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Association of free fatty acids with the insulin-resistant state but not with central obesity in individuals from Venezuela.

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Key words: Venezuelans, free fatty acids, insulin resistance, obesity, subcutaneous fat.

Abstract. Individuals with insulin resistance (IR) usually have upper body obesity phenotype, often accompanied by an increase in plasma free fatty acids (FFA). Since the Venezuelan population has a high frequency of IR and central obesity, the purpose of this work was to determine FFA levels in 47 Venezuelan individuals, men and women, 24-58 years old, and analyze their relationship with central obesity and parameters of carbohydrate and lipid metabolism. Basal concentrations of TG, total cholesterol, LDL-C, and HDL-C were measured, and FFA, glucose and insulin, at basal state and at different times after a glucose load. Eighteen individuals presented insulin resistance (HOMA-IR >2.7) and 29 were non-insulin resistant (non-IR). Insulin resistant individuals (IR) had higher waist circumference, BMI and basal concentrations of FFA than the non-IR. No differences were observed in skin folds and other basal lipids studied. The increased FFA seemed to be related to the IR associated to BMI and not to central obesity, since the difference between IR and non-IR disappeared when they were matched for waist circumference. After a glucose load, FFA decreased in both groups, but remained significantly elevated in IR subjects. This effect disappeared after matching for BMI or waist circumference, inferring that it was independent of anthropometrics. FFA were positively associated with HOMA-IR, glucose and TG levels; however, there was no association with BMI or waist circumference. These findings, and the lack of elements to support the presence of hepatic IR, common to increased visceral lipolysis, might suggest that the IR present in the obese individuals studied, might be due to an increase in subcutaneous fat.

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Asociación de los ácidos grasos libres con el estado de insulino-resistencia pero no con obesidad central en individuos venezolanos.

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Palabras clave: Venezolanos, ácidos grasos libres, insulino-resistencia, obesidad, grasa subcutánea

Resumen. Los individuos con insulino-resistencia (IR) usualmente presentan obesidad central, fenotipo comúnmente acompañado de incremento de ácidos grasos libres (AGL). Como los individuos venezolanos presentan una alta frecuencia de IR y obesidad central, el objetivo de este trabajo fue analizar, en un grupo de ellos, la relación entre AGL y obesidad central y parámetros relacionados con el metabolismo de carbohidratos y lípidos. En 47 venezolanos, hombres y mujeres, entre 24 y 58 años, se determinaron las concentraciones basales de TG, Colesterol total, LDL-C, HDL-C y AGL, glucemia e insulina a nivel basal y a diferentes tiempos después de una sobrecarga glucosada. Dieciocho individuos resultaron IR (HOMA-IR > 2,7) y 29 no IR. Los IR presentaron mayor circunferencia de cintura (CC), índice de masa corporal (IMC) y concentraciones basales de AGL. No hubo diferencias en los pliegues cutáneos ni en los otros lípidos. Los valores elevados de AGL parecieron relacionarse con la IR asociada al IMC y no a la obesidad central puesto que una vez apareados por CC, la diferencia en los valores de AGL entre IR y no-IR desapareció. Después de la sobrecarga glucosada los AGL disminuyeron en ambos grupos, pero permanecieron significativamente elevados en los IR. Esta diferencia desapareció al aparear por IMC o CC. Los AGL estuvieron significativamente asociados a HOMA-IR, glucemia y TG, sin embargo no se encontró asociación con IMC o CC. Estos hallazgos, más la falta de elementos que apoyen la presencia de IR hepática, común en un incremento de la lipólisis visceral, sugieren que la IR presente en estos individuos obesos pueda ser debida a incremento de la grasa subcutánea.

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INTRODUCTION

Insulin resistance is commonly associated with multiple adverse consequences such as dyslipidemia, impaired fasting glucose, and increased blood pressure, all of which predispose to endothelial dysfunction and atherosclerosis. Individuals with insulin resistance (IR) usually present with upper body obesity. This phenotype is often accompanied by an increase in plasma free fatty acids (FFA) flux and concentration. Increased plasma FFA may contribute to IR by promoting excess ectopic (non-adipose) triglyceride (TG) content of the liver and other organs, inhibiting the ability of insulin to stimulate muscle glucose uptake and to suppress hepatic glucose production (1). Excess FFA entry into pancreatic islets may be an important factor in the reduction in beta cell function, commonly seen in diabetic and pre-diabetic states. IR may, in

turn, contribute to increased plasma FFA since IR appears to reduce the ability of insulin to suppress hormone sensitive lipase and the release of FFA into the plasma by adipocytes (2). The Venezuelan population has a high frequency of IR, central obesity and hypertension (3-5), but we are aware of no published data on FFA levels in this group, or on their relationship to these conditions. The purpose of this work was to study FFA levels in individuals with or without IR, and the relationship of plasma FFA with central obesity and parameters of carbohydrate and lipid metabolism.

