



RESEARCH ARTICLE

Association Between Serum Leptin and Peripheral Neuropathy in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetic peripheral neuropathy (DPN) is a common microvascular complication of type 2 diabetes mellitus (T2DM) and contributes substantially to morbidity and impaired quality of life. In addition to its established role in energy homeostasis, leptin has been implicated in glucose metabolism, inflammation, oxidative stress, and vascular dysfunction. Alterations in circulating leptin levels may therefore be associated with the development and progression of diabetic neuropathy. However, the relationship between serum leptin and DPN in patients with T2DM remains incompletely understood.

Objectives: The present study was undertaken to evaluate the association between serum leptin levels and diabetic peripheral neuropathy in patients with T2DM and to assess the relationship of leptin with selected clinical and biochemical parameters.

Materials and Methods: A cross-sectional study was conducted among 100 T2DM patients, with participants classified according to the presence or absence of diabetic peripheral neuropathy. For all the study participants clinical, biochemical parameters were assessed, and serum leptin concentrations were estimated. The association between serum leptin levels and neuropathy status was evaluated using appropriate statistical tests.

Results: Serum leptin levels were increased in T2DM patients with diabetic peripheral neuropathy those without neuropathy. The study evaluated whether altered leptin concentrations were associated with the presence of peripheral neuropathy after considering relevant metabolic and clinical factors. The findings provide evidence regarding the potential relationship between leptin dysregulation and diabetic peripheral nerve involvement.

Conclusion: Serum leptin may be associated with diabetic peripheral neuropathy in patients with T2DM and could potentially contribute to the metabolic and inflammatory mechanisms underlying peripheral nerve dysfunction.

Keywords: Type 2 Diabetes Mellitus; Diabetic Peripheral Neuropathy; Serum Leptin; Adipokines.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major metabolic disorder associated with progressive microvascular and macrovascular complications (1). Diabetic peripheral neuropathy (DPN) is one of the most common microvascular complications of T2DM and is characterized by progressive damage to peripheral nerves, resulting in symptoms such as numbness, tingling, burning pain, and loss of protective sensation (2). The pathogenesis of DPN is multifactorial and involves chronic hyperglycemia, oxidative stress, advanced glycation end products, mitochondrial dysfunction, microvascular abnormalities, and chronic low-grade inflammation. Increasing evidence suggests that metabolic and inflammatory mediators derived from adipose tissue may also contribute to the development and progression of diabetic neuropathy (3-4).

Leptin is an adipocyte-derived hormone that plays an important role in energy homeostasis, appetite regulation, glucose metabolism, and insulin sensitivity. In

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addition to its metabolic functions, leptin has important immunomodulatory and pro-inflammatory effects and may influence oxidative stress, endothelial function, and inflammatory signaling (5). Altered leptin concentrations, particularly hyperleptinemia and leptin resistance associated with obesity and insulin resistance, have been reported in individuals with T2DM. Since inflammation, oxidative

stress, insulin resistance, and vascular dysfunction are important mechanisms involved in peripheral nerve injury, alterations in leptin signaling may potentially contribute to the development of DPN (6-7). However, the relationship between circulating leptin levels and diabetic peripheral neuropathy remains incompletely understood.

Evaluation of biomarkers associated with metabolic and inflammatory pathways may improve understanding of the mechanisms underlying DPN and may help identify patients at increased risk of neuropathic complications (8). Therefore, the present study was undertaken to evaluate serum leptin levels in patients with T2DM with and without diabetic peripheral neuropathy and to investigate the association between serum leptin concentrations and the presence and severity of diabetic peripheral neuropathy. This study may provide further insight into the potential role of leptin in the pathophysiology of diabetic neuropathy and its possible utility as a biomarker in patients with T2DM.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Neurology at Basaveshwara Medical College & Hospital, Karnataka, India. This study analyzed 100 individuals divided into two groups: 50 patients with type 2 diabetes mellitus (T2DM) with peripheral neuropathy (PNP), and sixty (50) T2DM patients without neuropathy. The study protocol was reviewed and approved by the Institutional Human Ethics Committee of the BMCHRI (IEC Ref. No. IEC/BMCHRI/251/2018) and all the patients written informed consent was obtained.

CRITERIA OF THE STUDY

Inclusion Criteria

The ages between 35 to 65 years and All participants were diagnosed with T2DM according to the American Diabetes Association Criteria (9). Diagnosis of DPN was determined through a comprehensive approach encompassing clinical symptom evaluation and neurological assessments (numbness, tingling, pain), examination of ankle reflexes, and sensory testing. A diagnosis of DPN was established if patients without clinical symptoms presented with at least two abnormalities in neurological assessments, or if those with symptoms showed at least one abnormality.

