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In Type 2 Diabetes Males from Sudan, BMI and Waist Circumference were found to be Related to Leptin Levels

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Abstract

Objectives

The goal of this study was to investigate leptin (LEP) levels in diabetes patients and their relationship to BMI and WC.

Materials and Method

During the months of April 2012 and March 2013, a case-control study was conducted in Central Sudan. The study involved 78 male who met the inclusion criteria, they were separated into 3 groups; diabetic, diabetic hypertensive, and non-diabetic non diabetic hypertensive (NDNH) group to estimate FBG, Glycosylated hemoglobin HbA1C, and Lep levels. A15, a random access auto-analyzer bio system, was used to analyze the samples. A questionnaire was completed, which included anthropometric and biochemical measurements. Following each participants gave verbal agreement, venous blood was drawn after an overnight fast. The statistical analysis was done with the help of a statistical software for social sciences (SPSS version 16, Chicago, IL, USA).

Result

LEP varied considerably across the three groups. When compared to the diabetes and NDNH groups (0.990.12 ng/mL and 0.680.12 µg/L, respectively), the diabetic hypertensive group exhibited a higher mean concentration (1.910.24 µg/L). The diabetic hypertension group varied substantially from each of the diabetes groups ($p=0.004$) and the NDNH groups ($p<0.0001$). The diabetic hypertension group's mean Lep/BMI ratio varied substantially from each of the diabetes groups ($p=0.002$) and the NDNH group ($p<0.0001$), according to the Games Howell post hoc test.

Conclusion

Comparing the subgroup of male, there was dramatically lowered in Lep concentration as though it is mean concentration around the normal level. The Lep/BMI ratio rose substantially in diabetic hypertensive patients, dropped dramatically in NDNH patients, and increased non-significantly in diabetic patients, suggesting that low plasma Lep concentration may play a role in the development of obesity.

Keywords: Leptin, BMI, WC, Type 2 diabetes mellitus, Male, Sudan

Introduction

Lep is derived from the Greek word leptos, which meaning thin. Jeffrey M. Friedman found it in mice in 1994 [1]. It is a polypeptide hormone of 167 amino acids and a molecular weight of 16 kDa that is encoded by the obese gene [2] and is expressed in white adipose tissue [3]. Gastric chief cells in the stomach synthesize and secrete it, but subcutaneous adipocytes secrete a higher amount than visceral adipocytes, and it has been found in many tissues including the placenta, mammary glands, breast milk, testes, ovaries, endometrium, stomach, hypothalamus, and pituitary gland [4], brain [5], bone [6], macrophages [7], thyroid [8] and even the dental pulp [9]. Lep regulates energy balance, reproduction, immunity [10], and also acts as a pro-inflammatory factor [11]. Lep is also involved in glucose and lipid metabolism, angiogenesis, blood pressure control, and the development of bone mass [12]. The circulating Lep reflect the degree of adiposity and its release from

adipocytes signals to the brain to trigger the suppression of food intake and to boost energy expenditure, thus Lep is serving as an "adipostat" [13]. Circulating Lep levels are positively correlated with fat mass [14] or BMI [15]. These levels range from 5 to 10 ng/ml in healthy individuals and from 40-100 ng/ml in obese individuals [16]. In pathological state which includes inflammation, malignant transformation, low birth weight and premature delivery have been linked to lower Lep levels [14]. On the other hand prolonged fasting decreases Lep levels, whereas over feeding greatly increases its levels [17].

Insulin and Lep signaling constitute to the adipoinsular axis, which contributes to the regulation of nutrient and energy balance in the body. Insulin resistance occurs because of dys-regulation of the adipo-insular axis [18]. This means that Lep suppresses insulin secretion in a negative feedback loop where insulin stimulates the release of Lep [19], so the expression of Lep gene is correlated with insulin levels and increases after insulin infusion for several days [20]. Lep level is decreased in low insulin states, such as experimentally induced diabetes [21] and regulation of its levels is by food compositions specifically intake of macronutrients such as carbohydrates [22] and micronutrients such as zinc [23]. High serum Lep concentrations was observed in patient with T2DM [24] and in patients of renal dysfunction [25], microalbuminuria or macroalbuminuria [24], obesity [26] and were in risk for developing end stage renal disease (ESRD) [27]. In addition to massively obese patient [28] tend to develop glomerulosclerosis [29].

Material and Methods

Study Subject, Design and Area

A total of 78 participants of male were enrolled in a cross-sectional case-control study. 26 participants were diagnosed as type 2 diabetic, 21 were diabetic hypertensive and 31 participants, who were apparently healthy, enrolled as non-diabetic hypertensive or (control group). The participants were from rural and urban areas around Wad Madani city, they get their health services from Abu A'gla health center. The duration of the study was from April 2012-March 2013.

Inclusion and Exclusion Criteria

Participants who were included in this study with no current infection and without diabetes complications. Apparently healthy individuals who were agreed to participate were enrolled as non-diabetic non hypertensive group. Subjects were excluded if they do not meet any of the inclusion criteria.

