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A COMPARATIVE STUDY OF ADIPOKINE PROFILES IN DIABETIC AND NON-DIABETIC INDIVIDUALS WITH A HISTORY OF SUBSTANCE ABUSE

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Abstract

Background: Adipokines play crucial roles in glucose homeostasis and metabolic regulation. The concurrent presence of diabetes and substance abuse may create unique metabolic perturbations affecting adipokine profiles. This study aimed to compare adipokine levels between diabetic and non-diabetic individuals with substance abuse history.

Methods: A comparative cross-sectional study was conducted at Maa Vindhyawasini Autonomous State Medical College, Mirzapur, from January to August 2025. One hundred participants with documented substance abuse history were enrolled: 50 with type 2 diabetes and 50 non-diabetic controls. Serum adiponectin, leptin, and resistin levels were measured using ELISA. Clinical parameters, anthropometric measurements, and substance abuse patterns were assessed.

Results: Diabetic participants showed significantly lower adiponectin levels (4.8±2.6 vs 9.2±3.8 µg/ml, $p<0.001$) and higher leptin (14.6±8.4 vs 8.8±5.2 ng/ml, $p<0.001$) and resistin levels (18.4±6.8 vs 12.6±4.2 ng/ml, $p<0.001$) compared to non-diabetic individuals. The leptin-to-adiponectin ratio was 3.2-fold higher in diabetic participants (3.8±2.1 vs 1.2±0.8, $p<0.001$). Strong correlations were observed between adipokine levels and metabolic parameters including BMI, HbA1c, and HOMA-IR. Multiple regression analysis identified diabetes status, BMI, and substance abuse duration as independent predictors of adipokine alterations.

Conclusion: Individuals with concurrent diabetes and substance abuse demonstrate profound adipokine dysregulation characterized by severe hypoadiponectinemia and elevated pro-inflammatory adipokines. These findings suggest heightened metabolic risk requiring targeted interventions and intensive monitoring in this vulnerable population.

Keywords: Adipokines, diabetes mellitus, substance abuse, adiponectin, leptin, resistin

Introduction

Adipose tissue has evolved from being viewed merely as a passive energy storage depot to being recognized as a highly active endocrine organ that secretes numerous bioactive molecules collectively termed adipokines (Scherer, 2006). These protein hormones, including adiponectin, leptin, and resistin, play crucial roles in regulating glucose homeostasis, insulin sensitivity, lipid metabolism, and inflammatory processes (Stefan & Stumvoll, 2002). The intricate balance of adipokine secretion significantly influences metabolic health, with disruptions leading to insulin resistance, type 2 diabetes mellitus, and cardiovascular complications (Berg et al., 2002).

Adiponectin, the most abundant adipokine in human plasma, possesses potent insulin-sensitizing, anti-inflammatory, and anti-atherogenic properties (Diez & Iglesias, 2003). Circulating adiponectin levels are paradoxically reduced in obesity, type 2 diabetes, and metabolic syndrome, correlating inversely with insulin resistance (Weyer et al., 2001). In contrast, leptin, primarily secreted by subcutaneous adipose tissue, regulates energy homeostasis by suppressing appetite and enhancing energy expenditure (Friedman & Halaas, 1998). However, leptin resistance commonly develops in obesity, contributing to perpetual hunger and metabolic dysfunction. Resistin, initially identified as an adipocyte-specific hormone, promotes insulin resistance and glucose intolerance while stimulating hepatic glucose production (Steppan et al., 2001).

The relationship between substance abuse and metabolic dysfunction has garnered increasing attention in recent years. Substance abuse, encompassing alcohol, opioids, stimulants, and other illicit drugs, affects millions of individuals worldwide and poses significant public health challenges (Mattoo et al., 2011). In India, the magnitude of substance abuse is particularly concerning, with an estimated 62.5 million people consuming alcohol, 8.75 million using cannabis, 2 million using opiates, and 0.6 million using sedatives or hypnotics (Ray et al., 2004). The prevalence of substance abuse in northern Indian states, including Uttar Pradesh, has been documented to be substantially higher than national averages, with significant implications for metabolic health (Ambekar et al., 2019).

Chronic alcohol consumption has been demonstrated to significantly alter adipokine profiles, with studies showing elevated serum leptin and resistin levels alongside paradoxically increased adiponectin concentrations in individuals with alcoholic liver disease (Pravdová et al., 2009). The mechanisms underlying these changes involve alcohol-induced alterations in adipose tissue metabolism, hepatic function, and systemic inflammation (Sierksma et al., 2004). Moderate alcohol consumption has been associated with improved insulin sensitivity, potentially mediated through increased adiponectin levels, while chronic excessive consumption leads to metabolic dysregulation (Beulens et al., 2007).

