Original Communication

CD36 polymorphism, sugary drinks, and sedentarism are associated with hypertriglyceridemic waist phenotype

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Abstract: *Background:* The hypertriglyceridemic waist (HTGW) phenotype is characterized by concomitant increases in waist circumference (WC) and blood triglyceride levels (TG), which have been identified as a predictor of metabolic disorders. This study aimed to analyze associations between food consumption, exercise, and the *CD36* gene rs1761667 G>A polymorphism with the HTGW phenotype in adult Mexicans. *Methods:* This cross-sectional study included a total of 255 participants (both genders, between 18–64 years of age). The HTGW phenotype was defined as WC >88 cm in women, WC >102 cm in men, and TG >150 mg/dL. Body composition was analyzed by electrical bioimpedance. Dietary intakes (macro and micronutrients) were evaluated through a validated 64-item food frequency questionnaire and a 24-h recall. Physical exercise was subjectively recorded asking the participants if they regularly performed some systematic exercise or sport of moderate intensity at least 150–300 minutes a week. Biochemical tests were determined by an automated system. A Taqman real-time assay was used to detect the rs1761667 (G>A) polymorphism of the *CD36* gene. A multivariate logistic regression model was performed to analyze the variables potentially associated with the HTGW phenotype (adjusted for age, energy intake, and total fat mass). *Results:* Overall, 21.6% of the population presented the HTGW phenotype; compared to the HTGW−, also, they were older, had more body fat, higher glucose, cholesterol and insulin levels, and high blood pressure. Female sex (OR=2.92, 95% CI: 1.12–7.60, p=0.028), body mass index (OR=1.19, 95% CI: 1.07–1.32, p=0.001), total cholesterol (OR=1.01, 95% CI:1.00–1.02, p=0.039), daily consumption of sugary drinks (OR=6.94, 95% CI: 1.80–26.8, p=0.005), and the *CD36* AG genotype (OR=3.81, 95% CI: 1.08–13.4, p=0.037) were positively associated with the HTGW phenotype, while performing exercise played a protective role (OR=0.23, 95% CI: 0.08–0.62, p=0.004). Overall, the model predicted the HTGW phenotype in 47% (R^2=0.47, p≤0.001). *Conclusion:* The *CD36* AG genotype, daily consumption of sugary drinks and sedentarism are risk factors for the HTGW phenotype in Mexicans.

Keywords: hypertriglyceridemic waist phenotype, cardiovascular risk, CD36 polymorphism, diet, nutrition, exercise

Introduction

Obesity is considered a risk factor for the onset and progression of several metabolic abnormalities, especially when excess adiposity predominates in the central body area [1]. In this context, individuals with abdominal obesity (AO) are more likely to develop insulin resistance, glucose intolerance, liver steatosis, hyperinflammation, and dyslipidemia [2]. Thus, the use of simple and accessible tools for forecasting cardiometabolic risk in people with obesity is clinically relevant [3].

The hypertriglyceridemic waist (HTGW) phenotype is a marker characterized by the concomitant increases of waist circumference (WC) and plasmatic triglycerides (TG), which has been associated with several metabolic disorders and diseases including atherogenesis [4], metabolic syndrome [5], type 2 diabetes mellitus [6], hypertension [7], and fatty liver [8]. Moreover, this phenotype has been identified as a reliable marker for prediction of visceral fat accumulation [9].

Epidemiological and observational studies have demonstrated that the habitual consumption of ultra-processed foods as well as the excessive intake of saturated/hydrogenated fats may increase the risk of presenting the HTGW phenotype [10]. Moreover, the adoption of sedentary lifestyles has been associated with the HTGW phenotype in some populations [11].

Furthermore, polymorphisms in key genes may also contribute to the pathogenesis of the HTGW phenotype [12].

