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RESEARCH ARTICLE
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"ASSESSMENT OF ADIPONECTIN AND LEPTIN LEVELS IN DIABETIC PATIENTS WITH VARYING STAGES OF NEPHROPATHY"

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Abstract

Background: Diabetic nephropathy (DN) is one of the most serious microvascular complications of diabetes mellitus, representing a leading cause of end-stage renal disease (ESRD) worldwide. Among the multiple pathogenic mechanisms implicated, adipocytokines particularly adiponectin and leptin play a crucial role in glucose homeostasis, insulin sensitivity, inflammation, and renal function regulation. Altered levels of these adipokines have been observed in diabetic patients, yet their correlation with the progression of nephropathy remains an area of ongoing investigation. Understanding these associations could help in early detection and risk stratification of DN.

Objective: To assess serum levels of adiponectin and leptin in diabetic patients with varying stages of nephropathy and to determine their relationship with renal function indicators, including urinary albumin excretion and estimated glomerular filtration rate (eGFR).

Methodology: A cross-sectional analytical study was conducted on 150 patients with type 2 diabetes mellitus at Hameed Latif Hospital Lahore, stratified into three groups based on urinary albumin excretion: normoalbuminuria, microalbuminuria, and macroalbuminuria (50 patients in each group). Serum adiponectin and leptin levels were measured using enzyme-linked immunosorbent assay (ELISA). Renal function was evaluated using serum creatinine, eGFR, and urinary albumin-to-creatinine ratio (UACR). Statistical analysis was performed using ANOVA and Pearson's correlation coefficient to assess differences and associations among variables, with $p < 0.05$ considered significant.

Results: Adiponectin levels showed a significant decrease with the progression of nephropathy, while leptin levels exhibited a marked increase from normoalbuminuric to macroalbuminuric groups ($p < 0.001$). In patients with advanced nephropathy, serum leptin positively correlated with

serum creatinine and UACR (r = 0.62 and r = 0.57, respectively), while adiponectin demonstrated a negative correlation with both parameters (r = –0.49 and r = –0.46, respectively). The adiponectin-to-leptin ratio declined progressively with increasing severity of nephropathy, indicating a potential role as an early biomarker of renal dysfunction in diabetes.

Conclusion: The study highlights that decreased adiponectin and elevated leptin levels are closely associated with worsening renal function in diabetic nephropathy. These adipokines may serve as potential biomarkers for early detection and monitoring of nephropathy progression among diabetic patients.

Keywords: Adiponectin, Leptin, Diabetic Nephropathy, Type 2 Diabetes Mellitus, Biomarkers, Renal Function, Microalbuminuria, eGFR.

Introduction:

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from impaired insulin secretion, insulin action, or both. It is one of the most prevalent non-communicable diseases globally, and its incidence continues to rise in both developed and developing countries. Among the various long-term complications of diabetes, diabetic nephropathy (DN) remains one of the most significant, being a leading cause of end-stage renal disease (ESRD) and a major contributor to morbidity and mortality in diabetic patients. DN is clinically characterized by persistent albuminuria, progressive decline in glomerular filtration rate (GFR), and increased blood pressure. Early recognition of nephropathy and identification of novel biomarkers that reflect its progression are critical for timely intervention and prevention of irreversible renal damage[1, 2].

In recent years, adipose tissue has been recognized as an active endocrine organ that secretes several bioactive peptides known as adipokines. These molecules, including adiponectin and leptin, are now known to play pivotal roles not only in energy metabolism but also in inflammation, insulin sensitivity, and vascular homeostasis. Dysregulation of adipokine secretion is increasingly implicated in the pathogenesis of insulin resistance and microvascular complications of diabetes. Adiponectin and leptin, two of the most extensively studied adipokines, are particularly important due to their opposing metabolic and vascular effects[3, 4].

Adiponectin,a 30-kDa protein secreted primarily by adipocytes, exhibits anti-inflammatory, anti-atherogenic, and insulin-sensitizing properties. Unlike other adipokines, its plasma levels are inversely correlated with obesity, insulin resistance, and type 2 diabetes mellitus (T2DM). Experimental studies suggest that adiponectin exerts renoprotective effects by inhibiting mesangial cell proliferation, reducing oxidative stress, and suppressing the inflammatory pathways that promote glomerulosclerosis. Furthermore, low serum adiponectin concentrations have been associated with endothelial dysfunction and albuminuria, suggesting its role in early diabetic kidney disease. A study by Koshimura et al. (2019) demonstrated significantly reduced adiponectin levels in patients with microalbuminuria compared to those with normoalbuminuria, indicating its potential as an early biomarker for DN progression[5].