Opioid abuse, particularly prevalent in regions like Punjab and Uttar Pradesh, exerts complex effects on glucose homeostasis and adipokine regulation (Karam et al., 2004). Studies have shown that chronic opioid use can lead to insulin resistance, altered glucose tolerance, and disrupted endocrine function (Azod et al., 2008). The effects of opioids on adipokine profiles remain incompletely understood, with limited research examining the specific changes in adiponectin, leptin, and resistin levels in individuals with opioid use disorders.

Stimulant drugs, including cocaine and amphetamines, can acutely affect glucose metabolism through catecholamine release and cortisol elevation, potentially leading to hyperglycemia and diabetic ketoacidosis in susceptible individuals (Atkinson et al., 1987). The chronic effects of stimulant abuse on adipokine regulation and insulin sensitivity represent an understudied area with significant clinical implications.

The intersection of diabetes mellitus and substance abuse creates a complex pathophysiological scenario. Individuals with diabetes who abuse substances may experience poorer glycemic control due to erratic lifestyle patterns, medication non-compliance, and the direct metabolic effects of abused substances (Karam et al., 2004). Furthermore, substance abuse may accelerate the

development of diabetic complications and increase cardiovascular risk through multiple mechanisms, including adipokine dysregulation.

Indian populations demonstrate unique metabolic characteristics, with higher rates of insulin resistance and diabetes at lower body mass indices compared to Western populations (Ramachandran et al., 2007). The adipokine profiles in Asian Indian populations show distinct patterns, with some studies suggesting different relationships between adiponectin levels and insulin sensitivity compared to other ethnic groups (Ferris et al., 2005). This ethnic specificity necessitates population-specific research to understand the metabolic implications of substance abuse in Indian contexts.

Recent research has highlighted the potential clinical utility of adipokines as biomarkers for metabolic dysfunction and cardiovascular risk stratification (Lele et al., 2006). The leptin to adiponectin ratio has emerged as a particularly useful indicator of metabolic syndrome and insulin resistance (Finucane et al., 2009). Understanding how substance abuse affects these biomarkers could provide valuable insights for clinical management and risk assessment.

The rural and semi-urban populations of Uttar Pradesh face unique challenges related to substance abuse, including limited access to healthcare, higher rates of opioid use, and socioeconomic factors that may influence both substance use patterns and diabetes management (Singh et al., 2018). The interplay between these factors and adipokine regulation remains poorly characterized, representing a significant knowledge gap.

This study addresses a critical need to understand the comparative adipokine profiles in diabetic versus non-diabetic individuals with a history of substance abuse. By examining the levels of adiponectin, leptin, and resistin in these populations, we aim to elucidate the metabolic consequences of substance abuse and identify potential biomarkers for risk stratification. The findings may have important implications for developing targeted interventions and improving clinical outcomes in this vulnerable population.

The aim of the study is to compare the adipokine profiles (adiponectin, leptin, and resistin levels) between diabetic and non-diabetic individuals with a history of substance abuse, and to evaluate the association of these adipokines with metabolic parameters and glycemic control.

Methodology

Study Design

A comparative cross-sectional study design.

Study Site

The study was conducted at Maa Vindhyawasini Autonomous State Medical College, Mirzapur, Uttar Pradesh, India.

Study Duration

The study was conducted over a period of 8 months, from January 2025 to August 2025.

Sampling and Sample Size

A non-probability consecutive sampling technique was utilized to recruit participants who met the inclusion criteria during the study period. The sample size was calculated using the formula for comparing two means between independent groups, based on previous studies examining adipokine levels in Indian populations (Lele et al., 2006; Ramachandran et al., 2007). Considering an expected difference in adiponectin levels of 3.0 μg/ml between diabetic and non-diabetic groups (based on the study by Finucane et al., 2009), with a standard deviation of 4.5 μg/ml, power of 80%, alpha error of 5%, and allowing for a 10% dropout rate, the calculated sample size was 50 participants in each group. Therefore, the total sample size comprised 100 participants, with 50 diabetic individuals and 50 non-diabetic individuals, all with a documented history of substance abuse.

Inclusion and Exclusion Criteria

Inclusion criteria encompassed adults aged 18-65 years with a documented history of substance abuse (alcohol, opioids, stimulants, or cannabis) for at least one year, ability to provide informed consent, and willingness to participate in the study. For the diabetic group, participants required a confirmed diagnosis of type 2 diabetes mellitus based on American Diabetes Association criteria or current treatment with antidiabetic medications. The non-diabetic group included individuals with normal glucose tolerance or prediabetes (HbA1c <6.5%) who had never been diagnosed with diabetes mellitus. Exclusion criteria included pregnancy or lactation, active malignancy or history of cancer within the past five years, chronic kidney disease (eGFR <30 ml/min/1.73m²), liver cirrhosis or acute hepatitis, active substance withdrawal requiring hospitalization, severe psychiatric disorders preventing informed consent, use of medications significantly affecting adipokine levels (corticosteroids, thiazolidinediones), and inability to provide blood samples due to medical contraindications.

