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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

LDL-C measurement. Adherence to treatment was calculated according to the Medical Possession Ratio: number of days of statin supply during 6 consecutive months divided by 183 days. The descriptive analysis classified patients' statin or ezetimibe exposure according to the cholesterol reduction capacity of the drug, as follows: low, <30%; moderate, 30% to 50%; high, 50% to 60%; and very high, >60%.[12]

The untreated LDL-C measurement closest to December 2014 in each patient record was used to estimate FH-P prevalence. LDL-C was considered untreated if there was no record of LLT purchases during at least 6 months before the LDL-C test. We used 10 multiple imputations by chained equations to replace missing pretreated LDL-C[13] in individuals with no record of untreated LDL-C (ie, they consistently purchased medication). The imputation of pretreated cholesterol levels for participants on medication at baseline has been shown to yield estimates consistent with reports of randomized clinical trials.[13] The variables included in the imputation model were age, sex, dose and type of LLT, treatment adherence (purchasing record), and the presence of diabetes mellitus. The LDL-C measurement closest to December 2014 was used to describe the level of LDL-C control, independently of LLT treatment.

Definition of case

It was impossible to make a diagnosis based on the full Dutch Lipid Clinic Network score because the SIDIAP database does not include information on familial history of premature CVD, presence of cholesterol deposits, or genetic tests. Thus, we defined FH according to validated age-adjusted LDL-C thresholds[14] and refer to individuals with FH as FH-P patients. In adults, HeFH-P was defined as untreated LDL-C >230 mg/dL for 18- to 30-year-olds; >239 mg/dL for 30- to 39-year-olds, >269 mg/dL for 40- to 48-year-olds, and >255 mg/dL for participants aged >48 years.[14] For all adults, HoFH-P was defined by LDL-C values ≥500 mg/dL.[2] In children and adolescents (aged 8–18 years), FH was defined by LDL-C values >190.[7]

CVD were defined as a composite of CHD (myocardial infarction, cardiac revascularization, or angina), peripheral arterial disease, and stroke. Diagnoses were determined using ICD-10 and ICD-9 codes obtained from primary care and hospital discharge records. The presence of cardiovascular risk factors (CVRF) diabetes mellitus, hypertension, hypercholesterolemia, and smoking were also determined from ICD-10 and ICD-9 codes in primary care and hospital discharge records. The following variables were also obtained from SIDIAP: baseline age, sex, systolic and diastolic blood pressure (SBP and DBP, respectively), body mass index, and laboratory tests: total cholesterol, LDL-C, high-density lipoprotein cholesterol, triglycerides, glucose, glycosylated hemoglobin (HBA1c), and creatinine.

Statistical analyses

Results were expressed as percentages for categorical variables and compared using the chi-square test; continuous variables are reported as mean and standard deviation (SD), or median (quartiles) and compared using Student *t*-test or Mann–Whitney test. Prevalence was standardized by age and sex using the 2014 European population age and sex distribution.[15] The association of CVRF and of CVD with FH-P was assessed using logistic regression models. Statistical analysis was carried out using R software.[16]

Results

At least 1 LDL-C measurement was recorded for each of the 2,764,917 individuals in the SIDIAP database. Of these, 2,554,644 patients fulfilled all inclusion criteria (Supplementary Fig. 1).

The FH-P definition criteria identified 14,699 individuals. The observed global FH-P prevalence was 0.58% (95% confidence interval [CI]: 0.58–0.60), or 1/172 individuals. The age- and sex-standardized prevalence of FH-P was slightly lower: 0.52% (95% CI: 0.51–0.53; 1/192). Prevalence of FH-P by age group and sex are represented in Figure 1. Six patients fulfilled HoFH-P criteria, representing a prevalence of 1/425,774 individuals. Mean (SD) age of these patients was 53.3 years (20.0), 50% of them were women, and mean (SD) LDL-C was 535 mg/dL (29.4). Fifty percent of patients presented hypertension, 1 in 3 presented diabetes. Two participants were under statin therapy, 1 was a current smoker, and none of them presented history of CVD.

Prevalence of FH-P among children aged 8 to 18 years was 0.46% (95% CI: 0.41–0.52; 249 cases in 53,737 individuals). In this age range, 895 individuals had LDL-C >160 mg/dL, considered the clinical threshold to suspect FH in children.

