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Original Article

Prevalence of dyslipidemia and its association with cardiometabolic factors and kidney function in the adult Romanian population: The PREDATORR study



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ABSTRACT

The aims were to assess the prevalence and characteristics of dyslipidemia phenotypes in a Romanian population-based sample from the PREDATORR study.

Methods: PREDATORR was an epidemiological study with a cross-sectional, cluster random sampling design. Participants were classified into four dyslipidemia phenotypes based on the NCEP ATP III criteria: isolated hypertriglyceridemia, isolated hypoHDL-C, isolated hyperLDL-C and mixed dyslipidemia (≥ 2 standard lipid abnormalities). Overall, 2656 were included in the analysis by dyslipidemia phenotypes.

Results: An estimated 67.1% of Romanian adults have at least one lipid abnormality: 27.5% (95%CI26.0–28.9%) have elevated TG, 29.4% (95%CI27.9–30.8%) have low HDL-C and 47.8% (95%CI46.3–49.2%) have elevated LDL-C (26.2% had LDL-C levels ≥ 2.58 mmol/l associated with CHD or CHD risk equivalent). Also, 30% Romanian adults have mixed dyslipidemia with 7.6% (95%CI6.1–9.0%) having all three lipid abnormalities.

The age- and sex-adjusted prevalence of isolated dyslipidemia phenotypes in Romanian adult population was 23.7% (95%CI22.2–25.1%) for hyperLDL-Cholesterolemia, 9.3% (95%CI7.8–10.7%) for hypoHDL-Cholesterolemia and 4.1% (95%CI2.6–5.5%) for hypertriglyceridemia.

Among participants with triglycerides ≥ 2.25 mmol/l, 15.2% (95%CI13.7–16.6%) of Romanian adults have non-HDL-C levels ≥ 3.36 mmol/l.

Conclusions: The PREDATORR survey indicated a high prevalence of dyslipidemia phenotypes in the Romanian population aged 20–79 years, providing data on its association with several cardiometabolic risk factors.

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1. Introduction

Cardiovascular diseases (CVD), despite being in a large proportion preventable, remain the leading cause of premature death and chronic disability worldwide and the association of CVD with lipid profile abnormalities is well established [1].

In Romania, limited data are available regarding the lipid

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abnormalities prevalence and relationship with cardiometabolic traits and renal function. PREDATORR (prevalence of diabetes mellitus, prediabetes, overweight, obesity, dyslipidaemia, hyperuricaemia and chronic kidney disease in Romania) study indicated a high gender and age adjusted prevalence of prediabetes (16.5%), diabetes (11.6%), overweight/obesity (34.7%/31.9%), smoking (18% for current smoking and 30.8% for smoking cessation) and chronic kidney disease (CKD) (6.74%) in the Romanian population aged 20–79 years [2–5].

To our knowledge, PREDATORR is the first epidemiological national study evaluating the association of dyslipidemia phenotypes with the cardiometabolic risk factors and kidney function in a representative adult Romanian population sample.

The goals of the actual study were to establish the prevalence of lipid abnormalities in the Romanian population aged 20–79 years and to assess the association of the dyslipidemia phenotypes with cardiometabolic profile, kidney function, lifestyle risk factors and sociodemographic data.

2. Subjects

The PREDATORR survey (EudraCT number: 2012-004803-12) was a population based study with a cross-sectional, stratified, two-cluster random sampling design, conducted according to the World Medical Association Declaration of Helsinki and the Good Clinical Practice Guidelines standards, between 2012 and 2014.

The study design was described previously [2]. In brief, participants were enrolled from the databases of 101 general practitioners (GPs) affiliated with the National Health Insurance House using an automated random computer selection, based on the inclusion criteria (age between 20 and 79 years, included on the list of a GP, living for the past 10 years mainly in Romania, born in Romania, no pregnancy or lactation).

Overall, 2728 participants aged 20–79 years were enrolled based on the 2002 Romanian Census in order to have representativeness of the sample for the adult Romanian population. All participants signed written informed consent before enrolment in the study.

3. Materials and methods

3.1. Clinical and biological data

Socio-demographic data (age, gender), life style data (alcohol drinking, smoking status, sedentarism) and personal medical history were recorded using an interviewer-administered questionnaire.

Non-drinkers were considered the participants who did not report alcohol consumption in the last month. According to smoking status, the participants were classified as nonsmokers (participants who never smoked) and smokers (participants who had smoked daily or occasionally more than one cigarette per day, anytime in their life).

Sedentarism was defined as physical activity performed less than 4 days/week. Overweight/obesity were defined as body mass index (BMI) ≥ 25 kg/m² and abdominal obesity was defined as abdominal circumference ≥ 80 cm in women and ≥ 94 cm in men.

