e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2023; 15(10); 1620-1624

Original Research Article

Peripheral Neuropathy in Type 2 Diabetes Mellitus: Strategies for Early Detection

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Received: 25-08-2023 / Revised: 23-09-2023 / Accepted: 18-10-2023
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Conflict of interest: Nil

Abstract:

Background: Diabetes is a common metabolic disorder linked to high blood sugar levels, causing issues like peripheral neuropathy. In India nearly 29.3% of people with diabetes experience peripheral neuropathy due to factors such as oxidative stress, vascular problems, and metabolic disturbances in Type 2 Diabetes Mellitus (T2DM). Early detection of neuropathy is crucial for better outcomes, prompting annual screening recommendations for T2DM patients.

Methodology: This study focused on T2DM patients aged 18 and older, categorized into three groups based on neuropathy severity: no neuropathy, mild neuropathy, and moderate to severe neuropathy. Exclusions encompassed unrelated conditions, test limitations, those under 18, and non-consenting individuals. A total of 80 patients underwent comprehensive medical and neurological assessments. Data collection involved standard tests like blood counts, liver and kidney function evaluations, HbA1c levels, serum interleukin-6 (IL-6) levels.

Results: Patients with severe neuropathy had longer diabetes duration, higher HbA1c levels, BMI, blood pressure, and cholesterol levels. Nerve conduction variations existed among groups, with serum IL-6 levels correlating with neuropathy severity. RNFL thickness, assessed using OCT, decreased with worsening neuropathy and directly related to nerve function.

Recommendations: Timely neuropathy detection and monitoring are crucial in T2DM. Disease duration, HbA1c levels, and IL-6 levels can predict neuropathy severity. Serum IL-6 levels and RNFL thickness are valuable markers for assessing neuropathy severity. Maintaining blood sugar control is pivotal in preventing diabetes-related complications, including neuropathy.

Conclusion: This study highlights factors influencing peripheral neuropathy in T2DM, offering diagnostic and monitoring markers. Effective blood sugar management is key to averting diabetes-related complications, emphasizing early neuropathy detection and management for improved outcomes.

Keywords: Diabetes, Peripheral Neuropathy, Type 2 Diabetes Mellitus (T2DM), Serum IL-6 Levels.

Introduction

An ongoing elevated blood sugar level is the hallmark of diabetes mellitus (DM), a prevalent metabolic illness. Heart disease, stroke, peripheral neuropathy, kidney issues, and blindness are just a few of the complications that may result from it. One of the main health issues facing the world today is type 2 diabetes mellitus (T2DM). 16.8% of Indians were reported to have diabetes in a research that was done there [1, 2].

Diabetic neuropathy is a term used when persons with diabetes have symptoms and evidence of nerve dysfunction, after ruling out other probable causes. The rate of peripheral neuropathy in diabetic individuals in India is about 29.3%. Oxidative stress, vascular problems, and metabolic abnormalities are important factors in the development of diabetic polyneuropathy in patients with type 2 diabetes [3, 4].

The prognosis and avoidance of serious consequences are significantly enhanced by early identification of diabetic polyneuropathy (DPN). From the time they receive a T2DM diagnosis onward, it is advised that all diabetic patients have a neuropathy screening at least annually [5].

The development of problems such as DPN is known to be greatly influenced by an inflammatory component of type 2 diabetes. Ex vivo research on diabetic neuropathic patients and diabetic patients with foot ulcers has demonstrated elevated expression of IL-6 in nerve biopsies as compared to non-neuropathic patients [6].

The retina is vulnerable to DPN-related injury because, similar to peripheral nerves, it has a large number of sensory neurons. Diabetes leads to the loss of photoreceptors and ganglion cells, as well as weakening of the retinal nerve fibre layer. A notable weakening of the macular retinal nerve fibre layer is also observed in patients with DPN. It is important to research retinal alterations since it can reveal possible early warning signs of problems. With the goal of early detection of peripheral neuropathy in T2DM patients, this study looked at clinical, radiographic, laboratory, and neurophysiological data [7].

The aim of the study is to early detection of neuropathy in patients having T2DM

Methodology

Study Design: This study is cross sectional in nature.

Study Setting and Participation: It was a cross-sectional study conducted in 80 diagnosed cases of T2DM patients attending the OPD, inpatient in department of Medicine and Neurology, GSVM medical college and hospital, Kanpur, between April 2022 to April 2023 and assessed for peripheral neuropathy. Ethics committee approval was duly taken with the study conducted in accordance with the guidelines. Informed consent was taken from each participant.

