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#### Original Article

## Association of obesity with leukocyte count in obese individuals without metabolic syndrome



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#### ABSTRACT

Aims: Inflammation in obesity is associated to insulin resistance (IR), hyperglycemia, hypertension and hyperlipidemia. Leukocytes play an important role in obesity associated inflammation. The initial factors that generate the inflammatory events in the obesity remain unclear. Therefore, the aim of this study was to determine the association of circulating leukocytes with clinical and biochemical parameters in obese individuals with clinical and biochemical parameters in normal range and with or without IR.

Methods: Nineteen obese non-diabetic and 9 lean subjects were studied for serum levels of insulin, lipids, glycated hemoglobin, glycemia, for clinical parameters as HOMA-IR, arterial pressure and anthropometric parameters, and for leukocyte counts. Neutrophil/lymphocyte ratio (N/L) was calculated using the  $\log_e$  of leukocyte counts. Association between leukocytes and studied parameters was determined by Pearson's correlation.

Results: Two groups of obese individuals were observed: with high levels of insulin (with IR) and with normal levels (without IR). Positive correlations were observed between leukocyte and lymphocyte counts with body mass index and HOMA-IR and negative correlation with decreased HDL levels. Lymphocytes correlated with increased levels of insulin. Leukocytes and neutrophils correlated positively with increased visceral fat and liver steatosis. These associations were absent in the obese group without IR. N/L ratio did not show correlations with studied parameters. The leukocyte associations were mainly observed in obese individuals with IR.

Conclusions: These data may represent initial leukocyte associations with morbidity features and define two different obese individuals that may evolve to the chronic inflammation observed in the obesity.

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#### 1. Introduction

Obesity is associated with pathologies that define the metabolic syndrome (MS). These include insulin resistance, hyperinsulinemia, impaired glucose tolerance, dyslipidemia, hypertension and obesity, in particular central adiposity [1]. The concurrence of any three of these conditions will result in a diagnosis of MS. Insulin resistance (IR) is a complication of chronic inflammation associated with obesity that increases the risk of developing metabolic diseases, resulting from the alteration of insulin-mediated signaling pathway

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leading to hyperglycemia and other alterations such as hypertension and hyperlipidemia [1]. This chronic inflammation has been focused on monocyte/macrophage infiltration and activation in the adipose tissue. However, unique roles have been shown for a variety of immune cells in this tissue, including cells from both innate and adaptive immune system [2–5]. Circulating leukocytes represent a key factor in the study of the pathogenesis of obesity. In this regard, association between leukocyte count and diabetes risk has been recently suggested [6,7]. It has been clearly demonstrated that the inflammatory status is a causative factor in diet-induced insulin resistance, but it remains unclear what is/are the initial(s) association of leukocytes and leukocyte subtypes with morbidity factors involved in MS. The obese individuals without clinical and biochemical alterations could represent an initial stage of inflammatory status during the

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obesity. Therefore, the aim of this study was to evaluate the associations of clinical and biochemical parameters with circulating leukocyte and leukocyte subtype counts in obese individuals with normal clinical and biochemical parameters and with or without IR.

#### 2. Subjects

Forty-four obese individuals were analyzed and chosen through a voluntary call to participate in the project. Only 19 obese nondiabetic subjects (20–55 years of age), with body mass index (BMI) greater than 30 kg/m<sup>2</sup> and 9 lean control individuals, whose BMI was less than 25 kg/m<sup>2</sup>, were selected in this study. All subjects fulfilled the inclusion criteria: absence of arterial hypertension, diabetes or other metabolic abnormalities, not evidence of hepatitis or HIV infection (determined by the absence of antibodies against the viruses), absence of any other current infectious processes, not taken any medications known to influence glucose or lipid metabolism or the inflammatory pathway, and in the case of women, not under hormonal contraceptive drugs. The project was approved by the Ethic Committee of the Instituto de Investigaciones Clínicas "Dr. Américo Negrette", University of Zulia in Maracaibo, Venezuela, according with the principles of the Declaration of Helsinki as revised in 2008. Written consent was obtained from all subjects.

Individual demographic information was collected including age, sex, qualifying criteria, current medications, height, weight and waist circumference. Body mass index was calculated from the formula: weight (kg)/height (m²), considering obesity when it was >30 kg/m². Absence of hypertension was confirmed by means of a sphyngomanometer. Ultrasound was used for the estimation of visceral fat and hepatic steatosis as described by Ryder et al. [8]. Grades of hepatic steatosis were assigned arbitrarely for statistical purposes; 1 represents: I/III, 2: I–II/III, 3: II/III and 4: II–III/III.

