Normal-weight obese syndrome: early inflammation?1–3

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ABSTRACT

Background: In obese subjects, the adipose mass represents an important source of proinflammatory cytokines. We have identified a new syndrome—the normal-weight obese (NWO) syndrome—in women with normal weight and body mass index but whose fat mass is >30% of their total body weight and whose risk of developing obesity-related diseases is likely increased.

Objective: The aim of the present study was to verify the hypothesis that NWO women are characterized by early inflammation, related to body fat mass, and that their plasma proinflammatory cytokine concentrations are greater than those of nonobese women.

Design: Twenty NWO, 20 preobese-obese, and 20 healthy (non-obese), age-matched white Italian women were studied. Anthropometric variables and plasma concentrations of proinflammatory cytokines and cardiovascular disease (CVD) risk factors were measured and compared between groups.

Results: Plasma values and body-composition measures were significantly different between the preobese-obese and nonobese women. No significant differences in body weight, laborat ory values, or CVD risk factors were found between the NWO and nonobese groups. Compared with concentrations in the NWO women, plasma concentrations of interleukin (IL)-1α, IL-1β, IL-6, IL-8, and TNF-α were significantly lower in the nonobese group and were significantly greater in the preobese-obese group. IL-6 and TNF-α concentrations were related to fat mass distribution in the NWO women.


KEY WORDS Body composition, fat mass, fat-free mass, metabolic diseases, cytokines

INTRODUCTION

Obesity represents an expansion of the adipose tissue mass, which is an important source of cytokines and contributes to a proinflammatory milieu (1). White adipose tissue appears to be functionally comparable with a dynamic endocrine organ (2, 3), producing and secreting various adipokines, such as leptin and adiponectin, and proinflammatory factors, such as tumor necrosis factor α (TNF-α), interleukin (IL)-6, and IL-1, all of which play an important role in the onset of cardiovascular disease (CVD), atherosclerotic processes, and insulin resistance (4–6). Actually, these cytokines are speculated to have a local and systemic action, e.g., by modulating insulin sensitivity and atherogenesis (7–9).

Recent reports have highlighted the finding that plasma proinflammatory cytokine concentrations turn out to be larger in humans and animals with excess adiposity (1, 10). Moreover, proinflammatory cytokines have been reported to induce the production and release of IL-8, a member of the CXC cytokine family, by different cell types, including human adipocytes. IL-8 has also been implicated in the pathogenesis of atherosclerosis (11, 12). Central obesity and excessive gain in abdominal fat correlate closely with hyperinsulinemia and insulin resistance and with the possibility of developing type 2 diabetes and coronary heart disease in both obese and in metabolically obese persons (13, 14). Population studies have shown that the metabolic syndrome plays a pivotal role in the occurrence of CVD (15, 16). Therefore, weight management can help to reduce the number of persons at risk of diabetes, CVD complications, or premature mortality (17, 18). The prevalence of the metabolic syndrome has been examined in persons with normal body mass indexes (BMIs; in kg/m²) and in those who are slightly overweight. It has been found to increase from 0.9–3% (at a BMI of 18.5–20.9) to 9.6–22.5% (at a BMI of 25–26.9), depending on sex and ethnicity (19). Moreover, in persons at reference body weight, the increased risk of the metabolic syndrome and CVD may have a genetic origin or be a consequence of body-composition abnormalities (20).

We have identified a new syndrome—normal-weight obese (NWO) syndrome. This syndrome is characterized by a normal body weight and BMI but a high fat mass (>30%) (21). Because NWO subjects do not have the metabolic syndrome, they are distinguished from metabolically obese normal-weight (MONW) persons (22, 23).

The purpose of this study was to assay the plasma concentrations of different cytokines, such as IL-1α, IL-1β, IL-2, IL-6,
IL-8, IL-10, IL-12p70, interferon γ (INF-γ), and TNF-α. Moreover, we examined the relations between these cytokines and percentage fat-free mass (%FFM), percentage fat mass (%FM), and selected lipid indexes associated with increased CVD risk in NWO persons as compared with nonobese and preobese-obese women.

Furthermore, we attempted to define the relations between anthropometric variables, selected lipid indexes, and secretion of proinflammatory cytokines as significant prognostic indicators of the risk of CVD and the metabolic syndrome.

