Abstract

Introduction: obesity affects more than a third of Mexican population. Oxidative stress participates actively in the etiology of this phenomenon. Glutathione peroxidase-1 (GPX-1) plays a protective role against oxidative stress. The SNP Pro200Leu (rs1050450) has been reported to affect the activity of the enzyme.

Objective: to determine the frequency of rs1050450 polymorphism in women with obesity and normal weight control, assess the concentration of peripheral TBARS and evaluate the consumption of pro and antioxidants.

Methods: 104 women with obesity and 70 healthy controls (CG) were included in the study. Anthropometric, biochemical, clinical and dietary features were evaluated. GPx-1 rs1050450 was determined by PCR/RFLP method. TBARS was assayed spectrophotometrically in plasma. The subjects were stratified and compared by obesity grades and by subgroups of prediabetes and diabetes condition. Statistical analysis included ANOVA of Kruskal Wallis, Xi squared and Pearson correlation.

Results: for rs1050450 polymorphism there were differences ($X^2 = 6; p = 0.01$) between frequency (0.61) of obese carriers (Pro/Leu plus Leu/Leu) and CG carriers (0.42), and between ($X^2 = 8; p = 0.004$) morbidity (IMC $> 40$) obesity (0.74) and CG carriers. The obese group (OB) showed a prevalence of 66% of prediabetes and diabetes. There were no differences in frequencies of rs1050450 in OB with pre or diabetes versus CG, or versus obese participants without diabetes. TBARS concentration was greater in all the degrees of OB versus CG.

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Conclusion: GPx-1 Pro200Leu polymorphism was associated with obesity especially with morbid obesity, but not with obese participants with prediabetes or diabetes. Oxidative stress is present in all grades of obesity significantly.

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Key words: Obesity. Glutathione peroxidase-1. rs1050450. Pro200Leu. Oxidative stress.

Abbreviations

RONS: Reactive oxygen and nitrogen species
GPx-1: Glutathione peroxidase-1
C: Cytosine
T: Thymine
Pro: Proline
Leu: Leucine
SNP: Single nucleotide polymorphism
TBARS: Thiobarbituric acid reactive species
BMI: Body mass index
CG: Control group
OB: Obese group
OB I: Obesity grade I
OB II: Obesity grade II
OB III: Obesity grade III
DM: Type 2 diabetes
IFG: Impaired fasting glucose
PCR-RLFP: Polymerase chain reaction-restriction length fragment polymorphism
BP: Blood pressure
RMR: Resting metabolic rate
TEE: Total energy expenditure
PAL: Physical activity level
SFA: Saturated fatty acids
MDA: Malondialdehyde
LDL: Low density lipoprotein
VLDL: Very low density lipoprotein

Introduction

Obesity is defined as the increase in total body fat percentage above a standard value as a result of an imbalance between energy intake and energy expenditure. The etiology is multifactorial and can be explained with the complex interaction between environmental, genetic and cultural factors.

Obesity is a public health problem worldwide due, it used to be considered disorder of high-income countries, but currently this phenomenon have increased in middle-income and even low-income countries. According to the National Institute of Public Health a total of 71.28% Mexican adults were reported to be overweight or obese in 2012, ranking Mexico second in the world in adult obesity.

Obese individuals display an increased risk to develop impaired fasting glucose and impaired glucose tolerance known as prediabetes which are related with a variety of diseases such as insulin resistance, type II diabetes, dyslipidemia, cardiovascular disease, metabolic syndrome, cancer and others. Diabetes is the main cause of mortality among Mexican adults, with a prevalence greater than 11% in 2013 there were 8.7 millions of people with diabetes and it is estimated that by 2035 there will be 15.7 millions.

The initiation and development of the afore mentioned diseases are related to pro-oxidant state caused by several mechanisms, where visceral fat is an important contributor to this phenomenon through the production of proinflammatory adipokines.

The oxidative stress condition is generated by continuous production of reactive oxygen and nitrogen species (RONS) by activating macrophages and neutrophils, under the pro-inflammatory milieu of the adipose tissue. Such leukocyte infiltration produces RONS through the activation of NADPH oxidase and myeloperoxidase.

