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Association of Serum Adiponectin and Leptin Levels with Glycemic Control in Type 2 Diabetes Mellitus

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Abstract

Emerging evidence implicates adiponectin and leptin in glucose homeostasis and metabolic regulation among individuals with type 2 diabetes mellitus (T2DM). The present experimental study investigated their association with glycemic control in a cross-sectional cohort of 120 adult T2DM patients, stratified into well-controlled (HbA1c $\leq 7\%$, $n = 60$) and poorly controlled (HbA1c $> 8\%$, $n = 60$) groups. Fasting serum adiponectin and leptin concentrations were measured via ELISA, and glycemic control was assessed by HbA1c. Adiponectin levels were significantly lower in poorly controlled participants (5.6 ± 1.4 µg/mL vs. 9.2 ± 2.1 µg/mL; $p < 0.001$), whereas leptin levels were notably higher (19.7 ± 3.8 ng/mL vs. 12.4 ± 2.9 ng/mL; $p < 0.001$). Pearson correlation analysis revealed a strong inverse relationship between adiponectin and HbA1c ($r = -0.62$, $p < 0.01$), and a moderate positive correlation for leptin ($r = 0.57$, $p < 0.01$). Multivariate regression, adjusted for age, BMI, and diabetes duration, confirmed that adiponectin ($\beta = -0.48$,

$p < 0.001$) and leptin ($\beta = 0.33$, $p < 0.01$) independently predicted HbA1c. These findings suggest that lower adiponectin and higher leptin levels are significantly associated with poorer glycemic control in T2DM, reinforcing their potential as non-invasive biomarkers. The study introduces a novel insight into adipokine-mediated glycemic regulation beyond insulin resistance, highlighting prospective utility in risk stratification and personalized diabetes management.

Keywords: adiponectin; leptin; glycemic control

Introduction

Type 2 diabetes mellitus (T2DM) remains a burgeoning public health challenge, characterized by chronic hyperglycemia resulting from insulin resistance and impaired insulin secretion. Its global prevalence continues to rise, with significant morbidity and mortality stemming from microvascular and macrovascular complications[1]. While glycemic indices such as HbA1c serve as established markers of metabolic control, they offer limited insight into underlying adipokine-mediated mechanisms that may influence disease progression. Adiponectin and leptin, secreted by adipose tissue, have garnered considerable attention as modulators of insulin sensitivity and energy homeostasis[2].

Adiponectin, noted for its anti-inflammatory and insulin-sensitizing effects, typically declines in obesity and T2DM[3]. Recent studies (2022–2024) have demonstrated its inverse association with glycemic deterioration, suggesting that adiponectin might hold diagnostic and therapeutic potential[4]. Conversely, leptin, primarily known for regulating satiety and energy expenditure, tends to increase in obesity, but its role in glycemic regulation is more complex[5]. Contemporary evidence indicates hyperleptinemia may correlate with insulin resistance and poor metabolic outcomes[6]. Despite these associations, literature remains inconclusive regarding the independent predictive utility of both adipokines in stratifying glycemic control among T2DM individuals. A 2022 cohort found only adiponectin correlated significantly with HbA1c after adjustment for BMI and inflammation[7], whereas a 2023 cross-sectional analysis reported both leptin and adiponectin as independent predictors in adjusted models[8].

Furthermore, emerging mechanistic research suggests that adiponectin promotes glucose uptake via AMPK pathways, whereas leptin modulates insulin signaling via JAK-STAT cascades[9]. However, few studies have examined both molecules concurrently in stratified T2DM cohorts, adjusting for demographic and anthropometric confounders[10].

The present study was designed to fill this gap by measuring fasting serum adiponectin and leptin

in well-controlled vs. poorly controlled T2DM patients, assessing correlation with HbA1c, and performing multivariate regression including age, BMI, and diabetes duration. By doing so, it seeks to elucidate the independent contributions of these adipokines to glycemic control in a contemporary T2DM sample.

This approach offers novelty by integrating both adipokines in stratified analysis and adjusted modeling, contrasting with prior research that mostly focused on one marker or lacked robust adjustment[11,12]. Moreover, the use of ELISA-based quantitative assays and multivariate statistics enhances the methodological rigor and translational relevance[13,14,15].

Methodology

A cross-sectional experimental study was conducted at Bolan Medical College a tertiary endocrinology cente, enrolling 120 adult T2DM patients aged 30–70 years. Sample size estimation via Epi Info® version 7 assumed 80% power, $\alpha = 0.05$, two-sided test, an expected difference of 2.5 µg/mL in adiponectin between groups, and SD of 3.0; yielding 58 participants per group, rounded to 60 for contingency. Patients were categorized based on HbA1c into well-controlled ($\leq 7\%$, n = 60) or poorly controlled ($> 8\%$, n = 60). Exclusion criteria encompassed type 1 diabetes, active infection, pregnancy, corticosteroid therapy, known malignancy, chronic kidney disease (stage 3+), or liver dysfunction. Eligible participants provided verbal informed consent following IRB-approved protocol. Demographic data including age, sex, BMI, diabetes duration, and current medications were recorded. After overnight fasting, venous blood samples were collected; serum was separated and stored at –80 °C. Serum adiponectin and leptin concentrations were measured using commercially available ELISA kits according to manufacturer instructions, ensuring duplicate assays and coefficient of variation <10%. HbA1c was analyzed via HPLC technique standardized per NGSP protocol. Data normality was assessed via Shapiro-Wilk test. Between-group comparisons of continuous variables employed Student's t-test or Mann–Whitney U as appropriate; categorical variables were compared using chi-square test. Pearson or Spearman correlations were performed between adipokines and HbA1c. Multivariate linear regression models included adiponectin, leptin, age, BMI, and disease duration to assess independent predictors of HbA1c. Statistical significance was set at two-tailed $p < 0.05$. Data were analyzed with SPSS® version 25.0 and the sample-size calculation details were included in the methods.

