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Serum leptin in obese type 2 diabetic females in South-Western Nigeria

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Abstract

Background: Obese people, especially females, are known to have high circulating levels of leptin, a hormone that increases energy expenditure and also regulates glucose metabolism. However, the link between obesity and type 2 diabetes (T2DM) through leptin is yet to be clearly defined.

Objectives: This study determined and compared the levels of serum leptin and HOMA-IR scores in obese and non-obese females with or without T2DM. We also determined the relationship between their serum leptin levels and glycaemic control.

Methodology: This was a cross sectional study involving 60 obese T2DM females, 60 non- obese T2DM females and 60 obese non-diabetic female adults who met selection criteria. Their demographic data and anthropometric parameters were obtained using standard methods. Fasting blood samples were collected aseptically from participants for determination of plasma glucose, serum leptin, HbA_{Ic} and HOMA-IR.

Results: Serum leptin levels in obese T2DM, obese non-diabetic and non-obese T2DM femaless were (15.61 ±10.63), (11.33±14.22) and (5.92±3.68) ng/ml respectively. There were significantly much higher serum leptin levels in obese T2DM than in obese non-diabetic females (p = 0.035S). In the obese T2DM participants, serum leptin levels had strong negative correlation with HOMA-IR (r = -0.293, p = 0.023) and HbA_{Ic} (r = -0.255, p = 0.049).

Conclusion: Serum leptin levels were much higher in obese females with diabetes than in those without diabetes. However, the strong negative correlation of serum leptin levels with improving glycaemic control may suggest a therapeutic potential of leptin for diabetes which needs to be further explored.

Keywords: *Obesity, Type 2 diabetes mellitus, Serum leptin, Insulin resistance, HOMA-IR, HbA_{Ic}*

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Résumé

Contexte : Les personnes obèses, en particulier les femmes, sont connues pour leurs taux élevés de leptine en circulation, une hormone qui augmente la dépense énergétique et régule également le métabolisme du glucose. Cependant, le lien entre l'obésité et le diabète de type 2 (DT2) par le biais de la leptine n'est pas encore clairement défini.

Objectifs: Cette étude a déterminé et comparé les taux de leptine sérique et de scores HOMA-IR chez les femmes obèses et non obèses avec ou sans DT2. Nous avons également déterminé la relation entre leurs taux sériques de leptine et le contrôle glycémique .

Méthodologie: Il s'agissait d'une étude transversale portant sur 60 femelles DT2 obèses, 60 femelles DT2 non obèses et 60 femelles obèses non diabétiques qui répondaient aux critères de sélection. Leurs données démographiques et paramètres anthropométriques ont été obtenus en utilisant des méthodes standard. Des échantillons de sang à jeun ont été prélevés de manière aseptique chez les participants pour la détermination du glucose plasmatique, de la leptine sérique, de l'HbA_{Ic} et de l'HOMA-IR.

Résultats: Les taux de leptine sérique des femelles DT2 obèses, obèses non diabétiques et non obèses DT2 étaient (15,61 ± 10,63), (11,33 ± 14,22) et (5,92 ± 3,68) ng/ml, respectivement. Les taux de leptine sérique étaient significativement plus élevés chez les femelles DT2 obèses que chez les femelles obèses non diabétiques (p = 0,035S). Chez les participantes DT2 obèses, les niveaux de leptine sérique avaient une forte corrélation négative avec l'HOMA-IR (r = -0,293, p = 0,023) et HbA_{Ic} (r = -0,255, p = 0,049).

Conclusion: Les taux de leptine sérique étaient beaucoup plus élevés chez les femelles obèses diabétiques que chez celles non diabétiques. Cependant, la forte corrélation négative des niveaux sériques de leptine avec l'amélioration du contrôle glycémique peut suggérer un potentiel thérapeutique de la leptine pour le diabète qui doit être davantage exploré.

