry, cracked, or shiny skin, with decreased moisture on the surface of affected areas. The TCNS consists of 6 clinical symptoms, 5 sensory tests & lower limbs reflexes, which give a maximal score of 19

0-5 points - without DPN
6-8 points - mild DPN
9 to 11 points - moderate DPN
12 to 19 points - severe DPN

For variables that were normally distributed, the mean ± standard deviation was used; for variables that were not, the median (interquartile range) was used. Percentages or proportions were used to express categorical variables. Depending on the sample size, the independent sample t-test was used to compare regularly distributed continuous data, the Mann-Whitney U test for abnormally distributed continuous variables, & the Chi-square or Fisher's exact test for categorical variables. SPSS version 25.0 was used for data analysis & validation. Every p-value that was less than 0.05 was considered statistically significant.

## RESULTS

Patients were divided on the basis of age group. Maximum patients were in the age group of 51-60 years (27.8%) & least were in the group of 81-90 yeas (1.3%). Out of 151 patients 56.3% were male & 43.7% were female as shown in table 1.

| Demographic Data | | N (%) |
|---|---|---|
| Age | 21-30 | 3 (1.9) |
| | 31-40 | 11 (7.2) |
| | 41-50 | 22 (14.5) |
| | 51-60 | 42 (27.8) |
| | 61-70 | 10 (6.6) |
| | 71-80 | 10 (6.6) |
| | 81-90 | 2 (1.3) |
| Gender | Male | 85 (56.3) |
| | Female | 66 (43.7) |

***Table 1: Demographic data of patients***

The mean duration of diabetes was 7.2±2.3 years, mean FBS was 157.49±23.1 mg/dl, mean PLBS was 270.42±31.5, mean HbA1C was 8.84±1.2 % & 71.5% of patients had symptoms of disease as shown in table 2.

| Clinical Parameters | Mean±SD /N (%) |
|---|---|
| Duration of diabetes | 7.2±2.3 |
| Mean FBS (mg/dl) | 157.49±23.1 |
| Mean PLBS (mg/dl) | 270.42±31.5 |
| HbA1C (%) | 8.84±1.2 |
| Presence of symptoms | 108 (71.5) |

***Table 2: Clinical parameters***

The mean TCNS score was 3.64±0.78. Out of 151 patients 102 (67.5%) were without DPN, 39 (25.8%) had mild DPN & 10 (6.62%) had moderate DPN as shown in figure 1.

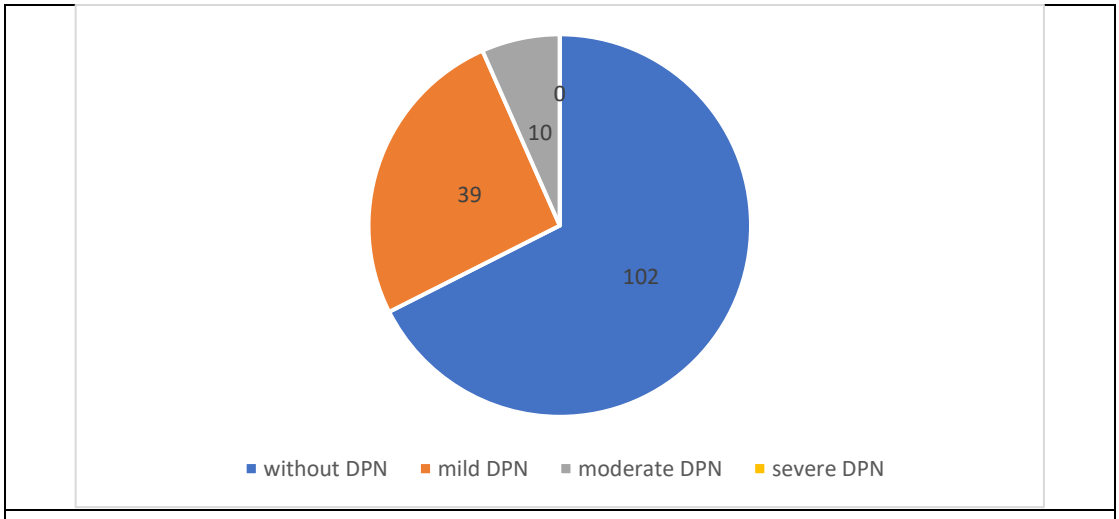


***Figure 1: Distribution of patients according to Toronto Clinical Neuropathy Scale***

On analysis of the risk factors, the duration of diabetes showed significant relationship (p=0.000) with the severity of diabetic neuropathy while no significant relationship was found between HbA1C & severity of DPN as shown in table 3.