Hypertension was considered in participants with systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or with previous diagnosis of hypertension, and/or with antihypertensive medication.

The fasting plasma levels of glucose (FPG), HbA1c, uric acid, creatinine, insulin, total cholesterol (TC), triglycerides (TG), HDL-Cholesterol (HDL-C), VLDL-Cholesterol (VLDL-C) and urinary creatinine and albumin levels were assessed at the Synevo Romania

SRL laboratories using standardized procedures (enzymatic method for assessment of FPG, TC, TG, HDL-C, uric acid, creatinine and urinary creatinine; immunoturbidimetric method for HbA1c and albuminuria and chemiluminiscent immunoassay for insulinemia determination).

LDL-Cholesterol (LDL-C) was calculated using Friedewald formula in participants with TG levels < 4.51 mmol/l ($LDL-C = TC - HDL-C - TG/5$). Non-HDL-C was calculated in participants with TG levels ≥ 2.25 mmol/l using the formula: $non-HDL-C = TC - HDL-C$. Homeostasis Model Assessment for insulin resistance (HOMA-IR) as a marker of insulin resistance was estimated using formula [6]: $HOMA-IR = \text{fasting insulinemia } (\mu\text{UI/mL}) \times \text{fasting glycemia } (\text{mg/dL})/405$.

Impaired glucose regulation (IGR) including prediabetes, known and unknown diabetes was defined based on FPG, 2h plasma glucose levels during oral glucose tolerance test, HbA1c, symptoms of hyperglycemia or previous diagnosis of diabetes, according to the 2012 American Diabetes Association guidelines [7].

The risk of occurrence of CVD was estimated using Framingham 10-year CVD risk score [8]. Participants with Framingham CVD risk score $< 10\%$ were considered as having low CVD risk and those with Framingham CVD risk score $\geq 10\%$ were considered as having moderate/high CVD risk.

Ischaemic vascular disease (IVD) - carotid artery disease, coronary heart disease, peripheral arterial disease - was diagnosed based on personal history (angina, myocardial infarction, stroke, gangrene, arterial by-pass, angioplasty), clinical examination and/or medical records (arterial Doppler ultrasound, ECG, angiography, etc) from GPs. Premature coronary heart disease (CHD) was considered in participants which reports that first-degree relatives had a myocardial infarction or angina before age 50 [9].

eGFR was estimated using CKD-EPI equation and albumin to creatinine ratio (ACR) was evaluated in a spot urine sample. CKD was defined as eGFR < 60 mL/min per 1.73 m² and/or ACR ≥ 30 mg/g, according to the KDIGO 2012 guidelines [10]. Hyperuricemia was defined as uric acid levels ≥ 416.3 $\mu\text{mol/l}$ in men or ≥ 356.8 $\mu\text{mol/l}$ in women.

3.2. Dyslipidemia phenotypes

LDL-C categories were established based on the presence of CHD, CHD risk equivalent (diabetes, peripheral arterial disease), major CHD risk factors (cigarette smoking, hypertension, HDL-C < 1.03 mmol/l, family history of premature CHD, age in men ≥ 45 years and in women ≥ 55 years) and Framingham CVD risk score ($\geq 20\%$, 10–20%, $< 10\%$) according to NCEPATP III definitions and components were matched as well as possible to the data recorded in PREDATORR [1].

Hypertriglyceridemia was considered when TG levels ≥ 1.69 mmol/l and elevated VLDL-C was considered when VLDL-C ≥ 0.78 mmol/l [1]. Hypercholesterolemia was defined as TC levels ≥ 5.17 mmol/l and elevated non-HDL-C was defined in subjects with TG ≥ 2.25 mmol/l as non-HDL-C ≥ 3.37 mmol/l [1]. HDL-C < 1.03 mmol/l in men and < 1.29 mmol/l in women was considered as hypoHDL-cholesterolemia [1].

Mixed dyslipidemia was defined as double or triple association of isolated dyslipidemia (hypertriglyceridemia, hypoHDL-cholesterolemia and elevated LDL-C).

3.3. Statistical analysis

Calculation of sample size was performed only for the primary objective of PREDATORR study (prediabetes and diabetes prevalence). The global prevalence of isolated dyslipidemia (elevated LDL-C, low HDL-C, elevated TG) and mixed dyslipidemia

(combination of 2 or 3 lipid abnormalities) was adjusted for the age and sex structure of the Romanian population aged 20–79 years, according to 2011 Romanian Census. A full analysis method was used in the case of missing data (i.e., absence of biochemical data, incomplete questionnaires).