Mots clés: *Obésité, diabète sucré de type 2, leptine sérique, résistance à l'insuline, HOMA-IR, HbA_{Ic}*

Introduction

Obesity is defined as an excess proportion of body fat relative to lean body mass of sufficient magnitude to produce adverse health consequences [1, 2]. It is associated with many chronic diseases including type 2 diabetes, cardiovascular disease and some cancers [3]. Type 2 diabetes is the most common metabolic disorder worldwide [4], and its prevalence is growing at an alarming rate in both developed and developing countries [5, 6]. This increase has been attributed to the rising prevalence of obesity which of itself, is also an independent health problem [6]. Worldwide, approximately 90% of people with diabetes are type 2, and of these, 44% are obese or overweight [7]. Globally, 23% of ischaemic heart disease burden and 7-41% of certain cancer burdens are also attributable to overweight and obesity [7].

The incidence of obesity is rapidly increasing in epidemic proportions all over the world [6, 8]. One billion of the approximately 6.5 billion people in the world are estimated to be overweight [body mass index (BMI) $\geq$ 25 kg/m^2] and, of these, at least 300 million are obese (BMI $S \geq$ 30 kg/m^2) [7]. In a population study in Ibadan, Nigeria, the prevalence of obesity and overweight were found to be comparable to rates seen in many industrialized countries, and rapidly emerging urbanized populations in Africa [9]. In that study, the prevalence of obesity among women was 17.27% and 2.75% among men [9].

A similar study in Ile-Ife, a semi urban region of Nigeria, also showed higher prevalence of obesity among women irrespective of the anthropometric indices of adiposity used [10]. It can be inferred from these findings that more Nigerian women than men are obese and at risk of obesity-related morbidity and mortality. There is therefore a need for better understanding of the physiological and pathological processes that balance energy intake and energy expenditure in order to help in combating the menace of obesity.

Leptin is the first obese gene product known to participate in many physiological processes such as: regulation of food intake and energy metabolism, cardiovascular function, glucose and lipid metabolism [11]. It is a protein hormone produced mainly by white adipocytes and it has structural similarities with the cytokine family [12]. In obesity, leptin looses the ability to inhibit energy intake and increase energy expenditure; this is termed leptin resistance [2]. There is also a suggestion that leptin could be a link between obesity and diabetes [13]. However, this link has not been clearly defined. It has been demonstrated that high serum leptin levels are associated with insulin resistance and the metabolic syndrome which is mediated by central obesity, independent of body mass index [14]. Studies also showed that plasma leptin levels are not affected by the presence of type 2 diabetes mellitus or by short-term treatment with diet or oral anti-diabetic drugs nor by the age of patients but rather related to glycaemic control in female patients with type 2 diabetes mellitus [15,16].

Other previous studies have also documented ethnic variations in serum leptin levels [17, 18], which may account for the variation in the relationship of circulating levels of leptin with the presence or absence of diabetes. In a study among non-obese Nigerian women with T2DM, Ajala et al., showed that plasma leptin levels in poorly-controlled diabetic patients were significantly increased compared to those obtained in well controlled diabetic subjects [19], though this study used HbA_{1c} value of less than 6% to determine subjects with controlled diabetes.

In Nigeria, there has not been a study designed purposely to determine the link between obesity, type 2 diabetes and serum leptin levels and it is plausible that a distinct relationship may exist. Therefore, this study determined and compared levels of serum leptin and HOMA-IR scores in three groups of participants i.e. obese female Nigerians with T2DM, obese female Nigerians without T2DM and non-obese female Nigerians with T2DM. We also determined the relationship between serum leptin and glycaemic control levels among the various groups.

Materials and methods

This was a cross-sectional, comparative hospital-based study carried out at the Endocrinology, Diabetes and Metabolism (EDM) Out-patient's Clinic of a tertiary hospital in Osun State, South-western Nigeria, between January and June 2012 following ethical approval from the institutional Ethics and Research Committee. In addition, signed informed consent was obtained from each participant after a discussion session explaining the required procedure.

Sixty obese and 60 non-obese females with type 2 diabetes mellitus and age comparable 60 obese apparently healthy female participants who met the inclusion criteria as stated below for each of the 3 groups were recruited consecutively from the EDM Unit outpatient's clinic, General Outpatient Department (GOPD) clinic and the hospital staff clinic. Inclusion criteria were obese females with BMI $\geq$ 30 kg/m^2 and non-obese female females with

BMI < 30 kg/m^2, type 2 diabetes mellitus was diagnosed based on the WHO criteria of 1998 [20], and participants were currently not on insulin treatment. Apparently healthy obese non-diabetic female Nigerians with fasting plasma glucose (FPG) less than 6.1 mmol/l as defined by WHO criteria of 1998 [20], and adult females aged between 30 years and 64 years based on the age range mostly affected by type 2 diabetes [21].

