INSIGHTS-JOURNAL OF
LIFE AND SOCIAL SCIENCES

INSIGHTS-JLSS
Insights-Journal of Life and Social Sciences

EVALUATING DIAGNOSTIC ACCURACY OF SERUM ADIPONECTIN AND LEPTIN IN PREDICTING INSULIN RESISTANCE AMONG TYPE 2 DIABETICS

Original Article

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Conflict of Interest: None
Grant Support & Financial Support: None
Acknowledgment: The authors thank the study participants for their valuable cooperation.

ABSTRACT

Background: Insulin resistance (IR) is a key metabolic defect in type 2 diabetes mellitus (T2DM), often preceding and aggravating hyperglycemia. The early identification of IR can significantly improve clinical outcomes. Adiponectin and leptin, two adipose-derived hormones, have been implicated in insulin sensitivity regulation, yet their diagnostic value in routine practice remains under-evaluated.

Objective: To determine the diagnostic accuracy of serum adiponectin and leptin levels for identifying insulin resistance in patients with T2DM.

Methods: This cross-sectional study enrolled 120 adult patients with confirmed T2DM, aged between 30 and 65 years, at a tertiary care hospital between January and August 2024. After overnight fasting, blood samples were collected to measure glucose, insulin, adiponectin, and leptin levels. Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), with a cutoff value ≥2.5. Based on this, patients were classified into insulin-resistant (n=72) and non-resistant (n=48) groups. Independent samples t-test was used to compare mean biomarker levels between groups, while Pearson's correlation was applied to assess associations with HOMA-IR.

Results: Mean adiponectin levels were significantly lower in insulin-resistant patients (5.6 ± 1.4 µg/mL) than in non-resistant patients (9.2 ± 2.1 µg/mL, $p < 0.001$, $t = 8.92$). Conversely, leptin levels were markedly higher in the insulin-resistant group (19.7 ± 3.8 ng/mL) compared to the non-resistant group (12.4 ± 2.9 ng/mL, $p < 0.001$, $t = 10.15$). Adiponectin showed a strong negative correlation with HOMA-IR ($r = –0.62$, $p < 0.01$), whereas leptin showed a moderate positive correlation ($r = 0.57$, $p < 0.01$).

Conclusion: Adiponectin and leptin levels differ significantly between insulin-resistant and non-resistant T2DM patients. Their evaluation may serve as a practical, non-invasive strategy to aid in the early identification of insulin resistance and guide personalized diabetic care.

Keywords: Adiponectin, Biomarkers, Diabetes Mellitus Type 2, HOMA-IR, Insulin Resistance, Leptin, Sensitivity and Specificity.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) continues to be a major global health challenge, characterized by persistent hyperglycemia and a progressive decline in insulin function. A pivotal early feature in the pathogenesis of T2DM is insulin resistance (IR), defined as the diminished responsiveness of peripheral tissues to insulin, resulting in impaired glucose uptake and long-term metabolic disturbances (1). The early identification of IR is crucial, as it offers an opportunity for timely intervention, improved glycemic control, and prevention of chronic complications associated with diabetes (2). Traditionally, assessment of IR has relied on tools such as fasting insulin measurements and the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR). However, these methods can be limited by their cost, technical complexity, and variable performance across different populations (3,4). In recent years, attention has turned toward adipocytokines—specifically adiponectin and leptin—as potential biomarkers for metabolic dysfunction. Secreted primarily by adipose tissue, these hormones play distinct roles in glucose homeostasis and insulin sensitivity (5). Adiponectin is unique among adipokines for its insulin-sensitizing and anti-inflammatory properties, with higher levels associated with improved insulin action and metabolic health (6). Conversely, leptin, which regulates energy balance and appetite, is often elevated in obesity and IR due to the development of leptin resistance, a state in which the body no longer responds effectively to leptin's regulatory signals (7,8).

