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Type 2 Diabetes Mellitus and Role of Adiponectin in Insulin Resistance

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Abstract

Background: Adiponectin an adipocyte - derived hormone is specifically and abundantly expressed in adipose tissue and directly sensitizes the body to insulin adipocytes, whose reduction plays a central role in obesity-related diseases, including type 2 diabetes mellitus (type 2 DM), insulin resistance and cardiovascular disease. The epidemic increase in type 2 DM can be prevented if markers of risk can be identified and it is a challenging task.

Aim of Study: To assess the role of adiponectin in insulin resistance among patients with type 2 DM.

Patients and Methods: 30 type 2 diabetic patients, 20 controls were studied. Fasting serum sample were used to measure Adiponectin, insulin, plasma glucose and lipid parameters (Cholesterol, high density lipoprotein HDL and low density lipoprotein LDL). Collecting data including height, weight and body mass index (BMI) were measured using a standard technique.

Results: Wilcoxon signed rank test shows the significant variation between adiponectin and other analyzes. The reduction of mean adiponectin value observed in patient's sample compared to control sample. Significant correlation between fasting blood sugar (FBS) and adiponectin. Significant correlation between adiponectin and insulin level observed. In lipid parameters, significant positive correlation between adiponectin and high density lipoprotein (HDL) observed.

Conclusion: Adiponectin plays a role in insulin sensitivity and might be as a potensial biomarker in type 2DM.

Key Words: *Type 2 DM – Adiponectin – Insulin resistant.*

Introduction

THE insulin resistance is a major component of metabolic disorders which concern a substantial fraction of the general population and is particularly prevalent in obese subjects **[1,2]**. These adipokines are key regulators of glucose metabolism, fatty acid intake, and inflammation **[3,4]**. The role of insulin resistance and its sequelae is gaining prominence. Understanding the role of insulin across a wide range of physiological processes and the influences on its synthesis and secretion, alongside its actions from the molecular to the whole body level, has significant implications for much chronic disease seen in populations **[5]**. β cell dysfunction is one of the major causes for insulin resistance in type 2 diabetes, also in some cases longstanding stress causes the elevation of cortisol, higher level of this hormone damages the β cell by the way decreases insulin production and increases the insulin resistant **[6]**.

Prolonged exposure of high level of fatty acids accumulates in the muscle and liver, causes the inhibition of glucose to enter in both tissues, in response more amount of insulin produced hyperinsulinemia to unlock the cell for utilization of glucose **[7]**. Frequent and longstanding of this type of mechanism end in apoptosis of islet cell also no more overproducing insulin to meet the requirement of muscle and liver which is also causative for insulin resistant **[8]**. More researches on central obesity reports, visceral lipid deposits are increased and the abdominal subcutaneous adipose tissue depot is decreased, in type 2 associated insulin resistance in Asian Indians, **[9]** and emphasised the involvement of adiponectin, one of the adipokines released from adipose tissue that regulates the metabolism of lipids and glucose also increases the insulin sensitivity **[10]**.

Early finding of insulin resistant through a biomarker will help to prevent from micro vascular and macro vascular complications **[11]**.

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Patients and Methods

Between September 2021 and February 2022, total of 50 serum samples were collected from Patient and Control study. The study has been conducted at Al-Gumhuria Modern Hospital - Aden Governorate - Yemen. Age range from 40 to 60 years including both genders categorized type 2 diabetes (Patients samples) and non-diabetes (Control samples). Written informed consent was obtained from each participant before commencement of the study.

The sample included with 20 samples normal healthy individuals, and the 30 samples of known Type 2 diabetes. Before blood collection individuals age, sex, height, weight noted. BMI was calculated using height and weight measurement.10-12 hours overnight fasting instructed for both the subjects. Overnight fasting Venous blood drawn from individuals, 2ml blood with EDTA anticoagulated tubes for fasting blood glucose estimation and the remaining 6ml blood was transferred in plain tubes (without anticoagulant) for estimation of serum fasting insulin, serum adiponectin, HDL and LDL. Serum insulin measured by chemiluminescence technique, Serum HDL measured by Peroxidase end point method and serum adiponectin measured by using enzyme immunoassay.

Statistical analysis:

SPSS (version 27) statistical software was used for analyses.