MATERIAL AND METHODS

The sample consisted in 47 Hispanic individuals, 21 men and 26 women, 24 to 58 years old, apparently healthy community volunteers selected at random from a cardiovascular prevention program. None were taken any medication related to carbohydrate or lipid metabolism. The study was approved by the Instituto de Investigaciones Clinicas Review Board and previous written consent was obtained from each individual. Clinical characteristics were evaluated by standardized questionnaires. Blood pressure was measured with individuals in the sitting position using a standard mercury sphygmomanometer. Anthropometric measurements (height, weight, waist circumference and skin folds) were obtained using standard techniques (4). BMI was expressed as Kg/m^2.

After a fast of 10-12 h, a blood sample was taken and all subjects went a 75 g glucose load. After the glucose load, samples were taken at 60 and 120 min. From the fasting sample, serum glucose, TG, total cholesterol and HDL-cholesterol (HDL-C) were determined by enzymatic methods (Human, Germany) and LDL-cholesterol (LDL-C) was estimated as in (6). Fasting samples and from each time point after the glucose load were frozen at –70°C for determination of serum insulin (Diagnostic Products, Inc. USA), and plasma FFA (Wako Chemicals, USA). Blood samples for the determination of FFA were collected in ice-cold tubes containing 0.1% EDTA, plasma was obtained after centrifugation at 4°C at 2000 rpm, frozen immediately and processed not later than 3 months.

The Homeostasis Model Assessment (7) was used as surrogate measure of the degree of insulin resistance (HOMA-IR = insulin (μU/mL) × glucose (mmol/L) / 22.5) and beta cell function (HOMA-beta cell = 20 x insulin (μU/mL) / glucose (mmol/L) – 3.5)). A cut off value of 2.7 was taken as representative of IR (8).

The matching process was manual, matching one dataset to another and comparing each value in one dataset with each value in a second data set grouping the most similar ones (9).

Statistical analysis. Data are presented as means ± standard deviations. To determine the normality of the variables, the Kolmogorov-Smirnov test was applied. In those variables with normal distribution, the significance of differences between the basal values, as well as the samples taken after the glucose load, from IR and non-IR individuals, were tested by the Student's t test, for independent samples. Those without normal distribution were analyzed using the Mann-Whitney U test. In order to establish the effect of BMI and waist, the anthropometric and biochemical data were matched for these two variables. Simple correlations and partial correlations, adjusted for BMI and waist were calculated by the Pearson's method. The responses of glucose, insulin and FFA to the glucose load in insulin resistant and non-IR individuals were analyzed by a t test adjusting by BMI and waist. A p value of 0.05 or less was considered significant. All statistical analyses were performed using SPSS 12.0.

RESULTS

The demographic and basal biochemical characteristics are shown in Table I. From the 47 individuals, 18 (38.3%) were found insulin resistant (HOMA-IR value >2.7) There were no significant differences in age or blood pressure between the two groups, but the IR individuals had significantly higher BMI and waist circumference, despite not having differences in skin folds. The mean values for basal cholesterol, TG and LDL-C were not abnormal in any of the two groups and there were no differences between them. The HDL-C values were low in both groups, with no statistical differences between them.

Fasting FFA, glucose and insulin values were significantly higher in the IR subjects, but only two of them had impaired fasting glucose (over 100 mg/dL). Although by design, HOMA-IR was higher in the IR individuals, they did not differ from non-IR subjects in calculated HOMA-beta cell function.

