**Name of Journal: *World Journal of Hepatology***

**ESPS Manuscript NO: 25637**

**Manuscript Type: Original Article**

***Retrospective Study***

***CD36* genetic variation, fat intake and liver fibrosis in chronic hepatitis C virus infection**

Ramos-LopezO *et al. CD36* taste receptor and hepatitis C

**Omar Ramos-Lopez, Sonia Roman, Erika Martinez-Lopez, Nora A Fierro, Karina Gonzalez-Aldaco, Alexis Jose-Abrego, Arturo Panduro**

**Omar Ramos-Lopez, Sonia Roman, Erika Martinez-Lopez, Nora A. Fierro, Karina Gonzalez-Aldaco, Alexis Jose-Abrego, Arturo Panduro,** Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara “Fray Antonio Alcalde”, Guadalajara, Jalisco 44280, Mexico

**Omar Ramos-Lopez, Sonia Roman, Erika Martinez-Lopez, Nora A. Fierro, Karina Gonzalez-Aldaco, Alexis Jose-Abrego, Arturo Panduro,** Health Sciences University Center, University of Guadalajara, Guadalajara, Jalisco 44340, Mexico

**Author contributions:** Lopez O performed the genotyping experiments, statistical analysis and prepared the first draft of the manuscript; Roman S wrote, integrated the final version and critically revised the content of this article; Martinez-Lopez E provided the biochemical tests and critically revised the manuscript; Ramos- Fierro NA wrote and critically revised the article; Gonzalez-Aldaco K and Jose-Abrego A wrote, revised statistical analysis and critically reviewed the manuscript; Panduro A conceived the study, performed clinical studies and transient elastography, wrote and critically revised the content of this article; all authors critically reviewed all drafts and approved the final manuscript.

**Supported by** Promep-University of Guadalajara to AP, No. UDG-CA-478.

**Institutional review board statement:** The study was reviewed and approved by the Ethics Committee of the Health Sciences University Center.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** The authors declare that they have no conflict of interest.

**Data sharing statement:** No additional data are available.

**Open-Access:** This is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Manuscript source:** Invited manuscript

**Correspondence to: Arturo Panduro, MD, PhD, FAASLD,** Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara, “Fray Antonio Alcalde”, Hospital # 278, Col. El Retiro, Guadalajara, Jalisco 44280, Mexico. apanduro@prodigy.net.mx

**Telephone:** +52-33-36147743

**Fax:** +52-33-36147743

**Received:** March 29, 2016

**Peer-review started:** March 31, 2016

**First decision:** June 12, 2016

**Revised:** June 28, 2016

**Accepted:** August 11, 2016

**Article in press:**

**Published online:**

**Abstract**

**AIM:** To analyze the association of the *CD36* polymorphism (rs1761667) with dietary intake and liver fibrosis (LF) in chronic hepatitis C (CHC) patients.

**METHODS:** In this study, 73 patients with CHC were recruited. The *CD36* genotype (G > A) was determined by a TaqMan Real-Time PCR system. Dietary assessment was carried out using a three-day food record to register the daily intake of macronutrients. Serum lipids and liver enzymes were measured by a dry chemistry assay. LF evaluated by transient elastography (Fibroscan®) and APRI score was classified as mild LF (F1-F2) and advanced LF (F3-F4).

**RESULTS**: Overall, the *CD36* genotypic frequencies were AA (30.1%), AG (54.8%), and GG (15.1%), whereas the allelic A and G frequencies were 57.5% and 42.5%, respectively. CHC patients who were carriers of the *CD36* AA genotype had a higher intake of calories attributable to total fat and saturated fatty acids (SFA) than those with the non-AA genotypes. Additionally, aspartate aminotransferase (AST) serum values were higher in AA genotype carriers compared to non-AA carriers (91.7 IU/L *vs* 69.8 IU/L, *P* = 0.02). Moreover, the AA genotype was associated with an increase of 30.23 IU/L of AST (β = 30.23, 95%CI: 9.0-51.46, *P* = 0.006). Likewise, the AA genotype was associated with advanced LF compared to the AG (OR = 3.60, 95%CI: 1.16-11.15, *P* = 0.02) or AG + GG genotypes (OR = 3.52, 95%CI: 1.18-10.45, *P* = 0.02).

**CONCLUSION:** This study suggests thatthe *CD36* (rs1761667) AA genotype is associated with higher fat intake and more instances of advanced LF in CHC patients.

**Key words:** Hepatitis C virus infection; *CD36* receptor; Lipids; Liver fibrosis; Mexico

**© The Author(s) 2016**. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** In this study, chronically infected hepatitis C patients who were carriers of the AA genotype of the *CD36* receptor polymorphism (rs1761667) showed a higher risk of advanced liver fibrosis compared to patients with an AG/GG genotype. This liver damage was associated with the consumption of a hepatopatogenic diet, high-calories and excessive intake of total and saturated fat, typical of the population of West Mexico. Thus, preventive nutritional intervention strategies based on the *CD36* genotype may be a useful tool to avoid further liver damage due to alterations in liver lipid metabolism and inflammation in patients with chronic hepatitis C infection.

Ramos-Lopez O, Roman S, Martinez-Lopez E, Fierro NA, Gonzalez-Aldaco K, Jose-Abrego A, Panduro A. CD36 genetic variation, fat intake and liver fibrosis in chronic HCV infection. *World J Hepatol* 2016; In press

**INTRODUCTION**

The hepatitis C virus (HCV) is a hepatotropic human RNA virus, member of the *Flaviviridae* family[1]. Globally, it is estimated that nearly 170 million individuals are infected with HCV, causing yearly 350,000 deaths[2]. Liver cirrhosis causes a high burden of liver disease in Mexico, and HCV infection represents one of its primary etiologies[3,4]. Approximately two million Mexican individuals are infected with HCV[5,6] and up to 64% of patients with acute HCV infection fail to undergo spontaneous viral clearance[7]. Thus, chronically infected patients may be at risk of liver fibrosis (LF), cirrhosis, and hepatocellular carcinoma (HCC) during a period of 20 to 30 years[4,8].

Regardless of etiology, the pathogenesis of LF is influenced both by genetic and environmental factors[9,10]. High-fat diets, which have a significant content of saturated fatty acids (SFA), have been associated with the pathological processes known to be involved in liver fibrogenesis, including steatosis, inflammation, and insulin resistance[11-13]. Recently, we reported that in West Mexico, the general population and patients with liver disease consume an excessive amount of red meat, fried foods, sausages, and pastry products[14]. Consequently, these dietary trends have increased the proportional intake of calories, total fat, and SFA, which could eventually lead to liver damage in individuals that consume this type of hepatopathogenic diet.

