ORIGINAL RESEARCH PAPER

Cardiology

DOES HOMOCYSTEINE LEVEL AFFECT THE SEVERITY OF CORONARY ARTERY DISEASE AND THE OUTCOME AFTER CORONARY ARTERY BYPASS GRAFTING – A PROSPECTIVE STUDY

KEY WORDS: Homocysteine, risk factor, Coronary artery, bypass graft.

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ABSTRACT

INTRODUCTION
Plasma Homocysteine is a known risk factor of Coronary artery disease (CAD).There are not many studies that correlate Homocysteine level with CAD and its effect on patients who are undergone coronary artery bypass (CABG) in Indian population or western population.

AIM
The aim of our study is to analyse the correlation of plasma Homocysteine levels in patients undergoing coronary artery bypass grafting (CABG) with respect to various patient variables like age, sex and also the severity of disease and outcome of surgery.

METHODS
The plasma Homocysteine levels of one hundred patients undergoing CABG, between January 2016 and January 2017 were analysed. Data about patient variables was obtained from questionnaires given to the patients during the preoperative period. The severity of disease was assessed based on Coronary angiogram (CAG) findings and perioperative findings. Homocysteine levels were assessed by CLIA method and levels of greater than 13mmol/L was taken as hyperhomocyteinemia.

RESULTS
Higher Homocysteine levels are associated with triple vessel disease (TVD) with greater severity of disease. It is also associated with poorer target vessels with increased morbidity and post operative mortality.

CONCLUSION
Homocysteine level is one of the independent risk factor for severity of CAD.
It can have predictive value in CABG but modifiable if preoperatively treated.

INTRODUCTION

Worldwide Coronary artery disease is a major cause of mortality and morbidity.[1] There are many risk factors that contribute to CAD such as Dyslipidemia, smoking, hypertension, diabetes and newer independent risk factor hyperhomocysteinemia.[2,3]

Many studies have been done which reveal the role of Homocysteine in atherosclerotic vascular disease and hypercoagulability states.Hyperhomocysteinaemia is associated with premature vascular diseases irrespective of age and cause.[4]

Plasma Homocysteine levels are a strong predictor of mortality in patients with CAD and increased incidence of myocardial infarction.[5,6]

Homocysteine affects the endothelial function, coagulation system in turn causes hyperproliferation of endothelium and hyperthrombotic endothelium. Studies that correlate plasma Homocysteine level with severity of CAD and predict outcome after CABG are few in number.

The objective of our study was to evaluate the correlation of plasma Homocysteine levels in patients with coronary artery disease undergoing CABG and the outcome of surgery.

MATERIALS AND METHODS

Ours was a prospective single centre study of 100 patients that took place in Dhiraj hospital from January 2016 to December 2017. All 100 patients underwent CABG in our centre for CAD.

The study was approved by the ethics committee. All patients gave us their informed written consent. The patient confidentiality was maintained.

Patient's detailed history was taken on admission with respect to presenting complaints, associated risk factors.
Homocysteine levels of all the patients was analysed in the pre operative period. Homocysteine levels were assessed by CLIA method and levels of greater than 13mmol/L was taken as hyperhomocyteinemia.

Patient's CAG was evaluated. The coronary vessel condition was visually assessed during CABG on operative table.The need of coronary endarterectomy was also decided per operatively.

Post operative recovery was assessed by the vital data, ventilator requirement, the number of ICU days, and the need for post operative inotropic support. Post operative morbidity and mortality analysed.

STATISTICAL ANALYSIS

The statistical software used for statistical analysis is SPSS 20.
We have applied chi square test to find significant level between two groups.

P value less than 0.05 was considered as significant value.

RESULT

One hundred patients were enlisted for the study. All hundred patients underwent CABG in Dhiraj Hospital, Vadodara.

