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LIPID PROFILE AND VARIATIONS IN WBC COUNT AND ESR IN ACUTE MYOCARDIAL INFARCTION

Deepa G[1], Vijayalakshmy.R[2]

ABSTRACT

Background: The incidence of acute myocardial infarction, an important manifestation of coronary artery disease, is very high in India. Dyslipidemia and inflammation are equally important in the process of atherosclerosis, leading to myocardial infarction.

Aims and objectives: The aim is to assess the influence of dyslipidemia in causing myocardial infarction by estimating the fasting lipid profile . The atherogenic index can be assessed by calculating LDL/HDL ratio. The estimation of total white blood cell count (WBC count) and erythrocyte sedimentation rate (ESR) seem to have a definite predictive value for the evidence of inflammation in acute myocardial infarction.

Materials and methods: 60 male patients of 40 - 65 years age, admitted with a diagnosis of acute myocardial infarction, during the period August -- November, 2004 were included in the study. They were compared with 62 healthy male subjects of the same age group, who had no history of coronary heart disease in the past.

Results: Serum total cholesterol, triglycerides, LDL, VLDL and LDL/HDL ratio showed statistically significant increase and HDL showed a statistically significant decrease in myocardial infarction. Both WBC count and ESR showed a significant increase in acute myocardial infarction.

Conclusions: Hyperlipidemia and inflammation definitely influences the occurrence of myocardial infarction. One of the novel findings in the present study was that hypertriglyceridemia puts middle-aged and old-aged men at increased risk for cardiovascular disease regardless of their HDL-cholesterol or LDL-cholesterol levels. Leucocytosis is significantly associated with acute myocardial infarction and is a weak, but independent laboratory predictor of this condition.

Keywords: myocardial infarction, dyslipidemia, lipoproteins, WBC count, inflammation, atherosclerosis

INTRODUCTION

Acute myocardial infarction, an important manifestation of coronary artery disease, can cause significant mortality and morbidity. Over the past four decades since serum cholesterol levels were first linked to atherosclerotic disease, a number of additional markers have been identified in an attempt to better characterize the atherogenic potential of the lipid profile[1,2]. Relationships of cholesterol ester rich lipoproteins (LDL and HDL) with atherosclerosis have been clearly established. Circulating blood cholesterol is strongly and positively associated with coronary heart disease (CHD) risk in men and women, both young and old. A series of large scale, randomized, controlled trials of blood cholesterol reduction demonstrate that this process is reversible and risk reductions of the magnitude predicted from the observational data can be produced through lowering of blood cholesterol. In a study by J.Michael Gaziano et al[3], it was revealed that elevated fasting triglyceride (TG) levels are strongly associated with the risk of myocardial infarction. In the Physician's Health Study[4], a 1-unit increase in the LDL/HDL ratio was associated with a 53% increase in the risk of myocardial infarction.

Recently much data has emerged about the evidence of systemic and local inflammation in atherosclerosis[5]. Stimulus for this local inflammation is not clear. In fact, the lesions of atherosclerosis represent a series of highly

[1]Assistant Professor, Department of Physiology, Government Medical College, Thiruvananthapuram, Kerela - 695 011.
[2]Prof & HOD, Department of Physiology, ACME, Pariyaram, Kannur.

specific cellular and molecular responses that can best be described, in aggregate, as an inflammatory disease. This concept has gained more attention to the role played by inflammation in the process of atherogenesis and the resultant rupture of fibrous plaques leading to myocardial infarction[6]. In patients with acute myocardial infarction, the evidence of inflammation is reflected by a high rise in leukocyte count and erythrocyte sedimentation rate. In the early 1980's, Kotis et al[7] suggested that total leukocyte count correlates with the severity of coronary atherosclerosis and that the initial leukocyte count during acute myocardial infarction independently predicts the frequency of ventricular fibrillation. Also WBC's may promote myocardial ischemia by capillary plugging and or release of toxic oxygen metabolites[8,9]. It is therefore an early measurable prognostic variable in the survivors of myocardial infarction. In acute myocardial infarction, where there has been tissue break down, the elevation of ESR may be a simple way of judging the severity of the condition.

