https://dx.doi.org/10.4314/dujopas.v11i1a.35
ISSN (Print): 2476-8316
ISSN (Online): 2635-3490
Dutse Journal of Pure and Applied Sciences (DUJOPAS), *Vol. 11 No. 1a March 2025*

Evaluation of Pain Threshold and Tolerance in Diabetics: Influence of Polyneuropathy and Age-Related Changes

***Kurawa M.I**[1]

[1]Department of Human Physiology,
Faculty of Basic Medical Sciences,
College of Health Sciences,
Bayero University Kano,
Kano State,
Nigeria.

Email: mikurawa2012@gmail.com

Abstract

Diabetes mellitus (DM) is an escalating global health issue, especially in developing countries. The disease is linked to various complications, with peripheral neuropathy being particularly noteworthy. While early detection is important, the lack of simple, bedside screening tool in the clinics may deter early detection and prompt management. The aim was to assess the changes in pain threshold and tolerance among diabetic patients with or without polyneuropathy and healthy controls and the factors associated with it. It is a cross-sectional comparative study involving 60 diabetic patients (28 with polyneuropathy (PNP), 32 without polyneuropathy (WPNP)), aged 20-85 years, and 40 apparently healthy controls. Pain threshold and tolerance in the feet, and polyneuropathy were assessed using the Cold Pressor Test (CPT) and Michigan Neuropathy Screening Index (MNSI) respectively. Results indicate that the majority of participants were not formally educated (54%), and the age group 40-49 had the highest representation (36%). Most participants were married (95%) and belonged to the Hausa/Fulani tribe (82%). The majority had been living with diabetes for around 5 years, and most had Type II DM (90%). Both pain threshold and tolerance of diabetic patients were significantly higher than those of healthy controls, and diabetic patients with PNP had a significantly higher pain threshold compared to those WPNP. Only the right foot pain threshold and tolerance of the DM patients WPNP and the left foot of DM patients with PNP were significantly different among different age groups. Significant differences in pain threshold and tolerance between different Duration of Diabetes (DOD) were observed only in PNP patients. Surprisingly, pain threshold and tolerance of the right foot was always higher than the left foot in DM patients with PNP. Values of pain threshold and tolerances in both feet increased steadily with advancing age and also longer DOD in patients with PNP. Significant positive correlations between pain threshold and tolerance and the DOD were observed in both feet of the DM patients with PNP. Significant positive correlations were found between left foot pain threshold, tolerance, and MNSI scores in PNP patients, whereas insignificant negative correlations were observed in those WPNP. In conclusion, pain threshold and tolerance were significantly higher among PNP compared to WPNP. Pain threshold and tolerance was significantly positively correlated with Age, DOD, and MNSI scores in DM patients with PNP.

Keywords: Diabetes mellitus, Pain threshold and tolerance, Polyneuropathy, Cold pressor test, Michigan neuropathy screening index.

**Author for Correspondence*

INTRODUCTION

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it has (Arokiasamy, *et al*., 2021). Hyperglycemia is a common effect of untreated or poorly managed diabetes which, over time, leads to severe damage to many body systems, especially nerves and blood vessels.

Diabetes mellitus (DM) is an escalating global health issue, especially in developing countries (Sincree, 2006; Ranjbar, 2008). Among its numerous complications, distal symmetric polyneuropathy (DSPN) is the most common (Callaghan *et al*., 2015; Callaghan *et al*., 2016; Pop-Busui *et al*., 2017). DSPN can lead to significant motor and sensory dysfunctions (Hunt, 2002; Booya *et al*., 2005; Janghorbani *et al*., 2006). One critical manifestation is peripheral sensory neuropathy, which heightens the risk of severe foot ulcers, amputations, and Charcot arthropathy (Aliasgharpour and Nayeri, 2012; Lavery *et al*., 2012).

Complications from DSPN are extensive and include severe pain, loss of sensation, foot ulcers, amputations, burns, infections, and various systemic impairments affecting sleep, mood, cardiovascular, gastrointestinal, and reproductive health (Booya *et al*., 2005; Pajouhi *et al*., 2007). These issues profoundly degrade quality of life, lead to frequent hospitalizations, and escalate healthcare costs (Aaberg, 2008; Bruce and Young, 2008).

Early detection and timely intervention are pivotal in mitigating the progression of diabetic polyneuropathy (Viswarothen *et al*., 2004). Regular monitoring of foot sensation in diabetic patients is crucial, with various screening methods, such as monofilaments, being commonly used to identify DPN (Malgrange *et al*., 2003; Modawal *et al*., 2006). Although nerve conduction studies are effective for diagnosing neuropathy, their high cost and time-consuming nature make them less feasible for routine outpatient care (Feng *et al*., 2009). Consequently, annual screenings for peripheral neuropathy are advised for all diabetic patients to effectively manage and reduce the risk of complications (Olaleye *et al*., 2001).

The intensity of pain in diabetic neuropathy seems to depend on small nerve fiber damage and differentiation. According to Kramer et al. Quantitative sensory threshold test, such as the Cold pressor test (CPT) in assessing pain threshold and tolerance, is an essential noninvasive tool for screening peripheral nerve lesion in the Diabetic patient. In addition, several devices/tools are used in physical therapy, rehabilitation settings, and research studies (Kramer, Rolke & Bicke, 2004).

Diabetes and its complications are significant contributors to global health expenditures, accounting for over 12% of worldwide healthcare costs, making diabetes one of the most critical health epidemics of the 21st century (Arokiasamy *et al*., 2021). Diabetic neuropathy, in particular, leads to considerable pain and economic burden, while significantly diminishing the quality of life for affected individuals (Pop-Busui *et al*., 2017). However, with early detection and appropriate intervention, the progression of polyneuropathy can be slowed or even prevented (Ismail, 2023).

