PON1Q192R polymorphism is associated with lipid profile in Mexican men with Mayan ascendency

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Available online 4 June 2008

Introduction

Human paraoxonase/arylesterase (PON1:aryldialkylphosphatase [E.C.3.1.8.1]) is an enzyme synthesized in the liver and secreted into the plasma where it is associated with high-density lipoproteins (HDL); PON1 gene is a member of a multigene family conformed also by PON2 and PON3 genes (Primo-Parmo et al., 1996). Several studies reveal a wide variation in serum PON1 activities (Eckerson et al., 1983; Geldmacher-von et al., 1983; Rojas-García et al., 2005) and this inter-individual variability was partially attributed to the presence of polymorphisms in PON1 gene.

HUMAN PON1 presents several polymorphisms in the promoter region, that at position −108C/T contributes with the most significant effect in PON1 activity (22.8%) (Leiviev and James, 2000; Brophy et al., 2001). Two polymorphisms in the coding region have been reported: at position 55 (Leu [L]/Met [M]) that is related with differences in PON1 activity, partially due to linkage disequilibrium with the −108C/T polymorphism (Brophy et al., 2001). Polymorphism at position 192 (Gln [Q]/Arg [R]) has been described as substrate-dependent: the alloenzyme 192R hydrolyzes paraoxon faster than the 192Q alloenzyme, whereas other compounds, such as diazoxon, are hydrolyzed faster by the 192Q alloenzyme (Davies et al., 1996). We previously showed by multiple logistic regression analysis that only PON1Q192R polymorphism was associated with PON1 activity towards paraoxon in a Mexican population (Rojas-García et al., 2005).

Initially, PON1 was characterized by its ability to hydrolyze and hence inactivate the oxygen analogues of organophosphorous (OP) compounds (e.g. paraoxon, from what it received its name) and several studies have demonstrated the relevance of PON1 in modulating OP toxicity (Costa et al., 2003). On the other hand, a role of PON1 as an antioxidant of lipoproteins has been established. As an HDL-associated enzyme, it was initially shown that PON1 prevents lipid-peroxide accumulation in low-density lipoproteins (LDL) that are involved in the initiation of atherosclerosis and constitute a major risk factor for the development of coronary heart disease (CHD) (Mackness et al., 1998).

Paraoxonase (PON1) enzyme is associated with high-density lipoproteins (HDL) that prevents low-density lipoprotein (LDL) oxidation. PON1Q192R polymorphism is associated with a risk of coronary heart disease and low HDL levels in case-control studies, but the issue is yet unresolved. Mexico has shown an increase in cardiovascular diseases, and some genetic factors may play a role. Our purpose was to evaluate the association between PON1Q192R and LDL5P polymorphisms and serum lipid profile in a healthy Mexican population. Ninety unrelated male inhabitants from southeastern Mexico with Mayan ancestry agreed to participate. Demographic characteristics, lifestyle and medical history were obtained by questionnaire. Lipid profile was determined by enzymatic methods, PON1 activity by using paraoxon and phenylacetate and PON1 genotype by real-time PCR. HDL-cholesterol (HDL-C) levels were associated with genotype: 192RR homozygote subjects had lower HDL-C levels than 192QQ homozygotes, and individuals with 192RR and 192QR genotypes had an odds ratio (OR)=7.05 (95% confidence interval (CI)=1.29-38.34) of having HDL-C <60 mg/dL. Individuals with higher paraoxonase activity (≥600.18 U/L) had a slight risk (OR=4.9, 95% CI=0.83-22.02) of having HDL-C <60 mg/dL. PON155LM polymorphism was associated with higher LDL-cholesterol. PON1Q192R polymorphism showed a role in modulating lipid profile: 192RR homozygotes showed the least favorable lipoprotein levels.