Non-parametric tests were used for comparisons between dyslipidemia phenotypes of categorical and continuous variables. Multivariate analysis by multinomial logistic regression was performed to evaluate the association of cardiometabolic parameters and renal function (independent variables) with dyslipidemia phenotypes (dependent variable). The analysis was adjusted for covariates (age, sex, smoking status, statin use, alcohol drinking, sedentariness), and “no lipid disorders” was considered reference category.

Two-tailed $p < 0.05$ was considered significant. Analyses were performed using the SPSS v19.0 (IBM Corp., Armonk, NY, USA).

4. Results

Of the 2728 participants enrolled in the PREDATORR study, 11 participants were lost to follow-up and 61 participants had incomplete data and were not included in the analyses. Overall, 2656 were included in the analysis by dyslipidemia phenotypes.

An estimated 67.1% of Romanian adults have at least one lipid abnormality: 47.8% have elevated LDL-C, 29.4% have low HDL-C, and 27.5% have elevated TG (Fig. 1, Table 1). The global prevalence of mixed dyslipidemia was 30% in the Romanian adult population. Approximately 7.6% of Romanian adults have all three lipid abnormalities (Fig. 1, Table 1), the triple association being more prevalent in 60–79 age group and in women (Table 2).

The age- and sex-adjusted overall prevalence of isolated hypoHDL-Cholesterolemia in Romanian adult population was 9.3% (95% CI 7.8–10.7%), the prevalence of isolated hyperLDL-Cholesterolemia was 23.7% (95% CI 22.2–25.1%) and that of isolated hypertriglyceridemia was 4.1% (95% CI 2.6–5.5%) (Fig. 1,

Table 2). The highest percentage of low HDL-C was in the 20–39 age group and in women, whereas, elevated LDL-C and TG were predominant in the 40–79 age group and in men (Table 2).

Among patients with elevated LDL-C levels, 26.2% had LDL-C levels ≥ 2.58 mmol/l associated with CHD or CHD risk equivalent (10-year risk $>20\%$) (Table 2).

The prevalence of elevated non-HDL-C levels was 15.2% in Romanian adults and 12.6% of adults have “high” and “very high” non-HDL-C levels according to the NCEP definition (Table 2).

Table 3 summarizes socio-demographic data, life style characteristics and cardiometabolic features for Romanian adults with different dyslipidemia phenotypes: isolated abnormal LDL-C, isolated low HDL-C, isolated elevated TG and mixed dyslipidemia (abnormal measurements for 2 or more standard lipid parameters - LDL-C, HDL-C, TG).

Moderate/high Framingham 10-year CVD risk was significantly higher in participants with isolated hyperLDL-Cholesterolemia compared to participants with isolated hypertriglyceridemia ($p < 0.01$) or hypoHDL-Cholesterolemia ($p < 0.001$), but lower than in those with mixed dyslipidemia ($p = 0.01$) (Table 3).

Elevated LDL-C was associated with a 2.1-fold increase risk for IVD compared to hypoHDL-Cholesterolemia (31.1% vs 14.3%), a 1.7-fold increased IVD risk compared to hypertriglyceridemia and a similar IVD risk as mixed dyslipidemia (Table 3).

Participants with isolated elevated TG had significantly higher values of HOMA-IR ($p < 0.01$ for LDL-C; $p = 0.04$ for HDL-C), VLDL-C ($p < 0.01$ for both), uric acid ($p < 0.01$ for both), waist ($p < 0.01$ for both), maximum BMI ($p < 0.01$ for both) and BMI ($p < 0.01$ for both) compared with participants with isolated elevated LDL-C and to those with isolated hypoHDL-C, and similar values of these parameters compared to participants with mixed dyslipidemia (Table 3).

IGR was highly prevalent among subjects with mixed dyslipidemia compared with subjects with isolated dyslipidemia, pre-diabetes and unknown diabetes being more frequent in subjects