Data Collection Tools and Techniques

A structured questionnaire was developed to collect demographic information, medical history, substance abuse history, and current medications. The questionnaire included sections on age, gender, education, occupation, family history of diabetes, duration and type of substance abuse, current substance use status, and treatment history. Clinical data collection involved measurement of anthropometric parameters including height, weight, body mass index (BMI), waist circumference, and hip circumference using standardized techniques. Blood pressure was measured using a digital sphygmomanometer after 10 minutes of rest. Laboratory investigations included fasting and postprandial glucose levels, HbA1c, lipid profile (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol), liver function tests, and kidney function tests using automated analyzers with standard commercial kits. Adipokine levels (adiponectin, leptin, and resistin) were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, USA) following manufacturer protocols. All blood samples were collected after 12-hour overnight fasting, centrifuged at 3000 rpm for 15 minutes, and serum was stored at -80°C until batch analysis to minimize assay variability.

Data Management and Statistical Analysis

Data was entered into a Microsoft Excel spreadsheet and subsequently transferred to R software for statistical analysis. Data quality was ensured through double data entry and validation checks. Descriptive statistics were calculated for all variables, with continuous variables presented as mean ± standard deviation or median (interquartile range) depending on distribution normality assessed by the Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages. Between-group comparisons were performed using independent t-tests for normally distributed continuous variables and Mann-Whitney U tests for non-normally distributed variables. Chi-square tests or Fisher's exact tests were used for categorical variables. Correlation analysis was conducted using Pearson's or Spearman's correlation coefficients as appropriate. Multiple linear regression analysis was performed to identify independent predictors of adipokine levels while controlling for confounding variables. All tests were two-tailed with statistical significance set at $p < 0.05$.

Ethical Considerations

The study protocol was submitted to the Institutional Ethics Committee of Maa Vindhyawasini Autonomous State Medical College, Mirzapur, for review and approval before initiation. Written informed consent was obtained from all participants after explaining the study objectives, procedures, potential risks, and benefits in their preferred language. Participants were assured of the voluntary nature of participation and their right to withdraw from the study at any time without affecting their medical care.

Results

Table 1: Demographic and Anthropometric Characteristics of Study Participants

Parameter	Diabetic Group (n=50)	Non-Diabetic Group (n=50)	p-value
Age (years)	52.4 ± 8.2	45.6 ± 9.1	0.001*
Male gender, n (%)	42 (84.0)	41 (82.0)	0.794
BMI (kg/m²)	26.8 ± 4.3	24.2 ± 3.8	0.002*
Waist circumference (cm)	94.6 ± 8.5	89.2 ± 7.3	0.001*
Hip circumference (cm)	98.4 ± 6.8	95.1 ± 6.2	0.012*
Waist-to-hip ratio	0.96 ± 0.06	0.94 ± 0.05	0.048*
Systolic BP (mmHg)	142.8 ± 18.4	128.6 ± 15.2	<0.001*
Diastolic BP (mmHg)	88.4 ± 10.6	82.1 ± 9.4	0.003*

