



# Warm Perception Threshold and Its Associated Factors to Detect Diabetic Peripheral Neuropathy: A Hospital-based Study

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## ABSTRACT

**Background:** To predict the efficacy of thermal perception threshold in case of diabetic peripheral neuropathy.

**Methods:** The study was conducted among 161 adults with type 2 diabetes mellitus (T2DM). Thermal perception thresholds [warm and cold perception threshold (WPT and CPT)] and vibration perception threshold (VPT) were measured bilaterally, and a *t*-test was performed for age, body mass index, and diabetic duration between the non-neuropathy and neuropathy groups, followed by correlation and regression analysis. Diagnostic accuracy was measured using receiver operating characteristic analysis and decision tree analysis done with the significant predictors.

**Results:** Among 161 participants, 96 (59.62%) had peripheral neuropathy based on VPT scores. We found WPT was significantly higher in the neuropathy group ( $44.3 \pm 4.51$  vs  $43.1 \pm 3.64$ ;  $p=0.012$ ). The duration of diabetes correlated positively with WPT ( $p=0.037$ ). Receiver operating characteristic (ROC) analysis and linear regression confirmed WPT as a reliable diagnostic indicator and independent predictor in peripheral neuropathy in T2DM.

**Conclusions:** Our study revealed WPT as a good diagnostic indicator in assessing peripheral neuropathy in T2DM. Therefore, our study emphasizes accurate and timely diagnoses of neuropathy, which enable appropriate treatment, preventative measures, and effective management of diseases, ultimately leading to improved patient health and potentially reducing healthcare costs.

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## INTRODUCTION

Diabetic peripheral neuropathy (DPN) is one of the most common chronic complications of T2DM, with prevalence estimates ranging widely from 2.4% to over 75% depending on population characteristics, diagnostic criteria, and disease duration.<sup>1,2</sup> It is primarily a consequence of prolonged hyperglycemia, leading to metabolic and microvascular damage that impairs nerve function. DPN not only diminishes the quality of life through symptoms such as pain, tingling, and numbness, but also predisposes patients to more severe outcomes, including foot ulceration, infections, and eventual lower limb amputation.

Screening and early diagnosis of DPN are crucial for preventing long-term complications. Vibration perception threshold (VPT) and 10-gm monofilament testing are commonly used and validated methods for detecting large-fiber dysfunction in peripheral neuropathy.<sup>3</sup> These tests are advantageous due to their simplicity, cost-effectiveness, and utility in primary care settings. VPT assesses large myelinated A-beta fibers responsible for proprioception and vibratory sensation, and is often used to grade the severity of neuropathy.<sup>4</sup>

However, a growing body of literature highlights the involvement of small nerve fibers—A-delta and unmyelinated C fibers—in early diabetic neuropathy. These fibers are primarily responsible for temperature perception and pain, and their dysfunction may precede detectable abnormalities in large fiber testing. Thus, reliance solely on VPT or monofilament testing may result in underdiagnosis of early or small-fiber neuropathy.

Thermal quantitative sensory testing (TQST), which measures warm perception threshold (WPT) and cold perception threshold (CPT), offers a more sensitive means of assessing small-fiber function. These tests are particularly useful in the evaluation of subclinical neuropathy and can reflect early pathophysiological changes in nerve function. Despite their diagnostic utility, TQST remains underutilized due to limited access to equipment, lack of familiarity, and the perceived complexity of the testing procedure.<sup>5,6</sup>

There are reports where they have shown alterations in thermal thresholds among diabetic patients and have proposed that these measures may serve as early markers of neuropathy and even predictors of complications such as diabetic nephropathy

and cardiovascular autonomic neuropathy.<sup>7-9</sup> Nevertheless, few studies have attempted to quantify the optimal threshold or cut-off of TQST in diabetic neuropathy.

In this study, we aimed to assess warm and cold thermal perception thresholds in diabetic patients with and without neuropathy as defined by VPT, and to examine the association of these thermal thresholds with duration of diabetes and other clinical parameters. By exploring this relationship, we aim to highlight the significance of incorporating small-fiber assessment into routine neuropathy screening protocols for early detection and improved patient outcomes. The study aimed to assess the diagnostic efficacy of thermal perception thresholds among diabetic patients with a VPT >15, indicative of neuropathy, and those with a VPT <15, indicative of non-neuropathy individuals.

