

Serum Homocysteine Level as a Risk Factor for Acute Coronary Syndrome in Middle Aged Persons- An Observational Study

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ABSTRACT

Background: Abnormal Homocysteine (HCY) level appear to contribute to atherosclerosis by direct toxic effect that damages the arterial linings, interfering with the clotting factors and oxidation of LDL. Some 10% to 20% of cases of Coronary heart disease have been linked to elevated level of serum Homocysteine. Objective: This is an observational study designed to study the Homocysteine levels in middle age group patients with acute coronary syndrome & to carry out statistical analysis to evaluate Homocysteine as an independent risk factor for MI. **Methods:** The mean serum Homocysteine in patients of MI and control was calculated and its association with fasting lipid profile, 2decho and ECG was done. **Results:** The mean serum Homocysteine in case and control was 29.77 $\mu\text{mol} / \text{L}$ with a significant p value of 0.001. The difference in Homocysteine levels observed between patients with LDL-C $\geq 100 \text{ mg}\%$ and those with LDL-C $< 100 \text{ mg}\%$ was not significant. The difference in Homocysteine levels observed between patient's very low ejection fraction with 20% EF and with high EF 50% has significant correlation with mortality more with low EF. Also in our study more common presentation was anterolateral wall MI but there was no significant correlation. **Conclusion:** From the above findings, in this study the low levels of LDL-C and high levels of HDL-C did not protect the patients against the Homocysteine induced coronary artery disease. Also increased levels of homocystiene are directly proportional to the complications of acute coronary syndrome henceforth, plasma total homocystiene plays a vital role and an independent risk factor for middle aged patients with acute coronary syndrome even without any conventional risk factors.

Keywords: Serum Homocystiene, Acute Coronary Syndrome.

INTRODUCTION

Acute myocardial infarction (ACS) refers to a group of health conditions due to reduced blood flow in the artery, and therefore cannot function properly or dies. The most common symptoms are chest pain, which usually radiates to the left or right corner of the jaw and is associated with nausea and sweating.^[1]

Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium; it typically occurs when there is an imbalance between myocardial oxygen supply and demand. The most common cause of myocardial ischemia is atherosclerotic disease of an epicardial coronary artery (or arteries)

sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery.

Patients with acute coronary syndrome (ACS) commonly are classified into two groups to facilitate evaluation and management, namely patients with acute myocardial infarction with ST-segment elevation (STEMI) on their presenting electrocardiogram (ECG) and those with non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS). The latter include patients with non-ST-segment elevation myocardial infarction (NSTEMI), who, by definition, have evidence of myocyte necrosis, and those with unstable angina (UA), who do not. The relative incidence of NSTEMI is rising due to the increasing burden of diabetes and chronic kidney disease in an aging population, while STEMI is declining due to greater use of aspirin, statins, and less smoking. Among patients with NSTEMI-ACS, the proportion with NSTEMI is rising while that with UA is falling because of the wider use of troponin

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assays with higher sensitivity to detect myocyte necrosis, thereby reclassifying UA as NSTEMI.^[1]

The Global Burden of Disease study estimate of age-standardized CVD death rate of 272 per 100 000 population in India is higher than the global average of 235 per 100000 population.

Hyperhomocysteinemia, described as an raised plasma total homocysteine levels (>13 μM), is one such factor.^[2]

Some studies have shown that elevated serum homocysteine is a major risk factor for Acute coronary syndrome in middle aged patients

Hyperhomocysteine is a major prothrombotic factor associated with acute coronary syndrome in middle-aged patients. Hyperhomocysteinemia is a major risk factor for arterial malfunction in mature, wellbeing individuals

Hyperhomocysteinemia leads to an increase in blood pressure, raising the complication of acute coronary syndrome. High plasma homocysteine will show to cause oxidative damage to endothelial some of the mechanisms involve platelet aggregation attachment to endothelial cells, promoting smooth muscle cell growth of vascular endothelium, and raised homocysteine binding to major factors of thrombosis such as β- thromboglobulin, factor VIIc and tissue plasminogen activator.

Through diet and genetic factors, plasma homocysteine levels are strongly influenced. The most effective food ingredients were folic acid and vitamins B6 and B12.

Pathophysiology of Acute Myocardial Infarction

Myocardial infarction usually occurs when there is a sudden decrease in coronary blood flow with flow after obstruction of coronary arterial thrombosis, previously narrowed by atherosclerotic fissures, rupture or ulcer, and when thrombosis is needed. Plaque position break and leads to occlusion of coronary artery.

The cascade of coagulation is stimulated by contacting a tissue element in place of a damaged plaque in endothelial cells. Activated factor 7 and factor 10, eventually helps in prothrombin to thrombin conversion, which then converts fibrinogen to fibrin. The artery of coronary to be injured will sooner or later be closed with a thrombus having platelet aggregates and fibrin strand.