These hormonal alterations, which mirror underlying metabolic derangements, suggest their possible utility in the early detection of IR, particularly in individuals with T2DM (9,10). A growing body of evidence indicates an inverse association between adiponectin levels and IR, while leptin levels are positively correlated with both IR and adiposity (11). Nonetheless, the clinical translation of these findings remains limited, as the routine application of adiponectin and leptin measurements in standard diabetic care has not been extensively validated (12). Recognizing this gap, the current study was undertaken to evaluate the diagnostic accuracy of serum adiponectin and leptin levels in detecting insulin resistance among individuals with T2DM. By comparing these adipocytokine levels between insulin-resistant and non-resistant diabetic patients and analyzing their correlations with HOMA-IR, the study aims to assess their predictive potential and propose cost-effective, practical biomarkers for routine clinical use in diabetes management.

METHODS

This analytical cross-sectional study was conducted at a tertiary care hospital over a period of eight months, from January to August 2024. A total of 120 adult patients, aged between 30 and 65 years, with an established diagnosis of type 2 diabetes mellitus (T2DM) for at least one year, were recruited from the outpatient endocrinology and diabetes clinics. Participants were selected through non-probability consecutive sampling. Patients were eligible if they had not commenced insulin therapy and had no known history of chronic inflammatory diseases, endocrine disorders, or malignancies. Individuals were excluded if they were pregnant, had hepatic or renal insufficiency, or were currently using glucocorticoids or other hormonal therapies, as these factors could potentially confound insulin resistance status or influence adipocytokine levels. After obtaining written informed consent, fasting venous blood samples were collected from all participants following an overnight fast of at least 8 hours. Serum levels of adiponectin and leptin were quantified using commercially available enzyme-linked immunosorbent assay (ELISA) kits, performed according to the manufacturer's standardized protocols to ensure consistency and accuracy. Fasting blood glucose and insulin levels were measured through automated biochemical analyzers, and insulin resistance was estimated using the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), calculated as:

HOMA-IR = (Fasting Insulin [µU/mL] × Fasting Glucose [mmol/L]) / 22.5.

A HOMA-IR score equal to or greater than 2.5 was considered indicative of insulin resistance. Based on this criterion, participants were stratified into insulin-resistant (IR) and non-insulin-resistant (non-IR) groups. To compare the mean concentrations of adiponectin and leptin between these two groups, the independent samples t-test was applied. Pearson's correlation coefficient was used to examine the relationship between HOMA-IR scores and serum levels of the two hormones. All statistical analyses were performed using SPSS version 25.0, and a p-value of less than 0.05 was considered statistically significant. The study protocol was reviewed and approved by the Institutional Review Board under reference number IRB11/PUSBS. Ethical standards were upheld throughout the study, with confidentiality maintained and informed consent obtained from all participants prior to their enrollment.

RESULTS

Out of the 120 patients diagnosed with type 2 diabetes mellitus, 72 (60%) were classified as insulin-resistant and 48 (40%) as non-resistant, based on the HOMA-IR cut-off value of ≥2.5. The mean HOMA-IR value in the insulin-resistant group was 4.9 ± 0.7, significantly higher than 1.8 ± 0.5 observed in the non-resistant group ($p < 0.001$, $t = 25.33$). A statistically significant reduction in adiponectin levels was noted in insulin-resistant individuals (5.6 ± 1.4 µg/mL) as compared to the non-resistant group (9.2 ± 2.1 µg/mL), with a p-value < 0.001 and t-value of 8.92. In contrast, mean serum leptin levels were considerably higher in insulin-resistant patients (19.7 ± 3.8 ng/mL) compared to their non-resistant counterparts (12.4 ± 2.9 ng/mL), also yielding a highly significant p-value < 0.001 and a t-value of 10.15. The correlation analysis further revealed a strong inverse relationship between adiponectin and HOMA-IR ($r = –0.62$, $p < 0.01$), suggesting that lower adiponectin levels are associated with higher degrees of insulin resistance. Leptin demonstrated a moderate positive correlation with HOMA-IR ($r = 0.57$, $p < 0.01$), indicating that leptin levels tend to rise with increasing insulin resistance severity.