Inclusion and Exclusion Criteria: The study included patients aged 18 or older diagnosed with (T2DM) following ADA criteria. They were grouped based on (TCNS): Group 1 (no neuropathy, TCNS 0-3), Group 2 (mild neuropathy, TCNS 6-8), and Group 3 (moderate to severe neuropathy, TCNS 9-18).

Exclusion criteria encompassed patients with conditions other than T2DM linked to neuropathy, contraindications or limitations for neurological exams, nerve conduction studies, OCT, or ELISA testing, individuals under 18, and those without informed consent.

Study Size: After fulfilling the inclusion criteria, 80 patients underwent thorough medical and neurological evaluation.

Data Collection and Analysis: Data were collected via. laboratory investigations included standard tests like complete blood count, liver and renal function assessments, and HbA1c levels. Additionally, a specific ELISA technique, (OCT) was used to measure (RNFL) thickness precisely. A circular profile of 3.4 mm centered on the optic disc, manually adjusted to the disc margins, assessed RNFL thickness.

Bias: To minimize bias, the goal of the research was not disclosed to the participants or healthcare providers during data collection. Additionally, data analysts were blinded to the identity of the participants.

Variables: In this study, various analyses were performed to understand the relationship between different variables and neuropathy severity. The variables examined included disease duration, HbA1c levels, BMI, systolic and diastolic blood pressure, serum interleukin-6 (IL-6) levels, and (RNFL) thickness measured by (OCT).

Statistical Analysis: Statistical analysis was carried out using SPSS version 24. Descriptive statistics were used to summarize the data. To compare mean values, an independent sample t-test was used, and differences among the three subject groups were assessed with a one-way analysis of variance (ANOVA) test. Post hoc Tukey tests were conducted to identify specific group differences. Logistic regression analysis examined the influence of independent variables on neuropathy severity, while Receiver Operating Characteristic (ROC) curve analysis evaluated the effectiveness of serum IL-6 levels and RNFL thickness in diagnosing neuropathy severity. A significance level of $p<0.05$ was employed throughout the analysis to determine statistical significance.

Ethical Considerations: The study was carried out in accordance with ethical guidelines, which included getting each participant's informed consent. The ethics committee examined and approved the study protocol.

Results

Table 1: Comparative Analysis of Clinical Characteristics in Patients Grouped by Neuropathy Severity"

Characteristic	Group 1 (No Neuropathy)	Group 2 (Mild Neuropathy)	Group 3 (Moderate to Severe Neuropathy)	Total (N=80)
Total Patients (n)	27	27	26	80
Gender Distribution (%)	33.75% M / 66.25% F	33.75% M / 66.25% F	33.75% M / 66.25% F	-
Age (Mean ± SD)	55.00 ± 6.22 years	54.10 ± 4.71 years	55.30 ± 5.75 years	-
Disease Duration (Mean ± SD)	3.30 ± 1.30 years	6.60 ± 1.39 years	12.75 ± 6.66 years	-
HbA1c Levels (Mean ± SD)	6.07 ± 0.13	7.70 ± 0.49	9.11 ± 0.79	-
BMI (Mean ± SD)	22.37 ± 1.82	24.97 ± 2.41	29.01 ± 2.57	-

Diastolic BP (Mean ± SD)	77.00 ± 7.33 mmHg	82.00 ± 7.68 mmHg	87.50 ± 7.16 mmHg	-
Systolic BP (Mean ± SD)	125.00 ± 11.12 mmHg	127.50 ± 15.85 mmHg	140.25 ± 19.63 mmHg	-
Total Cholesterol (Mean ± SD)	186.42 ± 12.83 mg/dl	196.41 ± 6.39 mg/dl	210.27 ± 18.00 mg/dl	-

In this study, 80 patients diagnosed with T2DM were meticulously examined according to the criteria established by the ADA. These patients were categorized into three groups based on their (TCNS) to assess the severity of neuropathy. Group 1 consisted of 27 patients without evident neuropathy, while Group 2 included 27 patients with mild neuropathy, and Group 3 comprised 26 patients with moderate to severe neuropathy. Importantly, the study excluded patients with underlying medical conditions that could potentially contribute to neuropathy, ensuring a focus solely on T2DM-related neuropathy.

The comprehensive assessment of these 80 patients involved extensive medical and neurological evaluations, including Nerve Conduction Studies, (OCT) to measure (RNFL) thickness, and a battery of laboratory tests, such as Serum Interleukin-6 (IL-6) levels. Statistical analyses were employed to explore the data, encompassing descriptive statistics, t-tests, one-way ANOVA, Tukey tests, and logistic regression. The diagnostic utility of serum IL-6 levels and RNFL thickness as markers for neuropathy severity was assessed using Receiver Operating Characteristic (ROC) curve analysis.

