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Leptin, Insulin and Lipid Profiles in Obese Subjects with and without Metabolic Syndrome in the Region of Cap-Bon: Tunisia

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Abstract

Aims: To evaluate the effect of obesity associated or not with Metabolic Syndrome (MS) on leptinemia, insulinemia and lipid profile in subjects from the region of Cap-Bon in northeastern Tunisia.

Methods: Ninety seven individuals were included in this study. Anthropometric parameters (Body Mass Index (BMI), Waist Circumference (WC) and Hip Circumference (HC), metabolic parameters (Total Cholesterol (TC), LDL-C, HDL-C, Non-Esterified Fatty Acids (NEFA), Triglycerides (TG), C-Reactive Protein (CRP), glucose) and hormones (insulin and leptin) were determined. Insulin resistance was estimated by Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). Metabolic syndrome was identified with the International Diabetes Federation (IDF) criteria. Results: Obese patients with and without MS, Ob-MS and Ob groups, have significantly increased plasma levels of glucose, TG, TC, LDL-C and decreased HDL-C. In obese subjects Ob and Ob-MS, plasma levels of insulin and the HOMA-IR index were increased especially when obesity is associated with MS, conversely to leptin which decreases slightly in the presence of MS. Leptinemia was positively correlated with BMI in the whole population. But, we did not find any correlation between leptinemia and HOMA-IR. In controls, plasma leptin concentrations were positively correlated to LDL-C ($p<0.05$). Conclusion: Our findings support the link between leptinemia in obesity, associated or not with MS. However, in the Tunisian population plasma leptin was not associated to insulin profile.

Keywords: Leptinemia; obesity; lipid profile; metabolic syndrome

Introduction

Obesity (Ob) and Metabolic Syndrome (MS) constitute a major public health problem throughout the world [1]. Several studies consider obesity as a key element in the development of several components of the MS [2]. This syndrome is associated with multiple metabolic and cardiovascular diseases [3] and refers to a constellation of metabolic abnormalities linked together [4]. However, several definitions of MS have been proposed, all take into account one way or another abdominal obesity, dyslipidemia, Insulin Resistance (IR) or Type 2 Diabetes Mellitus (T2DM) and Hypertension (HTA) [5]. Adipose tissue is an organ biologically active and multifunctional that releases a large number of cytokines and bioactive mediators that influence not only body weight homeostasis but also play roles in inflammation, hematopoiesis, angiogenesis, atherosclerosis, insulin resistance, diabetes, bone formation and healing, and some form of cancer [6]. Among the adipocyte-derived hormones, leptin is the greatest and the best known as a regulator of food intake and energy expenditure [7]. Leptin expression is enhanced by insulin and glucocorticoids, which are associated with positive energy balance, while catechol-amines decrease leptin production during negative energy balance. Leptin is a pleiotropic molecule, playing an important role in the regulation of endocrine and metabolic functions [8]. Interestingly, several studies have demonstrated that leptin was involved in the pathophysiology of obesity while playing a crucial role in regulating the size of body fat. Leptin is fundamentally a "starvation signal" that, when low prompts increased appetite and decreased energy expenditure. Furthermore, circulating levels of leptin appears always correlated with Body Mass Index (BMI), it is greatly increased in obese subjects [9,10]. Leptin is strongly associated with inflammatory factors. However, impaired immune responses or inflammatory reactions and susceptibility to bacterial infections have been reported in patients deficient in leptin and malnutrition in situations where there is a low level of leptin [8,11]. Thus, insulin controls the secretion of leptin [12]. It has been also reported that the increase in fat mass and increased serum leptin level, lead to a decrease in the production of insulin, explaining the bidirectional feedback loop between adipose tissue and pancreatic islets called the adipoinsular axis [13]. High concentration of leptin, commonly called hyperleptinemia, is nearly associated with ob-releated diseases including T2DM, dyslipidemia, HTA and cardiovascular disease. Also, Non-Esterified Fatty Acids (NEFA) plays important physiological roles in skeletal muscle, heart, liver and pancreas. Elevated NEFA concentrations are linked with the onset of peripheral and hepatic insulin resistance [14]. Currently, few studies are focused on MS and ob in developing countries, particularly in Tunisia, where the prevalence of Ob is increasing strikingly [15]. Besides, growing evidence suggests that hyperleptinemia may play an important role in the development of MS. In this work, we tried to study the influence of obesity associated or not with MS on lipid profile and some key control peptides i.e leptinemia and insulinemia in patients and control subjects in the region of Cap-Bon, Tunisia.

