

# Study on Homocysteine Levels in Ischemic Heart Disease Proved by 2D-Echocardiography

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## ABSTRACT

**Introduction:** Homocysteine is a risk factor for atherosclerotic vascular disease, with adverse influence on endothelial cells, vascular smooth muscle cells, connective tissue, interactions with plasma lipoproteins and platelets. This study was conducted to study the association between levels of homocysteine and IHD, the clinical profile of subjects in relation to their lifestyle, and the socio-demographic profile of patients with established Ischaemic heart disease.

**Material and Methods:** The data for this study was collected from patients who presented to Government General Hospital, Guntur from Nov 2016 to Oct 2017. 40 cases and 40 age and sex matched controls were taken. All cases taken were proven cases of IHD proved by 2D echocardiography. Homocysteine levels were compared between the two groups and the results drawn.

**Results:** Homocysteine levels were found to be significantly higher in cases with IHD when compared to controls. Both cases and controls with dyslipidemia and other risk factors for IHD like age above 50 years, diabetes mellitus, hypertension and a history of CVA were found to have significantly higher homocysteine levels.

**Conclusions:** A significant association was found between elevated serum homocysteine levels and both IHD and risk factors for IHD even in the absence of IHD. This suggests that elevated homocysteine levels are an independent risk factor for developing IHD.

**Keywords:** IHD; Homocysteine

established Ischaemic heart disease.

## MATERIAL AND METHODS

This was a case control/comparative study carried out in the department of Medicine, Government General Hospital, Guntur, A.P during November 2016 to October 2017

### Source of data

The data for the study has been collected from the in-patients who fulfill the inclusion and exclusion criteria in the Department of Medicine, Government General Hospital, Guntur, A.P who were proved as cases of IHD.

**Study period:** November 2016 to October 2017

**Type of study:** Case control / comparative study

**Sample size:** 40 cases and 40 controls

**Collection of data:** Data was collected by patient evaluation which was done by detailed history taking and clinical examination through a structured proforma specially designed for this study.

### Inclusion Criteria

All cases of IHD – This includes all patients both sexes established cases of IHD, who give history of myocardial infarction and their echocardiography shows motion wall abnormalities.

### Exclusion criteria

- Patients < 18 years
- Patients on Haemodialysis
- Patients with renal transplant
- Patients on drugs such as methotrexate, theophylline, metformin and niacin

**Controls:** Sex and age matched controls from general population without any evidence of IHD.

**Investigations:** All patients and controls included underwent detailed clinical examination and following investigations.

- RBS or FBS and PPBS
- Blood urea, S. creatinine
- Lipid profile

## INTRODUCTION

WHO<sup>1</sup> and World Bank data indicate that in India deaths attributed to IHD have increased markedly with the expanding population and will continue to increase.

Increasing recognition that as many as 30-50% of patients with established IHD lack the traditional risk factors has led to search for additional new risk factors that may predispose individuals to coronary artery disease over the past several years, observational and epidemiological studies have identified a host of new and potential risk factors for atherothrombotic vascular disease, the growing list of new and emerging risk factors include elevated blood levels of homocysteine<sup>2</sup>. Evidence from retrospective and prospective clinical studies indicates that elevated levels of homocysteine are associated with increased risk of IHD, Ischaemic stroke and peripheral vascular disease<sup>3</sup>.

Study aims and objectives were to assess the association between the levels of homocysteine and IHD, to assess the clinical profile of subjects in relation to their lifestyle and to study the socio-demographic profile of patients with

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- Plasma homocysteine
- ECG
- 2D echocardiography

**Method of detection of homocysteine:** Homocysteine is present in plasma primarily bound as disulfides with itself, and albumin. A moderate increase of homocysteine occurs in various diseases. These disorders justify the introduction of HCY assay in routine clinical chemistry laboratory.

### STATISTICAL ANALYSIS

Microsoft office 2007 was used for the analysis. Descriptive statistics like mean and percentages were used for the analysis.

### RESULTS

#### Study Design

A case-control study consisting of 40 IHD patients and 40 age and sex matched controls is undertaken to investigate the relationship of homocysteine with IHD, Clinical features, lipid profiles, risk factors.

#### Age distribution of cases and controls

Maximum number of cases are seen in the age group of 61 to 70 years. The youngest case being 30 and the oldest being 80 years

#### Sex Distribution

Among the 40 cases, 24 are male and 16 are female. Among the 40 controls, 27 are male and 13 are female. The cases and controls are well matched according to sex.