The characteristics of the population with FH-P are compared with the general population in Table 1, showing that patients with FH-P were older and had higher prevalence of CVRF. Mean values for pretreated and treated LDL-C by age group in the population with FH-P are shown in Figure 2. Mean values were higher at younger ages.

Among the FH-P population, 2578 patients had a history of CVD (2077 of them CHD). Considering the general population aged >18 years, patients with FH-P had 3.5 times higher CHD prevalence than the general population, which increased to 4.5 in the group aged 35 to 59 years (mean age 50.3 years); in the subgroup aged 35 to 44 years, the CHD prevalence was 8.2 times higher in women and 6.4 times higher in men, compared with the population without FH-P. Prevalence of CHD by sex, age group, and presence of FH-P is shown in Figure 3. Regardless of the specific CVD analyzed, the prevalence stratified by the presence of FH-P did not differ by sex (Table 2).

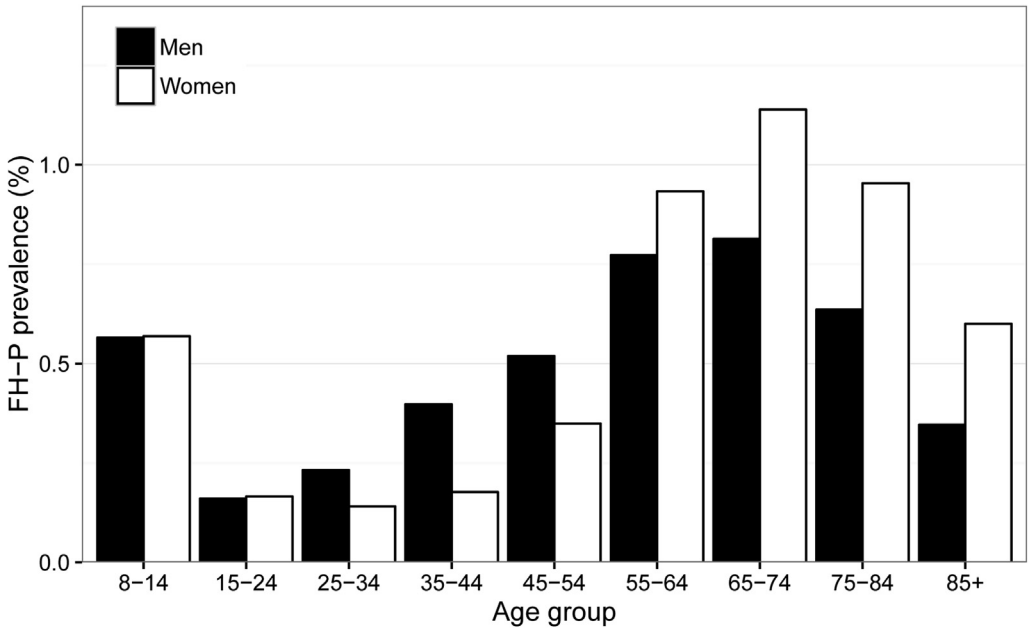

Figure 1 Prevalence of familial hypercholesterolemia phenotype (FH-P) by age and sex.

Clinical characteristics according to presence of CVD are shown in Table 3. In the multivariate analysis, age and classical CVRF, but not sex, were independently associated with the presence of CHD in the population with FH-P (Table 4).

The mean (SD) age at CHD onset was 64.9 (12.4) years for the whole study population, and 60.5 (12.0) years in participants with FH-P. At CHD onset, 31% of individuals were aged <55 years, and 63% were aged >65 years.

