Severe Hypertriglyceridemia in Argentina: Prevalence and Clinical Characteristics

Hipertrigliceridemia grave en Argentina: prevalencia y características clínicas

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ABSTRACT

Background: Severe hypertriglyceridemia (SHTG) is a metabolic disorder with multiple origins and management implications. Prevalence, clinical characteristics, and its possible causes are unknown in Argentina.
Objective: The aim of this study was to estimate the prevalence and describe the clinical characteristics and underlying SHTG causes in a third level hospital in the municipality of General Pueyrredón.
Methods: An observational, descriptive study was performed using an electronic database from a provincial Hospital. It included adult patients with triglyceride (TG) levels above 885 mg/dL (10 mmol/L) evaluated from January 2018 to December 2021. Medical records were collected, and patients were then contacted to obtain anthropometric measurements, sociodemographic variables, personal and family history, secondary causes of hypertriglyceridemia, and treatment received.
Results: Among 16 029 patients analyzed, 46 presented SHTG, representing a total prevalence of 0.28% (95% CI 0.20-0.40%). Finally, 19 participants with mean age 48.47±16 years and 84.2% men were included in the analysis. Median TG level was 1821 mg/dL (interquartile range 917-7000 mg/dL), and 17 participants (84.97%) had hypercholesterolemia (total cholesterol >200 mg/dL). Almost 50% reported alcohol consumption, 55% were obese and 68% had type II diabetes. Nine participants were under pharmacological treatment, 4 with fibrates and 5 with statins.
Conclusion: A prevalence of 0.28% SHTG was found, higher than that reported in other series. Another finding was the underuse of medication for this severe dyslipidemia.

Keywords: Hypertriglyceridemia - Triglycerides - Prevalence - Argentina

RESUMEN

Introducción: La hipertrigliceridemia grave (HTGG) es un desorden metabólico con múltiples causas e implicancias terapéuticas. Se desconocen hasta la fecha las características clínicas, la prevalencia y sus posibles causas en nuestra población.
Objetivo: Estimar la prevalencia, describir las características clínicas y causas subyacentes de la HTGG en un hospital de tercer nivel del municipio de General Pueyrredón.
Materia Y métodos: Estudio descriptivo y observacional realizado con pacientes ambulatorios e internados de un hospital provincial. Se incluyeron pacientes adultos con triglicéridos (TG) mayores que 885 mg/dL (10 mmol/L) evaluados desde enero de 2018 a diciembre de 2021. Se extrajeron sus historias clínicas y, luego, se los contactó para obtener medidas antropométricas, variables sociodemográficas, antecedentes personales y familiares, causas secundarias de hipertrigliceridemia y el tratamiento recibido.
Resultados: Se analizaron 16 029 muestras; 46 presentaron HTGG, lo que representa una prevalencia total del 0,28 % (IC 95% 0,20-0,40%); se incluyeron 19 participantes en el análisis. La edad media fue de 48,47 años (DE ±16); el 84,2 % de ellos eran hombres. La mediana de triglicéridos fue 1821 mg/dL (rango intercuartílico 917-7000 mg/dL); 17 participantes (84,97 %) presentaban hipercolesterolemia (colesterol total mayor que 200 mg/dL). Casi el 50 % refirió consumo de alcohol, el 55 % presentaba obesidad y el 68 % diabetes tipo II. Solo 9 participantes se encontraban en tratamiento, 4 con fibratos y 5 con estatinas.
Conclusión: Se encontró una prevalencia del 0,28 %, más alta que la esperada y reportada en series previas. Por otro lado, se destaca la subutilización de medicación para el tratamiento de esta dislipidemia grave.

Palabras claves: Hipertrigliceridemia - Triglicéridos - Prevalencia - Argentina

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INTRODUCTION

Hypertriglyceridemia (HTG) is defined as an elevation of triglycerides (TG) that exceeds 150 mg/dL (1.7 mmol/L). Several population surveys show that it is the most prevalent lipid disorder and the NHANES survey revealed that 24.7% present this disorder in the general population. (1,2) When classifying the severity of HTG, we define it as mild-moderate (up to 500-885 mg/dL) and severe HTG (SHTG), when it exceeds these cut-off points. (3) SHTG can be secondary to other pathologies, such as diabetes, alcohol abuse and hypothyroidism; to physiological situations, such as pregnancy; or secondary to drugs, such as contraceptives and protease inhibitors, as the most frequent ones. (4) Similarly, in a smaller percentage, SHTG is due to monogenic genetic disorders, such as familial chylomicronemia syndrome or lipodystrophies, or polygenic disorders, such as multifactorial chylomicronemia syndrome. (5) Once diagnosed, the treatment goal is to reduce the risk of pancreatitis, a complication directly associated with the TG level, which in SHTG has an incidence of 20%. (6)

The prevalence of SHTG in Argentina, as well as its potential causes, is currently unknown. The objective of this study was to estimate the prevalence of SHTG in a hospital population (outpatient and inpatient), as well as the characterization and discrimination of the potential causes of this condition.

