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Relationship of leptin hormone with body mass index and waist circumference in type 2 diabetes and non-diabetes in Sudanese

Abstract

Introduction: The high prevalence of type 2 diabetes mellitus was associated with an increase in WC, BMI, and therefore obesity in the Sudanese population which may be due to low physical activity and absence of routine exercises. Because there is little data on the metabolic effects of adipocytokines leptin (Lep) in the diabetic Sudanese population this study aims to find the association of Lep and obesity with increased risk of type 2 diabetes mellitus. A case-control study was made at Abu A"gla health center for diabetic care at Wad Madani, Gezira State, Sudan, during the period of April 2012-March 2013. A total of one hundred eighty-one were enrolled in the study, participants divided into diabetic and non-diabetic groups to estimate the levels of Lep, fasting plasma glucose (FPG), and HbA1c. A questionnaire including personal information was filled as well as anthropometric and biochemical measures. Venous blood was collected after an overnight fast. Statistical analysis was carried out using a statistical package for social sciences (SPSS version 16, Chicago, IL, USA).

Method: Samples were analyzed for different biochemical parameters, using A15, a random access auto-analyzer biosystem. Lep was measured by ELIZA according to the method of the human leptin ELISA kit. This kit allows the determination of Lep concentration in human serum, plasma, and other biological fluids.

Result: Analysis of variance (ANOVA) revealed that mean FPG and HbA1c concentration in the diabetic group were increased significantly than that in the non-diabetic group; F=(8,250)=(p=<0.0001) and F=(2.933) (p=0.056). Correlation analysis revealed that FPG and HbA1C had strong positive significant correlation with Lep concentration (r=0.198**, p=0.007) at 0.05 and (r=0.153*, p=0.040) at 0.01 respectively. WC and BMI mean was (98.06) and (29.01) respectively.

Conclusion: The main finding in this study was that; the Sudanese participants with type 2 diabetes had a normal mean concentration of adipocytokines Lep (6.9813ug/L) compared to the standard values. FPG, HbA1c, and Lep in the diabetic group had a significant mean concentration (<0.0001), (<0.0001), and (0.056) respectively compared with the non-diabetic group. FPG and HbA1c had a strong positive significant correlation (p=0.007) and (p=0.040) respectively with Lep concentration. BMI and WC had no significant correlation with Lep concentration.

Keywords: leptin, type 2 diabetes mellitus, BMI, WC, Sudan

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Abbreviations: T2DM, type 2 diabetes mellitus; WHO, world health organization; Lep, leptin; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; p, probability; r, correlation coefficient; F, degree of freedom; µg, microgram; mg, milligram; M, meter; FPG, fasting plasma glucose; WAT, white adipose tissue; BAT, brown adipose tissue

Introduction

Adipose tissue is a complex network of endocrine organs that has been divided into white adipose tissue (WAT) and brown adipose tissue (BAT) Hahn et al.[1] Approximately one-third of WAT is adipocyte related Geloen et al.[2] Although the primary function of the adipose tissue is to store fat, energy storage, and insulation Hahn et al.,[1] they also function as endocrine cells that release numerous regulatory molecules -collectively known as adipocytokines- such as Lep Champe et al.[3] Lep means (leptos=„thin") in Greek. It was discovered in mice in 1994 by Jeffrey M. Friedman Williams et al.[4] It is a polypeptide hormone composed of 167 amino acids, of 16 kDa, encoded by the obese gene Zhang et al.[5] and expressed in white adipose tissue Bluher et al.[6] Synthesis and secretion is by gastric chief cells in the stomach Bado et al.,[7] but a higher amount is secreted by subcutaneous adipocytes than by the visceral adipocytes Van Harmelen et al.[8] Functions of Lep include the regulation of energy balance De Vos et al.,[9] reproduction, immunity Caldefie-Chezet et al.,[10] and also as a pro-inflammatory factor Lago et al.[11] Moreover, Lep is involved in glucose and lipid metabolism, angiogenesis, blood pressure regulation, bone mass formation Housa et al.[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" Rosen et al.[13] Lep levels range from 5 to 10 ng/ml in healthy individuals and from 40-100 ng/ml in obese individuals Howard et al.[14] Moreover, circulating Lep levels are positively correlated with fat mass Mantzoros et al.,[15] or BMI Ruhl et al.[16]

