Atherosclerosis 277 (2018) 304–307

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Preliminary data of familial hypercholesterolemia (FH) patients in Romania

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HIGHLIGHTS

- We have enrolled 59 patients (0.7%) who had a FH score above 3.
- The mean LDL-c level upon enrollment was 229.84 mg/dl for the untreated patients.
- 91.52% of the patients had a possible FH score, while 6.7% a probable FH score and 1.6% had a definite FH score.
- Based on this data the prevalence of FH in Romania is: 1:213.

ARTICLE INFO

Keywords:
Familial hypercholesterolemia
Atherosclerosis
FHSC
Romania

ABSTRACT

Background and aims: Familial hypercholesterolemia (FH) is one of the most frequent monogenic cholesterol disorders. Its prevalence varies in adults between 1/500–1/217 individuals in the heterozygous form. The objective of this study was to uncover the FH prevalence in Romania to perform an adequate prevention for high risk individuals.

Methods: We have conducted an epidemiological study between January 2015 and January 2018 by recruiting patients from the CardioPrevent Foundation based on their FH score (taking into account their low density lipoprotein cholesterol (LDLc) levels, clinical characteristics such as premature coronary artery disease (CAD), and their family history of premature cardiovascular disease). We have calculated the probability of FH using the Dutch Lipid Clinic Network (DLCN) criteria and we have included patients with a score over 3 points.

Results: We have enrolled 59 patients, out of whom 61% were females. 8.4% of the patients recruited had a first degree relative with premature coronary artery disease and 5% had a relative with LDLc > 190 mg/dl (without statin treatment). 10.16% of the patients had coronary artery disease and 15.25% peripheral vascular disease. 91.52% of the patients had a possible FH, while 6.7% had a probable FH and 1.6% a definite FH diagnosis. Based on this data, the prevalence of FH in Romania is: 1:213.

Conclusions: To raise the suspicion for FH is easy at the level of the general practitioners, based on the analysis of LDLc levels and premature CAD occurrence. Diagnosis can be further refined using an available online free software.

1. Introduction

Familial hypercholesterolemia (FH) is a worldwide spread inherited disease with two main characteristics: its transmission is dominant autosomal, the offspring of an affected person having 50% chance of inheriting the disease, and low density lipoprotein cholesterol (LDLc) levels that are persistently and significantly higher than in the general population since early childhood [1]. This last feature leads to early atherosclerotic lesions, exposing patients with FH to a particularly high cardiovascular (CV) risk. This disease causes a dramatic 100-fold increase in coronary mortality among young patients (aged 20–40) [2]. It is estimated that the 30-year risk of having a CV event in FH patients is up to 5 times higher than in the general population [3], the severity of atherosclerotic lesions due to this monogenic lipid disorder being higher than in polygenic dyslipidemia [4]. On average, carriers of a low density lipoprotein cholesterol receptor (LDLR) mutation have coronary artery disease (CAD) 11 years earlier than their counterparts without this mutation [5]. The mean age of developing CAD is 35 years in

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https://doi.org/10.1016/j.atherosclerosis.2018.08.015
Received 30 March 2018; Received in revised form 26 July 2018; Accepted 21 August 2018

heterozygous FH patients [1].

Most importantly, with recommended optimal treatments, the CV risk of these patients might be significantly lowered to not being different from the risk in the general population [1]. Data from a prospective registry study in the United Kingdom showed an important reduction in CAD mortality in FH patients treated with statins, mainly in primary prevention and in women [6]. LDLc treatment targets are the same for FH patients as for other patients with high/very high risk of CV events: LDLc < 2.5 mmol/l (100 mg/dl) in FH patients without CAD or major CV risk factors and < 1.8 mmol/l (70 mg/dL) in FH patients with CAD or other major CV risk factors [7].

The reported prevalence of heterozygous FH ranges from 1/500 persons [8] to 1/217 persons in a recent Danish report [5], reported most often as 1:250. A study on the prevalence of heterozygous FH in the US, using the Dutch Clinic Lipid Network (DCLN) criteria for diagnosis, found that FH affects 1 in 250 Americans [9].

The level of knowledge about the FH population is rather scarce across Europe and there are still existing countries where little is known about FH. Romania is a great example of such a country, although in the last few years large efforts have been made to improve the situation. Since 2016, Romania has joined the Familial Hypercholesterolemia Studies Collaboration (FHSC) program, which aims to create national registries on FH patients to raise awareness for this disease and offer a better opportunity for treatment [10]. This registry is the base of our current study.

Our study aims to uncover the prevalence of FH patients in the setting of a cardiology private practice in Romania and describe the baseline characteristics of patients with FH.

2. Materials and methods

We have conducted an epidemiological retrospective study between January 2015 and January 2018 among consecutive patients admitted to our ambulatory practice, for a cardiology consultation. Data was collected from our electronic database ICMed, including, age, gender, laboratory test results (LDLc levels), recorded history of CAD or peripheral vascular disease (premature cerebrovascular atherosclerosis or peripheric arteriopathy), and prescription of statin medication. The majority of the patients included were not on statin therapy upon inclusion and, for those who were, we calculated their baseline LDLc levels by multiplying x 1.43 their current LDLc levels [9]. Other comorbidities such as hypertension or diabetes mellitus were not taken into account for this analysis.

