Journal of Clinical Lipidology (2018) ■, ■–■

Journal of Clinical Lipidology

Original Article

Prevalence, management, and outcomes of familial hypercholesterolemia in patients with acute coronary syndromes in the Arabian Gulf

Q4 Khalid Al-Rasadi*, Ibrahim Al-Zakwani, Alawi A. Alsheikh-Ali, Wael Almahmeed, Q1 Wafa Rashed, Mustafa Ridha, Raul D. Santos, Mohammad Zubaid

Department of Biochemistry, Sultan Qaboos University Hospital, Muscat, Oman (Dr Al-Rasadi); Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman (Dr Al-Zakwani); Gulf Health Research, Muscat, Oman (Dr Al-Zakwani); College of Medicine, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, UAE (Dr Alsheikh-Ali); Institute of Cardiac Sciences, Sheikh Khalifa Medical City, Abu Dhabi, UAE (Dr Alsheikh-Ali); Heart and Vascular Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, Q2 *UAE (Dr Almahmeed); Department of Medicine, Mubarak Al–Kabeer Hospital, Ministry of Health, Kuwait (Dr Rashed); Department of Medicine, Al–Adan Hospital, Ministry of Health, Kuwait (Dr Ridha); Lipid Clinic Heart Institute (InCor), University of Sao Paulo Medical School Hospital, Sao Paulo, Brazil (Dr Santos); Preventive Medicine Center and Cardiology Program, Hospital Israelita Albert Einstein, Sao Paulo, Brazil (Dr Santos); and Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait (Dr Zubaid)*

KEYWORDS:
Acute coronary syndrome;
Hypercholesterolemia;
Cardiovascular abnormality;
Diabetes;
Middle East;
Arabs

BACKGROUND: Information on the epidemiology of familial hypercholesterolemia (FH) in the Arabian Gulf region, which has an elevated rate of consanguinity and type II diabetes, is scarce.

OBJECTIVES: To assess the prevalence of FH, its management, and impact on atherosclerotic cardiovascular disease (ASCVD) outcomes in a multicenter cohort of Arabian Gulf patients with acute coronary syndrome (ACS).

METHODS: Patients (N = 3224) hospitalized with ACS were studied. FH was diagnosed using the Dutch Lipid Clinic Network criteria. A composite endpoint of nonfatal myocardial infarction, stroke, transient ischemic attack, and mortality between the "probable/definite" and the "unlikely" FH patients was assessed after 1 year. Analyses were performed using univariate and multivariate statistical techniques.

RESULTS: At admission, the proportion of "probable/definite", "possible", and "unlikely" FH in ACS patients was 3.7% (n = 119), 28% (n = 911), and 68% (n = 2194), respectively. Overall, 54% (n = 1730) of patients had diabetes, whereas 24% (n = 783) were current smokers. The "probable/definite" FH group was younger (50 vs 63 years; $P < .001$), had a greater prevalence of early coronary disease (38% vs 8.8%; $P < .001$), and previous statin use (87% vs 57%; $P < .001$) when compared with the "unlikely" FH group. After 1 year, the "probable/definite" FH cohort had worse lipid control (13% vs 23%; $P < .001$) and presented with a greater association with the composite ASCVD endpoint when

Funding: Gulf COAST is an investigator-initiated study that was supported by AstraZeneca and Kuwait University (project code XX02/11). Neither Kuwait University nor AstraZeneca had any role in the study design, data collection, data analysis, or writing the article.

* Corresponding author. Department of Biochemistry, Sultan Qaboos University Hospital, P.O. Box 38, Al-Khod, Muscat 123, Oman.
E-mail address: k.alrasadi@gmail.com

Submitted September 12, 2017. Accepted for publication February 8, 2018.

https://doi.org/10.1016/j.jacl.2018.02.003

compared with the "unlikely" FH group (odds ratio: 1.85; 95% confidence interval: 1.01–3.38; $P = .047$) after multivariable adjustment.

CONCLUSIONS: In Arabian Gulf citizens, FH was common in ACS patients, was undertreated, and was associated with a worse 1-year prognosis.

