EDITORIAL

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Dyslipidemia in the Arabian Gulf and its Impact on Cardiovascular Risk Outcome

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Cardiovascular disease (CVD) is considered the most common cause of death in the Arabian Gulf accounting for up to 45% of all mortalities.[1] Risk factors for CVD, like dyslipidemia and smoking, are prevalent in young Arab populations. The Gulf Registry of Acute Coronary Events (Gulf RACE)[2] and the INTERHEART[3] studies have shown that the first presentation of acute myocardial infarction (AMI) in this population is 10–12 years earlier than in their Western counterparts.[3]

The presence of high low-density lipoprotein (LDL-C) levels is a strong independent risk factor for CVD in several populations worldwide.[4] Therefore, LDL-C is accepted by several guidelines to be the primary target of cholesterol-lowering therapy.[5-9] However, in the Arabian Gulf, a significant proportion of patients on lipid-lowering drugs (LLDs), mainly those considered to be in the high and very high-risk groups for CVD, are not at their recommended therapeutic LDL-C targets. This was evident from the Centralized pan-Middle East Survey on the undertreatment of hypercholesterolemia (CEPHEUS), which was conducted in 5,276 patients in six Arabian Gulf countries on LLDs. The LDL-C goal was attained in 91.1% of low-risk, 52.7% of high-risk, and 32.0% of very high-risk category patients.[10] In a study conducted in 160 dyslipidemic patients in Oman the LDL-C goal was achieved in only 43% of high-risk, 50% of moderate risk, and 90% of low-risk patients.[11]

There is a high prevalence of diabetes mellitus (DM) and metabolic syndrome (MetS) in the Arabian Gulf in patients with acute coronary syndrome (ACS).[12,13] Atherogenic dyslipidemia in these populations is characterized by high triglyceride (TG), low high-density lipoprotein cholesterol (HDL-C), and elevated levels of small, dense LDL particles.[14] Patients with these pro-atherogenic lipoproteins remain at a higher risk for residual cardiovascular disease despite attaining optimal LDL-C targets.[15,16] In the Gulf RACE survey, 62% of patients with ACS had low HDL-C. This figure was the highest reported in studies on ACS in the region, which ranged from 28% to 57%.[17] Moreover, in this study, in-hospital mortality and cardiogenic shock were significantly associated with low levels of HDL-C. Other predictors of low HDL-C levels were a higher body mass index (BMI), prior myocardial infarction, DM, smoking, and renal impairment.[17] Despite the lack of evidence from clinical trials on the benefit of raising HDL-C levels to reduce CVD events,[18] low HDL-C remains a target for intervention, but mainly through lifestyle therapies especially exercise[19] and smoking cessation.[20]

Beyond LDL-C, both non-HDL-C and apolipoprotein B (ApoB) are considered important lipid markers for not only LDL particles but also for TG-rich lipoprotein concentrations, CVD risk prediction, and monitoring the efficacy of LLDs especially in patients with DM and MetS.[21,22] Both markers can be measured in the non-fasting state, but non-HDL-C is usually calculated by substracting the HDL-C concentration from the total cholesterol concentration. ApoB, however, is directly measured making the non-HDL-C a more preferable marker for monitoring lipid targets particularly in terms of cost. Patients with high non-HDL-C levels remained at an increased risk for cardiovascular events despite achieving low LDL-C levels[23] and, therefore, several guidelines recommend non-HDL-C as an additional therapeutic target particularly in patients with high triglyceride after reaching their primary LDL-C target.[5-9] However,

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in the Arabian Gulf, a large proportion of patients on LLDs in the high and very high-risk groups for CVD are not at their recommended therapeutic non-HDL-C and ApoB targets. In the CEPHEUS study,[24] which included 5,276 patients on LLDs in six Arabian Gulf countries, non-HDL-C and ApoB targets were achieved in 36% and 38% of patients, respectively, in the very high-risk group compared to 58% and 51% of patients, respectively, in the high-risk patients. Factors associated with not meeting targets included patients in the high-risk categories, not receiving optimum doses of statins, treating physicians not adhering to international guidelines, and difficulties with patient compliance.[24] Similarly, in a study conducted in Oman in 94 dyslipidemic patients taking LLDs found that the non-HDL-C target was achieved in 53% of patients and ApoB in only 39% of patients in the overall group.[25]

Another underdiagnosed and undertreated type of dyslipidemia in the Arabian Gulf is familial hypercholesterolemia (FH), which is a common genetic cause of premature coronary heart disease (CHD) due to lifelong elevated plasma LDL-C levels.[26,27] There are a few reports on the molecular characteristics of FH in the Middle East and the Arabian Gulf.[28-33] A systematic review to identify all FH-related mutations reported in the Middle East and in Western populations identified only 57 mutations in 17 Middle East and North Africa (MENA) countries compared to over 500 mutations in three Western nations.[34] The predicted prevalence of FH in the Arabian Gulf could be between 52,277 to 130,693 patients for heterozygous familial hypercholesterolemia (HeFH) (based on a rate of 1:200–500) and 87 to 163 patients for homozygous familial hypercholesterolemia (HoFH) (based on a rate of 1:300,000–600,000). These calculations are based on the National Centre for Statistical Information (NCSI) 2010–2015 census.[35] The FH numbers in the region could be higher than predicted due to high consanguinity in the Arabian Gulf.[36] The prevalence of FH in the Gulf Countries is unknown due to lack of national registries and genetic screening for FH.[34,37,38]

There is suboptimal management of dyslipidemia across the Arabian Gulf countries. More aggressive treatment management is required which would include aggressive lifestyle modifications, adherence to international guidelines for lipid management, and the use of optimal lipid lowering therapies.

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