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Association between Adiponectin and Insulin Resistance among Sudanese Males with Type 2 Diabetes Mellitus

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Abstract

Background: Adiponectin is associated with improved systemic insulin sensitivity and profound positive effects in adipose tissue, such as increased mitochondrial density in adipocytes, reducing adipocyte size, and effective esterification of free fatty acids on lipid storage The factor performs forward transcriptional regulation. Diabetes and its complications are considered to be one of the main causes of morbidity and mortality worldwide. **Aims and objectives:** The aim of this study was to correlate serum levels of adiponectin with insulin resistance in Sudanese males' type 2 diabetes mellitus. **Design and Methods:** A case-control community-based study carried out among 126 patients with T2DM as cases group (mean ages 45.2±5.4 years); and 126 normal healthy individuals as controls group (mean ages 44.7±5.4 years as) in Aldaraga Diabetic Center, Wad Medani, Gezira State, Sudan. About Five mL of fasting venous blood was obtained from all participants. HbA_{1c}, FPG, FPI, serum Adiponectin, and (HOMA)-IR were analyzed. SPSS (v 20.0) was used for data analysis. **Results:** The mean of serum adiponectin in the cases group (3.03±0.90µg/ml) was lower than the control group (6.02±4.24µg/ml) giving highly significant differences -between them (P=value ≤ 0.000). HbA1c and Homeostasis Model Assessment of Insulin Resistance index (HOMA-IR) differed significantly between the two groups (P-value ≤ 0.000). Serum adiponectin concentrations correlated significantly negative with HOMA IR (r = -0.149, P-value = 0.002). **Conclusion:** We concluded that low plasma adiponectin level was predictive of future development of Insulin resistance in Sudanese males.

Keywords: Adiponectin, Insulin resistance, Diabetes Mellitus, HOMA-IR, Sudanese males.

INTRODUCTION

Adipose tissue dose not simply store fat, energy storage, and insulation but is also an important endocrine organ that secretes bioactive proteins, into the circulation, such as tumor necrosis factor (TNF-α) and adiponectin [1], although it can also be secreted by epicardial fat, hepatocytes and skeletal muscle [2]. Adiponectin regulates the metabolism of lipids with anti-atherogenic and insulin-sensitizing activities; studies have shown an inverse relationship between adiponectin and metabolic syndrome [3]. Insulin resistance is a major feature in the etiology of obesity and type 2 diabetes [2]. Adiponectin is a regulator of glucose and energy homeostasis [4]. Homeostasis is the embodiment of integrated metabolic reactions and a large network of signaling pathways designed to stabilize life and function [5]. Insulin is an integral part of this regulatory network and affects all of its parts. Insulin resistance it was associated with other risk factors for the development of type 2 diabetes, obesity, dyslipidemia, hypertension, and hypercoagulopathy,

grouped under the term hyperinsulinemic/insulin resistance syndrome (X) or currently, the metabolic syndrome [6]. Adiponectin has been shown to increase insulin sensitivity and decrease plasma glucose by increasing tissue fat oxidation, adiponectin levels tend to decrease as a person ages and body mass index increase [7]. Obesity and hyperinsulinemia are suggested as the potential mechanisms for the suppression of adiponectin levels in the body and ethnicity may play a role in adiponectin regulation among different subjects [8]. Diabetes is a chronic disease that requires ongoing medical care and education to prevent acute complications and reduce the risk of long-term complications [9]. Patients with hyperglycemia should receive treatment and care by a team of health professionals coordinated by a doctor, including nurses, nutritionists, and social workers [10]. Diabetes was previously considered a rare disease in Sudan [9]. Diabetes mellitus is a chronic, lifelong disease resulting from a defect in insulin secretion, insulin resistance, or both. Insulin resistance occurs when cells in the body (liver, skeletal muscle, and adipose/fat tissue) become less sensitive and eventually resistant to insulin, Glucose can no longer be absorbed by the cells but remains in the blood, triggering the need for more and more insulin (hyperinsulinemia) to be produced in an attempt to process the glucose [11].

MATERIAL AND METHODS

Ethical approval

Ethical approval for the study was obtained from the Ethics and Research Committee, Faculty of Medicine, University of Gezira and Ministry of Health, Gezira State. The study objectives and procedure were explained to participants, and verbal consent was obtained from each participant.