In addition to the textural, olfactory, neural and hormonal mechanisms involved in food intake, taste perception is considered a critical determinant of dietary preferences[15,16]. There is growing evidence of the existence of a new taste modality related to fat preference[17]. Experimental studies suggest that the lingual cluster of differentiation 36 (CD36) receptor regulates the motivation for fatty food consumption in rodents[18,19]. This effect is carried out through the cellular capture of long-chain fatty acids (LCFA) by the CD36 receptors on the taste buds[20]; subsequently, lipid signals are transduced into the gustatory nervous pathway[21]. Therefore, genetic variations that lead to changes in the expression of CD36 could explain the interindividual differences in fat linking[15]. CD36 protein levels are modulated by several single nucleotide polymorphisms (SNPs) in the *CD36* gene on chromosome 7[22,23]. One SNP consists of a nucleotide substitution of guanine for adenine in the *CD36* gene promoter sequence (-31118G > A, rs1761667)[24]. This SNP has been associated with a significant reduction in the CD36 expression in several tissues[25,26].

Recently, we reported an association between *CD36* with a higher intake of fat portions and high serum cholesterol among the general population of West Mexico[27]. However, its role in dietary intake and HCV-related liver damage is currently unknown. Therefore, this study aimed to analyze the association of the rs1761667 *CD36* polymorphism with dietary intake and LF in patients chronically infected with hepatitis C.

**MATERIALS AND METHODS**

***Study design***

In this retrospective study, 73 chronic hepatitis C (CHC) patients were recruited at the Department of Molecular Biology in Medicine from January 2012 to December 2014. Chronic HCV infection was defined as a positive anti-HCV test result (ELISA Third-Generation, AxSYM, Abbott Laboratories, Illinois, USA) and the presence of serum HCV RNA for more than six months (COBAS® AmpliPrep/COBAS® Taqman® HCV Test; Roche Diagnostics, Pleasanton, CA, USA)[28,29]. Duration of infection (years) was estimated by the self-reported date of exposure to any known risk factor for HCV infection including the history of surgeries, blood transfusions, hemodialysis, acupuncture, injection drug use and tattooing[30]. Patients co-infected with the hepatitis B virus or human immunodeficiency virus, as well as alcohol abusers were excluded. Based on the pattern of alcohol intake in West Mexico, alcohol abusers were defined as those individuals that consumed more than two drinks per occasion, as previously described[31]. None of the CHC patients in the study group had received antiviral treatment for HCV infection.

***Viral genotyping***

A VERSANT HCV Genotype 2.0 line probe assay was used to determine the HCV genotypes (Innogenetics, Ghent, Belgium).

***Body mass index (BMI) measurement***

An electrical bioimpedance apparatus was used to assess body mass index (BMI, kg/m2) (INBODY 3.0, Analyzer Body Composition, Biospace, Korea).

***Dietary assessment***

A three-day food record (two weekdays and one weekend day) was used as a tool to assess the patient’s dietary intake, which has been previously used for our population[27,32-34]. This methodology provides accurate data concerning intake of food and nutrients[35]. Briefly, each subject was instructed on how to register the type, amount, and mode of preparation of all foods using food models[32]. The food records were coded by a qualified dietitian using a specialized software (Nutrikcal VO®, Mexico). This program calculated the total amount of calories, fat, protein, and carbohydrates as well as the daily intake of food group servings such as sugars, meat, fruits, vegetables, fats, milk, legumes, and cereals. Dietary data were averaged over the three-day food records and were compared with the recommended dietary intakes based on the Mexican System of Food and Equivalents[36,37].

***Biochemical tests***

Serum was obtained from ten mL blood samples after a 12-h overnight fast. Biochemical tests included glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), total cholesterol (TC), triglycerides (TG) and high-density lipoprotein cholesterol (HDL-c). The Friedewald formula was selected to estimate low-density lipoprotein cholesterol (LDL-c)[38]. The concentration of very low-density lipoprotein cholesterol (VLDL-c) was calculated as Total Cholesterol - (LDL-c + HDL-c). All biochemical tests were performed using a dry chemistry assay on a Vitros 250 Analyzer (Ortho-Clinical Diagnostics, Johnson & Johnson Co, Rochester, NY).

***Liver fibrosis evaluation***

Liver stiffness (fibrosis) was evaluated by transient elastography (TE) (FibroScan® Echosens, Paris, France). The average value of ten successful readings expressed in kilopascals (KPa) was used as an indicator of LF according to the following classification: F1 (< 7 KPa), F1-F2 (7 KPa-8.49 KPa), F2 (8.5 KPa-9.49 KPa), F3 (9.5 KPa-12.49 KPa) and F3-F4 (12.5 KPa-14.49 KPa) and F4 (> 14.5 KPa)[39]. For this study, patients in either the F1 or F2 stages were classified as having mild LF and those in the F3 or F4 stages were classified as having advanced LF[40]. This classification was corroborated by calculating the aspartate aminotransferase-to-platelet ratio index (APRI score), as previously described[41].

***CD36 genotyping***

Leukocyte genomic DNA was extracted by a modified salting-out method[42]. The rs1761667 *CD36* polymorphism was detected by an allelic discrimination assay (TaqMan, Applied Biosystems, ID C\_8314999\_10; Foster City, CA, USA) in a 96-well format (StepOnePlus thermocycler (Applied Biosystems, Foster City, CA, USA) as previously described[27,34].

***Statistical analysis***

The sample size was estimated by a formula for the comparison of proportions[43] resulting in a statistical power of 80% (β = 0.20) with a reliability of 95% (α = 0.05) based on the rs1761667 *CD36* allelic frequency in our population[24,27]. Quantitative variables were expressed as mean ± Standard Deviation (SD) and analyzed by one-way ANOVA adjusted for age, gender, and BMI. Subsequently, post hoc tests were run (Bonferroni’s test and Dunnett’s T3 test). Finally, to quantify the effect of the *CD36* genotypes on quantitative variables, linear regression was performed. The Hardy-Weinberg equilibrium (HWE) and qualitative variables were evaluated by the chi-square test. The association of the *CD36* genotypes with LF was assessed by odds ratio (OR) as well as logistic regression tests considering a confidence interval (CI) of 95%. A *P*-value of < 0.05 was considered significant. Statistical analyses were performed using Arlequin (version 3.1), Epi InfoTM 7 (CDC, Atlanta, GA) and SPSS Statistics, Version 20.0 (IBM Corp, Armonk, NY). All statistical analyses were reviewed and approved by an expert biomedical statistician.

