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Prevalence of atherogenic dyslipidemia: Association with risk factors and cardiovascular risk in Spanish working population. "ICARIA" study

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ABSTRACT

Objective: The aim of this study was to assess the prevalence of atherogenic dyslipidemia (AD) and the lipid triad (LT) in the working population in Spain, their associated variables and how far they are linked to cardiovascular risk (CVR).

Methods: Observational cross-sectional study of 70,609 workers (71.5% male (M), 28.5% female (F), mean age 39.2 ± 10), who attended medical checkups and agreed to participate. Plasma samples were analysed in a central laboratory. AD definition used was: triglycerides ≥150 mg/dl and HDL cholesterol <40 mg/dl (M)/<50 mg/dl (F) and LT when LDL cholesterol > 160 mg/dl is further added. Univariate comparisons in the absence and presence of AD and LT and the probability of AD according to different parameters and their possible association with CVR were assessed. CVR was stratified following the European SCORE model for low risk-population.

Results: 5.7% (95% CI 4.7–6.9) of the working population have AD and 1.1% (95% CI 1.0–1.2) LT. In univariate analysis, workers with AD and LT had a higher prevalence of obesity, hypertension, smoking and diabetes than those who had not ($p < 0.001$). In multivariate analysis, BMI, sex, age 40–49, diabetes, tobacco, uric acid, LDL or blood pressure significantly influenced the risk of AD. AD was significantly associated with CVR after adjusting for alcohol and obesity. However, most of the AD subjects (91.8%) were classified as low risk.

Conclusions: About 6% of the working population in Spain meets AD criteria. Assuming that these subjects have increased CVR, AD allows to identify additional 5% of subjects with increased CVR to that one the SCORE model detects, helping to improve cardiovascular risk stratification.

1. Introduction

From the epidemiological point of view, the presence of atherogenic dyslipidemia (AD), defined by the presence of elevated triglycerides and low HDL cholesterol (HDL-C), has been independently associated with increased cardiovascular risk in large cohort studies, contributing to residual risk [1–3]. Elevation of LDL small dense particles, contributes to the AD vascular risk. They are not usually detected by routine laboratory methods, and clinical diagnosis is based on the recognition of the first two features [4]. Concomitant elevation in LDL-C and triglycerides with low levels of HDL, is called lipid triad (LT), a highly atherogenic combination [5], where PPARα agonists have shown benefit in primary and secondary prevention [6].

It has been noted that, significantly, major cardiovascular events appear more frequently (51%) in subjects with AD with respect to patients with low isolated HDL concentrations or high triglycerides (33%) or normal HDL cholesterol and triglycerides above normal level [7]. From this evidence, the term residual risk is coined as the

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risk of a cardiovascular event once LDL cholesterol, blood pressure and glucose are controlled, which is also contributed by AD, among other factors [8–10].

The prevalence of AD in the general population is not well known [11]. AD is common in patients with type 2 diabetes, metabolic syndrome and/or cardiovascular disease (CVD) [5,12,13]. In the United States, about two-thirds of coronary heart disease (CHD), or CHD equivalent patients, treated with statins with controlled LDL cholesterol levels, have low levels of HDL cholesterol (<40 mg/dl in men and <50 mg/dl in women), and this remains despite reaching common LDL-c goals aggressively (≤70 mg/dl) [13]. High triglycerides (≥150 mg/dl) are also a common finding, affecting about 50% of adults with previous established CVD [14].

Previous ICARIA Group studies (Ibermutuamur Cardiovascular Risk Assessment) to which this study belongs, have investigated the prevalence of various components of dyslipidemia, and its association with other risk factors in a large sample of the Spanish working population [15–18]. However, the European SCORE model, used to estimate the global cardiovascular risk (CVR), does not provide the triglycerides among predictors [19,20]. This reinforces the importance of assessing their potential in improving the estimation of CVR in the population.

It seems justified, therefore, to investigate the prevalence of AD and LT in our working population, the associated variables and assess the degree of association with cardiovascular risk.

2. Methods

This study is part of the ICARIA study whose detailed description has been published elsewhere [15]. Observational cross-sectional study of 70,609 workers (71.5% male (M), 28.5% female (F), mean age 39.2 ± 10.0), recruited from March 2010 to December 2011, who attended medical checkups in all Spanish Autonomous Communities and agreed to participate in the study.