In Nigerian diabetes clinics, screening for polyneuropathy is infrequent, which hinders early detection and management (Ismail, 2023). Early detection and timely management are essential to avoid long-term complications associated with diabetic neuropathy.

This study was conducted to assess pain threshold and tolerance in the feet of diabetic patients, both with and without polyneuropathy, and compared these findings with age and sex-matched healthy controls. It aimed to explore the relationship between neuropathy status,

age, and the duration of diabetes. Given the cumbersome nature of the Michigan Neuropathy Screening Instrument (MNSI) test, the study proposed the Cold Pressor Test (CPT) as a simpler, alternative tool for early neuropathy screening in diabetic patients.

Materials and Methods

Study Area: the study was conducted at the Diabetic clinic of Murtala Muhammad Specialist Hospital Kano

Study Setting and Design: This descriptive cross-sectional study involved 60 Diabetics (30 men, 30 women) aged 17 to 85 years who met the inclusion criteria and 40 (20 men, 20 women) age and sex-matched controls.

Inclusion/ Exclusion Criteria: The study included diabetic patients with no other neurological disease, rheumatologic or psychosomatic disorder and who has no regular use of medications that might interfere with pain and who provided an informed consent to participate in the study and excludes those diabetics with other systemic diseases or those who denied consent.

Ethical Consideration: Ethical clearance was obtained from the ministry of health Kano state, with the reference (SHREC/2022/3738) and approval number (NHREC/17/03/2018), dated 24th January 2023. The procedures used in this study adhere to the tenets of the Declaration of Helsinki (as revised in Edinburgh 2000) (Deutsch, 2001).

Sample Size Determination: The sample size of 59 was determined using the formula below,

$$N = \frac{Z^2 \times P\,(1-P)}{e^2}$$

p-value derived from Hanewinckel *et al.,* (2016) was 4%, Z-score of 1.96 and e-value at 95% confidence interval.

Data Collection: An open questionnaire used to capture biodata, neuropathy-related data and physical examination of the participants. Michigan Neuropathy Screening Index (MNSI); Semmes Weinstein Monofilament, Instruments for Cold Pressor Test (CPT), Turning Fork, Patella Hammer, and Stop Watch were used to record the data.

Neuropathy Screening Test: Michigan neuropathy screening index was used to assess the level of polyneuropathy (MNSI; Lunetta *et al.,* 1998). It consists of two parts, i.e. interview and physical assessment part. The self-administered interview part contains 15 neuropathy-related questions. All the responses were added to obtain a total score of 15. A total score of ≥7 was considered abnormal (neuropathy) (Feldman *et al*., 1994). Semmes Weinstein Monofilament (5.07mmg) assessed the light sense touch of the participants on both ulnar and radial nerves of both hands (Birke & Sima, 1985; Lee, Kim & Choi, 2003; Mueller, 1996). The total possible score for physical assessment is ten points and a total score of ≥ 2.5 was considered abnormal (neuropathy) (Feldman *et al*., 1994).

Pain Threshold and Tolerance: Pain threshold and tolerance were assessed using the CPT. Participants submerged their foot in a bowl of ice water (maintained at 1°C). They were instructed to indicate when the cold sensation transformed into pain and to remove their feet when the pain became intolerable or after a maximum of 5 minutes. Pain threshold and tolerance of the left and right feet were recorded as the time of pain reporting and withdrawal, respectively.

Data Analysis: Data were presented as Tables and graphs. One way ANOVA and Tukey's HSD post hoc were used to compare between means and Pearson correlation was used to show relationships. Statistical significance was set at P≤0.05. Data was analyzed using SPSS and GraphPad Prism version 8.4.3.

RESULTS AND DISCUSSION

Sociodemographic Characteristics of Study Participants

The study involved 60 diabetic patients, divided into 32 without polyneuropathy (WPNP; 15 men, 17 women) and 28 with polyneuropathy (PNP; 15 men, 13 women), along with 40 healthy controls (20 men, 20 women). Most participants (54%) lacked formal education, with similar trends observed across diabetic subgroups. A majority of male participants were businessmen (73%), while most women were housewives (20%) (Table 1).

The largest age group was 40–49 years for diabetics (56%) and controls (47.5%). Most participants (95%) were married, predominantly from the Hausa/Fulani tribes (82%), followed by Egbira (10%) and Yoruba (8%). Around 90% of diabetic patients had Type II diabetes, with the majority living with diabetes for about five years. Significant sociodemographic differences were noted between diabetic and control groups, consistent with previous studies (Loi & Li *et al*., 2001) (Table 1).