Table 1 Comparison of baseline characteristics of population with familial hypercholesterolemia (FH) phenotype and general population

	FH phenotype	General population	*P* value
N	14,699	2,539,944	
Age, mean (SD)	61.5 (15.6)	54.1 (18.7)	<.001
Male sex, %	45.9	47.4	.004
Hypertension, %	50.3	33.6	<.001
Diabetes mellitus, %	19.7	13.1	<.001
Current smoker, %	38.1	35.9	<.001
Obesity, %	25.7	21.1	<.001
BMI, mean (SD)	28.3 (4.8)	27.5 (5.3)	<.001
Personal history of CVD, %	17.5	8.1	<.001
Personal history of CHD, %	11.8	4.8	<.001
Personal history of stroke, %	4.9	2.6	<.001
Personal history of PAD, %	4.3	2.1	<.001
Receiving lipid therapy, %	86.5	19.2	<.001
SBP mm Hg, mean (SD)	130.2 (15.4)	127.1 (15.5)	<.001
DBP mm Hg, mean (SD)	75.9 (10.1)	75.1 (10.3)	<.001
TC mg/dL, mean (SD)	254.7 (65.4)	196.9 (39.5)	<.001
Untreated LDL-C, mg/dL mean (SD)	284.1 (37.2)	129.4 (38.0)	<.001
LDL-C, mg/dL mean (SD) (LLT)	171.9 (60.2)	118.7 (33.8)	<.001
HDL-C, mg/dL mean (SD)	55.3 (13.8)	55.0 (14.9)	<.02
TG, mg/dL mean (SD)	153.9 (91.0)	121.1 (74.9)	<.001
HBA1c, mean (SD)	6.24 (1.4)	6.0 (1.2)	<.001
Creatinine, mean (SD)	0.92 (0.4)	0.9 (0.3)	<.001

BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular diseases; DBP, diastolic blood pressure; HBA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; PAD, peripheral artery disease; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglycerides.

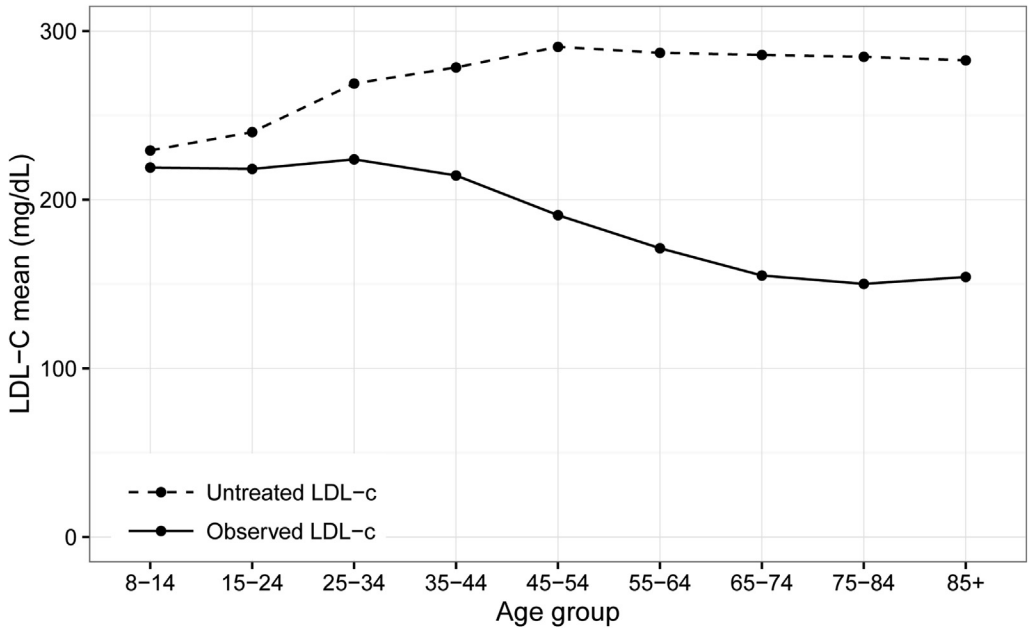

Figure 2 Mean LDL-C values by age in population with familial hypercholesterolemia phenotype (FH-P), with and without lipid-lowering therapy. LDL-C, Low-density lipoprotein cholesterol.

We found that 13.5% of patients with FH-P were not receiving LLT, but the proportion was 48.9% in participants aged >45 years. Among those treated, 73.1% were taking drugs with less than 50% lipid-lowering capacity; 24.5% were receiving high-intensity LLT (50%–60% lipid-lowering capacity); and 2.2% had a combined therapy, with LDL-C lowering potency >60% (Table 5). Mean LDL-C in patients with FH-P was 171.9 mg/dL; mean pretreated LDL-C was 284.1 mg/dL. On average, the percentage of participants who received high and very high-intensity LLT was 9% points lower in women than in men, regardless of age group. The Medical Possession Ratio exceeded 80% in more than half (51.2%) of the study participants with FH-P who were prescribed LLT.

