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Original Article

Twenty-first century epidemiology of dyslipidemia in Greece: EMENO national epidemiological study

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ABSTRACT

Background: Greece was recently reclassified from low- to medium-risk country in terms of cardiovascular disease, with 27% of cardiovascular deaths attributed to hypercholesterolemia. EMENO nationwide survey (2013-2016) assessed the epidemiology of dyslipidemia in the general population in Greece.
Methods: A random sample of adults was drawn by multistage stratified random sampling based on 2011 census. Standardized questionnaires and blood tests for total cholesterol (TC), low-density (LDL-C), and high-density lipoprotein cholesterol (HDL-C), and triglycerides were used. Hypercholesterolemia was defined as TC $\geq$ 240/200 mg/dL and/or the use of lipid-lowering drugs, hyper-LDL-cholesterolemia as LDL-C $\geq$160/130/100 mg/dL and/or the use of drugs, hypo-HDL-cholesterolemia as HDL-C <40 mg/dL, and hypertriglyceridemia as triglycerides $\geq$150 mg/dL. Weighted analysis was applied to adjust for study design, age/sex distribution discrepancies between sample and population and nonresponse.
Results: Of 6,006 individuals recruited, 4,298 were analyzed (mean [SD] age 49.2 [18.5] years, men 48.5%, BMI 28.2 [5.7] kg/m^2). Mean TC, LDL-C, HDL-C, and TG were 193.9 [44.4], 118.5 [37.6], 49.1 [14.9], and 130.8 [94.4] mg/dL, respectively. The prevalence of hypercholesterolemia was 27.6/52.4% for thresholds $\geq$240/200 mg/dL, and of hyper-LDL-cholesterolemia was 26.3/46.7/74% for thresholds $\geq$160/130/100 mg/dL, with no differences between sexes. The prevalence of hypo-HDL-cholesterolemia was 27.5% (men/women 38.1/17.5%, $p < 0.001$) and of hypertriglyceridemia was 27.8% (men/women 32.6/23.4%, $p < 0.001$). Lipid-lowering drugs were used by 14.1% of the participants (men/women 12.6/15.6%, $p < 0.001$).

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Conclusions: More than 50% of adults in Greece have some type of dyslipidemia (mainly TC ≥ 200 mg/dL) and 14% are treated. Nationwide programmes are needed to manage dyslipidemia and halt the increasing rate of cardiovascular disease in Greece.

1. Introduction

Cardiovascular disease accounts for almost half of deaths in Europe, with dyslipidemia ranked among the major modifiable risk factors for its development.[1] Greece was recently reclassified from low- to medium-risk country in terms of cardiovascular disease risk, with 27% of cardiovascular deaths attributed to hypercholesterolemia.[1,2]

In the last decades, the prevalence of dyslipidemia in Greece has increased, mainly driven by behavioral factors such as urbanization, dietary patterns, obesity, smoking, and physical inactivity, and the recent socioeconomic crisis had adversely affected the healthcare services and public health.[3,4]

In the last decades, several epidemiological studies have estimated the prevalence of dyslipidemia in Greece.[5-10] The Hellenic National Nutrition and Health Examination Survey (HNNHS)[6] in the period 2013-2015 showed that about 20% of Greek adults had dyslipidemia. The HYDRIA survey[7] in 2013-2014 also released brief analyses including so far only the total serum cholesterol (TC) and high-density lipoprotein (HDL-C) cholesterol levels. Other studies either included a selected sample or were conducted two decades ago or earlier.[8,9] A remarkable issue among these surveys is the lack of a universal definition for lipid disorders, which limits the comparability of their findings. This is probably because beyond the classic classification based on blood lipid levels,[11] current guidelines recommend different thresholds and intervention strategies according to the individual's total cardiovascular risk.[12]

This analysis of the National Survey of Morbidity and Risk Factors (EMENO) estimated the prevalence of dyslipidemia and its treatment in the general adult population in Greece.

2. Methods

The National Survey of Morbidity and Risk Factors (EMENO) is a cross-sectional health examination survey in a nationwide representative general population sample of adults living in Greece, aiming to assess cardiovascular and respiratory risk factors and diseases.[13]

2.1. Study design

The EMENO study was conducted in Greece from May 2013 to June 2016. Participants were assessed in two home visits through a standardized questionnaire, medical examination, anthropometric and blood pressure measurements, blood tests, and spirometry. The questionnaire included demographic, socio-economic and health status data, as well as behavioral data including adherence to Mediterranean diet (MEDAS score[14]) and physical activity (IPAQ-Short GR[15]). Details on the EMENO study design have been published.[13] The Ethics and Deontology Committee of the National and Kapodistrian University and the Hellenic Data Protection Authority approved the survey, and participants signed informed consent.