The primary objective of this study is to evaluate and compare thermal perception thresholds (TPT) and VPT in patients with type 2 diabetes mellitus (T2DM), with and without DPN, to assess their diagnostic utility in detecting sensory nerve dysfunction.

This objective is aligned with the following hypotheses:

- H1: Patients with DPN will demonstrate significantly elevated VPT values and altered TPT (both warm and cold) compared to T2DM patients without neuropathy.
- H2: TPT abnormalities will primarily reflect small fiber dysfunction, whereas VPT abnormalities will reflect large fiber involvement—allowing differentiation of neuropathic fiber subtype involvement.

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By testing these hypotheses, the study aims to provide a nuanced understanding of the sensory profile of DPN and to support the incorporation of TPT and VPT assessments into routine diabetic neuropathy screening protocols.

**Subjects:** 161 patients with T2DM aged 30–70 years attending the diabetic outpatient clinic of a tertiary care hospital were screened. Inclusion criteria included patients with a minimum diabetes duration of 1 year and the ability to provide informed consent.

Exclusion criteria were:

- History of stroke or other central nervous system disorders.
- Chronic alcohol use.
- Chronic kidney disease (stage III and above).
- Current foot ulcers or infections.
- Any diagnosed nondiabetic neuropathy or systemic disease affecting peripheral nerves.

Sample size was calculated considering the reported prevalence of diabetic peripheral neuropathy (DPN) among patients with type 2 diabetes mellitus (T2DM) in West Bengal, which ranges from approximately 32 to 59% according to recent studies.<sup>2,10,11</sup> Using a 95% confidence interval and a margin of error of 7.7%, the required sample size was calculated accordingly. A total of 161 participants were included in this study, aligning with these parameters. Participants were selected using convenience sampling during their routine clinic visits.

Each participant underwent a structured clinical evaluation, including:

- Detailed medical history and diabetes duration.
- Assessment of neuropathic symptoms (burning, tingling, numbness, cramping, etc.).
- Anthropometric measurements, including BMI using a calibrated portable stadiometer and digital scale.

## MATERIALS AND METHODS

This was a cross-sectional observational study conducted among patients diagnosed with T2DM, aimed at assessing thermal and vibration perception thresholds and their association with DPN. The patients coming from the OPD were recruited in the Department of Physiology for diagnostic evaluation of diabetic neuropathy. The study was approved by the Institutional Ethics Committee, All India Institute of Medical Sciences, Kalyani, on March 14, 2023, and the reference Id is IEC/AIIMS/Kalyani/Meeting/2023/029. The data was collected from the period May 2023 to

October 2024. The study was conducted in accordance with the 2013 revision of the Helsinki Declaration.

### Screening Test for Diabetic Neuropathy

All patients were screened by the Michigan neuropathy questionnaire and the 10-gm monofilament test according to standard protocol and recommendation.<sup>12,13</sup>

### Measurement of Vibration Perception Threshold and Temperature Perception Threshold

A conventional biothesiometer (Biothezi VPT from Kody Medical Electronics Pvt. Ltd., India) was used to measure VPT. A larger loss of sensory perception is indicated by a higher vibration stimulus unit. The machine produces vibration units that range from 1 to 50 V, or vibration amplitudes between 0.026 and 25  $\mu\text{m}$ . VPT measurements were taken at six different points on the foot's plantar surface: the great toe, the first, third, and fifth metatarsal heads, the medial side of the mid-foot, and the heel. The six spots on the foot were then examined for vibration sensitivity while the subject's eyes were closed. When the individual felt a buzzing sensation in the foot, they were instructed to respond "yes." Starting at 1 V, the vibration stimulus was progressively raised until the subject said they felt the experience. The VPT was determined by measuring the lowest vibrational intensity detected at each location. Each patient's average VPT was then calculated for each of the six-foot sites that were evaluated. The average VPT of all six points tested in the foot was then recorded for each patient.<sup>14</sup> After obtaining all data, the VPT values were graded as normal (<15 V), mild (15–20 V), moderate (20–25 V), and <25 V as severe neuropathy. Severe neuropathy can extend up to 50 V.<sup>12</sup>

Warm perception threshold and CPT were measured using Kodys HCP-Elite Instrument using methods of limits. This delivers rapidly rising warm and cool stimuli through a thermoelectric module placed in the probe and applied to the plantar surface of the patient. It has been used for the study of many small fiber syndromes with a good correlation with the density of C- and A $\delta$ -fibers in the superficial skin.<sup>5,15</sup>

All the above-mentioned tests were performed in both feet.