***Ethical guidelines***

This study was in compliance with the ethical guidelines defined by the Declaration of Helsinki 2013 and was approved by the Institutional Board Review (CI-01913). All patients who agreed to enter this study signed a written informed consent.

**RESULTS**

In this study, the genotypic frequencies were AA (30.1%), AG (54.8%), and GG (15.1%), whereas the allelic A and G frequencies were 57.5% and 42.5%, respectively. These genotypes were concordant with the HWE (*P* = 0.50). In Table 1, the demographical and clinical characteristics of the CHC patients by *CD36* genotypeare shown. No significant differences for the variables of age, gender, BMI, years of infection, and HCV genotypes between *CD36* genotypes were found. Only the CHC patients who were carriers of the AA genotype were overweight according to the WHO classification (BMI = 26.6 kg/m2). HCV genotype 1 was the most frequent with 68.4% of the total cases, followed by HCV genotype 2 (23.3%) and HCV genotype 3 (8.2%).

The daily dietary intake of the CHC patients classified by *CD36* genotype is shown in Table 2. CHC patients who were carriers of the *CD36* AA genotype had a higher caloric intake relative to total fat, and SFA than those with the AG and GG genotypes. No differences in protein and CH intakes between *CD36* genotypes were observed. Subsequently, the daily intake of several food groups classified by *CD36* genotype is shown in Table 3. Fats were the only food group associated with the *CD36* genotype. The lipid and liver profiles of the CHC patients by *CD36* genotype are shown in Table 4.CHC patients with the *CD36* AA genotype had more elevated serum levels of AST than the AG genotype carriers (91.7 IU/L *vs* 69.8 IU/L, *P* = 0.02). Furthermore, an increase of 30.23 IU/L of AST was attributed to the AA genotype when compared with the AG genotype (β = 30.23, 95%CI: 9.0-51.46, *P* = 0.006). No differences for ALT and GGT were observed (Table 4).

According to the categories of LF established in this study, 47.9% of the CHC patients had mild fibrosis, whereas 52.1% presented advanced fibrosis (Table 5). Among the CHC patients, the Kpa values and APRI score were higher in those with advanced fibrosis compared to those with mild fibrosis (22.7 KPa *vs* 6.5 Kpa, *P* < 0.001 and 1.78 *vs* 0.81, *P* < 0.001, respectively). CHC patients with advanced fibrosis had a higher frequency of the *CD36* AA genotype than those with mild fibrosis (42.1% *vs* 17.1%, *P* = 0.002), respectively (Table 6). Additionally, patients who were AA genotype carriers had a higher risk for advanced fibrosis than those with the AG genotype (OR = 3.60, 95%CI: 1.16-11.15, *P* = 0.02) and AG+GG genotypes (OR = 3.51 95%CI: 1.18-10.45, *P* = 0.02). A logistic regression test was used to corroborate this association (OR = 2.23 95%CI: 1.03-4.81, *P* = 0.041).

**DISCUSSION**

Genetic polymorphisms in fat taste perception may partially explain the interindividual variability in fat intake[15] and their association with the risk of developing chronic diseases[15,44]. Over recent years, it has been proposed that the CD36 receptor is an oral fat sensor that may influence an individual’s preference for high-fat foods[15-18]. Specifically, it has been shown that the *CD36* AA genotype decreases fat taste perception[45-48]. In this study, the frequency of *CD36* AA genotype was 30.1%. In regards to food consumption, despite that the three-day food record may not be representative of the long-term food variety, the amount of fat intake represented over 30% of the total daily calories. It has been documented that the prolonged ingestion of high-fat diets increases the risk for metabolic disorders[49]. These data were consistent with previous results found in overweight patients from the general population of West Mexico[27].

The association of high-fat diets with LF has been well documented in animal models[11-13] as well as in humans in different populations[50,51]. In this study, among the *CD36* AA genotype carriers, more cases of advanced LF were detected. This disease stage is characterized by steatosis and persistent inflammation[4]. Also, they exhibited significantly higher levels of AST, which is a better predictor of progression of LF than ALT or GGT[52]. Furthermore, two validated non-invasive methods (TE and APRI score) were used to evaluate LF[41,53]. Since no differences in demographic and viral characteristics between *CD36* genotypes were found, the likelihood of HCV-related LF seems to be enhanced because of the higher consumption of fat portions observed among the *CD36* AA genotype carriers.

The immunological mechanisms that regulate LF progression during HCV infection have been extensively studied[54-56]. However, alterations in lipid and lipoprotein metabolism have been reported to play a key role[9], considering that chronic HCV infection is characterized by hypocholesterolemia and reduced levels of LDL-c, TG and apoB[57]. Recently, a novel interaction of the CD36 receptor in liver VLDL-c metabolism has been proposed[58]. Findings in a further study, concurring with this hypothesis, have demonstrated that CD36 deletion can reduce VLDL output and liver fat in obese mice[59]. This finding was related to the enhanced production of the series-2 liver prostaglandins, which have been shown to suppress VLDL output and increase the hepatocyte triglyceride content in an inflammatory condition-dependent manner[60]. Thus, it is plausible that the AA genotype carriers may have a lower expression of the CD36 receptor that could contribute to liver steatosis and consequently to fibrosis similar to the effects of a CD36 deletion. Nonetheless, further investigation is required to elucidate the correlation between the *CD36* genotype and liver steatosis and clarify its interaction with other key molecules involved in this metabolic alteration, such as the microsomal triglyceride transfer protein (MTTP), apolipoprotein E (apoE) and apolipoprotein B (apoB)[61,62].

Concerning the nutritional management of liver disease, including HCV infection, the majority of international guidelines focus on the reduction of total fat and SFA intake[51,63] without taking into account the nutrigenetics and food cultures of individual populations. We advocate shifting towards a genome-based nutrition approach as a preventive and intervention strategy for chronic diseases given the fact that, worldwide, human populations differ[64]. Specifically, in the case of Mexico and most of Latin America, the people in these regions are genetically an admixture of Amerindian, Caucasian, and African ancestries with a heterogeneous inter-regional distribution[65,66]. Furthermore, 70% of the Mexican general population is overweight or obese due to the consumption of an obesogenic and hepatopatogenic diet that was previously described[4,14,64]. Thus, based on the gene-environmental interactions that currently prevail in the Mexican population, specific preventive strategies are crucial to diminish the progression of liver damage caused by alterations in lipid metabolism and inflammation.