2.2. Sample selection

The EMENO applied multistage stratified sampling methodology based on the 2011 census in Greece, aiming to collect data from a representative sample of adults. Greece was divided into 22 geographical areas, each of which was multiplied by 3 degrees of urbanization, and 577 sampling points were selected randomly. Within each sampling point, eligible households were selected according to the survey protocol[13], and door-to-door interviews were performed by study investigators at schedule appointments. One individual (aged ≥18 years) per household was recruited randomly. Details on the sampling methodology of the survey have been published elsewhere.[13]

2.3. Blood tests

Blood sampling was performed during home visits or at local healthcare centers by trained study physicians. Participants were asked to fast for 8 h before taking a blood sample from the antecubital vein in a sitting position. Samples were kept at 4°C until centrifugation within 12-18 h and were analyzed at the National Retrovirus Reference Center, Laboratory of Hygiene, Epidemiology and Medical Statistics of the Medical School, National and Kapodistrian University of Athens. Data on serum lipid profile, including TC, HDL-C, low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) were collected. TC was measured using a chromatographic enzymic method in a Technicon automatic analyzer RA-1000 (Dade Behring, Marburg, Germany), whereas LDL-C derived using the Friedewald formula [LDL-C (mg/dL) = TC (mg/dL) − HDL-C (mg/dL) − TG (mg/dL)/5, if TG < 400 mg/dL].[16]

2.4. Definitions

Hypercholesterolemia was defined using two TC thresholds (≥240/200 mg/dL) and/or the use of statins and/or ezetimibe. Hyper-LDL-cholesterolemia was defined using three LDL-C thresholds (≥160/130/100 mg/dL) and/or the use of statins and/or ezetimibe. Hypo-HDL-cholesterolemia was defined as HDL-C <40 mg/dL, and hypertriglyceridemia was defined as TG ≥ 150 mg/dL.

Cardiovascular disease was defined as participant reported history of stroke, coronary heart disease, myocardial infarction, or coronary artery bypass graft. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic ≥90 mmHg and/or taking antihypertensive medication. Diabetes mellitus was defined as fasting blood glucose ≥126 mg/dL and/or hemoglobin A1c ≥ 6.5% and/or taking antidiabetic treatment (including dietary intervention alone) and/or self-reported diabetes. Smoking status was self-reported and classified as current, ex-smoking, and never smoking. Current smoking versus the other two categories was considered in this analysis.

Body mass index (BMI) was calculated as weight (kg) divided by the square of standing height (meters). Obesity was defined as BMI ≥30 kg/m^2, while those with BMI 25-30 kg/m^2 were classified as overweight.

Lipid-lowering drugs included the following: (i) statins; (ii) cholesterol absorption inhibitor (ezetimibe); (iii) fibrates; and (iv) omega-3 fatty acids and were identified in the dataset according to the Anatomical Therapeutic Chemical Classification codes. There were no individuals receiving resins, nicotinic acid, and proprotein convertase subtilisin/kexin type 9 inhibitors in the dataset.

Questionnaires did not record the use of dietary supplements, such as phytosterols, monacoline, and red yeast rice.

2.5. Statistical analysis

Sampling weights were used to adjust for study design; sampling weights were multiplied with poststratification weights, applied to match the sample age, sex, and geographical distribution to that of the general population in Greece based on census 2011. Nonresponse, as not all interviewed subjects provided blood samples, was adjusted by inverse probability weighting, with weights being the reciprocal of the response probabilities. Weighted mean and standard deviations were provided for continuous variables, and weighted percentages were provided for categorical variables. The Chi-square test and weighted linear regression were used to test differences in categorical and continuous variables, respectively. Loess smoothing was applied to visualize the association between age and lipids separately for each sex. Based on that, weighted regression models were fitted using the appropriate functional form of age for men and women to estimate the mean values of lipids by age and sex. STATA (version 13.0; Stata Corp, College Station, TX) was used for the analysis.

3. Results

3.1. Participants' flow

A total of 6,006 individuals were enrolled in the EMENO study, with overall response rate at 72%. Thirteen individuals with unknown age were excluded. Of the remaining, TC, HDL-C, and/or TG measurements were available in 4,421. Of them, 110 individuals with TC < 200 mg/dL and missing information on lipid-lowering medication (4.6% of 2,380 individuals with TC < 200 mg/dL) and 13 individuals who reported receiving lipid-lowering medication but with an unknown drug class (1.6% of 788 individuals treated) were excluded. Thus, a total of 4,298 individuals were included in the current analysis. Excluded subjects were more likely to be aged >70 years, to live in urban areas and less likely to have kids, to be unemployed, to have a chronic disease, and to be of Greek origin. A weighted logistic regression model adjusted for all these factors was fitted to estimate response probabilities.