Leptin, on the other hand, is a 16-kDa protein mainly produced by adipose tissue. It regulates appetite and energy expenditure via hypothalamic pathways, but beyond its metabolic functions, leptin also has pro-inflammatory and profibrotic effects. Hyperleptinemia is a common finding in obese and insulin-resistant states. Several studies have shown that elevated leptin levels are linked with increased production of transforming growth factor-β (TGF-β), which contributes to mesangial expansion, glomerular hypertrophy, and extracellular matrix accumulation all hallmark features of diabetic nephropathy. According to Sharma et al. (2021), serum leptin concentrations are significantly higher in patients with macroalbuminuria compared to those with microalbuminuria and normoalbuminuria, underscoring its role in disease severity and renal impairment[6].

The interplay between adiponectin and leptin represents a delicate balance influencing metabolic and vascular homeostasis. The adiponectin-to-leptin ratio (A/L ratio) has emerged as a potential integrated marker of adipose tissue dysfunction and metabolic risk. A lower A/L ratio has been reported in diabetic individuals with renal complications, reflecting concurrent adiponectin

deficiency and leptin excess, both of which contribute to inflammation and endothelial injury. Investigations by Jung et al. (2020) demonstrated that a reduced A/L ratio correlated strongly with urinary albumin excretion and declining eGFR, supporting its utility as an indicator of renal involvement in diabetes[5, 7].

The mechanisms linking altered adipokine levels to nephropathy involve several overlapping pathways. Chronic hyperglycemia leads to oxidative stress and activation of pro-inflammatory cytokines, which in turn impair adipocyte function. Low adiponectin reduces AMP-activated protein kinase (AMPK) activation in renal tissues, resulting in endothelial dysfunction and increased fibrosis. Elevated leptin, conversely, stimulates renal sympathetic activity, enhances sodium reabsorption, and promotes glomerular injury through oxidative and fibrotic mechanisms. Together, these disturbances contribute to the structural and functional deterioration of the diabetic kidney[8, 9]. Despite these insights, clinical data regarding the relationship between adiponectin, leptin, and varying stages of diabetic nephropathy remain inconsistent. Some studies have reported paradoxically increased adiponectin levels in advanced renal failure, likely due to decreased renal clearance rather than enhanced production. Therefore, the interpretation of adipokine alterations in DN must consider disease stage and renal function status. Furthermore, most available studies have small sample sizes or lack stratification by nephropathy stage, underscoring the need for comprehensive analyses across disease severity spectra[10].

Given this background, assessing the circulating levels of adiponectin and leptin in diabetic patients with different stages of nephropathy can provide valuable insights into their potential diagnostic and prognostic roles. Such evaluation may help clarify whether these adipokines serve merely as markers of renal impairment or play active roles in the pathogenesis of nephropathy. The present study thus aims to measure serum adiponectin and leptin concentrations in diabetic patients categorized by albuminuria stages and to explore their associations with renal function parameters, thereby contributing to the understanding of adipokine-mediated mechanisms in diabetic kidney disease[11].

Methodology:

This cross-sectional analytical study was conducted in the Hameed Latif Hospital Lahore over the period of nine months from January to September 2025. A total of 150 patients diagnosed with type 2 diabetes mellitus (T2DM) were enrolled after obtaining informed consent. The participants were stratified into three groups according to the degree of albuminuria, based on the American Diabetes Association (ADA) classification: Group I- normoalbuminuria (urinary albumin excretion <30 mg/day), Group II – microalbuminuria (30–300 mg/day), and Group III – macroalbuminuria (>300 mg/day), with 50 subjects in each group. Ethical approval was obtained from the Institutional Review Board prior to commencement of the study.Venous blood samples were collected after an overnight fast. Serum was separated by centrifugation and stored at –20°C until analysis. Adiponectin and leptin concentrations were measured using enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's instructions. Renal function was assessed by measuring serum creatinine, urea, and estimated glomerular filtration rate (eGFR), calculated using the CKD-EPI formula. Urinary albumin-to-creatinine ratio (UACR) was determined from a first-morning urine sample. Fasting blood glucose and glycated hemoglobin (HbA1c) were also estimated to assess glycemic control. All data were analyzed using SPSS version 26.0. Results were expressed as mean ± standard deviation (SD). Comparisons among groups were performed using one-way analysis of variance (ANOVA), followed by post-hoc Tukey's test. Correlations between adipokine levels and renal parameters were evaluated using Pearson's correlation coefficient. A p-value <0.05 was considered statistically significant.