However, this is not the only source of RONS in people with obesity, since increased fat intake produces more generation of RONS by metabolic activity, and a deficient consumption of antioxidants drives the balance prooxidant-antioxidant towards the oxidative stress condition in this group of persons. Likewise, hyperglycemia and excessive carbohydrates intake generate reactive oxygen species inducing oxidative stress and contribute significantly to the development and progression of diabetes and related cardiovascular complications.

One important defense against the endogenous peroxide free radical is the antioxidant glutathione peroxidase-1 enzyme (GPx-1), which is located in the human chromosome 3p21.3. This selenoprotein produces water and alcohol after the reduction of hydrogen peroxide or organic peroxides, respectively, through the oxidation of glutathione. The enzyme shows a transition of cytosine to thymine (C > T), which generates a nonsynonymous change of the amino acid Proline (Pro) for Leucine (Leu). This SNP (GPx-1 Pro200Leu) previously named GPx-1 Pro198Leu (rs1050450), displays a decreased GPx-1 erythrocyte activity for the Leu allele, and has been implicated in diseases like cancer, diabetes, coronary and cardiovascular diseases.

In Mexican population the prevalence of this polymorphism in obese and normal weight population has not been yet determined.

Conclusion: el polimorfismo rs10504050 se asoció con obesidad, especialmente mórbida, pero no se asoció con diabetes o prediabetes. El estrés oxidativo está presente de manera significativa en todos los grados de obesidad.

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The adequate function of the GPx as well as other important antioxidant enzyme superoxide dismutase, require the presence of antioxidant minerals as cofactors for their optimal activity. In general the antioxidant minerals (copper, manganese, selenium and zinc) and vitamins (A, E and C), have to be obtained through daily consumption in the diet of vegetables, seeds and fruits, since they are not stored in the body in abundance.

A low consumption of antioxidants can enlarge the production of RONS to lead the appearance of oxidative stress condition, which has been described previously associated with the development of the main comorbidities of obesity.

The present study aimed to assess the frequency of the SNP GPx-1 Pro200Leu (rs1050450) in a Mexican population of women from the central plateau with normal weight and obesity, and in a subgroup of diabetes and prediabetes people with obesity. In addition the study aimed to evaluate the consumption of antioxidants and pro-oxidant macromolecules and correlate with TBARS (thiobarbituric acid reactive species) concentration in plasma as a marker of oxidative stress.

Material and methods

Study Population

The study included women who assisted to “Clínica de Nutrición de la Universidad Iberoamericana” in Mexico City. After determining their body mass index (BMI) 174 individuals were classified in normal weight or control group (CG) and obese group (OB). Normal weight group (BMI 18.5-24.9) included 70 individuals, and the obese group (BMI >30) included 104 individuals, from whom the obesity grades- I (OB-I), II (OB-II) and III (OB-III) included 36, 34 and 34 individuals, respectively. The study included women from Mexico City’s low-income community, between 19-60 years old, non-smokers, without history of thyroid disease, autoimmune, allergies, infectious disease, eating disorders and no consumption of antioxidant supplements within the past 6 months and women not pregnant or lactating. All the participants were informed about the study and signed a written informed consent statement if they decided to participate. The protocol was reviewed and approved by the scientific committee and institutional ethics.

Height was measured to all subjects in a standing position after removing the shoes with a Seca® Model 240 (Vogel & Halke GMBH & Co., Germany) stadiometer with a ±2mm accuracy. Weight measurements were performed with subjects under fasting condition using an Inbody model 720 (Biospace Co; Korea) bioimpedance body composition analyzer with a ±0.1kg accuracy and 250 kg capacity. BMI was determined as the ratio between weight (kg) and height squared meters (m²).

Individuals with obesity referring type 2 diabetes (DM) or that presented impaired fasting glucose (IFG; >100<125 mg/dl) at the moment of assessment were stratified into a different group to assess the GPx-1 Pro200Leu polymorphism. Then at the next nutrition counseling appointment fasting glucose concentration was measured again to corroborate the diagnostic.

Glucose concentration was measured with a glucose oxidase method (BioSystems; Spain) in our lab; inter and intra-assay precision was 4.5% and 3.8%. Blood pressure (BP) was measured to all patients using a sphygmomanometer (Diagnostix 972; USA) seated after 5 min of rest. There were taken four consecutive measurements; the first reading was discarded and the mean of the next three consecutive measures were used as the final BP.