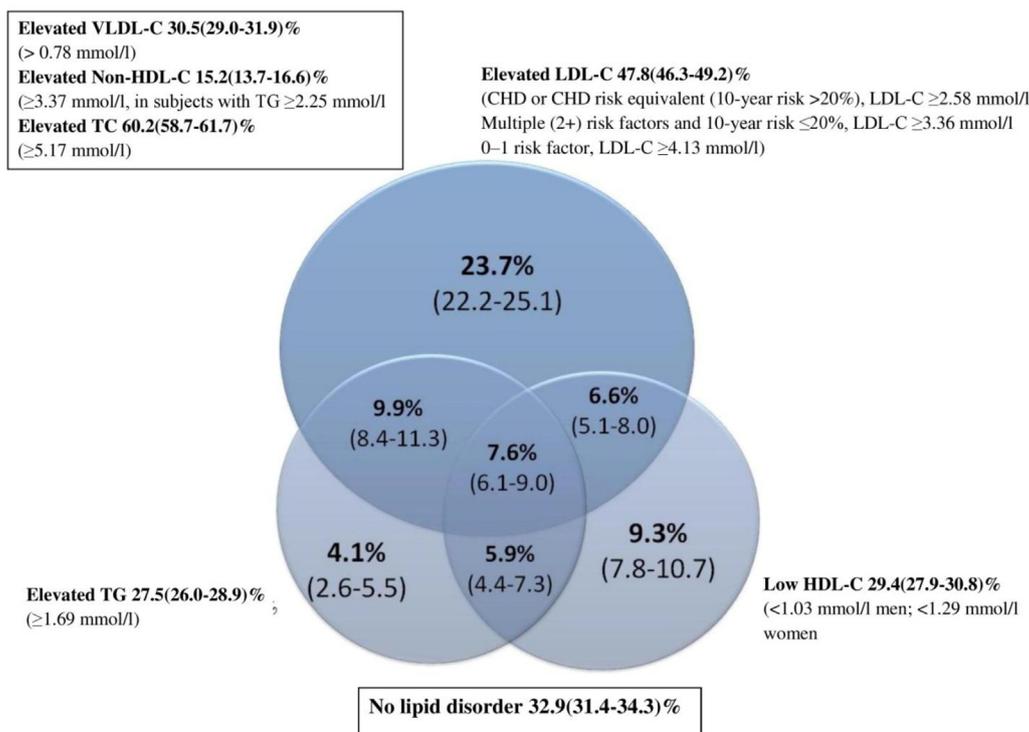


Fig. 1. Prevalence of lipids abnormalities in Romanian population aged 20–79 years.

Table 1
Prevalence of isolated and mixed dyslipidemia in Romanian population aged 20–79 years.

	Age groups			Overall
	20–39 years	40–59 years	60–79 years	
Isolated dyslipidemia				
Total population				
Elevated LDL-C alone	13.6(12.1–15.1)	28.6(27.1–30.1)	31.6(30.1–33.1)	23.7(22.2–25.2)
Low HDL-C alone	14.1(12.6–15.6)	6.1(4.6–7.6)	6.6(5.1–8.1)	9.3(7.8–10.8)
Elevated TG alone	4.0(2.5–5.5)	4.2(2.7–5.7)	4.2(2.7–5.7)	4.1(2.6–5.6)
Men				
Elevated LDL-C alone	15.8(14.3–17.3)	27.2(25.7–28.7)	36.5(35.0–38.0)	25.2(23.7–26.7)
Low HDL-C alone	7.6(6.1–9.1)	5.4(3.9–6.9)	4.9(3.4–6.4)	6.1(4.6–7.6)
Elevated TG alone	6.1(4.6–7.6)	6.8(5.3–8.3)	4.9(3.4–6.4)	6.0(4.5–7.5)
Women				
Elevated LDL-C alone	11.6(10.1–13.1)	29.9(28.4–31.4)	27.2(25.7–28.7)	22.5(21.0–24.0)
Low HDL-C alone	20.2(18.7–21.7)	6.7(5.2–8.2)	8.2(6.7–9.7)	12.0(10.5–13.5)
Elevated TG alone	2.0(0.5–3.5)	2.1(0.6–3.6)	3.5(2.0–5.0)	2.4(0.9–3.9)
Mixed dyslipidemia				
Total population				
Elevated LDL-C and low HDL-C and elevated TG	5.0(3.5–6.5)	9.1(7.6–10.6)	9.4(7.9–10.9)	7.6(6.1–9.1)
Elevated LDL-C and low HDL-C and normal TG	4.0(2.5–5.5)	8.2(6.7–9.7)	8.2(6.7–9.7)	6.6(5.1–8.1)
Elevated LDL-C and normal HDL-C and elevated TG	5.0(3.5–6.5)	12.6(11.1–14.1)	13.4(11.9–14.9)	9.9(8.4–11.4)
Normal LDL-C and low HDL-C and elevated TG	6.5(5.0–8.0)	6.1(4.6–7.6)	4.8(3.3–6.3)	5.9(4.4–7.4)
Men				
Elevated LDL-C and low HDL-C and elevated TG	6.5(5.0–8.0)	8.4(6.9–9.9)	6.8(5.3–8.3)	7.3(5.8–8.8)
Elevated LDL-C and low HDL-C and normal TG	3.9(2.4–5.4)	5.2(3.7–6.7)	6.5(5.0–8.0)	5.0(3.5–6.5)
Elevated LDL-C and normal HDL-C and elevated TG	8.7(7.2–10.2)	18.0(16.5–19.5)	15.6(14.1–17.1)	13.8(12.3–15.3)
Normal LDL-C and low HDL-C and elevated TG	9.8(8.3–11.3)	9.1(7.6–10.6)	4.6(3.1–6.1)	8.2(6.7–9.7)
Women				
Elevated LDL-C and low HDL-C and elevated TG	3.6(2.1–5.1)	9.6(8.1–11.1)	11.7(10.2–13.2)	7.9(6.4–9.4)
Elevated LDL-C and low HDL-C and normal TG	4.0(2.5–5.5)	10.8(9.3–12.3)	9.6(8.1–11.1)	8.0(6.5–9.5)
Elevated LDL-C and normal HDL-C and elevated TG	1.6(0.1–3.1)	8.1(6.6–9.6)	11.4(9.9–12.9)	6.5(5.0–8.0)
Normal LDL-C and low HDL-C and elevated TG	3.6(2.1–5.1)	3.7(2.2–5.2)	5.0(3.5–6.5)	4.0(2.5–5.5)