The exclusion criteria were unwilling participants, pregnancy, acute illness within a week before the study and participantts who were known or suspected to have chronic debilitating diseases. Females who were known or suspected to have other endocrine diseases related to diabetes mellitus or obesity such as Cushing's syndrome, hypothyroidism, polycystic ovarian syndrome, acromegaly, and those who were on long tern steroid use or currently on steroid therapy were also excluded.

Demographic data and clinical history were obtained with interviewer's administered structured questionnaire. Physical examination was performed on each eligible participant. Body weight, height, waist circumference (WC), hip circumference (HC), and blood pressure were measured in all participants according to standard protocol. BMI was calculated as weight in kilogrammes divided by square of height in metres and waist to hip ratio (WHR) was also calculated for each participant.

Fasting blood samples were collected aseptically from each participant after an overnight fast of between 8 to 12 hours for all laboratory blood tests. Glycosylated haemoglobin (HbA_{1C}) was measured only in participants with type 2 diabetes as a marker of glycaemic control. Based on HbA_{1C} results, type 2 diabetic participants were then categorized as controlled diabetic if HbA_{1C} was <7% or poorly controlled diabetics if $HbA_{1C} \geq 7\%$. All participants were assessed for insulin resistance using the homeostasis model assessment of insulin resistance (HOMA-IR) as described by Matthews *et al.* [22, 23].

Fasting plasma glucose was measured with the spectrophotometer using the principle of Trinder reaction [24]. HbA_{1C} was measured from the blood samples by the principle based on boronate affinity chromatography with Biorad in-2-it HbA_{1C} auto-analyser and its test catridges after the initial standardization of the analyser with a system check cartridge.

Fasting serum leptin levels were measured by double assay from the sera of subjects as total serum leptin. This quantitative estimation of human serum leptin assay was done using the human leptin test kit on a Chemwell 2910 microwell enzyme linked immunosorbent assay (ELISA) analyser. Assay sensitivity was 0.3 ng/ml and specificity of antibodies for human leptin was 100%. Intra assay coefficient of variation (CV) was 6.42% while the inter assay coefficient of variation (CV) was 10.11 %. The test kit laboratory reference values for a normal weight male = 3.84 ± 1.79 ng/ml and for a normal weight female = 7.36 ± 3.73 ng/ml.

Double assay for serum insulin were also done by a quantitative method with microwell ELISA human insulin test kits on Chemwell 2910 Auto-analyser. The test kit laboratory reference values for normal adults range from 0.7 to 9.0 µIU/ml and values for adults with type 2 diabetes mellitus range from 0.7 to 25 µIU/ml. The sensitivity of this assay was 0.75 µIU/ml and the test has no cross reactivity with C-peptide, proinsulin and glucagon. The HOMA-IR estimate for insulin resistance is as follows: HOMA-IR = Fasting Glucose (mmol/l) x Fasting Insulin (µIU/ml)/22.5 [22]. HOMA-IR scores of ≥ 2 was used to define individuals with insulin resistance as previously described by Oli et al. for Nigerians [25].

Data analysis

This was done using statistical package for social sciences (SPSS) version 17.0 (SPSS Inc. Chicago Illinois). The data were tested for normality using Kolmogorov–Smirnov test. Except where otherwise stated, results were expressed as mean ± standard deviation (SD) and number count (N) with proportions (%). Median ± Interquartile Range (IQR) were used to express the result of serum leptin, serum insulin and HOMA-IR data which were not normally distributed. Serum leptin levels, insulin and HOMA-IR levels of the three groups were compared using Kruskal-Wallis-H- test while other normally distributed continuous variables were compared among the three groups with Analysis of Variance (ANOVA).

Serum leptin levels, insulin and HOMA-IR levels were also compared between two groups using Mann-Whitney-U test while other normally distributed continuous variables were compared between participants with controlled and poorly controlled diabetes using Student's t-test. Spearman's correlation coefficient was used to determine the relationship between serum leptin levels, HbA_{1C} and other continuous variables. Proportion of participants based on diabetes control status of the obese and non-obese type 2 diabetic groups and other categorical variables were also compared using Chi-

square test, Level of statistical significance was set as p-value <_0.05.