Study design and area

This study was a case-control community-based study carried out at Aldaraga Center for Diabetes Care at Wad Medani, Gezira State, Central Sudan (located about 186.9 Km Southeast of Khartoum on the west bank of the Blue Nile River, It is the Capital of Gezira State).

Study sample

A total of 252 adult male participants (126 patients with T2DM as cases and 126 non-diabetic healthy subjects as control) with age range (40 – 65 years old). Both the non-diabetic control group and the diabetic group were selected to have matching BMI and a similar distribution of age that live in the same area. Data were collected by using a detailed and structure questionnaire, included close-ended questions. The duration of the study was from September 2019 – April 2020.

Inclusion Criteria

All T2DM with oral hypoglycemic agents, non-ketosis, and duration of diabetes >1 year, were in good general health and had normal kidney and liver function.

Exclusion Criteria

Who disagree to participate, if they had active cardiac, hepatic, or renal disease or if they had long-term complications from diabetes, diabetic subjects treated with insulin were not included in this study.

Sample collection

About Five mL of fasting venous blood was obtained from all participants. 1ml of blood was put in EDTA container for HbA_{1c} measurement; 1ml was put in fluoride oxalate container for measurement of plasma glucose, and 3 ml were put in lithium heparin container, then plasma was separated after centrifugation at 3000g for 10 minutes and used for biochemical measurements (lipid profiles and adiponectin concentration) using standard laboratory methods. The collected serum for adiponectin analysis was separated within one hr. of collection and was stored at -80°C until the measurement of total adiponectin concentration, which was within a month.

Sample analysis

Plasma samples were analyzed for different biochemical parameters, using A15, Biochemistry Calibrator (Bio-Systems code. 18011), and Serum adiponectin concentration was measured by using enzyme-linked immunoassay kits (ELISA Kit).

Software

A15 - Y15 service manual English, TESE00005-11-ING. May - 2010. Biosystems, S.A. Costa Brava, 30, 08030 Barcelona-Spain http://www.biosystems-sa.com

Statistical analysis

The data were statistically analyzed using IBM SPSS, Version 25 statistical program (SPSS Inc, Chicago, IL, USA) was used for descriptive and analytical statistics, Independent Sample T. test, and Pearson correlations to analyzed the associations' differences and correlations between the study groups. The significance was considered when the P-value is less than 0.05 ($P < 0.05$).

RESULTS

Comparison of means of anthropometric measurements and biochemical parameters between the study groups:

Table 1 showed Waist, HbA1c, FBG, fasting plasma insulin, and HOMA-I.R were significantly higher in diabetics compared to non-diabetics (P-value < 0.05) while serum adiponectin was significantly lower in diabetics compared to non-diabetics (P-value = 0.001).

Table 1: Comparison of anthropometric measurements and biochemical parameters between the study groups:

Anthropometric and Biochemical parameters	T2DM (n=126)	Control (n=126)	*P value*
	Mean ± SD		
Age (years)	45.2 ± 5.4	44.7 ± 5.4	0.070
BMI (kg/m^2)	26.03 ± 0.98	24.54 ± 2.55	0.287
Waist (cm)	104.14 ± 1.10	82.15 ± 1.67	0.002*
Serum Adiponectin (µg/ml)	3.03 ± 0.90	6.02 ± 4.24	0.001*
Glycated hemoglobin HbA_{1c}%	9.27 ± 1.51	5.03 ± 0.90	0.000*
Fasting blood glucose (mmol/l)	8.26 ± 1.22	5.62 ± 0.93	0.001*
Fasting plasma insulin (µIU/mL)	9.23 ± 0.98	6.00 ± 0.82	0.000*
HOMA-I.R	3.39 ± 0.64	1.49 ± 0.29	0.000*

Data were presented as means ± SD and t-test used for comparison. (HOMA-I.R) Homeostasis model assessment of insulin resistance. * P value ≤ 0.05

Comparison of means of Adiponectin (µg/ml) levels in T2DM patients according to the abdominal obesity prevalence (n=126)

The results in table 2 showed that diabetic males with abdominal obesity are 27% Adiponectin (3.11µg/ml), whereas 73% without abdominal obesity, Adiponectin (1.81 µg/ml), this result statistically significant (P-value ≤ 0.05).

