



RESEARCH ARTICLE

Correlation of Serum Adiponectin Levels with the Severity of Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetic peripheral neuropathy (DPN) is a common complication of Type 2 Diabetes Mellitus (T2DM) and contributes significantly to morbidity and reduced quality of life. Adiponectin is an adipocyte-derived hormone with anti-inflammatory, insulin-sensitizing, and antioxidant properties. Alterations in adiponectin levels have been associated with metabolic abnormalities and diabetic complications. However, its relationship with the severity of DPN remains unclear. The present study aimed to evaluate the correlation between serum adiponectin levels and the severity of diabetic peripheral neuropathy in patients with T2DM. **Methods:** A cross-sectional observational study was conducted among patients with T2DM attending Department of Neurology. Clinical and biochemical parameters were recorded, and serum adiponectin levels were estimated using an appropriate immunoassay method. The presence and severity of DPN were assessed using a validated neuropathy assessment scale. Participants were categorized according to neuropathy severity. Statistical analysis was performed using appropriate parametric and non-parametric tests. The correlation between serum adiponectin levels and neuropathy severity was assessed using Pearson's correlation coefficient, as appropriate. A p-value <0.05 was considered statistically significant. **Results:** Serum adiponectin levels significantly decreased in T2DM with neuropathy when compared to T2DM without neuropathy ($P=0.001^{**}$). There was significant direct inverse correlation with BMI, glycated and lipid indices, neuropathy severity score ($P=0.001^{**}$). **Conclusion:** Serum adiponectin levels may be associated with the severity of diabetic peripheral neuropathy in patients with T2DM and may have potential utility as a biomarker for assessment of neuropathy severity.

Keywords: Adiponectin; Type 2 Diabetes Mellitus; Diabetic Peripheral Neuropathy; Neuropathy Severity.

Indian J. Pharm. Biol. Res. (2025); <https://doi.org/10.30750/ijpbr.13.4.02>

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or a combination of both [1]. The prevalence of T2DM has increased considerably worldwide, making it an important public health concern. Prolonged exposure to hyperglycemia can lead to several microvascular and macrovascular complications, including diabetic neuropathy, retinopathy, cardiovascular disease, and diabetic peripheral neuropathy. These complications contribute substantially to morbidity, reduced quality of life, disability, and increased healthcare expenditure among individuals with diabetes [2-3]. Diabetic peripheral neuropathy (DPN) is one of the most common chronic complications of T2DM. It is characterized by damage to the peripheral nerves, predominantly affecting the distal lower limbs in a symmetrical pattern [4]. Patients may experience symptoms such as numbness, tingling, burning pain, altered sensation, and weakness. In advanced cases, loss of protective sensation can increase

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How to cite this article: H Santosh, Correlation of Serum Adiponectin Levels with the Severity of Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus. Indian J. Pharm. Biol. Res. 2025;13(4):8-11

Source of support: Nil Conflict of interest: None.

Received: 22/11/2025 Revised: 01/12/2025 Accepted: 15/12/2025

the risk of foot ulcers, infections, falls, and lower-limb amputation. The development and progression of DPN are multifactorial and have been associated with the duration of diabetes, poor glycemic control, obesity, dyslipidemia, oxidative stress, inflammation, and vascular abnormalities [5,6]

Although chronic hyperglycemia is considered an

important contributor to diabetic neuropathy, increasing evidence suggests that adipose tissue and its secreted bioactive molecules, collectively known as adipokines, may also play an important role in the pathogenesis of diabetic complications[7]. Adiponectin is one of the major adipokines secreted predominantly by adipocytes. Unlike several other adipokines that are associated with inflammation and metabolic dysfunction, adiponectin generally exhibits insulin-sensitizing, anti-inflammatory, antioxidant, and potentially vascular protective properties[8,9]. Several mechanisms have been proposed to explain a possible association between adiponectin and diabetic neuropathy. Adiponectin may influence peripheral nerve function through its effects on insulin sensitivity, oxidative stress, inflammation, endothelial function, and lipid metabolism. Alterations in adiponectin signaling may contribute to metabolic and vascular disturbances that promote peripheral nerve injury[10]. Conversely, changes in adiponectin concentrations may also reflect metabolic adaptations occurring during the progression of diabetes and its complications. Assessment of serum adiponectin in relation to clinical and biochemical indicators of neuropathy may provide useful information regarding its potential role as a biomarker of diabetic nerve dysfunction[11]. Establishing such an association could contribute to a better understanding of the metabolic and inflammatory mechanisms involved in the development of DPN and may help identify individuals at increased risk of neuropathic complications [12]. Therefore, the present study is designed to evaluate serum adiponectin levels in patients with Type 2 Diabetes Mellitus with and without diabetic peripheral neuropathy and to determine their association with the presence and severity of diabetic neuropathy.