Specifically, the cluster of differentiation 36 (CD36), is a scavenger receptor involved in many processes of lipid metabolism comprising the uptake and transport of long-chain fatty acids, secretion of peptides, regulation of hepatic lipoprotein output, beta oxidation activation, and regulation of the production of fatty acids-derived bioactive eicosanoids [13, 14]. Also, CD36 may influence immune cell differentiation and activation, and ultimately help determine cell fate [15]. Thus, it has been related to some metabolic complications of obesity such as inflammation, insulin resistance, atherosclerosis, and thrombosis under excessive fat supply [16, 17] and in presence of different genomic variants within the *CD36* gene, including the rs1761667 polymorphism [18].

In Mexico, high frequencies of obesity and dyslipidemia, including hypertriglyceridemia (HTG), have been reported [19]. HTG is a risk factor for developing insulin resistance and liver fibrosis, increasing the risk of diabetes mellitus and cardiovascular disease, the leading causes of morbidity and mortality in Mexico [20]. To the best of our knowledge, there is apparently no evidence that jointly evaluates genetic and non-genetic factors related to the HTGW phenotype in the Mexican population. This information may be helpful to the design of precision nutritional strategies aimed to prevent the HTGW and accompanying complications [21]. The present study aimed to analyze the association of food consumption, exercise, and the *CD36* gene rs1761667 G>A polymorphism with the HTGW phenotype in a Mexican adult population.

Methods

Population

A cross-sectional/analytical study was carried out. Two hundred fifty-five subjects, both genders, between 18–64 years of age were recruited at the Department of Genomic Medicine in Hepatology at the Civil Hospital of Guadalajara "Fray Antonio Alcalde" in Guadalajara, Jalisco, Mexico. Demographic and clinical data were obtained through a direct interview. The exclusion criteria included pregnant or breastfeeding women, smokers, subjects consuming a restrictive diet in the last three months, and individuals with prescribed medication that could affect the blood level of lipids and glucose. The study met the ethical requirements described in the 2013 Declaration of Helsinki and was approved (ID#HC141/09) by the Bioethics Committee of the Hospital Civil de Guadalajara "Fray Antonio Alcalde". There were no financial benefits for the participants. All participants were asked to sign an informed consent to be included in the study.

Anthropometric and blood pressure measurements

As reported elsewhere, the anthropometric measurements (height, weight, and WC circumference) were collected according to conventional standardized procedures [22]. The body mass index (BMI, kg/m^2) was calculated by dividing weight (kilograms) by height (squared meters). The World Health Organization (WHO) classification of BMI in adults was used for the categorization of normal-weight (BMI: 18.5–24.9 kg/m^2), overweight (BMI: 25.0–29.9 kg/m^2), and obesity (BMI: $\geq$30.0 kg/m^2). Body composition (including muscle and fat mass) was analyzed by tetrapolar electrical bioimpedance using an Inbody 3.0 (body composition analyzer, Biospace, Korea) following the manufacturer's instructions. The systolic and diastolic blood pressures were measured with an automated sphygmomanometer following the WHO criteria.

Biochemical profile

Venous blood samples were drawn after an overnight fast. Biochemical analyzes were determined by an automated system (*Vitros* 250 equipment, Ortho Clinical Diagnostics, Johnson and Johnson Co, Rochester, NY). Biochemical tests included fasting blood glucose, total cholesterol, TG, high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and the liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl-transferase (GGT). The homeostatic model assessment-insulin resistance (HOMA-IR index was calculated according to the Matthews formula as fasting insulin (μU/L) × fasting glucose (nmol/L)/22.5.

Definition of the HTGW phenotype

The definition of the HTGW phenotype was based on the NCEP/ATP-III criteria, considering as HTGW+ individuals with TG>150 mg/dL, WC >88 cm in women, and WC >102 cm in men [23]. The absence of the phenotype was defined as HTGW−.

