Short communication

Homocysteine in CAD patients-Does it matter?

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ABSTRACT

Introduction and Aim: Homocysteine (Hcy) is considered as an independent risk factor for coronary artery disease (CAD). Hyperhomocysteinemia (HHcy) may be caused due to the deficiency of vitamin B12, folic acid (FA), and pyridoxine (B6) or due to genetic polymorphism in methylenetetrahydrofolate reductase (MTHFR). A pilot study was undertaken to investigate Hcy levels and its association with lipid profile in patients with CAD.

Methods: Lipid profile values were obtained from laboratory reports and the Hcy levels were estimated by enzymatic cycling assay using the commercial kits in autoanalyzer in subjects with CAD (n=12).

Results: Hcy (14.58 ± 8.32 µmol/L), LDL (134.75 ± 45.02 mg/dl) and non-HDL (150.25 ± 56.89 mg/dl) levels were found to be elevated in patients with CAD.

Conclusion: Dyslipidemia was associated with variable Hcy levels. Few patients with HHcy showed concurrent upsurge in LDL and non-HDL levels.

Keywords: Coronary Artery Disease; Dyslipidemia; Homocysteine.

INTRODUCTION

Homocysteine (Hcy) is a sulfur-containing amino acid which is converted to cysteine or recycled into methionine with the aid of vitamins B12, folic acid (FA) and pyridoxine (B6). A deficiency of these vitamins can lead to hyperhomocysteinemia (HHcy). HHcy can also be caused due to inadequate enzyme activity of methylene tetra-hydrofolate reductase (MTHFR) due to genetic defects (1).

According to WHO, an estimated 17.9 million individuals died due to cardiovascular diseases (CVDs) in 2019, representing 32% of deaths world-wide. Of these deaths, 85% were caused due to stroke and heart attack (2). HHcy is considered a risk factor for coronary artery disease (CAD) (3). The prevalence of CAD in Indians is 21.4% among diabetics and 11% in non-diabetics (4).

Regular supplementation of FA (0.5–5.0 mg/day) typically lowers Hcy levels in plasma by approximately 25% in patients with HHcy (2).

Evaluation and management of HHcy remains controversial, since a meta-analysis conducted by the American Heart Association revealed that Hcy-lowering therapies did not significantly avert stroke and had a non-significant impact on CAD (1). According to the 2021 Canadian Cardiovascular Society Dyslipidemia Guidelines, low density lipoprotein (LDL) cholesterol is the main target while apolipoprotein B and non-high density lipoprotein cholesterol (non-HDL-C) remains the secondary target for myocardial infarction are all responsible for mortality (5) and have been validated as markers in the prediction of CAD risk. Based on the evidence obtained from earlier research, it is fair enough to say that non-HDL-C can be used for the primary screening and is a precise primary target for therapy (6).

A pilot study to explore the serum Hcy levels in small group of subjects with confirmed CAD and its association with the lipid profile was undertaken.

MATERIALS AND METHODS

Non-diabetic men and women (n=12) aged 40-59 years with known coronary artery disease confirmed by an elevation in ST segment of ECG or by angiography were included in the present study after obtaining the Institutional Ethical clearance (IEC KMC MLR 05-2020/171). Subjects with known diabetes, gastrointestinal and thyroid disorders, intrinsic factor deficiency, malignancy, chronic liver, kidney diseases and supplements of B12 and folic acid were excluded from the study. Lipid profile values were noted from the laboratory. Patient history was collected using structured proforma and medical records. Serum Hcy was estimated by enzymatic cycling assay using the commercial kits (Roche Diagnostics, USA) in autoanalyzer (COBAS 6000 c 501, USA).

RESULTS

The baseline data of the subjects are compiled in Table 1. Mean values of TC, TG, LDL and Non-HDL-C were above the normal reference range. Hcy values were found to be elevated in three of the subjects, with moderate elevation (16-30 µmol/L) (1) in one and an intermediate elevation (31-100 µmol/L) in two. These three subjects also had high LDL and non-HDL-C levels and were hypertensive on treatment (Fig. 1).