#### Age distribution with sex

There is a predominance of males in cases and controls, and it was seen that more females affected with IHD were in the age group of 30 to 50 years.(Table 1)

#### Risk factors

Hypertension was the most prevalent risk factor among controls. Cerebrovascular accident was the most common associated condition among IHD cases. In our study incidence of diabetes and hypertension was also significantly increased among cases. Family history of IHD and smoking were relatively less frequent(Table 2)

#### Homocysteine and family history of IHD

Among 40 cases, 16 cases were found to have positive family history out of which 11 have high homocysteine levels. 5 were found to have normal homocysteine levels. Among the 40 controls. 4 had positive family history of IHD and none of them had high homocysteine levels.(Table 3)

#### Clinical features

Recurrent angina, raised JVP, pedal oedema, basal crepitations, tachypnoea and PND, which are features of cardiac decompensation, were the most common clinical features present in the cases.(Table 4)

#### Lifestyle

Maximum cases and controls had sedentary lifestyle. However, 1/5 of patients with active lifestyle also had IHD but these patients were also found to have other risk factors such as diabetes, hypertension, dyslipidemia.

Age in years	IHD cases		Controls	
	Male	Female	Male	Female
≤ 30	-	1 (6.3)	-	1 (7.7)
31-40	3 (12.5)	4 (25.0)	4 (14.8)	3 (23.1)
41-50	3 (12.5)	3 (18.8)	6 (22.2)	3 (23.1)
51-60	9 (37.5)	1 (6.3)	9 (33.3)	2 (15.4)
61-70	8 (33.3)	4 (25.0)	4 (14.8)	2 (15.4)
>70	1 (4.2)	3 (18.8)	4 (14.8)	2 (15.4)
Total	24 (100.0)	16 (100.0)	27 (100.0)	13 (100.0)

Figures in parenthesis are percentages

**Table-1:** Age distribution with sex

Risk factors	IHD cases (n=40)		Controls (n=40)		P value
	No	%	No	%	
DM (+)	22	55.0	12	30.0	0.024*
HTN (+)	20	50.0	14	35.0	0.014*
CVA (+)	23	57.5	4	10.0	0.000**
Smoke (+)	16	40.0	13	32.5	0.485
Inference	DM, HTN and CVA are significantly positive associated with the IHD cases P<0.05				
* Significant at 5% ** Significant at 1%					

**Table-2:** Presentation of risk factors

Family History of IHD	IHD cases (n=40)		Controls (n=40)		P value
	No	%	No	%	
Normal Homocysteine (n=9)	5	12.5	4	10.0	P>0.05
Elevated Homocysteine (n=11)	11	27.5	-	-	0.010**
Over all (n=20)	16	40.0	4	10.0	0.030**
Inference	Patients with family history of IHD have been found to have significantly higher homocysteine levels (P<0.05)				

**Table-3:** Family history of IHD and homocysteine level

Clinical features	Number (n=40)	%
Recurrent angina	15	37.5
JVP increased	15	37.5
Pedal edema	17	42.5
Basal crepts	12	30.0
Tachypnea	14	35.0
PND	12	30.0

**Table-4:** Presentation of clinical features in IHD

#### Homocysteine levels and lipid profile

Serum homocysteine levels were found to be significantly elevated in cases with dyslipidemia, when compared to cases without dyslipidemia. However, the homocysteine levels in

cases without dyslipidemia was significantly higher than in controls.

### Homocysteine levels and clinical features

No significant association was found between clinical features and serum homocysteine levels. Homocysteine levels were compared with each risk factor for IHD, and it was found that homocysteine levels are elevated in cases without risk factors, but are even higher in cases with risk factors. This shows that elevated homocysteine levels are strongly associated with IHD and its various risk factors.

## DISCUSSION

It was first reported in Singapore<sup>4</sup> in 1986 that people hailing from Indian sub continent had a higher probability of dying from IHD. Studies in the past have shown that high rates of IHD in Indians are accompanied by paradoxically low prevalence of conventional risk factors such as

- HTN
- DM
- Dyslipidemia
- Smoking
- Sedentary life style

The strong evidence for above statement comes from studies analyzing risk factors for IHD among Asian Indians Physicians in UK<sup>5</sup>, where the prevalence of IHD was four fold higher than the national average. The data suggested the presence of powerful risk factor that is unaffected by even maximal modifications of conventional risk factors. The lack of epidemiological data in our population regarding homocysteine prompted us to undertake this study of defining their association to IHD. In the present study 40 cases of IHD and 40 controls were taken. It was found in this study, that IHD was higher in males 24/40 (60%) when compared to females – 16/40 (40%), and more commonly encountered in the sixth and seventh decade, which correlates well with many other studies done both within the country and abroad. In the present study, the youngest patient is a 30 year old female, and another four female patients were also in the age group of 31 to 40 years, all being in the reproductive age group. Though females are said to have hormonal protection during this age group from IHD, our study shows 5 females having loss of this hormonal protection. Among these five, three had CVA, with two to three other conventional risk factors. All of them had increased levels of homocysteine. Only one patient with proven IHD had CVA and no known risk factors, and normal levels of homocysteine. Though not investigated extensively, this patient could have developed IHD probably due to other undetected factors including anomalies of coronary vessels. Hence it may be concluded that higher homocysteine levels could be a risk factor for IHD in younger females.

