ORIGINAL ARTICLE

Prevalence of hypertriglyceridemia in adults and related cardiometabolic factors. SIMETAP-HTG study[☆]

Antonio Ruiz-García [a,*], Ezequiel Arranz-Martínez [b], Beatriz López-Uriarte [c],
Montserrat Rivera-Teijido [d], David Palacios-Martínez [d],
Gema M. Dávila-Blázquez [e], Antonio Rosillo-González [f],
José Antonio González-Posada Delgado [g], José Enrique Mariño-Suárez [g],
Enrique Revilla-Pascual [g], José Luis Quintana-Gómez [g], Ignacio Íscar-Valenzuela [g],
Rafael Alonso-Roca [h], Ana Pilar Javierre-Miranda [i], Rosa Ana Escrivá-Ferrairó [j],
Isabel Tello-Meco [k], Ana María Ibarra-Sánchez [l], M. Isabel Gutiérrez Sánchez [m],
Juan Ramón Iglesias Quintana [n], M. Inmaculada Hernández-Beltrán [n],
Montserrat Pérez Fernández [o], Elena Barrios-Rueda [p], Raúl Pérez Muñoz [q],
Miguel Prieto Marcos [r], Santiago Delgado Rodríguez [r], Raquel Pleite Raposo [s],
Rafael Rodríguez-Cabanillas [t], M. Rosario Morales-Chico [u],
Diana Fernández-Pacheco Vila [u], Beatriz Remón-Pérez [u],
M. Jesús del Villar Redondo [u], Joaquina Reguillo-Díaz [u], Paloma Aguilera Reija [v],
Ana Olga Rodríguez Rodríguez [w], Ofelia Gómez-Fernández [x],
M. del Carmen Antón-Sanz [y], Antonio Sánchez-Calso [z], Norma Alejandra Doria-Carlin [aa],
Manuel J. Frías-Vargas [bb]

[a] *Centro de Salud Universitario Pinto, Unidad de Lípidos y Prevención Cardiovascular, Pinto, Madrid, Spain*
[b] *Centro de Salud San Blas, Parla, Madrid, Spain*
[c] *Centro De Salud Humanes, Humanes de Madrid, Madrid, Spain*
[d] *Centro De Salud Universitario Isabel II, Parla, Madrid, Spain*
[e] *Centro De Salud Universitario Las Américas, Parla, Madrid, Spain*
[f] *Centro De Salud Tres Cantos II, Tres Cantos, Madrid, Spain*
[g] *Centro De Salud El Greco, Getafe, Madrid, Spain*
[h] *Centro De Salud Mar Báltico, Madrid, Spain*
[i] *Centro De Salud Montesa, Madrid, Spain*
[j] *Centro De Salud Santa Isabel, Leganés, Madrid, Spain*
[k] *Centro De Salud Los Alperchines, San Fernando de Henares, Madrid, Spain*
[l] *Centro De Salud Buenos Aires, Madrid, Spain*
[m] *Centro De Salud Guayaba, Madrid, Spain*

[n] *Centro De Salud Pavones, Madrid, Spain*

[o] *Centro De Salud Reyes Magos, Alcalá de Henares, Madrid, Spain*

[p] *Centro De Salud Vicente Soldevilla, Madrid, Spain*

[q] *Centro de Salud Huerta de los Frailes, Leganés, Madrid, Spain*

[r] *Centro De Salud Ntra, Sra. de Fátima, Madrid, Spain*

[s] *Centro De Salud Juncal, Torrejón de Ardoz, Madrid, Spain*

[t] *Centro de Salud Arroyo de la Media Legua, Madrid, Spain*

[u] *Centro De Salud Valdemoro, Valdemoro, Madrid, Spain*

[v] *Centro De Salud Miraflores, Alcobendas, Madrid, Spain*

[w] *Centro De Salud Margaritas, Getafe, Madrid, Spain*

[x] *Centro De Salud Daroca, Madrid, Spain*

[y] *Consultorio Alpedrete, Alpedrete, Madrid, Spain*

[z] *Centro De Salud Galapagar, Galapagar, Madrid, Spain*

[aa] *Centro De Salud Los Cármenes, Madrid, Spain*

[bb] *Centro De Salud Comillas, Madrid, Spain*

Abstract:

Aim: To determine in the adult population the crude and the sex- and age-adjusted prevalence rates of hypertriglyceridaemia (HTG) and to assess its association with cardiovascular risk factors, chronic kidney disease, cardiovascular and cardiometabolic diseases.

Methods: Cross-sectional observational study conducted in Primary Care, with 6,588 adult study subjects, randomly selected on base-population. Patients had HTG if the triglyceride level was $\geq$150 mg/dL ($\geq$1.7 mmol/L), or were on lipid-lowering therapy to lower triglyceride. Associations were assessed by univariate and multivariate analysis, and crude and sex- and age-adjusted prevalence rates were determined.

Results: The arithmetic and geometric means of triglyceride levels were respectively 120.5 and 104.2 mg/dL in global population, 135.7 and 116.0 mg/dL in men, and 108.6 and 95.7 mg/dL in women. The crude HTG prevalence rates were 29.6% in global population, 36.9% in men and 23.8% in women. The sex- and age-adjusted HTG prevalence rates were 27.0% in global population, 34.6% in men and 21.4% in women. The independent variables that were most associated with HTG were hypercholesterolemia (OR: 4.6), low HDL-C (OR: 4.1), hepatic steatosis (OR: 2.8), diabetes (OR: 2.0), and obesity. (OR: 1.9).

Conclusions: The means of triglyceride levels and HTG prevalence rates are intermediate between those of other national and international studies. A fifth of the female adult population and more than a third of the male population had HTG. The independent factors associated with HTG were hypercholesterolemia and low HDL-C, and the cardiometabolic variables diabetes, hepatic steatosis and obesity.

Prevalencia de hipertrigliceridemia en adultos y factores cardiometabólicos asociados. Estudio SIMETAP-HTG

Resumen

Objetivo: Determinar en la población adulta las tasas de prevalencia crudas y ajustadas por edad y sexo de hipertrigliceridemia (HTG) y valorar su asociación con factores de riesgo cardiovascular, enfermedad renal crónica, enfermedades cardiovasculares y cardiometabólicas.

Métodos: Estudio observacional transversal realizado en Atención Primaria, con 6.588 sujetos de estudio adultos, seleccionados aleatoriamente con base poblacional. Los pacientes tenían HTG si la concentración de triglicéridos era ≥150 mg/dL (≥1,7 mmol/L), o estaban en tratamiento hipolipemiante para reducir los triglicéridos. Se valoraron las asociaciones mediante análisis univariado y multivariante, y se determinaron las prevalencias crudas y ajustadas por edad y sexo.

Resultados: Las medias aritméticas y geométricas de las concentraciones de triglicéridos fueron respectivamente 120,5 y 104,2 mg/dL en la población global, 135,7 y 116,0 mg/dL en hombres, y 108,6 y 95,7 mg/dL en mujeres. Las prevalencias crudas de HTG fueron 29,6% en población global, 36,9% en hombres y 23,8% en mujeres. Las prevalencias ajustadas por edad y sexo de HTG fueron 27,0% en población global, 34,6% en hombres y 21,4% en mujeres. Las variables independientes que más se asociaban con la HTG fueron hipercolesterolemia (OR: 4,6), cHDL bajo (OR: 4,1), esteatosis hepática (OR: 2,8), diabetes (OR: 2,0) y obesidad (OR: 1,9).

Conclusiones: Las medias de triglicéridos y las prevalencias de HTG se encuentran intermedias entre las de otros estudios nacionales e internacionales. La quinta parte de la población adulta femenina y más de un tercio de la masculina presentaba HTG. Los factores independientes asociados con HTG fueron hipercolesterolemia y cHDL bajo, y las variables cardiometabólicas diabetes, esteatosis hepática y obesidad.