Data show adjusted percentages, with 95%CI in parentheses. LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglycerides.

Table 2
Prevalence of LDL-C, Non-HDL-C and triglycerides categories based on NCEP ATP III risk factor profile in Romanian population aged 20–79 years.

LDL-C		
CHD or CHD risk equivalent (10-year risk >20%) LDL-C ≥2.58 mmol/l 26.2(24.7–27.6)%	Multiple (2+) risk factors and 10-year risk ≤20% LDL-C ≥3.36 mmol/l 19.5(18.1–21.1)%	0–1 risk factor LDL-C ≥4.13 mmol/l 2.1(0.6–3.6)%
Non-HDL-C		
Borderline high 3.37–4.12 mmol/l 2.6(1.1–3.9)%*	High 4.14–4.90 mmol/l 3.8(2.3–5.2)%*	Very high ≥4.92 mmol/l 8.8(7.3–10.2)%*
Triglycerides		
Borderline high 1.69–2.24 mmol/l 13.5(12.0–14.9)%	High 2.25–5.63 mmol/l 11.0(9.5–12.4)%	Very high ≥5.64 mmol/l 3.0(1.5–4.4)%

Data show adjusted percentages, with 95%CI in parentheses; CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol; Non-HDL-C: Non-high-density lipoprotein cholesterol; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III. *Non-HDL-C was calculated in individuals with triglycerides ≥2.25 mmol/l.

with hyperLDL-Cholesterolemia, while known diabetes was frequently identified in subjects with hypertriglyceridemia (Table 3).

Compared to subjects with low HDL-C, participants with hyperLDL-Cholesterolemia had higher prevalence of CKD (0.02) and albuminuria ($p = 0.002$) and lower eGFR ($p < 0.01$) (Table 3).

Multivariate multinomial logistic regression analysis indicated that the isolated hyperLDL-Cholesterolemia phenotype had higher odds of being linked with moderate/high Framingham 10-year CVD risk and IVD ($p < 0.001$ for both), than the phenotype without any lipid disorders (Table 4). The isolated hypoHDL-cholesterolemia and isolated hypertriglyceridemia phenotypes were associated with overweight/obesity ($p = 0.04$ and respectively $p = 0.01$), but interestingly unrelated significantly with CVD risk (Table 4). Hyperuricemia was an independent predictor for the presence of the isolated hypertriglyceridemia ($p = 0.02$) (Table 4). Mixed

dyslipidemia (≥ 2 abnormal standard lipid parameters - LDL-C, HDL-C, TG) had higher odds of being associated with CVD risk ($p < 0.001$), IVD ($p < 0.001$), CKD ($p = 0.01$) and also with hyperuricemia ($p < 0.001$), overweight/obesity ($p = 0.001$) and abdominal obesity ($p = 0.01$) (Table 4).

5. Discussions

The PREDATORR survey was the first national study to assess the prevalence of cardiometabolic risk factors in the Romanian adult population. On the basis of the current analysis of PREDATORR data, an estimated 67.1% of Romanian adults have at least one lipid abnormality. Approximately half, 47.8%, have high LDL-C for their cardiovascular risk category, 29.4% have low HDL-C, more than one-quarter, 27.5% have elevated TG levels, and, among participants with TG ≥ 2.25 mmol/l, 15.2% have elevated Non-HDL-C.

Table 3
Clinical and biological characteristics by lipid disorders.

