

CASE REPORT

A STUDY ON EARLY ONSET CORONARY ARTERY DISEASE IN RELATION TO HYPER HOMOCYSTEINEMIA IN PATIENTS YOUNGER THAN 40 YEARS OF AGE

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ABSTRACT: There has been a rising incidence of myocardial infarction as a whole in recent times much because of changing pattern of life style, urbanization, changing food habits, and increase in cigarette smoking, psycho social stress and increase in the incidence of diabetes mellitus. Adding to this there is drastic increase in the incidence of MI in young people much to the influence of novel risk factors which are of current debate especially homocysteine, lipoprotein little (a), fibrinogen, anticardiolipin antibody, protein C, protein S and antithrombin deficiency. The first ever positive prospective study on plasma homocystein and CAD was reported in 1992 by Selhubetal who showed an association of plasma homocysteine with extracranial carotid stenosis in the elderly. We report our study to analyze the special risk factors of MI in patients younger than 40years of age in special reference to serum homocysteine levels.

KEYWORDS: Coronary Artery Disease, Hyper Homocysteinemia

INTRODUCTION: Atherosclerotic plaques are the most common cause of CAD ¹. More than 200 coronary risk factors have been reported. Recently homocysteine has been shown to be involved in the pathogenesis of CAD.

Homocysteine is a sulfur containing amino acid produced by demethylation of the essential amino acid methionine ². Homozygotes with homocystinuria have high levels of circulating tHcy (> 100Gmol/l) are at high risk for premature arteriosclerotic vascular disease and venous thrombosis. If homocystinuria remains untreated, about 50% of patients may experience thromboembolic events and mortality could reach 20% before the age of 30 years.

Although the exact mechanism of atherothrombosis associated with hyperhomocysteinemia is not clearly understood, in many of the reported effects of plasma homocysteine are thought to be mediated by its atherogenic effects, such as vascular smooth cell migration and proliferation ³ and prethrombotic properties, such as inhibition of thrombomodulin activity, reduction of protein C activationthe increase of platelet aggregation and predisposition to endothelial cell injury ⁴.The aim of this study is to analyze the clinical profile of myocardial infarction, study the sensitivity of cardiac markers in diagnosing AMI and to study the special risk factors of MI at this age in special reference to serum homocysteine levels, serum lipid profile, serum lipoprotein little (a), plasma fibrinogen in 40 patients below the age of 40 years.

AIMS AND OBJECTIVE:

1. To study the clinical profile of MI.
2. To study the sensitivity of Cardiac markers in diagnosing Acute MI.

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3. To study the Special risk factors of MI at this age in special referance to serum homocysteine levels, serum lipid profile, serum lipoprotein little (a), Plasma fibrinogen in profile cases.

MATERIALS AND METHODS:From Jan 2005 to Jan 2007, 40 consecutive patients initially admitted in M.G.M.H for MI with age less than 40 years were included in the study. Exclusion criteria for patients and controls included presence of congenital and or valvular heart disease, age above 40years and lack of ECG changes, no typical chest pain, and no 2D echo evidence of RWMA.

Every patient completed a detailed questionnaire providing information about history of hypertension, hyperlipidemia, smoking, diabetes mellitus and family history of premature CAD (documented CAD in at least one first-degree relative before the age of 55 years for men and 65 years for women).

Routine investigations like CBP, ESR and RBS were done in 4 hrs after admission.ECG was taken from every patient at arrival and hourly intervals thereafter for the first 4 hours. Serum cardiac enzymes levels were evaluated in all the patients. Serum lipid profile was done in all patients within 6hrs after the acute attack or after one month.

Considering the rising importance of newer risk factors, serum levels of hmocysteine, lipoprotein little (a) and plasma fibrinogen was done in all patients. 2D echo was done in the first hour after admission in patients shifted to ICCU and on subsequent day for those patients who stayed in MCW. Coronary angiogram was done in possible cases mostly 5 days after admission and with one month.

INCLUSION CRITERIA:

1. Age less than 40 years
2. ST elevation > 1 mm in limb leads, more than 2 mm in chest leads which is present in atleast 2 continuous leads.
3. No ST elevation but with typical prolonged chest pain, raised cardiac enzymes and 2D echo evidence of RWMA.
4. No ST elevation but typical prolonged chest pain, normal cardiac enzymes and, 2D echo evidence of RWMA

EXCLUSION CRITERIA:

1. Age more than 40 years.
2. No ECG changes, No typical chest pain, Normal cardiac enzymes and No 2D echo evidence of RWMA
3. Presence of congenital and / or valvular heart desease.

