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Evaluation of Apelin and Resistin in Individuals with Impaired Glucose Tolerance: A Case Control Study

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ABSTRACT

Introduction: Apelin is known to modulate adipogenesis, enhance fatty acid oxidation, and regulate insulin secretion in diabetes mellitus (DM). Furthermore, apelin-activated pathways are implicated in the development of DM-related complications. On the other hand, resistin is believed to function as a hormone with insulin antagonist properties, impacting glucose metabolism significantly.The primary aim of this investigation was to evaluate the levels of serum apelin and resistin among individuals with impaired fasting glucose, juxtaposed against a cohort of healthy controls.

Methods: In this study, we recruited a total of 200 participants diagnosed with impaired glucose tolerance (IGT), and 200 healthy controls. Comprehensive assessments encompassed the measurement of serum apelin and resistin levels, alongside evaluations of fasting and postprandial blood glucose, markers indicative of insulin resistance, and lipid profiles.

Results: Our analyses uncovered a noteworthy decrease in serum apelin levels within the IGT group when compared to the control group. Conversely, serum resistin levels demonstrated a marked elevation in the IGT cohort compared to their healthy counterparts.

Conclusion: These findings underscore the potential roles of apelin and resistin in influencing glucose metabolism and insulin resistance pathways. Particularly in the prediabetic phase, apelin emerges as a significant biomarker, holding promise for the early detection and management of type 2 diabetes mellitus (T2DM), thus aiding in the prevention of associated complications.

Key Words: Apelin, Resistin, Impaired Glucose Tolerance, Diabetes.

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INTRODUCTION

Diabetes mellitus (DM) represents a chronic metabolic disorder associated with both acute and chronic complications, imposing significant morbidity, mortality, and societal costs. Insulin resistance, a key aspect of DM, entails reduced biological response to normal insulin concentrations, leading to diminished stimulation of glucose use [1-3]. Genetic factors, including various gene defects, are pivotal in determining insulin sensitivity [4, 5].

Initial studies on resistin revealed elevated expression in obese animal models, with circulating resistin levels correlating with insulin resistance in rodents. Resistin is proposed to function as an insulin antagonist, affecting glucose metabolism [6, 7]. Elevated resistin levels are linked to an increased risk of developing type 2 diabetes (T2DM), especially in individuals with central obesity [8, 9]. Resistin plays a regulatory role in adipocyte metabolism in both mice and humans [10]. Thiazolidinedione (TZD), an antidiabetic medication targeting insulin resistance in T2DM treatment, is reported to decrease insulin resistance by inhibiting resistin production induced by adipocytes. This highlights the close relationship between increased circulating resistin, insulin resistance, and hyperglycemia [11].

Apelin, another significant factor, regulates adipogenesis, fatty acid oxidation, and insulin secretion in DM. Apelin's actions improve insulin sensitivity, stimulate glucose utilization in various tissues relevant to DM, and enhance brown adipogenesis. Furthermore, apelin mitigates DM-induced kidney and cardiac hypertrophy, as well as retinal angiogenesis in diabetic retinopathy. Plasma apelin levels positively correlate with body mass index (BMI), and although apelin inhibits insulin secretion in mice, its precise inhibitory mechanism remains unclear [12,13]. Human studies, such as that by Gourdy et al. [14], demonstrate that high-dose apelin administration increases insulin sensitivity and the apelin/APJ pathway in patients with T2DM, suggesting it as a potential therapeutic target.

Our study aims to explore apelin and resistin levels, alongside key biochemical markers reflecting glucose metabolism, in impaired glucose tolerance (IGT).

MATERIAL AND METHODS

This case-control study was conducted at the department of Biochemistry, Index Medical College, Indore, India. Ethical approval was obtained from the Ethics Committee of the institute, and written consent was obtained from all participants meeting the inclusion criteria.

The study included 200 individuals with IGT, and a control group of 200, totaling 400 participants matched by age and gender. Exclusion criteria encompassed type 1 diabetes mellitus, chronic hypertension, congenital anomalies, liver or renal diseases, acute infections, malignancy,

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psychiatric or neurological disorders affecting cognition, and ongoing insulin or oral anti-diabetic treatment.