METHODS

A descriptive, observational study was carried out using an electronic database (Plexus) of patients treated at HIGA Dr. Oscar E. Alende hospital in Mar del Plata. Medical records were included from January 2018 to December 2021 and the data was collected during the month of July 2022 by the research team of the EPAHiTS Project (Argentine Prevalence Study of Severe Hypertriglyceridemia). The inclusion criteria to participate in this study was to have a TG level ≥885 mg/dL and age ≥18 years.

Data collection

The clinical history of each of patient with inclusion criteria was reviewed. A trained physician reviewed the clinical history, previous hospitalizations, and the presence of a history of acute pancreatitis. Subsequently, all the patients were contacted by telephone and an appointment was made at the hospital to collect sociodemographic and anthropometric data (weight and height), and establish the medical history (diabetes, alcohol consumption, presence of hypothyroidism and renal failure). They were asked about personal and family history related with HTG: presence of recurrent abdominal pain, acalculous pancreatitis, family history of dyslipidemia, and treatment received. Secondary causes were also questioned: poorly controlled diabetes, hypothyroidism, renal failure, and pregnancy. Patients were examined to verify the presence of eruptive xanthomas. Finally, the last blood test obtained in the clinical history was considered for laboratory values: glycosylated hemoglobin (HbA1c), total cholesterol, LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), ultrasensitive thyrotropin, and apolipoprotein B (ApoB).

Anthropometric measurements were obtained using standard techniques and protocols. Weight was measured in light clothing, without shoes, and in kilograms to one decimal place using a foot scale. Height was measured in centimeters, without shoes and with only one decimal place. With these data, the body mass index (BMI) was calculated dividing body weight in kilograms by the square of height in meters (BMI = weight [kg]/height² [m²]). For alcohol consumption, a structured questionnaire based on the Hispanic Community Health Study was used adapted for its use in Argentina, (7) in which the type of alcoholic beverage (wine, beer, or both) and number of drinks per week were differentiated.

Definition of variables

Obesity was defined as the presence of a BMI ≥30 kg/m². Alcohol consumption was classified according to intensity as: no consumption, moderate consumption (up to 7 drinks in women and 14 in men), severe consumption (8 or more in women or 15 or more in men) and compulsive consumption. (4 to 5 drinks in 2 hours). Hypercholesterolemia was defined as LDL-C ≥200 mg/dL or use of statins. The presence of diabetes was identified by self-report or previous laboratory tests with fasting blood glucose ≥126 mg/dL, or use of insulin or oral antidiabetic agents. Poorly controlled diabetes was described as the presence of HbA1c >12%.

Statistical analysis

The frequency and distribution of the variables was analyzed at a global level. Categorical data are presented as percentages, and for continuous data, the mean was used for central tendency and standard deviation (SD) for dispersion in the case of normal distribution. For non-normal distribution of continuous data, median for central tendency and interquartile range for dispersion were used as summary measures.
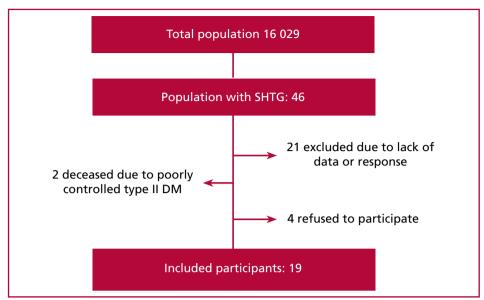
RESULTS

Study participants

The total number of participants analyzed was 16 029. Among them, 46 patients presented SHTG, representing a total prevalence of 0.28% (95% CI 0.20-0.40%). Finally, 19 patients were contacted and included in the analysis. (Figure 1) Of the 46 initial patients and the 19 finally analyzed, 10 and 3, respectively, were hospitalized at the time of data collection. Of the patients not contacted, 2 died. One was a female patient with human immunodeficiency virus (HIV) under treatment with protease inhibitors, and uncontrolled diabetes (HbA1c 14.7%) and the cause of death was sepsis due to skin and soft tissue injuries. The second case of death corresponded to a 42-year-old patient with poorly controlled diabetes (HbA1c 12.9%), chronic renal failure secondary to diabetes and SHTG (>3000 mg/dL) in different determinations, who died of diabetic ketoacidosis. Four patients refused to provide data; in 12, the telephone number did not correspond to what was registered in the system and the remaining 9 did not present contact information in the system.

Baseline characteristics of the 19 participants are presented in Table 1. Mean age was 48.47±16 years, and 84.2% were men. Median TG level was 1821 mg/dL (interquartile range 917-7000 mg/dL) and 17 participants (84.97%) had hypercholesterolemia (total

Fig. 1. Flowchart of the patients included in the study.