Genotyping of GPx-1 Pro200Leu

Peripheral fasting blood samples were collected into 7 mL heparin tubes (Becton Dickinson Vacutainer Systems; USA) from all of the patients and controls. Immediately after collection, the plasma was separated using centrifugation technique and all the samples were stored in aliquots at -80°C until use. Isolation of DNA was performed from whole blood (100 µL) using DNAzol (Molecular Research Center; USA) according to the manufacturer’s instructions.

GPx-1 genotypes were detected using a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. The SNP C>T in exon 10, was amplified to form undigested fragments of 338 bp (bases pairs) using primers: forward 5’- ATC GAG CCT GAC ATC GAA - 3´ and reverse 5´- AAG CAG CCG GGG TAG GAG - 3´. PCR conditions were 94°C for 4 minutes, included 35 cycles of 94°C for 35 seconds for denaturation, 62°C for 30 seconds for annealing and 72°C for 30 seconds for elongation. The amplified product was digested with Apal restriction enzyme (Invitrogen; USA) at 37 ºC for 5 hours and analyzed by electrophoresis using agarose gels (2.5%). The DNA-bands in the electrophoresis gel were identified by ethidium bromide using an image analyzer (Alphalmager Mini; USA). Digestion resulted in one fragment of 76 bp for homozygous carriers (Leu/Leu), two fragments of 42 and 34 bp for wild type (Pro/Pro) and three fragments of 34, 42 and 76 bp for heterozygous (Fig. 1).

Determination of Antioxidants/Pro-oxidants Consumption Frequency

A dietary assessment food frequency questionnaire for antioxidants validated by the National Institute of Public Health was applied. To ensure a standard approach to data collection, two dietitians were trained to undertake interviews using measures, portions and
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comparative models of food to facilitate understanding of the survey. Recalls were coded and transformed to daily nutrients of interest in mass units, with the use of a food-composition database program named Nutritional Vector Calculation System developed to accommodate the characteristics of the Mexican diet. The concentration of total fat, saturated fat, cholesterol and carbohydrates (g) were obtained by means of this methodology. The total daily energy intake was estimated by means of a food record method over three non-consecutive days including a weekend or a holiday.

**Total Energy Expenditure**

The Resting Metabolic Rate (RMR) was measured via indirect calorimetry method using a Cardio Coach Metabolic Monitor (KORR Medical Technologies; USA). The Total Energy Expenditure (TEE) was predicted as RMR times physical activity level (PAL). The PAL was calculated by means of the International Physical Activity Questionnaire Long version19.

**Determination of thiobarbituric reactive species**

The lipoperoxidation state of peripheral plasma from obese and control participants was determined by the Thiobarbituric Acid Technique described by Asakawa, modified by Estepa20. One hundred of peripheral plasma was assayed to evaluate the concentration of TBARS. The product of reaction of malondialdehye-thiobarbituric acid was detected spectrophotometrically at 532 nm, and the concentration evaluated in each samples was reported as µmoles/L of TBARS. The coefficients of variation intra and inter-assay were less than 5% and 10%, respectively. The concentration of TBARS was correlated with pro-oxidants: carbohydrates, total fat, saturated fat and cholesterol, and antioxidants: vitamin C, A and E, manganese, zinc, copper and selenium.

**Statistical Analysis**

Descriptive statistics was used to analyze the epidemiological variables, glucose, blood pressure, intake of macromolecules and antioxidants. The differences between groups were assessed by the Kruskal Wallis ANOVA. The associations between the polymorphism and obesity as well as the subgroups were assessed by X² squared. The correlation between TBARS and consumption of pro-oxidant and antioxidant was done by a Pearson correlation. Sigma Stat 3.5 program was used to do all analysis afore mentioned. A p value ≤0.05 was accepted as a significant difference.

**Results**

**Participants**

The study included 104 women stratified by obesity grade, and 70 included in normal weight group, the characteristics of the subject groups are shown in (Table I).

There was no statistical difference in the age between groups. BMI was significantly (p<0.05) greater in the obese groups as well as total energy expenditure and daily energy intake.