*p < 0.05 considered statistically significant

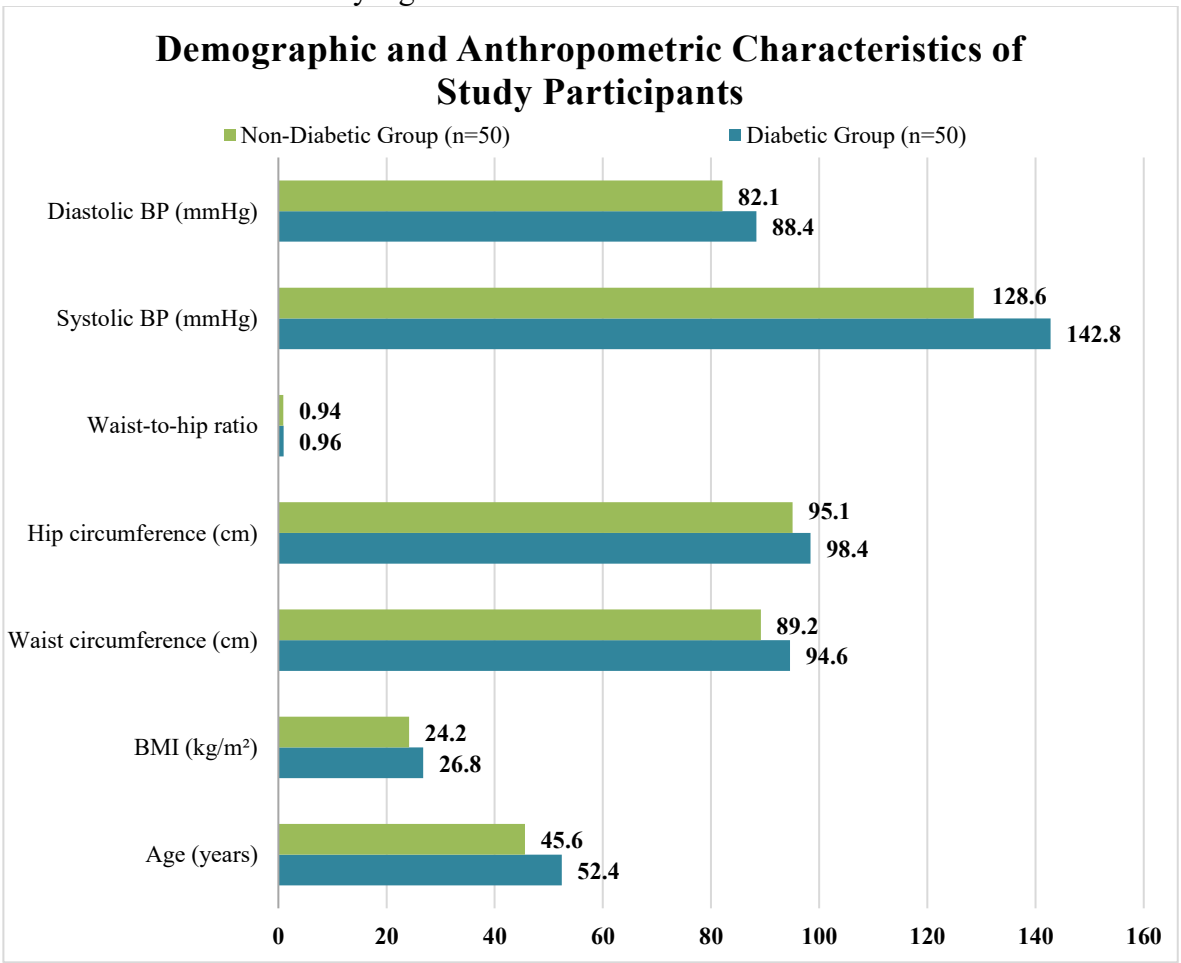

Fig: 1

Table 2: Laboratory Parameters and Glycemic Control

Parameter	Diabetic Group (n=50)	Non-Diabetic Group (n=50)	p-value
Fasting glucose (mg/dl)	164.2 ± 42.8	98.4 ± 12.6	<0.001*
Postprandial glucose (mg/dl)	248.6 ± 56.4	126.8 ± 18.2	<0.001*
HbA1c (%)	8.4 ± 1.8	5.6 ± 0.4	<0.001*
Total cholesterol (mg/dl)	198.6 ± 38.4	182.4 ± 32.6	0.028*
Triglycerides (mg/dl)	186.8 ± 64.2	142.6 ± 48.4	<0.001*

HDL-cholesterol (mg/dl)	38.4 ± 8.6	44.2 ± 9.8	0.003*
LDL-cholesterol (mg/dl)	122.8 ± 28.4	108.6 ± 24.2	0.009*
HOMA-IR	4.8 ± 2.1	2.1 ± 0.8	<0.001*