Table 1: **Socio-**Demographic Data of Participants Based on Group

Characteristics	Diabetic Patients		Control (%)	Overall (%)
	WPNP (%)	PNP (%)		
Gender				
Men	15 (46.9)	15 (53.6)	20 (50)	50 (50)
Women	17 (53.1)	13 (46.4)	20 (50)	50 (50)
Educational Level				
Non formal	18 (56.3)	15 (53.5)	21 (52.5)	54 (54)
Primary	8 (25.0)	8 (28.5)	9 (22.5)	25 (25)
Secondary	4 (12.5)	4 (14.3)	7 (17.5)	15 (15)
Tertiary	2 (6.25)	1 (3.7)	3 (7.5)	6 (6)
Occupation				
Business	24 (75.0)	23 (82.1)	26 (65)	73 (73)
Civil Servant	1 (3.1)	1 (3.6)	2 (5)	4 (4)
Full time house wives	6 (18.8)	4 (14.3)	10 (25)	20 (20)
Student	1 (3.1)	0 (0)	2 (5)	3 (3)
Age (years)				
20 – 29	2 (6.3)	2 (7.1)	0 (0)	4 (4)
30 – 39	7 (21.9)	2 (7.1)	15 (37.5)	24 (24)
40 – 49	10 (31.3)	7 (25.0)	19 (47.5)	36 (36)
50 – 59	11 (34.3)	6 (21.4)	6 (15)	23 (23)
60 – 69	2 (6.3)	5 (17.9)	0 (0)	7 (7)
70 and above	0 (0)	6 (21.4)	0 (0)	6 (6)
Marital Status				
Single	1 (3.1)	2 (7.1)	0 (0)	3 (3)
Married	27 (84.4)	26 (92.9)	38 (95)	38 (95)
Divorce/widow	4 (12.5)	0 (0)	2 (5)	6 (6)
Ethnicity				
Hausa/Fulani	27 (84.4)	23 (82.1)	32 (80)	82 (82)
Yoruba	3 (9.4)	1 (3.6)	4 (10)	8 (8)
Egbira	2 (6.3)	4 (14.3)	4 (10)	10 (10)
Diabetes Duration (years)				
0 – 5	20 (62.5)	12 (42.9)		
>5 – 10	8 (25.0)	8 (28.6)		
>10 – 15	2 (6.3)	3 (10.7)		

>15 – 20	0 (0)	2 (7.1)	
>20 – 25	0 (0)	3 (10.7)	
>25	2 (6.3)	0 (0)	
Diabetes Type			
Type I	3 (9.4)	3 (10.7)	6 (10)
Type II	29 (90.6)	25 (89.3)	54 (90)

Frequency Distribution Table. Without polyneuropathy (WPNP) n=32; polyneuropathy patients (PNP) n=28.

Pain Threshold and Tolerance in Diabetic Patients and Control Participants

Table 2 compares the pain threshold and tolerance of diabetic patients (with polyneuropathy, PNP, and without polyneuropathy, WPNP) to healthy controls. Both the pain threshold and tolerance in the right and left foot of diabetic patients were significantly higher than those in the control group. Specifically, diabetic patients with PNP had a notably higher pain threshold than those without PNP. Consistent with these findings, several studies have shown that diabetics with neuropathy exhibit the highest pain thresholds and tolerance levels (Telli and Cavlak, 2006; Kannan *et al*., 2014; Prakash *et al*., 2019). Moreover, Chantelau *et al*., (2012) discovered that perception thresholds for light cutaneous pressure pain were markedly elevated in diabetic neuropathic feet, especially in cases of Charcot foot (Chantelau *et al*., 2012). The cold pressor test (CPT) is an objective method used to assess pain by measuring pain threshold and tolerance (Meric, 1993). Despite its effectiveness, CPT has not been extensively used to evaluate pain in diabetic patients. Various studies have consistently reported that diabetic individuals exhibit higher pain thresholds compared to healthy controls (Sacca and Amadio, 1995; Lee and McCarty *et al*., 1992; Sierra-Silvestre *et al*., 2020).

Our findings align with those of Jessen *et al*., (1991), who found increased vibration and thermal pain thresholds in patients with more severe neuropathy. Similarly, Hiz, Claus, and Neurdorfer (1988) observed higher thermal pain thresholds and tolerances in diabetic patients compared to controls. These results suggest that diabetes mellitus elevates pain thresholds and tolerance, indicating peripheral nerve damage. This nerve damage is more pronounced in diabetic patients with polyneuropathy than in those without it (Ziegler *et al*., 2009; Akintoye *et al*., 2020). The damage typically involves small-fiber dysfunction, which is commonly associated with neuropathic pain in diabetic patients (Vlckova-Moravcova *et al*., 2008).

Table 2: Comparison of Pain Threshold and Tolerance Between Diabetic Patients and Healthy Controls

Variable (secs)	Control (n =40) Mean ± S.D	WPNP (n=32) Mean ± S.D	PNP (n = 28) Mean ± S.D	F	P
Pain Threshold					
Left Foot	46.6 ± 8.1^{ab}	92.3 ± 9.2^{bc}	104.5 ± 1.6^{ac}	605.1	0.001*
Right Foot	50.0 ± 8.8^{ab}	96.9 ± 9.9^{bc}	110.6 ± 2.7^{ac}	543.6	0.001*
Pain Tolerance					
Left Foot	90.6 ± 8.1^{ab}	174.3 ± 9.2^{bc}	181.5 ± 1.6^{ac}	1685.8	0.001*
Right Foot	95.3 ± 9.2^{ab}	180.9 ± 9.9^{bc}	190.6 ± 2.7^{ac}	1441.0	0.001*

One Way ANOVA. secs: seconds; *Indicates statistical significance. Tukey HSD Post Hoc Test:
Pain threshold: left and right: a, b, and c, p-values were 0.001.
Pain tolerance: left and right: a, b, and c, p-values were 0.001.

Pain Threshold and Tolerance Across Different Age Groups in Diabetic Patients

In diabetic patients without polyneuropathy, significant differences in pain threshold and tolerance were found only in the right foot across different age groups (Table 3). Conversely, in diabetic patients with polyneuropathy, significant differences were observed only in the left foot's pain threshold and tolerance across age groups (Table 4). Notably, pain threshold

and tolerance consistently increased with age, with the highest values recorded in patients aged 80 and above in the PNP group (Table 4).