Data were also categorized according to patients and control fasting serum insulin, serum HDL, LDL, BMI, fasting plasma glucose and were evaluated using a Pearson's correlation coefficient analysis. Comparisons of parameters in patients and control were performed with a significance level of $p<0.05$.

A non-parametric statistical test (Wilcoxon signed-rank test) used to give a data point of the two population samples mean with the standard score (z-score).

Results

A total of 50 consentin population were included in the study. These comprised of 30 patients with type 2 DM and 20 were healthy as control group. All subjects were men, with a mean ± SD age of 46±7.8 years.

Table (1): Comparison of parameters in patient and control samples.

Parameter	Patients Mean	Control Mean	*p*-value
Age (Years)	46.55±5.8	47.9±5.8	0.428
BMI (Kg/m^2)	22.62±0.88	20.75±3.6	0.786
FBS (Mg/dl)	192.35±12.5	103.06±22.6	<0.0001**
Fasting insulin (µIU/Ml)	11.72±3.2	9.86±9.6	0.026*
Adiponectin (µg/mL)	11.12±2.2	25.93±2.2	0.8
Triglyceride (Mg/dl)	110.07±8.64	115.20±12.75	0.773
Total cholesterol (Mg/dl)	146.99±3.87	143.96±5.75	0.518
LDL-cholesterol (Mg/dl)	93.9±38.02	88.3±28.03	0.082
HDL-cholesterol (Mg/dl)	41.3±13.6	55.8±6.9	0.065
Ratio (HDL/LDL)	0.566±1.72	0.57±0.03	0.630

*Significant ($p<0.05$). **Highly significant ($p<0.0001$).

Significant increase of insulin, and highly significant increase in fasting blood glucose in diabetic patient sample mean in compared with control samples mean. Low mean value of adiponectin and HDL in patient's sample compared with control sample was observed.

Table (2): Correlation of adiponectin with the other parameters in studied samples (n=50).

Parameters	Adiponectin	
	r-value	*p*-value
BMI	–0.111	0.326
FBS	0.035	0.376
Fasting insulin	0.100	0.755
Total cholesterol	0.012	0.659
Triglycerides	–0.337	0.002**
HDL-cholesterol	0.275	0.05*
LDL-cholesterol	0.023	0.840
Ratio (HDL/LDL)	0.171	0.079

Adiponectin correlated positively with HDL-cholesterol (0.275), having a significant *p*-value of 0.05* Triglycerides showed negative correlation and highly significant *p*-value 0.002** with adiponectin. No correlation was observed between adiponectin and the other parameter.

Table (3): Average value comparison of the two related samples.

Test Rank	Adipo-FBS	Adipo-Insulin	Adipo-BMI	Adipo-HDL	Adipo-LDL
Z score	1.2893	1.1842	1.2716	1.2811	1.2801
Asymp. Sig. (2-tailed)	0	0	0	0	0
Signed Rank	9.5	6-	1	4-	4

Wilcoxon signed rank test, Z-score (≥) 1.2816 statistically significant significant difference between the decreasing level of adiponectin with increasing level of fasting blood sugar.

Discussion

Adiponectin is abundant in the humans circulation with plasma levels in the microgram per ml range, thus accounting for approximately 0.01% of total plasma protein. In contrast to all other adipocytokines known to date, plasma adiponectin concentrations were found to be decreased, not increased, in individuals with obesity, type 2 diabetes, and cardiovascular disease, conditions commonly associated with insulin resistance and hyperinsulinemia **[12]**.

Asian and Americans are more likely than any other to have insulin resistance because of their race or ethnicity **[13]** and in South Indians insulin resistant observed due to central obesity **[14]**. In this study higher fasting blood sugar, fasting insulin are some of the causes for insulin resistance. Adiponectin is a protein encoded by ADIPOQ gene, secreted from adipose tissue, involves in glucose and lipid level regulation **[15]**. In the present study, the adiponectin in diabetic patients had a lower mean value than control samples, and the patient's adiponectin positively associated with HDL, both of these observations same like previous studies by Karamifar et al., 2013 **[16]**. Adiponectin level can be linked to whole-body insulin sensitivity, and hypoadiponectinemia can cause endothelial dysfunction by decreasing insulin sensitivity **[17]**.

