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Relationship between Serum Leptin and Adiponectin Levels in Obese Nigerians with Type 2 Diabetes Subjects

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Abstract

Background: Obesity is rising globally, independent of ethnicity, race and age, and is associated with increased risk of cardiovascular mortality and morbidity especially in persons living with diabetes. The effect of adipokines such as leptin, resistin and adiponectin which are secreted by adipose tissue factors has been linked to the increased risk of the cardiovascular mortality and morbidity. **Aim:** This study aims to assess the levels of serum leptin and serum adiponectin in obese type 2 diabetes subjects, and their relationship with cardio-metabolic component (using lipid profile). **Method:** This is a cross-sectional comparative hospital-based study in which one hundred and fifty participants grouped into 60 obese, 60 non-obese none diabetic and 30 non-obese non-diabetic adults with similar age from the Endocrinology outpatient's clinic, General outpatient department (GOPD) and staff clinic of Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC). Anthropometric parameters and other relevant clinical details of all subjects were obtained. Fasting venous blood samples were taken from all subjects for the determination of fasting plasma glucose (FPG), fasting lipid profile, glycosylated haemoglobin levels (HbA_{1C}), fasting serum insulin, leptin, and adiponectin. Data was analysed using the Statistical Package of Social Sciences (SPSS) version 23.0. **Results:** Twenty-eight (46.7%)) subjects were males while 32 subjects (53.3%) were females (in obese groups). There was no statistical difference between these two groups for both sexes ($p = 1.000$). The age range for all subjects was 34 to 64 years with their mean age being 52 ± 7.3 years, and for type 2 subjects and the obese non-diabetic 50.7 ± 7.3 years respec-

tively. The mean body mass index of the non-obese and non-diabetic was 23.7 ± 4 Kg/m^2 while the anthropometric measurements of the obese two groups were similar. The lipid profile, serum leptin and adiponectin in both the obese groups showed no difference. The relationship between components of obesity and serum leptin level in all subjects showed that serum leptin levels had significant positive correlation with BMI, WC, and serum insulin level. The correlation between adiponectin and lipid profile showed a positive correlation between serum adiponectin values and High-density lipoprotein (HDL) in obese diabetic ($p = 0.02$) but not in the non-diabetic group. **Conclusion:** In this study, there was no correlation in the serum leptin levels with the anthropometric parameters of obesity studied. For the components of the lipid profile, Triglycerides and low-density lipoprotein cholesterol (LDL) correlated with serum adiponectin and HDL showed a positive correlation with adiponectin. It is concluded that the effects of both serum adiponectin and serum leptin are driven by obesity rather than the glycaemic status of the obese subjects.

Keywords

Obesity, Type 2 DM, Leptin, Adipokines

1. Introduction

Obesity is an excessive proportion of body fat relative to lean body mass of sufficient magnitude to produce adverse health consequences. [1] It is an endemic health problem in both developed and developing countries. [2] The prevalence of obesity and overweight in Nigeria is comparable to that seen in industrialized countries. [3] Obesity is also associated with many chronic diseases including type 2 diabetes mellitus (T2DM) and remains an independent risk factor for cardiovascular disease. [4] This increased risk for cardiovascular events such as coronary heart disease is due in part to its strong association with atherogenic dyslipidaemia. [5] The implication on the basis of the association between obesity and T2 DM is subject to genetic susceptibility, environmental and dietary factors and sedentary life style. [6] Leptin and adiponectin are differentially expressed adipokines in obesity and cardiovascular diseases. Leptin levels are directly associated with adipose tissue mass, while adiponectin levels are downregulated in obesity. The proposed metabolic mechanism linking the two includes the effect of adipokines and their receptors and related factors such as leptin, resistin and adiponectin [7].

Leptin has been linked with obesity and the occurrence of T2DM. [8] [9] Leptin is the primary signal from energy stores and exerts negative feedback effects on energy intake. In most cases of obesity, leptin loses the ability to inhibit energy intake and increase energy expenditure; which is termed leptin resistance. [10] This may be responsible for higher levels of serum leptin in most cases of obesity.

Adiponectin, a marker with anti-atherogenic, anti-inflammatory, cardioprotective and insulin-sensitizing properties, modulates a number of metabolic processes. [11] A decline in plasma or serum levels of adiponectin due to genetic or environmental factors has been implicated in the development of diabetes, and some metabolic disorders, dyslipidemia, and abdominal obesity [12] [13].

This study aims to assess the levels of serum leptin and serum adiponectin in obese type 2 diabetes subjects, and their relationship with cardio-metabolic component (using lipid profile).

2. Methodology

This is a cross-sectional comparative hospital-based study in the Endocrinology, Diabetes and Metabolism (EDM) Unit Out-patient Clinic of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Osun State Nigeria. The study was carried out between March 2019 and April 2020.