Introduction

Familial hypercholesterolemia (FH) is more frequently found in patients with acute coronary syndrome (ACS) as suggested by some cross-sectional studies[1–5] and has been associated, in a prospective Swiss cohort, with worse in-hospital prognosis and recurrent atherosclerotic cardiovascular disease (ASCVD) events.[2,3] Nonetheless, FH remains largely underdiagnosed worldwide in the general population.[6,7]

Studies in Europe have shown that FH patients in the general population[6–8] and specially after an ACS event[2,3,9] are undertreated with lipid-lowering drugs (LLDs), and most patients fail to reach recommended low-density lipoprotein cholesterol (LDL-C) targets.[10–13]

There are currently no data available on the epidemiology of FH in ACS in the Arabian Gulf, a region where there is high prevalence of both consanguinity,[14,15] which is an important risk factor for FH, and type II diabetes,[16,17] a condition that severely aggravates the prognosis after an ACS event. Therefore, this study assessed the prevalence of FH, its management and ASCVD outcomes in a large multicenter cohort of Arabian Gulf patients who presented with ACS.

Methods

Study population

Details of the methods of the Gulf locals with ACS events (Gulf COAST) registry have been reported previously.[18] Briefly, Gulf COAST registry is a prospective, multicenter, multinational, longitudinal, observational, cohort-based registry of consecutive citizens, from the Gulf region of the Middle East, (Bahrain, Kuwait, Oman, and United Arab Emirates) admitted from January 2012 to January 2013 to 29 hospitals with a diagnosis of ACS. The registry enrolled a total of 4061 patients who were citizens, 18 years of age or older with ACS diagnosed according to American College of Cardiology clinical data standards.[19] Apart from excluding noncitizens and those who were not willing/able to sign an informed consent, there were no other exclusion criteria. An attempt was made to recruit all comers. This study was approved by the local institutional ethics committees of participating centers.

Diagnosis of FH

The diagnosis of FH was based on the Dutch Lipid Clinic Network (DLCN) criteria,[20] which consists of a point score system and includes information about personal and first-degree relatives with high LDL-C, tendon xanthomas, and premature coronary heart disease (CHD). Tendon xanthomas and genetic mutations were scored zero in this study because of the unavailaibility of information about these parameters. Definitive FH score was defined as >8 points, probable 6–8, possible 3–5, and unlikely <3. Owing to the small number of patients with definitive and probable FH, these 2 groups were combined as one "definitive/probable". The LDL-C on admission was corrected for prior statin use by multiplying a factor of 1.43 that considers an average 30% reduction in LDL-C by the use of average doses of statins as previously reported in similar studies.[21,22]

Data collection and clinical outcomes

Data collected included patient demographics, previous ASCVD history and risk factors, prior medication use, laboratory data, clinical presentation and management during hospital stay including medications, reperfusion therapy and procedures, and discharge medications. Follow-up was performed at 1, 6, and 12 months from the date of enrollment and was carried out by clinic visits or telephone interviews. ASCVD events during follow-up were defined as the first occurrence of the composite endpoint of nonfatal myocardial infarction, atherothrombotic stroke, transient ischemic attack, or mortality after hospital discharge.

Statistical analysis

For categorical variables, frequencies and percentages were reported. Differences among groups were analyzed using Pearson's χ^2 tests (or Fisher's exact tests for cells <5). For continuous variables, mean and standard deviation were used to present the data while analyses were performed using univariate ordinary least squares regression. The association between ASCVD event and FH status was evaluated by multivariable logistic regression utilizing the simultaneous method and adjusting for age, sex, body mass index (BMI), smoking, hypertension, and diabetes mellitus.[21–23] The goodness of fit of the multivariable logistic model was examined using the Hosmer & Lemeshow goodness-of-fit statistic[24] as well as the *C*-index.[25] An a *priori* 2-tailed level of significance was set at the 0.05 level. Statistical analyses were conducted using STATA version 13.1 (StataCorp, 2013, Stata Statistical Software, College Station, TX, USA).