Sir,

Dyslipidemia is one of the important risk factors for cardiovascular (CV) diseases. As per the current consensus, we assess lipid-derived risk by looking at traditional lipid parameters. We consider low-density lipoprotein cholesterol (LDLc) as a primary therapeutic target. However, many recent studies have claimed apolipoprotein B and non-high-density lipoprotein cholesterol (HDLc) are more accurate in this regard. In India, raised triglyceride levels are a unique and important feature of dyslipidemia. In the presence of high triglycerides, LDLc gets oxidized and becomes a small dense form that is considered more atherogenic than large buoyant LDL particles. Hence, in this subset of patients, LDL particle number and size would be more accurate measures of lipid parameters. To explore this aspect, we wrote this short communication to you. Lipoproteins (Lps) are the major contributor to atheromatous plaque formation. Among atherogenic Lps, LDLc has long been considered a major Lp and thus it became a major therapeutic target in all lipid-lowering therapies. Atherosclerotic CV disease (ASCVD) risk is linearly associated with LDLc level. It has been demonstrated that each mmol/lit decrease in LDLc level is associated with a 20–25% reduction in the risk of major ASCVD events. We have been assessing lipid-derived ASCVD risk by looking at traditional lipid parameters for the last few decades. However, traditional lipid parameters do not reflect the entire atherogenic Lps in the plasma such as Lp(a), and apolipoprotein-B. It has been found in several recent studies that a subset of patients, even with optimal LDLc levels they continue to get ASCVD events and atherosclerosis process progression. This phenomenon has been termed as “residual lipid risk” which cannot be identified by measuring LDLc level alone. Residual lipid risk is the difference between the estimated LDLc value and the actual quantity of circulating atherogenic Lp particles. Non-HDLc comprises cholesterol carried by all potential atherogenesis Lps including LDLc, VLDL, Lp(a), and remnant Lps. Apolipoprotein-B represents the total number of atherogenic Lps in the plasma as each Lp particle contains one molecule of apolipoprotein-B. LDLc represents the total cholesterol concentration of LDL, IDL, and Lp(a). However, LDLc level does not reflect the LDL particle number and size. For example, at the same level of LDLc people with small-sized LDL particles will have more number of LDLc particles than people with large-sized LDL particles. As it takes more small-sized LDL to traffic a given mass of cholesterol molecules per liter/deciliter. We know small dense LDL is more atherogenic than large buoyant LDL particles and more easily infiltrate into the arterial intima. In most circumstances, apolipoprotein-B and non-HDLc are highly correlated with each other but not identical as apolipoprotein-B and non-HDLc they also include triglyceride-rich Lps. Lp(a) is included in all three measurements. Among statin-treated patients, more pronounced discordance exists between these parameters as statin lowers LDLc more effectively than the other two parameters. Hence, it is important to identify this discordance and discordance pattern, particularly in statin-treated patients, otherwise they might have discordantly high apolipoprotein-B levels and they remain at higher risk for ASCVD events despite attainment of optimal LDLc. If we are able to identify that subset of patients, we can take appropriate
steps such as statin intensification, the addition of non-
statin therapy, or more aggressive procedures such as lipid
apheresis. To date, very small number of studies have been
directed to examine the relationship between these lipid
parameters in statin-treated patients. One study was done
by Qu et al.,11 they observed LDLc to be discordant with
apolipoprotein-B in 31% of cases and with non-HDLc in
20.1% of cases in their study cohort. They also reported
the brachial artery pulse wave velocity which is considered
a marker of subclinical atherosclerosis,12 was greater in
those with higher apolipoprotein-B or non-HDLc levels.
In the adjusted logistic regression model, low LDLc and
high apolipoprotein-B or non-HDLc discordance were
associated with a risk of arterial stiffness (OR: 13.41).13
Hence these discordant groups of patients need to be
identified to take necessary steps to reduce the residual
risk of CV events. Johannesen et al.,15 did concordance
discordance analysis and they concluded that statin-treated
patients, with elevated apolipoprotein-B and non-HDLc,
but not LDLc, are associated with residual risk of all-cause
mortality and myocardial infarction. It has been observed
that the amount of cholesterol within Lp particles is
very substantial. The analysis of the INTERHEART
study demonstrated that when apolipoprotein-B level
is higher than non-HDLc level that is when cholesterol-
depleted apolipoprotein-B particles are present, CV risk is
increased, whereas when non-HDLc level is higher
than apolipoprotein-B level that means when cholesterol-
 enriched apolipoprotein-B particles are present, CV risk is
less than the reference concordant group.14 When the mass
of cholesterol per apolipoprotein-B particle is normal, all
three measures are concordant. However, when a mass
of cholesterol within apolipoprotein-B particles is either
greater or lesser, LDLc and non-HDLc are discordant.
In both circumstances, the number of apolipoprotein-B
particles is not accurately represented by measures of the
mass of cholesterol within them.15 Hence, probably Lp
particle number, and size are more critical determinants
of CV risk than the mass of cholesterol within them.

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