Journal of Clinical Lipidology (2016) 10, 368–377

Journal of Clinical Lipidology

Non–high-density lipoprotein cholesterol target achievement in patients on lipid-lowering drugs and stratified by triglyceride levels in the Arabian Gulf

Khamis Al-Hashmi, MD, PhD, Ibrahim Al-Zakwani, PhD, Wael Al Mahmeed, MD, Mohammed Arafah, MD, Ali T. Al-Hinai, MD, Abdullah Shehab, MD, Omer Al Tamimi, MD, Mahmoud Al Awadhi, MD, Shorook Al Herz, MD, Faisal Al Anazi, MD, Khalid Al Nemer, MD, Othman Metwally, MD, Akram Alkhadra, MD, Mohammed Fakhry, MD, Hossam Elghetany, MD, Abdel Razak Medani, MD, Afzal Hussein Yusufali, MD, Obaid Al Jassim, MD, Omar Al Hallaq, MD, Fahad Omar Ahmed S. Baslaib, MD, Haitham Amin, MD, Raul D. Santos, MD, PhD, Khalid Al-Waili, MD, Khalid Al-Rasadi, MD*

Department of Physiology, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman (Dr Al-Hashmi); 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); Heart and Vascular Institute –Cleveland Clinic, Abu Dhabi, UAE (Dr Al Mahmeed); King Saud University Hospital, Riyadh, KSA (Dr Arafah); Ministry of Health, Muscat, Oman (Dr Al-Hinai); UAE University, AlAin, UAE (Dr Shehab); Hamad Medical Corporation, Doha, Qatar (Dr Al Tamimi); Al Amiri Hospital, Kuwait City, Kuwait (Dr Al Awadhi); King Fahad National Guard Hospital, Riyadh, KSA (Dr Al Herz); Ministry of Health, Riyadh, KSA (Dr Al Anazi); Al–Imam Mohammad Ibn Saud Islamic University (IMSIU), School of Medicine, Riyadh, KSA (Dr Al Nemer); King Fahad General Hospital, Jeddah, KSA (Dr Metwally); King Fahad Hospital of the University, Khobar, KSA (Drs Alkhadra, Fakhry); Soliman Fakieh Hospital, Jeddah, KSA (Dr Elghetany); Dubai Hospital, Dubai, UAE (Drs Medani, Yusufali, Al Jassim); American Hospital, Dubai, UAE (Dr Al Hallaq); Rashid Hospital, Dubai, UAE (Dr Baslaib); Bahrain Defense Force Hospital, Manama, Bahrain (Dr Amin); Lipid Clinic Heart Institute (InCor), University of Sao Paulo Medical School Hospital, Sao Paulo, Brazil (Dr Santos); and Department of Biochemistry, Sultan Qaboos University Hospital, Muscat, Oman (Drs Al-Waili, Al-Rasadi)

KEYWORDS:
Cardiovascular diseases;

BACKGROUND: Atherogenic dyslipidemia is highly prevalent in the Arabian Gulf. Non–high-density lipoprotein cholesterol (non-HDL-C) reduction has been proposed as an additional goal to low-density

The CEPHEUS project was sponsored by AstraZeneca. The sponsor had no involvement in the study conception or design; analysis or interpretation of data; writing, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

* 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 August 25, 2015. Accepted for publication December 16, 2015.

http://dx.doi.org/10.1016/j.jacl.2015.12.021

HDL cholesterol;
Triglycerides;
Non-HDL cholesterol;
LDL cholesterol;
Apolipoprotein B;
Diabetes mellitus;
Middle East

lipoprotein cholesterol (LDL-C) lowering to prevent atherosclerotic cardiovascular disease (ASCVD). Data on non–HDL-C goal attainment in patients with high triglycerides (TGs) on lipid-lowering drugs (LLDs) in the region is scarce.

OBJECTIVE: Evaluate non–HDL-C target attainment according to the National Lipid Association in patients on LLDs stratified by TG (<150 [1.69], 150–200 [1.69–2.26], >200 [2.26] mg/dL [mmol/L]) levels in the Arabian Gulf.

METHODS: Overall, 4383 patients on LLD treatment from 6 Middle Eastern countries participating in the Centralized Pan-Middle East Survey on the Undertreatment of Hypercholesterolemia study were evaluated. Patients were classified according to TG levels and ASCVD risk.