3.2. Demographics

Demographic characteristics of the study population are presented in Table 1. Of those analyzed, 48.5% were males, mean age was 49.2 years (36.2% were aged 18-39 years, 40.1% were aged 40-65 years, and 23.7% were aged ≥65 years). Participants from urban areas were 2,180 (63.8%), suburban were 805 (16.3%), and rural were 1,313 (20.0%). Education was primary in 1,582 (28.8%), secondary/postsecondary in 1,834 (46.2%), and high in 827 (23.9%). Household monthly income was ≤900 € for 1,784 participants (40.4%) and ≥1,700 € for 457 participants (11.4%). A total of 493 participants (15.3%) were unemployed, 2,917 (61.0%) were married or on cohabitation, and 1,340 were single (38.1%). The self-reported adherence to Mediterranean diet was classified as moderate in 3,433 participants (82.6%), low in 301 (9.6%), and high in 360 (7.8%). Physical activity was high in 1,900 participants (50.1%), moderate in 1,138 participants (33.3%), and low in 619 participants (16.6%).

Men were younger than women (Table 1). There was no difference between men and women in mean BMI, yet men had higher rate of overweight and lower rate of obesity. Smoking, hypertension, and history of cardiovascular disease were more common in men than in women. However, men had less frequent use of lipid-lowering agents. The vast majority of participants treated with lipid-lowering drug (92.2%) received monotherapy, 7.3% received two agents, and 0.5% received three agents. Statins were the most used agent (97.6%) of the treated individuals, of whom 51.8% received atorvastatin, 33.6% simvastatin, and 11.4% rosuvastatin, followed by ezetimibe (6.7%). Only 2.4% were receiving fibrates, and 1.6% were receiving omega-3 fatty acids.

3.3. Blood lipids

The overall mean TC, LDL-C, HDL-C, and TG levels were 193.9, 118.5, 49.1, and 130.8 mg/dL, respectively (Table 1; Supplementary Table 1). There was no difference in TC levels between men and women, but men had on average higher LDL-C (120.0 vs. 117.1 mg/dL, $p = 0.032$) and TG (144.9 vs. 117.5 mg/dL, $p < 0.001$), and lower HDL-C (44.4 vs. 53.5 mg/dL, $p < 0.001$).

TC and LDL-C levels followed a similar inverse U-shaped curve with aging for both sexes (Fig. 1A and 1B) but with an earlier peak (by about a decade) in men than women (at age about 50 and 60 years, respectively). Different curves were observed for TG and HDL-C according to sex. HDL-C in women showed a smooth decrease with aging (Fig. 1C). In men, HDL-C levels were substantially lower than in women in all age span and showed a U-shaped curve with aging, with nadir values at the fifth decade of life. Regarding TG, in women, there was a progressive increase, reaching a plateau at about the age of 80 years (Fig. 1D), whereas in men, the progressive increase peaked at the age of 60 years, with a gradual decrease thereafter (an inverse U-shaped function of age).

Table 1
Characteristics of the study participants and lipid levels overall and by sex. Weighted percentages and weighted summary statistics are presented.

Characteristic	Total	Men	Women	P
N (%)	4,298	1,837 (48.5)	2,461 (51.5)	
Age [years; mean (SD)]	49.2 (18.5)	48.1 (17.1)	50.2 (19.8)	0.003
Body mass index [kg/m^2; mean (SD)]	28.2 (5.7)	28.2 (4.5)	28.1 (6.8)	0.502
Overweight [N (%)]	1,600 (37.1)	823 (44.9)	777 (29.8)	<0.001
Obese [N (%)]	1,546 (32.4)	626 (30.6)	920 (34.1)	0.02
Current smokers [N (%)]	1,471 (38.4)	736 (44.1)	735 (33.0)	<0.001
Hypertension [N (%)]	1,945 (39.0)	925 (42.5)	1,020 (35.8)	<0.001
Diabetes mellitus [N (%)]	588 (11.7)	288 (12.4)	300 (11.0)	0.214
Cardiovascular disease [N (%)]	305 (5.8)	178 (7.2)	127 (4.5)	<0.001
Total cholesterol [mg/dL; mean (SD)]	193.9 (44.4)	193.3 (42.5)	194.4 (45.8)	0.489
LDL cholesterol [mg/dL; mean (SD)]	118.5 (37.6)	120.0 (36.0)	117.1 (38.9)	0.032
HDL cholesterol [mg/dL; mean (SD)]	49.1 (14.9)	44.4 (12.4)	53.5 (15.8)	<0.001
Triglycerides [mg/dL; mean (SD)]	130.8 (94.4)	144.9 (104.2)	117.5 (76.9)	<0.001
Use of lipid-lowering drugs [N (%)]	775 (14.1)	312 (12.6)	463 (15.6)	0.007