Introduction

Hypertriglyceridaemia (HTG) is important due to its high prevalence and its clinical relevance when associated with an increased risk of atherosclerotic cardiovascular disease (ASCVD). The increase in the prevalence of HTG in recent decades is similar to that of type 2 diabetes mellitus (DM) and obesity.[1]

Most circulating triglycerides (TG) are transported by TG-rich lipoproteins, which include chylomicrons, very low-density lipoproteins, and their remnants. Lipids and lipoproteins are measured to estimate cardiovascular risk (CVR) and to assist in the therapeutic management of cardiovascular disease. TG concentrations above 150 mg/dL indicate a higher CVR and necessitate a search for other cardiovascular risk factors (CVRF).[2–4]

Ischaemic heart disease and cerebrovascular diseases remain the 2 primary causes of mortality in Spain, over recent decades.[5] Epidemiological studies show a correlation between HTG and cardiovascular morbidity and mortality.[2,6,7] Subjects with similar plasma low-density cholesterol (LDL-C) levels may have different risk of ASCVD depending on their TG concentrations, and therefore individuals with HTG are at higher CVR.[8]

HTG is frequently associated with low concentrations of high-density lipoprotein cholesterol (HDL-C) and with a higher concentration of LDL-C particles, characterised by being small and dense. This association, known as atherogenic dyslipidaemia, increases the risk of ASCVD.[3] TG and HDL-C testing is necessary to estimate CVR more accurately, especially in patients with DM, metabolic syndrome (MS) or chronic kidney disease (CKD), where there is a higher concentration of atherogenic lipoproteins containing apolipoprotein B (ApoB).[4] The higher concentration of small, dense LDL-C particles associated with HTG can be reversed by lowering TG levels with drug treatment.[9]

Although HTG is associated with an increased risk of ASCVD, adjustment for HDL-C attenuates this relationship.[8,10] Scientific evidence has confirmed that retention within the arterial endothelium of LDL-C and other plasma particles containing ApoB within the arterial endothelium is responsible for the formation of ASCVD, the concentration of which is associated with cholesterol not bound to high-density lipoproteins (non-HDL-C),[11] and may even be more effective than LDL-C in predicting ASCVD when HTG is present.[12] The set of TG-rich lipoproteins and their remnants is associated with a risk of ASCVD but is determined more by the concentration of ApoB-containing particles than by TG content.[2,13,14]

Prevalence studies of CVRFs are needed to improve ASCVD prevention, plan health resources, and monitor and evaluate the strategies set out in the Global Plan of Action for the Prevention and Control of Non-Communicable Diseases.[15] Severe HTG (TG>885 mg/dL) is rare and is associated more with increased risk of pancreatitis.[16–19] However, the prevalence of mild to moderate HTG (HTG between 150 and 885 mg/dL) exceeds 10% of the adult population, with great variability between countries.[10,20,21]

This study aims to determine the gross and age- and sex-adjusted prevalence rates of HTG in the adult population in the primary care setting, and to assess the association of HTG with CVRF, CKD and cardiovascular and metabolic diseases.

Material and methods

The SIMETAP-HTG study is part of the SIMETAP project, approved by the Primary Care Management Research Commission of the Madrid Region Health System (SERMAS). This is a cross-sectional, observational study carried out by 121 general practitioners interested in participating in the SIMETAP research project, whose objective was to assess the prevalence of CVRFs, MS and related cardiovascular or metabolic diseases. The doctors worked in 64 SERMAS-dependent primary care centres (25% of the SERMAS health

centres). The participating doctors were selected competitively until the necessary sample size was achieved. The material and methods (design, sampling, selection, inclusion and exclusion criteria of the study subjects, data collection and statistical analysis) of the SIMETAP study have been detailed previously in this journal.[22] The study population was obtained through a simple random sample of the population over 18 years of age assigned to the SERMAS primary care physicians participating in the study. As per the study protocol, informed consent was obtained from all participants, and those for whom no information on biochemical variables was available were excluded, as were terminal, institutionalized patients, those with cognitive impairment and pregnant women. The final sample was 10,084 study subjects, whose response rate was 65.8%.

The statistical analysis was carried out using the Statistical Package for the Social Sciences (IBM® SPSS® Statistics). The means and standard deviation (SD) were determined for the analysis of continuous variables. The range, median and interquartile range (25th percentile; 75th percentile) of the age variable and the arithmetic mean (SD), median and geometric mean of the TG variable were determined. Qualitative variables were analysed using prevalence rates and percentages in each category, presented with lower and upper limits of the 95% confidence interval (95% CI). Prevalence rates were determined as gross rates and rates adjusted by age and sex, standardized with the Spanish population using the direct method.[23] The distributions by age and sex of the Spanish population in January 2015 were obtained from the National Institute of Statistics database.[24] It was decided to adjust the rates according to the Spanish population instead of the population of the Community of Madrid, because there were no significant differences in the results of the adjusted prevalence rates between both populations and to facilitate the comparison of results with other populations.

Comparisons of continuous variables were made using the Student t-test or analysis of variance. The chi-square test was used for analysis of categorical variables. Odds ratios (OR) were determined with 95% CI. All the tests were considered statistically significant if the 2-tailed p-value was less than .05. The multivariate logistic regression analysis with the introduce method was used to evaluate the effect on the dependent variable (HTG) of the independent variables (CVRF and comorbidities) whose previously performed univariate analysis would have shown a statistically significant association with the dependent variable, except for the age and sex variables, because they are strongly related to other cardiovascular or metabolic variables. The variables CUN-BAE,[25,26] MS, atherogenic dyslipidaemia, ASCVD and CKD were not entered in the multivariate analysis as they are complex parameters containing variables already included in the analysis.

In the present study we considered the definitions and criteria of the variables previously indicated in this journal.[22] It was also considered that the study subjects suffered from the syndromes or diseases analysed if their respective diagnoses or related codes from the International Classification of Primary Care 2nd edition[27] or the International Classification of Diseases, 9th revision, Clinical Modification,[28] were recorded in their clinical records. For the purposes of this study, the following criteria were given specific consideration:

- Abdominal or central obesity: waist circumference ≥ 102 cm in men or ≥ 88 cm in women.[29]
- Body mass index (BMI)[30]: weight (kg)/height (m).[2] Overweight: BMI 25.0–29.9 kg/m.[2] Obesity: BMI ≥ 30 kg/m.[2]
- Increased waist-height index[31]: waist circumference (cm)/height (cm) ≥ 0.6.
- Adiposity or body fat index determined by the CUN-BAE formula (Clínica Universitaria de Navarra-Body Adiposity Estimator)[25,26]: male sex $(\%) = -44.988 + (.503 \times age) + (3.172 \times BMI) - (.026 \times BMI^2) - (.02 \times BMI \times age) + (.00021 \times BMI^2 \times age)$; female sex $(\%) = -44.988 + (.503 \times age) + 10.689 + (3.353 \times BMI) - (.031 \times BMI^2) - (.02 \times BMI \times age) + (.00021 \times BMI^2 \times age)$. CUN-BAE-overweight: 20%-25% (men); 30%-35% (females); CUN-BAE-obesity: >25% (males); >35% (women).
- Hypercholesterolaemia[32] (International Classification of Primary Care 2nd edition: T93. International Classification of Diseases, 9th revision, Clinical Modification: 272.0; 272.2; 272.4): serum total cholesterol concentration (TC) >200 mg/dL, or if the patient was taking cholesterol-lowering drugs.
- HTG[32] (International Classification of Diseases, 9th revision, Clinical Modification: 272.1; 272.3): TG serum concentration ≥ 150 mg/dL, or if the patient was taking TG-lowering drugs.
- Low HDL-C:[33] serum concentration <40 mg/dL (men) or <50 mg/dL (women).
- Non-HDL-C:[4] difference between serum TC and HDL-C concentrations.
- LDL-C:[4] Friedewald's formula LDL-C = TC−HDL-C − TG/5 (mg/dL). Not determined whether TG ≥ 400 mg/dL.
- Cholesterol bound to very low-density lipoproteins and TG-rich lipoprotein remnants: TC−HDL-C − LDL-C. Not determined whether TG ≥ 400 mg/dL.
- Atherogenic dyslipidaemia:[33] HTG with low HDL-C.
- Castelli-I index:[34] TC/HDL-C.
- Castelli-II index:[34] LDL-C/HDL-C.
- Atherogenic coefficient: Non-HDL-C / HDL-C.
- TG index/HDL-C.
- Atherogenic index of plasma:[35] log (TG/HDL-C).
- TG index and glucose:[36] Ln [TG (mg/dL) × FPG (mg/dL)/2]
- Albuminuria:[37] albumin creatinine ratio ≥ 30 mg/g.
- Low glomerular filtration rate (GFR)[37]: <60 mL/min/1.73 m^2 estimated according to Chronic Kidney Disease EPIdemiology collaboration.
- CKD[37]: Low GFR and/or albuminuria.
- MS: 2009 IDF/NHLBI/AHA/WHF/IAS/IASO consensus criteria.[29]
- ASCVD: includes coronary disease, stroke, and peripheral arterial disease. Coronary disease includes ischaemic heart disease, previous acute myocardial infarction, acute coronary syndromes, coronary revascularisation, and other arterial revascularisation procedures. Stroke: includes cerebral vascular accident, cerebral ischaemia or intracranial haem-

Table 1 Description of age in the study populations.

	n	Range	Median (IQR)	Mean (SD)
With HTG	1.947	18.9−98.0	59.1 (48.3−69.9)	58.8 (15.4)
Men	1.072	19.7−96.7	56.1 (46.2−65.8)	56.1 (14.3)
Women	875	18.9−98.0	62.8 (52.0−74.5)	62.1 (16.0)
Without HTG	4.641	18.0−102.8	53.3 (39.5−67.3)	53.6 (18.1)
Men	1.832	18.0−102.1	54.2 (40.3−68.9)	54.7 (18.2)
Women	2.809	18.0−102.8	50.8 (38.966.4)	52.9 (18.1)
Global	6.588	18.0−102.8	54.7 (41.7−68.1)	55.1 (17.5)
Men	2.904	18.0−102.1	55.0 (42.4−67.5)	55.3 (16.9)
Women	3.684	18.0−102.8	54.5 (40.9−68.8)	55.0 (18.0)

SD: standard deviation; HTG: hypertriglyceridaemia; IQR: interquartile range.

orrhage and transient ischaemic attack. Peripheral arterial disease includes intermittent claudication or ankle brachial index ≤.9.

none- CVR: assessment according to recommendations of the European Guidelines,[38] using the Systematic Coronary Risk Estimation[38] and Systematic Coronary Risk Estimation O.P.[39] Extreme CVR:[40] patients with ASCVD and MD or CKD.