Patients

In total ninety seven subjects (mean age ± SD, 49.7 ± 16.4 years, range 18-85). These subjects were hospitalized in the Department of Endocrinology of Regional Hospital of Nabeul-Tunisia, or recruited from the outpatient clinic or even from the staff of the service, from January to April 2012. All objectives and procedures were explained to each volunteer. Obesity was defined as Body Mass Index (BMI) greater than or equal to 30 kg/m^2. Subjects were classified into three groups, according to obesity and the presence of MS; C group: 30

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controls non-obese without MS (15 men and 15 women), Ob group: 33 obese without MS (15 men and 18 women), and Ob-MS group: 34 obese with MS (16 men and 18 women). Almost of Ob-MS patients (23/34) are receiving anti-hypertensive treatment. The presence of metabolic syndrome in subjects was defined according to the criteria provided by the IDF (International Diabetes Federation) using ethnic-specific values [16]. Metabolic syndrome was defined as abdominal obesity (using the European-specific value for waist circumference (Wc ≥94 cm in men and ≥80 cm in women) plus two or more of the following four components; i) fasting blood glucose (≥5.60 mmol/l) or type 2 diabetes mellitus (T2DM); ii) triglycerides (≥1.70 mmol/l) or a specific drugs; iii) HDL-C (<1.03 mmol/l) in men and <1.29 mmol/l in women or a specific drugs; iiii) Systolic Blood Pressure (SBP) ≥130 mmHg or diastolic (DBP) ≥85 mmHg or antihypertensive treatment. Dyslipidemia was defined as an LDL-C concentration more or equal to 4.1mM and/or an HDL-C concentration less or equal to 1 mM and/or a TG concentration more or equal to 1.71 mM [17]. Exclusion criteria were nephropathy, hypothyroidism, inflammatory diseases, insulin intake and pregnancy. All subjects belonged to the same geographic origin from the governorate of Nabeul, in the region of Cap-Bon, Tunisia. Written and oral consent was obtained from all the patients and healthy subjects before the study. The protocol was approved by the Local Ethics Committee of the Regional Hospital of Nabeul, Tunisia.

Methods

Anthropometric and biochemical measurements

Medical examination and anthropometric measurements for each subject were performed by the experiment. Body weight was measured with the subjects wearing light clothing to the nearest of 0.1 kg on a digital scale. Height was measured with the subjects wearing no shoes to the nearest of 0.1 cm using a stadiometer. BMI (kg/m^2) was calculated as the ratio of weight (kg) to the square of the height (meter squared). Waist Circumference (Wc) and Hip Circumference (Hc) were measured and waist to hip ratio (Wc/Hc) was calculated. Blood pressure was measured twice with the subject in a seated position, by manual sphygmomanometer, and appropriately sized cuff, following 15 min of quite rest. The average of the two measurements was used for analysis. Blood samples were collected after a 12-hour overnight fast. Samples were collected in tubes containing EDTA and immediately centrifuged at 4°C, 3,000 rpm for 10 min. Plasma samples were stored at -80°C until analysis.

Plasma glucose, Total-Cholesterol (TC), LDL-Cholesterol (LDL-C), HDL-Cholesterol (HDL-C), Triglycerides (TG), C-Reactive Protein (CRP), urea, creatinine, and uric acid, were measured with standard laboratory techniques using enzymatic methods of commercial kits on a Konelab 30 analyzer.

Total plasma lipids were extracted by a modification of the method of Folch et al. [18], 3 ml of chloroform/methanol (2:1, v/v) were added to plasma (100 µl) and proteins were separated by centrifugation at 2000 g for 10 min, 750 µl distilled water were added to the superior phase, then shaken for 2 min at room temperature. The chloroform phase was transferred in new tubes, dried under N_2 and dissolved in 25 ml of ethanol/ether (1:1, v/v). Then, titrations of Nnon-Esterified Fatty Acids (NEFA) were carried with a 0.10 M alcoholic potassium hydroxide (KOH) solution.