Results

Table 1 presents the socio-demographic and clinical characteristics of study participants in each group. A total of 180 females participated in the study with 60 participants in each of the three groups. The age range for all participants was between 34 and 64 years with mean age of 52.0 ± 7.3 years. A large proportion (96.1%) of our participants were of Yoruba ethnicity.

In accordance to BMI grading by WHO [26], obesity class I, II and III were present in 41 (68.3%), 15 (25.0%) and 4 (6.7%) of the obese type 2 DM participants respectively. Among the obese non-diabetic participants, 27 (45.0%) had class I obesity, 18 (30.0%) had class II obesity and 15 (25.0%) had class III obesity. In the non-obese type 2 DM group, 21 (35.0%) participants had normal BMI and 39 (65.0%) participants were overweight. Central obesity as defined by waist circumference (WC) of at least 88 cm was present in all the obese T2DM participants, 59 (98.3 %) of the obese non-diabetic participants and in 43 (71.7%) of the non-obese T2DM participants. The anthropometric indices of participants are as shown in Table 2.

Table 1: Comparison of some clinical parameters of the study participants

Parameter	Obese T2DM	Obese Non- DM	Non-Obese T2DM	p-value
Age (Years)	52.8±7.3	50.7± 7.3	52.6±7.4	0.224
Family history of DM	25(41.7%)	17(28.3%)	16(26.7%)	0.036*
Family history of HTN	28 (46.7%)	21 (35.0%)	22 (36.7%)	0.286
Family history of obesity	50 (83.3%)	45 (75.0%)	25 (41.7%)	0.001*
Childhood history of obesity	27 (45.0%)	27 (45.0%)	14 (23.3%)	0.001*
Known HTN	46 (76.7%)	21 (35.0%)	38 (63.3%)	0.0001*
Antilipid drug use	19(31.7%)	0(0.0%)	13(21.7%)	0.0001*
DM Duration(Years)	3.8± 3.3	NA	5.5 ±4.3	0.017*

*HTN = Hypertension, DM – Diabetes Mellitus, T2DM = Type 2 DM, NA = Not Applicable, *p value <0.05 is statistically significant*

Table 2: Comparison of the anthropometric and biochemical parameters of the Study participants

			N = 180		
Parameter	Obese T2DM (a)	Obese Non-DM (b)	Non-Obese T2DM (c)	p-value (aVbVc)	p-value (aVb)
Ht(cm)	157.2±5.1	157.6±10.6	160.3±5.5	0.540	0.963
Wt (Kg)	85.6±10.1	92.1±14.0	66.1±7.6	0.0001*	0.014*
BMI (Kg/m^2)	34.5±3.4	36.5±5.1	25.9± 2.3	0.0001*	0.044*
WC(cm)	106.3±7.5	105.6±10.4	91.3±6.4	0.0001*	0.969
HC(cm)	113.7±8.9	19.9±10.4	97.9±5.5	0.0001*	0.003*
WHR	0.94±0.06	0.88±0.06	0.93±0.05	0.0001*	0.0001*
SBP(mmHg)	133.3 ±19.2	124.8±18.7	130.2±21.2	0.51	0.068
DBP(mmHg)	79.2 ±11.1	78.3±11.8	78.7±10.8	0.908	0.900
FPG (mmol/l)	8.1±2.9	5.4±0.5	8.3±2.9	0.0001*	0.0001*
HbA$_1$C (%)	8.3±2.9	NA	8.7±3.0	0.457	NA
Serum leptin(ng/ml)	15.61 ±10.63	11.33±14.22	5.92±3.68	0.0001*	0.035*
Serum Insulin (µIU/ml	13.37± 12.94	12.20± 2.37	6.72±1.42	0.0001 *	0.003*
HOMA-IR	5.23±4.38	2.90±0.86	2.25±1.18	0.0001*	0.0001*
Prevalence of IR	60 (100.0%)	59 (98.3%)	40 (66.7%)		