When the individuals were matched by waist (Table II), glucose, insulin and HOMA-IR were kept significantly higher ($p < 0.01$) in IR individuals, while the difference in FFA levels disappeared. However,

TABLE I
CHARACTERISTICS OF SUBJECTS WITHOUT AND WITH INSULIN RESISTANCE

	No insulin resistant (Homa-IR ≤ 2.7)	Insulin resistant (Homa-IR > 2.7)		
n (women/men)	29(18/11)	18(8/10)	*p	**p
Age (years)	41.27 ± 10.78	36.66 ± 11.17	0.245	
SBP (mmHg)	123.20 ± 15.32	122.05 ± 12.97		0.689
DBP (mmhg)	82.65 ± 11.45	87.27 ± 10.75		0.175
BMI (Kg/m^2)	29.20 ± 5.36	34.52 ± 7.05	0.011	
Waist (cm)	98.24 ±11.78	108.32 ± 14.62	0.023	
Bicipital skin fold (cm)	12.61 ± 6.27	14.98 ± 8.05	0.232	
Tricipital skin fold (cm)	21.28 ± 5.92	24.05 ± 8.34	0.203	
Subscapular skin fold (cm)	23.16 ± 6.41	25.16 ± 8.17	0.084	
B+T+SS (cm)	56.07 ± 14.87	63.54 ± 20.07	0.060	
Total Cholesterol (mg/dL)	152.31 ± 32.03	157.00 ± 36.83	0.808	
Triglycerides (mg/dL)	122.48 ± 81.98	144.38 ± 94.33		0.393
HDL-C (mg/dL)	39.79 ± 11.79	37.38 ± 8.61		0.681
LDL-C (mg/dL)	87.72 ± 29.21	90.66 ± 25.91	0.688	
FFA (mmol/L)	0.42 ± 0.11	0.50 ± 0.14		0.038
Insulin (μU/mL)	9.42 ± 2.87	19.23 ± 5.73	0.000	
Glucose (mg/dL)	76.48 ± 8.77	89.00 ± 25.18		0.005
HOMA-IR	1.75 ± 0.51	4.36 ± 1.89		0.000
HOMA-beta cell	372.85 ± 411.23	358.24 ± 158.90		0.085

Data are means ± SD. SBP: systolic blod pressure. DPB: diastolic blood pressure. BMI: body mass index. B+T+SS: sum of skin folds. FFA: free fatty acids. *p: t test for independent samples. **p: Mann-Whitney *U test*.

TABLE II
CHARACTERISTICS OF SUBJECTS WITHOUT AND WITH INSULIN RESISTANCE MATCHED FOR WAIST

	No insulin resistant (Homa-IR ≤ 2.7)	Insulin resistant (Homa-IR > 2.7)		
n (women/men)	9(5/4)	9(4/5)	*p	**p
Age (years)	38.67 ± 10.98	43.13 ± 9.70	0.388	
SBP (mmHg)	120.44 ± 11.15	126.25 ± 13.90	0.363	
DBP (mmhg)	82.33 ± 11.09	89.75 ± 11.72	0.202	
BMI (Kg/m^2)	29.74 ± 5.04	34.55 ± 4.10	0.047	
Waist (cm)	100.85 ± 13.71	106.25 ± 6.91	0.318	
Bicipital skin fold (cm)	11.88 ± 5.53	15.50 ± 8.70		0.277
Tricipital skin fold (cm)	22.03 ± 5.78	22.87 ± 9.37	0.830	
Subscapular skin fold (cm)	24.44 ± 7.07	26.00 ± 9.31	0.702	
B+T+SS (cm)	58.33 ± 16.02	68.12 ± 25.07	0.063	
Total Cholesterol (mg/dL)	159.33 ± 39.39	161.00 ± 43.77	0.936	
Triglycerides (mg/dL)	136.89 ± 76.37	133.00 ± 68.23	0.913	
HDL-C (mg/dL)	37.11 ± 8.53	37.00 ± 7.36	0.977	
LDL-C (mg/dL)	92.56 ± 26.02	97.38 ± 25.09	0.703	
FFA (mmol/L)	0.47 ± 0.13	0.50 ± 0.15	0.659	
Insulin (μU/mL)	10.44 ± 3.71	18.88 ± 7.11		0.007
Glucose (mg/dL)	74.89 ± 4.85	87.88 ± 8.02		0.002
HOMA-IR	1.91 ± 0.66	4.16 ± 2.06		0.000
HOMA-beta cell	468.20 ± 525.56	278.21 ± 64.64		0.743

Data are means ± SD. SBP: systolic blood pressure. DPB: diastolic blood pressure. BMI: body mass index. FFA: free fatty acids. B+T+SS: sum of skin folds. *p: t test for independent samples. **p: Mann-Whitney *U test*.

when matched by BMI (Table III) the same results were obtained, but the differences in FFA concentrations were even more significant. The responses of glucose, insulin and FFA after the glucose load are shown in Fig 1. Individuals with IR showed higher levels of glucose at all time-points, but only two of the IR subjects resulted with impaired fasting glucose and only one with impaired glucose tolerance (2 h post-challenge glucose over 140 mg/dL). Insulin levels were also significantly higher in individuals with IR at all time points.