LDL, low-density lipoprotein, HDL, high-density lipoprotein.

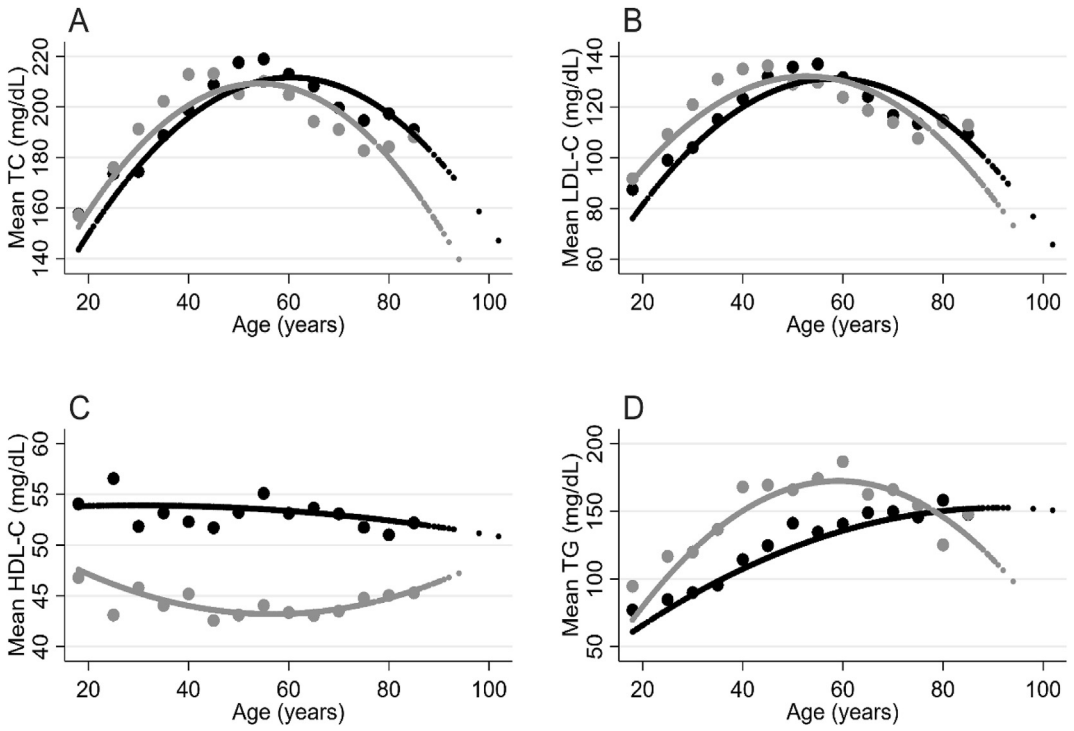

Figure 1. Mean total cholesterol (**A**), low-density cholesterol (LDL-C) (**B**), high-density cholesterol (HDL-C) (**C**), and triglycerides (TG) (**D**) according to age and sex, observed (dots) and estimated per 5-year age intervals through weighted regression models (lines) in men (grey) and in women (black).

3.4. Rates of elevated TC and LDL-C levels

A total of 2,033 participants (42.7%) had elevated TC (≥200 mg/dL) and 751 (15.4%) highly elevated (≥240 mg/dL) levels, with no significant overall differences between sexes (Supplementary Table 2). Elevated and highly elevated TC was more common in men than in women until the age of 50 years, whereas in older age, this relationship was reversed (Supplementary Fig. 1).

A total of 13.8% participants had LDL-C ≥160 mg/dL, 35.8% had LDL-C ≥130 mg/dL, and 67.6% had LDL-C ≥100 mg/dL (Supplementary Table 3). The differences between men and women by age group were similar as for TC (Supplementary Fig. 2).