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The association of PON1Q192R polymorphism with the development of cardiovascular diseases is yet unresolved. Epidemiological evidence suggests that PON1Q192R polymorphism may represent a risk factor to develop CHD, in particular the 192RR genotype (Durrington et al., 2001), but some studies have failed to find this relationship (Ko et al., 1998; Ombres et al., 1998). Few studies have observed an association between serum HDL-cholesterol (HDL-C) levels and PON1Q192R polymorphism (Hegele et al., 1995) or paraoxonase activity (Abbott et al., 1995), and other reports have shown that PON1 activity is lower in subjects with CHD regardless of PON1Q192R polymorphism (Mackness and Mackness, 2004). The association between PON1L55M polymorphism and lipid profile is scarcely studied. Deakin et al. (2002) reported that this polymorphism may be of particular relevance for vascular disease and impaired glucose metabolism. Being homozygous for the 55L allele with a history of premature coronary disease showed a trend to reduced insulin secretion and delayed glucose disposal compared with other genotypes. At present, most studies in this area are case-control in design and have reported controversial findings. This highlights the need to evaluate the association between PON1 polymorphisms and lipid profile, which is one of the risk factors to develop heart diseases, in general populations.

A leading cause of morbidity and mortality in developed countries is CHD (McGovern et al., 2001). In Mexico, heart diseases have been also among the most frequent causes of death in adults in the last decades (Chávez-Domínguez et al., 2003) and CHD and cerebrovascular diseases are among the first mortality causes in southern Mexico (INEGI, 2002), a region with a high density of Mayan population (INL, 1993). Considering that PON1 polymorphism may modulate serum lipid profile and be an important factor for cardiovascular diseases, and because of its dependency of ethnic characteristics, the aim of this study was to evaluate the influence of PON1Q192R and L55M genetic polymorphisms and PON1 phenotype (paraoxonase and arylesterase activities) on lipid profile in a population with Mayan ascendancy from southern Mexico.

Materials and methods

Study population

A cross-sectional study was performed in southern Mexico, during February to September 2005, to evaluate the association between PON1Q192R polymorphism and serum lipid profile. Eligible participants were men with an agrarian lifestyle residing in Muna, Yucatán, Mexico who were born in this state. Invitations to participate were men with an agrarian lifestyle residing in Muna, Yucatán, Mexico who were born in this state. Eligible men in a population with Mayan ascendancy from southern Mexico.

PON1 activity

PON1 enzymatic activities were assayed using paraoxon or phenylacetate as substrates to evaluate paraoxonase and arylesterase activities, respectively, as described by Eckerson et al. (1983). Arylesterase activity was determined by phenol production from the hydrolysis of phenylacetate (Sigma-Aldrich, Milwaukee, WI) using 10 mM Tris–HCl, pH 8.0, 1 mM CaCl₂ and 5 μM EDTA. Eserine sulfate (Sigma-Aldrich, San Louis, MO) was used to inhibit the unspecific hydrolysis due to serum albumin and serum cholinesterase. The increase in A₂₇₀ was followed for 5 min (the molar extinction coefficient of phenol is 1.31×10³), arylesterase activity was expressed as U/mL. Paraoxonase activity (hydrolysis of paraoxon; ChemService, West Chester, PA) was performed in the presence of 1 M NaCl (salt-stimulated) to get better identification of PON1 phenotype (Eckerson et al., 1983). The paraoxonase activity was assayed by monitoring the p-nitrophenol formation, the increase in A₄₀₅ was followed for 5 min (the molar extinction coefficient of p-nitrophenol is 18.05×10³), and paraoxonase activity was expressed as U/L.

PON1Q192R and L55M polymorphisms.