In our study, Comparing patients sample fasting blood sugar mean value with control sample mean value and patient sample fasting insulin mean value with control sample mean value shows higher and statistically significant. These observations seen same as previous studies done by Debbie et al., 2005 and Semple et al., 2007 **[18,19]**.

Our study revealed a non-significant but negative correlations of adiponectin with BMI. Indian researchers, Vikram et al., **[20]** who found that adiponectin levels correlate (inversely) strongly with BMI parameter in unlike our study were does not show a strong correlation. Possible explanation for such (negative but not statistically significant) findings in our study could be that, our participants included in this study were non-obese.

A strong negative correlation was found between adiponectin and triglyceride with statistically significant *p*-value of 0.002. We found significant positive correlation between adiponectin and HDL, *p*-value 0.05. Our study consistent with the findings Yamamota **[21]** and Hotta **[22]** however, the other parameters did not show any statistically significant correlation with Adiponectin.

In present study, Wilxon signed Rank test revealed a significance difference between the two sets of parameters analysed, adiponectin parameter and the overall other parameter, were showed there is significant difference between the decreasing level of adiponectin with increasing level of fasting blood sugar level, this agree with Böttner et al., **[23]** and disagree with Yanai and Yoshida 2019, **[24]** were they found, no difference association between plasma adiponectin levels and fasting blood sugar. Adiponectin levels are associated with incident diabetes and glycemic control and could be useful adjuncts for screening for insulin resistance and T2DM. The significant associations of adiponectin levels with clinical and cardiometabolic parameters reveal its potential as a biomarker in assessment of prediabetic state and T2DM screening **[25]**.

Conclusion:

From our study we can establish significant positive association between adiponectin and insulin resistance and could be useful adjuncts for screening insulin resistance and T2DM. Serum adiponectin level decreases with insulin resistance, also decreases in type 2 associated complications. These observations were well correlated and adiponectin can be used as a biomarker in Type 2 associated insulin resistant and its complication.

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داء السكرى من النوع الثانى ودور الأديبونكتين فى مقاومة الأنسولين

المقدمة : الأديبونكتين هرمون مشتق من الخلايا الشحمية بشكل خاص وفير فى الأنسجة الدهنية ويقوم بتوعية الجسم مباشرة بخلايا الأنسولين الدهنية، التى يلعب الحد منها دوراً رئيسياً فى الأمراض المرتبطة بالسمنة، بما فى ذلك داء السكرى من النوع الثانى مقاومة الأنسولين والقلب والأوعية الدموية. يمكن منع الزيادة الوبائية فى داء السكرى من النوع الثانى إذا أمكن تحديد علامات الخطر وهى مهمة صعبة.

هدف الدراسة : تقييم دور الأديبونيكتين فى مقاومة الأنسولين بين مرضى داء السكرى من النوع الثانى.

طرق البحث : تمت دراسة ٣٠ مريض السكرى من النوع الثانى و ٢٠ عنصر مجموعة التحكم. تم استخدام عينة مصل الصيام لقياس متغيرات الأديبوتكتين والأنسولين وجلوكوز البلازما والدهون الكوليسترول، البروتين الدهنى عالى الكثافة والبروتين الدهنى منخفض الكثافة. تم جمع البيانات بما فى ذلك الطول والوزن ومؤشر كتلة الجسم تم قياسها باستخدام تقنية قياسية.

النتائج : أظهر اختبار الرتبة الموقع من قبل ويلكوكسون التباين المعنوى بين الأديبونيكتين والتحاليل الأخرى، حيث لوحظ انخفاض متوسط قيمة الأديبونكتين فى عينة المريض مقارنة بعينة مجموعة التحكم ارتباط كبير بين سكر الدم الصائم والأديبونكتين. لوحظ وجود ارتباط كبير بين مستوى الأديبونكتين، الأنسولين. فى معاملات الدهن، لوحظ وجود ارتباط إيجابى معنوى بين الأديبونكتين والبروتين الدهنى عالى الكثافة.

الخلاصة : يلعب الأديبونكتين دوراً فى حساسية الأنسو لين وقد يكون بمثابة علامة حيوية محتملة فى النوع الثانى من داء السكرى.