Clinical Features of Acute Myocardial Infarction

- Chest Pain
- Breathlessness
- Sweating

Pathogenesis of Vascular Disease in Hyperhomocysteinemia

In research of atherogenesis, raised plasma total homocysteine levels are accompanied by dietary lipids, which cause intimate damage. An alternative hypothesis for the straight forward effect of decreased homocysteine on cells of endothelium

damage is the thing that homocysteine acts inversely by oxidizing it along simultaneously generating species of reactive oxygen

Atherosclerosis progression is involved with increased prooxidative activity, vascular disease of prematuration associated with elevated plasma homocysteine levels may get associated with raised pro-oxidative activity but not raised homocysteinemia. High levels of homocysteine have been shown to induce permanent damage to endothelial cells of artery, accelerating the thrombosis development with atherosclerosis and hence plaque rupture and clot formation and infarction.

MATERIALS AND METHODS

It's an observational prospective study where the homocysteine levels has been measured in patients diagnosed to have acute coronary syndrome in the age group of 30 to 60 years. Correlation of homocysteine as a risk factor in acute coronary syndrome is statistically analysed

Type of Study: Observational prospective study.

Source of data:

- The study is among the patients with acute coronary syndrome admitted in BLDE Hospital Vijayapur.
- The patients will be informed about study in all respects and informed consent will be obtained.
- Period of study will be from DECEMBER 2017 TO APRIL 2019 SAMPLE COLLECTION Oral and written consent will be taken from the subjects prior to the collection of specimens

Inclusion Criteria:

All the patients of either sex with acute coronary syndrome of middle age (30 to 60yrs) admitted in BLDE Hospital.

Exclusion criteria:

- 1) Recent history of surgery or trauma within the preceding 2 months.
- 2) Renal insufficiency (serum creatinine>1.
- 3) Patients with CVA or previous history of CVA.
- 4) Malignancy.
- 5) Patients having evidence of infection, inflammatory disease, active hepatic disease, severe dehydration.

List of Investigations Complete haemogram, Random blood sugar serum homocysteine levels. Ecg 2d echo/echo doppler Trop t, cpkmb Chest xray Lipid profile

Serum homocysteine level will be done by chemiluminiscense method in laboratory and considered high if it is > 13 mg/dl.

RESULTS

The study of serum homocysteine level as a risk factor for acute coronary syndrome in middle aged

patients was done in patients admitted to ICCU of Shri. B. M.Patil Medical College and Research Centre from December 2017 to April 2019. Total of 65 patients were admitted with acute coronary syndrome, who fulfilled the inclusion criteria

In our study of 65 patients, most of the patients came with complaints of chest pain with vomiting that is 27 patients (41.5%), with next most common presenting complaints with chest pain with sweating, 11 patients (16.9%) as shown in [Table 1]

In our study of 65 patients mean value of serum homocysteine level is higher in 17 patients (26.2%) with ejection fraction of 50% respectively and mean value of serum homocysteine least in 1 patient with ejection fraction 20%. However the death rate is more significant in patients with ejection fraction 20% as shown [Table 2].

Mean value of serum homocysteine level is higher in patients 20% ejection fraction with a mean of 42.0 with SD 0.0, than others with statistically significant p value 0.019 respectively as shown in [Figure 1]

In our study out of 65 patients, 9 deaths happened secondary to complications of acute coronary syndrome with very high homocysteine levels have more complications leading to death. Out of 9 patients with high homocysteine levels, ventricular tachycardia patients (4) have very high mortality rate (44.4%) as shown in [Table 3]

In our study of 65 patients with acute coronary syndrome, 9 patients (13.8%) had very high serum homocysteine levels and died and 56 patients (86.2%) of who are having moderately high serum homocysteine levels have been improved with medical therapy as shown in [Table 4]

This graph depicts among 65 patients with acute coronary syndrome mean value of homocysteine level is higher among death patients with significant p-value of as shown in [Figure 2]

Table 1: Distribution of Cases According to Symptoms

Symptoms	N	%
Breathlessness With Vomiting	2	3.1
Chest Pain	4	6.2
Chest Pain With Breathlessness	8	12.3
Chest Pain With Giddiness	4	6.2
Chest Pain With Nausea	5	7.7
Chest Pain With Sweating	11	16.9
Chest Pain With Vomiting	27	41.5
Chest Pain With Vomiting And Nausea	1	1.5
Chest Pain With Vomiting With Sweating	2	3.1
Chest Pain, Breathlessness And Vomiting	1	1.5
Total	65	100

Table 2: Distribution of Cases According to 2D Echo

2D Echo	N	%
20%	1	1.5
25%	2	3.1
30%	7	10.8
35%	10	15.4
40%	9	13.8
45%	11	16.9
50%	17	26.2
55%	2	3.1
60%	6	9.2
Total	65	100