According to the World Health Organization statistics, the prevalence of obesity worldwide is 400 million people with a projected increase to 700 million by 2015 WHO[17] and 1.5 billion will become overweight Ries et al.[18] The prevalence of obesity was doubled between the years 1980-2014 Islam et al.[19] The increase in BMI reflects the degree of obesity and it is used to classify overweight and obesity WHO.[20] Body mass index (BMI) is defined as a person's weight in kilograms divided by the square of his height in meters (kg/m^2) WHO.[20] It ranges from 19.5-25.5 in healthy individuals and from 25-29.9 in overweight individuals and greater than 30 for obese individuals Champe et al.[3] Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health WHO.[20] WC values are used to denote risk of metabolic disease in relation to BMI. Waist circumference (WC) is the measurement made at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest Farooq et al.[21] The cut-off values for men is >102 cm and for women is >88 cm Schuster.[22] The main cause of developing obesity is decreased physical activity and increase caloric intake and/or little energy expenditure besides the genetic tendency James.[23] The outcome is marked changes in the secretory functions of adipocytes, macrophages, and pre-adipocytes leading to chronic low-grade inflammation and an increased risk to develop insulin resistance, diabetes, and vascular disease Iacobellis et al.,[24] by secretion of set of adipocytokines such as Lep and adiponectin Trujillo et al.[25]

The secretary function of adipose tissues is not merely for the production of physiological functional molecules but also the increase or decrease in their concentrations leads to pathological states Ross.[26] These adipocytokines have been linked to the development of diabetes mellitus in case of increase Lep concentration Lindsay et al.[27] Diabetes mellitus is one of the common chronic diseases in the Sudan with a prevalence of 447,000 in 2000, and this prevalence is projected to increase in 2030 to reach 1,227,000 WHO.[28] The prevalence of T2DM in the Sudanese population is 3.4%, and T2DM accounts for 75% of all diagnosed cases in northern parts of Sudan in 1996 Elbagir et al.[29] Insulin is a positive regulator of Lep and it can modulate Lep production and increases its gene expression to suppress appetite Yamauchi et al.[30] On the other hand, Lep is thought to affect insulin action in other tissues and having a role on obesity-induced insulin resistance Hansen et al.[31]

Material and methods

Study Subject, design and area: This study was a cross-sectional case-control study. A total of 181 adults of both sexes were included in the study. Among them 100 were diagnosed type 2 diabetic and 81 participants who were apparently healthy, enrolled as control group or (non-diabetic). 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 were in the age range between 18 and 60 years with no current infection and without diabetes complications. Apparently healthy individuals who were agreed to participate were enrolled as non-diabetic 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 subjects after informed consents were obtained (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 et al.[32] Plasma samples were analyzed for different biochemical parameters, using A15, a random access auto-analyzer bio system. Lep was measured by ELIZA according to the method of human leptin ELISA kit. This kit allows the determination of Lep concentration in human serum, plasma and other biological fluids.

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). Correlation analysis was used to measure the strength of the association between two numerical variables. P-values were considered significant at 0.05 or lower ($p \leq 0.05$).

Results

100(55.2%) of study participants were diabetic and 81(44.8%) were non-diabetic. 128(70.7%) of study participants were female and 53(29.3%) were male Table 1. 16(8.8%) of male and 112(61.9%) of female had increased WC. Only 45(24.9%) of study participants were in normal BMI, 70(38.7%) were overweight and 65(36%) were obese. Physical activity was moderate in 109(60.2%) of study participants Table 2. 88(48.6%) of study participants had high FPG level and 44(24.3%) showed poor HbA1C control. 135(74.6%) with normal Lep level and only 1(0.6%) had high Lep concentration Table 3. Comparison of mean in ANOVA analysis revealed that WC mean had non-significant increased (98.06) and by calculating BMI, the mean was (29.01) indicating that the study participants were overweight. Comparing the mean concentration of FPG and HbA1c in diabetic and non-diabetic group revealed significant increase in their concentrations; F=(8,250)=(p=<0.0001) and F=(2.933) (p=0.056) respectively Table 4.

When we used Pearson"s correlation analysis to measure the extent of the association between the measured variables age, WC, BMI, Physical activity, FPG, HbA1C and Lep concentration, it revealed that, age had marginal positive significant correlation (r=0.140, p=0.061) with Lep concentration. WC, BMI and physical activity had no correlation with Lep concentration. FPG and HbA1C had strong positive significant correlation with Lep concentration (r=0.198**, p=0.007) at 0.05 and (r=0.153*, p=0.040) at 0.01 respectively Table 5.

Table 1 Diabetic and non-diabetic groups as well as gender

	Variables	Frequency	Percent %
Group	Diabetic	100	55.2
	Non-diabetic	81	44.8
Gender	Male	53	29.3
	Female	128	70.7

Table 2 Characteristic of WC, BMI and physical activity of the study participants

Variables	Characteristic	Frequency	Percent %
WC(cm)	Male<=102	37	20.4
	Male>102	16	8.8
	Female<=88	16	8.8
	Female>88	112	61.9
BMI (kg/m^2)	under weight (BMI<18.50)	1	0.6
	Normal (BMI 18.50-24.99)	45	24.9
	Overweight (BMI 25-29.99)	70	38.7
	Obese class I (BMI 30-34.99)	36	19.9
	Obese class II (BMI 35-39.99)	22	12.2
	Obese class III (BMI=>40.00)	7	3.9
Physical activity	Low	29	16
	Moderate	109	60.2
	High	43	23.8