The pattern of the decline response of FFA after the glucose load was similar in both groups; however, in individuals with IR, the levels of FFA were kept higher at all points.

When adjusted by waist, glucose and insulin levels were kept higher at 120 min, while no difference in FFA was observed. When adjusted by BMI, no differences were found for glucose, insulin or FFA (data not shown).

Simple Pearson's correlation coefficients were calculated to assess the rela-

TABLE III
CHARACTERISTICS OF SUBJECTS WITHOUT AND WITH INSULIN RESISTANCE MATCHED FOR BMI

	No insulin resistant (Homa-IR ≤ 2.7)	Insulin resistant (Homa-IR > 2.7)		
n (women/men)	10(8/2)	9(2/7)	*p	**p
Age (years)	41.40 ± 13.28	36.44 ± 9.22	0.355	
SBP (mmHg)	121.50 ± 15.07	124.67 ± 10.57		0.138
DBP (mmhg)	80.70 ± 9.04	88.33 ± 8.91	0.082	
BMI (Kg/m^2)	32.66 ± 5.81	33.00 ± 6.49		0.806
Waist (cm)	103.65 ± 7.76	106.92 ± 10.90	0.468	
Bicipital skin fold (cm)	16.70 ± 6.70	13.88 ± 8.16	0.427	
Tricipital skin fold (cm)	24.30 ± 5.96	22.33 ± 7.39	0.536	
Subscapular skin fold (cm)	28.44 ± 4.44	27.22 ± 7.18	0.671	
B+T+SS (cm)	68.22 ± 14.31	63.44 ± 20.67	0.578	
Total Cholesterol (mg/dL)	161.50 ± 39.21	160.22 ± 42.60	0.947	
Triglycerides (mg/dL)	131.00 ± 75.72	173.67 ± 117.96	0.370	
HDL-C (mg/dL)	34.10 ± 7.82	35.22 ± 6.03		0.594
LDL-C (mg/dL)	96.40 ± 26.36	92.67 ± 25.04	0.756	
FFA (mmol/L)	0.41 ± 0.11	0.58 ± 0.15	0.015	
Insulin (μU/mL)	9.99 ± 2.73	19.77 ± 5.10	0.000	
Glucose (mg/dL)	75.10 ± 8.93	94.33 ± 34.35		0.022
HOMA-IR	1.75 ± 0.52	5.11 ± 2.29	0.002	
HOMA-beta cell	252.92 ± 207.48	313.87 ± 179.28	0.515	

Data are means ± SD. SBP: systolic blod pressure. DPB: diastolic blood pressure. BMI: body mass index. FFA: free fatty acids. B+T+SS: sum of skin folds. *p: t test for independent samples; **p: Mann-Whitney *U test*.

tionship among basal FFA levels and anthropometric and biochemical parameters. In the IR individuals, FFA showed no association with BMI, waist circumferences, skin folds, insulin or HOMA-beta cell, but was positively associated with blood pressure, TG, glucose and with HOMA-IR (Table IV). Partial correlation analysis showed that these associations persisted after adjusting for waist (Table V) or BMI (Table VI). Interestingly, the relationship with HOMA-beta cell after adjusting for BMI became significant.

DISCUSSION

In the population studied, Venezuelans below 60 years of age, it was found that 38.3% of individuals were IR, similar to previously reported frequencies for this population (3-5). They did not differ from the non-IR in age, blood pressure or lipid profile, values that were between normal limits in both groups. However, the basal FFA levels were significantly higher, as previously shown by several authors (10-12) in IR individuals.