In this study, the frequency of the *CD36* AA genotype (30.1%) was comparable to the pattern of distribution (28.4%) observed in non-diabetic individuals of Caucasian origin[24]. These findings are consistent with the high Caucasian ancestry that prevails among Mexican-Mestizos and HCV patients that have been previously reported[7], whereas different frequencies have been reported elsewhere[67-69]. Thus, we consider that the detection of the *CD36* genotype, as well as other nutrient-interacting genes[31-34] could be used as auxiliary tools to predict the adherence to dietary regimens and for the implementation of genome-based intervention strategies[64] aimed at reducing fat intake and dyslipidemia in our population[27].

In conclusion,the AA genotype of the rs1761667 *CD36* polymorphism was associated with higher fat intake and more instances of advanced LF in CHC patients. However, further genomic studies are needed to analyze the role of the *CD36* polymorphism on liver disease in other populations within Mexico and worldwide.

**COMMENTS**

***Background***

Regardless of etiology, liver fibrosis (LF) pathogenesis is influenced by genetic and environmental factors, such as dietary intake. Diets that are high in saturated fatty acids have been associated with the pathological processes involved in liver fibrogenesis, including steatosis, inflammation, and insulin resistance. There is growing evidence that suggest that the lingual cluster of differentiation 36 (*CD36*) receptor regulates the motivation for fatty food consumption. Therefore, genetic variations in CD36 expression could explain the global heterogeneity of fat linking and its association with chronic diseases. This study aimed to analyze the association of the *CD36* polymorphism (rs1761667) with dietary fat intake and LF in chronically infected hepatitis C patients.

***Research frontiers***

The results of this study contribute to the understanding of the specific gene-environmental interactions that occur among a population with an admixture genome. The role of *CD36* genetic variation on hepatitis C virus (HCV)-related liver disease or other chronic diseases in distinct populations worldwide requires further studies.

***Innovations and breakthroughs***

In this study, we provide evidence regarding the effect of the *CD36* (AA) risk genotype on the consumption of a high-fat diet and its association with LF in HCV patients.

***Applications***

The detection of the *CD36* genotype together with other nutrient-sensing genes could be useful for the implementation of genome-based intervention strategies aimed at reducing fat intake and dyslipidemia in chronic hepatitis C patients.

***Peer-review***

The authors of this paper evaluated the dietary fat intake and the degree of LF in patients chronically infected with hepatitis C based on the *CD36* genotypes. The results suggest that the risk AA genotype of the *CD36* polymorphism was associated with higher dietary fat intake and more instances of advanced LF in chronic hepatitis C patients.

**REFERENCES**

1 **Zaltron S**, Spinetti A, Biasi L, Baiguera C, Castelli F. Chronic HCV infection: epidemiological and clinical relevance. *BMC Infect Dis* 2012; **12** Suppl 2: S2 [PMID: 23173556 DOI: 10.1186/1471-2334-12-S2-S2]

2 **Mohd Hanafiah K**, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology* 2013; **57**: 1333-1342 [PMID: 23172780 DOI: 10.1002/hep.26141]

3 **Méndez-Sánchez N**, Aguilar-Ramírez JR, Reyes A, Dehesa M, Juórez A, Castñeda B, Sánchez-Avila F, Poo JL, Guevara González L, Lizardi J, Valdovinos MA, Uribe M, Contreras AM, Tirado P, Aguirre J, Rivera-Benítez C, Santiago-Santiago R, Bosques-Padilla F, Muñoz L, Guerroro A, Ramos M, Rodríguez-Hernández H, Jacobo-Karam J. Etiology of liver cirrhosis in Mexico. *Ann Hepatol* 2004; **3**: 30-33 [PMID: 15118577]

4 **Ramos-Lopez O**, Martinez-Lopez E, Roman S, Fierro NA, Panduro A. Genetic, metabolic and environmental factors involved in the development of liver cirrhosis in Mexico. *World J Gastroenterol* 2015; **21**: 11552-11566 [PMID: 26556986 DOI: 10.3748/wjg.v21.i41.11552]

5 **Panduro A**, Escobedo Meléndez G, Fierro NA, Ruiz Madrigal B, Zepeda-Carrillo EA, Román S. [Epidemiology of viral hepatitis in Mexico]. *Salud Publica Mex* 2011; **53** Suppl 1: S37-S45 [PMID: 21877071 DOI: 10.1590/S0036-36342011000700008]

6 **Panduro A**, Roman S. Need of righteous attitudes towards eradication of hepatitis C virus infection in Latin America. *World J Gastroenterol* 2016; **22**: 5137-5142 [PMID: 27298556 DOI: 10.3748/wjg.v22.i22.5137]

7 **Gonzalez-Aldaco K**, Rebello Pinho JR, Roman S, Gleyzer K, Fierro NA, Oyakawa L, Ramos-Lopez O, Ferraz Santana RA, Sitnik R, Panduro A. Association with Spontaneous Hepatitis C Viral Clearance and Genetic Differentiation of IL28B/IFNL4 Haplotypes in Populations from Mexico. *PLoS One* 2016; **11**: e0146258 [PMID: 26741362 DOI: 10.1371/journal.pone.0146258]

8 **Roman S**, Panduro A. Genomic medicine in gastroenterology: A new approach or a new specialty? *World J Gastroenterol* 2015; **21**: 8227-8237 [PMID: 26217074 DOI: 10.3748/wjg.v21.i27.8227]

9 **Fierro NA**, Gonzalez-Aldaco K, Torres-Valadez R, Martinez-Lopez E, Roman S, Panduro A. Immunologic, metabolic and genetic factors in hepatitis C virus infection. *World J Gastroenterol* 2014; **20**: 3443-3456 [PMID: 24707127 DOI: 10.3748/wjg.v20.i13.3443]

10 **Papandreou D**, Andreou E. Role of diet on non-alcoholic fatty liver disease: An updated narrative review. *World J Hepatol* 2015; **7**: 575-582 [PMID: 25848481 DOI: 10.4254/wjh.v7.i3.575]

11 **Wang D**, Wei Y, Pagliassotti MJ. Saturated fatty acids promote endoplasmic reticulum stress and liver injury in rats with hepatic steatosis. *Endocrinology* 2006; **147**: 943-951 [PMID: 16269465 DOI: 10.1210/en.2005-0570]

12 **Ha SK**, Chae C. Inducible nitric oxide distribution in the fatty liver of a mouse with high fat diet-induced obesity. *Exp Anim* 2010; **59**: 595-604 [PMID: 21030787 DOI: 10.1538/expanim.59.595]

13 **Longato L**, Tong M, Wands JR, de la Monte SM. High fat diet induced hepatic steatosis and insulin resistance: Role of dysregulated ceramide metabolism. *Hepatol Res* 2012; **42**: 412-427 [PMID: 22176347 DOI: 10.1111/j.1872-034X.2011.00934.x]