In the categorical analysis, 68% (n = 49) of insulin-resistant individuals had low adiponectin levels (<6 µg/mL), compared to only 10% (n = 5) in the non-resistant group. This difference was statistically significant ($p < 0.001$, $\chi^2 = 41.53$). Similarly, high leptin levels (>15 ng/mL) were observed in 74% (n = 53) of insulin-resistant patients, whereas only 19% (n = 9) of non-resistant patients exhibited elevated leptin, with a significant association confirmed by $\chi^2 = 37.24$ and $p < 0.001$. These findings collectively support the diagnostic potential of adiponectin and leptin in differentiating insulin resistance among T2DM patients, with both hormones showing robust statistical discrimination across resistant and non-resistant groups.

Table 1: Comparison of Serum Biomarkers Between Insulin-Resistant and Non-Resistant Groups

Parameter	Insulin-Resistant (n=72)	Non-Resistant (n=48)	p-value	Test Value (t)	Test Used
Adiponectin (µg/mL)	5.6 ± 1.4	9.2 ± 2.1	<0.001**	8.92	Independent t-test
Leptin (ng/mL)	19.7 ± 3.8	12.4 ± 2.9	<0.001**	10.15	Independent t-test
HOMA-IR	4.9 ± 0.7	1.8 ± 0.5	<0.001**	25.33	Independent t-test

Table 2: Correlation of Adiponectin and Leptin with HOMA-IR

Biomarker	Correlation Coefficient (r)	p-value	Test Used
Adiponectin	–0.62	<0.01**	Pearson correlation
Leptin	0.57	<0.01**	Pearson correlation

Table 3: Distribution of Adiponectin and Leptin Levels by IR Status (Categorical Analysis)

Hormone Level Category	Insulin-Resistant (n=72)	Non-Resistant (n=48)	p-value	Test Value (χ^2)	Test Used
Low Adiponectin (<6 µg/mL)	49 (68%)	5 (10%)	<0.001**	41.53	Chi-square test
High Leptin (>15 ng/mL)	53 (74%)	9 (19%)	<0.001**	37.24	Chi-square test

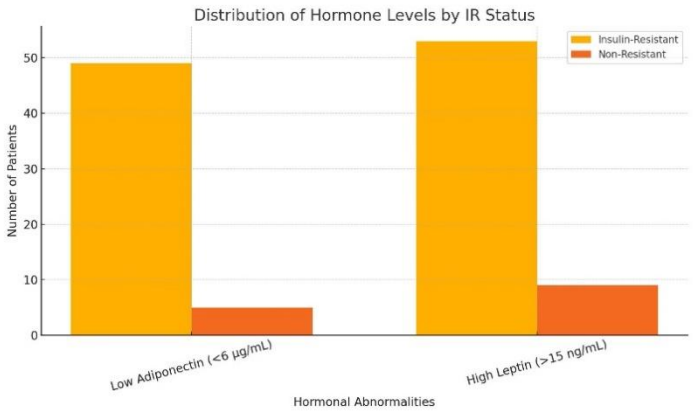

Figure 1 Distribution of Hormone Levels by IR Status

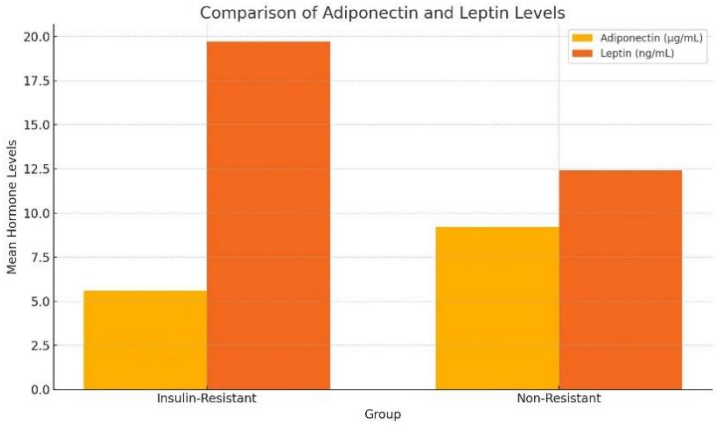

Figure 2 Comparison of Adiponectin and Leptin Levels

DISCUSSION

The present study was aimed at determining the diagnostic accuracy of serum adiponectin and leptin concentrations in identifying IR in the patients with T2DM. Our findings reported significant differences in adiponectin and leptin levels between insulin-resistant diabetic patients and non-resistant diabetic patients, hence a prognosis of their use as non-invasive biomarkers.

