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Lipoprotein (a) and comprehensive lipid tetrad index as a marker for coronary artery disease in NIDDM patients in South India

Medha Rajappa [a,*], M.G. Sridhar [b], J. Balachander [c], K.R. Sethuraman [d]

[a] Department of Biochemistry, Maulana Azad Medical College and associated hospitals, New Delhi – 110 002, India
[b] Department of Biochemistry, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry – 605 006, India
[c] Department of Cardiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry – 605 006, India
[d] Department of Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry – 605 006, India

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Abstract

Background: Coronary artery disease (CAD) is reaching epidemic proportions in India, in the absence of traditional risk factors. Lipoprotein (a) (Lp(a)) concentrations are related to both atherogenesis and thrombogenesis and may be a key link between lipid and CAD. We studied the role of Lp(a) and comprehensive lipid tetrad index as markers for CAD in South Indian patients with non-insulin-dependent diabetes mellitus (NIDDM).
Methods: Lp(a) concentrations and lipid profile were estimated in 53 NIDDM patients with CAD (Group 1), 53 NIDDM patients without CAD (Group 2), and 52 control subjects (Group 3). Comprehensive lipid tetrad index was calculated in all patients and controls.
Results: Lp(a) concentrations were significantly higher in Group 1 patients, when compared with Groups 2 and 3. In NIDDM patients with CAD, only total cholesterol and low-density cholesterol concentrations correlated significantly positively with lipoprotein (a) concentrations ($r=0.184$, $p=0.03$ and $r=0.168$, $p=0.02$). Mean comprehensive lipid tetrad index was 45,487±2747 in Group 1, 10,866±1163 in Group 2 and 4582±348 in Group 3 subjects.
Conclusion: Based on the foregoing data, high Lp(a) concentrations show strong correlation with CAD in NIDDM patients of South India. High concentrations of Lp(a) and comprehensive lipid tetrad index, along with high prevalence of NIDDM, may render Indians particularly vulnerable to malignant atherosclerosis at a young age. As NIDDM is increasing in prevalence in India, the above observations have ominous dimensions in terms of total burden of CAD in India.

Keywords: Lipoprotein (a); Comprehensive lipid tetrad index; Coronary artery disease; Acute myocardial infarction; Non-insulin-dependent diabetes mellitus; South Indians

1. Introduction

It was first reported in 1959 that people hailing from the Indian subcontinent had a higher probability of dying due to coronary artery disease. The last century has seen a rapid increase in the global prevalence of coronary artery disease (CAD). Estimates from the Global Burden of Disease study estimate that India is facing the greatest burden due to CAD [1]. In India, CAD has been predicted to assume epidemic proportions by the year 2015 [1–3]. The prevalence of CAD in India is not homogenous, being twofold higher in South than in North India [4]. In the quest for definitive pathogenic factors of atherosclerosis and CAD, a large number of environmental and genetic risk factors have been in focus for decades now.

Amidst several culprits identified through circumstantial evidences, a few have been shown beyond doubt to predispose to or to precipitate CAD. Factors presumed to be responsible for high prevalence of CAD among Asian Indians are decreased physical activity, increased central obesity, increased insulin resistance and plasma insulin concentrations, increased prevalence of type 2 diabetes mellitus and a peculiar atherogenic dyslipidemic profile [2]; characterized by low HDL cholesterol concentrations,

* Corresponding author. Department of Biochemistry, Maulana Azad Medical College, Bahadur Shah Zafar Marg, New Delhi – 110 002, India. Tel.: +91 98108 72175.
E-mail addresses: linkmedha@gmail.com, medha_rajappa@rediffmail.com (M. Rajappa).

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Table 1
Clinical characteristics of study groups

Parameters	Group 1: NIDDM with CAD (n=53)/ mean±S.D.	Group 2: NIDDM without CAD (n=53)/mean±S.D.	Group 3: Controls (n=52)/ mean±S.D.
Age (years)	56±9	54±5	55±11
BMI (kg/m^2)	27.8±3.4[a]	25.2±4.3[a]	19.0±4.6
Duration of diabetes (years)	12.5±7.3[b]	8.4±5.8	———
Fasting blood glucose (mg/dl)	165±58[a]	152±35[a]	88±21
HbA_{1c} (%)	8.9±2.2[a]	9.4±2.4[a]	4.5±0.6
Hypertension (%)	17.0	15.0	11.0
Smokers (%)	16.0	15.0	12.0
Family h/o CAD (%)	47.2	5.8	3.8

[a] Significantly high compared with control group (p<0.001).
[b] Significantly high compared with group 2 (p<0.05).

increased triglycerides and small dense LDL cholesterol concentrations and increased lipoprotein (a) concentrations [3].