14 **Ramos-López O**, Román S, Ojeda-Granados C, Sepúlveda-Villegas M, Martínez-López E, Torres-Valadez R, Trujillo-Trujillo E, Arturo Panduro. Patrón de ingesta alimentaria y actividad física en pacientes hepatópatas en el Occidente de México. *Rev Endocrinol Nutr* 2013; **21**: 7-15

15 **Garcia-Bailo B**, Toguri C, Eny KM, El-Sohemy A. Genetic variation in taste and its influence on food selection. *OMICS* 2009; **13**: 69-80 [PMID: 18687042 DOI: 10.1089/omi.2008.0031]

16 **Dransfield E**. The taste of fat. *Meat Sci* 2008; **80**: 37-42 [PMID: 22063168 DOI: 10.1016/j.meatsci.2008.05.030]

17 **Degrace-Passilly P**, Besnard P. CD36 and taste of fat. *Curr Opin Clin Nutr Metab Care* 2012; **15**: 107-111 [PMID: 22248592 DOI: 10.1097/MCO.0b013e32834ff19c]

18 **Laugerette F**, Passilly-Degrace P, Patris B, Niot I, Febbraio M, Montmayeur JP, Besnard P. CD36 involvement in orosensory detection of dietary lipids, spontaneous fat preference, and digestive secretions. *J Clin Invest* 2005; **115**: 3177-3184 [PMID: 16276419 DOI: 10.1172/JCI25299]

19 **Martin C**, Passilly-Degrace P, Gaillard D, Merlin JF, Chevrot M, Besnard P. The lipid-sensor candidates CD36 and GPR120 are differentially regulated by dietary lipids in mouse taste buds: impact on spontaneous fat preference. *PLoS One* 2011; **6**: e24014 [PMID: 21901153 DOI: 10.1371/journal.pone.0024014]

20 **Su X**, Abumrad NA. Cellular fatty acid uptake: a pathway under construction. *Trends Endocrinol Metab* 2009; **20**: 72-77 [PMID: 19185504 DOI: 10.1016/j.tem.2008.11.001]

21 **Aly R**, Maibach HI, Bagatell FK, Dittmar W, Hänel H, Falanga V, Leyden JJ, Roth HL, Stoughton RB, Willis I. Ciclopirox olamine lotion 1%: bioequivalence to ciclopirox olamine cream 1% and clinical efficacy in tinea pedis. *Clin Ther* 2016; **11**: 290-303 [PMID: 2663159 DOI: 10.1152/physrev.00002.2015]

22 **Rać ME**, Safranow K, Poncyljusz W. Molecular basis of human CD36 gene mutations. *Mol Med* 2007; **13**: 288-296 [PMID: 17673938 DOI: 10.2119/2006-00088.Rac]

23 **Fernández-Ruiz E**, Armesilla AL, Sánchez-Madrid F, Vega MA. Gene encoding the collagen type I and thrombospondin receptor CD36 is located on chromosome 7q11.2. *Genomics* 1993; **17**: 759-761 [PMID: 7503937 DOI: 10.1006/geno.1993.1401]

24 **Ma X**, Bacci S, Mlynarski W, Gottardo L, Soccio T, Menzaghi C, Iori E, Lager RA, Shroff AR, Gervino EV, Nesto RW, Johnstone MT, Abumrad NA, Avogaro A, Trischitta V, Doria A. A common haplotype at the CD36 locus is associated with high free fatty acid levels and increased cardiovascular risk in Caucasians. *Hum Mol Genet* 2004; **13**: 2197-2205 [PMID: 15282206 DOI: 10.1093/hmg/ddh233]

25 **Love-Gregory L**, Sherva R, Schappe T, Qi JS, McCrea J, Klein S, Connelly MA, Abumrad NA. Common CD36 SNPs reduce protein expression and may contribute to a protective atherogenic profile. *Hum Mol Genet* 2011; **20**: 193-201 [PMID: 20935172 DOI: 10.1093/hmg/ddq449]

26 **Ghosh A**, Murugesan G, Chen K, Zhang L, Wang Q, Febbraio M, Anselmo RM, Marchant K, Barnard J, Silverstein RL. Platelet CD36 surface expression levels affect functional responses to oxidized LDL and are associated with inheritance of specific genetic polymorphisms. *Blood* 2011; **117**: 6355-6366 [PMID: 21478428 DOI: 10.1182/blood-2011-02-338582]

27 **Ramos-Lopez O**, Panduro A, Martinez-Lopez E, Fierro NA, Ojeda-Granados C, Sepulveda-Villegas M, Roman S. Genetic variant in the CD36 gene (rs1761667) is associated with higher fat intake and high serum cholesterol among the population of West Mexico. *J Nutr Food Sci* 2015; **5**: 353 [DOI: 10.4172/2155-9600.1000353]

28 **European Association for Study of Liver**. EASL Clinical Practice Guidelines: management of hepatitis C virus infection. *J Hepatol* 2014; **60**: 392-420 [PMID: 24331294 DOI: 10.1016/j.jhep.2013.11.003]

29 **Ghany MG**, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology* 2009; **49**: 1335-1374 [PMID: 19330875 DOI: 10.1002/hep.22759]

30 **Muñoz-Espinosa LE**, Trujillo-Trujillo ME, Martínez-Macías RF, Panduro A, Rivas-Estilla AM, Fierro NA, Silvera-Linares AL, Torres-Valadez R, Cordero-Pérez P, González-Aldaco K, Chen-López CY, José-Abrego A, Zuñiga-Noriega JR, Gutiérrez-Ruiz MC, Roman S. Increase of drug use and genotype 3 in HCV-infected patients from Central West and Northeast Mexico. *Ann Hepatol* 2015; **14**: 642-651 [PMID: 26256892]

31 **Ramos-Lopez O**, Roman S, Martinez-Lopez E, Gonzalez-Aldaco K, Ojeda-Granados C, Sepulveda-Villegas M, Panduro A. Association of a novel TAS2R38 haplotype with alcohol intake among Mexican-Mestizo population. *Ann Hepatol* 2015; **14**: 729-734 [PMID: 26256902]

32 **Martinez-Lopez E**, Garcia-Garcia MR, Gonzalez-Avalos JM, Maldonado-Gonzalez M, Ruiz-Madrigal B, Vizmanos B, Hernandez-Nazara Z, Roman S, Panduro A. Effect of Ala54Thr polymorphism of FABP2 on anthropometric and biochemical variables in response to a moderate-fat diet. *Nutrition* 2013; **29**: 46-51 [PMID: 22817827 DOI: 10.1016/j.nut.2012.03.002.]