CD36 genotyping

Leukocyte genomic DNA was extracted by a modified salting-out method [24]. The *CD36* gene rs1761667 polymorphism was detected by real-time PCR using a specific allelic discrimination assay (TaqMan, Applied Biosystems, ID C_8314999_10; Foster City, CA, USA) and processed in the StepOnePlus thermocycler (Applied Biosystems,

Foster City, CA, USA). DNA was used at a final concentration of 70 ng. The conditions of the PCR polymerase were as follows: 95°C for 10 minutes, 40 subsequent cycles of denaturation at 92°C for 15 seconds, and annealing/extension at 60°C for 1 minute. Genotyping was verified using positive controls of DNA samples.

Lifestyle assessment

Food consumption was evaluated using a semiquantitative 64-item food frequency questionnaire (FFQ) previously validated in the Mexican population [25]. Thus, individuals were asked how often they had consumed each food item during the previous year based on the following time-frame categories: daily, weekly, monthly or never. For the purpose of this study, we report the number of persons and corresponding percentages that consumed daily each food item according to the recommended dietary allowances (RDA) for the Mexican population [26]. Instead, the average nutritional composition of the diet and the number of food equivalents were calculated using three 24-h recalls (including two weekdays and one weekend day), which were computed in the Nutrikcal VO software. The contributions of macro and micronutrients were contrasted with the recommendations for the Mexican population, as previously described [27, 28]. Reference values of food equivalent intakes were based on the number of food portions according to the Mexican System of Food and Equivalents [29]. For the exercise assessment, the participants were asked if they practiced some systematic physical exercise or sport (yes/no) of moderate intensity (i.e., walking briskly, dancing, and swimming) at least 150–300 minutes a week [30].

Statistical analyses

The sample size was calculated using the allelic frequencies of the *CD36* gene rs1761667 polymorphism in Mexican population as reference [31, 32]. It was estimated a total of 230 subjects to obtain a statistical power of 80% (β=0.20) and reliability of 95% (α=0.05). Normality of variables was assessed by the Kolmogorov-Smirnov test. Main variables (including HTGW phenotype, biochemical profile, and nutritional features) were normally distributed (p>0.05). Quantitative variables were expressed as means±standard deviation (SD), while qualitative variables were expressed as numbers and percentages. This study is a comparative cross-sectional study, where χ^2 was performed to compare qualitative variables between groups (HTGW+ vs. HTGW−). Student's t-test for independent samples or Mann-Whitney U test were conducted to compare the quantitative variables between groups (HTGW+ vs. HTGW) according to the normality of the variables. Moreover, a multivariate logistic regression model was run to assess the variables associated with the HTGW phenotype (adjusted for age, energy intake, and total fat mass). A p value <0.05 was considered statistically significant. The data were analyzed with the statistical package SPSS version 25 for Windows (IBM Inc, Armonk, NY, USA).

Table 1. Clinical, anthropometrical and biochemical parameters concerning the HTGW phenotype

Variables	HTGW−	HTGW+	P value
Sex n (%)			
Female	101 (50.5)	40 (72.7)	**0.003**
Male	99 (49.5)	15 (23.3)	
BMI n (%)			
Normal weight	66 (33.3)	0	**<0.001**
Overweight	86 (43.4)	15 (27.3)	
Obesity	46 (23.2)	40 (72.7)	
Age (years)	40.0±14.1	45.4±11.5	**0.010**
Muscle mass (kg)	13.1±2.61	13.6±2.75	0.206
Fat mass (kg)	22.0±9.36	33.0±11.1	**<0.001**
BMI (kg/m^2)	27.2±4.92	33.7±5.78	**<0.001**
Fat percentage (%)	29.1±9.41	37.9±7.84	**<0.001**
WC (cm)	88.3±12.2	102±9.93	**<0.001**
SBP (mmHg)	114±11.8	118±12.0	0.052
DBP (mmHg)	73.6±12.0	77.1±7.91	**0.007**
Fasting blood glucose (mg/dL)	98.1±49.4	104±23.0	**<0.001**
Total cholesterol (mg/dL)	185±53.2	202±42.3	**0.005**
TG (mg/dL)	144±107	266±206	**<0.001**
HDL-c (mg/dL)	42.5±16.0	41.0±11.6	0.576
LDL-c (mg/dL)	115±44.0	119±39.1	0.387
ALT (UI/L)	46.0±79.0	46.3±33.4	0.133
AST (UI/L)	43.9±48.4	40.5±26.8	0.269
GGT (UI/L)	50.6±94.5	50.0±61.2	0.111
HOMA-IR	2.01±1.59	4.23±3.55	**<0.001**