Total plasma leptin concentrations (pg/mL) were determined using an ELISA kit (Human leptin Immunoassay, catalog no. DLP00; R&D Systems). The minimum detectable concentration was typically less than 7.80 pg/mL. The intra-and inter-assay CVs were 3.10% and 4.50%, respectively.

Fasting insulin concentrations were measured by an ELISA kit (Human Insulin ELISA Kit, cat#: ELH-Insulin-001; RayBiotech, Inc.). The minimum detectable concentration was <4 µIU/mL. The intra-and inter-assay CVs were <10% and <12%, respectively. Insulin resistance was calculated with the homeostasis model assessment of insulin resistance (HOMA-IR) method using the following equation: fasting plasma insulin (µUI/mL) x fasting plasma glucose (mmol/L)/22.50 [19].

Statistical analysis

Statistical analyzes were performed using StatView ® software (version 5, SAS Institute Inc. Copyright © 1992-1998). Pearson's test (*r*) was used for correlating different parameters. Comparison of different variables in various groups was done using Student *t* test (two groups) and ANOVA (Bonferroni).. All numeric variables were expressed as mean ± Standard Deviation (SD). The statistical level of significance was established at 5%.

Results

Based on obesity (BMI ≥30 kg/m^2), the majority of patients enrolled were female. According to the IDF criteria, the prevalence of MS was significantly higher in women (70.59%) than in men (29.41%). As expected, mean levels of BMI, Waist Circumference (WC), Hip Circumference (HC), Waist to Hip Ratio (Wc/Hc), SBP, DBP, glucose, Triglycerides (TG), Total Cholesterol (TC), LDL-C, C-Reactive Protein (CRP) were significantly increased and HDL-C levels were significantly reduced in obese subjects with and without MS compared to controls. Anthropometric and biochemical parameters were shown in Tables 1 and 2, respectively.

Plasma leptin concentrations were higher in obese subjects with and without MS compared to control group (47.53 ± 19.27; 48.91 ± 31.11 and 23.09 ± 11.31, pg/mL, $p<0.01$ and $p<0.001$ respectively) (Figure 1A). In obese subjects Ob and Ob-MS, plasma insulin levels and HOMA-IR were increased (Figure 1B and 1C). The plasmatic Non-Esterified Fatty Acids (NEFA) concentrations, compared to control subjects (1.37 ± 0.32 mmol/L) showed significant differences between obese patients Ob (1.81 ± 0.51; $p<0.01$) and Ob-MS patients (1.92 ± 0.32, $p<0.001$) (Figure 1D).

Correlations of leptin and insulin with variables related to MS were performed. Overall, there were positive correlations between leptin and BMI ($r=0.581$, $p<0.001$) (Figure 2A), Wc ($r=0.365$, $p<0.01$), Hc ($r=0.478$, $p<0.001$) in the total population. Also, there were significant positive correlations for insulin with BMI ($r=0.344$, $p<0.05$) (Figure 2B), Wc ($r=0.468$, $p<0.01$), Hc ($r=0.358$, $p<0.05$), TC ($r=0.318$, $p<0.05$) and LDL-C ($r=0.343$, $p<0.05$) and SBP ($r=0.382$, $p<0.05$) in the total population. In addition, within the control group, insulin was significantly correlated to SBP ($r=0.625$, $p<0.05$).

The HOMA-IR was positively correlated to SBP only in the total population ($r=0.609$, $p<0.001$) and in the control group ($r=0.629$, $p<0.05$) but with DBP, HOMA-IR was positively correlated only in the total population ($r=0.339$, $p<0.05$) (Table 3).