33 **Garcia-Garcia MR**, Morales-Lanuza MA, Campos-Perez WY, Ruiz-Madrigal B, Maldonado-Gonzalez M, Vizmanos B, Hernandez-Cañaveral I, Yañez-Sanchez I, Roman S, Panduro A, Martinez-Lopez E. Effect of the ADIPOQ Gene -11391G/A Polymorphism Is Modulated by Lifestyle Factors in Mexican Subjects. *J Nutrigenet Nutrigenomics* 2014; **7**: 212-224 [PMID: 25790965 DOI: 10.1159/000371801]

34 **Ramos-Lopez O**, Panduro A, Martinez-Lopez E, Roman S. Sweet Taste Receptor TAS1R2 Polymorphism (Val191Val) Is Associated with a Higher Carbohydrate Intake and Hypertriglyceridemia among the Population of West Mexico. *Nutrients* 2016; **8**: 101 [PMID: 26907331 DOI: 10.3390/nu8020101]

35 **Thompson FE**, Byers T. Dietary assessment resource manual. *J Nutr* 1994; **124**: 2245S-2317S [PMID: 7965210]

36 **Marvan Laborde L**, Perez Lizaur AB, Palacios Gonzalez B. Sistema Mexicano de Alimentos Equivalentes. 2nd ed. Fomento de Nutricion y Salud, 2000: 1-84

37 **Perez Lizaur AB**, Marvan LL. Manual de dietas normales y terapéuticas: los alimentos en la salud y en la enfermedad. 5th ed. Mexico: DF La Prensa Médica Mexicana, 2005: 1-281

38 **Tremblay AJ**, Morrissette H, Gagné JM, Bergeron J, Gagné C, Couture P. Validation of the Friedewald formula for the determination of low-density lipoprotein cholesterol compared with beta-quantification in a large population. *Clin Biochem* 2004; **37**: 785-790 [PMID: 15329317 DOI: 10.1016/j.clinbiochem.2004.03.008]

39 **Foucher J**, Chanteloup E, Vergniol J, Castéra L, Le Bail B, Adhoute X, Bertet J, Couzigou P, de Lédinghen V. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut* 2006; **55**: 403-408 [PMID: 16020491 DOI: 10.1136/gut.2005.069153]

40 **do Carmo RF**, Vasconcelos LR, Mendonça TF, de Mendonça Cavalcanti Mdo S, Pereira LM, Moura P. Myeloperoxidase gene polymorphism predicts fibrosis severity in women with hepatitis C. *Hum Immunol* 2014; **75**: 766-770 [PMID: 24882572 DOI: 10.1016/j.humimm.2014.05.008]

41 **Lin ZH**, Xin YN, Dong QJ, Wang Q, Jiang XJ, Zhan SH, Sun Y, Xuan SY. Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: an updated meta-analysis. *Hepatology* 2011; **53**: 726-736 [PMID: 21319189 DOI: 10.1002/hep.24105]

42 **Miller SA**, Dykes DD, Polesky HF. A simple salting out procedure for extracting DNA from human nucleated cells. *Nucleic Acids Res* 1988; **16**: 1215 [PMID: 3344216]

43 **Flesis JL**, Levin B, Cho-Paik M. Statistical Methods for Rates and Proportions. 3rd ed. New York: John Wiley & Sons, 2003: 1-800

44 **Ramos-López O**, Ojeda-Granados C, Román S, Panduro A. Influencia genética en las preferencias alimentarias. *Rev Endocrinol Nutr* 2013; **21**: 74-83

45 **Pepino MY**, Love-Gregory L, Klein S, Abumrad NA. The fatty acid translocase gene CD36 and lingual lipase influence oral sensitivity to fat in obese subjects. *J Lipid Res* 2012; **53**: 561-566 [PMID: 22210925 DOI: 10.1194/jlr.M021873]

46 **Mrizak I**, Šerý O, Plesnik J, Arfa A, Fekih M, Bouslema A, Zaouali M, Tabka Z, Khan NA. The A allele of cluster of differentiation 36 (CD36) SNP 1761667 associates with decreased lipid taste perception in obese Tunisian women. *Br J Nutr* 2015; **113**: 1330-1337 [PMID: 25822988 DOI: 10.1017/S0007114515000343]

47 **Sayed A**, Šerý O, Plesnik J, Daoudi H, Rouabah A, Rouabah L, Khan NA. CD36 AA genotype is associated with decreased lipid taste perception in young obese, but not lean, children. *Int J Obes (Lond)* 2015; **39**: 920-924 [PMID: 25687220 DOI: 10.1038/ijo.2015.20]

48 **Melis M**, Sollai G, Muroni P, Crnjar R, Barbarossa IT. Associations between orosensory perception of oleic acid, the common single nucleotide polymorphisms (rs1761667 and rs1527483) in the CD36 gene, and 6-n-propylthiouracil (PROP) tasting. *Nutrients* 2015; **7**: 2068-2084 [PMID: 25803547 DOI: 10.3390/nu7032068]

49 **Zivkovic AM**, German JB, Sanyal AJ. Comparative review of diets for the metabolic syndrome: implications for nonalcoholic fatty liver disease. *Am J Clin Nutr* 2007; **86**: 285-300 [PMID: 17684197]

50 **Corrao G**, Ferrari PA, Galatola G. Exploring the role of diet in modifying the effect of known disease determinants: application to risk factors of liver cirrhosis. *Am J Epidemiol* 1995; **142**: 1136-1146 [PMID: 7485060]

51 **Freedman ND**, Cross AJ, McGlynn KA, Abnet CC, Park Y, Hollenbeck AR, Schatzkin A, Everhart JE, Sinha R. Association of meat and fat intake with liver disease and hepatocellular carcinoma in the NIH-AARP cohort. *J Natl Cancer Inst* 2010; **102**: 1354-1365 [PMID: 20729477 DOI: 10.1093/jnci/djq301]

52 **Stránský J**, Ryzlová M, Striteský J, Horák J. [Aspartate aminotransferase (AST) more than alanine aminotransferase (ALT) levels predict the progression of liver fibrosis in chronic HCV infection]. *Vnitr Lek* 2002; **48**: 924-928 [PMID: 16737138]

53 **Guéchot J**. [Noninvasive assessment of liver fibrosis in patients with chronic hepatitis virus C]. *Presse Med* 2006; **35**: 1317-1326 [PMID: 16969327 DOI: 10.1016/S0755-4982(06)74811-4]

54 **Fierro NA**, Castro-Garcia FP, Panduro A. Rethinking cytokine function during hepatitis A and hepatitis C infections. *Adv Biosci Biotechnol* 2013; **4**: 13-18 [DOI: 10.4236/abb.2013.47A1003]