3.5. Prevalence of dyslipidemia

The prevalence of hypercholesterolemia (TC ≥ 240 mg/dL and/or use of statins and/or ezetimibe) was 27.6% and reached 52.4% when a stricter cut-off (≥200 mg/dL) was applied (Supplementary Table 4, Supplementary Fig. 3A and 3B). The respective percentages for hyper-LDL-cholesterolemia were 26.3%, 46.7%, and 74.0% with thresholds 160, 130, and 100 mg/dL, respectively, and/or use of statins and/or ezetimibe (Supplementary Table 5, Fig. 2A, 2B, and 2C).

The prevalence of hypo-HDL-cholesterolemia was 27.5% (Supplementary Table 6) and hypertriglyceridemia was 27.8% (Supplementary Table 7), with both being higher in men than in women (38.1% vs. 17.5% and 32.6% vs. 23.4%, respectively; all $p < 0.001$) across all age span, apart from age ≥80 years, in which women tended to have higher hypertriglyceridemia rates. The overall, age-related prevalence curve was rather flat for hypo-HDL-cholesterolemia (Fig. 3A) but showed an increasing trend for hypertriglyceridemia (Fig. 3B), mainly in women.

3.6. Use of lipid-lowering drugs

In the entire sample, a total of 775 participants (14.1%) were on lipid-lowering drug treatment. Of the 298 participants with cardiovascular disease history and known lipid-lowering medication status, 151 (48.1%) were on lipid-lowering drug treatment. Lipid-lowering drugs were used by 23.7% of poststroke patients, 58.1% of those with coronary artery disease, 59.6% of those with post-myocardial infarction, and 62.6% of those with postcoronary artery bypass graft. There was a steep rise in lipid-lowering drug use with increasing age, with a peak at the age of 65-79 years (Supplementary Table 8). The use of lipid-lowering medication was higher in women (15.6% of the study population vs. 12.6% in men, $p = 0.007$), which was driven by the age group of 65-80 years, whereas the treatment rates were similar in younger men vs. women (Supplementary Fig. 4).

4. Discussion

The EMENO nationwide study in 4,298 adults provided methodologically appropriate epidemiological data on dyslipidemia in the general adult population in Greece in the years 2013-2016. Key findings are that there is a high prevalence of blood lipid abnormalities ranging from 28% to 52% for TC and from 26 to 74% for LDL-C, depending on the diagnostic threshold applied. Moreover, the rates of low HDL-C and hypertriglyceridemia were both at about 28%. Only 14% of the adult population in Greece was on lipid-lowering medications.

4.1. Epidemiology of hypercholesterolemia

In the current study, the mean TC and LDL-C levels were 193.9 and 118.5 mg/dL, respectively, which is in line with findings by

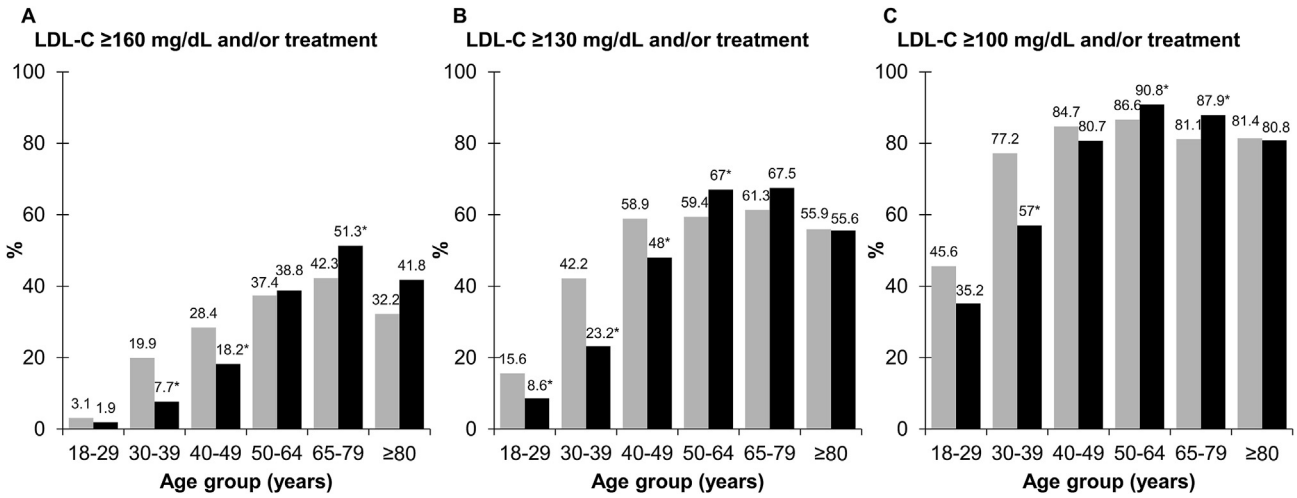

Figure 2. Prevalence of hyper-LDL-cholesterolemia defined as low-density lipoprotein cholesterol [LDL-C] ≥160 (**A**), ≥130 (**B**), and ≥100 mg/dL (**C**), and/or treatment by sex and age (men in grey; women in black). *, p < 0.05 for men vs. women.