The AD definition used was: TG ≥ 150 mg/dl and HDL-C <40 mg/dl (M)/<50 mg/dl (F) and LT, AD along with LDL-C above 160 mg/dl. In all cases an interview and anthropometric and biological parameters assessment was carried out [15], obtaining a fasting plasma sample of at least 12 h, which were sent to a central laboratory to perform the measurement of triglycerides and high density lipoprotein (HDL) cholesterol, among other parameters, according to standard protocols. Quality controls recommended by the Spanish Society of Clinical Biochemistry and Molecular Pathology (SEQC) were followed. The coefficient of variation of the main findings remained within the range accepted by the SEQC. LDL cholesterol was calculated by the Friedewald formula [21].

Cardiovascular risk was stratified following the cardiovascular SCORE for low-risk European countries [22] using the equation and coefficients published in Appendix A in which HDL cholesterol was not included. Subjects were classified as low, moderate and high risk [23]. Subjects with CV disease, type 2 diabetes, BP ≥ 180/≥110 mmHg, total cholesterol >320 mg/dl, LDL cholesterol >240 mg/dl and those with relative risk (RR) > 4 were considered high risk [24]. Because albuminuria was not assessed, patients with type 1 diabetes were stratified according to the SCORE model.

The following variables were also assessed: age, gender, type of occupation (white/blue-collar), uric acid (mg/dl), hypertension (previous diagnosis of hypertension or blood pressure > 140/90 mmHg), smoking (non-smoker or ex-smoker; at least one cigarette or pipe per day and people who quit smoking in the last year), alcohol intake (non-drinker or occasional drinker; regular daily moderate or significant drinking), LDL (mg/dl), diabetes (previous diagnosis of diabetes type 1 or type 2 or insulin therapy/oral hypoglycaemic or blood glucose level ≥126 mg/dl), Body Mass Index (BMI; kg/m^2), antihypertensive treatment (yes/no) and lipid lowering therapy (yes/no). The specific occupation of workers was classified into nine major categories according to the 1994 Spanish National Classification of Occupations. Workers in the first four categories were grouped as white-collar workers (non-manual), and workers in the last five categories were grouped as blue-collar workers (manual).

2.1. Statistical analysis

Descriptive statistics were calculated for all variables. For prevalence and categorical variables the results are shown as percentages with 95% confidence intervals (CI). For continuous variables means and standard deviations were used. The values were rounded to the first decimal.

Univariate analyses were performed to compare subjects with and without AD in the different demographic, anthropometric and biological variables. The same strategy was followed to compare subjects with and without the lipid triad. Comparisons on categorical variables were performed using χ^2 test. ANOVA was used to test differences between the two groups on continuous variables.

Multivariate associations of demographic, anthropometric and biological variables with AD were tested. Forward logistic regression (Wald) was used in order to reduce the number of covariates included in the final model.

Finally, crude and adjusted models to predict moderate-to-high vs. low cardiovascular risk were created. Two adjusted models were carried-out: 1) the first one entering gender, age, AD, alcohol and obesity as covariates; and 2) a second model adding LDL-cholesterol to the former set of predictors.

The Bonferroni correction was used to account for multiple comparisons.

All the analyses were carried-out with IBM SPSS Statistics v.17.0.

2.2. Ethical issues

The study was approved by the Ibermutuamur Scientific Ethics Committee and conformed to the international standards of the Declaration of Helsinki. Confidentiality established by the Organic Law on Data Protection was maintained. All participants signed an informed consent.

3. Results

Tables 1A and 1B show the prevalence of AD and LT, highlighting that this affect 5.7% and 1.1% of the Spanish working population, respectively, being higher among males in both cases. The age group most affected (in both men and women), corresponds to the 30–59 age range. In the subgroup of workers with lipid lowering therapy the prevalence rates of AD and LT were 11.1% ($n = 2710$; 95% CI 10–12.4) and 1.9 ($n = 2690$; 95% CI 1.5–2.5), respectively.

Demographic, anthropometric and biological characteristics are shown in Tables 2A and 2B in the presence and absence of AD and LT by gender, showing that age, BMI, waist circumference, glucose, uric acid, lipids (except HDL-C), systolic blood pressure (SBP) and diastolic blood pressure (DBP) values, as well as the prevalence of hypertension, smoking and diabetes were significantly higher in workers suffering AD and LT than those who were free of them. The percentage of workers with lipid lowering therapy or antihypertensive treatment was also higher among subjects with AD and LT. The only exception was the association between LT and lipid lowering therapy among male workers. Such association did not reach the statistical significance.

Multivariate analysis of variables associated with the presence of AD is presented in Table 3. Female gender, BMI ≥ 30 kg/m^2, age between 30 and 49 years-old vs. <30 years-old, diabetes,