#### 3. Materials and methods

#### 3.1. Biochemical and hematological measurements

To each subject a fasting blood sample was withdrawn for the determination of biochemical parameters. Glucose, total cholesterol and triglycerides were measured enzymatically; high density

lipoprotein (HDL)-cholesterol was measured after precipitation of the apo B-containing lipoproteins (Human GmbH, Germany). Plasma insulin was determined by chemiluminescence immunoassay (IMMULITE 1000, Siemens Diagnostics, USA) and total glycated hemoglobin by the method of Bioscience Medical SL, Spain. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as: fasting insulin (IU/L)  $\times$  fasting glucose (mmol/L)/22.5 according to Mathews et al. [9], and the cut off point to consider IR was 2.6 [10,11]. The number of leukocytes and leukocyte subtypes were computed with an autoanalyzer (Beckman Coulter Counter, Coulters Corporation, FL, USA). The neutrophil: lymphocyte ratio was defined as the loge neutrophil count/loge lymphocyte count.

#### 3.2. Statistical analysis

The data were normally distributed and are expressed as the mean  $\pm$  standard error of the mean. Significant differences among groups were analyzed by ANOVA followed by Dunnet's test for multiple comparisons. Pearson's correlations were estimated for various blood cell counts with the numbers of obesity, metabolic and clinical markers using PRISM statistical software (GraphPad Software). Differences were considered statistically significant at p < 0.05.

#### 4. Results

None of the lean and obese individuals in this study had hypertension, hyperglycemia or elevated glycated hemoglobin, and their mean values for total and LDL cholesterol were similar among the three groups. As expected, the BMI, HOMA-IR, waist circumference and visceral fat of the obese with IR and obese without IR were elevated in relation to the control group; however, the obese with IR showed significantly increased values of BMI, HOMA-IR and insulin compared to the obese without IR. Triglyceride values were higher and HDL cholesterol lower in both obese groups; however, the mean values were in the normal range for this population (Table 1). Increased total leukocyte, neutrophil and lymphocyte counts were observed in obese individuals with IR (Fig. 1); however, the total values remained into the normal range. Positive correlations were observed between total leukocyte and lymphocyte counts with BMI and

**Table 1**Clinical and laboratory parameters in obese individuals with or without insulin resistance and in healthy lean control individuals.

Parameter	Control (A)	Ob IR (B)	Ob no IR (C)	A vs. B p value	A vs. C p value	B vs. C
Age (yrs)	$29.7 \pm 3.3$	$33.3 \pm 4.2$	$\textbf{38.7} \pm \textbf{3.4}$	NS	NS	NS
Body mass index (kg/m <sup>2</sup> )	$22.4\pm0.5$	$\textbf{37.8} \pm \textbf{0.8}$	$34.6\pm1.2$	< 0.01	< 0.01	< 0.05
Systolic blood pressure (mmHg)	$112.5 \pm 2.5$	$122.2\pm2.8$	$114.0\pm2.7$	< 0.05	NS	NS
Diastolic blood pressure (mmHg)	$75\pm1.9$	$\textbf{85.1} \pm \textbf{1.7}$	$76\pm1.6$	< 0.01	NS	< 0.01
Homa-IR	$\boldsymbol{0.83 \pm 0.2}$	$\textbf{5.83} \pm \textbf{0.7}$	$\textbf{1.48} \pm \textbf{0.2}$	< 0.01	NS	< 0.01
Waist circumference (cm)	$77\pm2.0$	$114.9 \pm 4.2$	$106\pm2.4$	< 0.01	< 0.01	NS
Insulin (µU/mL)	$4.1\pm1.0$	$25.3 \pm 2.8$	$\textbf{6.93} \pm \textbf{0.9}$	< 0.01	NS	< 0.01
Glycemia (mg/dL)	$80.3 \pm 3.8$	$\textbf{92.8} \pm \textbf{3.4}$	$\textbf{86.4} \pm \textbf{1.6}$	< 0.05	NS	NS
Glycated hemoglobin (%)	$6.11 \pm 0.14$	$\textbf{6.37} \pm \textbf{0.36}$	$\textbf{6.44} \pm \textbf{0.14}$	NS	NS	NS
Triglycerides (mg/dL)	$\textbf{80.3} \pm \textbf{3.8}$	$126.6 \pm 14.7$	$\boldsymbol{127.9 \pm 13.2}$	< 0.05	< 0.05	NS
Cholesterol (mg/dL)	$163.9 \pm 7.9$	$186\pm14.0$	$187.1 \pm 14.4$	NS	NS	NS
HDL-cholesterol (mg/dL)	$51.8 \pm 2.5$	$41\pm2.4$	$42\pm3.3$	< 0.05	< 0.05	NS
LDL-cholesterol (mg/dL)	$99.8 \pm 6.2$	$119.5\pm11.0$	$117.4\pm14.5$	NS	NS	NS
Visceral fat (cm)	$2.36\pm0.3$	$6.2 \pm 0.6$	$\textbf{5.4} \pm \textbf{0.4}$	< 0.01	< 0.01	NS

Ob IR: obese with insulin resistance; Ob no IR: obese without insulin resistance; values are expressed as mean  $\pm$  standard error.

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