other national surveys in Greece performed in the same period. The HNNHS[6] (2013-15) in 1,094 individuals reported the mean TC and LDL-C levels at 192.0 and 115.1 mg/dL, respectively, whereas the HYDRIA[7] (2013-14) in a representative population of 4,011 adults reported mean TC at 195.4 mg/dL. Another national survey (2008-2010) by the Hellenic Heart Foundation in 32,736 individuals in 6 large Greek cities reported mean TC at 199.5 mg/dL.[17] These estimates are higher than those reported in the USA in 2013-2014 (LDL-C 111.3 mg/dL)[18] but lower than those in France in 2015 (LDL-C 129.9 mg/dL).[19]

Comparisons with studies performed 2-3 decades ago in Greece suggest that there is a trend toward decreased TC and LDL-C levels. A prospective cohort study in 11,645 volunteers from all over Greece, which was part of the European Prospective Investigation into Nutrition and Cancer (EPIC) study[9] conducted during the middle 1990s, reported mean TC levels of 222 mg/dL, and the ATTICA study[8] in a sample of cardiovascular disease-free adults in the region of Attica in 2001-2002 showed TC levels at 197 mg/dL. Although our results cannot be directly compared with those of these studies due to methodological differences (i.e., the EPIC[9] included volunteers and the ATTICA[8] inhabitants of one province around Athens, thus both being not representative of Greek population), the lower TC levels in the EMENO study might be attributed to increased use of statins in the last decades, despite the more Westernized lifestyle observed in Greece.

Regarding age-related trends in lipid parameters, TC and LDL-C levels increased with aging, peaked at the age of 50 years in men and a decade later in women, and were reduced thereafter. These changes might be due to increased use of lipid-lowering treatment in the elderly and the early death of people with hypercholesterolemia. The delayed TC and LDL-C peak in women is probably related with the loss of favorable effects of estrogens on lipids after menopause.[20] In addition, men had higher TC levels than women till the age of 50 years, but lower thereafter. This is in line with the findings by the HNNHS[6], which showed similar TC pattern in males and females but with a higher age threshold (i.e., 60 years, after which women had higher TC levels). The higher rate of hypercholesterolemia in older women may be due to the increased prevalence of obesity and early cardiovascular death of middle-aged men with hypercholesterolemia.

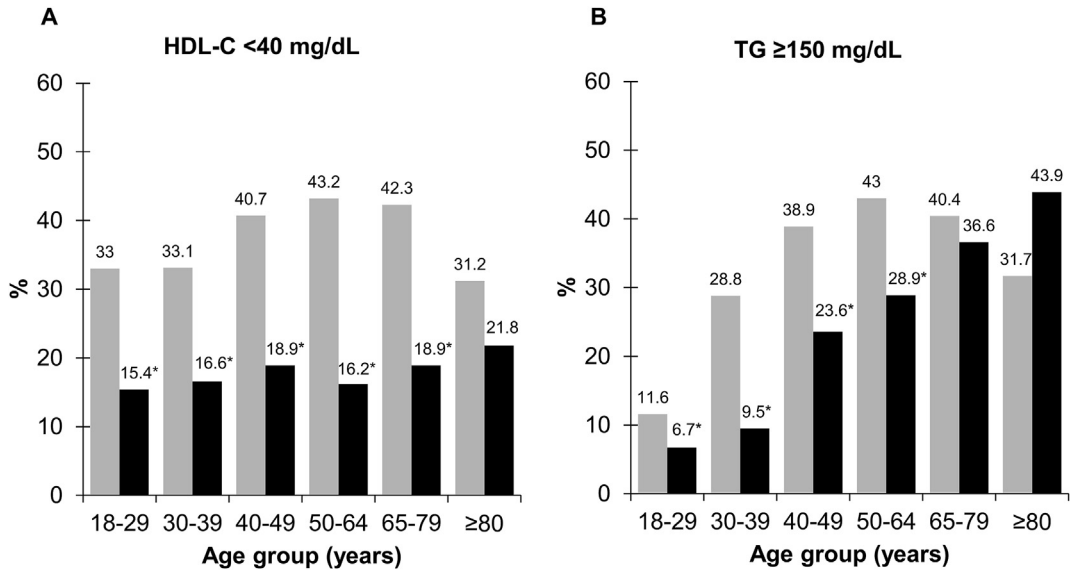

Figure 3. Prevalence of hypo-HDL-cholesterolemia (**A**) and hypertriglyceridemia (**B**) by sex and age (men in grey; women in black). *, p < 0.05 for men vs. women.