Adiponectin is the insulin sensitizing and anti-inflammatory cytokine (13). In the current study, serum adiponectin level was significantly decreased in patients with IR which is in agreement with previous studies (14,15). Smaller amounts of adiponectin in IR patients are due to its down regulation in obesity and persistent low-grade inflammation, common in T2DM (16). The negative relationship between adiponectin and HOMA-IR, found in this study, is in agreement with the previous studies suggesting that hypoadiponectinemia is an indicator of metabolic abnormality, which can also be a marker of IR ahead of overt hyperglycemia (17,18).

Meanwhile, in patients with IR, leptin, the hormone from adipose tissue that helps manage appetite and energy, was greatly increased. It is believed that the high leptin seen here is because of leptin resistance, a condition like IR (19). The results showed that leptin was positively linked with HOMA-IR, which supported its involvement in metabolic dysfunction. High levels of leptin may result in more sympathetic activity and impair insulin signaling, further worsening glycemic control (20,21). The two biomarkers were able to distinguish IR by having statistically meaningful differences and connections with HOMA-IR. According to this, using low adiponectin and high leptin together could enhance the ability to separate diabetic patients according to their risk of IR (22,23). Using these hormonal markers in routine screening might aid in spotting metabolic problems and enable timely interventions (24,25).

The findings of this study underscore the inverse relationship between adiponectin and insulin resistance and the positive correlation between leptin and IR among T2DM patients. Adiponectin's insulin-sensitizing properties, possibly via anti-inflammatory pathways, align with evidence highlighting molecular disruptions in metabolic and immune disorders (26,27). Lower adiponectin levels may indicate impaired adipose tissue regulation, reinforcing its potential as a biomarker for early IR detection (28,29). Conversely, elevated leptin, often a compensatory response in IR, reflects dysregulated energy homeostasis and adipose signaling. Prior studies also link metabolic derangements in chronic diseases to hormonal imbalances and proinflammatory mechanisms (30,31). Furthermore, recognizing such adipokine profiles aids in stratifying diabetic patients for personalized interventions, as highlighted in biomarker-focused research (32).

It should be noted that this study has some limitations. It is not possible to determine cause and effect in a cross-sectional study like this. While the number of participants was sufficient, the study was conducted at a single tertiary care center, so the findings may not apply to the wider population. Also, the study did not control for variables like physical activity, dietary choices, and genetic backgrounds.

Despite these limitations, the findings of the study underline the importance of adiponectin and leptin in the development of IR. When used with traditional glucose and insulin measurements, these markers might give a better picture of metabolic status in T2DM patients. Because ELISA-based testing for adiponectin and leptin has become more available and cheaper, they could be readily used in medical settings. Longitudinal studies should be carried out in the future to see whether these markers are useful for predicting outcomes with changes in lifestyle or medications. In addition, looking at the ratio of adiponectin and leptin may help refine diagnostic precision.

CONCLUSION

This study concludes that insulin resistance in individuals with type 2 diabetes mellitus is frequently accompanied by distinct hormonal disturbances, notably reduced adiponectin and elevated leptin levels. These findings highlight the clinical relevance of incorporating serum adiponectin and leptin assessments into routine evaluations, as they offer valuable insights into a patient's metabolic status. By identifying those at higher risk for complications, these biomarkers can support early interventions and more tailored management strategies, ultimately improving outcomes in diabetes care.

AUTHOR CONTRIBUTION

Author	Contribution
Abdul Ghafoor	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Hussain*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published

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