Values are mean±standard deviation unless where indicated. Bold numbers indicate P<0.05. BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglycerides; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; HOMA-IR: homeostatic model assessment for insulin resistance.

Results

Overall, 141 women (55.2%) and 114 men (44.8%) were included in this study. The mean age, BMI, WC, and TG were 41.1±13.7 years, 28.6±5.70 kg/m^2, 91.29±13.08 cm, and 170±161 mg/dL, respectively. The population was classified according to the presence (HTGW+) or absence (HTGW−) of the HTGW phenotype. In general, 21.6% of the participants met the criteria for the HTGW+. Table 1 shows the clinical, anthropometric, and biochemical differences between the studies groups (HTGW+ vs. HTGW−).

Table 2. Macronutrient intakes according to the HTGW phenotype

Variables	Reference values	HTGW−	HTGW+	P value
Energy (kcal/d)	–	2102±594	2106±587	0.868
Protein (%E/d)	15	16.4±4.20	16.8±3.98	0.574
Lipids (%E/d)	<30	33.5±9.43	30.1±8.71	**0.027**
SFAs (%E/d)	<7	8.74±3.55	8.87±3.87	0.129
MUFAs (%E/d)	10–15	11.5±5.01	9.96±4.59	**0.032**
PUFAs (%E/d)	10	5.25±2.59	5.04±2.54	0.508
Carbohydrates (%E/d)	55–60	52.0±10.8	54.5±10.1	0.183
Fiber (g/d)	30	20.2±11.1	22.0±13.3	0.538

Values are mean and standard deviation. Bold numbers indicate P<0.05. SFA: saturated fatty acids; MUFAs: monounsaturated fatty acids; PUFAs: polyunsaturated fatty acids. Reference values of macronutrient intakes for the Mexican population have been reported [26].

Table 3. Micronutrient intakes according to the HTGW phenotype

Variables	Reference values	HTGW−	HTGW+	P value
Vitamin A (mcg/d)	900	890±1003	937±985	0.341
Vitamin B1 (mcg/d)	1.5	1.23±0.62	1.30±0.73	0.426
Vitamin B2 (mcg/d)	1.7	1.38±0.68	1.54±0.97	0.622
Vitamin B3 (mg/d)	20	15.7±9.83	19.5±12.2	**0.017**
Vitamin B5 (mg/d)	10	2.36±2.71	2.31±1.38	0.567
Vitamin B6 (mg/d)	2	1.27±0.77	1.45±0.98	0.262
Vitamin B9 (mcg/d)	200	177±143	220±202	0.265
Vitamin 12 (mcg/d)	2	3.24±2.19	3.23±2.52	0.579
Vitamin C (mg/d)	60	80.7±88.4	121±150	0.176
Vitamin E (mg/d)	10	2.74±2.92	2.83±2.24	0.415
Ca (mg/d)	800	1028±469	991±431	0.793
K (mg/d)	1800	2044±799	2227±1019	0.260
Se (mcg/d)	55–70	46.8±34.5	55.2±44.3	0.166
Mg (mg/d)	350	275±166	320±235	0.468
Zn (mg/d)	15	7.25±7.47	7.13±3.60	0.374

Values are mean and standard deviation. Bold numbers indicate P<0.05. d: day. Reference values of micronutrient intakes for the Mexican population have been reported [25].

