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ROLE OF HOMOCYSTEINE AS A RISK FACTOR IN YOUNG ADULTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT:

Background: Coronary Artery Disease (CAD) occurs at a younger age in Indians. Atherosclerosis is the most common pathological process that leads to cardiovascular diseases. The Framingham risk score (FRS), known as an important instrument in predicting coronary artery disease in patients with traditional risk factors, such as dyslipidaemia, hypertension, diabetes mellitus (DM), and smoking, seems to have underestimated the coronary artery disease risk in individuals with high homocysteine plasmatic levels. Inborn errors of metabolism arising from a deficiency of Homocysteine (Hcy)-metabolizing enzymes result in extremely high Hcy concentrations and are associated with atherosclerosis and premature thrombosis. In this study we made an attempt to find out the role of homocysteine as a nontraditional risk factor in young adults with acute myocardial infarction

Materials and Methods: This is a cross-sectional, cohort study in young MI patients carried out in Department of General Medicine ACSR govt. medical college NELLORE. The Study subjects were Patients admitted in Intensive Care Unit for MI. Patients were interviewed and a designed questionnaire was used to collect demographic details, previous history of MI, presenting symptoms, the earlier medication and food supplementation used.

Results: In the study, Hcywas identified as a non-traditional risk factor for MI. It was found that 77.14% had higher homocysteine than control. In the study, mean plasma Hcy level in healthy subjects was 6.13±0.28µmol/l and in CAD patients the total plasma homocysteine was 15.6±1.8µmol/l (P=0.0377) indicating that Hcylevel is an independent marker of CAD.

Conclusions: Of the 35 MI patients, 8(22.85%) were having desirable plasma homocysteine levels (<10µmol/L), 15(42.85%) were having normal but undesirable homocysteine levels (10- 15µmol/L), 8(22.85%) had mild hyperhomocysteinemia (15-20µmol/L), 3(8.5%) were intermediate (20-50 µmol/L) and 1 (2.5%) had severe Hyperhomocysteinemia (>50%).

Keywords: Coronary Artery Disease, Myocardial Infarction, Homocysteine.

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INTRODUCTION: Coronary Artery Disease (CAD) occurs at a younger age in Indians, with over 50% of CAD mortality occurring in individuals aged less than 50 years, and one-fourth of all acute Myocardial Infarctions (MIs) are reported in patients below 40 years[1] . Clinical presentation of CAD in young Indians may vary from multiple vessel disease without any clues offered from risk factors to extensive ischemia in an asymptomatic individual[2] . Atherosclerosis is the most common pathological process that leads to cardiovascular diseases such as myocardial infarction (MI), heart failure, stroke and claudication[3] Occurrence of CAD in absence of any conventional risk factors at a young age makes it difficult to understand the aetiopathogenesis[1] . A number of populations at high CVD risk, including Celts and Indo-Asians, have regularly been shown to have high rates of folate and cyanocobalamin (vitamin B12) deficiencies, associated with increased levels of an intermediate in one carbon metabolism – homocysteine (HCY). Homocysteine is known as an independent risk factor for atherosclerosis[4]. Studies in animal models have shown that elevated HCY levels result in increased oxidant stress, impaired endothelial function and increased thrombogenicity, which act together to promote atherosclerosis[5].

The Framingham risk score (FRS), known as an important instrument in predicting coronary artery disease in patients with traditional risk factors, such as dyslipidaemia, hypertension, diabetes mellitus (DM), and smoking, seems to have underestimated the coronary artery disease risk in individuals with high homocysteine plasmatic levels[6]. The correlation between hyperhomocysteinemia and atherosclerotic disease was first proposed more than 40 years ago. It was first identified by McCully in 1969. Several cross-sectional and case control studies have pointed towards a clear correlation between total serum homocysteine and the incidence of coronary, carotid, and peripheral vascular disease[7].

Homocysteine has emerged as a significant marker of vascular disease, especially in patients of Asian origin[8]. HCY is a sulphur-containing amino acid in the body produced by conversion of methionine, an essential amino acid present in foods regularly consumed within the diet. Low levels of HCY (5–15 ìmol/L) are normally found in the plasma. However, genetic defects in the enzymes of HCY metabolism markedly increase HCY levels[5]. Data from epidemiological studies suggested that individuals with even moderately elevated levels of homocysteine (eg, fasting blood levels exceeding approximately 16 μmol/L) have small to moderate increased risks of cardiovascular disease (CVD)[9].