Genomic DNA was extracted using the High Pure PCR Template Preparation Kit (Roche). To prevent contamination, all PCR procedures were performed under an ultraviolet-irradiated hood. PON1Q192R and L55M polymorphisms were determined by real-time PCR (ABI Prism™ 7000 Sequence Detection System) using TaqMan® Universal PCR Master Mix (Applied Biosystems, Foster City, CA), according to Rojas-García et al. (2005). Briefly, the primers used were: CTCAGCATTCTT- TATGGCACAATAGTAACACCAATATACCATCTC for PON1Q192R polymorphism and ACAACCTGTATTTCTGGTCTCTTCTCTTG/ CAGACC-TAATGAACGCCAGTCCT for PON1L55M polymorphism and the VIC/FAM probes for PON1Q192R were CCTACTTACACTTG/ CCCTACTTACACTCGT and for PON1L55M were AATATCTCCATGCTGCTT and for PON1L55M were AATATCTCCATGCTGCTT. Reactions were performed using 5 μL of TaqMan Universal PCR Master Mix (containing AmpliTaq Gold DNA Polymerase, AmpErase UNG, dNTPs with dUTP, Passive Reference 1, and optimized buffer components), 0.25 μL of 40X primer–probe mix (containing primers at 36 μM and dye-labeled probes at 8 μM), and approximately 20 ng of genomic DNA; the reaction mixture was completed to 10 μL with water. Thermal cycling conditions were: a step at 50 °C for 2 min, a hot-start at 95 °C for 10 min, and a two step protocol was followed by 40 cycles: 95 °C for 15 s and 60 °C for 1 min. Allele discrimination was detected by two differentially labeled TaqMan probes labeled with two different fluorochromes, a reporter dye 6-carboxyfluorescein (6-FAM) and VIC® at the 5′ end.

Lipid profile

Serum total cholesterol (TC) and triglycerides (TG) were determined by enzymatic methods using CHOD-PAP (cholesterol oxidase-p-aminophenazone) (Roche/Hitachi, Mannheim, Germany) and GPO-PAP (glycerol phosphate oxidase-p-aminophenazone, Roche/Hitachi), respectively. HDL-C was measured using the cholesterol-esterase and cholesterol-oxidase enzymes modified with polyethylene glycol (PEG) (HDL-C Plus) (Roche/Hitachi, Mannheim, Germany). The detection limit was 3 mg/dL with a CV < 10%. LDL-cholesterol (LDL-C) was determined directly without sample pre-treatment, using the LDL-C plus 2nd generation kit from Roche/Hitachi (Mannheim, Germany). Results from the enzymatic techniques have proved to reach the standards from the National Cholesterol Education Program (Bachorik and Ross, 1995) and agree with those obtained with the precipitation or ultracentrifugation methods (Roche Diagnostics).
Table 1
General characteristics and lipid profile from the participating subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All (n=90)</th>
<th>Abnormal samples (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.4±15.4</td>
<td></td>
</tr>
<tr>
<td>Mayan ascendency (%)</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption (%)</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.6 (26.9–28.4)</td>
<td>77</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>165.5±34.4</td>
<td>20</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>188.5 (164.8–215.6)</td>
<td>63</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>41.3 (39.1–43.8)</td>
<td>42</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>90.0±27.7</td>
<td>10</td>
</tr>
<tr>
<td>LDL-C/HDL-C</td>
<td>2.1±0.67</td>
<td>98</td>
</tr>
<tr>
<td>Total cholesterol/HDL-C</td>
<td>4.0±0.99</td>
<td>71</td>
</tr>
</tbody>
</table>

a Percentage of samples outside the normal values.
b Data are expressed as arithmetic mean±SD.
c Data are expressed as geometric mean and confidence interval.
d Calculated as the weight divided by height squared (kg/m²); normal <25, overweight ≥ 25 to <30, obesity ≥ 30 to <40 (Flegal et al., 2004).