Variables	No lipid disorders	Isolated HyperLDL-C	Isolated HypoHDL-C	Isolated HyperTG	≥2 lipid disorders
No. participants	839	607	237	104	770
Age (years), mean ± SD	42.1 ± 15.1	52.8 ± 13.9 [#]	42.4 ± 15.9 ^{#E}	47.8 ± 13.8 ^{#&Y}	51.5 ± 13.6 [*]
Male, %	40.4	49.6 [*]	30.8 ^{#E}	68.3 ^{#&Y}	53.4 [*]
Alcohol drinking (yes), %	51.5	59.4 [*]	44.3 ^{#E}	73.8 ^{#&Y}	56.9 [*]
Smoker status (yes), %	42.4	56.7 [*]	46.4 ^{#E}	56.7 [*]	57.8 [*]
Sedentarism (yes), %	19.4	17.2	23.5 ^E	31.1 ^{#&Y}	18.5
BMI (kg/m ²), mean ± SD	25.6 ± 5.5	28.0 ± 5.3 [#]	27.2 ± 5.3 [#]	29.7 ± 6.0 ^{#&Y}	30.1 ± 5.2 [*]
Maximum BMI (kg/m ²), mean ± SD	27.8 ± 5.9	30.0 ± 6.1 [#]	29.2 ± 5.4 [#]	31.4 ± 6.0 ^{#&Y}	31.7 ± 5.5 [*]
Waist (cm), mean ± SD	88.9 ± 16.3	96.3 ± 14.4 [#]	92.5 ± 15.3 ^{#E}	101.5 ± 15.8 ^{#&Y}	102.4 ± 13.3 [*]
FPG (mmol/l), mean ± SD	4.5 ± 1.1	4.9 ± 1.3 [#]	4.8 ± 1.5 [#]	5.1 ± 2.3 ^{#&Y}	5.4 ± 2.0 [*]
HbA1c (%), mean ± SD	5.3 ± 0.6	5.6 ± 0.7 [#]	5.4 ± 0.7 ^{#E}	5.7 ± 1.1 ^{#&Y}	5.9 ± 1.1 [*]
HOMA-IR, mean ± SD	2.0 ± 2.3	2.2 ± 2.2 [#]	2.3 ± 1.7 ^{#E}	3.4 ± 3.2 ^{#&Y}	3.7 ± 3.0 [*]
Impaired glucose regulation, %	16.3	30.0 [#]	22.8 ^{#E}	26.0 [#]	40.4 [*]
Prediabetes, %	10.6	18.3	14.7	12.5	21.8
Known diabetes, %	5.1	8.6	7.1	12.5	14.3
Unknown diabetes, %	0.6	3.1	1.3	1.0	4.3
Uric acid (μmol/l), mean ± SD	273.6 ± 77.3	303.3 ± 83.2 [#]	273.6 ± 71.3 ^{#E}	327.1 ± 89.2 ^{#&Y}	333.0 ± 89.2 [*]
SBP (mmHg), mean ± SD	124.3 ± 16.9	135.1 ± 20.3 [*]	125.8 ± 16.6 ^{#E}	130.2 ± 16.8 ^{#&Y}	136.8 ± 18.8 [*]
DBP (mmHg), mean ± SD	74.7 ± 10.2	80.4 ± 11.3 [*]	75.8 ± 9.6 ^{#E}	78.0 ± 10.9 ^{#&Y}	80.7 ± 11.3 [*]
Framingham 10-year CVD risk (%), mean ± SD	7.4 ± 8.3	14.8 ± 10.4 [#]	8.8 ± 9.1 ^{#E}	11.8 ± 9.9 ^{#&Y}	16.9 ± 10.5 [*]
IVD (%)	10.8	31.1 [*]	14.3 ^{#E}	18 ^{#&Y}	32.2 [*]
Use of statins, %	18.0	18.8	17.7	22.1	17.1
eGFR (ml/min/1.73m ²), mean ± SD	102.8 ± 18.3	95.6 ± 17.4 [*]	104.2 ± 20.5 ^{#E}	98.5 ± 19.0 [#]	94.8 ± 18.3 [*]
ACR ≥30 mg/g, %	2.4	4.1	0.4 ^{#E}	2.9	4.2 [*]
CKD, %	5.1	7.2	3.4 ^{#E}	5.8	8.3 [*]
TC (mmol/l), mean ± SD	4.5 ± 0.7	6.1 ± 1.1 [#]	4.0 ± 0.7 ^{#E}	4.9 ± 0.7 ^{#&Y}	5.8 ± 1.2 [*]
TG (mmol/l), mean ± SD	0.9 ± 0.3	1.1 ± 0.3 [#]	1.0 ± 0.3 ^{#E}	2.2 ± 0.6 ^{#&Y}	2.1 ± 0.7 [*]
HDL-C (mmol/l), mean ± SD	1.6 ± 0.4	1.5 ± 0.3 [#]	1.1 ± 0.2 ^{#E}	1.4 ± 0.2 ^{#&Y}	1.2 ± 0.2 [*]
LDL-C (mmol/l), mean ± SD	2.5 ± 0.6	3.9 ± 1.0 [#]	2.4 ± 0.5 ^{#E}	2.5 ± 0.6 ^{#&Y}	3.7 ± 2.1 [*]
VLDL-C (mmol/l), mean ± SD	0.4 ± 0.2	0.5 ± 0.2 [#]	0.4 ± 0.1 ^{#E}	1.1 ± 0.3 ^{#&Y}	1.0 ± 0.4 [*]