Discussion

This study describes an age- and sex-standardized FH-P prevalence of 1/192 and 1/425,774 individuals (both heterozygous and homozygous, respectively) for the first time in a European Mediterranean population. It is also the first community-based study to assess the prevalence of FH-P in children aged 8 to 18 years. We found that prevalence of CHD was much higher in patients with FH-P than in the general population, despite of this, up to 14.1% of patients with FH-P were not under LLT, a gap that reached 48.9% in participants aged <45 years. These results suggest that FH-P is underdiagnosed and its therapeutic management is suboptimal and starts late.

HeFH-P prevalence

The observed prevalence of HeFH-P in our study is higher than that estimated in earlier studies,[2] similar to that reported in recent years in other populations,[5,6] and very close to that reported in Northern Europe.[3] The age- and sex-standardized prevalence figures were slightly lower than the crude prevalence because study participants were slightly older than the reference population.

The use of age-adjusted LDL-C levels to diagnose FH, in the absence of genetic criteria, has been previously validated in our population, with reported sensitivity values of 91% and positive predictive values (PPT) of 71% for the diagnosis of FH.[14] It appears that current FH-P criteria, based on age-adjusted LDL-C levels, may lead to some overestimation of the actual prevalence, mainly because of polygenic hypercholesterolemia or combined familial hyperlipidemia.

Only 3765 patients with FH are included in the official Catalan registry of FH, representing a very small proportion of all patients with FH according to the observed prevalence in this study, and only 1050 of them had undergone the corresponding genetic examination. This underdetection is comparable to that of other countries with active FH registers.[2]

Also in line with other studies,[5,6] we observed differences in HeFH-P prevalence across age groups. This result suggests that age could modulate the phenotypic expression of the disease,[6] as we based the FH-P diagnosis on LDL-C levels. Although no sex-related differences in FH-P prevalence were observed in children, in 25- to 54-year-olds, the prevalence was lower in women, probably due to the lower LDL-C levels in premenopausal women.[17]

HoFH-P prevalence

We found a higher prevalence of HoFH-P than that classically estimated in hospital patients, registry samples, or calculations using the Hardy–Weinberg equation,[2] and