As expected, obese individuals presented body fat percentage and waist-hip ratio higher than control group (p<0.001). The same differences were observed when the obese group (OB) was stratified by grades of obesity and compared with control group (CG).

Regarding obese participants 22% presented diabetes and 44% showed impaired fasting glucose, with a significant difference (p<0.005) in glucose concentration (both groups) compared with normal weight group. Although some patients of obesity group displayed higher values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) there were no statistical differences between control and study group or subgroup.
Prevalence of the GPx-1 Pro200Leu polymorphism

The frequency of the Pro200Leu polymorphism of GPx-1 in subjects with normal weight and obesity are shown in (Table II). The frequency of the CC homozygous genotype for control group showed a value of 0.58, while the obesity group value was 0.39. There was a statistical difference when analyzing the frequency of the mutated genotype (TC+TT) between people with normal weight (0.42) and obesity (0.61). When stratifying by obesity grade, only obesity grade III group showed significant difference (p=0.004) when compared to normal weight group. As expected, similar trends were observed for alleles analysis; allele T frequency corresponded to 0.22 for CG compared to 0.40 for OB showing a p=0.001.

When stratifying subjects with impaired fasting glucose (IFG) and type 2 diabetes (DM), we found that the frequency of the mutated genotype was considerable high; 0.62 for IFG and 0.59 for DM. However, there were no statistical differences when comparing these frequencies with subjects with obesity but not diabetes or prediabetes. These findings reinforce the idea that the GPx-1 Pro200Leu polymorphism at least in our group is associated with obesity, and more specifically with morbid obesity but not with prediabetes and diabetes. On the other hand, the genotype distribution was compatible with the Hardy-Weinberger equilibrium.

Pro-oxidant and antioxidant dietary intake

The ingestion of total carbohydrates in the diet was statistically greater in obesity groups in comparison with control subjects; this observation was also identified when obese group was stratified in obesity grades, as shown in (Table III). The consumption of lipids in OB was greater than in CG and the distribution of fatty acids was inadequate as saturated fatty acids (SFA) consumption by OB was higher 35.7 g corresponding to 10.4%, respect to CG that was of 20.4 g corresponding to 7.8% of total energy intake (p<0.05).

The imbalance of consumption of lipids is reinforced by the intake of cholesterol, since obese group showed a higher ingestion (324 mg/day) than the control group, also when stratified by obesity grade, the groups showed statistically difference when compared to CG (p<0.05).

The analysis of consumption of antioxidants was very similar between obese and control group and did not show statistically differences between obese groups.

<table>
<thead>
<tr>
<th>Table I</th>
<th>Characteristics of the participants included in the study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Weight n =70</td>
</tr>
<tr>
<td>Age</td>
<td>34.7 ± 7.8</td>
</tr>
<tr>
<td>BMI</td>
<td>21.4 ± 1.5</td>
</tr>
<tr>
<td>TEE (Kcal/day)</td>
<td>1821.2 ± 195.5</td>
</tr>
<tr>
<td>EI (Kcal/day)</td>
<td>1738.4 ± 540.5</td>
</tr>
<tr>
<td>BF%</td>
<td>24.7 ± 6.2</td>
</tr>
<tr>
<td>WHR</td>
<td>0.75 ± 0.1</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>89 ± 7.52</td>
</tr>
<tr>
<td>SBP mmHg</td>
<td>112.7 ± 8.4</td>
</tr>
<tr>
<td>DBP mmHg</td>
<td>75.2 ± 5.7</td>
</tr>
</tbody>
</table>

Data show: Mean ± SD; Median
OB I – III: Obese group. OB I: Obese grade I. OB II: Obese grade II. OB III: Obese grade III.
BF%: Body Fat percentage. WHR: Waist Hip Ratio. SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure
*Difference vs Normal Weight Group at p < 0.05
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and CG, except vitamin E for obese grade I group which consumed 19% less than CG. On the other hand, the mean of selenium dietary intake in normal weight individuals was of 38.7 µg/day and 40.8 µg/day for obesity group.

The Mexican Dietary Reference Intakes (RDA) for selenium according to 19-50 years is of 48 mg/day21, thus only 27% of CG met the RDA and 24% of OB.