The HTGW+ group was older and presented higher adiposity levels (including body fat) than those without the HTGW phenotype. Also, higher serum levels of glucose, total cholesterol, HOMA-IR, and DBP were found in HTGW+ participants compared to the HTGW− group. Moreover, the HTGW phenotype was associated with higher age regardless of sex, although women presented more metabolic abnormalities than men (data not shown).

The average consumption of energy and macronutrients according to the presence or absence of the HTGW phenotype groups is shown (Table 2). Both groups consumed excessive fat and saturated fatty acids (SFAs) and low amounts of fiber and polyunsaturated fatty acids (PUFAs) compared to reference values for the Mexican population. However, significantly higher consumptions of total fat and monounsaturated fatty acids (MUFAs) were found in subjects with the HTGW+ phenotype (Table 2). No significant differences were found in the groups' consumption of protein, fiber, and carbohydrates (Table 2).

Regarding micronutrients (vitamins and minerals), deficiencies in the intakes of vitamins B1, B2, B3, B5, B6, E, Mg, and Zn were found in both study groups compared to the reference standards (Table 3). The HTGW− subjects had a significantly higher intake of vitamin B3 than the HTGW+ participants (Table 3). In general, all individuals consumed equivalents of sugars, fats and meat above recommendations for the Mexican population, whereas the intakes of fruits, vegetables and legumes were insufficient (Table 4). The HTGW+ group tended to consumed more sugars and less vegetables than the HTGW− counterparts, although it did not reach statistical significance (Table 4).

Table 5 shows the differences in the frequencies of daily consumption of specific foods in both HTWG phenotype groups. The HTGW+ group presented a statistically higher consumption of sugary drinks than the HTGW−. No significant differences were found in the consumption of whole grains, fruits, vegetables, animal fats, or oilseeds. The frequencies in exercise performance between the HTGW

Table 4. Intakes of food equivalents according to the HTGW phenotype

Variables	Reference values	HTGW−	HTGW+	P value
Sugars (eq./d)	0–3	5.27±5.22	5.90±4.13	0.092
Fruits (eq./d)	2–4	1.52±1.99	1.98±2.18	0.225
Vegetables (eq./d)	3–5	2.55±2.23	2.35±2.91	0.060
Legumes (eq./d)	1–2	0.68±0.84	0.81±1.24	0.984
Fats (eq./d)	0–3	5.06±3.73	4.24±3.38	0.135
Meat (eq./d)	2–3	6.49±3.72	6.50±3.41	0.951

Values are mean and standard deviation. d: day; eq: equivalents. Equivalents refer to the number of food portions according to the Mexican System of Food and Equivalents [27].

Table 5. Frequencies of daily consumption of food groups according to the HTGW phenotype

Food group n (%)	RDA	HTGW−	HTGW+	P value
Whole grains	Daily	94 (48.0)	21 (38.9)	0.236
Legumes	Daily	177 (89.8)	51 (94.4)	0.300
Fruits	Daily	192 (97.5)	53 (98.1)	0.770
Vegetables	Daily	186 (94.4)	53 (98.1)	0.255
Beef meat	Daily	170 (86.3)	46 (85.2)	0.835
Chicken	Daily	175 (88.8)	48 (88.9)	0.991
Pork meat	Daily	123 (62.4)	38 (70.4)	0.281
Fish	Daily	119 (60.4)	32 (59.3)	0.879
Sea food	Daily	49 (24.9)	16 (29.6)	0.487
Dairy	Daily	181 (91.9)	50 (92.6)	0.864
Vegetables oils	Daily	85 (93.9)	50 (92.6)	0.726
Sausages	–	144 (73.1)	34 (63.0)	0.146
Fats	Daily	93 (47.2)	24 (44.4)	0.718
Fried foods	–	96 (49.0)	29 (53.7)	0.539
Oilseeds	Daily	166 (58.9)	30 (55.6)	0.661
Sugary drinks	–	139 (70.6)	46 (85.2)	**0.031**
Coffee	Daily	117 (59.7)	30 (55.6)	0.584
Grains with fats	Daily	135 (68.5)	34 (63.0)	0.440

Bold numbers indicate P<0.05. RDA: recommended dietary allowances. Frequencies are reported as number and corresponding percentage (n, %) of persons consuming daily each food group according to the Mexican RDA.

groups are shown (Figure 1). The HTGW+ group scored a higher prevalence of a sedentary lifestyle compared to subjects in the HTGW− group.

