ORIGINAL RESEARCH

Assessment of Adiponectin and Leptin in Individuals with Impaired Glucose Tolerance: A Case Control Study

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ABSTRACT

Introduction: Adiponectin is known for its role in modulating adipogenesis, enhancing fatty acid oxidation, and regulating insulin secretion in diabetes mellitus (DM). On the other hand, Leptin is believed to function as a hormone with insulin antagonist properties, significantly impacting glucose metabolism. This study aimed to evaluate serum adiponectin and leptin levels in individuals with impaired fasting glucose, compared to healthy controls. **Methods:** We recruited 200 participants diagnosed with impaired glucose tolerance (IGT) and 200 healthy controls. We measured serum adiponectin and leptin levels and assessed fasting and postprandial blood glucose, insulin resistance markers, and lipid profiles. **Results:** Our analysis revealed a notable decrease in serum adiponectin levels in the IGT group compared to controls. Conversely, serum leptin levels were significantly elevated in the IGT cohort compared to healthy controls. **Conclusion:** These findings highlight the potential roles of adiponectin and leptin in influencing glucose metabolism and insulin resistance pathways. Adiponectin, particularly in the prediabetic phase, emerges as a significant biomarker, offering promise for early detection and management of type 2 diabetes mellitus (T2DM) and preventing associated complications.

Key Words: Adiponectin, Leptin, Impaired Glucose Tolerance, Diabetes

INTRODUCTION

Adipose tissue is known to secrete various adipocytokines, including resistin, adiponectin, leptin, tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6). These molecules are thought to actively participate in metabolic regulation, influencing insulin resistance and diseases related to insulin resistance [1, 2]. While studies have indicated potential connections between adipocytokines and glucose tolerance states [3-5], the exact mechanism underlying these states in humans is not yet fully understood.

Adiponectin is a protein secreted specifically by adipocytes, and it plays a crucial role in enhancing the liver and muscle response to insulin, thereby regulating insulin sensitivity in both humans and rodents [6]. Reduced levels of circulating adiponectin have been observed in patients with insulin resistance, type 2 diabetes, and prediabetic conditions such as impaired glucose tolerance (IGT) [7-9]. However, clinical studies have reported inconsistent findings regarding adiponectin levels [10-12]. Apart from its role in insulin sensitivity, adiponectin also exhibits anti-inflammatory and anti-arteriosclerotic functions when present in circulation [14, 15, 19]. These additional functions contribute to the overall metabolic and cardiovascular benefits associated with adequate levels of adiponectin in the body.

Common obesity significantly increases the risk of developing type 2 diabetes (T2D) and is often characterized by elevated levels of leptin in circulation, termed hyperleptinemia. Despite the potent appetite-suppressing effects of leptin, these heightened levels fail to trigger an adequate physiological response. This is evident from the limited effectiveness of exogenous leptin in reducing body weight in obese individuals. Consequently, the term "leptin resistance" emerged to describe the failure of exogenous leptin to curb food intake and body weight effectively. This lack of response to exogenous leptin in obese patients led to questions about whether hyperleptinemia itself could contribute to metabolic disruptions and if it is a prerequisite for developing leptin resistance. Apart from its appetite-suppressing role, leptin plays a crucial role in insulin

action within the hypothalamus, aiding central insulin in maintaining blood glucose levels. Therefore, leptin resistance in the hypothalamus is associated with disturbances in overall glucose regulation. The arcuate nucleus (ARC) within the hypothalamus holds particular importance in energy metabolism regulation, and it becomes highly susceptible to leptin resistance during diet-induced obesity (DIO) [13-16].

The primary objective of our study was to investigate the levels of adiponectin and leptin, as well as key biochemical markers related to glucose metabolism, in individuals with Impaired Glucose Tolerance (IGT).

MATERIAL AND METHODS

This case-control study was conducted at the Department of Biochemistry, Index Medical College in Indore, India. Ethical clearance was obtained from the institute's Ethics Committee, and written consent was acquired from all participants who met the inclusion criteria.

The study encompassed 200 individuals diagnosed with Impaired Glucose Tolerance (IGT) and a control group of 200 participants, resulting in a total of 400 individuals matched based on age and gender. Exclusion criteria comprised Type 1 Diabetes Mellitus, chronic hypertension, congenital anomalies, liver or renal disorders, acute infections, malignancy, psychiatric or neurological conditions impacting cognition, and ongoing insulin or oral anti-diabetic therapies.

Data acquisition entailed collecting demographic information and biochemical parameters, such as anthropometric measurements, fasting and postprandial glucose levels, markers of insulin resistance, lipid profiles, and serum concentrations of apelin and resistin. Biochemical assays were performed using an automated biochemical analyzer, while the assessment of serum resistin and apelin levels was conducted utilizing enzyme-linked immunosorbent assay (ELISA) kits.

Statistical analysis, performed using IBM SPSS version 21, encompassed descriptive statistics and the unpaired t-test, with a significance level set at $\alpha = 0.05$. These analytical methods were employed to evaluate and compare the data between the IGT group and the control group, thereby elucidating potential associations and differences in the parameters studied.