To compare the HTG prevalence rates determined in the present study, a literature search was performed of the main studies published between 2005 and 2015 on PubMed, Medline, Embase, Google Scholar and Web of Science.

Results

Of the study population, 55.9 % (95 % CI: 54.7–57.1) were female. The difference in average age between men and women (.3 years) was not significant. The difference in mean ages (5.2 years) between the populations with and without HTG was significant (p < .001). In the population with HTG, the proportion of females was 44.9 % (95 % CI 42.7–47.2), with a significant (p < .001) difference in mean age (6.0 years) between men and women. In the population without HTG, the proportion of females was 60.5 % (95 %CI: 59.1–61.9), the difference in average age (1.8 years) between men and women being significant (p < .001) (Table 1).

The clinical characteristics and lipid profiles of the global study populations, with HTG and without HTG, are shown in Table 2. All parameters evaluated were significantly higher in the population with HTG, except HDL-G and GFR, which were significantly higher in the population without HTG. There was no significant difference in mean DM duration between the populations with and without HTG (Table 2).

Of the HTG population, 47.1 % (95 % CI 44.9–49.3) were on hypolipidaemic drug treatment. Of the population with HTG, 63.9 % (95 % CI, 61.8–66.1) had TG concentrations<200 mg/dL, and 23.3 % (95 % CI, 21.4–25.1) had TG concentrations<150 mg/dL.

In the study population, the mean (SD) TG was significantly higher (p < .001) in the men (135.7 [100.6] mg/dL) than in the women (108.6 [63.8] mg/dL). The geometric means and medians of TG were respectively: 104.2 and 101 mg/dL in the global population; 116.0 and 111 mg/dL in the male population; and 95.7 and 93 mg/dL in the female population.

In the population with HTG, the mean (SD) TG was significantly higher (p < .001) in the men (210.0 [131.6] mg/dL) than in the women (185.6 [82.4] mg/dL). The geometric and median TG were respectively: 180.6 and 176 mg/dL in the global population; 187.8 and 182 mg/dL in the male population; and 172.2 and 169 mg/dL in the female population.

In the population without HTG, the mean (SD) TG was significantly higher (p < .001) in the men (92.2.0 [28.3] mg/dL) than in the women (84.6.6 [28.3] mg/dL). The geometric means and medians of TG were respectively: 82.7 and 85 mg/dL in the global population; 87.6 and 92 mg/dL in the male population; and 79.7 and 82 mg/dL in the female population.

The gross and age- and sex-adjusted prevalence rates of the different types of GT are shown in Table 3. The crude prevalence of HTG was 29.6% (95%CI: 28.4–30.7), with a significant (p < .001) difference between the males (36.9% [95%CI: 35.2–38.7]) and the females (23.8 % [95%CI: 22.4–25.1]). The age- and sex-adjusted prevalence rates of HTG were slightly lower (Fig. 1).

The distribution of HTG prevalence rates by ten-year age group was adjusted (determination coefficient R^2 = .93) to the following polynomial function: $y = -.0147x^2 + .1521x - .0333$ (Fig. 2). The prevalence of HTG increased continuously with age, from the third to the sixth decade in the men and from the third to the eighth decade in the women, and then decreased. The male population had significantly higher prevalence rates of HTG than the female population in all age groups, except in the 70–79 age group, where the difference was not significant, and in the age group ≥80, where the prevalence of HTG was slightly higher in the female population.

The ORs for the comorbidities assessed among the populations with and without HTG are shown in Table 4. All comorbidities were significantly associated with HTG, except hypothyroidism and erectile dysfunction. The variables that showed a greater association with HTG were CUN-BAE,[25,26] DM, MS,[29] hepatic steatosis, hypercholesterolaemia, low HDL-C, low GFR and albuminuria. Hypoglycaemic, hypolipidaemic and antihypertensive therapy, and high, very high and extreme CVR were associated more with the population with HTG. Low CVR was significantly more associated with the population without HTG. Of the

Table 2 Clinical characteristics of the study population.

	Global		With HTG		Without HTG		Difference of means	p
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)		
BMI (kg/m^2)	6.588	27.5 (5.1)	1.947	29.3 (5.0)	4.641	26.8 (5.0)	2.5	<.001
Waist circumference (cm)	6.588	93.4 (14.1)	1.947	98.9 (13.2)	4.641	91.0 (13.8)	7.9	<.001
Waist-height ratio	6.588	0.57 (0.09)	1.947	0.60 (0.08)	4.641	0.56 (0.09)	0.04	<.001
CUN-BAE (%)	6.588	34.7 (8.7)	1.947	36.1 (8.6)	4.641	34.2 (8.7)	1.9	<.001
SBP (mmHg)	6.588	121.9 (15.4)	1.947	125.3 (14.6)	4.641	120.5 (15.6)	4.7	<.001
DBP (mmHg)	6.588	73.3 (9.8)	1.947	75.4 (9.6)	4.641	72.5 (9.7)	2.9	<.001
FPG (mg/dL)[a]	6.588	96.0 (26.0)	1.947	105.6 (33.5)	4.641	92.0 (20.8)	13.6	<.001
eAG (mg/dL)[a]	5.233	115.1 (25.8)	1.666	123.9 (31.5)	3.567	110.9 (21.4)	13.0	<.001
HbA$_{1c}$ (%)[b]	5.233	5.6 (0.9)	1.666	6.0 (1.0)	3.567	5.5 (0.8)	0.5	<.001
Duration of DM (years)	1.035	9.2 (6.8)	522	9.1 (6.3)	513	9.4 (7.4)	−0.3	.465
ITyG	6.588	8.5 (0.6)	1.947	9.1 (0.5)	4.641	8.2 (0.4)	0.9	<.001
CT (mg/dL)[c]	6.588	192.8 (39.3)	1.947	203.8 (42.8)	4.641	188.1 (36.8)	15.7	<.001
TG (mg/dL)[d]	6.588	120.5 (83.2)	1.947	199.0 (112.8)	4.641	87.6 (28.6)	111.4	<.001
HDL-C (mg/dL)[c]	6.588	54.8 (14.7)	1.947	47.8 (12.7)	4.641	57.8 (14.5)	−10.0	<.001
LDL-C (mg/dL)[c]	6.526	114.2 (34.5)	1.885	117.4 (38.1)	4.641	112.8 (32.8)	4.6	<.001
VLDLandR (mg/dL)[c]	6.526	22.9 (12.3)	1.885	35.8 (14.2)	4.641	17.5 (5.7)	18.3	<.001
Non-HDL-C (mg/dL)[c]	6.588	137.9 (38.4)	1.947	156.0 (41.0)	4.641	130.3 (34.6)	25.7	<.001
CT/ HDL-C	6.588	3.7 (1.1)	1.947	4.5 (1.3)	4.641	3.4 (0.9)	1.1	<.001
Non-HDL-C /HDL-C	6.588	2.7 (1.1)	1.947	3.5 (1.3)	4.641	2.4 (0.9)	1.1	<.001
LDL-C/HDL-C	6.526	2.2 (0.9)	1.885	2.6 (1.0)	4.461	2.1 (0.8)	0.5	<.001
TG/HDL-C	6.588	2.6 (2.6)	1.947	4.6 (3.8)	4.641	1.6 (0.8)	3.0	<.001
AIP	6.588	−0.07 (0.29)	1.947	0.23 (0.24)	4.641	−0.19 (0.21)	0.42	<.001
Uric acid (mg/dL)	6.168	5.0 (1.5)	1.849	5.5 (1.5)	4.319	4.8 (1.4)	0.7	<.001
AST (U/l)	4.812	23.1 (43.2)	1.448	24.8 (21.1)	3.364	22.3 (49.7)	2.5	<.001
ALT (U/l)	6.413	24.9 (16.9)	1.899	30.1 (20.3)	4.514	22.7 (14.8)	7.4	<.001
GGT (U/l)	6.075	33.4 (50.8)	1.788	47.8 (12.7)	4.287	27.3 (36.1)	20.5	<.001
Creatinine (mg/dL)	6.588	0.84 (0.29)	1.947	0.90 (0.34)	4.641	0.82 (0.27)	0.08	<.001
eGFR (mL/min/1.73 m^2)	6.588	90.6 (20.5)	1.947	85.9 (20.1)	4.641	92.5 (20.4)	−6.6	<.001
Albuminuria (mg/g)	4.451	14.7 (55.5)	1.447	20.3 (77.9)	3.004	12.1 (40.3)	8.2	<.001

ALT: alanine aminotransferase; AST: aspartate aminotransferase; HDL-C: cholesterol bound to high density lipoproteins; LDL-C: cholesterol bound to low density lipoproteins; Non-HDL-C: cholesterol not bound to high density lipoproteins; TC: total cholesterol; CUN-BAE: body fat index (*Clínica Universitaria* of Navarra-*Body Adiposity Estimator*); SD: standard deviation; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate according to CKD-EPI; GGT: Gamma-glutamyl transferase; eAG: estimated average glucose; FPG: fasting plasma glucose; HbA$_{1c}$: A$_{1c}$ glycosylated haemoglobin; HTG: hypertriglyceridaemia; AIP: atherogenic index of plasma [log (TG/HDL-C)]; BMI: body mass index; TyGI: triglyceride glucose index; DBP: diastolic blood pressure; SBP: systolic blood pressure; TG: triglycerides; VLDLandR: cholesterol bound to very low density lipoproteins and triglyceride-rich lipoprotein remnants.