### Quality Control Measures

- Testing was performed by trained clinicians blinded to the clinical scores.
- A standard script was used to instruct patients to minimize bias.

- Inter and intraobserver variability was minimized by repeating 10% of tests under supervision.
- All instruments were tested for technical error of measurement prior to study initiation.

### Statistical Analysis

The data from 161 patients were analyzed using Jamovi software (Version 2.5.5). An independent *t*-test was performed to assess thermal perception threshold comparing neuropathy and non-neuropathy groups. Spearman's correlation and linear regression analysis were used to explore the association between thermal perception threshold with age, body mass index, and diabetic duration. The diagnostic effectiveness of thermal perception threshold was evaluated using the receiver operating characteristic (ROC) curve and Youden's index. Data visualization and graphical representations were generated using R software (version 4.4.3). The *p*-value less than 0.05 was considered statistically significant.

## RESULTS

### Sociodemographic Data

A total of 161 subjects were enrolled in the study and completed all required assessments. Based on their Vibration Perception Threshold (VPT) scores, participants were categorized into two groups: those with peripheral neuropathy ( $n = 96$ ) and those without ( $n = 65$ ).

### Demographic Characteristics

Table 1 shows that the mean age of participants in the non-neuropathy group was  $51.40 \pm 8.79$  years, while the neuropathy group had a significantly higher mean age of  $57.40 \pm 9.49$  years ( $p < 0.001$ ). Body mass index (BMI) was similar between the two groups, with mean values of  $25.60 \pm 3.86$  in the non-neuropathy group and  $25.50 \pm 4.23$  in the neuropathy group; this difference was not statistically significant ( $p = 0.428$ ).

The duration of diabetes differed markedly between groups. Participants without neuropathy had a mean diabetes duration of  $3.97 \pm 2.14$  years, whereas those with neuropathy had a significantly longer duration, averaging  $9.49 \pm 2.93$  years ( $p < 0.001$ ).

Independent *t*-tests confirmed that age and duration of diabetes were significantly different between the neuropathy and non-neuropathy groups, while BMI did not show a statistically significant difference (Table 1).

### Vibration Perception Threshold Value

Among 161 patients, normal VPT or no neuropathy was observed in 65 (20.18%), and the remaining had neuropathy of varying

**Table 1:** Demographic characteristics

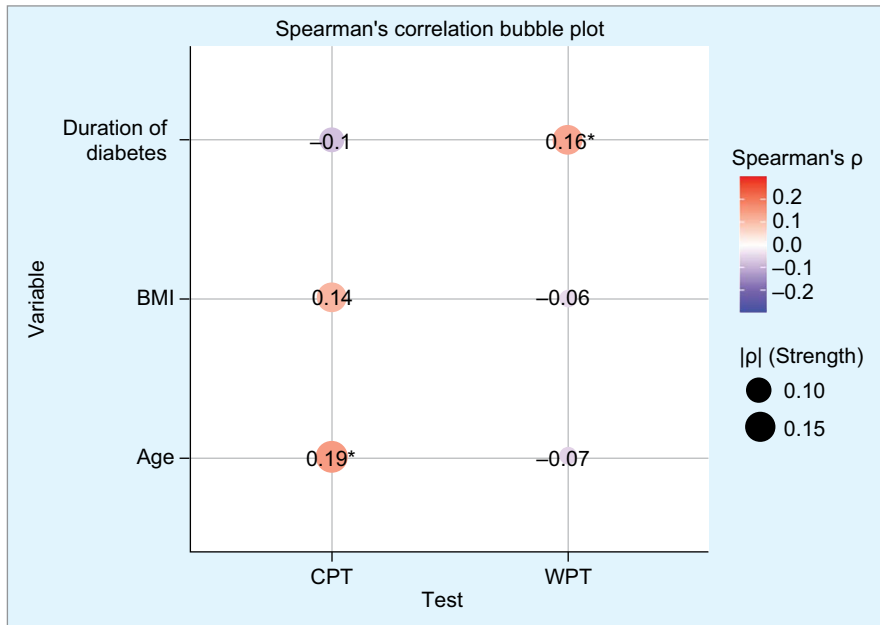
Variables	Non-neuropathy (n = 65)	Neuropathy (n = 96)	p-value
Age (years)	51.40 ± 8.79	57.40 ± 9.49	<0.001*
BMI (kg/m <sup>2</sup> )	25.60 ± 3.86	25.50 ± 4.23	0.428
Duration of diabetes (years)	3.97 ± 2.14	9.49 ± 2.93	< 0.001*

