Original Article

Evaluation of serum homocysteine level in acute myocardial infarction patients of Nanded district

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Abstract

Introduction: Coronary artery disease is a major cause of myocardial infarction. Abnormal Homocysteine level appear to damage the arterial lining leading to atherosclerosis and ultimately to coronary artery disease. **Objective:** To study the serum homocysteine level in acute myocardial infarction in young patients in Nanded district. Methods and Material: The serum homocysteine was done in 40 patients of MI and 40 healthy controls belonging to age group 35-45 yrs. Results: According to our study mean Homocysteine in normal healthy controls was 12.56 ± 3.1 µmol/L while in AMI patients mean homocysteine was 23.97 ± 9.7 µmol/L. The level of serum homocysteine level in myocardial infarction patients was significantly high. Conclusion: This study indicated a strong positive correlation of raised homocysteine level with myocardial infarction in patients of Nanded district and as possible risk factor for myocardial infarction.

Keywords: Homocysteine, Myocardial Infarction, Thrombomodulin.

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INTRODUCTION

From past few years there is sudden rise in cases of atherosclerosis, coronary artery diseases and myocardial infarction even in young patients with no family history and also there is an increase in its associated morbidity and mortality. Risk for myocardial infraction is multifactorial and to dissect out the relative contribution of each contributing factor is difficult but not near impossible. Factors contributing are male gender, family history, smoking, diet, hyperlipidemia, diabetes mellitus, hypertension. Although coronary artery disease primarily occurs in patients over the age of 40, younger men and women can also be affected[1]. In the Framingham heart study about 4 to 10 % of patients with MI were < or = 40 or 45 years. Researchers are trying to reduce the incidence of cardiovascular disease in young patients by working on homocysteine level instead of traditional risk factors. The effect of homocysteine on the cardiovascular system was first described by Mc Culty[2]. Homocysteine is a non essential, sulphur containing amino acid, Vigneaud described it first in 1931. It is a thiol containing amino acid and is an intermediate product which forms during the metabolic demethylation of dietary methionine while linking the methionine cycle to folate cycle. It is present in plasma in four forms ; a free thiol (1%), disulphide (5-10%),mixed disulphide (5-10%),and protein bound thiol groups (80-90%).The combined pool of all four forms of homocysteine is referred as "Total plasma homocysteine".[3] The total Homocysteine level in plasma has been reported to be in the range of 5-15 mM/L in healthy individuals[4]. Several studies conducted in different parts of the world have reported that elevated level of plasma homocysteine are associated with coronary artery disease independent of risk factor[5]. Genetic background is also one more factor influencing homocysteine level. Methylenetetrahydrofolate reductase

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gene mutation is responsible for elevation of plasma homocysteine. Vascular injuries caused by Homocysteine is put forth by many theories, according to Poddar R.shivsubramaniam *et al*, Homocysteine promotes leaucocyte recruitment by an upregulating chemoattractant protein –I and interleuin 8 expression and secretion[6]. It also causes oxidation of LDL which has lipid peroxidation effect. Homocysteine increases smooth muscle cell proliferation and enhances collagen production[7] and it also causes endothelial injury [8].Once luminal narrowing occurs complicated plaque formation takes place. Rupture of such plaque is especially susceptible to thrombus formation and often the final occlusive event is myocardial infraction. Several studies also describes relation of homocysteine with inhibition of thrombomodulin activity, reduction of protein C activation leading to increased platelet aggregation and predisposition to endothelial injury. Hyperhomocysteinemia induces smooth muscle proliferation, accelerates oxidation of LDL cholesterol, impairs endothelial derived nitric oxide, decreases synthesis of heparin sulphate proteoglycan and also induces proinflammatory changes in the vessel wall[9]. Several studies have showed that there is a clear close response relationship between Homocysteine concentration and cardiovascular mortality in patients with confirmed coronary artery disease[10.] Normal Homocysteine concentration ranges between 5 and 15 µmol/L and hyperhomocysteinemia has been classified as follows, moderate 15-30 µmol/L, Intermmediate 30-100 µmol/L, and severe more than 100 µmol/L.[11]

No literature or studies on Homocysteine levels in population of nanded district is available. So we have undertaken the present study to evaluate serum homocysteine level in Acute myocardial infarction patients in population of nanded district and it is the first of its kind of study in this district.

MATERIAL AND METHODS

Study was conducted at Dr. Shankar Rao Chavan Government medical college and Hospital, Vishnupuri, Nanded, Maharashtra and it was approved by institutional ethical committee.

Sample Size: 40 Patients admitted to intensive care unit of DR S.C.GMC and Hospital. AMI patients were diagnosed by positive clinical signs and symptoms with appropriate clinical examination and 12 lead ECG signs. All routine biochemical investigations, along with CPK-MB, serum glutamate Oxaloacetate transaminase, lactate dehydrogenase and serum homocysteine level performed in our laboratory was recorded and collected as data

The Inclusion Criteria Patients belonging to age group 35 – 45 years. Patients having elevated serum homocysteine level and CPK-MB along with significant changes in ECG.

The Exclusion Criteria

Patients with severe comorbid conditions, previous history of MI, Congenital heart disease. Patients above 50 years age. Patients not willing to give consent.