55 **Fierro NA**, González-Aldaco K, Torres-Valadez R, Trujillo-Trujillo ME, Roman S, Trujillo-Ochoa JL, Panduro A. Spontaneous hepatitis C viral clearance and hepatitis C chronic infection are associated with distinct cytokine profiles in Mexican patients. *Mem Inst Oswaldo Cruz* 2015; **110**: 267-271 [PMID: 25946254 DOI: 10.1590/0074-02760140377]

56 **Oshiumi H**, Matsumoto M, Seya T. [Chronic hepatitis C virus infection attenuates host antiviral innate immune response]. *Nihon Rinsho* 2015; **73**: 234-238 [PMID: 25764676]

57 **Chang ML**. Metabolic alterations and hepatitis C: From bench to bedside. *World J Gastroenterol* 2016; **22**: 1461-1476 [PMID: 26819514 DOI: 10.3748/wjg.v22.i4.1461]

58 **Pepino MY**, Kuda O, Samovski D, Abumrad NA. Structure-function of CD36 and importance of fatty acid signal transduction in fat metabolism. *Annu Rev Nutr* 2014; **34**: 281-303 [PMID: 24850384 DOI: 10.1146/annurev-nutr-071812-161220]

59 **Nassir F**, Adewole OL, Brunt EM, Abumrad NA. CD36 deletion reduces VLDL secretion, modulates liver prostaglandins, and exacerbates hepatic steatosis in ob/ob mice. *J Lipid Res* 2013; **54**: 2988-2997 [PMID: 23964120 DOI: 10.1194/jlr.M037812]

60 **Pérez S**, Aspichueta P, Ochoa B, Chico Y. The 2-series prostaglandins suppress VLDL secretion in an inflammatory condition-dependent manner in primary rat hepatocytes. *Biochim Biophys Acta* 2006; **1761**: 160-171 [PMID: 16545597 DOI: 10.1016/j.bbalip.2006.02.003]

61 **Mirandola S**, Bowman D, Hussain MM, Alberti A. Hepatic steatosis in hepatitis C is a storage disease due to HCV interaction with microsomal triglyceride transfer protein (MTP). *Nutr Metab (Lond)* 2010; **7**: 13 [PMID: 20178560 DOI: 10.1186/1743-7075-7-13]

62 **Bassendine MF**, Sheridan DA, Bridge SH, Felmlee DJ, Neely RD. Lipids and HCV. *Semin Immunopathol* 2013; **35**: 87-100 [PMID: 23111699 DOI: 10.1007/s00281-012-0356-2]

63 **Dietitians of Canada**. Hepatitis C: nutrition care Canadian guidelines for health care providers. *Can J Diet Pract Res* 2003; **64**: 139-141 [PMID: 12959661]

64 **Roman S**, Ojeda-Granados C, Ramos-Lopez O, Panduro A. Genome-based nutrition: an intervention strategy for the prevention and treatment of obesity and nonalcoholic steatohepatitis. *World J Gastroenterol* 2015; **21**: 3449-3461 [PMID: 25834309 DOI: 10.3748/wjg.v21.i12.3449]

65 **Aceves D**, Ruiz B, Nuño P, Roman S, Zepeda E, Panduro A. Heterogeneity of apolipoprotein E polymorphism in different Mexican populations. *Hum Biol* 2006; **78**: 65-75 [PMID: 16900882 DOI: 10.1353/hub.2006.0021]

66 **Martínez-Cortés G**, Salazar-Flores J, Haro-Guerrero J, Rubi-Castellanos R, Velarde-Félix JS, Muñoz-Valle JF, López-Casamichana M, Carrillo-Tapia E, Canseco-Avila LM, Bravi CM, López-Armenta M, Rangel-Villalobos H. Maternal admixture and population structure in Mexican-Mestizos based on mtDNA haplogroups. *Am J Phys Anthropol* 2013; **151**: 526-537 [PMID: 23754474 DOI: 10.1002/ajpa.22293]

67 **Bayoumy NM**, El-Shabrawi MM, Hassan HH. Association of cluster of differentiation 36 gene variant rs1761667 (G& gt; A) with metabolic syndrome in Egyptian adults. *Saudi Med J* 2012; **33**: 489-494 [PMID: 22588808]

68 **Keller KL**, Liang LC, Sakimura J, May D, van Belle C, Breen C, Driggin E, Tepper BJ, Lanzano PC, Deng L, Chung WK. Common variants in the CD36 gene are associated with oral fat perception, fat preferences, and obesity in African Americans. *Obesity (Silver Spring)* 2012; **20**: 1066-1073 [PMID: 22240721 DOI: 10.1038/oby.2011.374]

69 **Banerjee M**, Gautam S, Saxena M, Kumar Bid H, Agrawal CG. Association of CD36 gene variants rs1761667 (G > A) and rs1527483 (C > T) with Type 2 diabetes in North Indian population. *Int J Diabetes Mellit* 2010; **2**: 179-183 [DOI: 10.1016/j.ijdm.2010.08.002]

**P-Reviewer:** Sunami Y, Trovato FM **S-Editor:** Qiu S **L-Editor: E-Editor:**

**Table 1 Demographical and clinical characteristics of the chronic hepatitis C patients classified by *CD36* genotype**

|  |  |  |
| --- | --- | --- |
|  | ***CD36* genotype** |  |
| **Variable** | **AA** | **AG** | **GG** | ***P*-value** |
| Number of patients, *n* (%) | 22 (30.1) | 40 (54.8) | 11 (15.1) | --- |
| Age (yr) | 48.1 ± 11.7 | 51.4 ± 11.1 | 53.7 ± 15.3 | 0.38 |
| Gender (F/M), *n* (%) | (12/10) | (21/19) | (7/4) | 0.68 |
| BMI (kg/m2) | 26.6 ± 4.1 | 24.9 ± 4.2 | 24.4 ± 3.1 | 0.52 |
| Duration of infection (yr) | 26.9 ± 10.1 | 25.2 ± 8.1 | 25.4 ± 7.4 | 0.62 |
| HCV genotype 1, *n* (%) | 15 (68.2) | 27 (67.5) | 8 (72.7) | 0.40 |
| HCV genotype 2, *n* (%) | 5 (22.7) | 9 (22.5) | 3 (27.3) |
| HCV genotype 3, *n* (%) | 2 (9.1) | 4 (10) | 0 (0) |

Quantitative values are expressed as mean ± SD. Frequencies are expressed as percentage. CHC: Chronic hepatitis C; F/M: Female/male; BMI: Body mass index; HCV: Hepatitis C virus; *n* (%): Number of patients (percentage).