TBARS

The results of the concentration of peripheral TBARS in obese and control groups are shown in (Figure 2 Panel A). We observed a statistical difference (p<0.05) between the CG (X̅=0.48 +/- 0.29 µmol/L) and the OB (X̅= 1.15 +/- 0.84 µmol/L). When stratifying the participants of the study group in grades of obesity, we observed a statistical difference between the normal weight group and the three obesity grades (p<0.05).

When the TBARS concentrations were assessed by the genotype (Panel B) there was no significant difference between wild type genotype (CC) and carriers (TC and TT), not even for obese grade III. In the same context, no statistical difference was observed after stratifying DM and IFG subjects in function of the genotype; comparing the TBARS concentrations between wild type genotype and mutated carriers (data not shown).

No statistical difference was found in the correlation between total fat, cholesterol, saturated fat or antioxidants consumption and the concentration of peripheral TBARS by Pearson test (data not shown) even when we stratified as a function of the GPx-1 Pro200Leu polymorphism.

Discussion

In the present work we identified a higher frequency statistically significant of the GPx-1 rs1050450 polymorphism in Mexican mestizo women with obesity from the central plateau, compared with normal weight controls. The statistical results of mentioned analysis was “robust” (X²=6; p<0.01), however the stratification of the study group showed a more “robust” difference at the group III of obesity (X²=8; p<0.004), and only this degree of the pathology presented statistically significance.

The analysis of the allele Leu reinforced the same pattern of differences observed before, since the obe-

<table>
<thead>
<tr>
<th>Table II</th>
<th>GPx-1 Pro200Leu polymorphism identified in obese and control groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>Genotype carriers</td>
</tr>
<tr>
<td>CC</td>
<td>TC</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>41 (0.58)</td>
</tr>
<tr>
<td>OB I-III</td>
<td>40 (0.39)</td>
</tr>
<tr>
<td>OB I</td>
<td>15 (0.42)</td>
</tr>
<tr>
<td>OB II</td>
<td>16 (0.47)</td>
</tr>
<tr>
<td>OB III</td>
<td>9 (0.26)</td>
</tr>
<tr>
<td>OB without IFG/DM</td>
<td>13 (0.37)</td>
</tr>
<tr>
<td>IFG</td>
<td>18 (0.38)</td>
</tr>
<tr>
<td>DM</td>
<td>9 (0.26)</td>
</tr>
<tr>
<td>IFG + DM</td>
<td>27 (0.39)</td>
</tr>
</tbody>
</table>

OB I – III: Obese group. OB I: Obese grade I. OB II: Obese grade II. OB III: Obese grade III.

- Obese group, OB I, OB II and OB III subjects were compared versus normal weight group (IFG) Subjects with Impaired Fasting Glucose (≥100 <125 mg/dl) (DM) Type 2 Diabetes Mellitus (≥126 mg/dl)

- Subjects presenting IFG, DM and IFG+DM were compared versus subjects with obesity and without diabetes or impaired fasting glucose.
sity group increased the statistical value \((X_i^2=10; p<0.001)\) and the obese-III group reached a “strong” difference versus control group \((X_i^2=16; p<0.001)\). As such, it represents the first study to our knowledge that reports the frequency and differences of this polymorphism between Mexican women with obesity and normal weight control.

As it is known, the obesity is an important factor involved in the appearance of diabetes and other chronic pathologies. In our study we evaluated the concentration of fasting glucose in the participants, and identified a higher prevalence \((47\%)\) of prediabetic condition \((
\text{glucose: 100-125 mg/dl})\), which unfortunately, almost all the participants were not aware of this condition. This finding is a typical “picture” of the great percentage of people with obesity affected by this alteration in our country, on the way to get diabetes3.

For the case of diabetes we identified a prevalence of \(21\%)\) in our study group, a twofold value of prevalence reported for Mexican normal weight adults5. Due to the highest prevalence of prediabetes and diabetes in the study we analyzed the frequency of our polymorphism in this group of patients. The aggregation of participants with both conditions \((n=69)\) showed statistically difference \((X_i^2=6; p<0.033)\) versus control group, nonetheless there was not difference versus obese participants without diabetes \((n=35)\). Further, the obese group-III carriers of GPx-1 Pro-200Leu, who showed statistically differences versus control group, and by obvious reasons most of these participants could have prediabetes or diabetes, neither presented difference versus obese people without diabetes. Also the percentage of people with obesity with pre and diabetes showed a similar distribution between the grades I to III of \(63\%, 52\%\) and \(70\%\), respectively, and there were not statistically differences between groups (data not shown).