2.1. Subject Recruitment

It involved obese T2DM subjects with age and gender matched obese non-diabetic subjects. Also, non-obese non-diabetic subjects were recruited to serve as control and baseline measurement of serum leptin and adiponectin levels in the environment. All consecutive obese type 2 DM subjects defined as all previously diagnosed diabetic subjects based on the WHO classification and diagnostic criteria. [14] were recruited. Exclusion criteria were subjects with type 1 DM, patients on long term steroid therapy, pregnant female patients, as well as patients who were known or suspected to have Cushing's syndrome, hypothyroidism, polycystic ovarian syndrome and acromegaly.

2.2. Clinical Variables

All participants were examined and anthropometric measurement of weight, height, body mass index (BMI derived from calculation), waist circumference (WC), hip circumference (HC) and waist-hip-ratio (WHR) derived from calculation for males and females and documented. [14] [15] The central obesity is determined by ethnic specific cut off point for waist circumference and the IDF recommended cut off points for people of sub-Saharan Africa are WC ≥ 80 cm for female and WC ≥ 94 cm for male. [15] [16] Obese and non-obese females with type 2 diabetes mellitus diagnosed based on the WHO criteria of 1998.[14] Ethical approval was sought and granted by the hospital's Ethics and Research Committee.

2.3. Laboratory Investigations

Laboratory assessment was performed on blood samples that were collected after eight hours overnight fast for determination of blood glucose, glucose, glycated hemoglobin, serum levels of total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides was measured. Serum insulin,

serum leptin and serum adiponectin were also measured.

2.4. Data Analysis

Data was analyzed using the Statistical Package of Social Sciences (SPSS) version 23.0. Results were expressed as mean (SD), and proportions and presents as frequency tables. Continuous variables were analysed with analysis of variance ANOVA. Relationship between serum leptin, serum adiponectin and lipid profile in obese T2DM and obese non-DM were determined using student T test and chi square was used for categorical variables among the groups the level of statistical significance was set as $p \leq 0.05$.

3. Result

One hundred and fifty subjects made up of 60 T2D and 60 obese non-diabetic subjects and 30 non obese and none diabetic subjects were recruited. Twenty-eight (46.7%)) subjects were males while 32 subjects (53.3%) were females (in obese groups). There was no statistical difference between these two groups for both sexes ($p = 1.000$). The age range for all subjects was 34 to 64 years with their mean age being 52 ± 7.3 years for type 2 subjects was and the obese non-diabetic 50.7 ± 7.3 years respectively. The mean body mass index of the non-obese and non-diabetic was 23.7 ± 4 Kg/m^2 and the anthropometric measurements of the obese two groups are shown in Table 1.

The blood glucose assessment in the obese T2 DM group using HBA1c was <7% in 39 (65%) and ≥7% in 21 (35%) subjects. The lipid profile, serum leptin and adiponectin in both groups showed no difference (Table 2).

The mean baseline serum leptin levels of the non-obese and non-diabetic subjects was 7.59 ± 3.39 ng/ml, while for diabetic subjects with controlled and non-controlled glycaemia were 17.36 ± 7.65 ng/ml and 11.93 ± 7.30 ng/ml respectively with a statistically significant higher levels in subjects with controlled diabetes ($t = 2.020$, $df = 57.824$, $p = 0.048$) (Table 3).

Table 4 shows the relationship between components of obesity and serum leptin level. In all subjects, serum leptin levels had significant positive correlation with BMI, WC, and serum insulin level. In the Obese Type 2 DM subjects, serum

Table 1. Anthropometric Measurements of obesity in Participants.

Variable	Obese T2DM	Obese Non-DM	p value
Waist Circumference (cm)	106.3 ± 7.5	105.6 ± 10.4	0.969
Hip Circumference (cm)	113.7 ± 8.9	119.9 ± 10.8	0.003*
Waist/Hip Circumference ratio	0.94 ± 0.06	0.88 ± 0.06	0.0001*
Height (cm)	157.2 ± 5.1	157.6 ± 10.6	0.963
Weight (kg)	85.6 ± 10.1	92.1 ± 14.0	0.014*
BMI (kg/m^2)	34.5 ± 3.4	36.5 ± 5.1	0.044*

*p value significant.

Table 2. Laboratory parameters of the study participants.

Variable	Obese T2DM	Obese non DM	p value
Fasting Plasma Glucose (mmol/l)	8.1 ± 2.9	5.4 ± 0.5	0.0001*
HbA1C (%)	8.3 ± 2.9	-	-
HDL (mmol/l)	1.2 ± 0.3	1.2 ± 0.3	1.000
LDL (mmol/l)	3.4 ± 0.9	3.1 ± 0.8	0.447
TC (mmol/l)	5.4 ± 0.9	5.1 ± 0.8	0.363
TG (mmol/l)	1.6 ± 0.4	1.5 ± 0.4	0.959
Sr Leptin ng/ml	20.61 ± 15.13	20 94 ± 17.64	0.999
Serum Adiponectin (µg/ml)	3.0 ± 1.8 (µg/ml)	3.6 ± 1.8 (µg/ml)	0.13
Serum insulin µIU/ml	23.19 ± 1954	20.67 ± 20.24	0.866

HBA1c: Glycated heamoglobin; HDL: High density lipoprotein; TG: Triglycerides; LDL: Low density lipoprotein; TC: Total Cholesterol; *p value significant.