RESULTS: The overall non–HDL-C goal attainment was 41% of the subjects. Non–HDL-C goal was less likely attained in patients with high TGs (12% vs 27% vs 55%; $P < .001$). Very high ASCVD risk patients with high TGs attained less their non–HDL-C targets compared with those with lower TG levels (8% vs 23% vs 51%; $P < .001$). Similarly, high ASCVD risk patients with high TGs also failed more in attaining non–HDL-C targets compared with those with lower TGs (26% vs 42% vs 69%; $P < .001$). In addition, those with high TG also succeeded less in attaining LDL-C and apolipoprotein B goals ($P < .001$).

CONCLUSIONS: A large proportion of very high and high ASCVD patients on LLDs in the Arabian Gulf are not at recommended non–HDL-C targets and hence remain at a substantial residual risk.

Introduction

Non–high-density lipoprotein cholesterol (non-HDL-C) represents the cholesterol carried by all atherogenic particles[1] and is a good surrogate marker for triglyceride (TG) and TG-rich lipoprotein particles.[2] Although there is modest evidence for the association between fasting TG and atherosclerotic cardiovascular disease (ASCVD) risk, recent data suggest a stronger association between TG-rich lipoprotein particles and ASCVD.[3–5]

There is evidence that non–HDL-C is a better risk estimator than low-density lipoprotein cholesterol (LDL-C) in patients with high TG combined with diabetes mellitus, metabolic syndrome (MetS), or chronic kidney disease.[6] Moreover, non–HDL-C is considered a stronger predictor of ASCVD morbidity and mortality,[7] and changes in non–HDL-C levels are even a better predictor of coronary heart disease (CHD) events than on treatment levels of LDL-C in subjects receiving lipid-lowering therapy.[8,9] Therefore, several guidelines recognize non–HDL-C as a secondary therapeutic target particularly in patients with hypertriglyceridaemia.[10–14] The US National Lipid Association (NLA) in its recent published recommendation, recognizes both non–HDL-C and LDL-C as primary therapeutic targets.[15] In addition, a secondary optional target, apolipoprotein B (Apo B), a marker of proatherogenic lipoproteins, is also considered.

Data on non–HDL-C goal attainment stratified by TG and ASCVD in patients undergoing lipid-lowering therapy in the Arabian Gulf are scarce.[16] The main objective of this study was to evaluate non–HDL-C therapeutic target achievement in patients on lipid-lowering drugs (LLDs) stratified by TG levels in the Arabian Gulf region. Patients were also stratified according to ASCVD risk. The attainment of recommended LDL-C and Apo B targets was also evaluated.

Methods

The methods have already been previously described.[17] Briefly, the Centralized Pan-Middle East Survey on the Undertreatment of Hypercholesterolemia study (CEPHEUS) was a multicenter noninterventional survey of patients on LLDs in 6 Middle Eastern countries (Saudi Arabia, United Arab Emirates, Oman, Qatar, Bahrain, and Kuwait). A total of 5457 patients from outpatient clinics were enrolled in the survey by 177 specialists and primary care physicians. The study was conducted between November 22, 2009, and July 7, 2010. The inclusion criteria were age ≥18 years; use of LLDs for ≥3 months, with no dose change on the last 6 weeks.

A fasting blood sample was taken from each subject for measurement of total cholesterol, HDL-C, LDL-C, TG, apolipoprotein A1 (Apo A1), Apo B, glucose, and glycated hemoglobin A1c (HbA1c). Blood samples were collected in 3 tubes (5 mL in a gel tube, 2 mL in a fluoride tube, and 2 mL in an EDTA tube). Blood samples were shipped by air courier, and the tests were performed at the King Faisal specialist Hospital and Research Centre (Riyadh, Saudi Arabia). All laboratory tests underwent internal and external quality control checks. Low HDL-C was defined as levels of <40 mg/dL (1.0 mmol/L) for men and <50 mg/dL (1.3 mmol/L) for women.[15] TG levels were stratified into "normal" (<150 mg/dL [1.69 mmol/L]), "borderline" (150–200 mg/dL [1.69–2.26 mmol/L]), and "high" (>200 mg/dL [>2.26 mmol/L]).[15]

Criteria for ASCVD risk status was derived from the NLA recommendations for patient-centered management of dyslipidemia Part 1–Executive Summary.[15] High-risk group included patients with ≥3 major ASCVD risk factors, diabetes mellitus (type 1 or 2) with 0/1 other major ASCVD risk factor, or LDL-C ≥190 mg/dL (5.02 mmol/L; severe hypercholesterolemia). Very high-risk group