Table 2: Comparison of means of Adiponectin (µg/ml) levels ± SD in T2DM patients according to the abdominal obesity prevalence (n=126)

Variable	T2DM with abdominal obesity [a]	T2DM without abdominal obesity [a]	*P value*
Number and (%)	34 (27%)	92 (73%)	**0.004***
Adiponectin[b] (µg/ml)	3.11± 0.88	1.8 ± 0.94	

[a] Abdominal obesity was defined as WC ≥ 88 cm in male. [b] Data were presented as means ± SD and t-test used for comparison. * P value ≤ 0.05

Correlation of adiponectin (µg/ml) levels in T2DM patients

Table 3 illustrates that serum levels of adiponectin correlated negatively with WC, BMI, HOMA-IR and LDL (P-value < 0.05), and Pearson correlation (r values) were weak and positively correlated with HDL (r = 0.59, P-value = 0.001).

Table 3: Correlation of adiponectin (µg/ml) levels in T2DM patients (n=126)

Risk factors	r. value*	*P value* **
WC (cm)	-0.191	0.001
BMI (Kg/m^2)	-0.001	0.037
Insulin Resistance index (HOMA-I.R)	-0.015	0.002
High density lipoprotein	0.59	0.001
Low density lipoprotein	-0.101	0.001

*Pearson coefficient used for correlation. **P value ≤ 0.05

DISCUSSION

In the current study, we analyzed data to find the associations between different parameters in T2DM cases and control groups, after adjusting for age, gender and BMI. There were highly significant differences (P-value = 0.001) in comparison of means serum adiponectin among diabetics (3.03 ± 0.90 µg/ml) and non-diabetics (6.02 ± 4.24 µg/ml), but the difference no significant difference in the BMI distribution between the two study groups (P-value = 0.287). In T2DM there was a significant increase in WC mean and marginally decreased in control subjects (P-value = 0.002). This finding is in agreement with that of Bogan and Lodish's study, [12]. There were significant differences in HbA_{1c} differed significantly between the T2DM and control groups (P-value = 0.000), the T2DM group had a higher mean of (9.27 ± 1.51%). Similar reports have been published by Cnop *et al.* [13] and Valsamakis *et al.* [14] in 2003. Fasting plasma insulin and FPG differed significantly between the T2DM and control groups (P-value = 0.000 and 0.000 respectively). Homeostasis Model Assessment of Insulin Resistance index (HOMA-IR) was calculated by applying the following formula: (fasting serum insulin (µU/ml) × fasting plasma glucose (mmol/L)/22.5); the diabetic group had a higher mean of HOMA-IR (3.39 ± 0.64%), whereas the control group had a mean level of (1.49 ± 0.29%) giving the highly significant difference between the two groups (P-value = 0.000). Adiponectin concentrations significantly negative correlated with HOMA IR (r = -0.149, P-value = 0.002). This finding consistent with the study done by Yadav *et al*. [15]. Adiponectin levels are decreased in patients with T2DM, in the same way, high levels are predicted to reduce the risk for T2DM [16]. The effect of reduced plasma concentration of Adiponectin predisposes healthy individuals to the later development of insulin resistance [17].

Diabetic males with abdominal obesity are 27% (Adiponectin = 3.11 µg/ml), whereas 73% without abdominal obesity (Adiponectin = 1.81 µg/ml). This result statistically significant (P-value ≤ 0.05). Low levels of adiponectin are closely related to the development of insulin resistance. A negative correlation was also reported between adiponectin levels and WC and fasting serum insulin. Similar results were found in Hypoadiponectinemia in obesity and type 2 diabetes studies by Yamauchi *et al*. [7].

The serum levels of adiponectin correlated weakly negative with WC, BMI, HOMA-IR- and LDL (P value ≤ 0.05), and positively with HDL (r = 0.59, P-value < 0.001). Adiponectin concentration is negatively correlated with HOMA-IR, positively correlated with HDL cholesterol, and has nothing to do with age and BMI. Daimon also found a negative correlation between HOMA-IR (independent of BMI) and adiponectin (Daimon, 2003). These results indicated hyperglycemia in T2DM and decrease of FPG and HOMA-IR in control group, these result agree by Carling [18].

CONCLUSION

In conclusion, the modern lifestyle, high-fat, diet and lack of exercise have been shown to trigger the development of central obesity with hypoadiponectinemia, hyperlipidemia, insulin resistance, and type 2 diabetes. Now lifestyle changes, including weight loss and exercise, maybe a more effective strategy to improve health and limit insulin resistance.

Conflict of Interest Statement

The authors declare that they have no competing interests.

Author Contributions

All authors contributed to conception of research, the data analysis and manuscript writing. All authors have approved the final manuscript.

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