Independent t-test performed for comparison of age, body mass index, and duration of diabetes between non-neuropathy and neuropathy groups (n = 161). Values are presented as mean ± standard deviation; BMI, body mass index; \*p < 0.001

**Table 2:** Comparison of warm and cold perception thresholds between neuropathy and non-neuropathy groups

Variable	Non-neuropathy (n = 65)	Neuropathy (n = 96)	p-value	Cohen's d	95% CI
Warm perception threshold (°C)	43.1 ± 3.64	44.3 ± 4.51	0.012*	0.287	0.063–0.511
Cold perception threshold (°C)	23.1 ± 3.40	22.4 ± 3.29	> 0.05	−0.205	−0.428–0.018

Independent t-test used for comparison of thermal perception thresholds between non-neuropathy and neuropathy groups. Values are presented as mean ± standard deviation. Effect sizes (Cohen's d) are presented with 95% confidence intervals (n = 161)



**Fig. 1:** Correlation matrix: The bubble plot reflects the strength and direction of relationships between age, BMI, and duration of diabetes with the thermal threshold parameters (WPT and CPT). The size of each bubble corresponds to the value of rho (Spearman correlation coefficient). Bubbles are coloured orange, indicating positive correlation between the variables, and blue, indicating negative correlation between the variables. Larger bubbles correspond to stronger correlations, indicating a greater degree of association between the variables, and smaller bubbles or very small or no bubbles indicate weak or negligible correlation among the variables

degrees, with the majority (45, 23.43%) having severe neuropathy, followed by moderate neuropathy among (21, 10.93%), and mild neuropathy (30, 31.25%).

**Thermal Perception Threshold**

The mean of WPT in the non-neuropathy group was 43.1 ± 3.64 °C, compared to 44.3 ± 4.51°C in the neuropathy group. Independent t-test analysis revealed a statistically significant increase in WPT among patients with neuropathy (p = 0.012), with a small effect size [Cohen's d = 0.287; 95% CI: 0.063, 0.511] (Table 2).

For CPT, the non-neuropathy group had a mean value of 23.1 ± 3.40 °C, while the neuropathy group had a mean CPT of 22.4 ±

3.29 °C. This difference was not statistically significant (p > 0.05), and the effect size was small and negative [Cohen's d = −0.205; 95% CI: −0.428, 0.018] (Table 2).

**Correlation and Regression Analysis**

Spearman's rank correlation analysis was conducted to assess the associations between demographic/clinical variables (age, BMI, and duration of diabetes) and thermal perception thresholds.

For WPT, a statistically significant positive correlation was observed with duration of diabetes (p = 0.165, p = 0.037), indicating that individuals with longer diabetes duration tend to have higher warm perception thresholds.

No significant correlations were found between WPT and age (p = −0.048, p > 0.05) or BMI (p = −0.150, p > 0.05) (Fig. 1).

For CPT, a significant positive correlation was found with age (p = 0.189, p = 0.016), suggesting that cold detection sensitivity decreases with advancing age. No significant correlations were observed between CPT and BMI (p = −0.095, p > 0.05) or duration of diabetes (p = −0.034, p > 0.05) (Fig. 1).

Furthermore, Spearman's correlation bubble plot visualizes the strength and direction of associations between thermal perception thresholds (CPT and WPT) and three variables: Age, BMI, and duration of diabetes. Significant positive correlation was found between duration of diabetes and WPT (p = 0.165; p = 0.037), indicating that longer diabetes duration can impair warm perception threshold. Further, age shows a significant positive correlation with CPT (p = 0.189; p = 0.016), indicating that older age can cause impairment in CPT (Fig. 1).

A simple linear regression was conducted to examine the association between duration of diabetes and warm perception threshold (WPT). The model was statistically borderline, with the duration of diabetes emerging as a weak predictor of WPT, t = 1.93, p = 0.050. The overall model accounted for 2.3% of the variance in WPT (R = 0.152, R<sup>2</sup> = 0.023).

The unstandardized regression coefficient (B) for duration of diabetes was 0.199 (95% CI: −0.004 to 0.402), suggesting that each additional year of diabetes was associated with an estimated increase of 0.199 units in WPT. However, the confidence interval included zero, indicating that the effect may not be robust. The standardized beta coefficient was 0.152, reflecting a small effect size (Table 3).