Table 1: General characteristics and biochemical parameters estimated in CAD (n=12)

Variables (Reference range)	**Mean± SD**	**Range**
Age (40-59 years)	52.50 ± 5.12	41-58
TC (Upto 200 mg/dl)	200.92 ± 53.54	143-288
TG (Upto 150 mg/dl)	182.08 ±123.51	88-452
HDL (40-60 mg/dl)	45.80 ± 13.84	30-83.6
LDL (Upto 100 mg/dl)	134.75 ± 45.02	78-223
TC/HDL	4.5 ± 1.67	2-7
VLDL (0-40 mg/dl)	35.67 ± 25.35	9-90
Non-HDL (0-130 mg/dl)	150.25 ± 56.89	69-238
Homocysteine (5-15µm/L)	14.58 ± 8.32	6-34

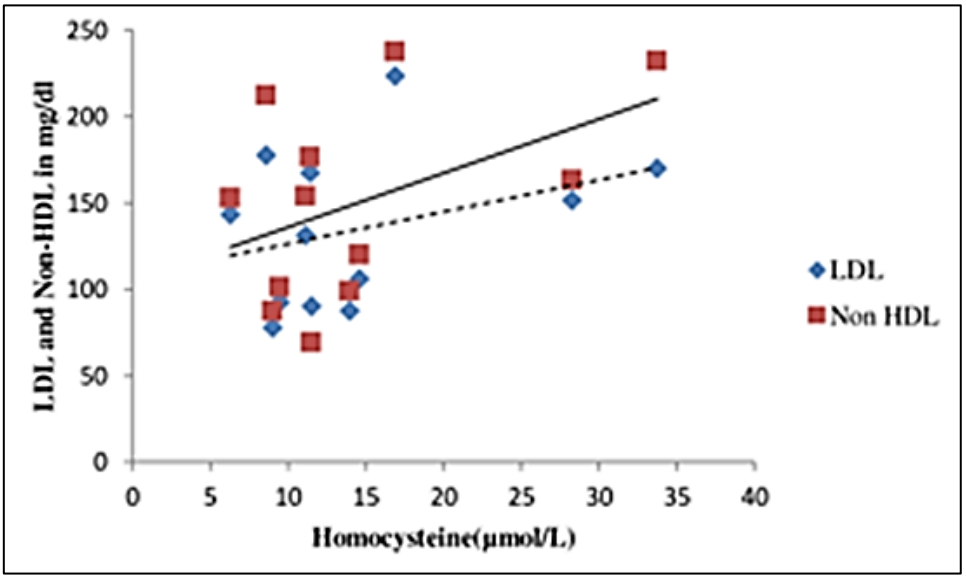

Fig 1: Comparison of Hcy to LDL and non-HDL

DISCUSSION

Epidemiology has shown that CAD is most commonly seen in subjects > 40 years and its occurrence rises significantly with age (7). Hence the present study was carried out in subjects aged between 40-59 years. CAD is linked to chronic diseases like diabetes and hypertension, which increase the difficulty of clinical treatment. Hence, timely diagnosis and evaluation of disease are very much essential for improving the prognosis (8).

Risk of CAD is monitored by lipid profile estimation especially the LDL and non-HDL-C levels. In a multi ethnic study conducted in patients (aged 52.3±17.9 years) with atherosclerotic cardiovascular disease, LDL levels were found to be higher than normal (9). The Copenhagen general population study conducted in 13,015 statin-treated patients found higher levels of apo B and Non-HDL-C were associated with the increased risk of all-cause mortality and myocardial infarction (6).

Hcy though implicated in CAD has not been validated as marker for the same. Hence a comparison of Hcy levels with the gold standard lipid profile was done in established cases of CAD as a part of the pilot study. Among the 12 subjects, three were found to have mild to moderate elevation in Hcy with associated high LDL and non-HDL levels (Fig. 1). It has been shown that mild to moderate HHcy leads to coronary artery, peripheral artery and even venous vessel diseases. This further elicits the vasomotor dysfunction leading to increased thrombosis, morbidity and mortality (10).

CONCLUSION

Dyslipidemia was associated with variable Hcy levels in the present pilot study. Select few patients with HHcy showed concurrent increase in LDL and non-HDL levels. Based on these findings, a detailed study in larger group of subjects with CAD is under progress.

CONFLICTS OF INTEREST

None declared.

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