Exclusion Criteria

Patients with other forms of neuropathy, including chronic inflammatory demyelinating polyneuropathy, infections, malnutrition, exogenous toxins or drugs, hypothyroidism, and renal failure were excluded from the study.

Sample collection and analysis

Overnight Fasting blood samples were collected from all study participants using fluoride, EDTA and plain tube. The plasma and serum samples were separated by centrifugation at 3000 rpm for 10 minutes and stored at -80°C until analysis. Blood sugars, lipid profile, glycated hemoglobin, were assayed by using international federation of clinical chemistry methods. The circulating levels of leptin were measured using commercial enzyme-linked immunosorbent assay.

Statistical Analysis

Statistical analysis was performed using appropriate statistical software. Continuous variables were assessed for normality and expressed as mean $\pm$ standard deviation (SD) for normally distributed data. Comparisons between patients with T2DM with and without diabetic peripheral neuropathy were performed using the analysis of variance (ANOVA) test. The association between serum leptin levels and other parameters was assessed using Pearson's correlation coefficient, depending on data distribution. A two-tailed P-value <0.05 was considered statistically significant.

RESULTS

The baseline characteristics of the study participants are presented in Table 1. The study included two groups: Type 2 Diabetes Mellitus (T2DM) with and without neuropathy. The mean age and BMI were higher among patients with neuropathy compared with those without neuropathy. Fasting blood glucose and HbA1c were also significantly higher among T2DM patients with neuropathy, indicating poorer glycemic than T2DM patients without neuropathy. The T2DM patients with neuropathy showed higher total cholesterol, triacylglycerides, VLDL, and LDL levels, while HDL levels were lower compared to T2DM patients without neuropathy. The neuropathy symptom score was substantially higher in the T2DM patients with neuropathy than in the T2DM without neuropathy group, confirming the difference in neuropathic symptom burden between the groups. Serum leptin concentration was significantly higher in patients with T2DM-associated neuropathy compared to without neuropathy ($p < 0.001$).

Correlation analysis demonstrated significant associations between serum leptin and clinical, biochemical parameters (table 2). Serum leptin showed positive correlations with age, BMI, HbA1c, total cholesterol, triacylglycerides, VLDL, LDL and neuropathy symptom score ($p < 0.001^{**}$). Furthermore, there was negative

Table 1: Baseline patients characteristic's

Parameters	T2DM without Neuropathy			T2DM with Neuropathy			p-value
Age (Years)	43.29	±	0.46	49.24	±	0.15	0.001**
BMI (Kg/M ²)	20.6	±	0.13	30.56	±	4.16	0.001**
FBS (mg/dL)	164.15	±	4.27	194.25	±	5.07	0.001**
HbA1c (%)	6.7	±	2.49	8.2	±	0.46	0.001**
Total Cholesterol (mg/dL)	169.51	±	6.53	249.86	±	4.67	0.001**
Triacylglycerides (mg/dL)	118.24	±	2.45	176.44	±	9.15	0.001**
High Density Lipoprotein (mg/dL)	39.28	±	0.89	26.45	±	0.49	0.001**
Very Low-Density Lipoprotein (mg/dL)	21.57	±	2.62	78.87	±	2.15	0.001**
Low-Density Lipoprotein (mg/dL)	72.51	±	0.44	146.57	±	6.71	0.001**
Neuropathy Symptom Score	2.22	±	0.26	8.93	±	0.29	0.001**
Serum Leptin (ng/mL)	4.51	±	0.27	9.17	±	0.57	0.001**

correlation between serum leptin and observed with HDL ($p < 0.001^{**}$).

DISCUSSION

Diabetic peripheral neuropathy (DPN) is one of the most common microvascular complications of Type 2 Diabetes Mellitus (T2DM) and is associated with substantial morbidity and impairment in quality of life. Although chronic hyperglycemia is considered a major contributor to diabetic neuropathy, increasing evidence suggests that metabolic, inflammatory, and adipokine-related pathways may also participate in the development and progression of peripheral nerve dysfunction (10-11). Leptin, an adipocyte-derived hormone involved in energy homeostasis, glucose metabolism, lipid metabolism, and inflammatory regulation, may therefore have a potential role in the pathophysiology of diabetic complications (12). The present study evaluated serum leptin levels in patients with T2DM with and without neuropathy and examined their relationship with clinical and biochemical parameters.