Discussion

The aim of our investigation was to evaluate the association of obesity, in the presence or not of MS, with leptinemia, insulinemia and lipid profile in subjects from the region of Cap-Bon in northeastern Tunisia. Over the past two decades, the MS has become a global problem of public health. As a developing country in the Eastern Mediterranean Region, Tunisia has seen socio-economic and urban changes, related to the adoption of sedentary lifestyles and new dietary habits that may lead to increased prevalence of Ob and MS [20,21]. Our

Sex	C (n=30)			Ob (n=33)			Ob-MS (n=34)		
	Total (n=30)	Men (n=15)	Women (n=15)	Total (n=33)	Men (n=30)	Women (n=30)	Total (n=34)	Men (n=30)	Women (n=30)
Age (years)	42.12 ± 21.03	52.50 ± 24.82	31.75 ± 9.23	51.64 ± 15.54	51.25 ± 17.29	51.77 ± 15.73	55.35 ± 12.75^{a}	60.80 ± 9.65	53.08 ± 13.55
BMI (kg/m^{2})	22.75 ± 2.26	22.55 ± 2.58	22.95 ± 2.06	31.46 ± 2.11^{aaa}	30.16 ± 0.14	31.86 ± 2.29	34.36 ± 4.58^{aaab}	32.27 ± 3.02	35.24 ± 4.94
Wc (m)	0.87 ± 0.08	0.91 ± 0.07	0.84 ± 0.09	1.03 ± 0.06^{aaa}	1.08 ± 0.08	1.02 ± 0.06	1.13 ± 0.12^{aaabb}	1.13 ± 0.14	1.14 ± 0.13
Hc (m)	0.98 ± 0.06	0.98 ± 0.06	0.99 ± 0.07	1.12 ± 0.08^{aaa}	1.11 ± 0.06	1.12 ± 0.09	1.13 ± 0.11^{aaa}	1.10 ± 0.05	1.15 ± 0.13
Wc/Hc	0.88 ± 0.05	0.93 ± 0.01	0.85 ± 0.05***	0.92 ± 0.07	0.97 ± 0.04	0.90 ± 0.08	0.99 ± 0.09^{aaab}	1.02 ± 0.10	0.98 ± 0.09
SBP (mmHg)	109.37 ± 9.28	110.00 ± 9.26	108.75 ± 9.91	120.58 ± 12.48^{aaa}	122.50 ± 18.93	120.00 ± 10.80	131.76 ± 15.50^{aaab}	138.00 ± 14.83	129.17 ± 15.64
DBP (mmHg)	63.12 ± 7.93	62.50 ± 4.63	63.75 ± 10.61	72.35 ± 11.47^{a}	72.50 ± 15.00	72.31 ± 10.92	76.47 ± 12.21^{aaa}	82.00 ± 13.04	74.17 ± 11.64

Table 1: Anthropometric and clinical parameters by sex type. Data are presented as mean ± SD. C: Control Group, Ob: Obese Without MS group, Ob-MS: Obese with MS group, BMI: Body Mass Index, Wc: Waist Circumference, Hc: Hip Circumference, Wc/Hc: Waist and Hip Circumference ratio, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure. ^{a}p<0.05; ^{aa}p<0.01; ^{aaa}p<0.001; difference from control group. ^{b}p<0.05; ^{bb}p<0.01; ^{bbb}p<0.001; difference from obese group without MS. *p<0.05; **p<0.01;***p<0.001; difference from men