[a] To convert mg/dL to mmol/L, multiply by .05556.
[b] To convert from % (Diabetes Control and Complications Trial) to mmol/mol (International Federation of Clinical Chemistry), multiply by .09148 and add 2.152.
[c] To convert mg/dL to mmol/L, multiply by .02586.
[d] To convert mg/dL to mmol/L, multiply by .01129.

patients with HGT, 42.1% (95% CI 39.9%–44.3%) had very high or extreme CVR (OR 2.0 [95% CI 1.8–2.3]). The result of the multivariate analysis of the independent factors significantly associated with HTG is shown in Table 5.

Discussion

This study updates the information on the prevalence of HTG and average values of TG in the adult population, offering intermediate results between those published by other national and international studies. Some countries such as the United States, Germany or China preferred to use geometric means to show the central trend in TG values, as these are less sensitive to extreme values than arithmetic means. In the present study, the geometric mean of TG (104 mg/dL) was lower than the arithmetic mean of TG (121 mg/dL). The geometric means of TG of the adult population of the United States[1,41] and Germany[21] were 107 and 111 mg/dL, respectively, being slightly higher than those of the SIMETAP-HTG study. The average TG in France[42] (121 mg/dL) was similar to that of the present study. The adjusted prevalence of HTG>200 mg/dL in Korea[43,44] (9.8%) was similar to that of the present study. The adjusted prevalence rates of HTG of the SIMETAP-HTG study and its mean

Table 3 Hypertriglyceridaemia prevalence rates in the study population.

TG concentration	Gross prevalence (IC95%), %	Adjusted prevalence[a], %
≥150 mg/dL (≥1.7 mmol/L)	22.7 (21.7; 23.7)	21.1
≥177 mg/dL (≥2.0 mmol/L)	14.7 (13.8; 15.6)	13.7
≥200 mg/dL (≥2.3 mmol/L)	10.7 (9.9; 11.4)	10.0
≥400 mg/dL (≥4.5 mmol/L)	.94 (.71; 1.12)	.97
≥885 mg/dL (≥10 mmol/L)	.09 (.02; .16)	.11
≥1.770 mg/dL (≥20 mmol/L)	.015 (−.01; −.04)	.021

Source: National Institute of Statistics.[24]
95%CI: lower and upper limits of 95% confidence interval; TG: triglycerides.
[a] Prevalence adjusted by age and sex to the Spanish population 2015.

TG concentrations were lower than those determined in the following countries: Mexico,[45] prevalence 31.5%; mean TG 140 mg/dL; China,[46] geometric mean TG 139 mg/dL. India,[47] prevalence 36.9%, mean TG 163 mg/dL (men) and 144 mg/dL (women).

The means of TG and adjusted prevalence rates of HTG in this study were slightly higher than those of other research studies in Spain,[48–57] except for the CORSAIB[58] study, which showed a mean of TG of 131 mg/dL in the population>35 of the Balearic Islands, and the CDC cohort in the Canary Islands,[59] which showed mean of TG of 141 mg/dL (men) and
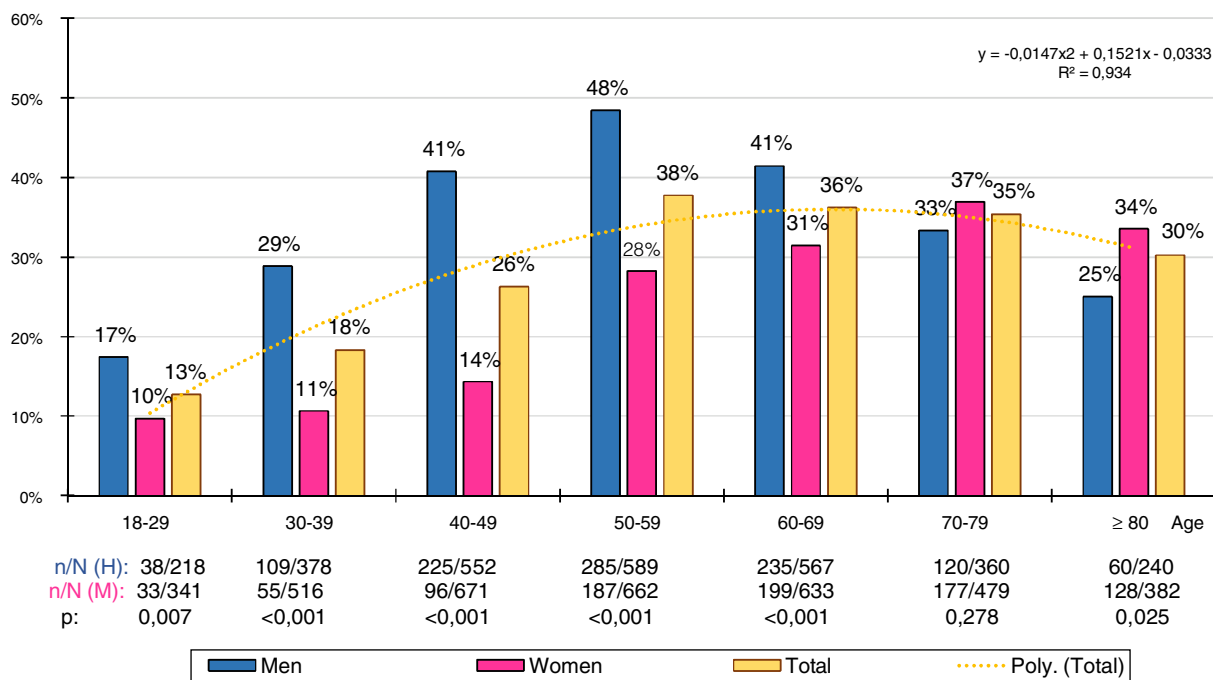
108 mg/dL (women). The GEVA48 group determined an average TG of 117 mg/dL in the population of Albacete, and a prevalence of HTG of 19.3%. The DINO[49] project determined an average TG of 109 mg/dL in the population of Murcia. The HERMEX[50] study determined a geometric mean TG of 96 mg/dL in the Badajoz population>25 years. In the Navarra population>35 years,[51] the mean TG were 132 mg/dL (men) and 98 mg/dL (women), and the prevalence of HTG was 22.6% and 9.1%, respectively. In the population between 35 and 74 years old in Gerona, REGICOR[52] researchers determined a prevalence of HTG>200 mg/dL of 13.6% (men) and 4.6% (women). In the population of the Community of Madrid between 30 and 74 years, the PREDIMERC[53] study showed a prevalence of HTG of 8.8%, and the MADRIC[54] study showed a prevalence of HTG of 21.0% in the population aged between 30 and 70 years. The ENRICA[55] study determined a prevalence of HTG of 17.4% and an average TG of 108 mg/dL in the Spanish population, excluding patients with TG>400 mg/dL. The di@bet.es[56] study showed a prevalence of HTG of 21.5% (men: 29.5%; women: 15.5%). The DARIOS[57] study analysed 11 studies carried out in Spain with populations between 35 and 74 years old, showing a mean TG of 142 mg/dL (men) and 108 mg/dL (women), similar to those of the present study (136 and 109 mg/dL, respectively).