Using the information from the patient records, we have calculated the DCLN score [11], which includes assessment of LDLc concentrations, clinical characteristics such as peripheral vascular disease and premature CAD, presence or absence of tendon xanthoma or arcus cornealis, and a family history of premature heart disease. The score determines the probability of an FH diagnosis as unlikely (< 3 points), possible (3–5 points), probable (6–8 points), or definite (> 8 points). Since genetic testing is not routinely possible in Romania, the diagnosis was solely based on the clinical DCLN score.

The inclusion criteria in this study was an FH score over 3 points indicating at least a possible FH diagnosis. All patients who did not meet these criteria were excluded from the study.

Descriptive statistics was calculated to describe patient characteristics. All analysis and results were calculated using the SPSS software. Descriptive statistics was used because the population involved was small and it may not have the same metabolic characteristics as the general population.

3. Results

Out of 8329 patients examined between January 2015 and January 2018 (Fig. 1), we have enrolled 59 patients (0.7%) who had an FH score above 3 (Fig. 2). The majority of the patients were not on statin

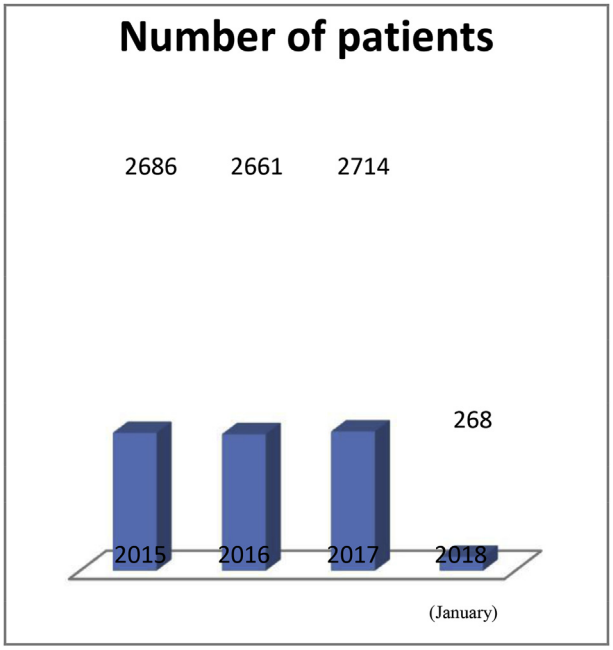

Fig. 1. Number of patients examined per year.

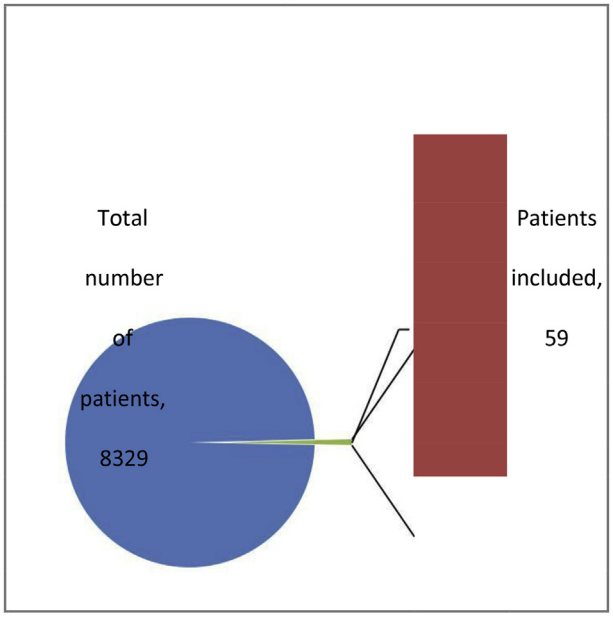

Fig. 2. Patients enrolled in our study.

treatment upon inclusion (88%). The mean LDLc level upon enrollment was 229.84 mg/dl for the untreated patients and 158.33 mg/dl for the treated patients. Taking into account that statin treatment would decrease LDLc levels by 30%, this corresponds to a mean value of 226.41 mg/dl before treatment. As previously mentioned, we calculated their baseline LDLc level by multiplying x 1.43 their current LDLc level [9].

61% of the patients included were females. The mean age was 54.9 years. Regarding the history of heredocolateral events, 8.4% of the patients had a first degree relative with premature CAD, while 5% had a relative with LDLc > 190 mg/dl. Personal history accounted for CAD in 10.16% of the patients and 15.25% had peripheral vascular disease (out of whom 6.7% had subclinical carotid atherosclerosis). (Fig. 3).

LDLc levels were measured before statin treatment and the cut-off value was above 190 mg/dl. For the few patients who were on statin