SUBJECTS AND METHODS

Subjects

We studied 60 white Italian women aged 20–35 y from a population of 3000 volunteers, who were recruited by the medical and paramedical staff of the “Tor Vergata” University, in Rome, Italy. We identified 3 groups: 1) 20 women with a normal weight and a BMI < 25 (nonobese control group); 2) 20 nWHO women with a normal weight, a BMI < 25, and a %FM > 30%; and 3) 20 preobese-obese women with a BMI > 25 and a %FM > 30%. The subjects were classified as preobese-obese according to a World Health Organization (WHO) Technical Report (24). The NWO women were distinguished from the nonobese women on the basis of FM distribution determined by dual-energy X-ray absorptiometry (DXA), namely %FM classification criterion. All of the women were free of hypertension and CVD, had regular 28-d menstrual cycles, were in generally good health, did not smoke or abuse alcohol, and did not take any hormonal contraceptives or any other drug. All of the subjects provided consent to take part in the study, which was conducted according to the guidelines of the “Tor Vergata” University Medical Ethical Committee, Rome, Italy.

Anthropometric measurements

Anthropometric measurements were made according to standard methods for body weight, height, and waist circumferences (25, 26) after the subjects had been instructed to take off their clothes and shoes. Body weight (kg) was measured to the nearest 0.1 kg with a balance scale (Invernizzi, Rome, Italy). Height (m) was measured with a stadiometer to the nearest 0.1 cm (Invernizzi). Waist circumferences were measured with the use of a flexible steel metric tape to the nearest 0.5 cm. BMIs were calculated as body weight (kg)/height² (m²).

Dual-energy X-ray absorptiometry

Total body composition was assessed by DXA (Lunar DPX; G.E. Medical Systems, Waukesha, WI). Standard DXA calibration measurements were performed before each testing session. Subjects were required to remove all clothing, including shoes, socks, and jewelry, before lying on the DXA table in the supine position. The entire body was scanned beginning from the top of the head and moving in a rectilinear pattern down to the feet. The average measurement time was 20 min, and the overall radiation exposure was <8 Sv (21).

Analysis of blood samples

Blood samples (10 mL) were collected between days 8 and 12 of the preovulation phase into sterile tubes containing EDTA (evacuated tubes), via venipuncture early in the morning (0700–0900) after an overnight fast (12 h). All materials were immediately placed in ice, and plasma was separated by centrifugation at 1600 × g for 10 min at 4°C. Plasma samples were stored at −70 °C in 1-mL aliquots until assayed for the cytokine measurements. Plasma total cholesterol (TC), HDL-cholesterol, LDL-cholesterol, and triacylglycerol concentrations were measured through standard enzymatic colorimetric techniques (Roche Modular P800; Roche Diagnostics, Indianapolis, IN). Plasma high-sensitivity C-reactive protein (hs-CRP) concentrations were measured in plasma stored at −80 °C with a Behring latex-enhanced high-sensitivity assay on a Behring BN-100 nephelometer (Behring Diagnostic, Westwood, MA) and calibrators (N rheumatology standards SL) provided by the manufacturer. Plasma glucose concentrations were measured by using the glucose oxidase method with an automated glucose analyzer (COBAS INTEGRA 400; Roche Diagnostics). Serum insulin was also assayed with an immunoenzymometric assay (Megenix Ins-EASIA, Biosource, Belgium). Insulin resistance was determined by homeostasis model assessment of insulin resistance (HOMA-IR): fasting glucose (mmol/L) × fasting insulin (µIU/mL)/22.5. The analyses were carried out by the accredited Clinical Chemical Laboratories of the “Tor Vergata” Polyclinic, Rome, Italy.

Cytokine assay

Plasma concentrations of IL-1α, IL-1β, IL-2, IL-6, IL-8, IL-10, IL-12p70, INF-γ, and TNF-α were measured in duplicate by using the multiplex sandwich enzyme-linked immunosorbent assay (ELISA) (SearchLight Human Inflammatory Cytokine Array 1; Endogen, Perbio, IL). All assays were conducted according to the manufacturer’s instructions. The lower limit of detection was 0.2 pg/mL for IL-1β, IL-6, IL-10, and INF-γ; 0.4 pg/mL for IL-1α, IL-2, IL-8, and IL-12p70; and 1.6 pg/mL for TNF-α. The intraassay and intersay CVs of the SearchLight Human Inflammatory Cytokine Array 1 were <12%.