*p < 0.05 considered statistically significant

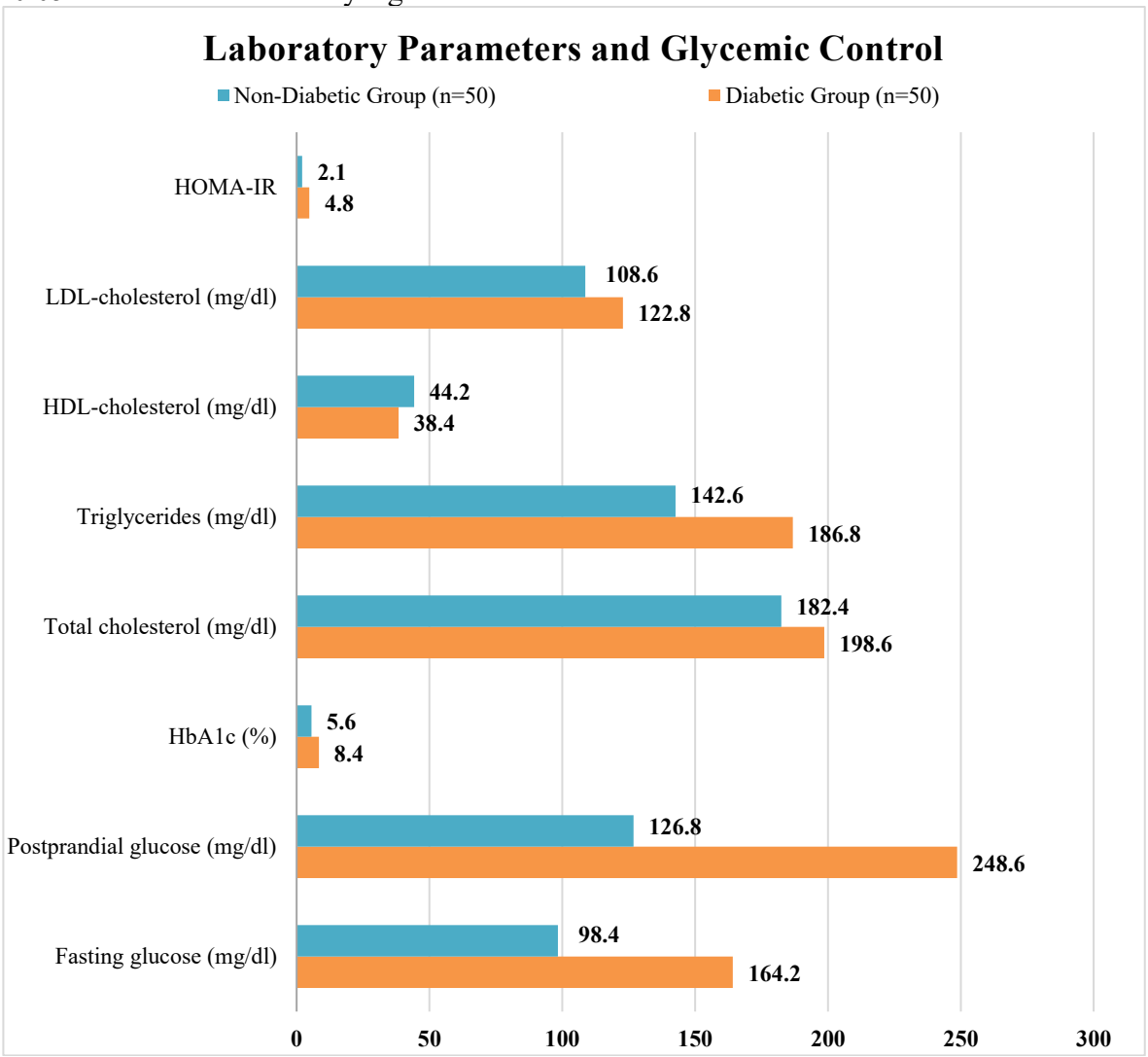

Fig: 2

Table 3: Adipokine Levels Comparison between Groups

Adipokine	Diabetic Group (n=50)	Non-Diabetic Group (n=50)	p-value	Effect Size (Cohen's d)
Adiponectin (µg/ml)	4.8 ± 2.6	9.2 ± 3.8	<0.001*	1.36
Leptin (ng/ml)	14.6 ± 8.4	8.8 ± 5.2	<0.001*	0.82
Resistin (ng/ml)	18.4 ± 6.8	12.6 ± 4.2	<0.001*	1.02
Leptin/Adiponectin ratio	3.8 ± 2.1	1.2 ± 0.8	<0.001*	1.68