| Risk factors | | Without DPN | Mild DPN | Moderate DPN | P value |
|---|---|---|---|---|---|
| Duration of diabetes | ≤5 | 67 (65.7) | 6 (15.4) | 1 (10) | .000 |
| | 6-10 | 30 (29.4) | 17 (43.6) | 2 (20) | |
| | ≥11 | 5 (4.9) | 16 (41) | 7 (70) | |
| HbA1C | <9 | 62 (60.8) | 18 (46.2) | 4 (40) | 0.173 |
| | >9 | 40 (39.2) | 21 (53.8) | 6 (60) | |

***Table 3: Correlation of severity of neuropathy with risk factors***

## DISCUSSION

The majority of peripheral neuropathy patients exhibit simultaneous involvement of large & small nerve fibres; however, the damage to distinct fibre types may be unequal at times. Some diseases primarily induce damage to large fibres (e.g., vitamin B12 deficiency), whereas others mostly affect small fibre lesions (e.g., Fabry's disease). Moreover, specialised structures, such as axons & myelin, are often engaged differently.[14]

Diabetes is a highly widespread metabolic condition globally, resulting in considerable morbidity & mortality. Several research have been conducted about the correlation between TCNS & diabetic neuropathy. Notable studies including those conducted by Bril V et al.[13,15,16] & Bostani A & Homayuonfar H.[17] It is crucial to juxtapose the current study with their findings.

The mean age in the current study was 53.9 years, consistent with the previously cited studies.[14] Of the 151 patients, 56.3% were male & 43.7% were female. This contrasts with the study of Bostani A & Homayuonfar H, which reported 20% male participants & 80% female participants.[17] Nevertheless, some writers, such Bril V et al., have demonstrated that the distribution among males ranges from 61% to 65%, while for females it ranges from 35% to 38%.[16]

The mean duration of diabetes in this study was determined to be 7.3±2.3 years. This markedly contrasts with other studies in which the mean duration of diabetes exceeded 11 years.

Despite indicating that individuals in the current study had a relatively brief history of diabetes, the length of diabetes exhibited a statistically significant link with the severity of diabetic neuropathy. Ashok S et al. & Gill HK et al. revealed analogous findings in their studies on the risk variables linked to diabetic neuropathy.[3,18]

The study population exhibited same diabetes control (mean HbA1C 8.84±1.2%) compared to the patients in Bril V et al. (mean HbA1C 8.5±1.7%). Interestingly, in this investigation, the severity of neuropathy exhibited no connection with HbA1C levels. Gill HK et al have shown a comparable absence of association between HbA1C & diabetic neuropathy, suggesting that any elevation of glucose above a specific threshold may predispose individuals to neuropathy, rather than indicating a linear relationship.[3,18]

Concerning the severity of neuropathy, evaluated by TCNS, among the 151 patients in this study, 102 (67.5%) were without DPN, 39 (25.8%) had mild DPN & 10 (6.62%) had moderate DPN. A comparable study conducted by Bril V et al with 65 patients revealed that 12.3%, 21.5%, 27.7%, & 38.5% had no neuropathy, mild neuropathy, moderate neuropathy, & severe diabetic neuropathy, respectively.[15] In a study done by Pal E et al patients were divided into no DPN (n=20, 9.2%); subclinical DPN (n=19, 8.8%); possible DPN (n=9, 4.2%); probable DPN (n=6, 2.8%); & confirmed DPN (n=111, 51.4%).[14]

The diagnosis of small fibre neuropathy remains problematic despite advancing understanding & available diagnostic methods. Clinical criteria were defined solely for the length-dependent variant; in other instances, diagnosis is more challenging. The evaluation of the IENFD is a noninvasive & sensitive technique for diagnosing the condition; it was endorsed by the European Federation of Neurological Societies (EFNS) & the Peripheral Nerve Society (PNS) in 2010, supported by level A evidence. Furthermore, the evaluation of intraepidermal nerves yields not only quantitative metrics but also prognostically significant morphological alterations, including length, branching, & axonal swelling.[19,20,21]

The current study has several limitations, one of which is that it was conducted in a hospital setting, so the findings may not be applicable to the broader community population. The distinctions between patients with type 1 & type 2 diabetes were not analysed.

## CONCLUSION

The diagnosis of small fibre neuropathy is mostly based on patient history & physical examination; however, techniques such as skin biopsy, intraepidermal nerve fibre density (IENFD) measurement, & corneal confocal microscopy have been utilised to evaluate small diameter nerve disease in diabetes. To examine the function, the Toronto Clinical Neuropathy Scale, quantitative sensory tests, laser-evoked potentials, & sudomotor function may be evaluated. The necessity for dependable criteria for diagnosing small fibre neuropathy (SFN) arises from both clinical practice & research, rendering early diagnosis crucial for appropriate patient treatment.

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