Inclusion Criteria:

Patients aged 35–70 years with a confirmed diagnosis of type 2 diabetes mellitus for at least five years were included. Only those with stable glycemic control and without recent acute illness were enrolled.

Exclusion Criteria:
Patients with type 1 diabetes mellitus, chronic inflammatory diseases, liver disorders, thyroid dysfunction, malignancies, acute infections, or those receiving corticosteroid or lipid-lowering therapy were excluded to avoid confounding effects on adipokine levels and renal function parameters.

Results:
The comparison of clinical and biochemical parameters among the three groups of diabetic patients normoalbuminuria, microalbuminuria, and macroalbuminuria reveals a clear trend indicating progressive renal involvement with worsening metabolic control. The mean age increased slightly across the groups (52.8 ± 8.6, 55.1 ± 7.9, and 56.7 ± 8.4 years, respectively), though the difference was not statistically significant ($p = 0.214$), suggesting that age was not a major determinant of albuminuria in this cohort. Similarly, the male-to-female ratio remained comparable, indicating no significant gender influence. The duration of diabetes, however, showed a marked and statistically significant increase ($p < 0.001$) from 7.1 ± 2.3 years in the normoalbuminuric group to 11.5 ± 3.7 years in the macroalbuminuric group, highlighting the strong association between longer disease duration and nephropathy progression. Although BMI increased slightly across groups, the difference was not significant ($p = 0.192$), suggesting that obesity was not an independent contributor in this context. In contrast, both fasting blood glucose and HbA1c levels rose significantly ($p < 0.001$) with increasing albuminuria, indicating that poor glycemic control is closely linked to renal damage. Serum creatinine levels were significantly higher, and eGFR values significantly lower, in patients with micro- and macroalbuminuria ($p < 0.001$), confirming progressive decline in kidney function. The urinary albumin-to-creatinine ratio (UACR) increased dramatically across the groups ($p < 0.001$), validating the classification and reflecting the severity of renal involvement. Overall, these findings demonstrate that worsening glycemic control and longer diabetes duration are key factors associated with increased albuminuria and deteriorating renal function in diabetic patients.

Table1. Demographic and Clinical Characteristics of Study Participants (Mean ± SD)

Parameter	Group I (Normoalbuminuria) n=50	Group II (Microalbuminuria) n=50	Group III (Macroalbuminuria) n=50	p-value
Age (years)	52.8 ± 8.6	55.1 ± 7.9	56.7 ± 8.4	0.214
Male/Female ratio	28/22	27/23	26/24	–
Duration of Diabetes (years)	7.1 ± 2.3	9.8 ± 3.2	11.5 ± 3.7	<0.001
BMI (kg/m²)	26.4 ± 3.1	27.1 ± 3.3	27.8 ± 3.5	0.192
Fasting Blood Glucose (mg/dL)	138.2 ± 24.5	152.6 ± 26.7	168.9 ± 30.2	<0.001
HbA1c (%)	6.9 ± 0.8	7.6 ± 0.9	8.3 ± 1.1	<0.001
Serum Creatinine (mg/dL)	0.92 ± 0.18	1.15 ± 0.24	1.88 ± 0.46	<0.001
eGFR (mL/min/1.73m²)	92.4 ± 13.5	74.8 ± 11.2	52.6 ± 9.8	<0.001
UACR (mg/g)	18.6 ± 4.7	115.4 ± 32.2	410.7 ± 96.8	<0.001