We think these results reinforces the idea that the GPx-1 rs1050450 at least in our study population is associated with obesity and in particular with the morbid grade, and the pre and diabetes conditions are not impacted by the presence of herein studied polymorphism.

However, the presence of the allele Leu in its heterozygous way has been associated with an increased value of coronary artery calcification in Japanese patients with diabetes type 223. Further, Hamanishi et al.23 reported a higher prevalence of cardiovascular disease.

### Table III

Pro-oxidant and antioxidant dietary intake shown by participants

<table>
<thead>
<tr>
<th>Macronutrient or Micronutrient</th>
<th>Normal Weight</th>
<th>OB I - III</th>
<th>OB I</th>
<th>OB II</th>
<th>OB III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates (g)</td>
<td>205 ± 66</td>
<td>329 ± 81 *</td>
<td>319 ± 84 *</td>
<td>329 ± 85 *</td>
<td>339 ± 74 *</td>
</tr>
<tr>
<td>Total Fat (g)</td>
<td>66.2 ± 31</td>
<td>92.8 ± 92</td>
<td>93 ± 95</td>
<td>96.3 ± 29.7</td>
<td>116 ± 123</td>
</tr>
<tr>
<td>Saturated Fats (g)</td>
<td>20.4 ± 10</td>
<td>35.7 ± 41 *</td>
<td>34.4 ± 36 *</td>
<td>25 ± 10</td>
<td>47.8 ± 59 *</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>205 ± 104</td>
<td>324 ± 389 *</td>
<td>396 ± 595 *</td>
<td>242 ± 168 *</td>
<td>328 ± 241 *</td>
</tr>
<tr>
<td>Vitamin C (mg)</td>
<td>173 ± 83</td>
<td>199 ± 163</td>
<td>202 ± 163</td>
<td>174 ± 180</td>
<td>222 ± 146</td>
</tr>
<tr>
<td>Vitamin A (µg)</td>
<td>956 ± 322</td>
<td>1146 ± 651</td>
<td>1077 ± 549</td>
<td>1038 ± 593</td>
<td>1326 ± 776</td>
</tr>
<tr>
<td>Vitamin E (mg)</td>
<td>9.3 ± 4</td>
<td>8.1 ± 5</td>
<td>7.8 ± 5.1 *</td>
<td>8.9 ± 5.9</td>
<td>7.7 ± 4</td>
</tr>
<tr>
<td>Manganese (mg)</td>
<td>20.4 ± 32.3</td>
<td>20.5 ± 20.3</td>
<td>19.3 ± 18.3</td>
<td>18.2 ± 26.9</td>
<td>24 ± 13.7 26.4</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>16 ± 12.5</td>
<td>18.3 ± 14.7</td>
<td>18.1 ± 14.2</td>
<td>18.4 ± 17.7</td>
<td>18.4 ± 12.2</td>
</tr>
<tr>
<td>Copper (mg)</td>
<td>2.8 ± 2.3 2.4</td>
<td>2.2 ± 1.9</td>
<td>2.1 ± 1.5</td>
<td>2.3 ± 2.7</td>
<td>2.2 ± 1.3</td>
</tr>
<tr>
<td>Selenium (µg)</td>
<td>38.7 ± 18.7</td>
<td>40.8 ± 29.5</td>
<td>37.2 ± 18.3</td>
<td>35.6 ± 22</td>
<td>49.8 ± 41.9</td>
</tr>
</tbody>
</table>

Data show Mean ± SD; Median OB I – III: Obese group. OB I: Obese grade I. OB II: Obese grade II. OB III: Obese grade III.

*Different from normal weight group at \(p<0.05\)
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and peripheral vascular disease in diabetic Japanese patients heterozygous for the Leu allele. Those reports reinforce the importance of the GPx-1 rs1050450 polymorphism in pathologies associated to obesity and the metabolism of carbohydrates. Nevertheless, more studies are necessary in our population, as well as assessing the frequency of the polymorphism in Mexican men, to evaluate whether this polymorphism is relevant in mentioned pathologies.