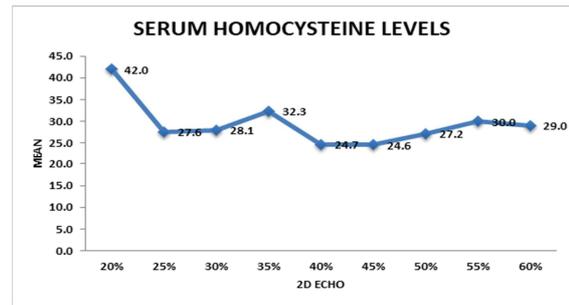


Figure 1: Mean Level of Serum Homocysteine According To 2D Echo

Table 3: Distribution of Cases According to Complications

Complications Of Acute Coronary Syndrome	Number Of Deaths Due To Complications With High Homocysteine Levels(N)	Serum Homocysteine Levels Range	%
Ventricular Fibrillation	2	32 -34	22.2
Ventricular Tachycardia	4	35 -40	44.4
Cardiogenic Shock	2	30-33	22.2
Acute Lv Failure	1	30-34	11.2
Total Deaths	9	30-40	100

Table 4: Distribution of Cases According to Outcome

Outcome	N	%
Death	9	13.8
Improved	56	86.2
Total	65	100

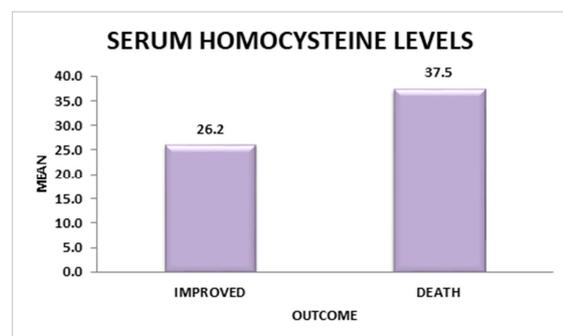


Figure 2: Mean Level Of Serum Homocysteine According To Outcome

DISCUSSION

A total of 65 patients included in this study and were analyzed to study homocysteine levels in acute coronary syndrome patients.

We measured fasting plasma total homocysteine levels by HPLC with fluorescence detection in 65 patients presenting with acute coronary syndromes.^[3] Demographic data, classical risk factors (systolic blood pressure, diabetes mellitus, smoking, ethanol intake, family history of ischaemic heart disease) and life-style habits were recorded. Lipid fractions including total cholesterol, triglycerides, HDL-cholesterol, total cholesterol/HDL-cholesterol ratio,

serum creatinine, LDL-cholesterol and vitamins involved in the metabolism of homocysteine, folic acid and vitamin B12 were also assessed.^[4]

In our study, the most common age group affected is 50-60 years more compared to other age groups with mean range of 52.1 and SD OF 7.8 observed respectively.

Another study done by Mesas C et al,^[5] in 50 patients hospitalized with acute coronary syndrome in Southern Brazil, they observed that, mean age group was 59 years (standard deviation SD = 10.5 years) which was significantly similar as in this study.^[6]

In this study there was male predominance i.e, 69.2% of patients and female patients were 30.8%, which was similar to study done by Scholz K et al,^[7] where male patients were 74% and female patients were 26%.^[8]

In our study of 65 patients, 63 patients (96.9%) had chest pain with vomiting and nausea, 2 patients (3.1%) had breathlessness with vomiting.^[9] The common presenting symptom was chest pain (63 patients).^[10]

In a study done by Vijetha Shenoy, Veena Mehendale et al,^[11] found out that homocysteine was an independent risk factor for cardiovascular disease and it estimated that 10 % of population's CVD risk is attributed to the elevated levels of homocysteine.^[12] In this study they had shown that homocysteine suppresses the vasodilator nitric oxide by increasing the levels of asymmetric dimethylarginine (ADMA), a strong inhibitor of nitric oxide synthase (eNOS).^[13]

Out of 65 patients, 10 patients had ejection fraction of 35%, 11 patients had EF (ejection fraction) of 45%, 17 patients had EF of 50%, 6 patients had EF of 60%, 2 patients had EF of 25% and 1 patient had EF of 20%. In our study patients with anterior wall MI with EF of less than 40% had higher mortality.^[14]

The main pathological phenomenon here is toxic effects on vascular endothelium, impaired endothelium dependant relaxation, a hypercoagulable state due to downregulation of thrombomodulin expression, activation of factor V, inhibition of protein C, increased platelet aggregation, henceforth all of these explain that hyperhomocysteinemia will leads to adverse cardiac events in acute coronary syndrome by indirectly affecting the coagulation cascade.^[15]

CONCLUSION

We can conclude from our study that hyperhomocysteinemia is a strong risk factor for developing atherosclerosis and thrombus formation leads to ischemic heart disease in middle aged patients.

Also increased levels of homocystiene are directly proportional to the complications of acute coronary syndrome. So hyperhomocysteinemia should be

considered in the work-up of acute Myocardial infarction in middle aged people and those without conventional risk factors.

Henceforth, plasma total homocystiene plays a vital role and an independent risk factor for middle aged patients with acute coronary syndrome even without any conventional risk factors.

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