The proportion of participants with TC ≥ 200 mg/dL was 42.7%, which is higher than the HNNHS estimate (38.6%).[6] Using the ≥240 mg/dL TC threshold, the prevalence of hypercholesterolemia was 15.4%, which is comparable to the HYDRIA[7] study estimate (13.4%) and NHANES report (12.4-12.8%).[21,22] By taking into account the older data from the ATTICA[8] study (2001-2002; 43% with TC ≥ 200 mg/dL and 14% TC ≥ 240 mg/dL) and the European report for Cardiovascular Disease Statistics[1] for Greece (2008 data; 12.8% with TC ≥ 240 mg/dL), the EMENO data are reassuring that in Greece the prevalence of hypercholesterolemia did not increase in the last two decades.

4.2. Epidemiology of hypo-HDL-cholesterolemia

The mean HDL-C level was 49.1 mg/dL, which was considerably lower than in the synchronous HNNHS (57.8 mg/dL)[6] and HYDRIA (58.1 mg/dL)[7], but similar to the older EPIC[9] study in Greece (47.8 mg/dL). Differences in study populations probably contributed to HDL-C differences, as e.g., the HNNHS[6] included younger individuals (44 vs. 49 years), more women (59 vs. 52%), less obese individuals (16 vs. 32%), less smokers (34 vs. 38%), and less diabetic individuals (5 vs. 12%) than the EMENO study. A recent report by a large Danish primary healthcare cohort reported that HDL-C levels remained stable between 2001 and 2018.[23]

As expected, men had considerably lower HDL-C levels than women and a more than double prevalence of hypo-HDL-cholesterolemia. Females showed a smooth decrease in HDL-C with ageing, which is probably due to the effects of menopause.[20] The U-shaped curve in HDL-C levels with aging in men may be due to an increased death rate of those with low HDL-C in middle age. Low HDL-C levels were more common in the EMENO (27.5%) than in the HYDRIA (9.7%)[7], as well as in the NHANES 2007-2014 (20.2%)[21] and 2015-2016 (18%).[22]

4.3. Epidemiology of hypertriglyceridemia

In the EMENO study, the mean TG was 130.8 mg/dL, which is considerably higher than in the HNNHS (83 mg/dL)[6] in Greece, as well as in other countries such as the USA (NHANES, 103.5 mg/dL)[18] and France (Esteban Study, 104.5 mg/dL).[19] Same factors as discussed above for HDL-C may explain these differences, as TG and HDL-C are inversely associated.[24] Overall, 27.8% of study participants had hypertriglyceridemia, which is similar as in USA NHANES (24.2%)[18] but higher than in previous studies in Greece (HNNHS 13.9%[6], ATTICA 20.4%[8]). However, the ATTICA study[8] was conducted two decades ago and included younger participants (47 years) with lower prevalence of obesity (20%) and diabetes (8%). Of note, the Greek Dyslipidemia International Study (DYSIS)[25] in 2012 reported that 39.9% of patients had hypertriglyceridemia, despite statin treatment.

Men had considerably higher TG levels than women (144.9 vs. 117.5 mg/dL) and had a more frequent hypertriglyceridemia (32.6 vs. 23.4%). There was an increase in the prevalence of hypertriglyceridemia with aging, which is probably linked with increasing overweight/obesity rate than with aging per se. Women showed a progressive rise in hypertriglyceridemia prevalence with aging, whereas men had a much steeper and earlier rise that peaked in the sixth decade of life and smoothly declined in older men.

4.4. Use of hypolipidemic medications

Lipid-lowering medications were received by 14.1% of the study participants. These findings are similar as in the HNNHS (12.2%)[6] but lower than in the HYDRIA (20.5%)[7] or the NHANES (18%).[18] For secondary prevention, this percentage was higher (48.1%), yet still inadequate in participants with cardiovascular disease history (24% in poststroke patients; 60% in those with coronary artery disease).[12] In the US NHANES 2011-2012[26], 71% of participants aged 40 years or older with cardiovascular disease were on cholesterol-lowering medication (28% in all participants aged 40 years and over), compared to 49.4% and 22%, respectively, in the EMENO participants aged 40 years or older.