RESULTS

Table 1: Demographic and anthropometric data of cases vs controls

Parameter	Cases (n=200)	Controls (n=200)	p Value
Age; years	41.39 ± 14.09	42.67 ± 16.93	0.412
Height; cms	154.98 ± 9.2	169.16 ± 6.93	<0.05
Weight; Kgs	82.13 ± 8.82	75.2 ± 7.44	<0.05
BMI; Kg/m2	34.58 ± 5.7	26.48 ± 3.94	<0.05
Gender			
Males	90	88	-
Females	110	112	-

Table 2: Blood sugar profile parameters in cases vs controls

Parameter	Cases (n=200)	Controls (n=200)	p Value
FBS; mg/dL	119.6 ± 2.41	89.37 ± 15.11	<0.05
PPBS; mg/dL	170.35 ± 16.6	131.24 ± 21.43	<0.05
HbA1c; %	6.61 ± 1.1	4.91 ± 0.59	<0.05
S.Insulin; µIU/ml	12.24 ± 1.43	9.31 ± 1.4	<0.05

Table 3: Serum adipocytokines comparison in cases vs controls

Parameter	Cases (n=200)	Controls (n=200)	p Value
S. Adiponectin; µg/ml	3.17 ± 0.42	12.14 ± 3.2	<0.05
S. Leptin; ng/ml	23.48 ± 7.9	9.79 ± 2.94	<0.05

Table 4: Lipid profile parameters in cases vs controls

Parameter	Cases (n=200)	Controls (n=200)	p Value
TG; mg/dl	206.22 ± 96.65	155.14 ± 29.33	<0.05
LDL-c; mg/dl	134.99 ± 18.83	79.13 ± 17.7	<0.05
HDL-c; mg/dl	45.81 ± 9.65	63.8 ± 10.47	<0.05
TC; mg/dl	222.04 ± 30.14	173.97 ± 24.67	<0.05

DISCUSSION

Adipose tissue is now acknowledged as an endocrine organ crucial for insulin resistance and glucose regulation, as it releases signaling molecules termed adipocytokines. The precise role and physiological function of adipocytokines like adiponectin and resistin in human glucose metabolism are currently under investigation.

The relationship between circulating adiponectin levels and glucose tolerance remains a topic of debate. While it's well-established that adiponectin decreases in individuals with insulin resistance-related conditions like obesity and type 2 diabetes [17-19], its association with impaired glucose tolerance (IGT) is less clear. Adiponectin has been shown to enhance fat oxidation and glucose transport in muscle cells in laboratory settings [20]. Some studies have reported an inverse correlation between serum adiponectin levels and glucose tolerance, indicating reduced adiponectin levels in individuals with IGT [6, 12, 19, 20]. However, conflicting findings exist, with other studies suggesting normal adiponectin levels in individuals with IGT [10-12]. In the current study, adiponectin concentrations were notably lower in the IGT group compared to the normal glucose tolerance (NGT) group, suggesting a potential link between circulating adiponectin levels and glucose tolerance.

Human studies have provided evidence supporting the idea that hyperleptinemia can disrupt energy metabolism. For instance, hyperleptinemia is strongly linked to low-grade systemic inflammation and metabolic dysfunction in obese individuals [21]. Interestingly, when obese subjects were categorized based on their initial leptin levels and then treated with metreleptin for weight loss, those with lower baseline leptin levels experienced more significant weight loss, indicating higher sensitivity to leptin in these individuals [22]. Conversely, individuals with higher baseline leptin levels were more likely to regain lost weight [23]. Participants undergoing weight-loss interventions showed decreased leptin levels, which did not counteract weight loss; instead, it was associated with further weight reduction [24]. These findings suggest that an individual's leptin levels may correlate with their sensitivity to leptin, indicating the presence of a threshold for physiological responses to leptin. Once this threshold is surpassed, disruptions in energy homeostasis may occur, leading to ongoing weight gain. In healthy individuals with normal weight, leptin levels remain low with minor fluctuations based on nutritional status [25]. These fluctuations play a crucial role in regulating energy metabolism, but they can be overshadowed by chronic increases in leptin levels seen in hyperleptinemia.

Our study focused on investigating adiponectin and leptin levels, as well as biochemical parameters related to glucose metabolism, in individuals with impaired glucose tolerance (IGT), a precursor to diabetes. Our goal was to understand the roles of these factors in insulin resistance and the development of diabetes. We observed that serum apelin levels were notably lower in the IGT group compared to the control group, while resistin levels were significantly higher in the IGT group [26].Our findings demonstrate significant changes in glucose metabolism, insulin resistance, and the secretion of adipokines in individuals with IGT, representing an early stage of diabetes. These alterations in cytokine expression could serve as valuable indicators for the early detection and prevention of complications in individuals at risk of progressing to type 2 diabetes mellitus (T2DM).

CONCLUSION

This study emphasize the critical roles of adiponectin and leptin in regulating glucose metabolism and insulin resistance mechanisms. In the prediabetic stage, adiponectin emerges as a crucial biomarker. Its levels are inversely related to insulin resistance and body fat mass, making it a promising candidate for early detection and management of T2DM. Further, adiponectin's anti-inflammatory and vasoprotective properties contribute to its therapeutic potential, suggesting that interventions aimed at increasing adiponectin levels or enhancing its signaling pathways could be effective strategies in preventing and managing diabetes and its associated complications.

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