AIM & OBJECTIVES-

To study the possible role of homocysteine as non-traditional risk factor in young patients presenting with acute myocardial infarction in a tertiary care teaching hospital.

MATERIALS AND METHODS

This study was carried out in Department of General Medicine ACSR Govt. Medical College Nellore. This is a cross-sectional, cohort study carried out in young MI patients. The Study subjects were Patients admitted in Intensive Care Unit between January 2022 to December 2022, for MI were enrolled in the study. Patients were interviewed and a designed questionnaire was used to collect demographic details, previous history of MI, presenting symptoms, the earlier medication and food supplementation used. The investigator obtained permission and ethical clearance from the authorities, prior to the data collection and assured confidentiality to the subject to get their cooperation and explained the purpose of the study. The results were analyzed through descriptive and inferential statistics using Graph-Pad software.

INCLUSION CRITERIA:

The following categories of patients from cardiology / intensive care units department are included in the study.

1. Inpatients admitted for myocardial infarction.
2. Patients with age 45 years and below only.

EXCLUSION CRITERIA:

1. Patients with age above 45 years.
2. Patients suffering from diseases such as renal failure, hypothyroidism, psoriasis,

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any malignancies and psychiatric disorders.
3. Patients taking drugs such as Methotrexate, oral contraceptive pills, L-dopa, nicotinic acid and Theophylline.
4. Patients taking folic acid or any vitamin supplement.
5. Patients without cardio-respiratory infections
6. Patients who are not willing to participate were excluded from the study.

ESTIMATIONOF HOMOCYSTEINE

Estimation of Homocysteine was performed by automated immunoassay analyzer – IMX ABBOTT System (USA).

OBSERVATIONS:

The study included 35 cases presenting with MI and 6 healthy subjects as controls.

Risk Factors:

Of the 35 patients with MI, 29 (82.85%) were males and 6 (17.14%) were males. 3 (80%) were Normal, 28 (8.5%) were Underweight, 4 (11.42%) were Overweight.

Of the 35 patients with MI, 22 (62.85%) were smokers, 15 (42.85%) were alcoholics, 7 (20%) were Diabetics and 6 (17.14%) were hypertensive. Of the 35 patients with MI, 7 (20%) had a significant family history and 28 (80%) had no family history.14 had past history of MI.

Homocysteine levels:

Of the 35 patients with MI, 8 (22.85%) had normal homocysteine and the remaining had abnormal values.

Comparison of Homocysteine levels of groups:

Table-1

C = Control.

T0 = Patients with normal cholesterol

T1 = Patients with hypercholesterolemia

Comparison of Homocysteine levels of group T1 with group C was found to be significant with the P value of 0.0292.

Comparison of Homocysteine levels of group T0 with group C gave P value 0.0621 and was considered to be not quite significant.

TABLE-1. Comparison of mean Homocysteine of patients with (T1), (T0) and group C.

Group	Mean Homocysteine +/- SEM	S. D
C	6.1333 +/- 0.2765	0.6772
T1	14.7217 +/- 1.878	9.007
T0	17.466 +/- 3.873	13.417

DISCUSSION:

The prevalence of CAD is 89% – 300% higher among Indian men than among whites in the US. The burden of CVD varies markedly within India, with Kerala, Punjab, and Tamil Nadu having the highest prevalence of CAD, high cholesterol, and high blood pressure. The prevalence of CAD has increased seven-fold in urban India and fourfold in rural areas between 1970 and 2013. Current prevalence of 14% in the urban and 7% in the rural populations. The number of patients with CAD also increased to 24 million in 2016. CAD was the leading cause of deaths (18% of all deaths) in India in2016. Only a few nationwide studies that have evaluated prevalence of known CHD are available. These include the India Migration Study (1.45%),47 India Heart Watch (2.55%),48 and PURE (2.04%)49 study[10].

According to the Indian studies, the prevalence rate of CAD was 9.7% in Delhi, 3.5% in Rajasthan and 11% in urban population of South India[11]. Among all the ethnic groups studied, the standard mortality ratio for men born in the Indian subcontinent and aged between 20 and 69 years was by far the highest[12].