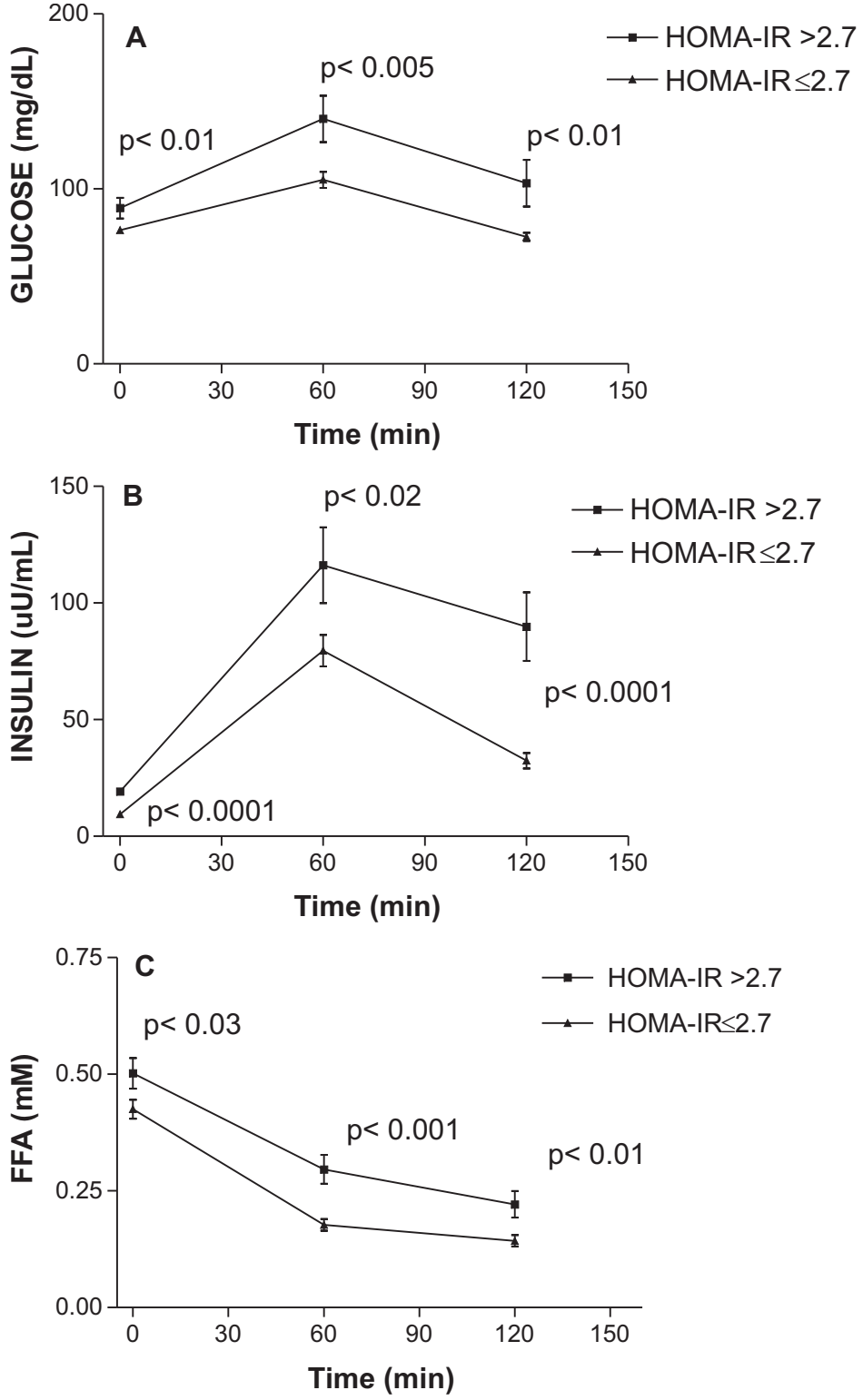

Fig. 1. Pattern of response of glucose (A), insulin (B) and free fatty acids (C) after the glucose load in individuals with and without insulin resistance. Data are expressed as means ± standard deviation.