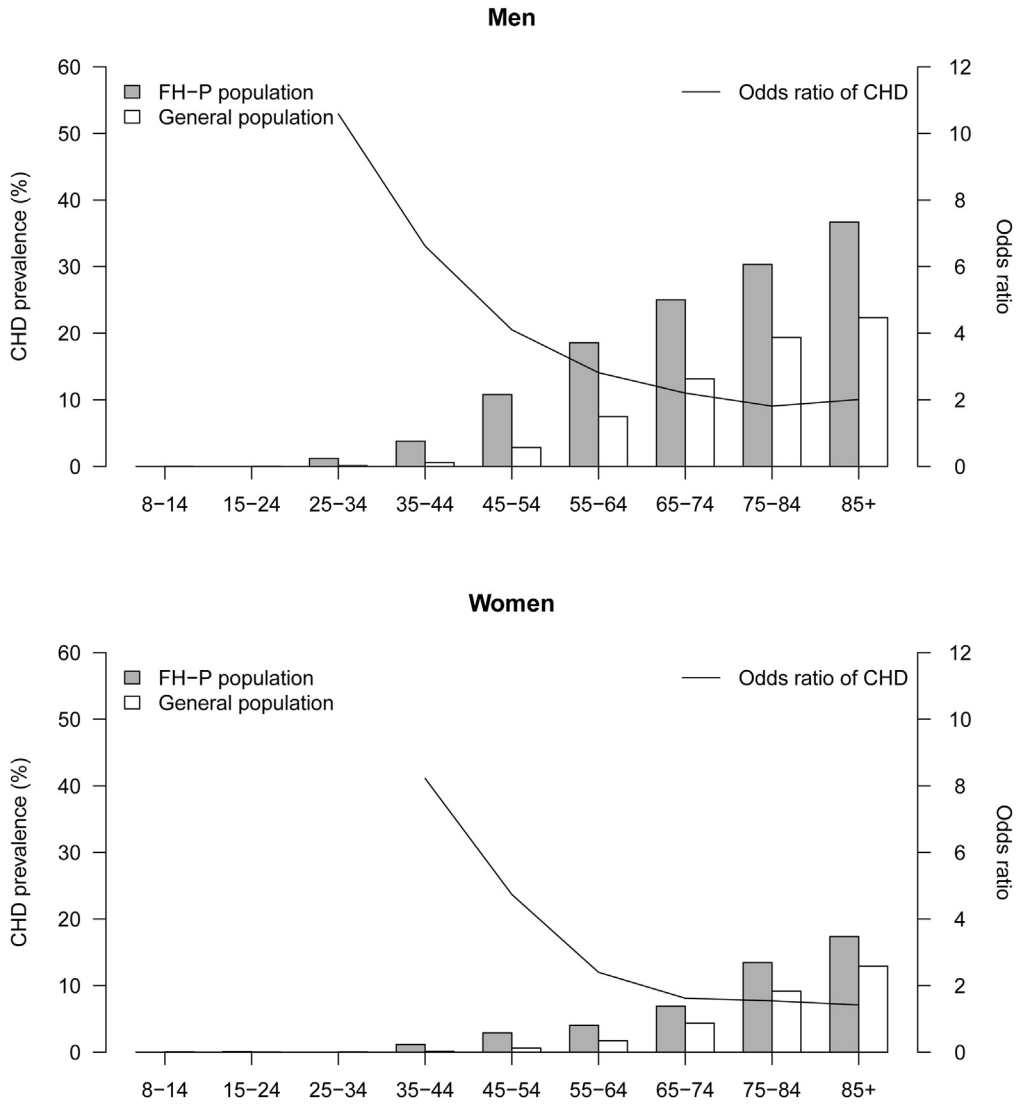

Figure 3 Comparison of coronary heart disease (CHD) prevalence in the population with familial hypercholesterolemia phenotype (FH-P) vs general population, and odds ratio of CHD in the FH-F population with respect to general population, by age and sex.

very similar to that recently described in the Spanish population.[18] Given the variability in the genetic expressiveness of patients with homozygous FH, and the use of LDL-C values >500 mg/dL to define the homozygous FH, null and defective homozygous patients[19] have probably been included in our study.

Table 2 Proportion of cardiovascular diseases by sex in individuals with FH phenotype and general population

Cardiovascular diseases	Sex	FH phenotype	General population	Ratio	*P* value
N	Men	6747	1,203,924		
	Women	7952	1,336,021		
Coronary heart disease	Men	17.6%	7.0%	2.50	.80
	Women	7.0%	2.9%	2.39	
Peripheral artery disease	Men	6.6%	3.3%	2.00	.14
	Women	2.5%	1.2%	2.13	
Stroke	Men	5.9%	3.2%	1.80	.13
	Women	4.1%	2.1%	1.90	
Cardiovascular disease	Men	24.6%	11.2%	2.19	.48
	Women	11.6%	5.4%	2.12	

FH, familial hypercholesterolemia.

Table 3 Comparison of baseline characteristics of population with FH phenotype, with and without CVD

	With CVD	Without CVD	*P* value
N	2578	12,121	
Age mean (SD)	69.3 (11.4)	59.0 (15.9)	<.001
Male sex %	64.3	42.0	<.001
Hypertension %	74.4	45.1	<.001
Diabetes mellitus %	34.8	16.5	<.001
Current smoker %	52.9	35.4	<.001
Obesity %	32.4	24.3	<.001
BMI mean (SD)	29.1 (4.6)	28.2 (4.9)	<.001
Receiving lipid therapy %	97.8	84.1	<.001
SBP mm Hg mean (SD)	132.2 (16.1)	129.9 (15.2)	<.001
DBP mm Hg mean (SD)	74.1 (10.3)	76.3 (10.0)	<.001
TC mg/dL mean (SD)	216.2 (56.2)	262.9 (64.3)	<.001
LDL-C mg/dL mean (SD)	137.0 (49.1)	179.4 (59.8)	<.001
Untreated LDL-C mg/dL mean (SD)	288.0 (35.5)	283.3 (37.5)	<.001
HDL-C mg/dL mean (SD)	50.8 (12.8)	56.3 (13.8)	<.001
TG mg/dL mean (SD)	153.9 (91.2)	154.8 (89.6)	.4
HBA1c mean (SD)	6.5 (1.4)	6.2 (1.3)	<.001
Creatinine mean (SD)	1.06 (0.5)	0.9 (0.3)	<.001

BMI, body mass index; DBP, diastolic blood pressure; HBA1c, glycosylated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, Triglycerides.

