Indian Journal of Clinical Biochemistry, 2005, 20 (1) 18-20

HOMOCYSTEINE STATUS AND ACUTE MYOCARDIAL INFARCTION AMONG TAMILIANS

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ABSTRACT

Myocardial infarction is a major consequence of coronary artery disease. Apart from the traditional risk factors of myocardial infarction, recently many reports have suggested that hyperhomocysteinemia plays important role in myocardial infarction. Plasma homocysteine level was determined in 60 myocardial infarction patients and in 35 age matched healthy individuals. Statistically significant differences ($p<0.01$) were observed in the mean of plasma homocysteine concentrations between the acute myocardial infarction patients (24.59 ± 6.14mM/L) and in normal healthy individuals (13.73 ± 3.54 mM/L). The level of homocysteine in myocardial infarction patients is significantly high ($p <0.01$) among myocardial infarction patients when compared to that of the controls. The the present study indicates a strong association between plasma homocysteine and acute myocardial infarction among Tamilians, thus implying plasma homocysteine as a possible risk factor for myocardial infarction.

KEYWORDS

Hyperhomocysteinemia, Acute myocardial infarction, Proaggregant.

INTRODUCTION

During the past 20 years, the battle to reduce the incidence of cardiovascular disease has led researchers to the discovery of various clinical markers. There are some cases with myocardial infarction those who do not have any of the traditional risk factors. So, attention has been focused on other predisposing factors, which may contribute to myocardial infarction. Researchers have taken effort to find the possible association between plasma homocysteine levels and acute myocardial infarction (AMI).

Homocysteine is a nonessential, sulphur containing aminoacid and it is an intermediate from the metabolic demethylation of dietary methionine. It is present in plasma in four forms: a free thiol (1%); disulfide (5-10%); mixed disulfide (5-10%) and protein bound thiol groups (80-90%). The combined pool of all four forms of homocysteine is referred as "total plasma homocysteine"(1). The total homocysteine levels in plasma has been reported to be in the range of 5-15 mM/L in healthy individuals. (2) Altered homocysteine metabolism play a potential role in the pathogenesis of atherosclerosis, thromboembolism and vascular endothelial damage. Individuals untreated for hyperhomocysteinemia may have major cardiovascular events before the age of 30 years.(3) Several studies conducted in different parts of the world have reported that elevated levels of plasma homocysteine are associated with coronary artery disease, independent of other risk factors(4,5).As the concentrations of homocysteine is also influenced by genetic background there is need to study on homocysteine levels in different ethnic groups. Studies are inadequate among Tamilians to establish the role of homocysteine as an independent risk factor for acute myocardial infarction. Therefore this study has been undertaken among Tamilians in whom the incidence of mortality due to myocardial infarction is high.

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MATERIALS AND METHODS

60 patients admitted to the intensive care unit of the Vadamalayan Hospital, Madurai, Tamil Nadu, with documented AMI showing characteristic ECG signs and rise in troponin I concentration were included in this study.

Fasting blood was collected from the patients and also from 35 healthy individuals. All subjects gave their informed consent.Plasma was separated using EDTA coated tubes. Analysis for plasma homocysteine was performed using homocysteine microplate substrate trapping enzyme assay(Diazyme laboratories). This

technology employs genetically engineered enzymes that lack catalytic activity but specifically and tightly trap their substrate or product molecules as the basis for diagnostic tests.The values were considered normal when below 15.0 μMol/L All values are expressed in mean ± S.E . Student 't' test was used to compare the means.

RESULTS AND DISCUSSION

There is an elevation of plasma homocysteine in acute myocardial infarction patients when compared with the control group (Table-1). Statistically significant differences ($p<0.01$) were observed in the mean of plasma homocysteine concentrations between the acute myocardial infarction patients (24.59 ± 6.14mM/ L) and in controls (13.73 ± 3.54 mM/L). Recent reports on homocysteine suggest that it is an independent predictor of vascular disease, including stroke and coronary artery disease. Studies on the association of hyperhomocysteinemia with coronary artery disease in different populations have yielded conflicting results with some studies providing evidence for an association (6,7) while others have found none (8,9). This may be attributed to ethnic differences or due to differences in the definition of cases. As genetic background and nutritional intake vary in different populations, the homocysteine level varies in different ethnic groups and this may be due to the polymorphism seen in the genes encoding enzymes involved in the metabolism of homocysteine. Mutations in the methylenetetrahydrofolate reductase gene is one of the most frequent causes of moderately elevated plasma homocysteine. Hyperhomocysteinemia may also occur due to nutritional deficiency that leads to low blood concentrations of folate, vitamin- B12, or vitamin- B6 (10). A meta analysis conducted by Boushey *et al* , showed that homocysteine was an independent, graded risk factor for atherosclerotic disease in the coronary, cerebral and peripheral vessels (5). Plasma homocysteine concentration are found to be higher in Indian Asian overseas compared to the North Americans and European whites.(4,11)A study conducted by Stampfer *et al* (12) have concluded that moderately high levels of plasma homocysteine are associated with subsequent risk of myocardial infarction . Chamber *et al*., have reported that elevated plasma homocysteine concentration is a risk factor for coronary heart disease , independent of conventional risk factors (4). Homocysteine is known to induce atherothrombosis in many ways: homocysteine thiolactate, a by product of oxidation of homocysteine combines with LDL to form foam cells(13). The LDL rich foam cells embed themselves in the vascular endothelium and become fatty streak, which is the beginning of an atherosclerotic plaque. Homocysteine thiolactate has also been suggested to impair oxidative phosphorylation and enhancement of the proliferation and fibrosis of smooth muscle cells (14). Homocysteine may also induce atherosclerosis by affecting endothelial–derived relaxing factor, nitric oxide (NO). NO combined with homocysteine in the presence of oxygen to form s-nitroso homocysteine, which inhibits sulfhydryl dependent generation of hydrogen peroxide .The bioavailability of NO is decreased due to endothelial cell injury . This dysfunctional endothelium may be due to generation of oxygen radicals produced by homocysteine. Homocysteine enhances lipid peroxidation which may decrease the expression of endothelial NO synthase and directly degrade NO (13). Auto oxidation of homocysteine results in oxidation of LDL through generation of the superoxide anion radical. Homocysteine may also reduce the antioxidant status which could injure endothelial cells. Homocysteine stimulates platelet generation of thromboxaneA2, which is a vasoconstrictor and proaggregant (15).

Table:1Characteristics and laboratory data of the study subjects.

Parameters	AMI Patients (n= 60)	Normal Healthy Individuals (n= 35)
Age (Years) Mean	46.5 ±10.5	44.4 ±12.6
Gender (M/F)	49/11	28/7
tHcy (μmol/ L)	24.596.14	13.73 ± 3.54

Data was expressed as the mean ± S.E. unless otherwise noted.

This is one of the very few studies to document the prevalence of hyperhomocysteinemia in south Indian population. As the level of plasma homocysteine is very high among the myocardial infarction patients, the findings of this study underscores the importance of determining the levels of plasma homocysteine in individuals who are at high risk of developing myocardial infarction among the Tamil Nadu population. In conclusion,our data provide evidence that plasma total homocysteine levels are markedly elevated in acute myocardial infarction patients.

ACKNOWLEDGEMENT

This work was supported by UBCHEA. The authors are grateful to the Director of Vadamalayan Hospital , Madurai and all the staff members in the clinical laboratory

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