Table 3: Comparison of Pain Threshold and Tolerance Among Different Age Groups in Diabetic Patients Without Polyneuropathy

Variable (secs)	Age (years) 20 – 29 (n=1)	30 – 39 (n=8)	40 – 49 (n=10)	50 – 59 (n=11)	60 – 69 (n=2)	F	P
Pain Threshold							
Left Foot	92.0	85.5±12.4	93.3±4.8	96.6±8.5	90.0±1.4	2.0	0.12
Right Foot	96.0	88.6±9.1	96.9±8.6	103.6±8.8	93.5±0.7	3.5	0.02*
Pain Tolerance							
Left Foot	174.0	167.5±12.4	175.3±4.8	178.6±8.5	172.0±1.4	2.0	0.12
Right Foot	180.0	172.6±9.1	180.9±8.6	187.6±8.87	177.5±0.7	3.5	0.02*

One Way ANOVA. secs: seconds; *Indicates statistical significance.

Table 4: Comparison of Pain Threshold and Tolerance Among Different Age Groups in Diabetic Patients with Polyneuropathy

Variable (Sec)	Age (years) ≤20 (n=1)	20 – 29 (n=1)	30 – 39 (n=2)	40 – 49 (n=7)	50 – 59 (n=6)	60 – 69 (n=5)	70-80 (n=4)	≥80 (n=2)	F	Sig.
Pain threshold										
Left Foot	101.0	102.0	103.0±1.4	104.6±1.1	103.8±0.8	105.2±1.6	105.3±1.3	107.0±1.4	4.07	0.006*
Right Foot	106.0	105.0	110.5±2.1	110.1±2.7	111.8±2.3	111.0±2.2	111.3±1.5	112.0±5.7	4.07	0.006*
Pain tolerance										
Left Foot	178.0	179.0	180.0±1.4	181.6±1.1	180.8±0.8	182.2±1.6	182.3±1.3	184.0±1.4	1.50	0.226
Right Foot	186.0	185.0	190.5±2.1	190.1±2.7	191.8±2.3	191.0±2.2	190.8±1.5	192.0±5.7	1.50	0.226

One Way ANOVA. secs: seconds; *Indicates statistical significance.

Pain Threshold and Tolerance Across Different Durations of Diabetes

In patients without polyneuropathy, there were no significant differences in pain threshold and tolerance related to the duration of diabetes (Table 5). Conversely, significant differences were noted between duration of diabetes (DOD) groups in patients with polyneuropathy (Table 6). Pain threshold and tolerance increased with longer durations of diabetes, with higher values observed in the right foot compared to the left among diabetic patients with polyneuropathy (Table 6).

Table 5: Comparison of Pain Threshold and Tolerance Based on the Duration of Diabetes in Patients Without Polyneuropathy

Variable (secs)	Duration of Diabetes (years) 0 - 5 (n=21)	>5–10 (n=8)	>10–15 (n=2)	>15–20 (n=0)	>20–25 (n=0)	>25 (n=1)	F	P
Pain threshold								
Left Foot	90.09.8	94.8±4.9	100.0±9.9	-	-	105.0	1.9	0.15
Right Foot	94.1±8.1	101.1±9.0	100.0±22.6	-	-	116.0	1.9	0.15
Pain tolerance								
Left Foot	172.0±9.8	176.8±4.9	182.0±9.9	-	-	187.0	2.7	0.06
Right Foot	178.1±8.1	185.1±9.0	184.0±22.6	-	-	200.0	2.7	0.06

One-Way ANOVA, secs: seconds, *Indicates statistical significance. p≤0.05.

Table 6: Comparison of Pain Threshold and Tolerance Based on the Duration of Diabetes in Patients with Polyneuropathy

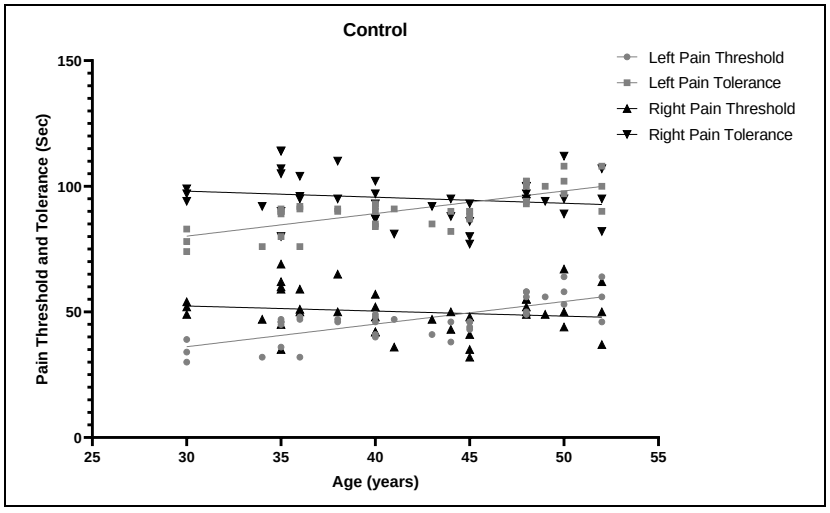
Variable (secs)	DM Duration (years) 0 - 5 (n=12)	>5 – 10 (n=8)	>10 – 15 (n=3)	>15 – 20 (n=2)	>20 – 25 (n=3)	F	Sig.
Pain Threshold							
Left Foot	108.8±1.6	104.1±1.4	104.7±1.2	106.5±0.7	106.3±1.5	2.9	0.04*
Reft Foot	109.2±2.6	111.1±1.7	113.3±2.9	109.0±1.4	113.7±2.1	2.9	0.04*
Pain Tolerance							
Left Foot	180.8±1.6	181.1±1.4	181.7±1.2	183.5±0.7	183.3±1.5	4.0	0.01*
Right Foot	189.2±2.6	191.1±1.7	193.3±2.9	189.0±1.4	193.0±3.0	4.0	0.01*

One-Way ANOVA, secs: seconds, *Indicates statistical significance.