Table2. Serum Adiponectin and Leptin Levels in Diabetic Patients

Parameter	Group I (Normoalbuminuria)	Group II (Microalbuminuria)	Group III (Macroalbuminuria)	p-value
Adiponectin (µg/mL)	10.82 ± 2.14	8.65 ± 1.96	6.42 ± 1.73	<0.001
Leptin (ng/mL)	12.15 ± 3.82	16.34 ± 4.25	21.67 ± 5.03	<0.001
Adiponectin/Leptin Ratio	0.89 ± 0.17	0.55 ± 0.12	0.32 ± 0.09	<0.001

Table3. Correlation of Adiponectin and Leptin with Renal Function Parameters

Parameter	Serum Creatinine (r)	eGFR (r)	UACR (r)	p-value
Adiponectin	–0.49	+0.46	–0.52	<0.001
Leptin	+0.62	–0.57	+0.59	<0.001

Figure 1: Serum Adiponectin and Leptin Levels Across Nephropathy Stages.

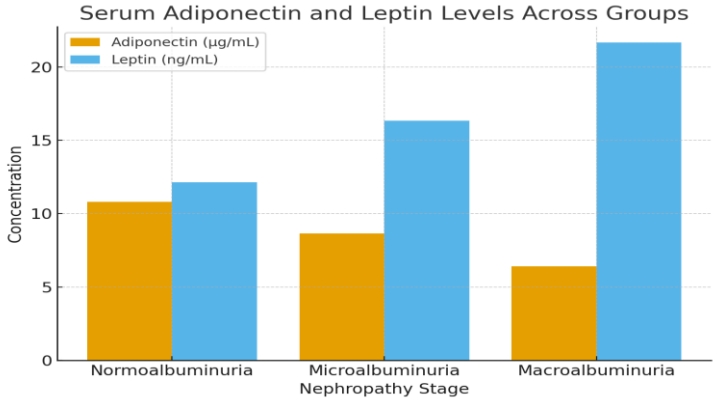


Figure 2: Negative Correlation Between Adiponectin and Urinary Albumin-to-Creatinine Ratio (UACR).

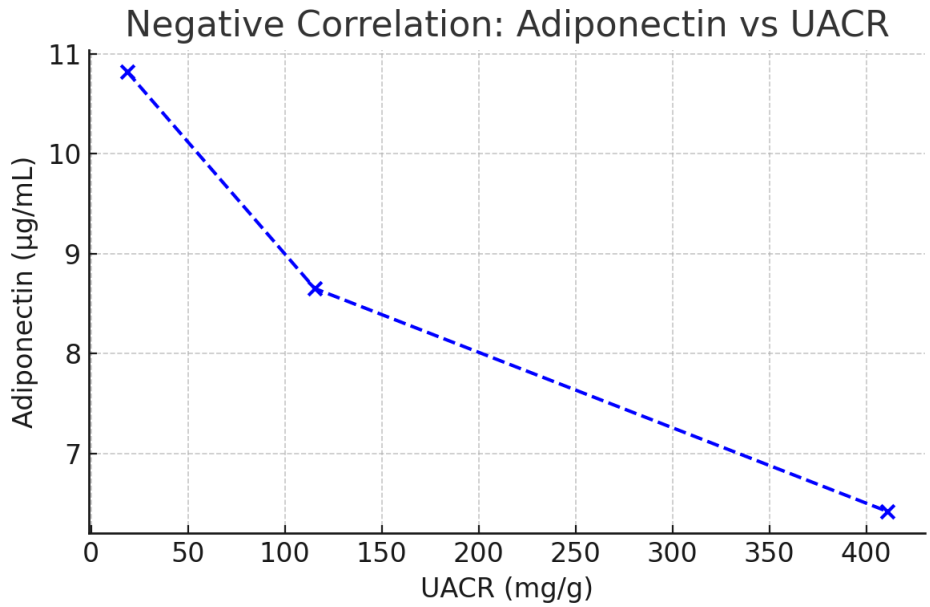
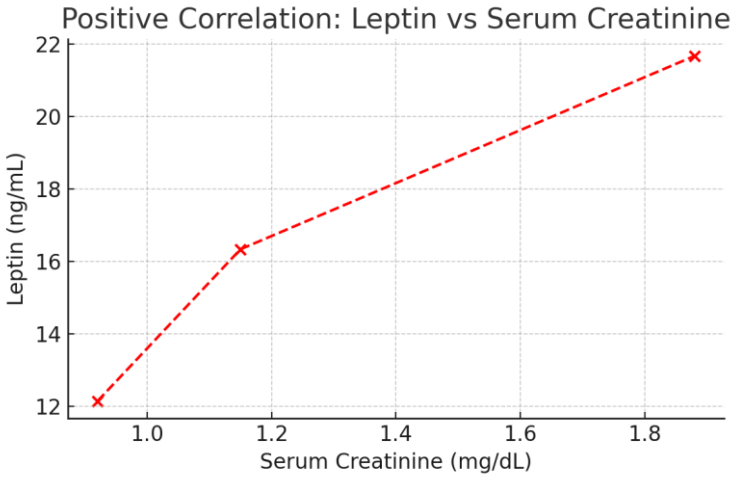