*p < 0.05 considered statistically significant

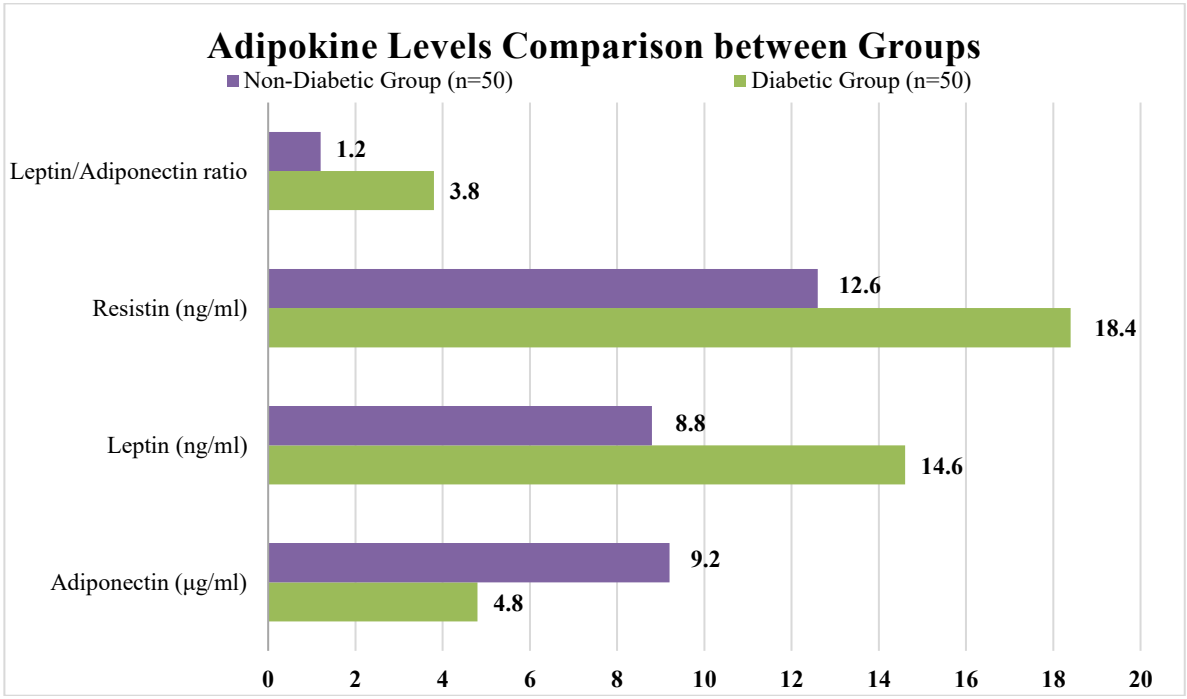

Fig: 3

Table 4: Substance Abuse Patterns in Study Population

Substance Type	Diabetic Group (n=50)	Non-Diabetic Group (n=50)	p-value
Alcohol, n (%)	38 (76.0)	36 (72.0)	0.654
Opioids, n (%)	28 (56.0)	22 (44.0)	0.231
Cannabis, n (%)	18 (36.0)	20 (40.0)	0.688
Stimulants, n (%)	8 (16.0)	12 (24.0)	0.316
Poly-substance use, n (%)	32 (64.0)	28 (56.0)	0.414
Duration of abuse (years)	16.8 ± 8.4	14.2 ± 7.6	0.122
Currently abstinent, n (%)	22 (44.0)	28 (56.0)	0.231

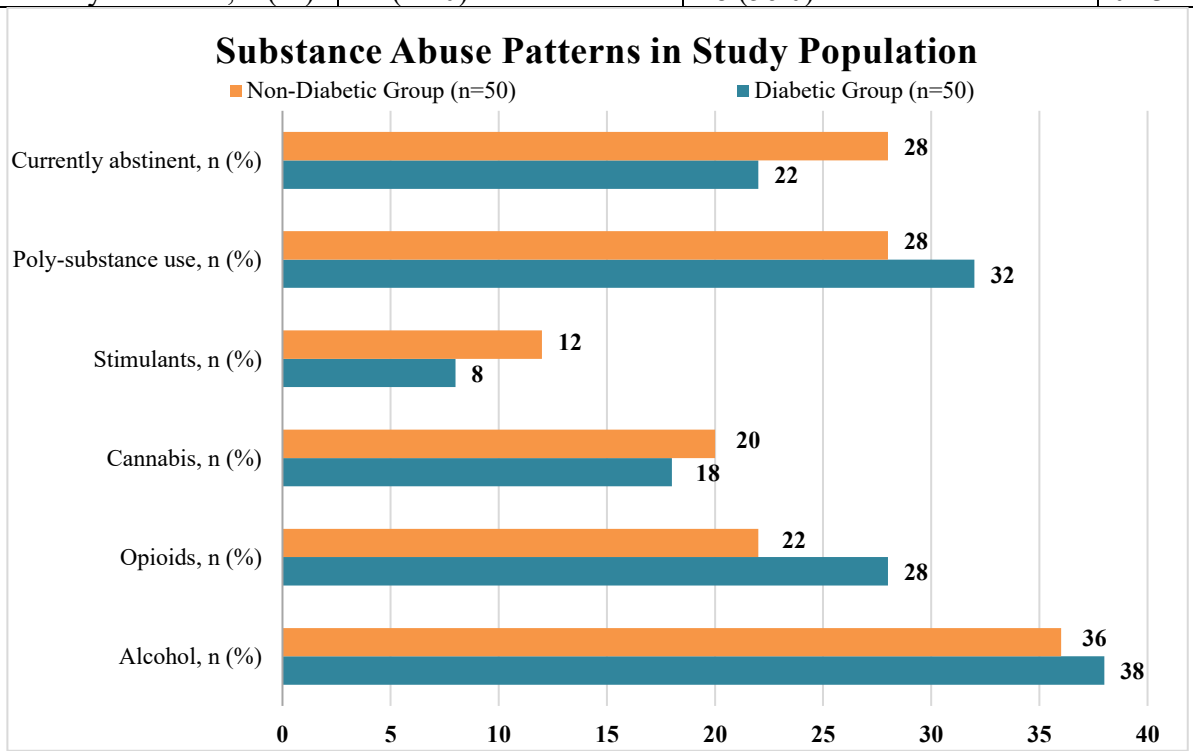

Fig: 4

Table 5: Correlation Analysis Between Adipokines and Clinical Parameters

Parameter	Adiponectin	Leptin	Resistin
BMI	-0.624**	0.518**	0.412**
Waist circumference	-0.586**	0.496**	0.384**
HbA1c	-0.678**	0.445**	0.524**
HOMA-IR	-0.592**	0.472**	0.498**
Triglycerides	-0.384**	0.368**	0.426**
HDL-cholesterol	0.442**	-0.398**	-0.324**
Duration of substance abuse	-0.286*	0.234*	0.312**
Systolic BP	-0.368**	0.284*	0.346**