Table 2
Paraoxonase and arylesterase activities according to PON1Q192R and L55M polymorphisms

<table>
<thead>
<tr>
<th>Activity</th>
<th>PON1Q192R (n=90)</th>
<th>PON1L55M (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>QQ (n=18)</td>
<td>RR (n=29)</td>
</tr>
<tr>
<td>Paraoxonase (U/L)</td>
<td>196.7±154.1 (256.2)</td>
<td>523.7±449.9 (609.5)</td>
</tr>
<tr>
<td>Arylesterase (U/mL)</td>
<td>112.1±28.5 (576–163.3)</td>
<td>138.1±273 (922–1940)</td>
</tr>
</tbody>
</table>

a Evaluated by ANOVA.
b Data are expressed as geometric mean and confidence interval and log-transformed for statistical analysis.
c Evaluated by Mann–Whitney.
d Expressed as arithmetic mean±SD.
e Evaluated by Student’s t test. Genotyping of PON1Q192R polymorphism was done in 90 subjects and PON1L55M polymorphism in 75 subjects.

Statistical analyses

The chi square test was used to evaluate the deviation of genotype frequencies from the Hardy–Weinberg equilibrium, and to evaluate the genotype and allele distributions between the study subjects and other populations. Logarithmic transformation of HDL-C and paraoxonase activity, and reciprocation of squared root transformation of TG were performed to improve normality. Differences between PON1Q192R and L55M polymorphisms and serum lipids and PON1 activities were evaluated by ANOVA and Bonferroni multiple comparison and Mann–Whitney or Student’s t tests, respectively. To estimate the risk of having serum lipid profile below normal values with PON1Q192R genotype, odds ratios were calculated by the multiple logistic regression analysis. Cut-offs for HDL-C (<40 and ≥ 60 mg/dL) were established according to literature: HDL-C values <40 mg/dL have been associated with a high risk of cardiovascular diseases and values >60 mg/dL with protection from cardiovascular diseases (Stone et al., 2005). We evaluated covariates associated with lipid profile, including age, body mass index (BMI), smoking, alcohol consumption and fat diet; finally, only smoking was included in the final model. Simple logistic regression was applied to test the association between PON1 paraoxonase activity and lipid profile after categorization of paraoxonase activity into its median distribution (>600.18 vs ≤ 600.18 U/L). The power of the study was calculated according to method of Fleiss (1981). All statistical analyses were conducted using the STATA version 8.1 (STATA, Corp.).

Results

The general characteristics of the studied population are shown in Table 1. Participants mean age was 48 ± 15 years and 49% had Mayan ascendency (at least one Mayan surname). According to the BMI, a high percentage of subjects (77%) showed different grades of overweight (BMI ≥ 25 kg/m²; Flegal et al., 2004).

PON1 L55M and Q192R genotypes and phenotype

Frequencies for 192Q and 192R alleles were 0.44 and 0.56, respectively and for 55M and 55L alleles were 0.18 and 0.82, respectively. The genotype frequencies were: PON1Q1/PON1Q=0.20, PON1Q1/PON1R=0.48 and PON1R/PON1R=0.32 and PON1L/PON1M=0.37 and PON1L/PON1L=0.63, the PON1M/PON1M genotype was not observed. There was no significant deviation of PON1L55M and Q192R genotype frequencies from those predicted by the Hardy–Weinberg law (p values of 0.15 and 0.96, respectively).

PON1 activities (paraoxonase and arylesterase) as a function of PON1Q192R and L55M polymorphisms revealed significant differences (p<0.05) among genotypes (Table 2). Individuals with the 192RR and 55LL genotypes had the highest activity, both paraoxonase and arylesterase. General characteristics of the study population were similar among PON1 different genotypes. A marked inter-individual variation was shown, particularly for paraoxonase activity and an inverse relationship was found between paraoxonase activity and fat intake (p=0.051).

Lipid profile

Regarding serum lipid levels, data are depicted in Table 1. Only serum triglycerides showed a mean value (188.5 mg/dL) higher than the normal level (<150 mg/dL); 63% of subjects showed abnormal levels. Total cholesterol and LDL-C levels were within normality, and although HDL-C mean value was within the normal range, approximately 40% of subjects showed values lower than 40 mg/dL (minimal normal concentration) (Stone et al., 2005). On the other hand, LDL-C/HDL-C and TC/HDL-C ratios were significantly higher than normal values, with frequencies of abnormality of 98% and 71%, respectively.