A simple linear regression was performed to examine the effect of age on CPT. The analysis revealed a statistically significant positive association, t = 2.32, p = 0.022. The

model accounted for 3.3% of the variance in CPT ( $R = 0.181, R^2 = 0.033$ ).

The unstandardized coefficient for age was  $B = 0.058$  (95% CI: 0.008–0.109),

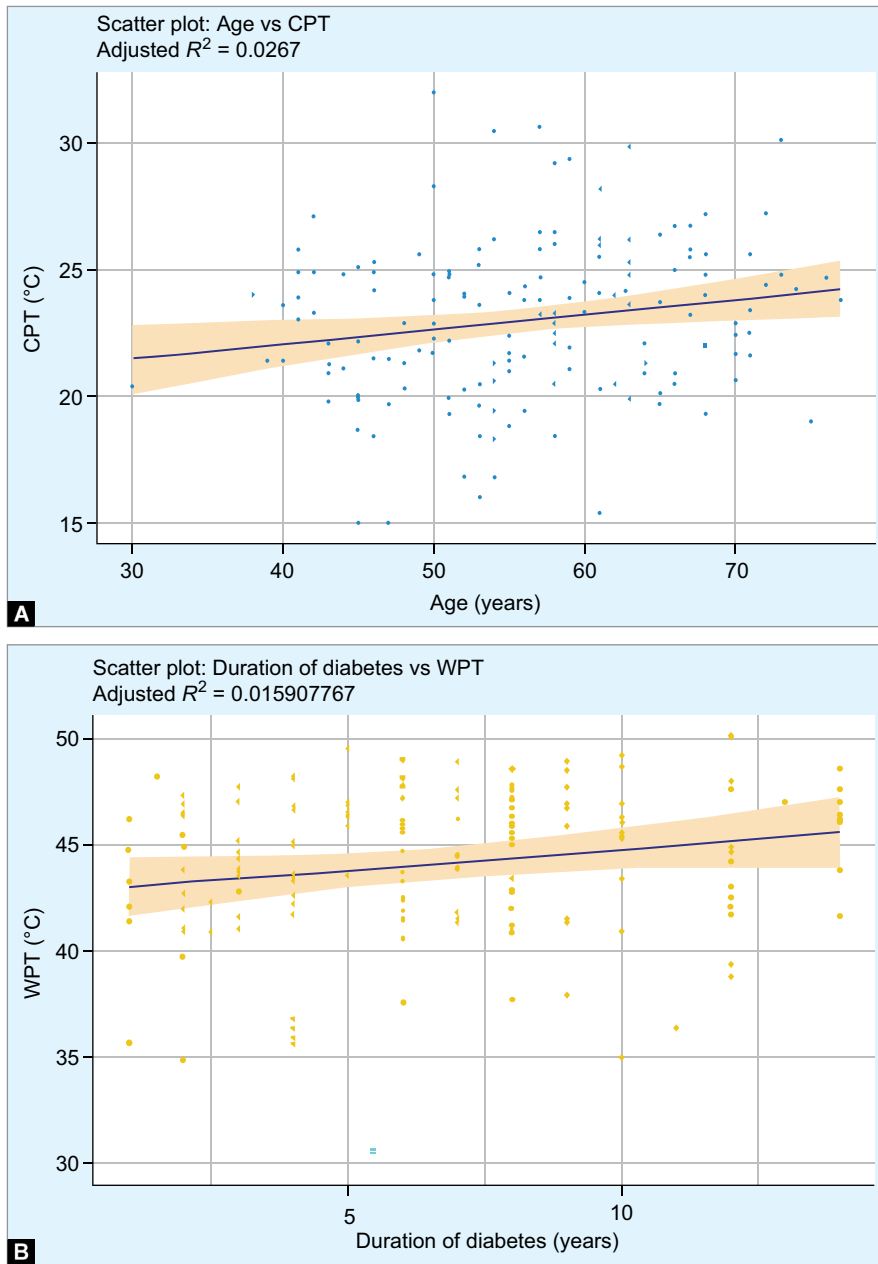
indicating that each additional year of age was associated with a 0.058 unit increase in CPT. The standardized beta coefficient was 0.181, reflecting a small but significant effect size (Table 4). The results suggest that age is a statistically significant predictor of cold perception threshold. As individuals age, there is a modest increase in CPT, implying a reduced sensitivity to cold stimuli with advancing age. While the effect size is small, the relationship is statistically meaningful, and the confidence interval does not include zero, indicating a reliable association. However, since age explains only a small portion (3.3%) of the variance in CPT, other contributing factors should be explored in future studies.