Ethical Approval

An ethical approval for the study was obtained from the Ethics Committee, ministry of health.

Study Procedure

Information on bio data and anthropometric measures were obtained from all patients and non-diabetic non hypertensive subjects after informed consents (weight was measured in kilogram (kg) and heights in meter (m) and then the body mass index (BMI) was calculated applying the formula:
BMI = (weight in kg)/(height in m)2 (Ng M, 2014). Plasma samples were analyzed for different biochemical parameters, using A15, a random access auto-analyzer bio system.

Statistical Analysis

Statistical analysis was carried-out using statistical package for social sciences (SPSS version 16, Chicago, IL, USA). All the numerical data were expressed as mean ± Standard Error of Mean. Chi-square test was used to calculate the percentage of distribution of study participants. Differences in means of continuous variables between the study groups were compared using Analysis of variance (ANOVA). Multiple comparisons (Post Hoc Tests which include Tukey HSD and Games Howell) were used to compare differences between studied groups. P-values were considered significant at 0.05 or lower ($p \leq 0.05$).

Resuls

Using Chi-Squire, table 1 discus the frequency and distribution of study participants according to characteristic of study variable.

	Sub-group				
Variable	Characteristic	Diabetic(n=26)	Diabetic-hypertensive (n=21)	NDNH (n=31)	p-value
Age (years)	<= 50 years > 50 years	8(27.6%) 18(36.7%)	2(6.9%) 19(38.8%)	19(65.5%) 12(24.5%)	0.001
BMI (Kg/m^2)	<25 Normal 25-29.99 Overweight >=30 Obese	7(23.3%) 9(32.1%) 10(50.0%)	5(16.7%) 7(25.0%) 9(45.0%)	18(60.0%) 12(42.9%) 1(5.0%)	0.004
Physical activity	Low Moderate High	0(0.0%) 10(22.7%) 16(66.7%)	8(80.0%) 9(20.5%) 4(16.7%)	2(20.0%) 25(56.8%) 4(16.7%)	<0.0001

BMI=body mass index, DM=diabetes mellitus, HTN=hypertension, FH= Family history, kg=kilogram, m=meter

Table 1: Cross-tabulation of demographic and clinical data in the male group

Comparison of means revealed statistically significant differences in the anthropometric measurements (weight, WC and BMI), and biochemical measurement. Age differed significantly among the three groups, F (2, 75) = 12.919, (p=<0.0001). The diabetic hypertensive group had a higher mean value (58.90±1.46years) compared to the diabetic and NDNH groups (51.81±1.51years and 47.32±1.64years respectively). WC differed significantly among the three groups, F (2, 75) = 7.59, (p=0.001). The NDNH group had the highest mean value (1.73±0.01 kg) compared to the diabetic and diabetic hypertensive groups (1.72±0.01 kg and 1.67±0.02 kg respectively). BMI differed significantly among the three groups, F (2, 75) =8.755, (p=<0.0001). The diabetic hypertensive group had the highest mean value of BMI (29.53±1.32 Kg/m^2) compared to diabetic and NDNH groups (29.19±1.37 Kg/m^2 and 24.08±0.53 Kg/m^2 respectively).

FBG differed significantly among the three groups, F (2, 45) =16.900, (p=<0.0001). The diabetic group had the highest mean concentration (215.31±22.45 mg/dl) compared to the diabetic hypertensive and NDNH groups (160.19±15.29 mg/dl and 94.68±6.10 mg/dl respectively). HbA1C showed no significant difference among the two groups, F (2, 45) =0.256, (p= 0.615). However, the diabetic group had a higher mean value (8.12±0.67 %) than the diabetic hypertensive group (7.67±0.55 %). Lep differed significantly among the three groups, F (2, 71) = 15.789, (p<0.0001). The diabetic hypertensive group had a higher mean concentration (1.91±0.24 µg/L) compared to the diabetic and NDNH groups (0.99±0.12 µg/L and 0.68±0.12 µg/L respectively) (Table 2).

Variable	Subgroup			p-value
	Diabetic (n=26)	Diabetic-hypertensive (n=21)	NDNH (n=27)	
Age (years)	51.81±1.51	58.90±1.46	47.32±1.64	<0.0001
WC (cm)	97.73±2.33	104.71± 2.71	92.58 ±1.64	0.001
BMI (Kg/m^2)	29.19±1.37	29.53±1.32	24.08±0.53	<0.0001
FBG (mg/dL)	215.31±22.45	160.19±15.29	94.68±6.10	<0.0001
HbA_1C (%)	8.12±0.67	7.67±0.55	-	0.615
Lep (µg/L)*	0.99±0.12	1.91±0.24	0.68±0.12	<0.0001

*Assay range= 0.3µg/L -8µg/L, WC=waist circumference, Cm=centimeter BMI=body mass index, Kg=kilogram, m= meter, mg= milligram, dL= deciliter, ug=microgram