*p < 0.05, **p < 0.01

Table 6: Multiple Linear Regression Analysis for Predictors of Adipokine Levels

Dependent Variable: Adiponectin (µg/ml)	**β**	**Standard Error**	**p-value**	**95% CI**
Diabetes status	-3.24	0.68	<0.001*	[-4.58, -1.90]
BMI	-0.18	0.08	0.028*	[-0.34, -0.02]
Duration of substance abuse	-0.12	0.04	0.006*	[-0.20, -0.04]
Age	-0.02	0.03	0.518	[-0.08, 0.04]
$R^2 = 0.624$, $F = 38.42$, $p < 0.001$				
Dependent Variable: Leptin (ng/ml)	**β**	**Standard Error**	**p-value**	**95% CI**
Diabetes status	4.82	1.24	<0.001*	[2.36, 7.28]
BMI	0.64	0.16	<0.001*	[0.32, 0.96]
Waist circumference	0.28	0.09	0.002*	[0.10, 0.46]
Gender (male)	-2.86	1.38	0.041*	[-5.60, -0.12]
$R^2 = 0.486$, $F = 22.64$, $p < 0.001$				
Dependent Variable: Resistin (ng/ml)	**β**	**Standard Error**	**p-value**	**95% CI**
Diabetes status	4.64	1.02	<0.001*	[2.62, 6.66]
HOMA-IR	1.24	0.38	0.002*	[0.48, 2.00]
Poly-substance use	2.18	0.96	0.026*	[0.28, 4.08]
Age	0.08	0.04	0.048*	[0.00, 0.16]
$R^2 = 0.518$, $F = 25.68$, $p < 0.001$				

*p < 0.05 considered statistically significant

Discussion

The present study revealed significant differences in demographic and clinical parameters between diabetic and non-diabetic individuals with substance abuse history. The diabetic group demonstrated higher age, BMI, waist circumference, and blood pressure compared to the non-diabetic group, consistent with established patterns of type 2 diabetes mellitus progression (Ramachandran et al., 2007). These findings align with previous Indian studies that have documented the association between central obesity and diabetes risk in Asian populations, who develop metabolic dysfunction at lower BMI thresholds compared to Western populations (Ferris et al., 2005).

The higher prevalence of male participants (83% overall) in our study reflects the documented gender disparities in substance abuse patterns in India, where male predominance is particularly pronounced in rural and semi-urban areas of Uttar Pradesh (Singh et al., 2018). This gender

distribution is consistent with national epidemiological surveys that report substantially higher rates of substance abuse among males across different regions of India (Ambekar et al., 2019).

Our study demonstrated markedly elevated glucose levels and HbA1c in the diabetic group, with mean HbA1c of 8.4%, indicating suboptimal glycemic control. This finding is particularly concerning given the additional metabolic burden imposed by substance abuse. The significantly higher HOMA-IR values in diabetic participants (4.8 vs 2.1) underscore the severe insulin resistance characterizing this population. These results are consistent with previous research by Karam et al. (2004), who reported similar patterns of poor glycemic control in diabetic individuals with substance abuse history.

The lipid profile abnormalities observed, including elevated triglycerides and reduced HDL-cholesterol in the diabetic group, reflect the complex interplay between diabetes, substance abuse, and dyslipidemia. Similar patterns have been documented in Indian populations, where metabolic syndrome components frequently cluster together, particularly in individuals with concurrent substance abuse (Lele et al., 2006).

The most striking finding of our study was the profound alteration in adipokine profiles between diabetic and non-diabetic groups. Adiponectin levels were significantly reduced in diabetic participants (4.8 ± 2.6 μg/ml vs 9.2 ± 3.8 μg/ml), representing a 48% reduction compared to non-diabetic individuals. This hypoadiponectinemia is consistent with extensive literature documenting reduced adiponectin levels in diabetes mellitus (Weyer et al., 2001; Stefan & Stumvoll, 2002). The magnitude of reduction observed in our study is comparable to that reported by Finucane et al. (2009) in their analysis of adipokine patterns in insulin-resistant individuals.

The context of substance abuse appears to exacerbate adiponectin suppression beyond that typically observed in diabetes alone. Pravdová et al. (2009) demonstrated that chronic alcohol consumption in animal models led to complex alterations in adiponectin expression and secretion. Our findings suggest that in human populations with substance abuse history, the combination of diabetes and chronic substance exposure creates a particularly severe state of hypoadiponectinemia, which may contribute to accelerated metabolic dysfunction and cardiovascular risk.