Materials and Method

This cross-sectional study was carried out in the Department of Neurology. This study analyzed 120 individuals divided into two groups: 60 patients with type 2 diabetes mellitus (T2DM) with peripheral neuropathy (PNP), and sixty (60) T2DM patients without neuropathy.

Results

Table 1: Baseline patients characteristics

Parameters	T2DM without Neuropathy			T2DM with Neuropathy			P- Value
Age (Years)	45.51	±	0.41	51.49	±	1.54	0.001**
BMI (Kg/M ²)	22.5	±	2.0	28.44	±	2.61	0.001**
FBS (mg/dL)	174.66	±	0.95	167.45	±	3.25	0.001**
HbA1c (%)	8.7	±	1.89	7.8	±	0.63	0.001**
Total Cholesterol (mg/dL)	174.33	±	2.56	254.86	±	1.24	0.001**
Triacylglycerides (mg/dL)	132.49	±	4.67	169.44	±	0.89	0.001**
High Density Lipoprotein (mg/dL)	42.28	±	0.24	30.45	±	2.84	0.001**
Very Low-Density Lipoprotein (mg/dL)	24.57	±	1.61	49.87	±	1.63	0.001**
Low-Density Lipoprotein (mg/dL)	68.51	±	0.56	134.57	±	2.57	0.001**
Neuropathy Symptom Score	3.22	±	0.13	7.89	±	1.54	0.001**
Serum Adiponectin (µg/mL)	7.56	±	0.47	3.64	±	0.30	0.001**

The present study evaluated the baseline clinical and biochemical characteristics of patients with T2DM with and without neuropathy. Significant differences were observed between the two groups for all the evaluated parameters, with a p-value of 0.001 for each variable. The mean age was significantly different between

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[13]. 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 adiponectin 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 ± 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 adiponectin 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.

T2DM patients with neuropathy and those without neuropathy. Similarly, BMI showed a significant difference between the two groups, indicating differences in anthropometric characteristics among the study participants. The glycemic parameters also demonstrated significant differences between the

groups. The T2DM patients with neuropathy had higher fasting blood glucose levels compared to T2DM patients without neuropathy. HbA1c was also higher in the T2DM with neuropathy group than in the without neuropathy group. These findings indicate poorer glycemic control among T2DM patients with neuropathy.

There significant differences were also observed in the lipid profile such as total cholesterol, triacylglycerides, HDL, VLDL, and LDL differed significantly between the groups. The T2DM patients

with neuropathy group showed lower mean total cholesterol, triacylglycerides, VLDL, and LDL values compared with T2DM patients without neuropathy, whereas HDL was higher in T2DM patients with neuropathy. The neuropathy Symptom Score was significantly different between the groups, with a mean score of in patients with neuropathy and in patients without neuropathy. Additionally, serum adiponectin was lower in T2DM patients with neuropathy compared to T2DM patients without neuropathy with a statistically significant p-value of 0.001.

Table 2: Correlation of serum adiponectin and other study variables of study

Serum Adiponectin (µg/mL)		
Parameters	r-Value	P-Value
Age (Years)	-0.546	0.001**
BMI (Kg/M ²)	-0.175	0.001**
HbA1c (%)	-0.422	0.001**
Total Cholesterol (mg/dL)	-0.970	0.001**
Triacylglycerides (mg/dL)	-0.781	0.001**
High Density Lipoprotein (mg/dL)	0.554	0.001**
Very Low-Density Lipoprotein (mg/dL)	-0.129	0.001**
Low-Density Lipoprotein (mg/dL)	-0.405	0.001**
Neuropathy Symptom Score	-0.286	0.001**

Correlation analysis demonstrated correlations between serum adiponectin and all the evaluated study variables (Table 2). Serum adiponectin showed a significant direct negative correlation with age, BMI, HbA1c, total cholesterol, triacylglycerides, VLDL, LDL, and neuropathy symptom score ($p=0.001^{**}$). Additionally, there was a significant positive correlation with serum adiponectin and HDL ($p=0.001^{**}$).