Therefore the classic concept of atherosclerosis as a disorder of lipid metabolism extends beyond dyslipidemia. Moreover, the biology linking the lipid disorder to vascular involvement during atherogenesis and subsequent clinical manifestation indicates a far more complex pathophysiology than mere lipid storage.

MATERIALS AND METHODS

60 male patients of 40 - 65 years age, admitted in the cardiology ICU with a diagnosis of acute myocardial infarction, within 24 hours of chest pain during the period August -- November, 2004 were included in the study. They were compared with 62 healthy male subjects of the same age group, who had no history of coronary heart disease in the past. The study protocol was approved by the Ethical Committee of the institution. Females were not included in this study so as to exclude the influence of oestrogen on the pathogenesis of coronary heart disease. Acute myocardial infarction was diagnosed by either increased CK-MB levels or electrocardiogram changes or both. Patients with cardiogenic shock, cerebrovascular accident and significant hepatic or renal diseases were excluded. Patients with clear evidence of infection elsewhere in the body were also excluded. Patients with repeated myocardial infarction were excluded. The control group selected included healthy male bystanders of 40 – 65 age group, who had no history of coronary heart disease in the past and who were not the first degree relatives of the patients. Screening was done based on a proforma. Detailed history was noted in proforma.

After over night fasting, 5 ml of blood was drawn from anticubital vein, under aseptic precautions, to do the total WBC count, ESR and lipid profile. The samples were kept in the refrigerator at 4^{0}C.

The following biochemical parameters were estimated. Cholesterol is detected by CHOD-PAP method[10]. HDL-cholesterol was estimated from the supernatant after precipitation by phosphotungstic acid and magnesium chloride. LDL-cholesterol and VLDL- cholesterol was calculated using the Friedewald's formula[11] and triglycerides by GPO-PAP method[12].

The total WBC count was done in an automated instrument for measuring haematological parameters, by using electrical impedance method, in which the cells are counted and sized as they pass through the aperture of the von Behrens WBC transducer.

ESR was determined by Esserite method.

RESULTS AND ANALYSIS

Statistical Analysis

Analyses of observations was done by using significance of difference in means (Z test).

$$Z = \frac{\text{Difference in means.}}{\text{Standard Error}}$$

The comparison of lipid profile, total WBC count and ESR in males of 40-65 age group in acute myocardial infarction and normal subjects are tabulated in the table given below.

Table 1: Serum lipid profile and inflammatory parameters in Normal and Acute myocardial infarction patients

	NORMAL SUBJECTS		ACUTE MYOCARDIAL INFARCTION PATIENTS		
	MEAN	SD	MEAN	SD	P VALUE
T.CHL	171.92	30.61	220.63	36.31	< 0.001
TRIGLY	79.84	23.19	162.10	34.94	< 0.001
VLDL	15.97	4.64	32.62	6.94	< 0.001
LDL	86.44	35.36	146.95	35.3	< 0.001
HDL	69.52	11.83	42.20	12.03	< 0.001
LDL/HDL	1.34	0.71	3.8	1.68	< 0.001
T.WBC	5616.13	1097.12	9618.33	2799	< 0.001
ESR	8.34	4.22	39.27	25.21	< 0.001

Lipid parameters showed a statistically significant increase in the serum total cholesterol, triglycerides, LDL-cholesterol and LDL/HDL ratio, whereas HDL-cholesterol showed a statistically significant decrease in myocardial infarction. In our study, among the 60 patients, 28 (50%) had total leucocyte count more than 8000/cmm and 42 patients (70%) had ESR more than 30mm/1st hour, indicating a strong and direct correlation of inflammation.