The Relationship Between Pain Threshold, Tolerance, and Age

Correlation analysis revealed significant positive correlations between pain threshold, tolerance, and age in controls, particularly in the left foot (r^2=0.5, p<0.0001). In the right foot of controls, correlations were very low and statistically insignificant (threshold: r^2=0.02, p=0.4; tolerance: r^2=0.03, p=0.3). Among diabetic patients without polyneuropathy (WPNP), only the right foot showed significant very low positive correlations for both threshold and tolerance (r^2=0.1, p=0.04). In contrast, diabetic patients with polyneuropathy (PNP) exhibited significant positive correlations in both feet for threshold and tolerance (left foot: r^2=0.4, p=0.0002; right foot: r^2=0.2, p=0.03 and 0.04) (Figure 1).

Several studies have also identified age, glycemic control, and duration of diabetes as risk factors for developing peripheral nerve dysfunction (Valensi *et al*., 1997; Ziegler *et al*., 2009).



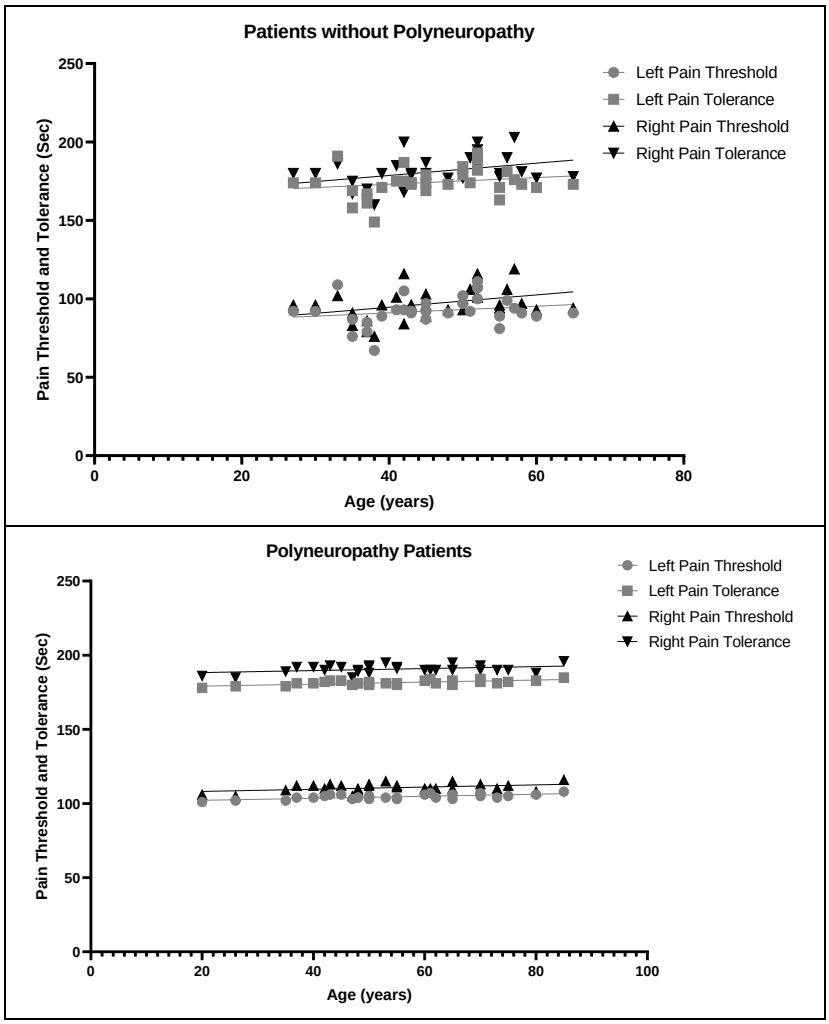


Figure 1: Correlation between pain threshold and tolerances and the age (years) in the control and diabetic patients with and without polyneuropathy.

Pearson correlation, (Control, left foot threshold and tolerance, r^2=0.5, p<0.0001; right foot threshold (r^2=0.02) and tolerance (r^2=0.03), p=0.4 and 0.3 respectively), (WPNP, left-foot threshold and tolerance, r^2=0.05, p=0.2; right-foot threshold and tolerance, r^2=0.1, p=0.04), (PNP, left foot threshold and tolerance, r^2=0.4, p=0.0002; right foot threshold and tolerance, r^2=0.2, p=0.03 and 0.04 respectively).

The Relationship Between Pain Threshold, Tolerance, and Duration of Diabetes

Significant positive correlations were observed between pain threshold, tolerance, and duration of diabetes (DOD) in diabetic patients with polyneuropathy (PNP) (left foot: r^2=0.4, p=0.0005; right foot: threshold r^2=0.2, p=0.008, tolerance r^2=0.2, p=0.02) and without polyneuropathy (WPNP) (left foot: r^2=0.1, p=0.04; right foot: r^2=0.2, p=0.02) (Figure 2). These findings are consistent with those of Nisar *et al.* (2015), who reported a significant association between diabetic neuropathy and duration of diabetes. Additionally, Lee *et al*. (2016) identified elevated HbA1c levels as a risk factor for polyneuropathy in diabetic patients, correlating with the severity of the condition.