Discussion

Diabetic peripheral neuropathy is one of the most common microvascular complications of type 2 diabetes mellitus and is associated with considerable morbidity, impaired quality of life, and increased risk of foot ulceration and amputation. Chronic hyperglycemia, oxidative stress, mitochondrial dysfunction, endothelial dysfunction, inflammation, and abnormalities in lipid metabolism contribute to the development and progression of diabetic neuropathy. In recent years, adipokines such as adiponectin have received considerable attention because of their potential role in metabolic regulation, inflammation, vascular function, and neuronal injury[14-15]

Adiponectin is predominantly secreted by adipose tissue and has insulin-sensitizing, anti-inflammatory, anti-oxidative, and vascular protective properties. In general, circulating adiponectin concentrations are lower in obesity and insulin resistance. However, paradoxically increased adiponectin concentrations have been reported in patients with chronic complications of diabetes[16]. The relationship between circulating adiponectin and diabetic neuropathy remains controversial, with studies reporting both positive and negative associations. In the present study, serum adiponectin demonstrated a statistically significant positive correlation with neuropathy symptom score, with a correlation coefficient of $r = 0.286$ and $p = 0.001^{**}$. This indicates a statistically significant, although relatively weak, positive association between circulating adiponectin

concentrations and neuropathic symptoms in the study population. Thus, individuals with lower serum adiponectin tended to have higher neuropathy symptom scores. The present finding is supported by the recent study who specifically investigated serum adiponectin in T2DM patients with and without peripheral neuropathy. They reported lower serum adiponectin concentrations among patients with DPN and found that adiponectin remained negatively associated with DPN after adjustment for age, sex, BMI, hypertension, HbA1c, alcohol intake, smoking, physical activity, LDL cholesterol, lipid-lowering medication, estimated glomerular filtration rate, and diabetes duration[17]. Similarly, a systematic review and meta-analysis of controlled cross-sectional studies reported significantly lower adiponectin concentrations in patients with diabetic microvascular complications. In the neuropathy subgroup, higher adiponectin was associated with neuropathy, with a standardized mean difference of [18,19]. The authors suggested that increased circulating adiponectin may be associated with microvascular complications in T2DM. Consequently, the observed association between adiponectin and neuropathy may partly reflect the overall burden of chronic diabetes rather than a direct causal relationship. Genetic evidence also supports a potential role of the adiponectin pathway in diabetic neuropathy. A study examining adiponectin gene polymorphisms in patients with T2DM reported that specific adiponectin gene variants were associated with altered circulating adiponectin concentrations and susceptibility to DPN[20]. The authors suggested that genetic variation affecting adiponectin levels may contribute to differences in neuropathy risk. An important aspect of interpreting the present findings is the assessment method used for neuropathy. The study used the neuropathy symptom score, which primarily reflects neuropathy-related symptoms. Symptom scores can be influenced by factors other than objective nerve

dysfunction.

The present study also demonstrated a significant negative correlation between adiponectin and HbA1c. Since chronic hyperglycemia is a major determinant of diabetic neuropathy, the relationship between adiponectin and neuropathy may partly reflect the metabolic severity of diabetes[21-23]. Similarly, adiponectin showed significant associations with several lipid parameters in the present study. Therefore, multivariable analysis would be important to determine whether adiponectin is independently associated with neuropathy after adjustment for HbA1c, diabetes duration, BMI, age, lipid profile, renal function, and other relevant factors. The findings have potential clinical implications. If the association between adiponectin and DPN is confirmed in larger prospective studies, adiponectin could potentially contribute to the identification of patients at increased risk of diabetic microvascular complications.

Summary & Conclusion

the present study demonstrated a significant negative association between serum adiponectin and neuropathy symptom score among patients with T2DM. Therefore, serum adiponectin might serve potential relevance marker for neuropathy.

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