DISCUSSION

Our data are consistent with earlier reports that elevated fasting levels of total cholesterol, LDL and TG are associated with coronary heart disease risk[1]. In MRFIT trial[7], and Adult Treatment Panel II study[13], it was revealed that high blood cholesterol level was a major risk factor for coronary heart disease. The higher the blood cholesterol, the greater was the risk for coronary heart disease. In our study also, acute myocardial infarction patients showed significantly higher cholesterol than the control group (Table1). The independent effect of hypertriglycedemia on risk for myocardial infarction was also found in subgroup analyses in other population studies like Glynn R J et al[14] and Alberg H et al[15]. In our study, TG value observed in MI patients (162.10 ± 34.94) was significantly higher when compared with controls (79.84 ± 23.19). In the prospective cardiovascular Monster study (The PROCAM study) [16], the fasting level of triglycerides was an independent risk factor for coronary heart disease events irrespective of serum levels of HDL or LDL-cholesterol. Considering the LDL and VLDL-cholesterol concentrations in the two study groups , a significant increase in their values was observed in the acute myocardial infarction patients (table –1), when compared to normal. Similar findings were seen in Helniski Heart study[17]. The higher the LDL level, the greater was the risk for coronary heart disease. A portion of the total cholesterol will be carried by the triglyceride-rich VLDL particles. The elevated triglycerides and cholesterol can decrease the lipoprotein lipase activity, leading to higher chylomicron remnant and VLDL levels (both of which may be atherogenic). In addition, lower lipoprotein lipase activity could result in increased density of VLDL particles. HDL – cholesterol is referred as the good cholesterol - 'good' because it protects the heart. HDL picks up cholesterol from peripheral tissues, and transports it to the liver, thus lowering plasma cholesterol. Extensive studies have established that HDL levels are inversely associated with cardiovascular risk. In the Framingham Heart Study[18], the significance of serum HDL and LDL – cholesterol levels with coronary heart disease were studied and it was observed that the risk associated with HDL –cholesterol was totally independent of LDL – cholesterol. The PROCAM Study[16] confirmed the above finding. The PROCAM Study also suggested that a high concentration of HDL was more protective than a low level of LDL, and that a low level of HDL may be more of a coronary heart disease risk than a moderately increased LDL –

cholesterol. Similar finding was got in our study also (table-1).

Data from the Lipid Research Clinics and the Framingham Heart Study[18] suggest that the LDL/HDL ratio may have a greater predictive value for coronary heart disease than total cholesterol, LDL or HDL – cholesterol alone. In our study also, there was a significant decrease in LDL/HDL ratio in the acute myocardial infarction patients. A value of $\leqslant 2.2 \pm 0.2$ is considered to be desirable as far as coronary heart disease is concerned and a low ratio may be a good indicator of abnormal cholesterol metabolism. Hence this ratio is also called atherogenic index. In the Physician's Health Study[4], a 1 – unit increase in the LDL/HDL ratio was associated with a 53% increase in the risk of myocardial infarction.

Observations made on inflammatory status in acute myocardial infarction by doing the total WBC count and ESR revealed that both these parameters were significantly increased in acute myocardial infarction patients, when compared to the normal(table–1). In acute myocardial infarction, where there has been tissue breakdown, the ESR may be a simple way of judging the disease. Along with total WBC count, it helps in confirming an inflammatory state, although it does not have any independent diagnostic value[8]. In a retrospective comparative study conducted in the Department of Emergency Medicine, Loma Linda University, USA[19], it was found that the initial WBC count was significantly higher for the subjects who had acute myocardial infraction. While CK-MB alone was 93 % specific and 73 % sensitive to acute myocardial infarction, the combination of CK-MB and raised WBC count increased these as 99 % and 79 % respectively. The site of action of WBCs are the areas of serious infection and inflammation. Hence they can be considered as important inflammatory markers. The ubiquitous monocyte, the precursor of macrophages in all tissues, is present in every phase of atherogenesis along with neutrophils. Monocyte-derived macrophages are scavenging and antigen-presenting cells and they secrete cytokines, chemokines, growth-regulating molecules and other hydrolytic enzymes. The ability of macrophages to produce cytokines, proteolytic enzymes and growth factors may be critical in the role of these cells in the damage and repair that ensue as the lesion progresses.

SUMMARY AND CONCLUSSION

Our study shows that elevated lipid parameters and inflammatory changes observed as increased inflammatory markers significantly increase the occurrence of acute myocardial infarction. The current medical treatment strategy for coronary heart disease is mainly oriented towards maintaining a near-normal lipid profile and due to this reason, the control of inflammatory status has been ignored. Inflammation occupies a very important central position in all phases of atherosclerosis, although inflammation must smolder for decades before resulting in a clinical event. The medical community now seems prepared to go beyond lipids and embrace inflammation as a common pathway by which a variety of risk factors may alter arterial biology and promote atherogenesis. This new viewpoint not only increases our mechanistic understanding of atherosclerosis, but also affords novel opportunities for therapeutic intervention.

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