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EVALUATION OF THE ASSOCIATION BETWEEN PLASMINOGEN ACTIVATOR INHIBITOR-1 AND ADIPONECTIN LEVELS IN PREDIABETIC PATIENTS

Medicine

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ABSTRACT

Background: Diabetes mellitus (DM) is a significant global health issue, and prediabetes is a precursor to type 2 diabetes (T2DM), marked by elevated blood glucose levels and insulin resistance. Both adiponectin and plasminogen activator inhibitor-1 (PAI-1) play a crucial role in glucose metabolism and cardiovascular risk. **Aims & Objectives:** This study aimed to evaluate the association between adiponectin and PAI-1 levels in prediabetic patients. The primary objective was to determine whether these biomarkers could be used to assess the risk of developing T2DM and its related complications. **Methods:** A cross-sectional study was conducted on 100 prediabetic patients and controls, aged 18-60 years, from CSS Hospital, Subharti Medical College, Meerut. Fasting plasma glucose (FPG), adiponectin, and PAI-1 levels were measured using standard laboratory techniques. Statistical analysis was performed using chi-square tests, analysis of covariance, and multivariate general linear models to assess the association between biomarkers and prediabetes. **Results:** The study found significantly lower adiponectin levels (3.69 µg/ml) in prediabetic patients compared to controls (10.29 µg/ml) and higher PAI-1 levels (56.16 ng/ml vs. 21.91 ng/ml), with p-values of 0.0304 and 0.0208, respectively. Both markers correlated with BMI, as adiponectin decreased and PAI-1 increased with higher BMI, especially in overweight and obese patients, highlighting notable metabolic differences between the groups. **Conclusions:** Adiponectin and PAI-1 levels show a significant association with BMI in prediabetic patients, suggesting that these markers could be valuable for early risk assessment of T2DM and cardiovascular complications. Further research is required to explore their potential in preventive interventions.

KEYWORDS

Adiponectin, Plasminogen Activator Inhibitor-1, Prediabetes, Type 2 Diabetes, Cardiovascular Risk

INTRODUCTION

Diabetes mellitus (DM) is a widespread metabolic disorder, characterized by elevated blood glucose levels resulting from impairments in insulin action or production.[1] Type 2 diabetes (T2DM), the most common form, is marked by insulin resistance (IR) coupled with a relative deficiency in insulin.[2] This metabolic imbalance, if unchecked, adversely impacts the vascular system, leading to complications like microvascular and macrovascular diseases. Long-term hyperglycemia is linked to significant damage to critical organs, including the heart, kidneys, eyes, and nervous system.[3]

The global burden of diabetes is staggering, with over 415 million people affected worldwide, a number expected to escalate to 642 million by 2040.[4] In India, the situation is equally alarming, with 69.2 million individuals currently living with diabetes, projected to soar to 123.5 million by 2040.[4] Prediabetes, a precursor to T2DM, is a condition marked by elevated blood glucose levels that are not high enough for a diabetes diagnosis.[5] Globally, 9.1% of adults (aged 20 to 79) are estimated to be prediabetic, and this is expected to rise to 10% by 2045.[4] The increase in prediabetes cases is closely tied to rising obesity rates, poor dietary habits, and sedentary lifestyles.[6]

Prediabetes is increasingly recognized as a significant health risk in itself. It not only predisposes individuals to diabetes but also to a range of vascular complications. Insulin resistance and obesity in prediabetic patients lead to endothelial dysfunction, increasing the risk of cardiovascular disease.[3,5] Plasminogen activator inhibitor-1 (PAI-1), a key regulator of fibrinolysis, is elevated in diabetic patients and has been linked to coronary heart disease (CHD) and thrombosis. Meanwhile, adiponectin, a peptide hormone produced by adipocytes, plays a crucial role in enhancing insulin sensitivity and reducing inflammation. Low adiponectin levels are associated with insulin resistance and increased risk of T2DM.[7]

This study seeks to explore the relationship between PAI-1 and adiponectin levels in prediabetic patients. By understanding this association, we can better predict the progression of prediabetes to T2DM and its related complications, potentially offering insights for early intervention.

MATERIALS AND METHODS

Study Design

This cross-sectional study was conducted to evaluate the association between plasminogen activator inhibitor-1 (PAI-1) and adiponectin levels in prediabetic patients.

Study Population

Pre-diabetic subjects of both sexes, aged 18–60, were enrolled from the Department of Medicine at CSS Hospital, Subharti Medical College, Meerut. The study was carried out from September 2022 to August 2024.

Ethical Approval and Consent

Informed consent was obtained from all participants. The study was approved by the Institutional Ethical Committee of CSS Hospital, Subharti Medical College, Meerut.

Sample Size

A total of 100 prediabetic patients were selected based on inclusion and exclusion criteria.

