

## Assessing Framingham cardiovascular risk scores in subjects with diabetes and their correlation with diabetic retinopathy-Comment

Sir,

I read the article "Assessing Framingham cardiovascular risk scores in subjects with diabetes and their correlation with diabetic retinopathy" published in your journal Jan-Feb 2012 issue<sup>[1]</sup> with interest and I offer following comment.

The authors report unique (risk factor) finding of "higher serum total High Density Lipoprotein-cholesterol (HDLC level", in diabetic (retinopathy) patients.

Currently, the residual risk of coronary events, despite aggressive LDL lowering therapy, results in renewed interest in serum total HDLC. Serum Total HDLC is a complex and heterogeneous in terms of size, shape, electrophoretic mobility, and composition of protein, cholesterol, triglyceride, and phospholipids, where each particle plays different roles such as anti-atherogenic due to reverse cholesterol transport<sup>[2]</sup> and other roles. Thus not all raised total serum HDLC are equally anti-atherogenic emphasizing HDLC particle composition rather than total HDLC, as an important determinant of its specific functional property (and role) as agreed by the expert clinical lipidologists.<sup>[1]</sup> Moreover, the inverse correlation between serum HDLC concentration and risk of CHD (Coronary Heart Disease) and decreased cardiovascular (CVD) risk with increasing HDLC levels have been known for years, particularly South Asians are not only notorious to have lower HDLC levels but also have a higher concentration of small, decreased-cardio-protective HDL particles.<sup>[3,4]</sup>

Additionally appropriate risk classification of patients based on the established cut points mandates the use of accurate methods for HDLC measurement. The NCEP (National Education Programme) measurement goal is total error

[combines imprecision (random error) and inaccuracy or bias (systematic error), represents the maximum tolerable error in measurement of a single specimen] within 13% of the true value. At low HDLC values, this proportional target becomes difficult to achieve. (For example, at 25 mg/dL the proportional goal would be  $\pm 1$  mg/dL). A recent report on comparative study of performance where most of the currently used HDLC assays across the United Kingdom (UK) laboratories reveals clinically unacceptable overestimation (positive bias ranging up to +32%) and this is worse when processing samples with even moderate amounts of triglycerides,<sup>[5]</sup> justifying that many of the currently available (homogeneous) assays cannot be confidently recommended for use in long-term clinical trials and other research applications without thorough validation.

In these contexts, the scientific soundness of the statement "higher serum HDLC levels, a unique (risk factor)" finding requires the evidences of HDLC numbers with its measurement methodology and its validation (including steps to ensure optimal long-term stability of those results), which are missing (in this evidence based era) not only in this paper even in their methodology published in the Ophthalmic Epidemiology in 2005 as referred by the authors.

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