Sex	C (n=30)			Ob (n=33)			Ob-MS (n=34)		
	C (n=30)	Men (n=15)	Women (n=15)	Ob (n=33)	Men (n=30)	Women (n=30)	Ob-MS (n=34)	Men (n=30)	Women (n=30)
Glucose (mmol/L)	5.14 ± 0.39	5.09 ± 0.45	5.20 ± 0.33	5.88 ± 1.17^{a}	5.57 ± 1.06	5.98 ± 1.23	11.47 ± 4.93^{aaabbb}	9.22 ± 2.32	12.42 ± 5.49
TG (mmol/L)	0.87 ± 0.50	1.01 ± 0.62	0.74 ± 0.35	1.39 ± 0.69^{a}	1.67 ± 1.05	1.31 ± 0.58	2.02 ± 0.71^{aaab}	2.24 ± 0.69	1.94 ± 0.73
TC (mmol/L)	3.70 ± 0.98	3.85 ± 1.11	3.55 ± 0.87	4.91 ± 1.02^{aa}	5.50 ± 1.44	4.74 ± 0.86	5.24 ± 1.77^{aa}	5.94 ± 2.13	4.95 ± 1.61
LDL-C (mmol/L)	2.35 ± 0.92	2.34 ± 0.94	2.38 ± 0.98	3.34 ± 0.93^{a}	4.16 ± 1.12	3.09 ± 0.75*	3.55 ± 1.44^{aa}	4.25 ± 1.98	3.26 ± 1.14
HDL-C (mmol/L)	0.94 ± 0.39	1.05 ± 0.20	0.84 ± 0.52	0.85 ± 0.31^{a}	0.59 ± 0.40	1.05 ± 1.91**	0.72 ± 0.30^{aab}	0.68 ± 0.22	0.74 ± 0.34
C-RP (mg/L)	2.32 ± 2.09	2.21 ± 1.06	2.40 ± 1.95	4.45 ± 3.58^{aaa}	4.02 ± 2.65	4.50 ± 3.37	5.67 ± 3.78^{aaabb}	5.37 ± 3.52	5.40 ± 3.34
Urea (mmol/L)	4.78 ± 2.29	5.59 ± 3.00	3.97 ± 0.86	5.11 ± 1.54	5.60 ± 1.09	4.96 ± 1.67	6.45 ± 2.48	6.24 ± 3.24	6.55 ± 2.27
Creatinine(umol/L)	72.18 ± 13.09	80.00 ± 3.00	64.37 ± 11.22*	72 ± 8.32	76.75 ± 7.45	70.54 ± 8.28	79 ± 12.42	87.00 ± 12.35	75.67 ± 11.30
Ur-ac (umol/L)	218.25 ± 105.14	261.50 ± 134.26	175.00 ± 37.28	222.23 ± 43.50	249.25 ± 18.21	213.92 ± 46.07	307.05 ± 110.60^{aabb}	353.40 ± 97.57	287.75 ± 113.79

Table 2: Biochemical Parameters by sex type. C: control group, Ob: Obese Without MS group, Ob-MS: Obese with MS group, TG: Triglycerides, TC: Total-Cholesterol, LDL-C: Low Density Lipoprotein-Cholesterol, HDL-C: High Density Lipoprotein-Cholesterol, CRP: C-Reactive Protein, Ur-ac: Uric Acid. ^{a}p<0.05; ^{aa}p<0.01; ^{aaa}p<0.001; difference from control group. ^{b}p<0.05; ^{bb}p<0.01; ^{bbb}p<0.001; difference from obese group without MS. *p<0.05; **p<0.01;***p<0.001; difference from men.

findings showed obesity is significantly different among different age groups. In a previous study, Gharipour et al. showed an increasing in management of individual components of MS such diabetes, HTA and dyslipidemia [22], also, the prevalence of MS in subjects aged over 60 years was significantly higher than those under 60 [23].

The MS was identified according to the IDF criteria, because the prevalence of MS according to WHO and NCEP ATP III definitions are similar 28.4 and 24%, but they will still be remarkably lower than those of the IDF. The main reasons seem to be the main square concerned abdominal obesity, in addition to the position of IR, and more specifically of T2DM, which is particularly very common in the Arab population and its frequency is increasing significantly in most regions of the world [24]. Our data based on the IDF criteria showed that approximately one third of the studied population had MS. In the same context, national studies showed that the prevalence of MS increase with age in both sexes, especially among women (70.59%) than in men (29.41%) [25,26].

The aim of our investigation was to evaluate the relationship between leptin levels in obesity associated or not with MS. In total population, leptin levels were positively correlated to BMI, Wc, Hc and SBP. These results clarified the association of leptin with obesity, confirming earlier findings [9,10]. Furthermore, plasma leptin concentrations were higher in obese subjects with and without MS, with a minor decrease in the last one. According to the study of Paz-Filho et al. [27], the production of leptin by the adipose tissue is reduced in obese subjects meeting three or more criteria of MS, which explain the slight decrease in leptin levels observed in the Ob-MS group compared to the Ob group. The mechanism by which leptin levels decrease in presence of MS is still unclear, this finding suggest a state of relative leptin deficiency in obesity associated with more advanced stages of MS. Additional studies are needed to verify this hypothesis and if it proves in the future to be true, leptin can be useful in selected obese patients to prevent or to ameliorate some components of MS.

The prevalence of hypertension was correlated with the degree of insulin and insulin resistance. It has been reported that MS is present in approximately one third of patients with hypertension [28]. We found also that circulating concentrations of CRP were increased according to obesity, with higher values in Ob-MS group (p<0.001) compared to the Ob group, which is in line with other studies [29,30], showing simultaneous increasing levels of circulating CRP, TNF-α and IL-6 depending on the presence of the MS and diabetes. But the mechanism linking leptin and CRP is yet to be explained.