Association between PON1Q192R and L55M polymorphisms and lipid profile

Regarding to serum lipid profile, PON1Q192R polymorphism was only associated with HDL-C levels (Table 3); significantly lower (p<0.40 mg/dL and although there were few subjects (n=11) with HDL-C values >60 mg/dL, 5 and 2 subjects had the 192QQ and 192RR genotypes, respectively (data not shown). This suggests that 192RR genotype may be related to HDL-C concentrations. No significant differences were found between PON1Q192R polymorphism and LDL-C or TC values or with LDL-C/HDL-C or TC/HDL-C ratios (Table 3). Finally, there was no significant difference in HDL-C values according to PON1 L55M genotype; however, individuals with the 55LM genotype had higher LDL-C levels than 55LL homozygote subjects (Table 3).
Multivariate analysis of HDL-C and PON1Q192R polymorphism was done to estimate the risk of having low HDL-C levels and results are shown in Table 4. Considering HDL-C as <40 mg/dL (value associated with cardiovascular disease risks), subjects carrying the 192R allele (homozygotes or heterozygotes) did not show an increased risk of having lower values of HDL-C. Whereas, when HDL-C concentration of ≥60 mg/dL was used as the reference (value that protects against cardiovascular diseases), subjects carrying the 192R allele (homozygotes or heterozygotes) were 7-fold (OR=7.05, 95% CI=1.29–40.34; p=0.024) as likely of having lower values of HDL-C. Homozygote subjects for the 192R allele had lower levels of HDL-C compared to heterozygote subjects (OR=0.38, 95% CI=0.20–0.73; p=0.009). This suggests that PON1 may be a determinant of serum lipid levels, and was included in the final model.

Related to PON1 phenotype, no associations were observed between PON1 activities (paraoxonase or arylesterase) and the lipid profile, modeled as continuous variables (data not shown). However, to evaluate the risk of having low HDL-C levels (<60 mg/dL as the reference value) according to paraoxonase activity (categorized into the median value of 600.18 U/L), a slight association (p=0.08) was observed (Table 4); those individuals with paraoxonase activity above the median value of 600.18 U/L (all of them with the 192RR genotype) had an OR=4.93 of having less than 60 mg/dL of HDL-C. There was neither an effect of PON1 phenotype on HDL-C, taking 40 mg/dL as the reference value, nor an association between HDL-C and arylesterase activity (data not shown).

**Table 3**

<p>| Lipid profile from the participating subjects according to PON1Q192R and L55M polymorphisms |</p>
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Polymorphism</th>
<th>QQ (n=18)</th>
<th>QR (n=43)</th>
<th>RR (n=29)</th>
<th>p</th>
<th>PQ1L55M (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides (mg/dL)^a</td>
<td>177.9 (122.3–258.8)</td>
<td>168.1 (141.5–199.8)</td>
<td>231.5 (180.9–296.3)</td>
<td>0.09</td>
<td>178.7 (142.1–224.5)</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)^b</td>
<td>178.0 ± 13.7 (130–239)</td>
<td>160.8 ± 32.8 (80–236)</td>
<td>164.6 ± 36.5 (110–250)</td>
<td>0.20</td>
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<tr>
<td>HDL-C (mg/dL)^b</td>
<td>47.7 (41.3–54.9)</td>
<td>40.5 (37.2–44.1)</td>
<td>39.1 (35.4–42.8)</td>
<td>0.03^a</td>
<td>41.6 (37.5–46.3)</td>
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<tr>
<td>LDL-C (mg/dL)^b</td>
<td>95.3 ± 29.9 (15–147)</td>
<td>91.9 ± 28.1 (27–161)</td>
<td>83.8 ± 25.6 (42–144)</td>
<td>0.32</td>
<td>101.0 ± 36.2 (37–161)</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol/HDL-C</td>
<td>3.75 ± 0.82 (2.2–5.1)</td>
<td>4.0 ± 0.98 (2.1–5.8)</td>
<td>4.25 ± 1.06 (2.1–6.8)</td>
<td>0.22</td>
<td>4.1 ± 1.0 (2.2–5.7)</td>
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<td>LDL-C/HDL-C</td>
<td>2.0 ± 0.75 (0.12–3.1)</td>
<td>2.21 ± 0.63 (0.94–3.5)</td>
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^a Evaluated by ANOVA. ^b Data are expressed as arithmetic mean±SD (range is in parenthesis). ^c Evaluated by Mann-Whitney. ^d Data are expressed as arithmetic mean±SD (range is in parenthesis). ^e Evaluated by Student’s t test. ^f Data are expressed as arithmetic mean±SD (range is in parenthesis).