There is a very weak positive linear relationship between diabetes duration and WPT. As diabetes duration increases, WPT tends to rise slightly—indicating worsening warm perception (i.e., patients detect warmth at higher temperatures). However, the  $R^2$  value (0.016) indicates that only ~1.6% of the variance in WPT is explained by diabetes duration—meaning this relationship is statistically weak. Despite the low  $R^2$ , the bubble plot shows this correlation was statistically significant ( $p = 0.16$ ), so it might be relevant in larger or more homogeneous samples (Fig. 2).

A very weak positive association exists between age and CPT. Higher CPT means that individuals perceive cold at higher temperatures, suggesting reduced cold sensitivity with advancing age. The  $R^2 = 0.027$  indicates that age explains only 2.7% of the variation in CPT, again a weak relationship (Fig. 2).

Both age and diabetes duration are significantly (but weakly) associated with impaired thermal perception. The regression models show low explanatory power, meaning that other factors (e.g., neuropathy severity, comorbidities, metabolic control) may contribute more to changes in TPT. These findings align with the idea that thermal sensory loss in diabetes develops gradually and is multifactorial.

Receiver operating characteristic analysis was conducted to evaluate the diagnostic performance of two predictors: CPT and WPT. The area under the curve (AUC) for CPT was 0.554 (95% CI: 0.464–0.645), with a bootstrap standard error of 0.046 and a bootstrap ratio



**Figs 2A and B:** (A) Scatter plot showing the association between duration of diabetes and warm perception threshold (WPT). A linear regression line with 95% confidence interval (shaded area) is plotted to show the trend. A weak positive association was observed (adjusted  $R^2 = 0.016$ ), indicating that longer diabetes duration is associated with a higher WPT, suggestive of impaired warm perception. (B) Scatter plot showing the association between age and cold perception threshold (CPT). A linear regression line with 95% confidence interval (shaded area) is shown. A weak positive association was found (adjusted  $R^2 = 0.027$ ), suggesting that increasing age is associated with a higher CPT, reflecting reduced cold sensitivity

**Table 3:** Linear regression analysis of the association between duration of diabetes and warm perception threshold (WPT)

Predictor	B (Unstandardized)	Std error	$\beta$ (Standardized)	t	Sig	95% CI for B
Constant	42.764	0.800	–	53.48	0.000	41.18–44.34
Duration of diabetes (years)	0.199	0.103	0.152	1.93	0.050	–0.004–0.402

Dependent variable: WPT, warm perception threshold. Predictor: duration of diabetes. Model summary  $R = 0.152; R^2 = 0.023$ . Therefore, the equation will be,  $WWPT = 0.152$  (duration of diabetes) + 42.76

**Table 4:** Linear regression analysis of the association between age and cold perception threshold (CPT)

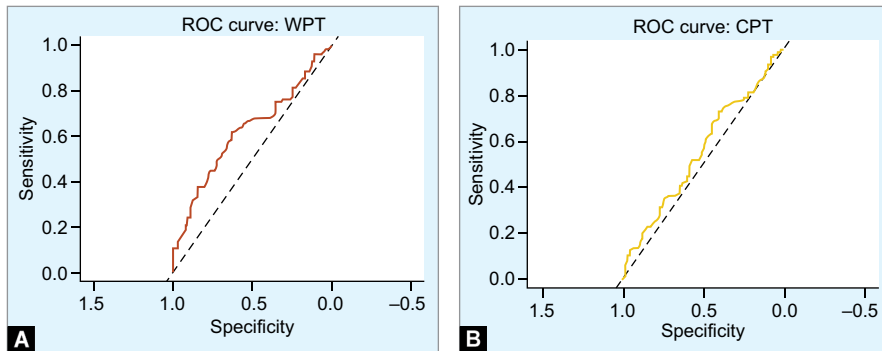
Predictor	B (Unstandardized)	Std error	$\beta$ (Standardized)	t	p	95% CI for B
Constant	19.700	1.430	–	13.75	0.000	16.87–22.53
Age (years)	0.058	0.025	0.181	2.321	0.022	0.008–0.109