The socioeconomic or cultural differences, the different concept of HTG or the exclusion of populations <35 or >70 years, or with TG >400 mg/dL, can justify the variability of the results shown. The differences diminish when the study is extended to the entire adult population, prevalence rates are adjusted, or other measures of centralisation are offered as medians or geometric means. The prevalence of HTG is strongly influenced by age and sex. In the present study, one-fifth of the female population is affected by HTG, and more than one-third of the male population. The prevalence of HTG increases with age until the 50 s and then declines. There are significant differences in favour of the male popu-
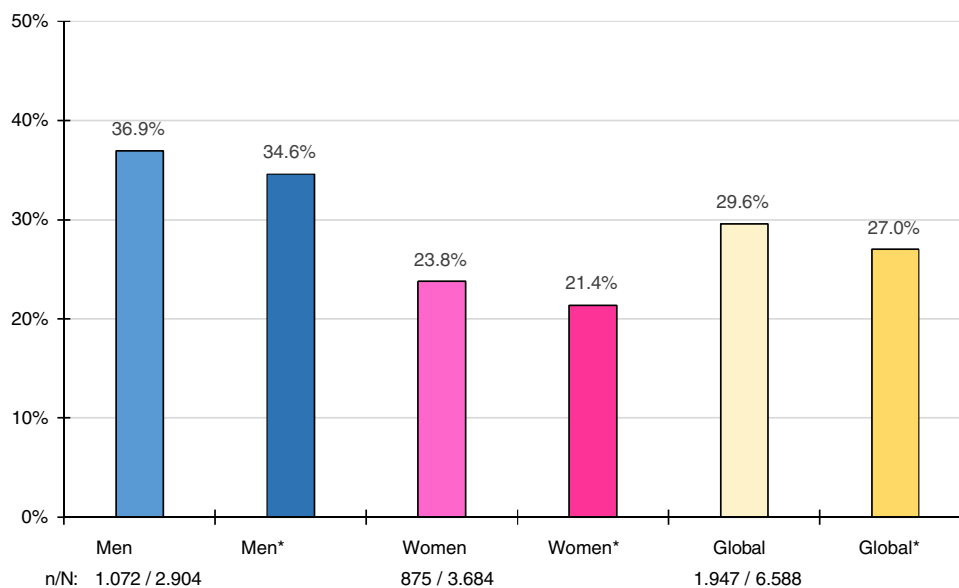
Figure 1 Gross and adjusted (asterisk) prevalence by age and sex of adult hypertriglyceridaemia in the Spanish population of 2015. n: number of cases; N: sample size.
Source: National Institute of Statistics.[24]

$$y = -0{,}0147x2 + 0{,}1521x - 0{,}0333$$
$$R^2 = 0{,}934$$

	18-29	30-39	40-49	50-59	60-69	70-79	≥ 80	Age
n/N (H):	38/218	109/378	225/552	285/589	235/567	120/360	60/240	
n/N (M):	33/341	55/516	96/671	187/662	199/633	177/479	128/382	
p:	0,007	<0,001	<0,001	<0,001	<0,001	0,278	0,025	

Figure 2 Prevalence of hypertriglyceridaemia according to age and sex.
M: men; W: women; n: number of cases; N: sample size.

lation in all age groups until the 70 s, when it becomes equal, and higher in the female population thereafter. HTG prevalence is also significant in the populations<30 years (13%) and>80 years (30%), and therefore it would be advisable to include them in HTG prevalence studies.

The prevalence rates of severe and very severe HTG shown in the present study (Table 2) were similar to those published in other papers.[16–19]

The Castelli-I index[34] (TC/HDL-C) has been considered a more sensitive and specific index of risk of coronary disease than TC in individuals with HTG. It has been associated with greater risk[60] when it is ≥4. In the population with HTG, the TC/HDL-C index was 4.5, which shows that the risk was high. The atherogenic coefficient (non-HDL-C /HDL-C) reflects the atherogenic potential of ApoB[12]-containing lipoproteins. This coefficient was significantly higher in the population with HTG, which points to a higher atherogenic load. According to Dobiasova,[35] plasma atherogenic index values between −.3 and .11 are associated with low risk of atherosclerosis; between .1 and .21, with moderate risk; and >.21, with high risk.[61] The plasma atherogenic index of the population with HTG was .23, which also shows that the risk was high. The TyG insulin resistance index[36] was significantly higher in the population with HTG, as they had higher concentrations of glucose and TG (Table 2).

Lipid metabolism could explain why hypercholesterolaemia and low HDL-C are strongly associated with HTG. MS was the comorbidity with the highest association with HTG, as HTG and low HDL-C were included in its definition. Liver steatosis, DM, pre-diabetes and alcoholism were also significantly associated with HTG, both in the univariate and the multivariate analysis (Tables 4 and 5), probably because liver fat content and plasma glucose correlate with the produc-

tion of very low density lipoproteins, TG and ApoB.[62] The increased association with hepatic steatosis could explain the significantly higher concentrations of transaminases in the HTG population (Table 2).

Hypercholesterolaemia, high blood pressure and DM were associated with the HTG population, which may explain anti-diabetic, hypolipidaemic and antihypertensive therapies being associated more in the HTG population. Increased waist-height index, abdominal obesity, overweight, obesity and adiposity (as measured by the body fat index CUN-BAE-obesity[25,26]) were significantly associated with HTG, although only obesity and overweight were independent factors associated with HTG (Tables 4 and 5).

The variables involving renal function (reduced eGFR, albuminuria) were significantly associated with HTG, although they were not significant in the multivariate analysis (Tables 4 and 5).

The Hypertriglyceridaemia Registry of the Spanish Society of Arteriosclerosis[63] included 1182 patients selected in the Lipid Units of this society, with HTG ≥200 mg/dL. The means of TG in the Register of the Spanish Society of Arteriosclerosis[63] were higher than those of the present study, although the prevalence of comorbidities associated with HTG (high blood pressure, DM, MS, coronary disease) was quite similar in both studies.

Of the HTG population in the SIMETAP-HTG study, 66% had high or very high/extreme CVR. The greater association with HTG of high blood pressure, smoking, DM, obesity, MS, hypercholesterolaemia and ASCVD could explain their close association with high CVR (OR: 2.3) and very high/extreme CVR (OR: 2.0).

The main limitations of the present study were the inability of a cross-sectional study to determine causality and

Table 4 Associated comorbidity in the populations with and without hypertriglyceridaemia.

	With HTG[a], n (%)	Without HTG, n (%)	p[b]	OR (CI)[c]	OR[d]
Smoking[e]	510 (26.2)	916 (19.7)	<.001	1.4 (1.3−1.6)	1.6
COPD	89 (4.6)	157 (1.2)	.020	1.4 (1.0−1.7)	1.2
Alcoholism[f]	277 (14.2)	333 (7.2)	<.001	2.1 (1.8−2.5)	2.4
Physical inactivity[g]	974 (50.0)	2105 (45.4)	.001	1.2 (1.1−1.3)	1.2
Overweight[h]	815 (41.9)	1701 (36.7)	<.001	1.2 (1.1−1.4)	1.2
Obesity[i]	766 (39.3)	1067 (23.0)	<.001	2.2 (1.9−2.4)	2.1
CUN-BAE-overweight[j]	200 (10.3)	873 (18.8)	<.001	.5 (.4−.6)	.6
CUN-BAE-obesity[k]	1.687 (86.7)	3145 (67.8)	<.001	3.1 (2.7−3.6)	2.2
Central obesity[l]	1.110 (57.0)	1812 (39.0)	<.001	2.1 (1.9−2.3)	1.8
Increased WHR[m]	949 (48.7)	1412 (30.4)	<.001	2.2 (2.0−2.4)	1.8
Prediabetes ADA[n]	553 (28.4)	896 (19.3)	<.001	1.7 (1.5−1.9)	1.6
Prediabetes CDA[o]	226 (11.6)	297 (6.4)	<.001	1.9 (1.6−2.3)	1.8
Diabetes	522 (26.8)	513 (11.1)	<.001	2.9 (2.6−3.4)	2.2
High blood pressure	1.008 (51.8)	1539 (33.2)	<.001	2.2 (1.9−2.4)	1.5
Hypercholesterolaemia[p]	1.636 (84.0)	2465 (53.1)	<.001	4.6 (4.1−5.3)	3.9
Low HDL-C[q]	941 (48.3)	878 (18.9)	<.001	4.0 (3.6−4.5)	3.9
Hypothyroidism	212 (10.9)	443 (9.6)	.096	1.2 (.0−1.4)	1.0
Hepatic steatosis	352 (18.1)	228 (4.9)	<.001	4.3 (3.6−5.1)	4.1
Metabolic syndrome	1.490 (76.5)	1361 (29.3)	<.001	7.9 (7.0−8.9)	5.2
Heart disease	136 (7.0)	185 (4.0)	<.001	1.8 (1.4−2.3)	1.6
Stroke	99 (5.1)	151 (3.3)	.001	1.6 (1.2−2.1)	1.4
PAD	68 (3.5)	82 (1.8)	<.001	2.0 (1.4−2.8)	1.7
ASCVD	250 (12.8)	365 (7.9)	.001	1.7 (1.4−2.0)	1.7
Heart failure	71 (3.7)	113 (2.4)	.006	1.5 (1.1−2.1)	1.3
Atrial fibrillation	95 (4.9)	155 (3.3)	.003	1.5 (1.1−1.9)	1.3
Erectile dysfunction	202 (18.8)	302 (16.5)	.105	1.6 (1.4−2.0)	1.3
Albuminuria[r]	164 (11.3)	211 (4.7)	<.001	2.6 (2.1−3.2)	1.7
Low eGFR[s]	214 (11.0)	310 (6.7)	<.001	3.3 (2.7−4.0)	1.5
Chronic kidney disease	286 (27.6)	470 (8.4)	<.001	1.5 (1.3−1.8)	1.6
Hypoglycaemic treatment	442 (22.7)	211 (7.0)	<.001	6.2 (5.2−7.3)	2.4
Anti-hypertensive treatment	933 (47.9)	1406 (30.3)	<.001	2.4 (2.1−2.7)	1.5
Hypolipidaemic treatment	917 (47.1)	934 (20.1)	<.001	3.5 (3.2−4.0)	2.7
Low CVR	216 (11.1)	1929 (41.6)	<.001	.2 (.2−.2)	.3
Moderate CVR	444 (22.8)	935 (20.2)	.106	1.2 (1.0−1.3)	1.5
High CVR	467 (24.0)	556 (12.0)	<.001	2.3 (2.0−2.7)	2.4
Very high CVR	671 (34.4)	1051 (22.7)	<.001	1.8 (1.6−2.0)	1.4
Extreme CVR[t]	149 (7.7)	170 (3.7)	<.001	2.2 (1.7−2.7)	2.1

ADA: American Diabetes Association; HDL-C: Cholesterol bound to high density lipoproteins; CDA: Canadian Diabetes Association; CUN-BAE: Body fat index (*Clínica Universitaria* of Navarra-*Body Adiposity Estimator*); PAD: Peripheral artery disease; ASCVD: Atherosclerotic cardiovascular disease; COPD: Chronic obstructive pulmonary disease; eGFR: Estimated glomerular filtration rate according to CKD-EPI; HTG: hypertriglyceridaemia; WHR: Waist-height ratio; CVR: Cardiovascular risk.