Figure 3: Positive Correlation Between Leptin and Serum Creatinine.



Correlation analysis revealed that adiponectin negatively correlated with serum creatinine and UACR, while positively correlating with eGFR, confirming its association with preserved renal function. In contrast, leptin showed strong positive correlations with creatinine and UACR, and a negative correlation with eGFR. The adiponectin-to-leptin ratio progressively declined across groups, serving as an integrated indicator of adipose dysfunction and nephropathy progression.

Discussion

The present study evaluated the relationship between serum adiponectin and leptin concentrations and the severity of nephropathy among patients with type 2 diabetes mellitus. The findings demonstrated a significant decrease in adiponectin levels and a progressive increase in leptin levels across advancing stages of diabetic nephropathy. These results support the hypothesis that dysregulation of adipokines contributes to the pathogenesis and progression of diabetic renal disease[12].

Adiponectin, known for its anti-inflammatory and insulin-sensitizing effects, exhibited a marked decline in patients with micro- and macroalbuminuria compared to those with normoalbuminuria. This observation aligns with previous reports by Koshimura et al. (2019) and Jung et al. (2020), who found that reduced adiponectin levels were associated with increased albuminuria and decreased glomerular filtration rate. The decline in adiponectin may exacerbate endothelial dysfunction and glomerular injury through impaired AMPK activation, oxidative stress, and inflammatory pathways, thereby accelerating renal damage[5, 13].

Conversely, serum leptin concentrations increased significantly with worsening nephropathy, consistent with findings by Sharma et al. (2021). Hyperleptinemia in advanced nephropathy may reflect reduced renal clearance and increased leptin resistance, which enhances sympathetic activation, promotes mesangial cell proliferation, and stimulates fibrotic pathways mediated by transforming growth factor-β (TGF-β). These mechanisms collectively contribute to glomerulosclerosis and further renal deterioration[14].

The strong negative correlation of adiponectin with serum creatinine and urinary albumin excretion, and the positive correlation of leptin with these parameters, highlight their potential as biochemical indicators of renal dysfunction in diabetic patients. The declining adiponectin-to-leptin ratio with disease severity also emphasizes the imbalance in adipose tissue homeostasis as a key metabolic signature of diabetic nephropathy[15, 16].

Overall, this study reinforces the emerging role of adipokines as pathophysiological mediators and potential biomarkers for early detection and monitoring of nephropathy in diabetes.

Conclusion:

This study demonstrates that serum adiponectin levels decrease while leptin levels increase progressively with advancing stages of diabetic nephropathy. The significant correlations of these adipokines with renal function parameters such as serum creatinine, eGFR, and urinary albumin excretion suggest their potential utility as biomarkers for early detection and monitoring of nephropathy in patients with type 2 diabetes mellitus. The declining adiponectin-to-leptin ratio reflects the metabolic and inflammatory imbalance underlying renal dysfunction. Incorporating adipokine assessment into clinical evaluation may enhance risk stratification and guide timely therapeutic interventions to prevent disease progression.

Limitations:

The present study has certain limitations. It was conducted with a relatively small sample size from a single center, which may limit the generalizability of the findings. The cross-sectional design restricts the ability to establish causal relationships between adipokine levels and nephropathy progression. Additionally, potential confounding factors such as dietary habits, medication use, and body fat distribution were not extensively controlled, which may have influenced adipokine concentrations.

Implications:

The findings suggest that monitoring adiponectin and leptin levels can aid in early detection and risk assessment of diabetic nephropathy. Incorporating these adipokines as adjunct biomarkers in routine clinical practice may enhance patient stratification, enable timely interventions, and improve management strategies to prevent renal complications in diabetes.

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