*WC = Waist Circumference, HC = Hip Circumference, Ht= Height, Wt = Weight, WHR = Waist to Hip Circumference Ratio, BMI = Body Mass Index, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, FPG =Fasting Plasmal Glucose, HbA$_1$C = Glycosylated Haemoglobin, HOMA-IR = Homeostasis Model Assessment of Insulin Resistance, NA = Not Applicable, IR = Insulin Resistance, *p value < 0.05 is statistically significant*

Comparison of biochemical parameters between the obese type 2 diabetic and obese non-diabetic female participants are also shown in Table 2. Serum leptin levels were significantly higher among obese T2DM participants than in obese non-diabetic participants (15.61± 10.63 ng/ml vs. 11.33±14.22 ng/ml, p = 0.035). In the obese T2DM participants, serum leptin levels had weak correlation with BMI, WC, and serum insulin levels but a strong negative correlation with HOMA-IR and HbA_{1C}. Among the obese non-diabetic participants, serum leptin levels had strong positive correlation with BMI, serum insulin and HOMA-IR but a weak positive correlation with WC. Among the non-obese type 2 DM participants, serum leptin levels had weak correlation with BMI, WC, serum insulin levels, HOMA-IR, and HbA_{1C} .Further detail on the relationship of serum leptin and HOMA-IR levels with BMI, WC, serum insulin levels and HbAIC in all the three study groups are as shown in Tables 3 and 4.

41.7% had controlled diabetes while 38.3% of the non-obese T2DM group had controlled diabetes. There were no statistically significant differences in the proportion of participants with controlled and poorly-controlled diabetes in both groups (X^2 =1.39, p = 0.709).

The serum leptin levels of the obese T2DM participants with controlled diabetes were not significantly higher than the serum leptin levels in those with poorly- controlled diabetes (16.41±22.85 ng/ml vs.15.11±9.50 ng/ml, p = 0.092). The serum insulin levels of obese T2DM participants with controlled diabetes were significantly higher than the serum insulin levels in those with poorly-controlled diabetes (14.03 ± 32.66 µIU/ml vs.12.93 ± 5.36 µIU/ml, p = 0.036). The HOMA-IR levels of the obese T2DM participants with controlled diabetes were not significantly lower than the HOMA-IR levels in those with poorly-controlled diabetes (5.01±8.71 vs. 5.51 ±2.81, p = 0.333S). There were no statistical significant differences

Table 3: Relationship of serum leptin levels with BMI, WC, serum insulin levels, HOMA-IR, and HbA_{1C} by group.

	Obese T2DM		Obese Non-DM		Non-ObeseT2DM	
Parameter	r-value	p- value	r-value	p- value	r-value	p- value
BMI	+0.038	0.776	+0.281	0.030*	+0.039	0.769
WC	0.025	-0.849	+0.237	0.068	+0.058	0.660
Serum insulin	-0.077	0.558	+0.446	0.0001*	+0.030	0.821
HOMA-IR	-0.293	0.023*	+0.385	0.002*	0.000	0.996
HbA_{1C}	-0.255	0.049*	NA	NA	-0.170	0.195

*BMI = Body Mass Index, WC= Waist Circumference, r= Spearman's simple correlation coefficient, *p < 0.05 is statistically significant, NA = Not Applicable.*

Table 4: Relationship of HOMA-IR with BMI, WC, serum insulin levels, and HbA1C by Group.

	Obese T2DM		Obese Non-DM		Non-Obese T2DM	
Parameter	r-value	p- value	r-value	p- value	r-value	p- value
BMI	-0.105	0.424	+0.432	0.001*	-0.011	0.932
WC	+0.008	0.951	+0.454	0.0001*	-0.007	0.956
Serum insulin	+0.483	0.0001*	+0.385	0.002*	+0.279	0.031*
HbA_{1C}	+0.196	0.134	NA	NA	+0.163	0.214

*BMI = Body Mass Index, WC= Waist Circumference, r = Spearman's simple correlation coefficient, *p<0.05 is statistically significant, NA = Not Applicable*

The total number of the diabetic participants was 120 of whom 40% were assessed to have controlled diabetes with a mean HbA_{1C} of 5.09 ± 0.7%. Among the obese T2DM participant group, between the non-obese diabetic females with controlled and poorly-controlled diabetes in their levels of serum leptin, insulin and HOMA-IR as shown inTable 5.