### Risk factors

American heart association in 1992 proposed the development of risk factors and their relationship to incidence of IHD. In 1996 Pearson et al<sup>6</sup> at the 27<sup>th</sup> Bethesda Conference categorized risk factors based on matching the intensity of

risk factor management with hazard of IHD. The risk factors were categorized into four groups.

**Category I** (Risk factors for which intervention have proven to lower IHD)

- Smoking • LDL Cholesterol • HTN • LVH

**Category II** (Risk factors for which intervention are likely to lower IHD)

- DM • Sedentary life style • HDL • Obesity • Postmenopausal

**Category III** (Risk factors associated with IHD that if modified might lower the risk)

- Psychosocial factors • Lipoprotein (a) • Homocysteine • Oxidative stress • Alcohol abstinence

**Category IV** (Non-modifiable risk factors)

- Age • Male gender • Family history

Hypertension was one of the most prevalent risk factors among cases and controls. Many studies done in India and abroad show that hypertension does bring an increase in the homocysteine levels. It was seen that homocysteine levels in hypertensive cases and controls was much higher when compared to non hypertensive persons.

### Correlation of homocysteine levels with diabetes

Diabetes mellitus was present in 42% of our cases and 30% controls. Diabetic patients were also found to have higher homocysteine levels when compared to non diabetics. Cannon et al<sup>7</sup>, in 1991, conducted a meta analysis and found the incidence of diabetes in IHD 32 to 67%.

### Correlation of homocysteine levels with physical activity

In the present study, most of the cases and controls were found to be sedentary workers. However, 20% of the patients, despite an active lifestyle, were found to have IHD. These cases had other conventional risk factors.

### Clinical profile of cases with IHD

In the present study, it was found that most of our cases (34 out of 40) had features of congestive cardiac failure. This could be explained on the basis of the presence of cardiac decompensation along with the presence of other risk factors such as diabetes, hypertension and dyslipidemia, which per se are also known to affect the vasculature of the heart.

### Homocysteine levels

In our study, the mean homocysteine levels above which an increased risk of developing IHD was found was 13.5  $\mu\text{mol/l}$ . In the present study, homocysteine levels in cases were found to be almost twice to that of controls. Graham et al<sup>8</sup> 1998 in large European study ECAP showed that HCY levels were significantly higher in patients than controls. Giles et al<sup>9</sup> in 2000 (3<sup>rd</sup> NHANES Study) also concluded that a 2 fold increase in MI occurred in patients with a mean concentration of HCY  $> 15 \text{ mmol/m}^2$ .

### Correlation of homocysteine levels with sex

No significant difference between homocysteine levels was found in males and females. Some studies done in India and abroad show that males have higher homocysteine levels as

compared to females the reason being more muscle mass in males. However patients coming to our hospital mostly belong to the lower socioeconomic strata and have poor nutritional status and therefore the comparable values of homocysteine in males and females can be explained on that basis, There was an increase in homocysteine levels with increasing age. According to other studies also conducted by lussier et al (1992) and bree etal(2001) showed that homocysteine levels increase with age. Our study though validating the view that increased HCY levels are associated with IHD needs further verification in large prospective case control studies. The mean HCY level were significantly higher than those reported in other studies. This can be attributed to the inclusion of patients with severe IHD in our study.

### CONCLUSION

In the case control study with 40 cases of IHD and 40 age and sex matched controls conducted at Government General Hospital Guntur A.P the following conclusions were drawn.

- Homocysteine levels are comparable in cases and controls.
- With advancing age there is an increased in level of HCY.
- Lifestyle and personal habits were not significantly associated with HCY levels.
- Hypertension was found to bring an increase in homocysteine levels.
- Absence of hypertension in IHD cases was also associated with increased HCY levels hence proving the association between IHD and HCY.
- Similarly, diabetes and stroke and dyslipidemia were found to increase HCY levels marginally but their absence was also associated with increased levels of homocysteine in IHD cases, hence proving the correlation between HCY and IHD.
- No clinical feature was found to be statistically significant with level of homocysteine.

40 cases of coronary artery disease were studied and among them homocysteine levels were estimated. Homocysteine levels were also estimated in 40 adults with coronary artery disease as controls. Homocysteine levels were found to be raised in the coronary artery disease patients and there was statistically significant difference in plasma homocysteine levels between patients with coronary artery disease and controls.

Our study also shows that the homocysteine levels were raised in the coronary artery disease patients with traditional risk factors (hypertension, diabetes, smoking, sedentary lifestyle, tobacco chewing and family history of ischaemic heart disease) as compared to the controls. Our study although validating the view that increased homocysteine levels are associated with coronary artery disease needs further verification in large prospective case controls studies. In conclusion, homocysteine levels were increased in patients with coronary artery disease, which shows that it is an independent risk factor for coronary artery disease.

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