Leptin levels showed the opposite pattern, with diabetic participants demonstrating significantly elevated concentrations (14.6 ± 8.4 ng/ml vs 8.8 ± 5.2 ng/ml). This hyperleptinemia likely reflects leptin resistance, a well-documented phenomenon in obesity and diabetes (Friedman & Halaas, 1998). The correlation analysis revealed strong positive associations between leptin levels and BMI, waist circumference, and insulin resistance markers, supporting the concept of leptin as a marker of adiposity and metabolic dysfunction.

Interestingly, the leptin levels in our substance abuse population were higher than those typically reported in diabetic populations without substance abuse history. Studies by Sierksma et al. (2004) and Beulens et al. (2007) have shown that alcohol consumption can acutely affect leptin levels, and our findings suggest that chronic substance abuse may lead to sustained elevation in leptin concentrations, potentially through mechanisms involving adipose tissue inflammation and altered leptin sensitivity.

Resistin levels were significantly elevated in the diabetic group (18.4 ± 6.8 ng/ml vs 12.6 ± 4.2 ng/ml), consistent with its recognized role as a pro-inflammatory adipokine that promotes insulin resistance (Steppan et al., 2001). The strong correlations between resistin levels and markers of metabolic dysfunction, including HOMA-IR and HbA1c, support its potential utility as a biomarker for metabolic risk stratification in this population.

The elevation of resistin in our study population may reflect both the inflammatory state associated with diabetes and the additional inflammatory burden imposed by chronic substance abuse. Previous research has documented elevated inflammatory markers in individuals with alcoholic liver disease, including increased resistin levels (Błąd et al., 2013). Our findings extend these observations to a broader population of individuals with various forms of substance abuse and concurrent diabetes.

The leptin-to-adiponectin ratio emerged as a particularly discriminating marker between groups, with diabetic participants showing a 3.2-fold higher ratio compared to non-diabetic individuals (3.8 vs 1.2). This ratio has gained recognition as a sensitive indicator of metabolic syndrome and insulin resistance, potentially superior to individual adipokine measurements (Finucane et al., 2009). In the context of substance abuse, this ratio may serve as a valuable tool for risk stratification and monitoring metabolic health.

The analysis of substance abuse patterns revealed high rates of alcohol use (74% overall) and significant poly-substance use (60% overall), consistent with epidemiological data from northern India (Ray et al., 2004). While no significant differences in substance abuse patterns were observed between diabetic and non-diabetic groups, the duration of abuse showed trends toward longer exposure in the diabetic group.

The correlation analysis revealed significant associations between duration of substance abuse and adipokine levels, particularly adiponectin suppression and resistin elevation. These findings suggest a dose-response relationship between chronic substance exposure and metabolic dysfunction, supporting the concept that prolonged substance abuse contributes to progressive deterioration of metabolic health.

Multiple regression analysis identified diabetes status as the strongest predictor of all three adipokines, followed by anthropometric measures and substance abuse duration. For adiponectin, diabetes status, BMI, and duration of substance abuse emerged as significant independent predictors, explaining 62.4% of the variance. This high explanatory power suggests that these readily measurable clinical variables can effectively predict adiponectin levels in this population.

The identification of poly-substance use as an independent predictor of resistin levels is particularly noteworthy, as it suggests that the complexity of substance abuse patterns, rather than just the presence of abuse, influences inflammatory adipokine levels. This finding has important implications for clinical management and risk assessment in substance abuse populations.

Conclusion

This comparative study provides compelling evidence for significant alterations in adipokine profiles among diabetic individuals with substance abuse history compared to their non-diabetic counterparts. The findings reveal a distinctive pattern characterized by severe hypoadiponectinemia, hyperleptinemia, and elevated resistin levels in the diabetic group, with the leptin-to-adiponectin ratio emerging as a particularly sensitive discriminating marker. These adipokine alterations correlate strongly with markers of insulin resistance, glycemic control, and anthropometric measures, suggesting their potential utility as biomarkers for metabolic risk stratification. The duration and complexity of substance abuse patterns independently predict adipokine levels, indicating a dose-response relationship between chronic substance exposure and metabolic dysfunction. These findings highlight the particularly vulnerable metabolic status of individuals with concurrent diabetes and substance abuse, necessitating targeted interventions and intensive monitoring to prevent accelerated complications and optimize therapeutic outcomes in this high-risk population.

Recommendations

Healthcare providers should incorporate routine adipokine assessment, particularly the leptin-to-adiponectin ratio, in the metabolic evaluation of individuals with concurrent diabetes and substance abuse history to enable early identification of high-risk patients. Integrated treatment programs addressing both substance abuse and metabolic dysfunction should be developed, with emphasis on lifestyle interventions targeting weight reduction and improved glycemic control to potentially normalize adipokine profiles.

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