Table 5: Comparison of biochemical parameters between non-obese T2DM participants with controlled and poorly-controlled diabetes.

Parameters	Controlled DM n (%) = 23 (38.3%)	Poorly- Controlled DM n (%) = 37 (61.7%)	p-value
HbA_{1c} (%)	5.9±0.7	10.4±2.4	0.0001*
Serum leptin(ng/ml)	6.33±4.38	5.63±2.81	0.407
Serum Insulin(μIU/ml)	6.53±1.62	6.93±1.35	0.964
HOMA-IR	2.07±0.80	2.40 ±1.29	0.058

*T2DM = Type 2 Diabetes Mellitus, n = number of subjects, DM = Diabetes Mellitus, HOMA-IR = Homeostasis Model Assessment of Insulin Resistance, *p < 0.05 is statistically significant*

Discussion

The mean duration of T2DM was shorter in obese T2DM participants compared to non-obese T2DM participants. This may suggest that the non-obese T2DM participants had over time been subjected to life style modification and other diabetes treatment modalities that could have resulted in their present lower body mass index. More than 50% of all diabetic participants were known to be hypertensive while about one third of the obese non-diabetic participants were also found to be hypertensive. These finding are suggestive of the presence of metabolic syndrome in our participants. Hypertension, obesity and T2DM are essential components of metabolic syndrome [27], which is known to be associated with increased risk of cardiovascular morbidity and mortality.

There were many participants with combined family history of T2DM and obesity among the obese T2DM participants compared with non-obese T2DM participants. Similarly, participants with family history of obesity were more among the obese participants compared with non-obese participants. These findings give credence to the familial tendencies of these non-communicable diseases. Twin studies have demonstrated that familial aggregation of obesity has a genetic component and is not only due to cultural or environmental factors clustered in families [28]. In addition, linkage studies have also identified markers and genes related to obesity in virtually all human chromosomes [28]. Majority of the participants in each of the groups had documented evidence of central obesity by waist circumference irrespective of their BMI. The high prevalence of central obesity among diabetic participants was similar to that reported by Fasanmade et al. [29] in Lagos among Nigerian females with T2DM. Central obesity is particularly recognized as an independent risk factor for increased cardiovascular morbidity and mortality.

Serum leptin levels were significantly higher in both obese participants with or without type 2 diabetes mellitus than in non-obese type 2 diabetic participants. Higher serum leptin levels in obese participants have been previously reported [14, 16]. The higher levels of leptin in obese participants reflects the fact that leptin is produced by adipose tissue and in proportion to the amount of the adipose tissue in the body [30, 31]. The serum leptin levels in our participants were lower when compared to the levels reported in other populations [18, 32]. This could be due to ethnic variations in serum levels of leptin and possibly to variations in the severity of obesity [17, 18]. Luke et al. [18] have earlier demonstrated that serum leptin levels in Nigerians were lower when compared to that of Jamaicans and Americans respectively.

Our study showed that levels of serum leptin in obese T2DM participants were significantly much higher than the levels in the obese non-diabetic participants. Liuzzi et al. [16] found similar serum leptin levels in obese diabetic participants and obese non-diabetics, while Guler et al. [15] reported that leptin levels were not affected by the presence or absence of type 2 diabetes mellitus among Turkish women. However, Buyukbese et al. [33], in another study among Turkish obese women with and without type 2 diabetes mellitus demonstrated significantly higher serum levels of leptin in the group without type 2 diabetes mellitus. This disparity could be as a result of variation in insulin secretion and sensitivity in T2DM since insulin is also known to increase leptin production [34]. The leptin levels in our non-obese T2DM participants were also similar to the levels previously reported for non -obese females with type 2 diabetes mellitus in Nigeria [19], perhaps because of their common ethnic background.