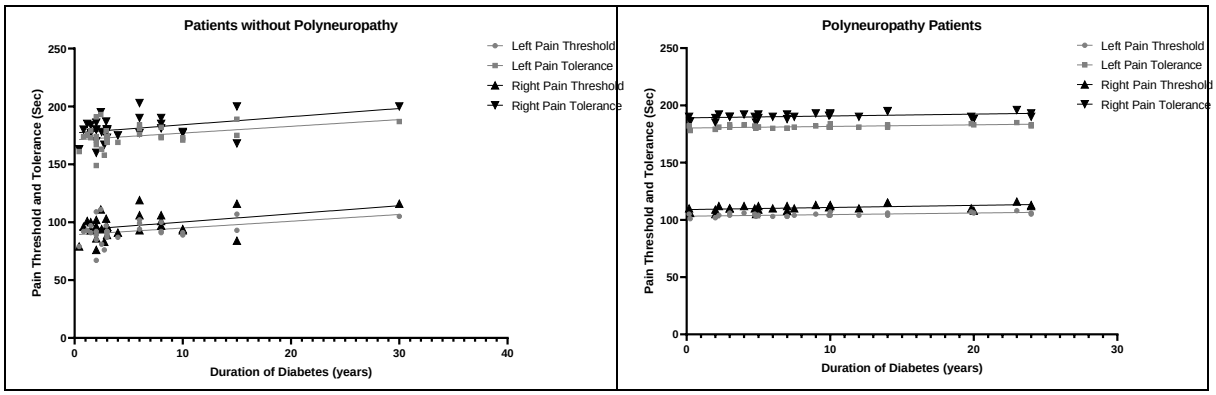


Figure 2: Correlation between pain threshold and tolerances and the duration of Diabetes (years) in the diabetic patients with and without polyneuropathy.
Pearson correlation, (WPNP: left foot threshold and tolerance, r^2=0.1, p=0.04; right foot threshold and tolerance, r^2=0.2, p=0.02), (PNP: left foot threshold and tolerance, r^2=0.4, p=0.0005; right foot threshold and tolerance, r^2=0.2, p=0.008 and 0.02 respectively).

The Relationship Between Pain Threshold, Tolerance, and Michigan Neuropathy Screening Index

Significant positive correlations were observed only in the left foot for pain threshold and tolerance among diabetic patients with polyneuropathy (PNP) (left foot: r^2=0.2, p=0.02; right foot: r^2=0.06, p=0.2) (Figure 3). This suggests that there is no significant association between Michigan Neuropathy Screening Index (MNSI) scores and pain threshold or tolerance in patients without polyneuropathy. Kumar *et al.* (2023) found a significant association between the duration of diabetes and the severity of neuropathy, indicating that patients with longer diabetes durations experience more severe peripheral neuropathy.

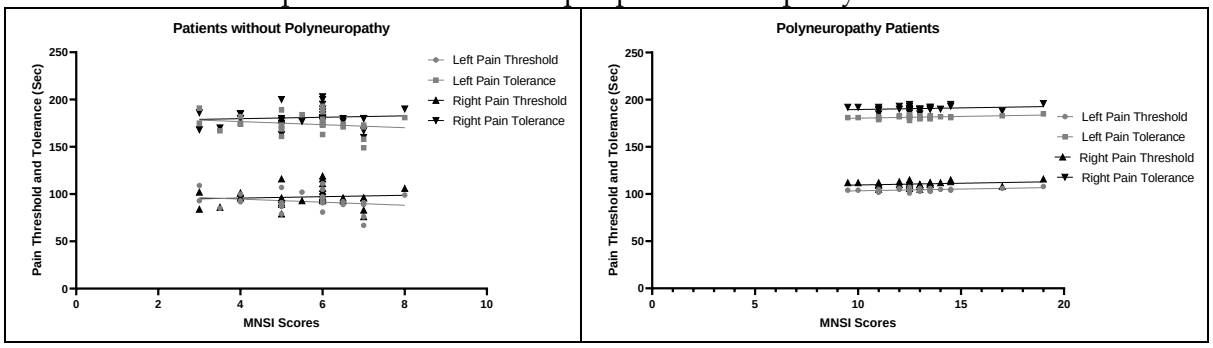


Figure 3: Correlation between pain threshold and tolerances and the MNSI scores in the diabetic patients with and without polyneuropathy.
Pearson correlation, (WPNP, left foot threshold and tolerance, r^2= 0.05, p=0.2; right foot threshold and tolerance, r^2= 0.008, p=0.6), (PNP, left foot threshold and tolerance, r^2=0.2, p=0.02; right foot threshold and tolerance, r^2=0.06, p=0.2).

CONCLUSION AND RECOMMENDATION

In Nigerian diabetes clinics, screening for polyneuropathy is infrequent, which impedes early detection and management of the condition. Early identification and timely intervention are however crucial to prevent the long-term complications associated with diabetic neuropathy. Due to the cumbersome nature of the Michigan Neuropathy Screening Instrument (MNSI), this study suggests using the Cold Pressor Test (CPT) as a simpler and more cost-effective alternative for early neuropathy screening in diabetic patients.