^{*}p < 0.05 for Isolated HyperLDL-C or Isolated HyperTG or Isolated HypoHDL-C or ≥2 lipid disorders category vs No lipid disorders category.

[#]p < 0.05 Isolated HyperLDL-C or Isolated HyperTG or Isolated HypoHDL-C vs ≥2 lipid disorders category.

[&]p < 0.05 for Isolated HyperLDL-C vs Isolated HyperTG.

^Ep < 0.05 for Isolated HyperLDL-C vs Isolated HypoHDL-C.

^Yp < 0.05 for Isolated HypoHDL-C vs Isolated HyperTG.

FPG, fasting plasma glucose; HOMA-IR, homeostasis model assessment for insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein CVD, cardiovascular diseases; IVD, ischaemic vascular disease; eGFR, estimated glomerular filtration rate, ACR, albumin-to-creatinine ratio, CKD, chronic kidney disease.

Table 4
Factors associated with isolated dyslipidemia categories (Multivariate multinomial logistic regression).

Variables	Isolated HyperLDL-C OR(95%CI)	Isolated HypoHDL-C OR(95%CI)	Isolated HyperTG OR(95%CI)	≥2 lipid disorders
Framingham 10-year CVD risk ≥10%	2.8(2.1–3.7) [*]	1.2(0.8–1.8)	1.1(0.6–1.9)	3.4(2.5–4.5) [*]
IVD	1.8(1.4–2.5) [*]	1.3(0.9–2.1)	1.2(0.6–2.0)	1.6(1.2–2.2) [*]
BMI ≥25 kg/m [2]	1.2(0.9–1.8)	1.7(0.9–2.9) [*]	3.1(1.3–7.1) [*]	1.9(1.3–2.8) [*]
Maximum BMI ≥25 kg/m [2]	1.1(0.7–1.8)	1.9(0.9–4.0)	0.9(0.3–2.7)	1.2(0.7–2.1)
Abdominal obesity	1.2(0.8–1.7)	0.9(0.5–1.7)	1.0(0.4–2.3)	1.6(1.1–2.4) [*]
IGR	0.7(0.5–1.0)	1.1(0.7–1.7)	0.9(0.5–1.6)	1.1(0.8–1.4)
Hypertension	1.1(0.8–1.4)	1.1(0.7–1.6)	1.4(0.8–2.4)	0.9(0.7–1.2)
Hyperuricemia	0.9(0.6–1.3)	0.7(0.4–1.3)	1.9(1.1–3.4) [*]	1.9(1.4–2.7) [*]
ACR ≥30 mg/g	2.0(0.8–4.6)	0.1(0.01–1.3)	2.1(0.4–9.8)	1.6(0.7–3.6)
CKD	0.5(0.3–1.0)	1.0(0.5–2.1)	0.5(0.1–1.6)	0.5(0.3–0.8) [*]

OR, odds ratio; CI, confidence interval; BMI, body mass index; CVD, cardiovascular disease; CKD, chronic kidney disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein, IVD: ischaemic vascular disease.

The regression analysis was adjusted for covariates (age, sex, alcohol drinking, sedentariness, smoking status, statin use). "No lipid disorders" was considered reference category. ^{*}p < 0.05.

The most comprehensive assessment of the lipid abnormalities in the United States came from The National Health and Nutrition Examination Survey (NHANES) 2003–2006. In this survey it was estimated that prevalence dyslipidemia (at list one lipid abnormality) was 53% [11]. In France at least one dyslipidemia was detected in 50.8% of all patients [12].

The hyperLDL-Cholesterolemia prevalence in PREDATORR study was 47.8%, higher than the prevalence reported in United States (26.9%), hyperLDL-Cholesterolemia being defined using similar criteria from PREDATORR [11]. It is difficult to compare these results

with the prevalence reported in other studies because there is no currently harmonized threshold of optimal LDL-C.