Among the notable findings, the gender distribution revealed that 33.75% of the patients were male, while 66.25% were female. Clinical parameters varied significantly among the patient groups, with Group 3 showing the most pronounced differences, including longer disease duration, higher HbA1c levels, increased BMI, elevated blood pressure readings (both systolic and diastolic), and higher total cholesterol levels. Nerve conduction parameters also exhibited substantial differences across the three patient groups.

Discussion

This study expanded upon previous findings by conducting a thorough examination of 80 T2DM patients, shedding light on the intricate relationships between clinical and laboratory parameters, neuropathy severity, and potential diagnostic markers. It reaffirmed the diagnostic significance of both serum IL-6 levels and RNFL thickness, as measured by OCT, in assessing neuropathy severity within this extended patient cohort. These findings represent a valuable contribution to the field of diabetic neuropathy research.

One serious side effect of diabetes is (DPN), which is characterized by peripheral nerve injury. Diagnosing this problem usually involves excluding other possible causes of neuropathy and evaluating symptoms and indicators of nerve loss in diabetes patients. Further evidence for the diagnosis comes from investigations on nerve conduction, especially in relation to the lower leg nerves. Based on the degree of their neuropathy, the study divided the patients into three groups: no neuropathy, mild to moderate neuropathy, and severe neuropathy [8].

The research reveals several interesting findings regarding the factors associated with the development and severity of DPN. One key factor is the duration of (DM). The study found significant variations among the groups in terms of how long they had been diagnosed with DM. Patients with no neuropathy had the shortest duration, while those with severe neuropathy had been diagnosed for the longest time. This suggests that the longer a person has DM, the more likely they are to develop neuropathy [9].

The glycated haemoglobin (HbA1c) level, which represents the average blood glucose levels over a period of two to three months, is another important component. The onset and severity of DPN were substantially correlated with high HbA1c values. This is consistent with the knowledge that keeping HbA1c levels at ideal levels is essential for preventing or delaying the consequences of diabetes, including neuropathy [10].

The study also examined the relationship between serum interleukin-6 (IL-6) levels and DPN. IL-6 is a cytokine involved in inflammation and immune responses, and its elevated levels were found in patients with more severe DPN. Interestingly, there was a direct correlation between IL-6 levels, disease duration, and HbA1c levels, and an inverse correlation with nerve function, particularly in the sural nerve. This suggests that high IL-6 levels could be indicative of more severe nerve damage in diabetic patients [11].

In addition to biochemical markers, the study also explored structural changes associated with DPN, particularly in (RNFL). Using (OCT), it was found that the thickness of the RNFL decreased with the progression of neuropathy. This decrease in RNFL thickness was directly correlated with nerve function, suggesting that changes in the retina

could be indicative of peripheral neuropathy development and progression [12].

Conclusion

The study's findings are significant because they offer new insights into the mechanisms underlying DPN and provide potential biomarkers for its diagnosis and progression. The correlation between serum IL-6 levels, RNFL thickness, and neuropathy severity in T2DM patients could lead to more effective strategies for early detection, monitoring, and management of DPN. These findings also underscore the importance of long-term glycemic control in preventing or delaying the onset of diabetic complications.

Limitations: The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: Timely neuropathy detection and monitoring are crucial in T2DM. Disease duration, HbA1c levels, and IL-6 levels can predict neuropathy severity. Serum IL-6 levels and RNFL thickness are valuable markers for assessing neuropathy severity. Maintaining blood sugar control is pivotal in preventing diabetes-related complications, including neuropathy

Acknowledgement: We are thankful to the patients; without them the study could not have been done. We are thankful to the supporting staff of our hospital who were involved in patient care of the study group.

List of abbreviations:

1. DM - Diabetes Mellitus
2. T2DM - Type 2 Diabetes Mellitus
3. ADA - American Diabetes Association
4. TCNS - Toronto Clinical Neuropathy Score
5. IL-6 - Interleukin-6
6. RNFL - Retinal Nerve Fiber Layer
7. OCT - Optical Coherence Tomography
8. BMI - Body Mass Index
9. HbA1c - Hemoglobin A1c
10. BP - Blood Pressure
11. SD - Standard Deviation
12. DPN - Diabetic Polyneuropathy
13. SPSS - Statistical Package for the Social Sciences
14. ANOVA - Analysis of Variance
15. ROC - Receiver Operating Characteristic

Source of Funding: No funding received.

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