On the other hand, we identified a solid increased concentration of peripheral TBARS in OB versus CG, and the stratified degrees of the pathology showed a very similar pattern as showed by OB. This data is in line with a previous study made by our group by means of lipid peroxidation, where we found significant differences between obesity groups versus control group.

When we separated the control and study groups in carriers of GPx-1 rs1050450 and compared the concentration of TBARS versus respective wild type participants, a very similar pattern was observed in both groups. Also the comparison of GPx-1 rs1050450 carriers with prediabetes, diabetes and both conditions did not showed any differences between them, neither when they were compared versus their respective wild-type group. The higher concentration of TBARS in OB is in line with previous studies where a higher concentration of MDA (malondialdehyde) and oxidizability of LDL and VLDL were found in obese subjects.

These results support the idea that oxidative stress in people with obesity is the accumulation of diverse factors involved in the process as enzyme antioxidant defense, hyperglycemia, chronic inflammation, hyperleptinemia, elevated tissue lipid levels, inadequate concentration of organic and inorganic cellular antioxidants, etc. Hyperglycemia as we identified in the 68% of the participants, can activate several biochemical pathways as poliot in which sorbitol is obtained from glucose by action of aldose reductase. Excess sorbitol activates stress genes and cause oxidative damage. Hyperglycemia also promotes the production of NADPH by increasing the activity of NADPH oxidase that produces superoxide, especially in the endothelium. Likewise, the auto-oxidation of glucose produces reactive species similar to hydroxyl and superoxide radicals.

In this regards, we observed that the OB presented greater carbohydrate consumption than control group, and although we did not evaluate the difference between the consumption of simple and complex carbohydrates, Mexican population consumes an important percentage of simple carbohydrate present in soft drinks, fruit juices, typical sweet bread, desserts, sweet cookies and chocolates. For example more than 70% of a sample of adolescents consumed more than 25 g/day of sugar from sugar-sweetened beverages.

Also Mexico is the country with the world’s highest per capita consumption of soft drinks (163 liters at year), and ranks second globally in added sugar consumption per person.

Other important mechanism involved in the generation of oxidative stress is the consumption of antioxidants. In our study we found that OB intake had the same amount of the antioxidants evaluated herein in comparison with CG. These results agree with previous reports in Mexican population where obese group had higher intake of energy and lipids, but similar intake of micronutrients compared with normal weight group.

Although there were no differences between the consumption of antioxidants between OB and CG, in general all the participants did not reach the recommended intake. This characteristic was more dramatic in OB, where just 10% of participants reached the recommendation for vitamin E and 65% for cooper and zinc. The deficit consumption of antioxidants is directly associa-
ted with the actual diet in our country, since one of the main source of dietary antioxidants are fruits and vegetables, and these products are consumed in a lower value by Mexican population. Pérez-Lizaur et al34 found that Mexican children consumed on average only once a day these food products. This data is supported by a previous report, where a deficient consumption of selenium in health population where around 50% of male and female participants were below of the necessary concentration in plasma of this mineral35.

In our study we found that 73% of the individuals with obesity did not meet the RDA for selenium, and these levels could be lower than that needed for optimal GPx-1 activity, and genotypes could modulate their expression, promoting the appearance of oxidative stress condition in this group.

Even though in our study we did not analyze the expression or activity of the GPx-1, it has been described an interaction between genotype and selenium, due to nutritional intake of selenium and plasmatic selenium concentration could modulate the GPx-1 expression and activity, depending on the allelic forms, identifying a decreased GPx-1 activity of cells carrying the Leu variant36.

The development of obesity and its principal comorbidities have an important genetic component, which in a complex relationship with environment and behavior of each person, promotes the appearance of obesity and other chronic-degenerative diseases. Nevertheless each ethnic group have a specific set of genes implicated in this phenomenon, as a result of the own “gene-imprinting and gene-transfer”, diet, geographic area of habitat, way of life, etc.

Increasing the knowledge of the genetic characteristics involved in the appearance and development of obesity and its comorbidities in specific populations, is a necessary activity to understand better the etiology of the phenomenon, and improve the strategies related to the diagnostic, prognostic and treatment of the diseases.

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References

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