In the analysis by Balarajan, the excess mortality seen among immigrants from the subcontinent steadily increased with decreasing

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age. Men in the age group 20-29 and 30-39 years had SMRs of 313 and 210, respectively. The rate of first MI was five times higher among Indian men compared to the Europeans in the study[13].

Further, the mean age at first MI was about 5 years lower for the Indian men (50.2 v 55.5 years). Indians also suffered larger infarcts as estimated from peak creatine kinase (CK) levels and degree of left ventricular dysfunction. Lowry et al., found a small increase in the atheroma score among South Asian patients when compared to the Europeans in the study. More South Asian patients (38% v. 22%) were found unsuitable for surgery because of extensive disease. CAD tends to occur earlier in life among people of Indian descent[14].

In addition to the conventional risk factors such as smoking, HT, DM, hypercholesterolemia, obesity and reduced physical activity Hyperhomocysteinemia was found to be independent risk factor of CAD. Identification of new markers such as Homocysteine 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 measures.

Normal values of plasma total Homocysteine are between 5 and 15 +/- mol/L. In our study, the mean plasma Homocysteine in healthy subjects was 6.133 +/- 0.2765 and in CAD patients, the total plasma Homocysteine was 15.5942 +/- 1.801 (P = 0.0377) indicating that Homocysteine level is an independent marker of CAD. A twofold increase in likelihood of MI among persons with a total Hcy concentration more than or equal to 15 +/- mol/L has been noted in a United States study[15]. An Indian study which gave a mean value of 22.81 +/- 13.9 in cases and 7.77 +/- 7.3 in controls showed a significant difference of Homocysteine values between the two groups and hence showed increased Homocysteine levels among patients with coronary artery disease[16].

However, another Indian study with a mean Homocysteine value of four cases as 18.30 +/- 10.08 +/- mol/L and control 18.04 +/- 10.65 reported a negative association between Homocysteine with MI[17].

Homocysteine and hypercholesterolemia:

In the Hordaland study in Norway, increasing plasma levels of cholesterol, triglycerides and smoking were associated with increasing levels of Homocysteine. In our study, Homocysteine levels were actually less (14.721) in CAD patients with hypercholesterolemia when compared to CAD patients (17.45) without this risk factor. Lowered Hcy may be due to change in life style adopted by patients as part of treatment for high cholesterol. In addition, majority of our patients were manual workers, not having sedentary life style pattern.

HDL was comparatively less in patients (40.6) as compared to controls (45.66). VLDL was relatively high in patients (42.3) as compared to controls. These results help to confirm the fact that hyperhomocysteinemia along with conventional risk factors give rise to CAD and MI in young individuals. Alarmingly, out of 35 patients studied (65.7%) 23.5 had hypercholesterolemia.

Limitations of the study: -

However, as the study was limited to a small population, analysis of a larger group would definitely give an insight into the various causative factors leading to hyperhomocysteinemia and its role in CAD amongst the young Indian population.

CONCLUSION

In the study, Homocysteine was identified as a nontraditional risk factor for MI. Among the study population of MI, it was found that 77.14% had higher Homocysteine than control. In the study, the mean plasma Homocysteine level in healthy subjects was 6.13±0.28µmol/l and in CAD patients the total plasma Homocysteine was 15.6±1.8µmol/l(P=0.0377) indicating that Homocysteine level is an independent marker of CAD. It was also found that Homocysteine levels were higher in patients who had additional conventional risk factors when compared to patients without such risk factors except hypercholesterolemia.

As such Asian Indians are genetically predisposed to CAD. Hence it is mandatory to determine Homocysteine levels in people after thirties so that preventive measures such as

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vitamin supplementation and life style modifications could be undertaken and thus reduce the incidence and mortality due to CAD.

DECLARATIONS

Conflict of interest: There was no conflict of interest.

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Contribution Details:

Role (Concepts, Design, Definition of intellectual content, investigation, manuscript writing, etc.)	Contributor 1	Contributor 2	Contributor 3	Contributor 4
Concepts	✓			
Design	✓	✓	✓	
Definition of intellectual content	✓		✓	
investigation	✓	✓		✓
manuscript writing	✓		✓	✓
Proof reading	✓		✓	
Literature search	✓	✓	✓	
Final submission	✓	✓		✓
Plagiarism check			✓	