In Table 6, the frequencies of the *CD36* gene polymorphism were analyzed by study groups. Higher frequencies of the AG genotype were found in the HTGW+ group than HTGW− individuals. According to the multivariate logistic regression model (Table 7), the main risk variables present among the patients with the HTGW phenotype were female sex, BMI, total cholesterol, and daily consumption of sugary drinks. On the other hand, performing exercise was shown to have a protective effect.

Discussion

This study is the first to jointly analyze a Mexican population's lifestyle and genetic factors with the HTGW phenotype. This information is of epidemiological and clinical value given the relationship of this phenotype with the development of chronic illnesses, where has been found to be a valuable, sensitive, and integrative mirror of metabolic syndrome traits [33].

There is little evidence linking genetic factors to the HTGW phenotype. In this study, when analyzing the relationship between the rs1761667 *CD36* gene polymorphism and the HTGW phenotype, it was found that individuals carrying the AG genotype had up to four times more risk of presenting the HTGW phenotype compared to homozygotes. Different genetic studies have reported the physiopathological role of the CD36 receptor in humans, associating mutations in this gene with insulin resistance, low levels of adiponectin, type 2 diabetes mellitus [34], liver fibrosis [31], and hypercholesterolemia [32]. Likewise, variants in this gene have also been related to adiposity measurements [35], evidencing their prominent role in obesity [36]. Interactions with other lipid-related genes highly prevalent in the Mexican population, such as *APOE* and *FABP2* [37, 38] need further research.

This study shows that 21.6% of the population presented the HTGW phenotype. This frequency is similar to elderly subjects (27.1%) from northeast Brazil [39], but higher than young adults (5.90%) from the Southern Region of Brazil [40], as well as in Iranian adolescents (6.40%), as reported elsewhere [41]. Moreover, in this study, the most affected population was women (72.7%), showing a difference with other studies reporting a prevalence of the HTGW phenotype in women between 30–40% [42, 43].

Studies have indicated that individuals with the HTGW phenotype show lower adherence to a healthy diet [44]. In this study, all subjects consumed fat and SFAs above the recommendations for the Mexican population, whereas the intakes of fiber, PUFA as well as some B-complex vitamins and minerals were deficient. The analysis of food equivalents in this research revealed that the aforementioned nutritional features appears to be related to the overconsumption of red meat and animal fats and the poor intakes of vegetables, fruits, and legumes. Moreover, although the HTGW− group consumed more fats than the HTGW+ counterparts, these were mainly essential

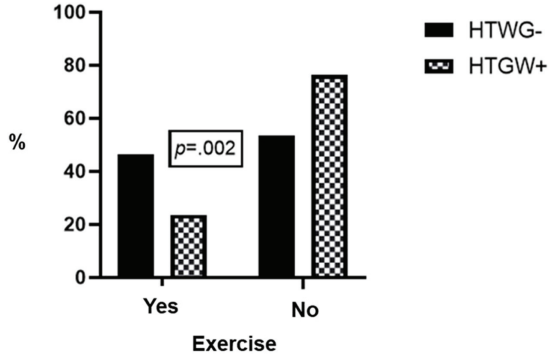

Figure 1. Differences in the performing of exercise according to the HTGW phenotype. For the exercise assessment, the participants were asked if they practiced some systematic exercise or sport (yes/no) of moderate intensity at least 150–300 minutes a week [29].