DM: diabetes mellitus. SHTG: severe hypertriglyceridemia

Table 1. Baseline characteristics of the population with hypertriglyceridemia

Categorical variables, n (%)	
Men	16 (84.21)
Diabetes	13 (68.42)
Alcohol consumption	9 (47.37)
History of familial hypercholesterolemia	9 (47.37)
History of hypertriglyceridemia	8 (42.1)
Recurrent abdominal pain	6 (31.58)
Abdominal pain in childhood	1 (5.26)
Acalculous pancreatitis	1 (5.26)
Xanthomas	0
Fibrates	4 (21)
Statins	5 (26)
Quantitative variables	
Age, years (mean ±SD)	48.47±16
BMI kg/m² (median, IQR)	31 (21-45)
Glycosylated hemoglobin (mean±SD)	9.3 ±2.8
Total cholesterol, mg/dL (median, IQR)	282 (166-721)
HDL cholesterol, mg/dL (mean±SD)	31 ±5.8
Triglycerides, mg/dL (median, IQR)	1821 (917-7000)

BMI: body mass index; IQR: Interquartile Range; SD: Standard Deviation

cholesterol >200 mg/dL). Almost 50% reported alcohol consumption; however, all drinking patterns were classified as moderate (up to 7 drinks per week for women and up to 14 for men); 55% presented obesity and 68% type II diabetes. Only 6 participants (31%) reported the presence of recurrent and chronic abdominal pain, and 1 case of pancreatitis was recorded. Nine participants were on pharmacological treatment, 4 with fibrates and 5 with statins.

DISCUSSION

This study shows that the prevalence of SHTG in a tertiary level hospital in Argentina is 0.28% (95% CI 0.20-0.40%). This value is at the upper end of the range reported by different series of studies worldwide. The prevalence described, though low, presents a great discrepancy and variability according to the region studied. For example, in Japan, Tada et al. described a prevalence of 0.3% SHTG; in Israel, Zafrir et al., 0.09%; in Norway, Retterstøl et al., 0.13% and in Russia, Karpov reported only 0.037%. (8-11)

In the detailed analysis of our sample, we observed that median BMI was 31, which suggests an associated underlying metabolic disorder, independently of other comorbidities, and a probable cause of SHTG. This was reflected in 52% (10/19) of the patients. On the other hand, 3 patients had HbA1c >10%, without obesity. These data are even higher than those reported in the work of Masson et al., whose population with SHTG presented obesity in 38.6% and diabetes only in 28.1% of cases. (12) Regarding the use of drugs with an established association with SHTG, 2 patients used protease inhibitors to control their HIV. (3) Thus, we can confirm that 79% (15/19) of the screened patients had a secondary condition as the potential cause of their SHTG. Two of the four remaining patients presented a transient elevation of TG, a situation that may be the consequence of not respecting fasting prior to blood withdrawal, alcohol intake or physical exercise; (3) one of the patients was undergoing tuberculostatic treatment in maintenance phase with rifampin and isoniazid, a drug that, according to animal studies, could be related to SHTG. (13) Finally, the remaining participant met the criteria for familial combined hyperlipidemia, (14) since he presented

elevated total cholesterol and TG in successive blood tests with a first-degree relative relationship with a similar lipid profile. Regarding the results observed in terms of underutilization of pharmacological treatment, this finding is coincident with that reported by the group of Masson et al., which states that only 21% of patients received treatment for their lipidic disorder (statins or fibrates). (12)

As limitations to our work, we can mention that the study period (2018-2021) was notably influenced by the COVID-19 pandemic, which reduced the number of consultations and blood extractions. A second limitation is that since the Argentine health system is fragmented and segmented, a tertiary public hospital dependent on the province of Buenos Aires does not cover the complete universe of patients that are treated in this system; there is also a public municipal health system which is not interconnected with the former, with the consequent lack of information flow between one system and the other. The third limitation is linked to what was stated above: being a third-level hospital, outpatients are mostly referrals from primary care centers, or they are patients with multiple comorbidities who require multidisciplinary care, which cannot be achieved at the first level. Moreover, in our universe of study there were hospitalized patients, who per se presented an intrinsic complexity.

The systematization and continuous process of detecting patients with SHTG based on values obtained from the laboratory, constitutes a simple and accessible strategy, which allows real-time research of patients affected by this dyslipidemia.

In conclusion, a prevalence of 0.28% was found, which was within the upper range of what was expected according to previous reports. Our value at the higher end of the range may probably be due to the fact that our study included outpatients and inpatients at a tertiary hospital. On the other hand, the underuse of medication for the treatment of this severe dyslipidemia with a high risk of pancreatitis stands out, despite the fact that more than half of the patients had cardiovascular risk factors.

Conflicts of interest
None declared.

(See authors' conflict of interests forms on the web/Additional material.)

Ethical considerations
Not applicable.

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