Inclusion Criteria

Participants aged 18 to 60 years diagnosed with prediabetes, according to the American Diabetes Association (ADA) criteria, were included in the study.

Exclusion Criteria

Exclusion criteria included pregnant females, individuals with liver cirrhosis, chronic kidney disease, cardiac insufficiency, malignant tumors, hypertension, hyperlipidemia, cardiovascular or cerebrovascular diseases, or mental illness. Patients on antidiabetic drugs or diagnosed with diabetes, as well as those using drugs, supplements, or functional foods more than three times per week for over three months, were also excluded.

Data Collection

Venous blood samples were collected after an overnight fast of at least 8 hours. Fasting plasma glucose (FPG), triglycerides (TG), total cholesterol (TC), LDL-C, and HDL-C levels were measured using an autoanalyzer. Adiponectin levels were analyzed via latex-enhanced immunoturbidimetry, while PAI-1 levels were determined using enzyme-linked immunosorbent assay (ELISA).

Statistical Analysis

Chi-square tests were used to compare categorical variables, while analysis of covariance was used for continuous variables. Multivariate general linear models (GLM) were employed to assess the association between PAI-1 and prediabetes, with adjusted odds ratios (ORs) and 95% confidence intervals (CIs). A p-value of less than 0.05 was considered statistically significant. SPSS version 21 was used for data analysis.

RESULTS

Table 1 Patient Demographics and BMI Distribution

Variable	Pre-diabetic	Control
Mean Age (years)	49.31	48.89
Age SD	7.73	7.73
Males (%)	46.67	49.33
Females (%)	53.33	50.67
Healthy Weight (%)	33.33	46.67
Overweight (%)	37.33	42.67
Obesity (%)	18.67	8.00
Severe Obesity (%)	10.67	2.66
Mean BMI (Kg/m²)	28.85	26.73
BMI SD	5.69	3.92

This table provides a concise overview of the prediabetic and control groups, comparing their mean age, gender distribution, and BMI classifications. It highlights that the prediabetic group had a higher proportion of obesity and severe obesity compared to the control group, with a statistically significant difference in BMI.

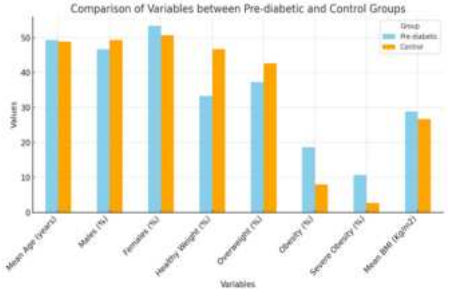


Table 2 Comparison of Adiponectin Levels Between Pre-diabetic and Control Groups Based on BMI

Group/BMI	Adiponectin (µg/ml)		
	Mean	**SD**	**p-value**
Pre-diabetic Group	3.69	1.46	0.0304
Control Group	10.29	1.22	0.0304
Healthy Weight (Control)	11.55	3.90	0.0012
Overweight (Control)	9.86	1.90	0.0012
Obesity (Control)	8.08	1.30	0.0012
Severe Obesity (Control)	1.53	0.00	0.0012

This table compares the adiponectin levels between pre-diabetic and control groups, with a further breakdown of adiponectin levels in different BMI categories among the control group. It shows a significant decline in adiponectin levels as BMI increases, highlighting a strong relationship between higher BMI and lower adiponectin in the control group.

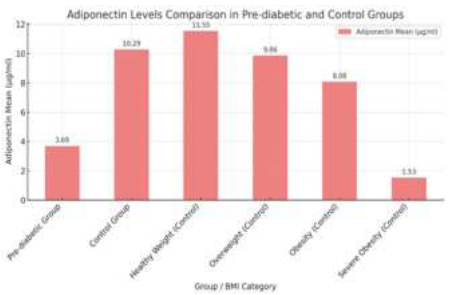


Table 3 Plasminogen Activator Inhibitor-1 Levels Across Pre-diabetic and Control Groups by BMI

Group/BMI	Plasminogen Activator Inhibitor-1 (ng/ml)		
	Mean	**SD**	**p-value**
Pre-diabetic Group	56.16	16.57	0.0208
Control Group	21.91	2.51	0.0208
Healthy Weight (Control)	19.14	3.98	0.0017
Overweight (Control)	22.78	4.11	0.0017
Obesity (Control)	25.29	5.38	0.0017
Severe Obesity (Control)	64.81	0.66	0.0017

This table illustrates the significant differences in plasminogen activator inhibitor-1 (PAI-1) levels between pre-diabetic and control groups, with a further breakdown by BMI categories within the control group. A notable increase in PAI-1 levels is observed as BMI rises, particularly in the severe obesity group.