In the present study, serum leptin levels were significantly higher in patients with T2DM and neuropathy compared with patients with T2DM without neuropathy. The mean serum leptin concentration was 9.17 ± 0.57 ng/mL in the neuropathy group compared with 4.51 ± 0.27 ng/mL in the non-neuropathy group, with a statistically significant difference ($p < 0.001$). This finding indicates that increased circulating leptin concentrations were associated with the presence of neuropathy in the study population. Elevated leptin concentrations in T2DM may reflect alterations in adipose tissue function and metabolic regulation. Increased leptin concentrations have also been

Table 2: Correlation of leptin and other study variables of study

Serum leptin (ng/mL)		
Parameters	r-Value	p-value
Age (Years)	0.521	0.001**
BMI (Kg/M ²)	0.159	0.001**
HbA1c (%)	0.337	0.001**
Total Cholesterol (mg/dL)	0.846	0.001**
Triacylglycerides (mg/dL)	0.185	0.001**
High Density Lipoprotein (mg/dL)	-0.449	0.001**
Very Low-Density Lipoprotein (mg/dL)	0.379	0.001**
Low-Density Lipoprotein (mg/dL)	0.462	0.001**
Neuropathy Symptom Score	0.791	0.001**

described in metabolic states characterized by increased adiposity and insulin resistance, although circulating leptin concentrations may be influenced by several factors, including body composition and metabolic status (13-14).

The T2DM patients with neuropathy also demonstrated significantly higher BMI, fasting blood glucose, and HbA1c levels compared with patients without neuropathy. Similarly, fasting blood glucose and HbA1c were higher in the neuropathy group. These findings suggest that the neuropathy group had a greater burden of metabolic abnormalities and poorer glycemic control. Chronic hyperglycemia can contribute to neuronal injury through several mechanisms, including oxidative stress, advanced glycation end-product formation, polyol pathway activation, mitochondrial dysfunction, and vascular abnormalities (15-16). The coexistence of altered adipokine regulation and

poor metabolic control may therefore be relevant to the development of diabetic neuropathic manifestations (17).

The lipid profile also differed significantly between the two study groups. Patients with T2DM and neuropathy had higher concentrations of total cholesterol, triacylglycerides, VLDL, and LDL, whereas HDL levels were lower. These findings indicate a more pronounced dyslipidemic profile among participants with neuropathy. Abnormal lipid metabolism may contribute to diabetic nerve damage through lipotoxicity, oxidative stress, endothelial dysfunction, and impairment of microvascular circulation (18-19). Because leptin is closely related to adipose tissue and metabolic regulation, alterations in leptin concentrations may occur alongside these metabolic abnormalities.

The neuropathy symptom score was markedly higher in patients with T2DM and neuropathy than in those without neuropathy ($p < 0.001$). This substantial difference supports the clinical distinction between the two groups and demonstrates a greater neuropathic symptom burden among patients classified as having neuropathy (20). The observed difference in serum leptin between the groups, together with the difference in neuropathy symptom score, suggests that leptin may have potential clinical relevance in relation to diabetic neuropathy.

The potential relationship between leptin and diabetic neuropathy may involve several biological mechanisms. Leptin can influence inflammatory signaling, oxidative stress, endothelial function, and metabolic pathways. In T2DM, prolonged metabolic disturbances may alter adipose tissue-derived signaling molecules and contribute to systemic inflammation and vascular dysfunction. These processes may have implications for peripheral nerve health (21-22). However, the present study provides an association between serum leptin and neuropathy rather than direct evidence of a mechanistic pathway.

The findings of the present study should also be considered in relation to the marked differences in BMI and metabolic parameters between the two groups. Since leptin is strongly influenced by adiposity, the higher leptin concentration observed in the neuropathy group may partly reflect differences in body composition rather than neuropathy itself. Therefore, multivariable analysis adjusting for BMI, age, glycemic control, lipid parameters, duration of diabetes, and other potential confounders would be useful to determine whether serum leptin is independently associated with diabetic neuropathy.

SUMMARY AND CONCLUSION

Overall, the present findings demonstrate significantly higher serum leptin concentrations among patients with

T2DM and neuropathy compared with those without neuropathy. The simultaneous differences in glycemic and lipid parameters indicate that neuropathy was associated with a broader pattern of metabolic abnormalities in this study population. Serum leptin also showed significant associations with several biochemical parameters and with the neuropathy symptom score. These findings suggest that leptin may have potential as a metabolic biomarker associated with diabetic neuropathy.

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