The study aimed to evaluate pain threshold and tolerance in the feet of diabetic patients, both with and without polyneuropathy, and compare these results with age and sex-matched healthy controls. The objective was to explore the relationship between neuropathy status,

age, duration of diabetes, and MNSI scores. Our findings showed that diabetic patients with polyneuropathy had significantly higher pain thresholds and tolerance compared to those without polyneuropathy. Additionally, pain threshold and tolerance were significantly, positively correlated with age, duration of diabetes, and MNSI scores in diabetic patients with polyneuropathy.

Based on these results, we propose that the Cold Pressor Test could be an effective and simple screening tool for polyneuropathy in diabetic patients, especially in resource-constrained settings.

REFERENCES

Aaberg, M. L., Burch, D. M., Hud, Z. R., & Zacharias, M. P. (2008). Gender differences in the onset of diabetic neuropathy. *Journal of Diabetes and its Complications*, **22**(2), 83-87.

Akintoye, O. O., Owoyele, B. V., Fabunmi, O. A., Raimi, T. H., Oniyide, A. A., Akintoye, A. O., ... & Adeleye, G. S. (2020). Diabetic neuropathy is associated with increased pain perception, low serum beta-endorphin and increase insulin resistance among Nigerian cohorts in Ekiti State. *Heliyon*, **6**(7), 1-7.

Aliasgharpour, M., & Nayeri, N. D. (2012). The care process of diabetic foot ulcer patients: a qualitative study in Iran. *Journal of Diabetes & Metabolic Disorders*, **11**, 1-9.

Arokiasamy, P., Salvi, S., & Selvamani, Y. (2021). Global burden of diabetes mellitus. In Handbook of Global Health. Pp. 1-44. Cham: Springer International Publishing.

Birke, J.A., & Sima, P.S (1985). Plantar Sensory Threshold in Ulcerative foot. Read at the Proceedings of International Conference on Biomechanics and Clinical Kinesiology of Hand and Foot, *Madro*, India.

Booya, F., Bandarian, F., Larijani, B., Pajouhi, M., Nooraei, M., & Lotfi, J. (2005). Potential risk factors for diabetic neuropathy: a case control study. BMC neurology, 5, 1-5.

Bruce, S. G., & Young, T. K. (2008). Prevalence and risk factors for neuropathy in a Canadian First Nation community. *Diabetes care*, **31**(9), 1837-1841.

Callaghan, B. C., Xia, R., Banerjee, M., de Rekeneire, N., Harris, T. B., Newman, A. B., ... & Strotmeyer, E. S. (2016). Metabolic syndrome components are associated with symptomatic polyneuropathy independent of glycemic status. *Diabetes care*, **39**(5), 801-807.

Callaghan, B. C., Price, R. S., Chen, K. S., & Feldman, E. L. (2015). The importance of rare subtypes in diagnosis and treatment of peripheral neuropathy: a review. *JAMA neurology*, **72**(12), 1510-1518.

Chantelau, E., Wienemann, T., & Richter, A. (2012). Pressure pain thresholds at the diabetic Charcot-foot: an exploratory study. *J Musculoskelet Neuronal Interact*, **12**(2), 95-101.

Deutsch, E. (2001). The Declaration of Helsinki Revised by the World Medical Organisation, Edinburgh 2000. Victoria U. Wellington L. Rev., 32, 633.

Feldman, E. L., Stevens, M. J., Thomas, P. K., Brown, M. B., Canal, N., & Greene, D. A. (1994). A practical two-step quantitative clinical and electrophysiological assessment for the diagnosis and staging of diabetic neuropathy. *Diabetes care*, **17**(11), 1281-1289.

Feng, Y., Schlösser, F. J., & Sumpio, B. E. (2009). The Semmes Weinstein monofilament examination as a screening tool for diabetic peripheral neuropathy. *Journal of vascular surgery*, **50**(3), 675-682.

Hiz, M., Claus, D., & Neurdorfer, B. (1988). Early diagnosis of diabetic small fiber neuropathy by cold perception. *Diabetes Complications*, **2**(1), 38 – 43.

Hunt, D. (2002). Using evidence in practice: foot care in diabetes. *Endocrinology and Metabolism Clinics*, **31**(3), 603-611.

Ismail, C. A. N. (2023). Issues and challenges in diabetic neuropathy management: a narrative review. *World Journal of Diabetes*, **14**(6), 741.

Janghorbani, M., Rezvanian, H., Kachooei, A., Ghorbani, A., Chitsaz, A., Izadi, F., & Amini, M. (2006). Peripheral neuropathy in type 2 diabetes mellitus in Isfahan, Iran: prevalence and risk factors. *International Journal of Diabetes and Metabolism*, **14**(3), 126-133.

Jensen, T. S., Bach, F. W., Kastrup, J., Deigaard, A., & Brennum, J. (1991). Vibratory and thermal thresholds in diabetics with and without clinical neuropathy. *Acta neurologica scandinavica*, **84**(4), 326-333.

Kannan, M. A., Sarva, S., Kandadai, R. M., Paturi, V. R., Jabeen, S. A., & Borgohain, R. (2014). Prevalence of neuropathy in patients with impaired glucose tolerance using various electrophysiological tests. *Neurology India*, **62**(6), 656-661.

Kumar U., Anjali S., Deepak S., and Nivesh A. (2023). Relationship between the duration of diabetes and severity of neuropathy in patients of peripheral neuropathic diabetic foot ulcers. International Journal of Research in Medical Sciences. *Int J Res Med Sci.* **11**(5):1549-1552

Kim, Y., Kim, H., Choi, S., Park, Y., Lee, S., & Cho, B. (2003). Clinical usefulness of the two-site Semmes-Weinstein monofilament test for detecting diabetic peripheral neuropathy. *Journal of Korean medical science*, **18**(1), 103-107.