Few men and women received therapy under the age of 50 years, with a steep rise in treatment rates thereafter (Supplementary Fig. 4). Women older than 65 years were more often treated than men. This finding could be attributed to sex differences in healthcare seeking behaviors, with women visiting their primary care providers more often and thus having more opportunities to receive lipid-lowering medication.[27] However, other studies showed lower use of lipid-lowering treatment in women[19], which may be due to underestimation by doctors of the cardiovascular risk in postmenopausal women.

The vast majority of treated participants (92.2%) were on lipid-lowering drug monotherapy, with statins being by far the most widely used hypolipidemic (97.6%). This treatment pattern is in agreement with previous studies.[28,29] In the DA VINCI cross-sectional, observational study in 18 countries, 83% of patients receiving lipid-lowering treatment for primary or secondary prevention were on monotherapy with statins, and 9% received a statin with ezetimibe.[29] The higher monotherapy treatment rate in the present study compared to the DA VINCI reflects the different composition of the population, with the vast majority of EMENO participants being in primary prevention, where LDL-C targets can usually be achieved with statin monotherapy. This treatment strategy is also in line with current guidelines, recommending statins as first-line therapy for hypercholesterolemia, and the addition of ezetimibe if LDL-C target is not achieved.[12]

4.5. Limitations

The EMENO study data should be interpreted by considering its limitations. First, 4,298 of 6,006 participants had data on area of interest and were analyzed, and those who were excluded differed in several characteristics. To limit the potential of bias, the inverse probability weighting method was applied. Second, questionnaires did not assess nonpharmacological approaches for dyslipidemia management, such as diet or nutritional supplements, and not all participants were fasting for 8 h before the blood sample. Third, the presence of cardiovascular disease was based on the medical history reported by the participant. Fourth, EMENO was conducted in 2013-2016, and since then the prevalence of dyslipidemia and treatment strategies may have changed in response to recent guidelines recommending stricter treatment thresholds and goals of therapy.[12,30,31] In addition, the recent financial recession and the COVID-19 pandemic may have limited patients' health priorities and their access to healthcare services, affecting adversely health outcomes.[32,33]

5. Conclusions

EMENO demonstrated the high prevalence of dyslipidemia in Greece, with more than half of the adults having some type of dyslipidemia (mainly TC ≥ 200 mg/dL) and 14% receiving pharmacological treatment. These recent epidemiological data showed a higher rate of dyslipidemia in Greece than in other national and international surveys, with less use of drug treatment, and certainly contributed to the recent reclassification of the Greek population from low to medium cardiovascular risk. Nationwide public awareness programs are urgently needed to prevent and manage

dyslipidemia, aiming to halt the increasing rate of cardiovascular disease in Greece.

Authors Contribution

GSS, MG, AV, GC, CH, GT, PVV, YA, AK and GT conceptualized and designed the study. MG, AV, GC, CH, GT, PVV, YA, AK and GT acquired the data. AN, NK and GT analyzed the data. GSS, AN, AM, NK, CV, ENL, LR, DR and GT interpreted the data. GSS, AN, AM, NK, CV, ENL, LR, DR and GT drafted the article. GSS, MG, AV, GC, CH, GT, PVV, YA, AK and GT made critical revision of the article for important intellectual content.

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Declaration of competing interest

GSS reports advisory and lecture fees from Astra-Zeneca, Menarini, Novartis, Sanofi-Aventis, Servier. CV reports research grants and honoraria from Amgen, Vianex, Elpen, Pfizer, Lilly, Menarini, Servier, Sanofi, Viatris, Winmedica. ENL reports personal fees paid to his institution from Amgen, Novartis, Sanofi, Novo Nordisk, Lilly and Servier, outside the submitted work. LR reports research grants and honoraria from Amgen, Elpen, Sanofi-Aventis, Mylan, Novartis, and Servier. DR reports personal fees for lectures and AB from Amgen, Novartis, Sanofi, Novo Nordisk, Lilly and Servier, Menarini, Viatris, Recordati, Boehringer, Elpen, Bayer, Roche, Medtronic, Edwards, Astra-Zeneca, Demo, outside the submitted work. MG received honoraria paid through her institution from Merck, for advisory boards and lectures unrelated to this study. GT has received EU and National resources grants as well as a grant from the Hellenic Diabetes Association, all paid to her institution, to support this study and grants unrelated to this study and paid to her institution from Gilead Sciences Europe, UCL, ECDC, EU, and National funds. The other authors report no relationships that could be construed as a conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hjc.2022.10.002.

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