Data collection involved demographic and biochemical parameters, including anthropometric measurements, fasting and postprandial glucose levels, insulin resistance markers, lipid profiles, and serum apelin and resistin levels. Biochemical investigations were conducted using an automatic biochemical analyzer, while serum resistin and apelin levels were measured via enzyme-linked immunosorbent assay (ELISA) kits.

Statistical analysis using IBM SPSS 21 included descriptive statistics, and unpaired t test with a significance level set at $\alpha = 0.05$.

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. Resistin; ng/ml	9.19 ± 1.29	5.44 ± 2.52	<0.05
S. Apelin; ng/ml	0.65 ± 0.1	1.04 ± 0.41	<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

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DISCUSSION

The diagnosis and early intervention during pre-diabetes stages are crucial for preventing diabetes and its associated complications. This study was designed to assess a group of adipokines expressed in adipose tissues of patients with IGT, aiming to contribute to the diagnosis and management of pre-diabetes and early diabetes stages.

Steppan et al. [11] conducted a study in mice where they observed that the secretion of resistin from adipocytes increased with rosiglitazone, an oral antidiabetic medication, as well as with dietary/genetic obesity. They found that diet-induced obesity in mice led to elevated resistin levels and insulin activity, resulting in improved blood sugar levels. Furthermore, they noted that administering recombinant resistin to normal mice led to impaired glucose tolerance and insulin activity. Interestingly, insulin-sensitive glucose uptake by adipocytes decreased with resistin application but increased when resistin was inactivated. Based on these findings, researchers suggested that resistin acts as an insulin antagonist and may contribute to the development of diabetes in obesity.

The statistically significant increase in serum resistin levels observed in the IGT group indicates a rise in these peptide hormones due to increased hyperglycemia. This finding supports the theory that adipokines expressed from adipose tissue, including resistin, are a consequence rather than a cause of diabetes. The elevation of plasma resistin levels in the progression towards T2DM likely contributes to the development of complications in these patients, as resistin can decrease glucose tolerance and impair insulin's effect on cells through similar cellular pathways.

Boucher et al. [15] noted that insulin stimulates the synthesis and release of apelin from adipose tissue. In obese individuals with increased body fat and hyperinsulinemia, there is a concurrent rise in plasma apelin levels and mRNA expression of apelin in adipocytes, indicating that obesity and insulin induce apelin synthesis. However, despite this association, apelin has been shown to increase glucose utilization while inhibiting insulin secretion [16, 17]. Yue et al. [18] further demonstrated that mice with total apelin deficiency developed insulin resistance, which improved upon administering apelin to these mice, highlighting the role of apelin in modulating insulin sensitivity.

In our study, we observed lower serum apelin levels in individuals with impaired glucose tolerance (IGT) compared to the control group. This finding supports the notion that apelin plays a role in increasing insulin sensitivity. Similarly, Zhang et al. [19] also reported low plasma apelin levels in newly diagnosed type 2 diabetes mellitus (T2DM) patients, showing a negative correlation between apelin levels and markers such as C-reactive protein (CRP), fasting blood glucose (FBG), HbA1c, and the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), while positively correlating with insulin sensitivity. They concluded that apelin's effect on glucose metabolism is likely indirect, mediated through adipocyte stimulation.

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Our study aimed to investigate apelin and resistin levels, alongside biochemical parameters reflecting glucose metabolism in individuals with IGT, a pre-diabetic stage. By examining these parameters and their interplay, we aimed to understand their roles in insulin resistance and diabetes development. We found that while serum apelin levels were significantly lower in the IGT group compared to the control group, resistin levels were significantly higher in the IGT group [20].

In summary, changes in glucose metabolism, insulin resistance, and the secretion of adipokines such as apelin and resistin from adipose tissue show significant alterations in individuals with IGT, which is a pre-diabetic stage. These changes in cytokine expression could serve as useful markers for early diagnosis and prevention of complications in individuals at risk of progressing to T2DM.

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CONCLUSION

These findings underscore the potential roles of apelin and resistin in influencing glucose metabolism and insulin resistance pathways. Particularly in the prediabetic phase, apelin emerges as a significant biomarker, holding promise for the early detection and management of T2DM, thus aiding in the prevention of associated complications.

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