TABLE IV
PEARSON CORRELATION BETWEEN BASAL FFA AND DIFFERENT PARAMETERS IN SUBJECTS WITH AND WITHOUT INSULIN RESISTANCE

	No insulin resistant (Homa-IR ≤ 2.7) *29(18/11)		Insulin resistant (Homa-IR > 2.7) *18(8/10)	
Basal FFA vs:	r	p	r	p
SBP (mmHg)	0.33	0.07	0.57	0.01
DBP (mmHg)	0.28	0.13	0.52	0.02
BMI (Kg/m^2)	0.13	0.49	0.03	0.88
Waist (cm)	0.18	0.33	0.09	0.71
Bicipital skin fold (cm)	0.21	0.28	0.07	0.76
Tricipital skin fold (cm)	0.16	0.39	0.07	0.77
Subscapular skin fold (cm)	–0.02	0.88	0.12	0.61
B+T+SS (cm)	0.18	0.33	–0.05	0.83
Total Cholesterol (mg/dL)	0.15	0.43	0.22	0.37
Triglycerides (mg/dL)	–0.028	0.88	0.52	0.02
HDL-C (mg/dL)	0.01	0.97	–0.33	0.17
LDL-C (mg/dL)	0.18	0.33	0.04	0.85
Insulin (μU/mL)	0.26	0.16	0.32	0.19
Glucose (mg/dL)	0.11	0.54	0.74	0.001
Homa-IR	0.30	0.1	0.67	0.002
Homa-beta cell	0.05	0.78	–0.43	0.07

*n (women/men). SBP: systolic blood pressure. DBP: diastolic blood pressure. BMI: body mass index. FFA: free fatty acids. B+T+SS: sum of skin folds.

These higher levels of FFA seemed to be more related to the IR associated to BMI and not to the central obesity present in the IR individuals, since when matched by BMI, this difference was still more evident, while when matched by waist, the difference in FFA between IR and non-IR disappeared. However this difference on the effect of body anthropometrics was not seen in the response pattern after the glucose load, because the differences observed in glucose, insulin and FFA levels after the load were abolished once adjusted for both, BMI and waist. It might be that the impaired fatty acid suppression in the IR subjects was independent of anthropometrics, since it has been described, at least in females, that the antilipolytic effect of insulin is reduced in omental adipocytes as compared to subcutaneous adipocytes (13).

On the other hand, in this study we could establish an obese group that was no insulin resistant and whose FFA concentrations were similar to the insulin-resistant; however, the BMI in this particular non-IR group was significantly lower than the BMI of the IR. The paradox of finding obesity without the presence of insulin resistance has been described in experimental animals (14, 15) and humans (16). Non diabetics Polynesians of New Caledonia, despite a high prevalence of central obesity, as

TABLE V
PARTIAL CORRELATION BETWEEN BASAL FFA AND DIFFERENT PARAMETERS, ADJUSTED FOR WAIST, IN SUBJECTS WITH AND WITHOUT INSULIN RESISTANCE

	No insulin resistant (Homa-IR ≤ 2.7) *29(18/11)		Insulin resistant (Homa-IR > 2.7) *18(8/10)	
Basal FFA vs:	r	p	r	p
SBP (mmHg)	0.18	0.37	0.57	0.02
DBP (mmHg)	0.04	0.83	0.54	0.03
BMI (Kg/m^2)	0.09	0.64	–0.15	0.58
Bicipital skin fold (cm)	0.40	0.05	0.01	0.95
Tricipital skin fold (cm)	0.04	0.84	0.02	0.92
Subscapular skin fold (cm)	0.07	0.71	0.20	0.44
B+T+SS (cm)	0.21	0.31	0.10	0.71
Total Cholesterol (mg/dL)	0.02	0.91	0.36	0.16
Triglycerides (mg/dL)	–0.29	0.15	0.57	0.02
HDL-C (mg/dL)	0.37	0.07	–0.39	0.13
LDL-C (mg/dL)	–0.02	0.92	0.22	0.41
Insulin (μU/mL)	0.22	0.28	0.25	0.33
Glucose (mg/dL)	–0.31	0.13	0.75	0.001
Homa-IR	0.14	0.49	0.67	0.004
Homa-beta cell	0.13	0.52	–0.47	0.06

*n (women/men). SBP: systolic blood pressure. DBP: diastolic blood pressure. BMI: body mass index. B+T+SS: sum of skin folds. FFA: free fatty acids.

judged by high BMI and waist, had low fasting insulin values and low degree of HOMA-estimated insulin resistance (16, 17). In this ethnic group these findings might be due to their genetic background or to their great physical activity, however we can not apply these concepts to our group.

As investigation into the relation between obesity and insulin resistance has intensified, certain fat compartments, in particular visceral fat, have been shown to be more functionally active than others.