We had patients between age group of 31 to 80 years and the homocysteine levels varied among them with the highest number of hyperhomocysteinaemia being in the age group of 50 to 70 years. (Figure -1)

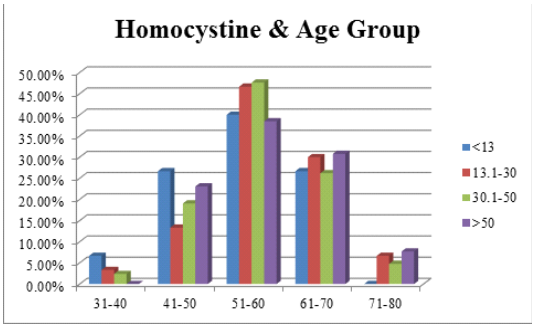

Figure -1

We had 82 males (82%) and 18 females (18%) in our study. There was no significant difference between Homocysteine levels in male

and female. (Figure -2)

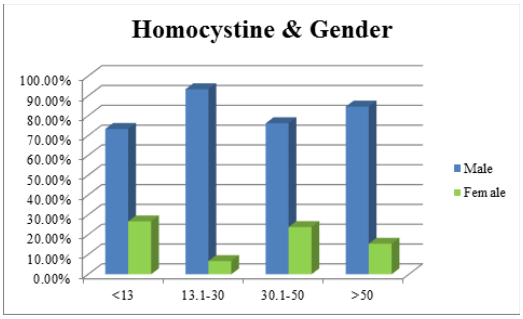

Figure -2

There were 66 smokers in our study group. There was a ignificant association of higher Homocysteine level with Smoking. (p value 0.009) (Table -1)(Figure-3)

Homocystine Level	Smoker				p value
	Yes	%	No	%	
<13	6	40.00%	9	60.00%	0.009
13.1-30	16	53.33%	14	46.67%	
30.1-50	34	80.95%	8	19.05%	
>50	10	76.92%	3	23.08%	

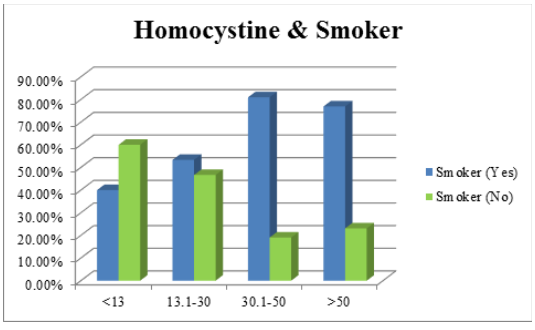

Figure -3

64 patients in our study were hypertensive. There was no significant Correlation between hypertension and Homocysteine level. (Figure -4)

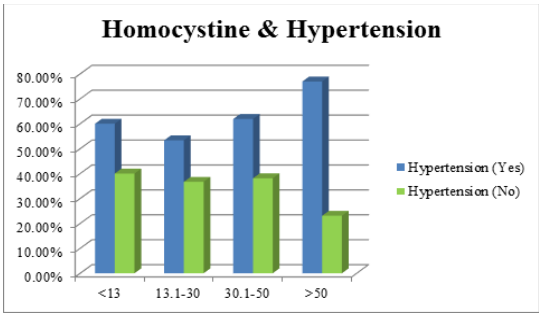

Figure -4

57 patients were diabetic with no significant difference in the Homocysteine level between the diabetic and the non diabetic patients. (Table-2)

Homocysteine Level	Diabetes				p value
	Yes	%	No	%	
<13	7	46.67%	8	53.33%	0.754
13.1-30	19	63.33%	11	36.67%	
30.1-50	24	57.14%	18	42.86%	
>50	7	53.85%	6	46.15%	

Table – 2

Two patients had single vessel disease with Left main coronary artery involvement (LMCA).

15 patients had double vessel disease of which 2 had LMCA disease. 83 patients had triple vessel disease with 28 having LMCA disease. (Figure - 5)

LIMA/Vein	N	%
LIMA	68	68.00%
RGSVG	32	32.00%
Total	100	100.00%

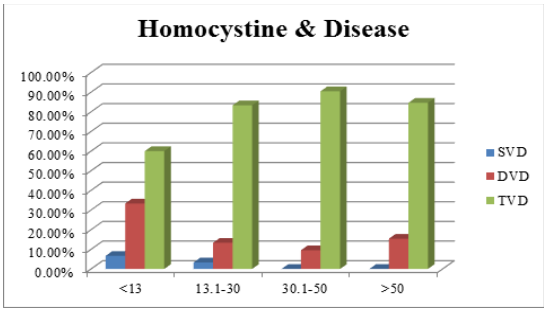

Figure-5

Out of the 100 patients, 68 patients had grafting of left internal mammary artery grafting (LIMA) to left anterior descending artery (LAD). (Table -3)

