ORIGINAL ARTICLE

Retrospective Study

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

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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 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 ($\beta = 30.23$, 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 that the *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

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.

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 350000 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 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 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, United States) and the presence of serum HCV RNA for more than six months (COBAS® AmpliPrep/COBAS® Taqman® HCV Test; Roche Diagnostics, Pleasanton, CA, United States)[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 measurement
An electrical bioimpedance apparatus was used to assess body mass index (BMI, kg/m^2) (INBODY 3.0, Analyzer Body Composition, Biospace, South Korea).

Dietary assessment
A three-day food record (two weekdays and one week-end 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 10 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 and 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, United States) in a 96-well format (StepOnePlus thermocycler (Applied Biosystems, Foster City, CA, United States) 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 ± 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 χ^2 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 Info™ 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%),

Table 1 Demographical and clinical characteristics of the chronic hepatitis C patients classified by cluster of differentiation 36 genotype

Variable	*CD36* genotype			*P*-value
	AA	**AG**	**GG**	
No. 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)	(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; *CD36*: Cluster of differentiation 36.

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* genotype are 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 apolipoprotein B (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

Table 2 Daily dietary intake of the chronic hepatitis C patients classified by cluster of differentiation 36 genotype

Variable	Reference values	CD36 genotype			P-value
		AA	AG	GG	
Total calories	-	2531.3 ± 301.3	1902.5 ± 396.1	1873.5 ± 345.7	0.021[a]
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	0.001299[a]
SFA (%)	< 7	16.1 ± 6.1	8.1 ± 3.2	8.4 ± 2.7	0.2×10^{-6a}
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

[a]By 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, $P = 0.2 \times 10^{-6}$, AA *vs* GG, $P = 0.185 \times 10^{-4}$. Quantitative values are expressed as mean ± SD. CH: Carbohydrates; SFA: Saturated fatty acids; MUFA: Monounsaturated fatty acids; PUFAs: Polyunsaturated fatty acids; *CD36*: Cluster of differentiation 36.

Table 3 Daily intake of food group servings in chronic hepatitis C patients classified by cluster of differentiation 36 genotype

Variable	Reference values	CD36 genotype			P-value
		AA	AG	GG	
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	0.003207[1]
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. [1]By Post hoc tests: Fats: AA *vs* GG, *P* = 0.011608. *CD36*: Cluster of differentiation 36.

Table 4 Biochemical profile of the chronic hepatitis C patients classified by cluster of differentiation 36 genotype

Variable	CD36 genotype			P-value
	AA	AG	GG	
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	0.028[1]
GGT (IU/L)	85.9 ± 56.2	66.4 ± 40.8	43.1 ± 33.2	0.18

[1]By post hoc tests: AA genotype *vs* AG genotype, *P* = 0.024. 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; *CD36*: Cluster of differentiation 36.

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
No. 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.

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 and 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

Table 6 Association of the cluster of differentiation 36 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

CD36: Cluster of differentiation 36.

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, the authors 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.

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