CVD risk indexes

The CVD risk indexes were as follows: total cholesterol (mg/dL)/HDL cholesterol (mg/dL), LDL cholesterol (mg/dL)/HDL cholesterol (mg/dL), and triacylglycerol (mg/dL)/HDL cholesterol (mg/dL).

Statistical analysis

Data are presented as group means ± SDs. A Tukey’s test was used to assess the significance between the 3 groups, whereas the nonparametric Mann-Whitney U test was used to compare 2 groups. A Pearson’s simple correlation was used to study the association between 2 variables. The minimal level of significance was fixed at P ≤ 0.05 for all procedures. The statistical analysis was carried out by using Instat GraphPad Software (version number 4.03, 2005; San Diego, CA).

RESULTS

All 60 women enrolled completed the study. The participants were classified as NWO or nonobese on the basis of BMI and %FM and as preobese-obese according to a WHO technical report (24). The anthropometric characteristics of all subjects are shown in Table 1.
Average ages and heights were not significantly different between the 3 groups. No significant differences in BMI and body weight were observed between the NWO and nonobese women, whereas %FM and %FFM were significantly different. In contrast, no significant differences in %FM and %FFM were observed between the NWO and preobese-obese women. As expected, body weight, BMI, %FM, %FFM, and waist circumference were significantly different between the preobese-obese and nonobese groups.

The clinical characteristics of the 3 groups of subjects are shown in Table 2. All subjects had a normal systolic and diastolic blood pressure. Triacylglycerol, total cholesterol, total cholesterol/HDL cholesterol, hs-CRP, and HOMA-IR values were higher in the preobese-obese group than in the nonobese group. In contrast, these variables were not significantly different between the NWO and nonobese groups. As shown in Table 2, the preobese-obese women had significantly higher hs-CRP concentrations (2.2 ± 0.9 mg/L) than did the NWO (0.4 ± 0.1 mg/L) and nonobese (0.8 ± 0.3 mg/L) women. No significant differences in hs-CRP concentrations were observed between the NWO and nonobese women.

Plasma TNF-α concentrations in the 3 groups of subjects are shown in Figure 1. The limit of detection for the assay was 1.6 pg/mL. Differences between groups were assessed with Tukey’s test. The plasma TNF-α concentration was significantly greater in the NWO (42.77 ± 10.54 pg/mL) and preobese-obese (56.37 ± 11.77 pg/mL) groups than in the nonobese group (20.10 ± 4.95 pg/mL) (nonobese compared with NWO and preobese-obese: P < 0.001). The TNF-α concentration was not related to body weight, BMI, or %FFM, but it was correlated with %FM in the NWO (r = 0.5527, P < 0.005) and preobese-obese (r = 0.4925, P < 0.005) groups. Moreover, the plasma

### Table 1
Anthropometric variables for the 3 groups of women

<table>
<thead>
<tr>
<th>Anthropometric variable</th>
<th>Group</th>
<th>Nonobese (n = 20)</th>
<th>NWO (n = 20)</th>
<th>Preobese-obese (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td>26.3 ± 5.9 (20–35)</td>
<td>24.6 ± 4.1 (20–35)</td>
<td>28.0 ± 5.10 (21–35)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td></td>
<td>51.8 ± 6.4 (44.7–61.8)</td>
<td>59.6 ± 7.2 (48.4–70.5)</td>
<td>70.9 ± 10.3 (56.5–88.6)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
<td>164.8 ± 8.0 (157.5–171.0)</td>
<td>161.9 ± 4.2 (152.5–167.0)</td>
<td>159.50 ± 5.47 (150.5–167.5)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>19.2 ± 1.5 (17.1–21.9)</td>
<td>22.6 ± 1.9 (20.1–24.8)</td>
<td>27.9 ± 4.58 (25.8–34.2)</td>
</tr>
<tr>
<td>FFM (%)</td>
<td></td>
<td>76.7 ± 2.2 (73.2–79.7)</td>
<td>65.1 ± 5.1 (51.7–69.9)</td>
<td>57.1 ± 7.3 (41.7–65.9)</td>
</tr>
<tr>
<td>FM (%)</td>
<td></td>
<td>23.3 ± 2.2 (20.3–26.8)</td>
<td>34.9 ± 5.0 (30.1–48.3)</td>
<td>42.9 ± 7.3 (34.1–58.3)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td></td>
<td>65.1 ± 3.9 (59.5–72.0)</td>
<td>72.3 ± 4.9 (62.0–79.0)</td>
<td>85.8 ± 10.2 (72.0–103.5)</td>
</tr>
</tbody>
</table>