Results

Table 1. Demographic and Clinical Characteristics of Study Participants

Variables compared across well-controlled (HbA1c ≤ 7%) and poorly controlled (> 8%) groups. Continuous data shown as mean ± SD; categorical as n (%).

- Age (years): 54.2 ± 8.0 vs. 56.5 ± 7.2; p = 0.08
- Sex (F/M): 34/26 vs. 30/30; p = 0.47
- BMI (kg/m²): 28.6 ± 3.4 vs. 30.2 ± 3.8; p = 0.01
- Diabetes duration (years): 6.8 ± 2.5 vs. 8.1 ± 3.0; p = 0.01

This table indicates comparable demographics except slightly higher BMI and disease duration in poorly controlled group.

Table 2. Serum Adiponectin, Leptin, and HbA1c Levels

Variables displayed as mean ± SD with intergroup comparisons.

- Adiponectin (μg/mL): 9.2 ± 2.1 vs. 5.6 ± 1.4; p < 0.001
- Leptin (ng/mL): 12.4 ± 2.9 vs. 19.7 ± 3.8; p < 0.001
- HbA1c (%): 6.5 ± 0.3 vs. 9.1 ± 0.6; p < 0.001

This highlights significantly lower adiponectin and higher leptin in poorly controlled diabetics.

Table 3. Correlation and Regression Analyses with HbA1c

- Adiponectin–HbA1c: r = –0.62, p < 0.01
- Leptin–HbA1c: r = 0.57, p < 0.01
- Multivariate regression (adjusted): adiponectin β = –0.48, p < 0.001; leptin β = 0.33, p < 0.01; age, BMI, and duration retained significance.

These data confirm independent predictive value of adipokine levels for glycemic control.

Discussion

The present study identifies significantly lower adiponectin and higher leptin concentrations in poorly controlled T2DM, aligning with growing literature that positions these adipokines as critical metabolic regulators[16]. The inverse correlation between adiponectin and HbA1c corroborates findings from a 2022 analysis where adiponectin independently predicted glycemic outcomes after adjustment for adiposity and inflammation[17]. The current data extend this by demonstrating that leptin, in parallel, retains independent association with HbA1c, reflecting hyperleptinemia's potential role in insulin resistance and metabolic dysregulation[18]. Mechanistically, adiponectin's enhancement of AMPK signaling and downregulation of hepatic gluconeogenesis offers plausible pathways through which lower adiponectin may contribute to

poorer glycemic control[19]. In contrast, leptin-induced SOCS-3 upregulation may impair insulin receptor signaling, thereby exacerbating hyperglycemia[20]. These distinct mechanisms support the dual-adipokine model observed in this study.

Multivariate analysis adjusted for age, BMI, and disease duration further strengthens the argument that adipokine levels exert an impact on glycemic control independent of conventional risk factors, addressing limitations in earlier studies that lacked such adjustment[21]. The moderate correlation coefficients ($|r| > 0.5$) and β-values reinforce clinical relevance and potential utility in routine risk stratification[22].

Comparative analysis with prior cohorts indicates consistency across diverse populations, although absolute levels may vary by ethnicity and assay sensitivity. This study's use of validated ELISA methods with low inter-assay variation boosts reproducibility[23].

Some limitations should be acknowledged: the cross-sectional design precludes causal inference, and single-time measurements prevent evaluation of temporality; nonetheless, the robust associations suggest a need for longitudinal follow-up[24]. Future interventional studies examining whether adiponectin modulation can improve glycemic outcomes would be valuable[25].

In addition, exploration into adiponectin/leptin ratios as composite biomarkers may enhance predictive utility, given their opposing associations[26]. Lastly, incorporating inflammatory markers and adipokine receptors could offer mechanistic depth in future analyses[27].

Overall, this study adds to a growing body of evidence positioning adiponectin and leptin as non-invasive biomarkers for glycemic control in T2DM[28]. These findings emphasize the potential for integrating adipokine profiling in personalized diabetes management and risk stratification protocols[29].

Conclusion

Lower serum adiponectin and higher leptin concentrations are significantly associated with poor glycemic control in type 2 diabetes, independent of age, BMI, and disease duration. This study fills the research gap by concurrently analyzing both adipokines in a stratified, adjusted cohort, underscoring their potential utility as biomarkers. Future longitudinal and interventional studies should investigate whether adipokine modulation can improve glycemic outcomes.

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