Within the total population there was a positive correlation of leptin with Wc and Hc but waist and hip circumference ratio has not shown such correlation. This is probably due to the association of Wc/Hc ratio with elevated levels of abdominal fat easily mobilized during android obesity, like in obese adolescent [31]. Or, probabely, another explanation is that it lies in a small sample from the general population and some associations may be not detected because we lack some statistical power.

Non-Esterified Fatty Acids (NEFA) play a complex role in glucidic homeostasis. This role led us to investigate their quantification in obese patients with and without metabolic syndrome. We found that plasma NEFA levels are elevated in obesity, mainly when it is associated with

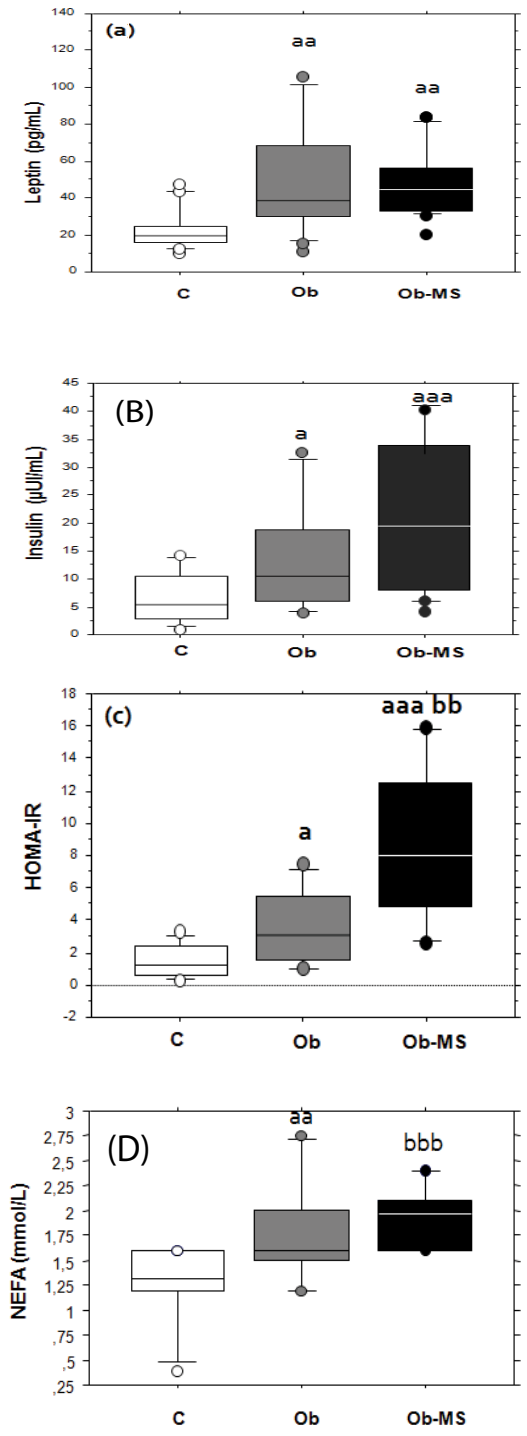

Figure 1: Means of Leptin (A), Insulin (B), HOMA-IR (C) and NEFA (D) in controls and obese with and without metabolic syndrome. HOMA: homeostasis model assessment, NFEA-non esterified fatty acid, C(n=30), Ob(n=33), Ob-MS(n=34). $^{a}p<0.05$; $^{aa}p<0.01$; $^{aaa}p<0.001$; from control group. $^{b}p<0.05$; $^{bb}p<0.01$; $^{bbb}p<0.001$; from obese group without MS

MS. Our results are consistent with earlier research. Thus, in all major insulin target organs (skeletal muscle, liver, endothelial cells), NEFA cause insulin resistance and have emerged as a major link between obesity, the development of MS, and atherosclerotic vascular diseases [32].