RESULTS: Out of the 40 patients, 19(47.5%) had hyperhomocysteinemia of which 13(32.5) had moderate elevation (15-30 μ m/l) and 6(5%) had marked elevation > 30 μ m/l. this study shows a very high association of increased homocysteine levels to coronary heart disease probably because Indian population have high baseline levels, which has to be confirmed by measuring the same in control population. This is because of poor nourishment in most Indians particularly food rich in Vitamine B6, B12 and folic acid. These patients were not followed with vitamin therapy subsequently. 6(15%) patients had plasma fibrinogen greater than 360 mg/dl which is a significant association. Out of 9 patients in whom anticardiolipin antibody was done only one (11.1%) patients had levels greater than 20 GPLU/ml. This particular patient did not have evidence of arterial or venous thrombosis

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anywhere else. Serum Lipoproteins little (a) was more than 30 mg/dl in 5 patients (12.5%). The association of the same with CDH is less in Indians when compared to that of homocysteinemia.

DISCUSSION: The studies in relation to myocardial infarction in young patients have taken a cut off limit for age as 45 years. We have taken upper age limit as 40 to increase the sensitivity maximum incidence of MI in this study was between 26 – 30 years (35%) and least between 21 – 25 years (15%) in contrast to 35 – 40 years age group (45%) in Jitsinghetal study. The mean age occurrence was 30.5 in contrast to 38.40 in Jitsinghetal study. The male to female ratio is similar to Jitsingh study. About novel risk factors in MI, moderate elevation of homocysteine was present in 13(32.5%) patients and marked elevation in 6(15%) patients. The SHARE study had found increased homocysteine levels to about 11.22% in South Asia,10% in Europeans and 3.79% in the Chinese.

Boers etal gathered a data from a number of studies and demonstrated that mild hyperhomocysteinemia after a methionine load test occurs in 21%, 24% and 32% of patients with CAD, CVD and peripheral vascular disease respectively. Selhubetal, found that from a group of 1160 elderly patients in between ages 67-96 in the Framingham heart study<hyperhomocysteine (>15µm/l) was present in 29.3%. This study also showed that plasma homocystein increase with age. In a group of 304 patients with CAD vs Controls, Robinson etal found that CAD increased as plasma homocystein increased even within the normal range. The present study shows a very high association of CHD to hyperhomocysteinemia because Indian people have high baseline levels, which has to be confirmed by measuring the same in control population.

Identification of new markers associated with an increased risk of CAD may provide a better insight into the pathology of coronary atherosclerosis and facilitate the development of preventive and therapeutic measures⁵. Ten of 13 case-control studies that assessed the association between fasting tHcy levels and CAD showed significantly higher levels of tHcy in patients with CAD compared to those without CAD.

The results of the Multiple Risk Intervention Trial failed to find any association between CAD and tHcy⁶. In a review of 43 studies, Christen observed that, in contrast to cross-sectional and case-control studies, prospective studies indicated less or no predictive ability for tHcy in cardiovascular disease⁷. Therefore, whether tHcy is a Furthermore risk factor, seven of the 13 case-control studies adjusted the tHcy levels for CAD risk factors and six of them observed an increased risk of CAD. Al Obaidi and associates showed that increased homocysteine levels are associated with a higher risk of ischemic myocardial injury in patients presenting with acute coronary syndromes⁸.

Some studies support the hypothesis that elevated plasma tHcy levels and low folate are independent risk factors for MI among youngwomen⁹ and that elevated tHcy is a strong predictor of late cardiac events in acute coronarysyndromes¹⁰, therefore early diagnosis and treatment of hyperhomocysteinemia in patients with CAD are very important. In recent studies by Schynder and Bozkurt, increased tHcy level is associated with severely narrowed major coronary arteries. Plasma homocysteine levels can easily be decreased with folic acid or vitamin B6, B12 supplementation. Several randomized studies are currently underway to assess the effects such therapy on progression of angiographic extent of CAD.

CONCLUSION:Many people claim that up to 10% of cardiovascular events could be prevented by a reduction in total homocysteine in patients with hyperhomocysteinaemia. A high dietary intake of

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folate, low coffee consumption, cessation of smoking and an increase in physical exercise can all contribute to a reduction in homocysteine in the general population. As far as therapy is concerned, folic acid is used widely and safely, its combination with B12 is becoming more accepted, whereas the usefulness and safety of B6 need further investigation. On the initial diagnosis of hyperhomocysteinaemia the aetiology must first be investigated and the cause must be treated if it is apparent. Methionine loading may also be of help in the diagnosis of hyperhomocysteinaemia in patients with borderline values (around 15 $\mu\text{mol/L}$).

Treatment with B12/folate/B6 may be given initially until plasma levels have normalised, from this point B12/folate treatment may be continued. Even though the value of this treatment in the prevention of CAD has not been fully determined, there is no reason not to give it (unless there is some other contraindication) since it causes no side effects and has a relatively low cost.

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