[a] $\geq$150 mg/dL.
[b] p of the difference between gross prevalence rates.
[c] *Odds ratio* between gross prevalence rates (95% confidence interval).
[d] *Odds ratio* adjusted by age and sex.
[e] Consumption of cigarettes or tobacco of any type over the past month.
[f] Regular alcohol consumption >210 g per week (men) or >140 g per week (women).
[g] Physical activity <150 min/week.
[h] Body mass index 25.0−29.9 kg/m^2.
[i] Body mass index $\geq$30 kg/m^2.
[j] 20%−25% (men); 30%−35% (women).
[k] >25 % (men); >35% (women).
[l] Waist circumference$\geq$102 cm (men); $\geq$88 cm (women).
[m] $\geq$.6.
[n] Fasting plasma glucose 100−125 mg/dL, or HbA$_{1c}$ 5.7%−6.4%.
[o] Fasting plasma glucose 110−125 mg/dL, or HbA$_{1c}$ 6.0%−6.4%.
[p] Total cholesterol $\geq$200 mg/dL.
[q] <40 mg/dL (men); <50 mg/dL (women).
[r] Albumin creatinine ratio > 30 mg/g.
[s] Glomerular filtrate < 60 mL/min/1.73 m^2 according to CKD-EPI.
[t] Atherosclerotic cardiovascular disease with diabetes or chronic kidney disease.

Table 5 Independent factors associated with hypertriglyceridaemia.

	β[a]	Wald[b]	p[c]	OR Exp(β)[d]
Hypercholesterolaemia[e]	1.52 (.08)	399.0	<.001	4.6 (3.9–5.3)
Low HDL-C[f]	1.40 (.07)	429.0	<.001	4.1 (3.6–4.6)
Hepatic steatosis	1.01 (.10)	97.5	<.001	2.8 (2.3–3.4)
Diabetes	.67 (.08)	63.4	<.001	2.0 (1.7–2.3)
Obesity[g]	.64 (.09)	56.5	<.001	1.9 (1.6–2.2)
Alcoholism[h]	.53 (.10)	25.6	<.001	1.7 (1.4–2.1)
Overweight[i]	.49 (.08)	37.1	<.001	1.6 (1.4–1.9)
Prediabetes ADA[j]	.43 (.08)	32.9	<.001	1.5 (1.3–1.8)
Smoking[k]	.38 (.08)	25.1	<.001	1.5 (1.3–1.7)
Intersection	−10.9 (.42)	677.7	<.001	NA

ADA: American Diabetes Association; HDL-C: cholesterol bound to high density lipoproteins; NA: not applicable.

[a] β coefficient (deviation).
[b] Wald statistic Z value.
[c] p-value of Wald test with one degree of freedom.
[d] Odds ratio parameter Exp (β) (95% confidence interval).
[e] Total cholesterol ≥ 200 mg/dL.
[f] <40 mg/dL (men); <50 mg/dL (women).
[g] Body mass index ≥ 30 kg/m^2.
[h] Regular alcohol consumption >210 g per week (men) or >140 g per week (women).
[i] Body mass index 25.0–29.9 kg/m^2.
[j] Fasting plasma glucose 100–125 mg/dL, or HbA$_{1c}$ 5.7%–6.4%.
[k] Consumption of tobacco of any type over past month.

possible under-diagnosis by excluding pregnant women and terminal, institutionalised or cognitively impaired patients as per protocol. The age and sex variables were not used in the multivariate analysis because they were strongly associated with CVRFs, cardiovascular or metabolic diseases, to highlight the independent cardiometabolic variables that could be associated with HTG. Furthermore, the researchers had to collect information on the most recent biochemical parameters determined in the analyses carried out over the last year, so that the cross-sectional observation carried out could have been influenced by the diseases that the participants were suffering from at that time, and by their treatments. When comparing the hypolipidaemic treatment variable, there is a significant difference between the populations with and without HTG, and therefore it is plausible that the prevalence of HTG could be somewhat higher if the population with HTG was not under the influence of hypolipidaemic therapy, a circumstance that cannot be avoided ethically in this observational study.

One of the strengths of the present study was the random selection of the study subjects on a population basis, a large sample that included people aged between 18 and 102 years, while other studies in the same field exclude the population <35 years and >70 years. Also noteworthy are the presentation of TG values with various measures of centralisation, small differences between gross and adjusted prevalence rates of HTG (2.3% in the male population and 2.4% in the female population), and the evaluation of the possible association between HTG and numerous CVRFs, CKD, metabolic diseases and ASCVD. Given that HTG is influenced by sex and age variables, another strength of this study is the global and sex-based description of HTG prevalence rates in all adult ten-year age groups, and the presentation with age- and sex-adjusted rates to be able to compare with other populations.

The high prevalence of HTG has serious socioeconomic and health consequences by increasing cardiovascular morbidity and mortality. Assessing the prevalence of HGT is especially important to better plan cardiovascular prevention intervention policies, optimizing available health resources and improving the medical care and quality of life of patients with HGT. Given the progression in the prevalence of obesity, DM and, simultaneously, HTG in recent years, the need for further epidemiological studies aimed at the entire population is clear, and in this regard, we hope this study will contribute towards improving epidemiological knowledge of HTG and assessing the importance of the association between HTG and ASCVD.

Conclusions

Studies on testing for mean TG concentrations and prevalence rates of HTG in the adult population show highly variable results. The SIMETAP-HTG study confirms intermediate results with respect to previous studies. The mean TG concentrations in the adult population in this study were lower than those in Mexico, China, and India, and similar to those in the United States, Korea, Germany, and France. The adjusted prevalence rates of TG were lower than those obtained in the Balearic Islands and the Canary Islands, and slightly higher than those of other studies conducted in Spain.

The present study also reinforces the idea that the prevalence of HTG in the adult population is highly influenced by the variables of sex and age, and therefore it is necessary to adjust the results by these variables. It shows that one-fifth of the adult female population and more than one-third of the adult male population had HTG, and that prevalence increases through life up to the fifth decade. The prevalence

of HTG is higher in the male population up to the 6th decade, is equal in the 7th, and is higher in the female population thereafter.

The SIMETAP-HTG study shows that the cardiometabolic factors related to HTG were DM, pre-diabetes, hepatic steatosis, overweight and obesity. It also shows that the elevation of atherogenic indices in the lipid profile demonstrates that HTG is associated with higher atherogenic potential and higher risk of ASCVD. The present study highlights that the lipid parameters most strongly associated with HTG were hypercholesterolaemia and low HDL-C concentration.

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Conflict of interests

The authors have no conflict of interests to declare.

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References

1. Carroll MD, Kit BK, Lacher DA, Shero ST, Mussolino ME. Trends in lipids and lipoproteins in US adults, 1988–2010. JAMA. 2012;308:1545–54, http://dx.doi.org/10.1001/jama.2012.13260.

2. Sarwar N, Butterworth AS, Di Angelantonio E, Ouwehand W, Watkins H, Lawlor D, et al. Triglyceride Coronary Disease Genetics Consortium, Emerging Risk Factors Collaboration. Triglyceride-mediated pathways and coronary disease: collaborative analysis of 101 studies. Lancet. 2010;375:1634–9, http://dx.doi.org/10.1016/S0140-6736(10)60545-4.

3. Hegele RA, Ginsberg HN, Chapman MJ, Nordestgaard BG, Kuivenhoven JA, Averna M, et al. European Atherosclerosis Society Consensus Panel. The polygenic nature of hypertriglyceridaemia: implications for definition, diagnosis, and management. Lancet Diabetes Endocrinol. 2014;2:655–66, http://dx.doi.org/10.1016/S2213-8587(13)70191-8.

4. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. ESC Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2019;00:1–78, http://dx.doi.org/10.1093/eurheartj/ehz455.

5. Instituto Nacional de Estadística. INEbase. Sociedad. Salud. Estadística de defunciones según la causa de muerte. [Accessed 23 March 2020]. Available from: https://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736176780&menu=ultiDatos&idp=1254735573175.

6. Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, Wareham N, Bingham S, et al. Triglycerides and the risk of coronary heart disease: 10,158 incident cases among 262,525 participants in 29 Western prospective studies. Circulation. 2007;115:450–8, http://dx.doi.org/10.1161/CIRCULATIONAHA.106.637793.

7. Patel A, Barzi F, Jamrozik K, Lam TH, Ueshima H, Whitlock G, et al. Asia Pacific Cohort Studies Collaboration. Serum triglycerides as a risk factor for cardiovascular diseases in the Asia-Pacific region. Circulation. 2004;110:2678–86, http://dx.doi.org/10.1161/01.CIR.0000145615.33955.83.

8. Kannel WB, Vasan RS. Triglycerides as vascular risk factors: new epidemiologic insights. Curr Opin Cardiol. 2009;24:345–50, http://dx.doi.org/10.1097/HCO.0b013e32832c1284.

9. Asztalos BF, Collins D, Horvath KV, Bloomfield HE, Robins SJ, Schaefer EJ. Relation of gemfibrozil treatment and high-density lipoprotein subpopulation profile with cardiovascular events in the Veterans Affairs High-Density Lipoprotein Intervention Trial. Metabolism. 2008;57:77–83, http://dx.doi.org/10.1016/j.metabol.2007.08.009.

10. Laufs U, Parhofer KG, Ginsberg HN, Hegele RA. Clinical review on triglycerides. Eur Heart J. 2020;41, http://dx.doi.org/10.1093/eurheartj/ehz785, 99–109c.

11. Ference BA, Ginsberg HN, Graham I, Ray KK, Packard CJ, Bruckert E, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2017;38:2459–72, http://dx.doi.org/10.1093/eurheartj/ehx144.

12. Ridker PM, Rifai N, Cook NR, Bradwin G, Buring JE. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. JAMA. 2005;294:326–33, http://dx.doi.org/10.1001/jama.294.3.326.

13. Emerging Risk Factors Collaboration, Di Angelantonio E, Gao P, Pennells L, Kaptoge S, Caslake M, Thompson A, et al. Lipid-related markers and cardiovascular disease prediction. JAMA. 2012;307:2499–506, http://dx.doi.org/10.1001/jama.2012.6571.

14. Varbo A, Benn M, Tybjaerg-Hansen A, Jorgensen AB, Frikke-Schmidt R, Nordestgaard BG. Remnant cholesterol as a causal risk factor for ischemic heart disease. J Am Coll Cardiol. 2013;61:427–36, http://dx.doi.org/10.1016/j.jacc.2012.08.1026.

15. World Health Organization [Accessed 23 March 2020]. Available from: https://www.who.int/nmh/publications/ncd-status-report-2014/en/, 2014.

16. Retterstol K, Narverud I, Selmer R, Berge KE, Osnes IV, Ulven SM, et al. Severe hypertriglyceridemia in Norway: prevalence, clinical and genetic characteristics. Lipids Health Dis. 2017;16:115, http://dx.doi.org/10.1186/s12944-017-0511-9.

17. Dron JS, Wang J, Cao H, McIntyre AD, Iacocca MA, Menard JR, et al. Severe hypertriglyceridemia is primarily polygenic. J Clin Lipidol. 2019;13:80–8, http://dx.doi.org/10.1016/j.jacl.2018.10.006.

18. Christian JB, Bourgeois N, Snipes R, Lowe KA. Prevalence of severe (500 to 2,000 mg/dl) hypertriglyceridemia in United States adults. Am J Cardiol. 2011;107:891–7, http://dx.doi.org/10.1016/j.amjcard.2010.11.008.

19. Chyzhyk V, Kozmic S, Brown AS, Hudgins LC, Starc TJ, Davila AD, et al. Extreme hypertriglyceridemia: genetic diversity, pancreatitis, pregnancy, and prevalence. J Clin Lipidol. 2019;13:89–99, http://dx.doi.org/10.1016/j.jacl.2018.09.007.

20. Jaross W, Assmann G, Bergmann S, Schulte H. Comparison of risk factors for coronary heart disease in Dresden and Munster. Results of the DRECAN (Dresden Cardiovascular Risk and Nutrition) study and the PROCAM (Prospective Cardiovascular Munster) Study. Eur J Epidemiol. 1994;10:307–15, http://dx.doi.org/10.1007/bf01719355.

21. Truthmann J, Schienkiewitz A, Busch MA, Mensink GB, Du Y, Bosy-Westphal A, et al. Changes in mean serum lipids among adults in Germany: results from National Health Surveys 1997-99 and 2008-11. BMC Public Health. 2016;16:240, http://dx.doi.org/10.1186/s12889-016-2826-2.

22. Ruiz-García A, Arranz-Martínez E, García-Álvarez JC, Morales-Cobos LE, García-Fernández ME, de la Peña-Antón N, et al. Población y metodología del estudio SIMETAP: prevalencia de factores de riesgo cardiovascular, enfermedades cardiovasculares y enfermedades metabólicas relacionadas. Clin Investig Arterioscler. 2018;30:197–208, http://dx.doi.org/10.1016/j.arteri.2018.04.006.

23. Armitage R, Berry G, Matthews JNS [Accessed 23 March 2020]. Available from: Statistical methods in medical research. 4th ed. Blackwell Science; 2002. p. 659–67 https://scholar.google.com/scholar?start=10&hl=es&as_sdt=0,5&cluster=3836887590140374505

24. Instituto Nacional de Estadística. INEbase. Demografía y población. Cifras de población y Censos demográficos. Cifras de población. [Accessed 23 March 2020]. Disponible en: http://www.ine.es/dynt3/inebase/es/index.htm?padre=1894&capsel=1895.

25. Zubiaga Toro L, Ruiz-Tovar Polo J, Díez-Tabernilla M, Giner Bernal L, Arroyo Sebastián A, Calpena Rico R. Fórmula CUN-BAE y factores bioquímicos como marcadores predictivos de obesidad y enfermedad cardiovascular en pacientes pre y post gastrectomía vertical. Nutr Hosp. 2014;30:281–6, http://dx.doi.org/10.3305/nh.2014.30.2.7581.

26. Fuster-Parra P, Bennasar-Veny M, Tauler P, Yañez A, López-González AA, Aguiló A. A comparison between multiple regression models and CUN-BAE equation to predict body fat in adults. PLoS One. 2015;10:e0122291, http://dx.doi.org/10.1371/journal.pone.0122291.

27. Comité Internacional de Clasificación de la WONCA. Clasificación Internacional de la Atención Primaria. 2ª ed Barcelona: Masson; 1999.

28. Ministerio de Sanidad, Servicios Sociales e Igualdad. Clasificación Internacional de Enfermedades: 9ª Revisión. Modificación Clínica. CIE-9-MC. 9ª ed; 2014.

29. KGMM Alberti, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation task force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120:1640–5, http://dx.doi.org/10.1161/CIRCULATIONAHA.109.192644.

30. Salas-Salvadó J, Rubio MA, Barbany M, Moreno B, Grupo colaborativo de la SEEDO. Consenso SEEDO 2007 para la evaluación del sobrepeso y la obesidad y el establecimiento de criterios de intervención terapéutica. Med Clin (Barc). 2007;128:184–96, http://dx.doi.org/10.1016/S0025-7753(07)72531-9.

31. Schneider HJ, Klotsche J, Silber S, Stalla GK, Wittchen HU. Measuring abdominal obesity: Effects of height on distribution of cardiometabolic risk factors risk using waist circumference and waist-to-height ratio. Diabetes Care. 2011;34:e7, http://dx.doi.org/10.2337/dc10-1794.

32. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults. Executive summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001;285:2486–97, http://dx.doi.org/10.1001/jama.285.19.2486.

33. Ascaso JF, Millán J, Hernández-Mijares A, Blasco M, Brea A, Díaz A, et al. Documento de consenso sobre el manejo de la dislipemia aterogénica de la Sociedad Española de Arteriosclerosis. Clin Investig Arterioscler. 2017;29:86–91, http://dx.doi.org/10.1016/j.arteri.2016.11.001.

34. Castelli WP, Abbott RD, McNamara PM. Summary estimates of cholesterol used to predict coronary heart disease. Circulation. 1983;67:730–4, http://dx.doi.org/10.1161/01.cir.67.4.730.

35. Dobiasova M. AIP-atherogenic index of plasma as a significant predictor of cardiovascular risk: From research to practice. Vnitr Lek. 2006;52:64–71 [Accessed 23 March 2020]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16526201

36. Simental-Mendia LE, Rodriguez-Moran M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndr Relat Disord. 2008;6:299–304, http://dx.doi.org/10.1089/met.2008.0034.

37. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco ALM, De Jong PE, et al. Kidney Disease: Improving Global Outcomes (KDIGO) CKD work group. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3:1–150, http://dx.doi.org/10.1038/kisup.2012.73.

38. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice. The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016;37:2315–81, http://dx.doi.org/10.1093/eurheartj/ehw106.