The prevalence of atherosclerotic vascular disease is several-fold higher in diabetic than in non-diabetic subjects. The most common and life-threatening disorder that besets type 2 diabetic patients is CAD. Diabetes itself may confer 75–90% excess risk of CAD in diabetic subjects and enhances the deleterious effects of other major cardiovascular risk factors [5]. Diabetes is also becoming an Indian epidemic, with India accounting for 20% of the world's diabetic population [6,7]. 35.5 million Indians are diabetic and this figure is expected to rise to 80 million by 2030. Therefore, the above figures have ominous dimensions in terms of total burden of CAD in Indians [7].

Lipoprotein (a) (Lp(a)), a genetically determined lipoprotein in blood, is one of the most powerful [8–10] and most prevalent [11–13] independent risk factors for CAD in Asian Indians. Several studies performed in Indians have confirmed the above findings [14–18]. Lp(a) is a complex of apolipoprotein (a) and LDL. Apo(a) is a atherothrombogenic moiety, which can competitively inhibit plasminogen activity leading to impaired fibrinolysis. Lp(a) has also been implicated in enhanced oxidation and foam cell formation. It functions as a dual pathogen, which is related to both atherogenesis and thrombogenesis [19,20]. It forms a link between genetic and two major explanations of the pathogenesis of atherosclerosis: fibrin deposition theory of Rokitansky and lipid hypothesis of Virchow [21]. Recently, it has been proposed that in settings of enhanced oxidative stress and increased Lp(a) lipoprotein concentrations, a pro-inflammatory milieu may predominate that contributes to the clinical expression of CAD [22].

Lp(a) correlation to CAD in diabetes is controversial. Some reports found that Lp(a) is an independent risk factor for CAD in diabetics [23–25]; while others were unable to show a significant relationship between Lp(a) and CAD [26–28]. Comprehensive lipid tetrad index (CLTI), proposed by Enas EA [29,30], is designed to magnify the subtle abnormalities of the various atherogenic and anti-atherogenic lipoproteins [15,29–31] and is derived by multiplying the three commonly measured lipids directly associated with CAD and dividing the product by HDL, which is inversely associated with CAD (total cholesterol × triglyceride × Lp(a)/HDL). We addressed the role of Lp(a) and CLTI as determinants of CAD in NIDDM patients in South India.

2. Methods

This study was conducted in the departments of Biochemistry, Medicine and Cardiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India. The following groups of subjects were studied: Group 1 was composed of 53 NIDDM patients with CAD, who were between the ages of 35 and 79 years. CAD was diagnosed if the patient had a documented episode of myocardial infarction, substantiated by ECG evidence of Q waves or symptoms of angina supported by ECG

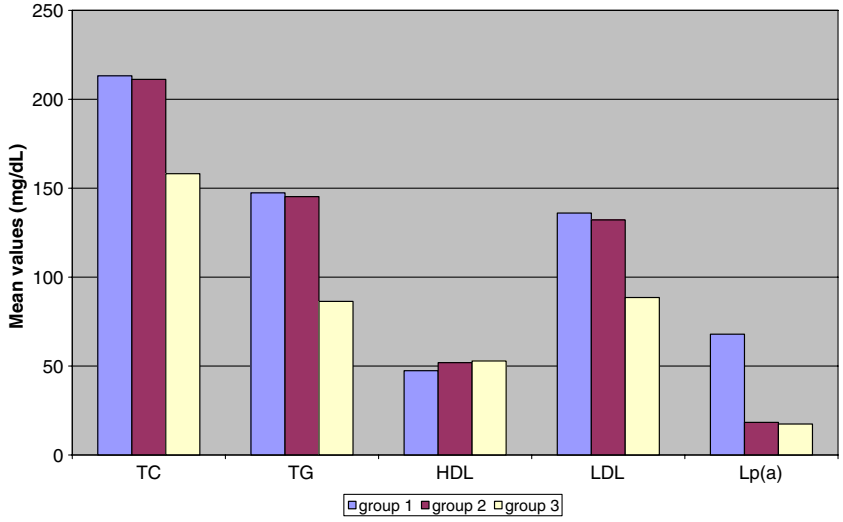

Fig. 1. Lipid profile and Lp(a) concentrations in all study groups. Groups: 1 – NIDDM with CAD, 2 – NIDDM without CAD, 3 – Controls.