The hypertriglyceridemia prevalence reported in PREDATORR study (27.5%) was lower than the prevalence estimated in EURO-ASPIRE III study in Europe (34.7%) and Romania (40%) [13], but similar with the prevalence reported in United States (29.6%) [11] and France (28.7%) [12].

The prevalence of the hypoHDL-Cholesterolemia in the adult Romanian population reported in PREDATORR study was higher than the prevalence reported for US, where approximately 23.3% of

the adult population has low HDL-C [11], but lower with the reports from EUROASPIRE III where the estimated prevalence was 36.7% in Europe and 51.5% in Romania [13].

Compared to results reported in the DYSIS (Dyslipidemia International Study), Romanian participants have a higher prevalence of low HDL-C (29.4% vs 26.3%), similar prevalence of elevated LDL-C (47.8% vs 48.2%), and lower prevalence of elevated triglycerides (27.5% vs 38.2%) [12].

The overall age adjusted prevalence of hypercholesterolemia ($TC \geq 5.17$ mmol/l) in the Romanian adult population in PREDATORR study was 60.2%, higher than the global European (51.1%) hypercholesterolemia prevalence ($TC \geq 4.5$ mmol/l) [14]. For the Romanian adult population, the prevalence of hypercholesterolemia was reported to be 40% ($TC \geq 5.17$ mmol/l) in SEPHAR study and 53.2% ($TC \geq 4.5$ mmol/l) in EUROASPIRE III study [13–17].

The discrepancies in the dyslipidemia prevalence pattern may be explained by the different time period when the studies were conducted, diagnostic thresholds and criteria for dyslipidemia phenotypes, or different prevalence of risk factors for dyslipidemia in different populations (presence of CHD, specific age groups) included in the surveys.

Results of PREDATORR study indicated that the lipid profile of Romanian adult population is predominantly atherogenic, characterized by high prevalence of elevated LDL-C, which may explain that Romania is one of the European countries with high cardiovascular risk [18].

In our study hypertriglyceridemia was associated predominantly with metabolic traits such as obesity/overweight, abdominal obesity, known diabetes, insulin resistance and hyperuricemia, while hyperLDL-Cholesterolemia was more related with prediabetes, unknown diabetes, high SBP, IVD and high CVD risk, data that are similar to those reported in other studies [2,3,11,19–21].

These observations highlights the importance of evaluating patients with hypertriglyceridemia for evidence of insulin resistance syndrome and initiating appropriate lifestyle and pharmacologic interventions and the importance of screening patients with elevated LDL-C for IGR and cardiovascular disease.

Given the fact that 14.1% of those with low HDL-C were in the 20–39 years age group, dyslipidemia should be actively identified at age 20 years and older in order to initiate precocious comprehensive management of dyslipidemia. It is important to identify, using novel methods [22], some molecules that would allow early detection of lipid abnormalities and also to identify potential genetic factors involved in the pathogenesis of dyslipidemia [23].

The strengths of the PREDATORR survey are the representativeness of the sample for the Romanian population aged 20–79 years, and the comprehensive diagnosis criteria of dyslipidemia phenotypes used. Furthermore, lifestyle characteristics and anamnestic data were collected using an interviewer–administered questionnaire, and all biochemical assessment were performed in the same certified laboratory.

The cross-sectional design of the PREDATORR survey represents a limitation of the study because it does not allow evaluating the causal relationship between cardiometabolic risk factors and dyslipidemia phenotypes. Another limitation is that the data required to establish the NCEP ATP III categories of hyperLDL-Cholesterolemia does not exactly match the data available in PREDATORR. NCEP ATP III defined family history of premature CHD as CHD in a female first-degree relative <65 years and in a male first-degree relative <55 years, while in PREDATORR study the family history of premature CHD was defined as CHD in first degree relatives <50 years. Also, data regarding symptomatic carotid artery disease and abdominal aortic aneurysm are not available in PREDATORR.

In conclusion, the PREDATORR study, indicate a high prevalence

of dyslipidemia phenotypes in a representative sample of the Romanian adult population and provide data on the relationship of dyslipidemia with important risk factors. These results suggest that dyslipidemia is a significant public health problem and calls for immediate action to initiate the implementation of prevention programs that may reduce the economic burden of dyslipidemia in Romania.

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Conflicts of interest

The authors declare that they have no conflict of interest. The sponsors had no role in the design of the study, in the execution, interpretation of the data or the decision to submit the results.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the Romanian National Ethics Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.dsx.2018.11.033>.

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