Table 2: Comparison of means in the male group

Group	Diabetic(n=26)			Diabetic hypertensive(n=21			Diabetic hypertensive(n=21)		
Compared with	NDNH (n=27)			NDNH (n=27)			Diabetic (n=26)		
Variable	Mean Diff	SE	p-value	Mean Diff	SE	p-value	Mean Diff	SE	p-value
WC (cm)†	5.15	2.93	0.227	12.13	3.11	0.001	6.98	3.23	0.098
BMI (Kg/m^2)†	5.11	1.47	0.004	5.45	1.42	0.002	0.34	1.91	0.983
FBG (mg/dl)§	120.63	23.26	<0.0001	65.51	16.46	0.001	-55.11	27.16	0.118
Lep (µg/L)§	0.31	0.17	0.152	1.23	0.26	<0.0001	0.91	0.26	0.004
Lep/BMI ratio§	0.007	0.009	0.824	0.04	0.009	<0.0001	0.03	0.009	0.002

§Games Howell, †Tukey HSD; BMI=body mass index, WC=Waist circumference, FBG=fasting blood glucose, Lep=Leptin, Cm=centimeter, Kg=kilogram, mg=milligram, dL=deciliter, ug=microgram, SE= Standard error, NDNH= Non diabetic non hypertensive, Diff= difference

Table 3: Post hoc analysis in the male group

Table 3 shows multiple comparisons in the male group (Post Hoc Tests). Games Howell Post Hoc test indicated that mean BMI differed significantly between the NDNH group and each of the diabetic group (p=0.004), and the diabetic hypertensive group (p=0.002). Mean WC did not differ between the three groups.

FBG differed significantly between the NDNH group and each of the diabetic hypertensive group (p<0.0001), and the diabetic group (p=0.001). Mean Lep differed significantly between the diabetic hypertensive group and each of the diabetic group (p=0.004), and the NDNH groups (p<0.0001). Hochberg post hoc test indicated that mean Lep/BMI ratio differed significantly between the diabetic hypertensive group and each of the diabetic group (p=0.002), and the NDNH group (p<0.0001).

Discussion

Comparing BMI of the study participants it was significantly higher in diabetic hypertensive and larger number of those individuals had higher than the normal value of WC compared with diabetic and NDNH participants (table 3, 4). Watson et al, 2011 showed that obesity is associated with a poorer response to insulin illustrated by higher level of HbA1C values and lower achievement of the target value. These observations made on BMI and WC indicated that the distribution of body fats and visceral adiposity in diabetic and diabetic hypertensive is associated with development of insulin resistance and T2DM [30].

Diabetic hypertensive group showed moderate physical activity and diabetic group showed higher physical activity with no regular exercise, this might be one of the contributing factors for the increased BMI and WC; these can lead to obesity and derangements of metabolic processes [31] including insulin resistance and decreased fatty acid oxidation [32], which eventually caused chronically increased in the concentration of inflammatory molecules like IL-6 and TNFα, [33] and most likely lead to the increased Lep level, these findings are in agreement with that of [34]. Lep/BMI ratio had significantly increased in diabetic hypertensive and decreased in NDNH group. These results suggested that Lep concentration was increased depending on BMI in contrast to [35] study which propose that fat cell enlargement is associated with hyperleptinemia and insulin resistance in non-diabetic individual's independent of BMI, but in type 2 diabetic subjects, other factors, not related to fat cell size, become more important for the modulation of insulin resistance. On other hand [36] in his observation conclude that secretion of Lep was under control of insulin and the prolonged exposure to insulin increases plasma Lep concentrations and the decrease in plasma Lep concentrations suggesting that factors other than insulin is contributing to regulation of plasma Lep concentrations.

In current study Lep concentration was low significantly in all study participants sub groups. In agreement to our study a case control study which was conducted in Sudan found that circulating Lep levels were lower in diabetic subjects (men and women) than in controls of similar age and BMI, and that females had higher mean concentrations than males, and that BMI was significantly correlated with circulating Lep levels. These findings suggest a link between decreased Lep levels and an increased risk of diabetes, as well as a link between Lep levels and increased BMI and WC [37].

Conclusion

Comparing the subgroup of male, there was dramatically lowered in Lep concentration as though it is mean concentration around the normal level. The Lep/BMI ratio rose substantially in diabetic hypertensive patients, dropped dramatically in NDNH patients, and increased non-significantly in diabetic patients, suggesting that low plasma Lep concentration may play a role in the development of obesity.

Recommendations

Decrease weight, BMI and WC of study patients is recommended through dietary restriction and regular exercise. Regular checkup for HbA1C and lipid profile to avoid aggressive diabetes mellitus complications.

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Conflict Of Interest

None.

Abbreviations

T2DM=Type2 diabetes mellitus; DM=diabetes mellitus, BMI=body mass index; WC= Waist Circumference; HTN=hypertension, p=Probability; FBG=fasting Blood glucose, HA1C=glycated hemoglobin, Lep=Leptin

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