Lavery, L. A., Lavery, D. E., Lavery, D. C., LaFontaine, J., Bharara, M., & Najafi, B. (2012). Accuracy and durability of Semmes–Weinstein monofilaments: What is the useful service life? *Diabetes research and clinical practice*, **97**(3), 399-404.

Lee, J. H., & Mc Carty, R. (1992). Pain threshold in diabetic rats: Effects of good versus poor diabetic control. *Muscle and Nerve*, **15** (12), 1334 – 1339.

Lee, W. J., Jang, S., Lee, S. H., & Lee, H. S. (2016). Correlation between the severity of diabetic peripheral polyneuropathy and glycosylated hemoglobin levels: a quantitative study. *Annals of rehabilitation medicine*, **40**(2), 263-270.

Loi, S. W., & Li, T. C. (2001). Body mass index and its related factor in the elderly. International *Journal of Obesity and Related Metabolic Disorder*, **8** (1), 56 – 60.

Lunetta, M., Le Moli, R., Grasso, G., & Sangiorgio, L. (1998). A simplified diagnostic test for ambulatory screening of peripheral diabetic neuropathy. *Diabetes research and clinical practice*, **39**(3), 165-172.

Malgrange, D., Richard, J. L., Leymarie, F., & French Working Group on the Diabetic Foot. (2003). Screening diabetic patients at risk for foot ulceration. A multi-centre hospital-based study in France. *Diabetes & metabolism*, **29**(3), 261-268.

Meric¸, A. (1993). Comparison of the effects of analgesic currents on pain threshold and tolerance, Hacettepe University Institute of Health Sciences Physical Therapy and Rehabilitation Programme Master thesis, Ankara.

Modawal, A., Fley, J., Shukla, R., Rudawsky, D., Welge, J., & Yang, J. (2006). Use of monofilament in the detection of foot lesions in older adults. *The Journal of foot and ankle surgery*, **45**(2), 76-81.

Mueller, M. J. (1996). Identifying patients with diabetes mellitus who are at risk for lower-extremity complications: use of Semmes-Weinstein monofilaments. *Physical Therapy*, **76**(1), 68-71.

Nisar, M. U., Asad, A., Waqas, A., Ali, N., Nisar, A., Qayyum, M. A., & Jamil, M. Association of diabetic neuropathy with duration of type 2 diabetes and glycemic control. *Cureus*, **7**(8): e302.

Olaleye, D., Perkins, B. A., & Bril, V. (2001). Evaluation of three screening tests and a risk assessment model for diagnosing peripheral neuropathy in the diabetes clinic. *Diabetes research and clinical practice*, **54**(2), 115-128.

Pajouhi, M., & MR, M. T. (2007). Evaluation and prevention of diabetic neuropathy. *Tehran University of Medical Sciences Journal*, **65**(3), 1-6.

Pop-Busui, R., Boulton, A. J., Feldman, E. L., Bril, V., Freeman, R., Malik, R. A., ... & Ziegler, D. (2017). Diabetic neuropathy: a position statement by the American Diabetes Association. *Diabetes care*, **40**(1), 136-154.

Prakash, S.B., Shankarappa, V., and Prabha V. (2019). A Comparative Study of Pain Thresholds between Diabetic Neuropathy Patients & Non Diabetic Subjects. *International Journal of Physiology*, **7**(2);185-187. DOI Number: 10.5958/2320-608X.2019.00070.2

Ranjbar, H. (2008). Overview of diabetic foot; novel treatments in diabetic foot ulcer. *DARU Journal of Pharmaceutical Sciences*, **16**(1), 1-6.

Sacca, I. C. N., & Amadio, A. C. (1995). Peak pressure pain tolerance threshold in gait analysis of neuropathic patients. *Journal of Bone and Joint Surgery*, **7**(6), 78 – 85.

Sicree, R. (2006). Diabetes and impaired glucose tolerance. *Diabetes atlas*, 15-109.

Sierra-Silvestre, E., Somerville, M., Bisset, L., & Coppieters, M. W. (2020). Altered pain processing in patients with type 1 and 2 diabetes: systematic review and meta-analysis of pain detection thresholds and pain modulation mechanisms. *BMJ Open Diabetes Research and Care*, **8**(1), e001566.

Telli, O., & Cavlak, U. (2006). Measuring the pain threshold and tolerance using electrical stimulation in patients with Type II diabetes mellitus. *Journal of Diabetes and its Complications*, **20**(5), 308-316.

Valensi, P., Giroux, C., Seeboth-Ghalayini, B., & Attali, J. R. (1997). Diabetic peripheral neuropathy: effects of age, duration of diabetes, glycemic control, and vascular factors. *Journal of Diabetes and its Complications*, **11**(1), 27-34.

Viswanathan, V., Seena, R., Nair, M. B., Snehalatha, C., Bhoopathy, R. M., & Ramachandran, A. (2004). Nerve conduction abnormalities in different stages of glucose intolerance. *Neurology India*, **52**(4), 466-469.

Vlckova-Moravcova, E., Bednarik, J., Belobradkova, J., & Sommer, C. (2008). Small-fibre involvement in diabetic patients with neuropathic foot pain. *Diabetic medicine*, **25**(6), 692-699.

Ziegler, D., Rathmann, W., Dickhaus, T., Meisinger, C., & Mielck, A. (2009). Neuropathic pain in diabetes, prediabetes and normal glucose tolerance: the MONICA/KORA Augsburg Surveys S2 and S3. *Pain medicine*, **10**(2), 393-400.