Control group included 40 subjects without any coronary heart disease and normal serum Homocysteine level and ECG signs and all above laboratory investigations were also performed on them.

Method

About 2 ml of 12 hr Fasting blood sample was collected from the AMI patients and healthy controls in EDTA coated bulb.. Blood sample was centrifuged within 30 minutes. Serum homocysteine was estimated by using XL-640 Fully Automated Analyser in our laboratory. The Diazyme Hcy Enzyme kits (commercial and standard) were used for estimation.

Principle

The Diazyme Hcy Enzymatic Assay is based on a novel assay principle that assesses the co-substrate conversion product. In the assay, oxidized Hcy is first reduced to free Hcy which then reacts with a co-substrate, SAM, catalyzed by a homocysteine S-methyltransferase. The co-substrate conversion product is amplified by coupled enzymatic cycling reactions. The tHcy level in the sample is directly proportional to the amount of NADH conversion to NAD+ (ΔA 340nm). The values were considered normal when < or = 15.0 µmol/L in our institutional laboratory.

Statistical Analysis

All values were expressed in mean ± S.D. ‘ z’ test was used to compare the mean as samples were 40.

RESULT

Table 1: Laboratory data of control group

	Control group (n=40)
Age in years (mean)	42 ± 4.8
Gender (M/F)	33/07
tHcy µmol/L	12.56 ± 3.1

Table 1 laboratory data shows that out of 40 normal subjects 33 (82.5%) subjects were male and 7 (17.5%) subjects were female. The mean of the age in control group was 42 and it’s S.D. 4.8. Mean of plasma homocysteine concentration in control group was 12.56 and S.D 3.1.

Table 2: Laboratory data from Acute Myocardial infarction patients

	AMI patient (n=40)
Age in years (Mean)	43.61± 4.3
Gender (M/F)	35/5
tHcy µmol/L	23.97 ± 9.7

TABLE 2: Laboratory data shows out of 40 Acute Myocardial Infraction patients 35 (87.5 %) were male and 5 (12.5%) were female. Mean of the age of AMI patients was 43.61 and it's S.D. 4.3. Mean of plasma homocysteine concentration in acute myocardial infraction patients was 23.97 and its S.D. 9.7

DISCUSSION

There is marked increase in plasma homocysteine concentration of acute myocardial infraction patients (table 2) in comparison with control group (table 1). Statistically significant difference of ($p < 0.05$) was observed in the mean of plasma homocysteine concentration in acute myocardial infraction patients (23.97 ± 9.7 µmol/L) and normal healthy individuals of control group (12.56 ± 3.1 µmol/L) and statistical association between them is well established. The results of our study indicates that there is association between high serum homocysteine level and increased risk of cardiovascular disease. Studies on association of hyperhomocysteinemia with coronary artery disease in different populations have yielded conflicting results with some positive evidence for an association[12.] While few other authors found no association[13.] This variation may be due to differences in ethnic group, genetic background, polymorphism in genes encoding enzyme, dietary intake in population, and different views of authors in definition of cases taken for their study. Homocysteine plays a role in inducing atherothrombosis in many ways, Homocysteine thiolactone a by product of oxidation of homocysteine combines with LDL to form foam cells. [14] The LDL rich foam cell embed themselves in the vascular endothelium and become fatty streak which is the precursor to atherosclerotic plaque. Homocysteine thiolactate probably impairs the oxidative phosphorylation and enhancement of the proliferation and fibrosis of smooth muscle cell.[15] It may also induce atherosclerosis by affecting endothelial derived relaxing factor, nitric oxide(NO). NO combines with homocysteine in the presence of oxygen to form S-Nitrosohomocysteine which inhibits sulfhydryl dependent generation of hydrogen peroxide. The bioavailabilty 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.[16] Auto oxidation of homocysteine causes oxidation of LDL by generation of superoxide anion radical. Homocysteine may also reduce the antioxidant status which could injure endothelial cells.[17] Homocysteine stimulates platelet aggregation of thromxane A2 which is vasoconstrictor and proaggregant.[18] Hyperhomocysteinemia may also occur due to nutritional deficiency which leads to low blood concentration of folate, vitamin B_{12} or vitamin B_6.[19] Plasma homocysteine concentration are found to be higher in Indian Asian overseas compared to the north Americans and European whites[20]. A metanalysis conducted by Boushey *et al* showed that homocysteine was a graded independent risk factor for atherosclerotic disease in coronary, cerebral and peripheral vessel[21]. McCully *et al* concluded that moderately high level of plasma homocysteine are associated with subsequent risk of myocardial linfarction.[22] Recent reports on homocysteine suggests that it is an important single largest risk factor of vascular disease, including stroke and coronary artery disease.[23] Neverthless a plethora of studies, show that elevated serum homocysteine is an independent risk factor for myocardial infraction.

CONCLUSION

This study indicates that, there is a significant positive correlation between raised homocystine level and Acute myocardial infraction. Our data appeals with evidence that plasma total homocysteine level is markedly raised in acute myocardial infraction patients of Nanded district. This study indicates the importance of determining plasma homocysteine level in individuals who are at high risk of developing Acute myocardial infraction and taking necessary precaution may prevent and reduce mortality in patients of Nanded district.

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