Waist circumference has been taken as a good parameter to reveal visceral obesity; however, upper body obesity is determined by the accumulation of visceral plus subcutaneous fat. Visceral fat has been suggested to be causally related to insulin resistance (18), however several authors (19-22) have raised the opinion that subcutaneous abdominal adiposity was of greater importance than visceral adiposity in the presence of insulin resistance.

The group of Jensen (23) found that 20-30% of hepatic FFA delivery was originated from visceral lipolysis in obese subjects, while the contribution of splanchnic FFA release to systemic FFA was 15%. Therefore, they concluded that the contribution of visceral lipolysis to peripheral FFA is limited, even in obese adults, and it is unlikely to be a cause of insulin resistance in extrahepatic tissues, although it could con-

TABLE VI
PARTIAL CORRELATION BETWEEN BASAL FFA AND DIFFERENT PARAMETERS, ADJUSTED FOR BMI, IN SUBJECTS WITH AND WITHOUT INSULIN RESISTANCE

	No insulin resistant (Homa-IR ≤ 2.7) *29(18/11)		Insulin resistant (Homa-IR > 2.7) *18(8/10)	
Basal FFA vs:	r	p	r	p
SBP (mmHg)	0.18	0.38	0.58	0.02
DBP (mmHg)	0.04	0.82	0.54	0.03
Waist (cm)	0.01	0.95	0.17	0.51
Bicipital skin fold (cm)	0.38	0.06	0.06	0.82
Tricipital skin fold (cm)	0.002	0.99	0.09	0.73
Subscapular skin fold (cm)	0.02	0.90	0.28	0.28
B+T+SS (cm)	–0.004	0.98	0.18	0.49
Total Cholesterol (mg/dL)	0.03	0.86	0.29	0.26
Triglycerides (mg/dL)	–0.26	0.20	0.56	0.02
HDL-C (mg/dL)	0.31	0.12	–0.39	0.12
LDL-C (mg/dL)	–0.01	0.96	0.19	0.47
Insulin (μU/mL)	0.20	0.32	0.27	0.29
Glucose (mg/dL)	–0.30	0.13	0.74	0.001
Homa-IR	0.12	0.55	0.75	0.001
Homa-beta cell	0.13	0.51	–0.62	0.01

*n (women/men). SBP: systolic blood pressure. DBP: diastolic blood pressure. BMI: body mass index. B+T+SS: sum of skin folds. FFA: free fatty acids.

tribute to hepatic insulin resistance. The same conclusion has been pointed out by Klein (24).

Intrabdominal fat is composed of smaller but lipolytically active adipocytes and the FFA released by them go directly into the portal vein, increasing the levels of FFA in the liver, with subsequent increase in circulating TG. Moreover, visceral fat mass has been associated with glucose intolerance. In Mexican Americans (25), it was demonstrated that normal glucose-tolerant offspring of diabetic parents are insulin resistant in muscle and liver and, that the deficit in insulin action precedes the development of insulin secretion; however in these lean, normal glucose tolerant insulin resistant individuals, the disturbances in FFA metabolism were already well established.

Since, in the present study, most of the IR individuals did not show increase in TG concentrations or impaired fasting glucose or glucose intolerance, it might be assumed that the FFA released by visceral fat were not producing hepatic insulin resistance. Furthermore, the higher levels of FFA in the basal state, as well as after the glucose load, did not have any effect on HOMA-beta cell, suggesting no interference with insulin secretion at the present moment, although it can not be ruled out that the observed correlation among basal FFA levels and some components of the meta-

bolic syndrome (TG, blood pressure and the significant negative correlation with HOMA-beta cell observed when matched by BMI) might be indicative of future abnormalities in these individuals.

Koutsari and Jensen (22) refer that upper body subcutaneous fat was by far the major contributor to systemic FFA in both lean and obese humans under postabsortive conditions. Moreover, the same group and others (19-21) concluded that it appears that visceral fat has very little, if any, role in the oversupply of FFA to extra hepatic tissues. Based on those assumptions, it is suggested that general obesity or subcutaneous fat, especially in the upper body, is probably, in the individuals of the present study, the major contributor of this mediator to their insulin resistance. Although the lack of significance in skin folds measurements between the two groups might blunt this hypothesis, the trend observed in those measures, might suggest that increasing the number of studied cases, it could probably become significative.

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