**Table 2 Daily dietary intake of the chronic hepatitis C patients classified by *CD36* genotype**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | ***CD36* genotype** |  |
| **Variable** | **Reference values** | **AA** | **AG** | **GG** | ***P*-value** |
| Total calories | - | 2531.3 ± 301.3 | 1902.5 ± 396.1 | 1873.5 ± 345.7 | 0.0211 |
| CH (%) | 50-60 | 55.4 ± 10.5 | 54.3 ± 8.9 | 53.2 ± 6.4 | 0.76 |
| Protein (%) | 15 | 17.2 ± 4.6 | 16.3 ± 3.9 | 16.4 ± 2.9 | 0.81 |
| Fat (%) | < 30 | 34.9 ± 7.5 | 27.5 ± 7.2 | 24.9 ± 1.1 | 0.0012991 |
| SFA (%) | < 7 | 16.1 ± 6.1 | 8.1 ± 3.2 | 8.4 ± 2.7 | 0.2 × 10-61 |
| MUFA (%) | 20 | 13.1 ± 3.4 | 12.8 ± 7.6 | 12.1 ± 5.4 | 0.94 |
| PUFA (%) | 10 | 8.8 ± 6.5 | 5.6 ± 4.2 | 5.2 ± 1.3 | 0.11 |
| Quantitative values are expressed as mean ± SD. CH: Carbohydrates; SFA: Saturated fatty acids; MUFA: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids. 1By post hoc tests: Total calories: AA genotype *vs* AG and GG genotypes, *P* = 0.027. Fat: AA *vs* AG, *P* = 0.006; AA *vs* GG, *P* = 0.002; SFA: AA *vs* AG, *P* = 0.2 x 10-6, AA *vs* GG, *P* = 0.185 x 10-4. |

**Table 3 Daily intake of food group servings in chronic hepatitis C patients classified by *CD36* genotype**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | ***CD36* genotype** |  |
| **Variable** | **Reference values** | **AA** | **AG** | **GG** | ***P*-value** |
| Sugars | 0-3 | 5.7 ± 4.3 | 5.5 ± 4.8 | 5.2 ± 4.1 | 0.85 |
| Meat | 2-3 | 5.7 ± 1.6 | 5.1 ± 2.8 | 4.4 ± 2.2 | 0.15 |
| Fruits | 2-4 | 2.0 ± 1.8 | 1.7 ± 0.9 | 1.4 ± 1.1 | 0.43 |
| Vegetables | 3-5 | 2.1 ± 1.6 | 1.9 ± 1.1 | 1.6 ± 0.8 | 0.42 |
| Fats | 0-3 | 6.5 ± 1.7 | 4.3 ± 3.1 | 3.9 ± 2.2 | 0.0032071 |
| Milk | 1-3 | 1.0 ± 0.7 | 0.8 ± 0.7 | 0.8 ± 0.9 | 0.86 |
| Legumes | 1-2 | 1.0 ± 0.7 | 0.9 ± 0.7 | 0.8 ± 0.7 | 0.88 |
| Cereals | 6-11 | 10.3 ± 5.4 | 9.6 ± 5.8 | 9.0 ± 5.1 | 0.77 |

Quantitative values are expressed as mean ± SD. 1By Post hoc tests: fats: AA *vs* GG, *P* = 0.011608.

**Table 4 Biochemical profile of the chronic hepatitis C patients classified by *CD36* genotype**

|  |  |  |
| --- | --- | --- |
|  | ***CD36* genotype** |  |
| **Variable** | **AA** | **AG** | **GG** | ***P*-value** |
| Glucose (mg/dL) | 109.5 ± 59.3 | 106.7 ± 42.9 | 97.4 ± 19.8 | 0.78 |
| TC (mg/dL) | 146.8 ± 35.1 | 162.2 ± 44.2 | 157.8 ± 51.1 | 0.40 |
| TG (mg/dL) | 112.8 ± 43.3 | 140.8 ± 60.8 | 142.3 ± 51.1 | 0.30 |
| HDL-c (mg/dL) | 42.7 ± 15.1 | 40.4 ± 13.1 | 33.8 ± 9.8 | 0.21 |
| LDL-c (mg/dL) | 83.1 ± 28.8 | 95.4 ± 42.6 | 101.1 ± 42.6 | 0.44 |
| VLDL-c (mg/dL) | 22.6 ± 8.7 | 28.2 ± 12.1 | 28.9 ± 10.1 | 0.27 |
| ALT (IU/L) | 93.8 ± 42.6 | 73.4 ± 73.1 | 71.5 ± 46.4 | 0.38 |
| AST (IU/L) | 91.7 ± 41.3 | 61.5 ± 40.3 | 69.8 ± 53.9 | 0.0281 |
| GGT (IU/L) | 85.9 ± 56.2 | 66.4 ± 40.8 | 43.1 ± 33.2 | 0.18 |

Quantitative values are expressed as mean ± SD. TC: Total cholesterol; TG: Triglycerides; HDL-c: High-density lipoprotein cholesterol; LDL-c: Low-density lipoprotein cholesterol; VLDL-c: Very low-density lipoprotein cholesterol; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyl-transferase. 1By post hoc tests: AA genotype *vs* AG genotype, *P* = 0.024.

**Table 5 Kilopascals and aspartate aminotransferase to platelet ratio index score values by the severity of liver fibrosis among chronic hepatitis C patients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Mild fibrosis** | **Advanced fibrosis** | ***P*-value** |
| Number of patients, *n* (%) | 35 (47.9) | 38 (52.1) | - |
| KPa | 6.5 ± 1.7 | 22.7 ± 13.4 | < 0.001 |
| APRI score | 0.81 ± 0.33 | 1.78 ± 0.53 | < 0.001 |

Quantitative values are expressed as mean ± SD. Kpa: Kilopascals; APRI: Aspartate aminotransferase to platelet ratio index; *n* (%): Number of patients (percentage).

**Table 6 Association of the *CD36* genotype with the severity of liver fibrosis among chronic hepatitis C patients**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***CD36* genotype** | **Mild fibrosis****n (%)** | **Advanced fibrosis****n (%)** | **Genotype****comparison** | **Odds ratio****(95%CI)** | ***P*-value** |
| AA | 6 (17.1) | 16 (42.1) | AA *vs* GG | 3.20(0.70-14.52) | 0.12 |
| AG | 23 (65.7) | 17 (44.7) | AA *vs* AG | 3.60(1.16-11.15) | 0.02 |
| GG | 6 (17.1) | 5 (13.2) | AA *vs* AG/GG | 3.51(1.18-10.45) | 0.02 |

*n* (%): Number of patients (percentage).