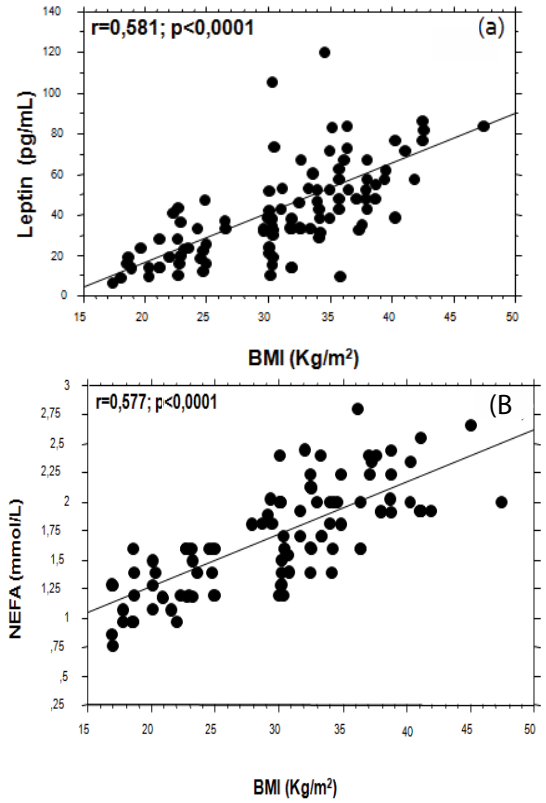

Figure 2: Correlation of Leptin (A) and NEFA (B) with BMI in all three groups. NFEA: Non Esterified Fatty Acid, BMI: Body Mass Index.

Leptin	C group (n=30)		Ob (n=33)		Ob-MS (n=34)	
	r	p	r	p	r	p
Insulin	0.134	0.685	0.284	0.333	-0.388	1.125
HOMA-IR	0.093	0.779	0.095	0.774	-0.472	0.124

Table 3: Correlation between Leptin, Insulin and HOMA-IR. C: Control Group, Ob: Obese without MS group, Ob-MS: Obese with MS group, HOMA-IR: Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

In addition, insulin was positively correlated with TC and LDL-C in the total population ($p < 0.05$). Our results are consistent with those reported by other studies. Reduced number of LDL receptors appears secondary to relative insulin deficiency. However, insulin induces the expression of LDL receptors and the treatment of patients with T2DM restores a normal number of LDL receptors [33].

We note in the total population a positive correlation between leptin and SBP. Similar results were reported by Gálvez Prieto et al. [34] who found that leptin induces vasodilation by the production of nitric oxide in the segments of the aorta. In control group, there was a positive correlation of leptin with LDL-C. These results suggest that there is a consisting link between LDL-C and leptin levels only in subjects with normal weight. However, when the individual becomes obese cases of Ob and Ob-MS groups, there would be no correlation. Hence, the increase of LDL-C in obesity may be a compensatory mechanism for the development of leptin resistance at an early stage.

Moreover, no significant correlation was observed between leptin and insulin or HOMA-IR. Increased fat mass and decreased leptin increases insulin production. However, there is a feedback loop,

called insulin adipo-axis where insulin increases leptin secretion that in response inhibits insulin secretion. However, in insulin-resistant patients, the loop is disrupted and therefore it would be responsible for hyper-leptinemia and hyper-insulinemia observed in T2DM. These data highlight the central role of adipocyte dysfunction in pathogenesis of insulin resistance. In a prospective study, leptin plasma levels, when controlling for BMI, predicted the development of MS as well as the development of glucose intolerance and insulin resistance [35].

Several limitations of the present study must be considered. First, this study was performed on limited sample size and requiring confirmation by prospective studies. Second, despite its advantages, the HOMA-IR showed limitations. In this context, Inoue et al. [36] have found that this index cannot diagnose insulin resistance in diabetic subjects with moderate hyperglycemia, where the ability of insulin secretion can no longer ensure glucose homeostasis. Similarly, a study on people with normal and impaired glucose tolerance showed that HOMA-IR was poor correlation in patients with type 2 diabetes [37].

Conclusion

In total, results from the population of Cap-Bon, show that the degree of obesity is more pronounced in the MS. Insulinemia and HOMA-IR were increased in obesity more severely if it is associated with the MS *vs.* leptinemia which decreased slightly with MS. However no associations were found between leptinemia and insulinemia.

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Conflict of Interest

The authors declare no conflict of interest.

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