Many investigators demonstrated that leptin had a significant correlation with BMI [33, 35, 36] In this study, leptin correlated significantly with BMI

only in obese non-diabetic participants. This positive correlation was also observed in the relationship between their serum leptin and serum insulin. However among the obese diabetic participants, there were poor correlations between serum leptin levels, BMI and serum insulin levels. These may be because of ongoing therapeutic intervention such as lifestyle modifications and use of anti-diabetes agents for our diabetic participants which may modulate insulin secretion and also influence leptin secretion [15]. Serum leptin levels were inversely related to HOMA-IR in obese T2DM participants and it did not correlate with HOMA-IR in non-obese T2DM participants while it had had a significant positive correlation with HOMA-IR in obese non diabetic participants. This suggests that increase in endogenous serum leptin levels may reduce insulin resistance in obese T2DM patients and therefore be a potential therapeutic agent if it can be augmented from an exogenous source or by any another physiological means.

The potential therapeutic role of leptin for diabetes mellitus is further supported by higher serum leptin levels in the obese type 2 diabetic participants with controlled diabetes than the levels in those with poorly-controlled diabetes, though these differences in leptin levels had no statistical significance. There was also a significant negative correlation between serum leptin levels and HbA_{1c} levels among obese diabetic participants. The HbA_{1c} is an established marker of long term glycaemic control and its levels reduce with improving glycaemic control. The findings of this study are similar to that of Buyukbese *et al.* [33] who reported elevated levels of leptin in obese females with controlled diabetes. Another previous study similarly demonstrated a weak but significant negative correlation between serum levels of leptin and glycaemic control before and after a period of treatment of diabetes [15]. Even among our non-obese T2DM participants, those with controlled diabetes also had elevation in their serum leptin levels than their poorly-controlled diabetes counterparts. The elevated serum leptin levels in participants with controlled diabetes and the significant negative correlation of serum leptin levels with glycosylated haemoglobin levels among obese diabetic participants may be attributable to the known regulatory function of leptin on glucose metabolism [11, 15]. Elevated serum leptin levels therefore appear to be good for glycaemic control either as a therapeutic agent or as a biochemical marker of glycaemic control.

HOMA-IR is a surrogate marker of insulin resistance that has been found to be well correlated with the measure of insulin resistance determined by euglycaemic clamp which is the gold standard [22]. The higher the HOMA-IR score, the higher the severity of insulin resistance [22, 23]. In this study, HOMA-IR scores increased across the groups with the lowest scores recorded in non-obese T2DM participants and the highest scores recorded in obese T2DM participants. In addition, the proportions of participants with insulin resistance were 100% among obese T2DM participants, 98.3 % among obese non-diabetic participants, and 66.7% among non-obese T2DM participants. This finding further illustrates the fact that obesity is strongly associated with insulin resistance which is a known cause of type 2 diabetes mellitus. Oli et al. [25] in Enugu, Nigeria previously reported that insulin resistance estimated by HOMA-IR is a major feature of type 2 diabetes mellitus in Nigerians and that obesity consistently correlates with and predicts insulin resistance. The higher degree of insulin resistance among obese non -diabetic participants in this present study also suggests that obese individuals should be routinely investigated and treated for insulin resistance in order to prevent or delay future occurrence of T2DM in them.

There were no significant correlations between BMI or WC with HOMA~IR in both obese T2DM participants and non-obese T2DM participants unlike their statistically significant correlations in obese non-diabetic participants. Liuzzi et al. [16] similarly demonstrated a significant positive correlation between HOMA-IR and BMI in a population of obese non-diabetic Italians. The weak correlation between BMI and WC with HOMA-IR in all our diabetic participants may be due to the modulatory effect of therapy on insulin resistance and body weight control in diabetic patients.

Conclusion

Serum leptin levels were significantly higher in obese participants than in non-obese participants and there were significantly much higher serum leptin levels in obese women with T2DM than in those without T2DM. Serum levels of leptin appear to be higher in obese participants with controlled diabetes than in those with poorly-controlled diabetes. In particular, serum leptin levels had a significant negative correlation with HbA_{1c} levels among the obese diabetic participants thus suggesting a potential role for leptin either as a marker of glycaemic control and or as a therapeutic agent for diabetes mellitus.

HOMA-IR showed that the severity of insulin resistance worsened with obesity and more so when obesity and T2DM co-exist. This finding therefore gives additional evidence in support of the fact that both non pharmacological and pharmacological interventions that can reduce insulin resistance should continue to form part of the management plan for obese patients with or without T2DM.

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