Prevalence of FH-P in children

To our knowledge, this is the largest study to estimate FH-P prevalence in a European population including children aged 8 to 14 years. However, only 7% of the Catalan population aged between 8 and 14 years had a lipid test including LDL-C on record, and many of them may have been performed within an FH cascade screening, so we cannot discard some selection bias affecting the prevalence estimation. The FH-P prevalence in this group is slightly lower than that observed in a sample of American children.[20] In general, the only lipid variable measured in children is TC, but we chose to use LDL-C because of its higher potential to diagnose FH-P.[21] Sex-specific LDL-C cut-off values are designed to be the most accurate diagnostic tool to screen the relatives of patients with FH when a genetic diagnosis is absent.[22] The recommendation of a universal screening criterion based on lipid testing in children has generated controversy.[22] Our findings support at least opportunistic screening for the pediatric population, and several authors have proposed that the ideal screening strategy would be the integration of direct and reverse screening cascades.[23]

Table 4 OR for association of coronary heart disease in the population with familial hypercholesterolemia phenotype (multivariate analysis)

Diagnostic	OR (CI)	*P* value
Age (10 y)	1.10 (1.14–1.18)	<.001
LDL-C (20 mg)	2.02 (1.90–2.04)	<.001
Diabetes	2.00 (1.90–2.04)	<.001
Hypertension	1.55 (1.48–1.62)	<.001
Creatinine (1 mg)	1.22 (1.14–1.29)	<.001
Smoking	1.16 (1.10–1.22)	<.001
Obesity	1.06 (1.01–1.11)	.01
HDL-C (10 mg)	1.05 (1.03–1.07)	<.001
Triglycerides (20 mg)	1.03 (1.02–1.03)	<.001
Sex (men)	0.97 (0.92–1.02)	.34

CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio.

FH-P, CVRF, and CVD

Participants with FH-P were older than the general population without FH-P and had a higher prevalence of CVRF. These differences in age and CVRF status coincide with a previous report in the Spanish population.[24] Diabetes mellitus, hypertension, renal function, smoking, and obesity proved to be important risk factors for CVD in patients with FH-P.[2] Hence, a global approach is needed to tackle CVRF levels in this population. However, high-intensity LLT should be the management cornerstone, as we observed a strong association between LDL-C levels and the presence of CHD in patients with FH-P.

The CVRF prevalence in our study is higher than that observed in SAFEHEART, a Spanish cohort study in a population with HeFH (defined by genetic criteria),[24] and moreover, Besseling et al.[25] found a lower prevalence of diabetes in FH individuals than in normolipidemic patients. This discrepancy could be explained by the older age of the FH population in our study. In individuals with FH-P, we would emphasize the observed CVD prevalence of 24.6% in men, (17.6% CHD). In women, the CVD prevalence was 11.6% (7% CHD). There were no differences between men and women with FH-P in CVD prevalence, compared

Table 5 Distribution and use for age and LDL-C value of LLT in patients with familial hypercholesterolemia phenotype

Age groups (y)	N	% Treated	Mean LDL-C (mg/dL)	Low <30%	Moderate, 30%–50%	High, 50%–60%	Very high, >60%
8–14	160	15.6	219	69.5%	19.7%	4.0%	6.8%
15–24	207	28.0	218	23.5%	52.3%	22.1%	2.1%
25–34	452	43.6	224	8.4%	60.9%	24.9%	5.0%
35–44	1221	58.7	214	8.8%	65.1%	21.8%	4.1%
45–54	2024	82.1	191	8.8%	62.6%	26.0%	2.4%
55–64	3775	91.1	171	9.6%	63.3%	24.4%	2.4%
65–74	3920	96.3	155	10.4%	61.9%	25.4%	1.9%
75–84	2296	97.1	150	11.8%	61.9%	24.6%	1.4%
>84	644	96.0	154	15.1%	63.8%	19.8%	1.0%

LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy.

with the general population. These results diverge from a recent systematic review, in which the odds ratios for CHD when comparing patients with FH vs non-FH patients were 10.3 (95% CI: 7.8–13.8) in the subgroup treated with LLT and 13.2 (95% CI: 10.0–17.4) in the nontreated patients.[26] The younger age of the population in our study might explain this discrepancy. Within the population aged 35 to 59 years (with a mean age of 50.3 years), the prevalence of CHD was 4.75 times higher in patients with FH-P, compared with general population. This difference was even more remarkable in women with FH-P. In the 36 to 45 years age group, CHD prevalence was 8.2 and 6.4 times higher in women and men, respectively, than in the general population. The mean age of CVD onset (60.5 years) was higher than expected, probably because of the selection criterion based on LDL-C.

The PAD prevalence in the present study is lower than that described in the Spanish population.[24] The prevalence ratio of ischemic stroke between individuals with FH-P and the general population in our study was also lower than in other studies.[24]

FH-P and LLT

In our study, 13.5% of patients with FH-P were not receiving LLT, a result comparable to other population studies.[4–6] In a recently published study, 20% of patients with FH-P were not treated with LLT.[6] Moreover, only 26.7% of patients with FH-P under LLT received intensive or very intensive treatment. Our results also highlight the low use of combination therapy (ie, a statin plus ezetimibe).[27] It is noteworthy that 48.9% of patients aged 8 to 45 years were not under LLT and only 26.7% of those treated received high-intensity LLT. This is particularly important because 40% of CHD occurs before 54 years of age. This important delay in the start of treatment, often until after the first CVD event, is exacerbated by treatment that has LDL-C reduction capacity lower than needed. Women with FH-P receive even less potent LLT than men, calling attention to sex-related differences, as in other aspects of CVD management.[28] Another aspect to emphasize is the low adherence to treatment. Only 51.2% of FH-P participants reported high LLT adherence, similar to other studies.[29]

If treatment were started before 18 years of age, the LDL burden in patients with FH could be delayed by 5 years compared with current initiation in older patients.[30] Only 13% of children aged between 8 and 18 years with FH-P received statin treatment in our study, compared with 65% of the patients listed in the FH pediatric register in the United Kingdom.[30] This clearly indicates an underdiagnosis and undertreatment in our pediatric population.

Clinical implications

In our study, age-adjusted LDL-C thresholds were useful to screen FH. Considering that LDL-C assessment is frequently done in clinical practice, a high proportion of individuals with FH-P could be identified in primary healthcare settings.[31] Using electronic health records data, we detected 3.9 times more patients with FH-P than were recorded in the official FH Register. Our results also support opportunistic phenotypic screening in pediatric populations, together with the use of reverse screening.[32] Further research is required to determine the optimal cut-off points of LDL-C values to identify FH-P by sex. A better understanding of the specific characteristics of FH-P should enable the detection of those patients with FH-P at higher risk of CVD.

Strengths and limitations of the study

SIDIAP includes epidemiologic and medical data from 85% of the Catalan population; it has enormous potential to provide a global vision of the FH epidemiology based on real-world data. Our study population included all individuals who had an LDL-C test in the last 10 years, which was 53.8% of our general population aged older than 7 years and 68.2% in subjects aged older than 45 years; hence, we cannot discard some selection bias, especially at younger ages. Another limitation of the study is the lack of availability of lipoprotein (a) measurements because high levels of it have been implied in the diagnostic of FH.[33]

Conclusions

Prevalence of FH-P in Southern Europe was higher than initially expected. This disease is underreported and application of the otherwise helpful genetic studies is scarce. FH-P treatment is suboptimal, especially in women, and could be considered at a younger age, given the high incidence of CVD associated with FH.

Each author is required to declare his or her individual contribution to the article: all authors must have materially participated in the research and/or article preparation, so roles for all authors should be described. The statement that all authors have approved the final article should be true and included in the disclosure.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jacl.2017.05.012.

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