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^a Evaluated by ANOVA. ^b Data are expressed as geometric mean and confidence interval. ^c From reciprocal square root-transformed values. ^d Evaluated by Student’s t test. ^e Data are expressed as arithmetic mean±SD (range is in parenthesis). ^f Evaluated by Student’s t test.
This study was conducted in healthy individuals with no clinical diagnosis of cardiovascular diseases, while most evidence has been obtained from case-control studies. Rozek et al. (2005) reported that the association between PON1 activity and HDL-C levels is different in carotid artery disease cases compared to control healthy individuals. In addition, PON1 activity can be inhibited by oxidative stress, depending on the PON1Q192R polymorphism; a worse protection against oxidation is observed with the 192R alloenzyme and it is more easily impaired than the 192Q alloenzyme (Aviram et al., 1998). Therefore, low PON1 activity in patients with a cardiovascular outcome or other adverse oxidative stress-associated illness may not be related to their genotype. On the other hand, our studied population had a wide range of HDL-C levels and a high number of individuals (32%) with the unfavorable genotype (192RR) than those reported in other studies (Blatter Garin et al., 2005; Gamboa et al., 2006), this may account for the association observed between PON1Q192R polymorphism and HDL-C. In addition, although we are aware that the low number of participants (n = 90) may be an inherent limitation of our study, the estimated power was 77%, very close to the standard (80%) (Fleiss, 1981) and the allele frequencies were according to the Hardy-Weinberg law. Finally, another possible explanation for differences among studies may be that PON1 activity and lipid levels can be modified by environmental factors, such as diet (Tomás et al., 2001) or physical activity (Sentí et al., 2000). Participants in the present study had homogenous alimentary habits, in which consumption of fatty food (derived from pork) was common; however, BMI was not a confounder nor was the fat intake.

In our study, 42% of subjects had HDL-C values lower than 40 mg/dL, from which 14 subjects (36%) were 192RR homozygotes and 5 (13%) were homozygote for the 192Q allele. Although the metabolic syndrome was not diagnosed in our participants (mean age of 48 years), 3 of the criteria that define it: increased TG, low HDL-C and increased abdominal circumference (taken as overweight in this study) (Stone et al., 2005) were more frequently observed in 192RR individuals compared with 192QQ homozygote subjects (data not shown). Considering that high values of HDL-C may act as a protective mechanism against cardiovascular diseases, our data suggest that there may be more 192RR individuals at risk for developing these pathologies. In this regard, previous studies reported a high frequency of subjects with the 192R allele with CHD and myocardial infarction (Serrato and Marian, 1995; Sanghara et al., 1997), although some studies have failed to find this relationship (Ko et al., 1998; Ombres et al., 1998). Furthermore, Marra et al. (2006) observed that 192RR genotype was associated with a high prevalence of arterial hypertension, and suggested that PON1Q192R polymorphism may help to identify subjects at early stages of cardiovascular diseases.