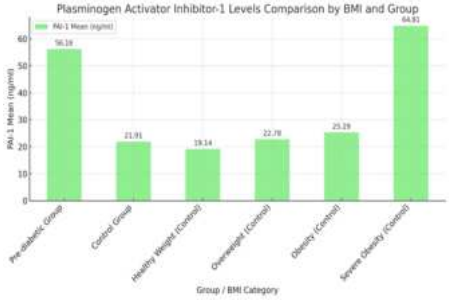


Table 4 Association of Adiponectin and Plasminogen Activator Inhibitor-1 (PAI-1) Levels Across BMI Categories in Prediabetic Patients

BMI Category	Adiponectin Mean (µg/ml)	Adiponectin SD	PAI-1 Mean (ng/ml)	PAI-1 SD	p-value
Less than 24.9 Kg/m² (Healthy weight)	5.32	2.3	37.94	9.9	0.0002 (Adiponectin) / 0.0003 (PAI-1)
≥25 Kg/m² to <30 Kg/m² (Overweight)	3.36	1.2	56.14	2.1	0.0002 (Adiponectin) / 0.0003 (PAI-1)
≥30 Kg/m² to <40 Kg/m² (Obesity)	2.62	0.9	73.22	10.1	0.0002 (Adiponectin) / 0.0003 (PAI-1)
≥40 Kg/m² (Severe obesity)	1.88	0.5	81.08	52.8	0.0002 (Adiponectin)

This table highlights the relationship between BMI and both adiponectin and PAI-1 levels in prediabetic patients. As BMI increases, adiponectin levels decrease significantly, while PAI-1 levels show a marked rise, reflecting a clear association between higher BMI and worsening metabolic markers.

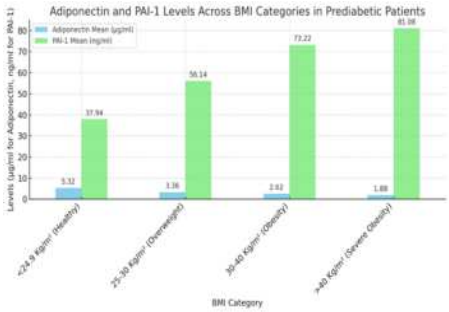


Table 5 Individual Group Comparisons of Adiponectin and Plasminogen Activator Inhibitor-1 (PAI-1) Levels Among Prediabetic Subjects

Comparison	Adiponectin p-value	PAI-1 p-value
Healthy weight vs Overweight	0.019*	0.003*
Healthy weight vs Obesity	0.005*	0.004*
Healthy weight vs Severe Obesity	0.001*	0.000*
Overweight vs Obesity	0.553	0.042*

Overweight vs Severe Obesity	0.002*	0.000*
Obesity vs Severe Obesity	0.000*	0.000*

This table compares the significance of differences in adiponectin and PAI-1 levels across various BMI categories in prediabetic subjects. The results highlight significant differences in both markers as BMI increases, particularly between the healthy weight group and the severe obesity group.

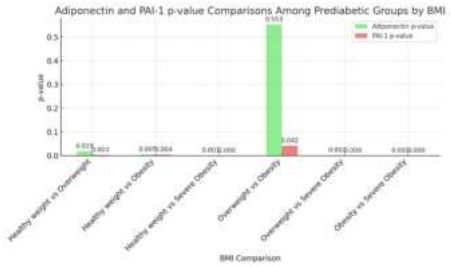
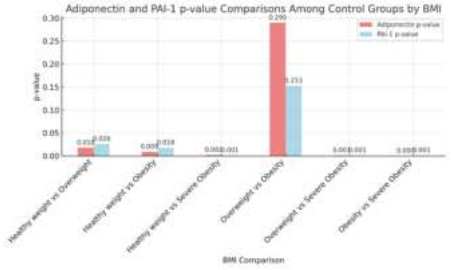


Table 6 Individual Group Comparisons of Adiponectin and Plasminogen Activator Inhibitor-1 (PAI-1) Levels Among Control Subjects

Comparison	Adiponectin p-value (control)	PAI-1 p-value (control)
Healthy weight vs Overweight	0.018*	0.026*
Healthy weight vs Obesity	0.009*	0.018*
Healthy weight vs Severe Obesity	0.002*	0.001*
Overweight vs Obesity	0.290	0.153
Overweight vs Severe Obesity	0.001*	0.001*
Obesity vs Severe Obesity	0.000*	0.001*

This table shows the statistical significance of differences in adiponectin and PAI-1 levels across BMI categories among control subjects. The results demonstrate significant variations, particularly between the healthy weight group and the severe obesity group, indicating a strong correlation between increased BMI and changes in these biomarkers.