39. Cooney MT, Selmer R, Lindman A, Tverdal A, Menotti A, Thomsen T, et al. Cardiovascular disease risk estimation in older persons: SCORE O.P. Eur J Prev Cardiol. 2016;23:1093–103, http://dx.doi.org/10.1177/2047487315588390.

40. Garber AJ, Abrahamson MJ, Barzilay JI, Blonde L, Bloomgarden ZT, Bush MA, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm — 2019 Executive summary. Endocr Pract. 2019;25:69–100, http://dx.doi.org/10.4158/CS-2018-0535.

41. Ghandehari H, Kamal-Bahl S, Wong ND. Prevalence and extent of dyslipidemia and recommended lipid levels in US adults with and without cardiovascular comorbidities: The National Health and Nutrition Examination Survey 2003–2004. Am Heart J. 2008;156:112–9, http://dx.doi.org/10.1016/j.ahj.2008.03.005.

42. Ferrières J, Bongard V, Dallongeville J, Arveiler D, Cottel D, Haas B, et al. Trends in plasma lipids, lipoproteins and dyslipidaemias in French adults, 1996–2007. Arch Cardiovasc Dis. 2009;102:293–301, http://dx.doi.org/10.1016/j.acvd.2009.02.002.

43. Lee MH, Kim HC, Ahn SV, Hur NW, Choi DP, Park CG, et al. Prevalence of dyslipidemia among Korean adults: Korea National Health and Nutrition Survey 1998-2005. Diabetes Metab J. 2012;36:43–55, http://dx.doi.org/10.4093/dmj.2012.36.1.43.

44. Roh E, Ko SH, Kwon HS, Kim NH, Kim JH, Kim C, et al. Prevalence and management of dyslipidemia in Korea: Korea National Health and Nutrition Examination Survey during 1998 to 2010. Diabetes Metab J. 2013;37:433–49, http://dx.doi.org/10.4093/dmj.2013.37.6.433.

45. Aguilar-Salinas CA, Gómez-Pérez FJ, Rull J, Villalpando S, Barquera S, Rojas R. Prevalence of dyslipidemias in the Mexican National Health and Nutrition Survey 2006. Salud Publica Mex. 2010;52:S44–53, http://dx.doi.org/10.1590/s0036-36342010000700008.

46. Yang W, Xiao J, Yang Z, Ji L, Jia W, Weng J, et al. China National Diabetes and Metabolic Disorders Study Investigators. Serum lipids and lipoproteins in Chinese men and women. Circulation. 2012;125:2212–21, http://dx.doi.org/10.1161/CIRCULATIONAHA.111.065904.

47. Guptha S, Gupta R, Deedwania P, Bhansali A, Maheshwari A, Gupta A, et al. Cholesterol lipoproteins and prevalence of dyslipidemias in urban Asian Indians: a cross sectional study. Indian Heart J. 2014;66:280–8, http://dx.doi.org/10.1016/j.ihj.2014.03.005.

48. Divisón Garrote JA, Massó Orozco J, Carrión Valero L, López Abril J, Carbayo Herencia JA, Artigao Rodenas LM, et al. Evolución de la prevalencia de los factores de riesgo y del riesgo cardiovascular global en población mayor de 18 años de la provincia de Albacete (1992-94 a 2004-06). Rev Esp Salud Pública. 2011;85:275–84 [Accessed 23 March 2020]. Available from: https://www.redalyc.org/articulo.oa?id=17020115006

49. Valverde JC, Tormo MJ, Navarro C, Rodríguez-Barranco M, Marco R, Egea JM, et al. Prevalence of diabetes in Murcia (Spain): a Mediterranean area characterised by obesity. Diabetes Res Clin Pract. 2006;71:202–9, http://dx.doi.org/10.1016/j.diabres.2005.06.009.

50. Félix-Redondo FJ, Fernández-Bergés D, Fernando Pérez J, Zaro MJ, García A, Lozano L, et al. Prevalencia, detección, tratamiento y grado de control de los factores de riesgo cardiovascular en la población de Extremadura (España). Estudio HERMEX. Aten Primaria. 2011;43:426–34, http://dx.doi.org/10.1016/j.aprim.2010.07.008.

51. Viñes JJ, Díez J, Guembe MJ, González P, Amézqueta C, Barba J, et al. Estudio de riesgo vascular en Navarra: objetivos y diseño. Prevalencia del síndrome metabólico y de los factores mayores de riesgo vascular. An Sist Sanit Navar. 2007;30:113–24 [Accessed 23 March 2020]. Available from: https://recyt.fecyt.es/index.php/ASSN/article/view/2118

52. Grau M, Subirana I, Elosua R, Solanas P, Ramos R, Masiá R, et al. REGICOR Investigators. Trends in cardiovascular risk factor prevalence (1995-2000-2005) in northeastern Spain. Eur J Cardiovasc Prev Rehabil. 2007;14:653–9, http://dx.doi.org/10.1097/HJR.0b013e3281764429.

53. Gil-Montalbán E, Zorrilla-Torras B, Ortiz-Marrón H, Martínez-Cortés M, Donoso-Navarro E, Nogales-Aguado P, et al. Prevalencia de diabetes mellitus y factores de riesgo cardiovascular en la población adulta de la Comunidad de Madrid: estudio PREDIMERC. Gac Sanit. 2010;24:233–40, http://dx.doi.org/10.1016/j.gaceta.2010.01.010.

54. Rosado-Martín J, Martínez-López MA, Mantilla-Morató T, Dujovne-Kohan I, Palau-Cuevas FJ, Torres-Jiménez R, et al. Prevalencia de diabetes en una población adulta de Madrid (España). Estudio MADRIC (MADrid RIesgo Cardiovascular). Gac Sanit. 2012;26:243–50, http://dx.doi.org/10.1016/j.gaceta.2011.09.013.

55. Guallar-Castillón P, Gil-Montero M, León-Muñoz LM, Graciani A, Bayán-Bravo A, Taboada JM, et al. Magnitud y manejo de la hipercolesterolemia en la población adulta de España, 2008-2010: el estudio ENRICA. Rev Esp Cardiol. 2012;65:551–8, http://dx.doi.org/10.1016/j.recesp.2012.02.005.

56. Martínez-Hervás S, Carmena R, Ascaso JF, Real JT, Masana L, Catalá M, et al. Prevalence of plasma lipid abnormalities and its association with glucose metabolism in Spain: The di@bet.es study. Clin Invest Arterioscl. 2014;26:107–14, http://dx.doi.org/10.1016/j.arteri.2013.12.001.

57. Grau M, Elosua R, Cabrera de León A, Guembe MJ, Baena-Díez JM, Vega Alonso T, et al. Factores de riesgo cardiovascular en España en la primera década del siglo XXI: análisis agrupado con datos individuales de 11 estudios de base poblacional, estudio DARIOS. Rev Esp Cardiol. 2011;64:295–304, http://dx.doi.org/10.1016/j.recesp.2010.11.005.

58. Rigo Carratalá F, Frontera Juan G, Llobera Cànaves J, Rodríguez Ruiz T, Borrás Bosch I, Fuentespina Vidal E. Prevalencia de factores de riesgo cardiovascular en las Islas Baleares (estudio CORSAIB). Rev Esp Cardiol. 2005;58:1411–9, http://dx.doi.org/10.1016/S0300-8932(05)74071-9.

59. Cabrera de León A, Rodríguez Pérez MC, Almeida González D, Domínguez Coello S, Aguirre Jaime A, Brito Díaz B, et al. Presentación de la cohorte ''CDC de Canarias'': objetivos, diseño y resultados preliminares. Rev Esp Salud Pública. 2008;82:519–34 [Accessed 23 March 2020]. Available from: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1135-57272008000500007&lng=es

60. Millán J, Pintó X, Muñoz A, Zúñiga M, Rubiés-Prat J, Pallardo LF, et al. Foro HDL. Cocientes lipoproteicos: significado fisiológico y utilidad clínica de los índices aterogénicos en prevención cardiovascular. Clin Invest Arterioscl. 2010;22:25–32, http://dx.doi.org/10.1016/S0214-9168(10)70005-X.

61. Rašlová K, Dobiášová M, Hubáček JA, Bencová D, Siváková D, Danková Z, et al. Association of metabolic and genetic factors with cholesterol esterification rate in HDL plasma and atherogenic index of plasma in a 40 years old slovak population. Physiol

Res. 2011;60:785–95 [Accessed 31 March 2020]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21812522

62. Adiels M, Taskinen MR, Packard C, Caslake MJ, Soro-Paavonen A, Westerbacka J, et al. Overproduction of large VLDL particles is driven by increased liver fat content in man. Diabetologia. 2006;49:755–65, http://dx.doi.org/10.1007/s00125-005-0125-z.

63. Ascaso JF, Millán J, Mateo-Gallego R, Ruiz-García A, Suárez-Tembra M, Borrallo RM, et al. Hypertriglyceridemia Registry of the Spanish Arteriosclerosis Society. Prevalence of metabolic syndrome and cardiovascular disease in a hypertriglyceridemic population. Eur J Intern Med. 2011;22:177–81, http://dx.doi.org/10.1016/j.ejim.2010.12.011.