Table 3. Comparison of serum leptin levels in diabetes subjects with controlled and non-controlled glycaemia.

Parameters	Controlled DM	Non-Controlled DM	p value
HbA_{1C} (%)	5.9 ± 0.7	10.2 ± 2.4	0.0001*
Serum leptin (ng/ml)	17.36 ± 7.65	11.93 ± 7.30	0.048*
Serum Insulin (µIU/ml)	17.62 ± 8.21	13.83 ± 4.43	0.229

DM = Diabetes Mellitus; *$p < 0.05$ is statistically significant.

Table 4. Relationship between serum leptin level with indices of obesity.

Parameter	Obese DM		Obese non-DM	
	r value	p value	r value	p value
BMI	+0.038	0.776	+0.281*	0.030
WC	−0.25	0.849	+0.237	0.068
Serum insulin	−0.077	0.558	+0.446*	0.0001

r = Spearman's simple correlation coefficient; *$p < 0.05$ is statistically significant.

leptin levels were not significantly correlated with BMI, WC, and serum insulin levels but in the Obese non-diabetic subjects, serum leptin levels were significantly and positively correlated with BMI, serum insulin but did not correlate with WC. There was also no correlation between the serum leptin levels and HbA_{1C} in all subjects with controlled diabetes ($r = 0.018$, $p = 0.905$) and in subjects without controlled diabetes ($r = -0.208$, $p = 0.080$).

The mean serum adiponectin levels of non-obese and non-diabetic subjects was 5.3 ± 0.8 µg/ml while that of the diabetic subjects with controlled and uncontrolled glycemic status were 3.3 µg/ml ± 1.7 and 3.5 µg/ml ± 2.0 respectively and this was also not statistically significant ($t = 0.497$, $df = 118$, $p = 0.620$). **Table 5** shows the correlation between adiponectin and lipid profile. There is a

Table 5. Correlation between Adiponectin and Lipid profile in subjects.

Lipid profile	Obese T2 DM		Obese Non DM	
	r	p value	r	p value
HDL	0.30	0.02*	0.20	0.13
TG	0.09	0.49	−0.12	0.37
LDL	0.13	0.31	0.08	0.56
Total Cholesterol	0.23	0.07	0.12	0.36

HDL: High density lipoprotein; TG: Triglycerides; LDL: Low density lipoprotein; *p value significant; r: Correlation co-efficient.

positive correlation between serum adiponectin values and High-density lipoprotein (HDL) in obese diabetic (p = 0.02) but not in the non-diabetic group.

4. Discussion

The increasing prevalence of obesity is a driving force for T2 DM. [17] Leptin and adiponectin are cytokines produced excessively by adipocytes. Generally, obesity is associated with high levels of the circulating hormone leptin (hyperleptinemia) and low levels of adiponectin on the other hand, as opposed to leptin's generally detrimental effects on the cardiovascular system, adiponectin is cardioprotective. Thus, Leptin is thought to be responsible for several cardiovascular diseases associated with obesity, while adiponectin is considered to be cardioprotective.

Serum leptin is known to be high in obese subjects because of the variation, proportion of obesity and ethnicity due to the proportion of adipose tissue. [18] [19] In this study, the serum leptin levels were high in both the obese groups compared to none obese. Serum leptin levels were noted to be high in obese subjects with or without diabetes. This is due to the fact that leptin is produced by adipose tissue in proportion to the severity of obesity. Variation in the production of leptin level also depends on insulin levels as insulin is known to increase leptin production. [20] Though the leptin levels are high, this is not as high as in other studied populations, and this may be due to ethnic variation in severity of obesity. [20] [21] [22] In this study, there was no correlation in the serum leptin levels with the anthropometric parameters of obesity studied, this may suggest that though subjects with diabetes may have associated insulin resistance states, it is the obesity that drives the level of leptin.

Plasma levels of adiponectin are decreased significantly in obese patients, and negatively correlated with body mass index (BMI). People with T2DM have lower plasma adiponectin concentrations compared to non-diabetic individuals, regardless of BMI. In this study, serum adiponectin levels in all subjects were comparable, this could be because both groups are obese and the effect of diabetes is not seen. It is also known that since adiponectin also acts as an insulin-sensitizing hormone in muscle and liver, lower levels of adiponectin further

contribute to peripheral insulin resistance in obesity. [23] [24] However, higher adiponectin values were seen only in the diabetic subjects with poor glycemic control.

For the components of the lipid profile: Total cholesterol, Triglycerides and low-density lipoprotein cholesterol (LDL) correlated with serum adiponectin. Serum levels of adiponectin are thought to correlate positively with high density lipoprotein (HDL) and negatively with Total cholesterol, LDL and Triglycerides due to its anti-atherogenic properties. [25] The positive correlation adiponectin has with HDL is known and expected because HDL is well-recognized as an independent predictor of cardiovascular risk.

In conclusion, the effects of both serum adiponectin and serum leptin are driven by obesity rather than the glycaemic status of the obese subjects.

Limitations: The sample size of this study may be a limitation as it may result in non-significant associations where larger studies would have shown significance.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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