DISCUSSION

In the present study, 53.33% of prediabetic patients were aged 51-60 years, with a mean age of 48.61 years, and 46.67% were males. Among the control group, 50.67% were aged 51-60 years, with a mean age of 49.12 years, and 49.33% were males. In comparison, studies by **Xu et al.[8] and Huang K et al.9** reported higher mean ages, ranging from 56.88 to 58.7 years for prediabetic and control groups, while **Ganesh V et al.[10]** and **Banerjee A et al.[11]** found mean ages closer to our study, around 45.51 to 50.08 years. Gender-wise, **Xu et al.[8], Ganesh V et al**.[10], and **Banerjee A et al.[11]** reported a similar male distribution, with males comprising 45% to 54.79% of the prediabetic group. Regarding BMI, 37.33% of prediabetic patients in this study were overweight, with 18.67% obese and 10.67% severely obese. **Ganesh V et al.[10]** observed a much higher mean BMI of 31.29 Kg/m² in prediabetic patients, while **Banerjee A et al**.[11] reported a mean BMI of 26.19 Kg/m², more in line with our findings. These comparisons highlight consistent demographic trends across different studies.

In the present study, mean adiponectin levels were significantly lower in prediabetic patients (3.64 µg/ml) compared to controls (10.53 µg/ml), and a significant inverse correlation between BMI and adiponectin levels was observed. Among prediabetics, adiponectin levels decreased from 5.7 µg/ml in healthy weight individuals to 1.1 µg/ml in those with severe obesity. Comparably, **Banerjee et al.[11]** found lower adiponectin levels in prediabetics (5.77 µg/ml) than controls (8.15 µg/ml). **Ganesh V et al.[10]** reported levels of 3.22 µg/ml in prediabetics and 5.36 µg/ml in controls. **Jiang et al.[12]** observed a significant negative correlation between BMI and adiponectin in prediabetes, while **Liu W et al.[13]** highlighted adiponectin's role in improving insulin sensitivity and preventing T2DM. Other studies, including those by **Kong SE et al.[14]** and **Gateva et al.[15],** consistently reported lower adiponectin levels in individuals progressing to prediabetes or T2DM, emphasizing adiponectin's role as a potential biomarker for disease progression and metabolic health.

In this study, mean plasminogen activator inhibitor-1 (PAI-1) levels were significantly higher in prediabetic patients (56.88 ng/ml) compared to controls (21.24 ng/ml). A significant positive correlation between BMI and PAI-1 levels was observed, with levels rising from 22.9 ng/ml in healthy-weight individuals to 95.3 ng/ml in severely obese patients. **Laryushina Y et al.[16]** found PAI-1 levels of 24.692 ng/ml in prediabetics and 194.611 ng/ml in controls, while **Xu L et al.[21]** observed levels of 185 ng/ml in prediabetics and 153 ng/ml in controls. **Festa A et al.[17],** in the IRAS study, noted that increased PAI-1 levels were associated with a higher risk of developing prediabetes and diabetes. Similarly, **Benyamin AF et al**.[18] confirmed greater PAI-1 activity in prediabetic individuals compared to healthy controls. Research also suggests that elevated PAI-1 levels are linked to insulin resistance, inflammation, and increased risk of cardiovascular disease (CVD) and thromboembolic events, as supported by studies from **Adam G. et al.[19], Petrauskiene V et al.[20]**, and others. These findings emphasize PAI-1 as a potential marker for assessing the risk of CVD and diabetes in prediabetic patients.

CONCLUSION

The present study demonstrated that prediabetic patients exhibit significantly lower adiponectin levels and higher plasminogen activator inhibitor-1 (PAI-1) levels compared to controls, with both markers showing a strong correlation with BMI. As BMI increases, adiponectin levels decrease, while PAI-1 levels rise significantly, particularly in obese and severely obese individuals. These findings suggest that adiponectin and PAI-1 could serve as valuable biomarkers for assessing the risk of developing type 2 diabetes and cardiovascular complications in prediabetic individuals. The results are consistent with previous studies, which also reported similar trends of decreased adiponectin and elevated PAI-1 levels in prediabetes. The association of these markers with metabolic disturbances highlights their potential role in early intervention strategies to prevent the progression of prediabetes to diabetes and its related complications.

Limitations

This study was limited by its cross-sectional design, which precludes establishing causal relationships. Additionally, the sample size may not be representative of broader populations, and external factors such as diet and physical activity were not accounted for.

Recommendations

Future studies should include larger, more diverse populations and adopt a longitudinal approach to better understand the temporal relationships between adiponectin, PAI-1, and the progression to diabetes. Moreover, incorporating lifestyle factors could provide deeper insights into modifiable risk factors that influence these biomarkers.

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Consent: Written consent from participants has been obtained and preserved.
Ethical Approval: Ethical approval was obtained and documented as per institutional guidelines.

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