Table -3

18 patients needed right coronary artery endarterectomy on table during CABG. All of these patients had hyperhomocyteinemia. (Figure-6)

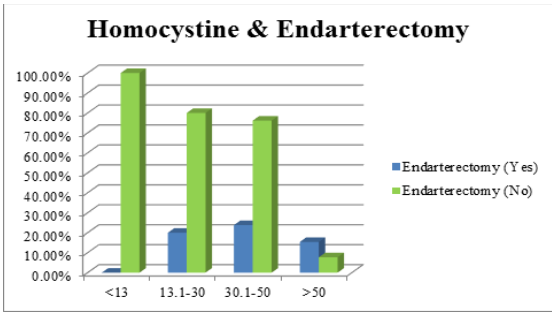

Figure-6

In our study, we found significant association of hyperhomocyteinemia with increased requirement of inotropic support and increased ICU stay. (Figure-7)

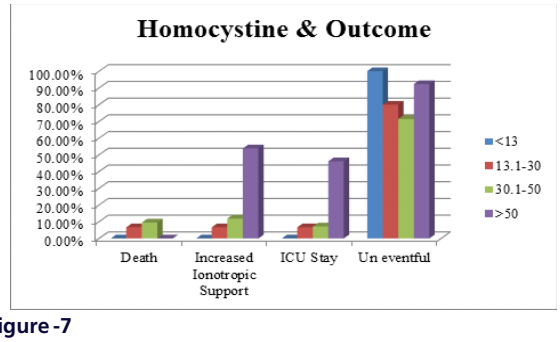

Figure -7

DISCUSSION

Homocystein is an aminoacid produced by catabolism of methionine. Homocysteine dependent on various Vitamins as cofactor for its degradation, any deficiency of such vitamin increases the level. It also increases with age and particularly evidently increased in male population .higher creatinine with renal dysfunction increases level of Homocysteine. Hyperhomocysteinaemia induces endothelial dysfunction with its endothelial proliferation, enhance platelet aggregation, affect

coagulation cascade eventually turns endothelium prothromotic.[7]

Hyperhomocyteinemia is modifiable, independent known risk factor for CAD and increases incidence of myocardial infarction.[8,9]

Uniformly it involves all vasculature of body. It consistently involves coronary artery, peripheral vasculature and cerebrovascular vessel .it has evident role in increased incidence of venous thrombosis .[10]

In 1969, McCully made the correlation between high Homocysteine and vascular disease and proved hyperhomocysteinaemia induce atherosclerosis. [11] In 1976, Wilken et al showed that hyperhomocysteinaemia was associated with CAD and increased incidence of mortality.[12]

Although, some studies conducted in India, did not show increased Homocysteine levels among patients with CAD, but they studied in very small group of patients.[13, 14] our study showed significant association of hyperhomocyteinemia with increased severity of CAD.

Our study suggests that prevalence of hyperhomocysteinemia in preoperative patients is high involving 85% of our study population. This is consistent with the findings of other western studies.

Our study revealed increased Homocysteine levels evidently associated with smoking. This is consistent with the finding in other studies.[15,16]

In this study, we found increased severity of coronary artery disease in patients with hyperhomocysteinaemia ,on operating table during CABG. We also found increased necessity for right coronary artery endarterectomy and same proved in other studies as well.[17]

In our study, we found significant association of hyperhomocysteinaemia with increased requirement of inotropic support , increased ICU stay with increased moriddty and mortality .

Recently completed large randomized controlled trials, Folic acid, vitamin B6, and vitamin B12 has been shown to decrease Homocysteine levels,[18] however that treating patients with hyper homocysteinemia with supplementation of vitamin B has failed to decrease cardiovascular morbidity and mortality.[19]

CONCLUSION

Our data suggests that Homocysteine level can predict morbidity and mortality risk in patients who are undergoing cardiac surgery. Identification of hyperhomocysteinemia in patients may allow the surgeon to modify and plan his procedure and helps to intense management in ICU postoperatively, for better outcome.

It requires aggressive management with anticoagulants in view of increased risk of thrombo-embolic events, which is inherent character of hyperhomocysteinaemia.

Routine supplementation of folic acid and other Vitamin has to be evaluated further in such cases to look out long term benefits.

Limitations

Our study is a single centre study with limited number of patients.

The conclusions of our study need to be validated with further trials.

In patients undergoing emergency CABG, Homocysteine evaluation avoided.

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