Table 3 Biochemical measurement of the study participants

Variables	Characteristic	Frequency	Percent %
FPG (mg/dl)	Low <75	14	7.7
	Normal 75-115	79	43.6
	High >115	88	48.6
HbA1c (%)	Excellent <6.5	105	58
	Good 6.5-7.5	12	6.6
	Moderate 7.5-8.9	20	11
	Poor >=9	44	24.3
Lep (ug/L)	Low <0.3	45	24.9
	Normal 0.3- 8	135	74.6
	High >8	1	0.6

Table 4 One way ANOVA

Variables	Minimum	Maximum	Mean	Std. Deviation	F	Sig
Age (years)	22	65	48.22	7.648	0.422	0.656
Weight (kg)	40	171	76.3	16.29	2.319	0.101
Height (m)	1.4	1.9	1.624	0.09268	0.356	0.701
WC(cm)	52	127	98.06	11.455	0.356	0.701
BMI (kg/m^2)	17.31	55.2	29.01	5.99723	0.419	0.658
SBP (mmHg)	80	170	116.52	11.476	0.017	0.983
DBP (mmHg)	30	100	75.51	9.247	1.987	0.14
FPG (mg/dl)	46	442	160.1	96.851	8.25	0.0001
HbA1c (%)	3.1	15	6.9813	2.63963	2.933	0.056

Table 5 Correlations analysis

Variables		Lep (ug/L)
Gender	r	0.058
	p	0.437
Age	r	0.14
	p	0.061
WC(cm)	r	0.044
	p	0.554
BMI (kg/m^2)	r	0.058
	p	0.437
Physical activity	r	0.008
	p	0.914

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Table Continued...

Variables		Lep (ug/L)
FPG (mg/dl)	r	0.198**
	p	0.007
HbA1c (%)	r	0.153*
	p	0.04

*Correlation is significant at the 0.01 and **Correlation is significant at the 0.05 levels (2-tailed)

Discussion

In this study 70.7% of study participants were female. WC mean showed non statistical significant compared to Lep concentration and neither statistical correlation though the mean of WC was 98.6. Overweight and obese account for 135(74.7%) of study participants and the mean of BMI of study participants was 29.00, presented no statistical significant and no any correlation with Lep concentrations. In contrast to this, previous studies reveals that increases in WC, BMI, distribution of body fats and visceral adiposity were associated with increased Lep concentration and so obesity and insulin resistance Antuna-Puente et al.[33]; Montague et al.[34] Pervious case control study that conducted in Sudan showed that circulating Lep levels were lower in diabetic subjects than in non-diabetic of similar age and BMI, those finding were agreed with our results in this recent study Abdelgadir et al.[35]; Jung et al.[36] In contrast to our study, Blair, 1993 confirmed that obesity and derangements of metabolic processes including insulin resistance and decreased fatty acid oxidation were associated with increased WC and BMI and most likely lead to the increased Lep level. Fortunately 109(60.2%) of total participants showed moderate physical activity with no regular exercise, this help them to reduce their WC and BMI. Islam et al.,[19] find that prevention of diabetes can be achieved by thirty minutes of moderate-intensity physical activity on most days. The effect of exercise training in reducing HbA1c -but not FPG- is by an amount that should decrease the risk of diabetic complications Boule et al.[37]

The main finding in this study was that 135(74.6%) of those participants showed normal Lep concentration with significant positive correlation and significant mean concentration between Lep concentration and increased FPG and HbA1Clevels. Malmstrom et al. confirmed that secretion of Lep was under control of insulin and the prolonged exposure to insulin, increases plasma leptin concentrations and that the decrease in plasma leptin concentrations suggesting factors other than insulin is contributing to regulation of plasma leptin concentrations. These finding were in line with our results because our study participant showed normal concentration of Lep level and higher FPG with poor glycated hemoglobin. The increased in FPG and HbA1C indicates that there was insufficient amount of insulin secretion or insulin couldn't exert its action as result of decreased in its receptors leading to change in the level of major metabolites like electrolyte which depends on insulin stimuli to pass through the plasma membrane of cells and so alteration on hormones levels Perseghin et al.[38] and change in the metabolism in the insulin dependent cells from carbohydrates to fats and other non-carbohydrate molecules to maintain energy and adequate amount of glucose to the tissues Alberti et al.[39]

Recommendations

Scientific research must be directed to the adipocytokines Lep because it is promised to become a new laboratory marker of insulin resistance in T2DM and to discover its association with insulin secretion and the availability of DM treatment by compound other than insulin or insulin stimulators.

Conclusion

The main finding in this study was that; the Sudanese participants with type 2 diabetes had a normal mean concentration of adipocytokines Lep (6.9813ug/L) compared to the standard values. FPG and HbA1c had strong positive significant correlation with Lep concentration. BMI and WC had no significant correlation with Lep concentration.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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