Table 6. Comparison of *CD36* genotype according to the HTGW phenotype

CD36 genotype	HTGW− n (%)	HTGW+ n (%)	P value
AA	70 (35.0)	16 (29.1)	**0.037**
AG	84 (42.0)	33 (60.0)	
GG	46 (23.0)	6 (10.9)	

Bold numbers indicate P<0.05.

Table 7. Multivariate logistic regression model analyzing variables associated with the presence of the HTGW phenotype

Variables	OR	95% CI Lower	95% CI Upper	P value
Age	1.04	0.99	1.07	0.107
Sex (female)	2.92	1.12	7.60	**0.028**
BMI (kg/m^2)	1.19	1.07	1.32	**0.001**
Total cholesterol (mg/dL)	1.01	1.00	1.02	**0.039**
LDL-c (mg/dL)	0.34	0.11	1.09	0.070
Exercise (yes)	0.23	0.08	0.62	**0.004**
MUFAs (%/day)	0.98	0.90	1.07	0.645
Daily sugary drinks consumption (yes)	6.94	1.80	26.80	**0.005**
CD36 (AG genotype)	3.81	1.08	13.40	**0.037**

Nagelkerke R^2=0.47, p≤0.001. Bold numbers indicate P<0.05. BMI: body mass index; LDL-c: low-density lipoprotein cholesterol; MUFAs: monounsaturated fatty acids.

MUFA, which exert several health benefits, including the prevention of metabolic syndrome and its complications [45]. Overall, these findings are consistent with previous nutritional reports in the Mexican population, where excessive consumption of ultra-processed foods rich in saturated fats and deficiencies in the intakes of antioxidants as part of a hepatopathogenic diet have been documented [46].

In addition, consuming daily sugary drinks was the only food significantly associated with the HTGW phenotype in this investigation. While the precise quantities of sugary drinks were not estimated in this study, this finding is important since a high consumption (more than 180 liters/person/year) of sugary drinks has been reported in the Mexican population [47]. Based on this information, the consumption of half a liter of sugary drinks per day may be sufficient to present metabolic disturbances among Mexicans including the HTGW phenotype. Accordingly, the regular consumption of sugary drinks has been systematically associated with weight gain and the development of obesity related chronic metabolic diseases, such as metabolic syndrome and type 2 diabetes [48].

Lifestyle modifications are of clinical relevance to avoid comorbidities associated with metabolic syndrome, where studies have shown the efficacy of performing exercise in preventing cardiometabolic diseases [49]. In this study, subjects with the HTGW phenotype predominantly adhere to a sedentary lifestyle that could be related to the fact that the majority had obesity. This data agrees with the results of other studies that have highlighted that people with excessive abdominal fat do not perform exercise regularly [50, 51]. Also, it has been shown that individuals with the HTGW phenotype have lower adherence to regular exercise programs, where people who did not present the HTGW phenotype are physically more active, resulting in a protective effect even in subjects with overweight or obesity and in older adults at high risk of cardiovascular disease [52].

A limitation of this study is the nature of the design, where causality cannot be analyzed. Another drawback is the difference in age within the study groups; however, this variable was controlled as shown in the multivariate logistic regression analysis. Also, it is important to consider that the determination of physical activity was based on subjective questions. Additionally, type I and type II statistical errors cannot be discarded despite appropriate settings. Furthermore, additional studies with a larger number of individuals are convenient.

In conclusion, the *CD36* (rs1761667) G>A polymorphism, daily consumption of sugary drinks and sedentarism are risk factors associated with HTGW phenotype in Mexican adult population. This knowledge may be helpful for the identification of genetically susceptible groups as well as the design and implementation of personalized strategies for the precision clinical/nutritional management of the HTGW phenotype and related metabolic comorbidities.

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Conflict of interest
The authors declare that there are no conflicts of interest.

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O.R.L conceived and designed the study. D.N.R analyzed the data and wrote the first draft of the manuscript. A.P and S.R wrote and review the data. All authors contributed to and approved the final draft of the manuscript.

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