Dependent variable: cold perception threshold (CPT). Predictor: age model summary  $R = 0.181$ ,  $R^2 = 0.033$ ; Therefore, the equation will be,  $CPT = 0.181$  (Age) + 19.70

**Table 5:** Comparison of diagnostic performance of CPT and WPT using ROC curve analysis

Predictors	AUC	95% CI (lower–upper)	Bootstrap SE	Bootstrap ratio	Cut-off threshold	Sensitivity (%)	Specificity (%)	Youden's index
CPT	0.554	0.464–0.645	0.046	12.002	24.45	72.9	40.0	0.129
WPT	0.621	0.535–0.708	0.044	14.066	44.95	61.5	63.1	0.245

AUC, area under the curve; CI, confidence interval; SE, standard error; CPT, cold perception threshold; WPT, warm perception threshold; Note: Thresholds were determined based on the maximum Youden's Index. Sensitivity and specificity are expressed as percentages



**Figs 3A and B:** (A) ROC curve for warm perception threshold (WPT): ROC curve depicting the diagnostic performance of WPT in distinguishing patients with and without diabetic neuropathy. The area under the curve (AUC) indicates moderate diagnostic accuracy, with the curve deviating significantly above the diagonal reference line, suggesting good discriminative ability. (B) ROC curve for cold perception threshold (CPT): ROC curve showing the diagnostic utility of CPT in identifying diabetic neuropathy. The curve lies close to the diagonal reference line, indicating lower discriminative capacity and limited diagnostic performance compared to WPT

of 12.002, indicating poor discriminatory ability. The optimal threshold for CPT was 24.45°C, yielding a sensitivity of 72.9% and a specificity of 40.0%, with a corresponding Youden's index of 0.129 (Table 5 and Fig. 3).

In comparison, the WPT showed a better performance with an AUC of 0.621 (95% CI: 0.535–0.708), a bootstrap standard error of 0.044, and a bootstrap ratio of 14.066. At the optimal threshold of 44.95°C, WPT demonstrated a sensitivity of 61.5% and a specificity of 63.1%, with a Youden's index of 0.245, suggesting modest discriminatory ability (Table 5 and Fig. 3).

Hence, the results showed that the warm perception threshold is more reliable and a good predictor of small fiber neuropathy as compared to CPT.

## DISCUSSION

Our present study showed 31.78% subjects were diabetic with no peripheral neuropathy, whereas 68.21% subjects had peripheral neuropathy in type 2 diabetes mellitus.

In our present study, we observed a significant association between age and

duration of diabetes between the two groups. There are several studies documenting an association of age with peripheral neuropathy among diabetic population. Previous studies have already shown that sensory neuropathy is strongly related to age at diagnosis. In 2014, Bansal et al. showed that age was significantly associated with diabetic microvascular complications, including diabetic neuropathy. All of these studies support our findings.<sup>10</sup>

We could not find any significant change in body mass index between neuropathy and no neuropathy group. This could be attributed to genetic predisposition, age of onset of diabetes, existing healthcare facilities, sample selection, and different clinical signs and symptoms. As high blood sugar or hyperglycemia, not just body weight, is the main cause of nerve damage in diabetes, BMI is frequently regarded as irrelevant in the development of diabetic neuropathy. This means that even people with a "normal" BMI can develop neuropathy if their blood sugar levels are poorly controlled, and some obese people with well-managed diabetes may not suffer from significant nerve damage.<sup>2</sup>

We observed the duration of diabetes as a significant variable between the no neuropathy and neuropathy groups. Literature suggests that the duration of diabetic neuropathy was significantly associated with the risk of having diabetic neuropathy. They interpreted that the duration of diabetes above 5 years can significantly develop neuropathy.<sup>16,17</sup>

The first published research work on thermal quantitative sensory testing (TQST) revealed that QST is a crucial component of somatic small-fiber used for neuropathy diagnosis in diabetes mellitus patients.<sup>8</sup> We found a significant increase in the warm perception threshold in the neuropathy group as compared to the no neuropathy group. This is because diabetes people develop neuropathy, which damages the small nerve fibers in the lower limbs. Our findings are in line with other previous studies. One very early study done by Bertelsmann in 1985 did thermal discrimination threshold between normal and diabetic patients and observed a significant increase in warm threshold and decrease in cold threshold. Another study observed that both perceptions getting deteriorated in diabetes. They interpreted that this is due to the damage of C and A-delta fibers. The threshold values for warm and cold perception in the foot can vary based on several factors, including age and individual differences. However, general reference values of WPT in healthy adults were around 40°C (104°F), and CPT was around 28°C (82°F), which had already been reported. These values are determined using quantitative sensory testing (QST) methods, such as the method-of-limits, to assess small nerve fiber function.<sup>7</sup> Another study reported in the year of 2020 where thermal perception threshold was used as a significant predictor of diabetic kidney disease in type 2 diabetes mellitus.<sup>18</sup> We also observed a significant positive association between duration of diabetes and warm perception threshold. Gaur et al.,

