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Familial hypercholesterolemia in a European Mediterranean population—Prevalence and clinical data from 2.5 million primary care patients

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BACKGROUND: Familial hypercholesterolemia (FH), the most frequent hereditary cause of premature coronary heart disease (CHD), is underdiagnosed and insufficiently treated.

OBJECTIVES: The objectives of the study were to estimate the prevalence of the FH phenotype (FH-P) and to describe its clinical characteristics in a Mediterranean population.

METHODS: Data were obtained from the Catalan primary care system's clinical records database (Catalan acronym: SIDIAP). Patients aged >7 years with at least 1 low-density lipoprotein cholesterol measurement recorded between 2006 and 2014 (n = 2,554,644) were included. Heterozygous FH-P and homozygous FH-P were defined by untreated low-density lipoprotein cholesterol plasma

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concentrations. The presence of cardiovascular diseases and risk factors was defined by coded medical records from primary care and hospital discharge databases.

RESULTS: The age- and sex-standardized prevalence of heterozygous FH-P and homozygous FH-P were 1/192 individuals and 1/425,774 individuals, respectively. In the group aged 8 to 18 years, 0.46% (95% confidence interval: 0.41–0.52) had FH-P; overall prevalence was 0.58% (95% confidence interval: 0.58–0.60). Among patients with FH-P aged >18 years, cardiovascular disease prevalence was 3.5 times higher than in general population, and CHD prevalence in those aged 35 to 59 years was 4.5 times higher than in those without FH-P. Lipid-lowering therapy was lacking in 13.5% of patients with FH-P, and only 31.6% of men and 22.7 of women were receiving high or very high-intensity lipid-lowering therapy.

CONCLUSION: Prevalence of FH-P was higher than expected, but underdiagnosed and suboptimally treated, especially in women. Moreover, treatment started late considering the high CHD incidence associated with this condition.

Introduction

Familial hypercholesterolemia (FH) is an autosomal dominant disorder associated with premature coronary heart disease (CHD).[1] If untreated, men with FH have a 50% risk of fatal or nonfatal CHD by 50 years of age, whereas untreated women are at 30% risk at 60 years.[1] Prevalence of heterozygous FH (HeFH) and homozygous FH (HoFH) in general population has been estimated at 1:500 and 1:1,000,000 respectively,[2] except in regions with high consanguinity rates, such as South Africa, Lebanon, and Quebec, where prevalence is close to 1/100. However, recent population studies disagree with these classical prevalence rates, reporting estimates of 1/200 to 1/250.[3–6] Despite this uncertainty, FH is a major public health concern, and studies assessing its prevalence and clinical characteristics in Mediterranean populations[7] are lacking.

Knowledge about population prevalence and identification of clinical characteristics related to the FH phenotypes (FH-Ps) associated with high risk of cardiovascular diseases (CVD) is a priority for the development of health policies to minimize the disease burden, both to relieve FH effects on the population and to optimize the use of therapeutic resources. The present study aimed to estimate FH prevalence and to describe its clinical characteristics in a European Mediterranean population.

Methods

Study design

A cross-sectional study was carried out using data from 2,554,644 patients.

Data source

The Information System for the Development of Research in Primary Care (Catalan acronym: SIDIAP) is a clinical database of anonymized longitudinal records containing the information collected from 6,177,972 patients between 2005 and 2014. This database includes information on the clinical activity of 3414 general practitioners and 853 primary care pediatricians in the 274 primary care practices of the Catalan Institute of Health, a public entity providing healthcare coverage to 85% of the population in Catalonia (Spain).[8]

The information recorded includes demographic and lifestyle factors, along with diagnoses (International Classification of Diseases [ICD-10]), hospital discharge information (ICD-9), laboratory tests, and prescribed medications dispensed by community pharmacies. The quality of SIDIAP data for research use has been previously documented, and the database has been widely used to study the epidemiology of CVD and risk factors.[9–11] The authors state that this study complies with the Declaration of Helsinki, and ethics approval for observational research using SIDIAP data was obtained from a local ethics committee.

Inclusion criteria

All SIDIAP records for individuals aged ≥8 years, alive on December 2014, and with at least 1 low-density lipoprotein cholesterol (LDL-C) measurement between 2006 and 2014 were eligible for inclusion.

Exclusion criteria

Patients with a history of hypothyroidism, nephrotic syndrome, or basal triglyceride values ≥400 mg/dL were excluded.

Variables and definitions

Participants were defined as receiving lipid-lowering therapy (LLT) if their records showed at least 2 purchases of statin or ezetimibe within the 6 months before their