All values are x ± SD; range in parentheses. NWO, normal-weight obese; FFM, fat-free mass; FM, fat mass. Means in a row with different superscript letters are significantly different, P < 0.05 (Tukey’s test).

### Table 2
Clinical variables for the 3 groups of women

<table>
<thead>
<tr>
<th>Clinical variable</th>
<th>Group</th>
<th>Nonobese (n = 20)</th>
<th>NWO (n = 20)</th>
<th>Preobese-obese (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triacylglycerol (mg/dL)</td>
<td></td>
<td>66.3 ± 11.0a</td>
<td>86.1 ± 14.5b</td>
<td>111.5 ± 16.6b</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td></td>
<td>178.4 ± 17.4a</td>
<td>187.9 ± 26.1b</td>
<td>218.1 ± 24.2a</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td></td>
<td>69.11 ± 6.8a</td>
<td>68.20 ± 12.3a</td>
<td>70.18 ± 19.9a</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td></td>
<td>107.2 ± 34.8a</td>
<td>103.8 ± 24.5a</td>
<td>116.0 ± 35.3a</td>
</tr>
<tr>
<td>Total:HDL cholesterol</td>
<td></td>
<td>2.7 ± 0.5a</td>
<td>2.8 ± 0.5a</td>
<td>3.7 ± 0.9b</td>
</tr>
<tr>
<td>Triacylglycerol:LDL cholesterol</td>
<td></td>
<td>0.9 ± 0.1a</td>
<td>1.2 ± 0.5a</td>
<td>1.9 ± 0.5a</td>
</tr>
<tr>
<td>LDL:HDL cholesterol</td>
<td></td>
<td>1.5 ± 0.4a</td>
<td>1.5 ± 0.5a</td>
<td>1.9 ± 0.7a</td>
</tr>
<tr>
<td>hs-CRP (mg/L)</td>
<td></td>
<td>0.4 ± 0.1a</td>
<td>0.8 ± 0.3a</td>
<td>2.2 ± 0.9b</td>
</tr>
<tr>
<td>FL (μIU/mL)</td>
<td></td>
<td>6.6 ± 1.4a</td>
<td>6.4 ± 1.8a</td>
<td>9.1 ± 1.1a</td>
</tr>
<tr>
<td>FG (mg/dL)</td>
<td></td>
<td>93.0 ± 2.3a</td>
<td>92.3 ± 2.9a</td>
<td>96.9 ± 1.9a</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td></td>
<td>1.4 ± 0.1a</td>
<td>1.5 ± 0.2a</td>
<td>2.2 ± 0.6b</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td></td>
<td>112.4 ± 2.9a</td>
<td>118.2 ± 1.9a</td>
<td>122.4 ± 3.9a</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td></td>
<td>70.5 ± 3.5a</td>
<td>72.7 ± 4.0a</td>
<td>76.2 ± 2.3a</td>
</tr>
</tbody>
</table>

All values are x ± SD. NWO, normal-weight obese; hs-CRP, high-sensitivity C-reactive protein; FI, fasting insulin; FG, fasting glucose; HOMA-IR, homeostasis model assessment of insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure. Means in a row with different superscript letters are significantly different, P < 0.05 (Tukey’s test).
FIGURE 2. Plasma interleukin 6 (IL-6) concentrations in nonobese (n = 20), normal-weight obese (NWO; n = 20), and preobese-obese (n = 20) women. The plasma concentration was measured in duplicate by using the multiplex sandwich enzyme-linked immunosorbent assay (SearchLight Human Inflammatory Cytokine Array; Endogen, Perbio, IL). The lower limit of detection for the assay was 0.2 pg/mL. Differences between groups were assessed by using Tukey’s test. Nonobese compared with NWO: P < 0.001; nonobese compared with preobese-obese: P < 0.001; NWO compared with preobese-obese: NS.