Several studies have focused on HDL as a protective factor against LDL liperoxidation. Mackness et al. (1993) first reported the antioxidant activity of HDL by decreasing the accumulation of lipid-peroxides on LDL, due in part, by the HDL-associated enzymes, such as PON1. PON1-associated HDL particle destroys the active LDL-derived oxidized lipids once they are formed and also prevents their formation (Mackness et al., 1993; Aviram et al., 1998). On the other hand, PON1Q192R polymorphism has been controversially associated with the capacity to protect LDL lipoperoxidation; HDL containing the 192Q alloenzyme better retained the protective antioxidative effect than the 192R alloenzyme (Mackness et al., 1998). In addition, Cao et al. (1999) reported that PON1 protection against LDL oxidation shows different enzymatic efficiency according to PON1Q192R polymorphism, corresponding to a better protection per unit of enzyme to the 192QQ genotype. Other HDL-associated enzymes that metabolize LDL lipid-peroxides as well, may contribute in protecting LDL against oxidative mechanisms, such as the platelet activating factor-acetylhydrolase (PAFAH) (Watson et al., 1995), and the lactonase activity of serum PON1 anchored on HDL with apolipoprotein A (Gaidukov and Tawfik, 2005).

Few studies have explored the genetic characteristics of Mayan populations. Herrera et al. (2007) reported a wide variability among Mayan groups from southern Mexico, evaluating ten polymorphic Alu insertion (PAI) loci, while Ferrel et al. (1990) reported the presence of the APO C-III*D allele in Mayans from this region, which is associated with low levels of plasma APO C-III, a component of HDL and VLDL (very low density lipoproteins). The lowest levels of TC and TG were observed in homozygous subjects for the deficient allele. In addition, Ahn et al. (1991) reported that polymorphisms in the apolipoprotein AI/CI/IV gene cluster had significant effects in plasma lipid levels in Mayan Indians. These polymorphisms, together with PON1Q192R, may account for the high prevalence of cardiovascular diseases, observed in this region of southern Mexico (Epidemiological and DeathStatistical System/SSA-Yucatán, Mexico, 2006).

Regarding PON1 phenotype, our results showed a slight association between paraoxonase activity and HDL-C levels; those individuals with values above the median (all had the 192RR genotype) had an OR = 4.93 of having less than 60 mg/dL of HDL-C. Lin et al. (2002) reported a significant correlation between HDL-C and PON1 phenotype in Taiwanese individuals and Singh et al. (1999) did not observe any association in healthy Indian Punjabis.

PON1Q192R alloenzymes have different efficiencies for the hydrolysis of some organophosphates; 192R has higher activity by paraoxon but lower by diazoxon than 192Q (Davies et al., 1996). Thus, it is not unexpected that activities of 192Q and 192RR alloenzymes may not be the same for protection against LDL oxidation (Aviram et al., 1998). This suggests that PON1Q192R alloenzymes may possess different sensitivities to peroxides formed during LDL oxidation, therefore, different antioxidant capacities.

The association between PON1L55M polymorphism and lipid profile has been less studied. We did not observe an association between PON1L55M polymorphism and HDL-C, but significant higher levels of HDL-C in 55LM heterozygote subjects. Fanella et al. (2000) and Deakin et al. (2002) reported a trend of higher LDL-C and lower HDL-C levels according to PON1L55M polymorphism, 55MM subjects had the less favorable profile.

In summary, data generated in this study will contribute to support the role of PON1Q192R genetic polymorphism as one determinant of plasma lipid levels in healthy populations who may be at higher risk if environmental factors (e.g. diet, exercise, etc.) are combined on their lifestyle. In addition, it is important to explore the effect of PON1 genetic polymorphisms on lipid metabolism in diverse populations with different ethnicities. Authors are aware that lipid profile is a multifactorial characteristic that cannot be explained by only one factor and caution must be taken when comparing data from different populations.

Acknowledgments

Authors are grateful to Dr. Jorge Alvarado-Mejía, Dr. Leticia González-Navarrete, Hilda Polanco-Minaya and Elsa Salazar-Arredondo for collaborating during the survey and María de Jesús Solís-Heredia and Gerardo Martínez-Aguilar for their technical assistance. NPH had a scholarship from CONACyT-Mexico. This study was financially supported by CONACyT-Mexico (Grant #CO1-134).

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