in 2024, reported one study where they assessed diabetic neuropathy based on the temperature perception threshold and found a significant change in both warm and cold temperature perception thresholds. Diabetes mellitus with warm perception threshold in the lower limb is strongly correlated with small fiber neuropathy, with warm perception threshold being more sensitive than cold perception threshold for diagnosis.<sup>19</sup>

Spearman correlation analysis followed by a linear regression study confirmed it as a potent predictor for diabetic neuropathy. Studies also suggested a similar finding to what we observed. They have mentioned that if the duration of diabetes is above 5 years, neuropathy may develop. Furthermore, we did correlation analysis between Age, BMI, and Duration of diabetes with warm and cold temperature perception threshold. WPT and CPT showed a significant correlation with duration of diabetes and age ( $p < 0.05$ ), respectively. Gaur et al., in 2024, reported a strong positive correlation between WPT and duration of diabetes, similar to our findings.<sup>19</sup>

Although CPT had a significant correlation with age, CPT did not significantly differ between the non-neuropathy and neuropathy groups. Further, the ROC analysis elucidated an AUC of 0.554 for CPT and 0.621 for WPT (Fig. 3), indicating that WPT can be considered as having good diagnostic accuracy. Table 5 provides an important insight into the diagnostic accuracy of WPT and CPT to identify neuropathy in T2DM patients. Hence, according to our findings, CPT has a poor ability to diagnose neuropathy at an early stage in diabetic patients. At the optimal threshold of 44.95°C, WPT demonstrated a sensitivity of 61.5% and a specificity of 63.1%, suggesting good discriminatory ability between diabetic patients with or without neuropathy. There are studies where both warm and cold perception thresholds showed greater sensitivity and specificity as compared to our present study.<sup>9,19</sup> Those studies concluded thermal perception threshold as a significant diagnostic predictor for neuropathy. In our study, CPT did not emerge as a significant diagnostic marker for neuropathy, contrasting with prior reports that emphasized its utility in detecting early small-fiber dysfunction. Gaur et al., in 2024, found hot and cold perception thresholds as a reliable marker for identification of peripheral neuropathy in diabetic patients. However, according to this study, hot perception threshold is more significant and reliable marker than CPT. This discrepancy may be attributed to differences in patient populations, neuropathy severity,

and testing methodologies. Notably, cold sensation is primarily mediated by thinly myelinated A $\delta$  fibers, which are known to be more vulnerable to metabolic and ischemic injury in early diabetic neuropathy. Consequently, CPT is often reported as being affected earlier than WPT, which is mediated by unmyelinated C fibers. Devigili et al. demonstrated that cold detection thresholds are impaired early in small fiber neuropathy, supporting its role as an early marker of small fiber involvement. However, the sensitivity of CPT may be reduced in populations with mixed or advanced neuropathy, where large fiber involvement predominates, or in settings with high intertest variability. These factors may explain the lack of significance of CPT observed in our cohort.<sup>20</sup> Therefore, the results found that WPT remained as an independent predictor of neuropathy in type 2 diabetes mellitus patients.

Therefore, our study emphasizes accurate and timely diagnoses of neuropathy, which enable appropriate treatment, preventative measures, and effective management of diseases, ultimately leading to improved patient health and potentially reducing healthcare costs.

## ACKNOWLEDGMENTS

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## DATA AVAILABILITY

The datasets used and/or analyzed during the present study are available from the corresponding author upon reasonable request.

## AUTHORS' CONTRIBUTIONS

Arpita Chakraborty: Data collection, analysis, interpretation, and writing the draft of the manuscript; Shaikh Alpa Nasrin Samuel: Helped in manuscript writing; Rubia Mondal: Helped with manuscript writing; Subhadeep Ghoshal: Helped in data analysis and graphical representation in R software; Manjusha A Shinde: Helped in manuscript writing; Boudhayan Das Munshi: Helped in patient data collection; Tandra Ghosh: Conceptualization

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