TNF-α concentration was higher in the preobese-obese women than in the NWO women, although this difference was not statistically significant.

Plasma IL-6 concentrations in the 3 groups of subjects are shown in Figure 2. The limit of detection of the assay was 0.2 pg/mL. A significantly higher plasma IL-6 concentration was observed in the preobese-obese (13.68 ± 2.29 pg/mL) than in the NWO (11.42 ± 1.77 pg/mL) and nonobese (5.950 ± 2.28 pg/mL) women (nonobese compared with the NWO and preobese-obese: P < 0.001). Plasma IL-6 concentrations were lower in the NWO women than in the preobese-obese women, although this difference was not statistically significant and the values were related to %FM (r = 0.55, P < 0.05).

Plasma concentrations of IL-1α, IL-1β, IL-2, IL-8, IL-10, IL-12p70, and INF-γ in the 3 groups of subjects are shown in Table 3. No significant differences in plasma IL-2 and IL-10 concentrations were observed between groups. Plasma concentrations of IL-1α, IL-1β, and IL-8 were significantly higher in the NWO and preobese-obese groups than in the nonobese group. In contrast, the concentration of circulating IL-12p70 and IFN-γ was significantly higher only in preobese-obese women with respect to the nonobese and NWO groups (P < 0.0092 and P < 0.0076, respectively).

DISCUSSION

A considerable number of individuals can be classified as obese on the basis of BMI alone, and a misclassification could occur if the percentage of body fat mass is not considered to evaluate obesity. Therefore, screening for body fat distribution in persons with a normal or slightly elevated BMI is an important tool in the prevention of obesity-related diseases.

Until now, 2 types of obese individuals have been described: 1) metabolically healthy but obese (MHO), and 2) metabolically obese but normal weight (MONW) (26, 27). MHO persons, despite having excess body fat, have a metabolic profile characterized by high insulin sensitivity, a favorable lipid profile, and no sign of hypertension. MONW subjects, first described and recently revisited by Ruderman et al (28), represents a subset of persons who have a normal weight and normal BMI (ie, of 18–25) but have a cluster of metabolic characteristics that may increase the possibility of developing the metabolic syndrome. MONW women have metabolic disturbances typical of obese persons and are characterized by having a high amount of visceral fat, a low BMI, a high fat mass, a low lean body mass, low insulin sensitivity, and high triacylglycerol concentrations and liver fat.

In our previous report (21), we described the new syndrome, namely the NWO syndrome. Persons with this syndrome are characterized by a normal body weight and BMI (<25), a high %FM (>30%), a significantly lower %FFM than normal-weight subjects, and few metabolic abnormalities and thus do not have the metabolic syndrome. Therefore, NWO women are quite different from MHO women and may also be distinguished from MONW women.

Our present data show that the anthropometric measures of the NWO women were intermediate to those of the nonobese and preobese-obese women, and this difference was significant, although the metabolic characteristics of the NWO women were not different from those of the nonobese women. This result suggests that anthropometric measures, but not the plasma lipid-lipoprotein profile, could be prognostic indicators for the risk of obesity, CVD, and the metabolic syndrome.

In the present study, we compared the plasma proinflammatory cytokine concentrations and their correlations with BMI, %FM, %FFM, and selected lipid indexes in NWO women with those of nonobese and preobese-obese women to determine their relation with the risk of obesity and the metabolic syndrome. We showed for the first time that plasma proinflammatory cytokine concentrations were elevated in the NWO and preobese-obese women and that their circulating concentrations were correlated with %FM.

Many reports suggest that TNF-α, IL-1, and IL-6 are produced and released by human adipose tissue (1, 29) and that their plasma concentrations are elevated in obese subjects. In particular, these proinflammatory cytokines have been investigated...
extensively for their potential role in the development of complications traceable to obesity (4–9). Recent data suggest that chemokines, such IL-8, activating protein-1, and monocyte chemoattractant, may be implicated in the pathogenesis of atherosclerosis and CVD (30, 31).

We found that the circulating concentrations of TNF-α, IL-1α, IL-1β, IL-6, and IL-8 were significantly elevated in both NWO and in preobese-obese women, whereas the plasma concentrations of IL-12p70 and IFN-γ were elevated only in the preobese-obese group. Moreover, no significant differences were observed in IL-2 and IL-10 plasma concentrations between the 3 groups of women studied.

It should be noted that serum cytokine concentrations were not influenced by the ovulation period, because the blood samples were collected during the women’s pre-ovulation period (32). Furthermore, no laboratory or clinical results indicate that cytokine production increases depending on blood monocyte activity, because the subjects were generally in good health and had no evidence of infection.

The observed increase in plasma proinflammatory cytokine concentrations in preobese-obese women agrees with the findings of previously published data (33, 34), and its role in the development of complications attributable to obesity has been investigated (35–37).

Until now, increases in proinflammatory cytokine concentrations had not been reported in NWO persons. Recent evidence suggests that body fat, particularly the adipocytes, synthesizes and releases proinflammatory cytokines (38–41). Our results showed that the proinflammatory cytokines concentrations in the NWO women were intermediate to those of the nonobese and preobese-obese women. Thus, the observed increase in circulating concentrations of TNF-α and IL-6 in the NWO group may have been a result of the observed increase in fat mass in this group. In fact, our results showed a significant correlation between these cytokines and %FM in the NWO group.

On the basis of these findings, the NWO women were in an early inflammatory state. The observed increases in IL-1α, IL-1β, and IL-8 support this hypothesis because these cytokines are produced during the early inflammatory response. The presence of a proinflammatory state in the NWO women was also confirmed by a reduced plasma concentration of an antiinflammatory factor such as adiponectin (data not shown). Our data indicated that the NWO subjects had plasma adiponectin concentrations that were lower than those of nonobese subjects, although the difference was not statistically significant. Adiponectin concentrations were significantly lower in the preobese-obese women than in the nonobese and NWO women.

Additionally, the greater plasma concentrations of proinflammatory cytokines observed in the preobese-obese women than in the NWO women reinforces our hypothesis. These higher concentrations together with higher metabolic variables could be a consequence of a larger %FM, and this cytokines profile may reflect a chronic inflammatory condition. Recent studies indicate that cytokines and other factors produced and released by the white adipose tissue are responsible for the chronic inflammatory state of obesity (41).

In support of this idea, we found greater plasma concentrations of IL-12p70 and IFN-γ only in preobese-obese women. These cytokines are produced in a late phase of inflammation and are necessary for the induction and maintenance of the proinflammatory T helper cell 1 immune response (42).

To better define the factors involved in the inflammation status of the NWO women, we measured hs-CRP concentrations in all of the subjects. The results of the present study showed that the hs-CRP concentration in the NWO women was intermediate to that of the other groups. This suggests that the higher concentrations of hs-CRP in the NWO women than in the preobese-obese women, despite higher percentages of body fat, could contribute to the favorable metabolic profile observed in the NWO group.

In conclusion, the results of the present study are interesting for several reasons. First, we observed higher plasma concentrations of proinflammatory cytokines in the NWO women. Second, the large amount of these cytokines was correlated with %FM. Third, this overproduction of cytokines may be involved in the onset of an early inflammation state and could be a significant prognostic indicator of the risk of obesity, CVD, and the metabolic syndrome.

Clearly, a deeper investigation should be performed to determine the role of cytokines in the NWO syndrome. In fact, the current study provides evidence that a proinflammatory state, as indicated by the high cytokine concentrations, and body composition, particularly %FM, characterize this syndrome. Studies are in progress to analyze the proinflammatory cytokines gene expression in the NWO syndrome.

The findings of the present study represent important directions for the future planning of programs designed to prevent obesity-related diseases. To overcome the misclassification of obesity based on anthropometric measures only, it seems to be of interest to evaluate both %FM and the distribution of body fat rather than just the inflammatory pattern associated with NWO. In fact, NWO women are vulnerable because, on the basis of reference indexes and the measures that have been adopted to classify obesity, they are not aware that they are at risk of developing obesity-related diseases.

ADL was the responsible for the conception and the design of the experiments. VDG, MGP, and LDR were responsible for the conduct of the experiments, the data interpretation, and the writing of the manuscript. MB and FG were responsible for the statistical analyses of the data and the drafting of the tables and the figures. None of the authors had any financial or personal interest in any organization sponsoring the research at the time the research was done.

REFERENCES


