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RELATIONSHIP BETWEEN HYPERHOMOCYSTEINEMIA AND SEVERITY OF PERIPHERAL VASCULAR DISEASE AND ITS OUTCOMES.

Cardiology

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ABSTRACT

AIM: The study is aimed to evaluate homocysteine levels in patients with peripheral arterial disease (PVD) with relation to the severity of peripheral vascular disease and its outcomes.

MATERIAL AND METHOD

The study is a prospective study that was conducted in dhiraj hospital in Gujarat where a sum of one hundred patients underwent vascular surgery between January 2016 and April 2018. Data about patient variables was obtained from questionnaires given to the patients during the preoperative period. Homocysteine levels are assessed by CLIA method and levels greater than 13mmol/L were consider as hyperhomocysteinemia.
Bilateral lower limb CT angiography was done in each and every patient. The 78 patients underwent coronary angiogram.
All patients underwent surgical vascular intervention in form of either embolectomy or vascular graft bypass.
The outcomes were evaluated by need for redo surgery and amputation post operatively.

RESULTS

Peripheral vascular disease is quite common in male population.82 of our study subjects were male. And 78 of the patients were smokers.
12 out of 100 patients required amputation.
We found hyperhomocysteinemia to be associated with more severe peripheral vascular disease.

CONCLUSION

Homocysteine levels can predict the severity of the peripheral vascular disease and its poor outcomes

KEYWORDS

Homocysteine, Hyperhomocyteinemia, Peripheral arterial disease, CT angiogram.

INTRODUCTION

Hyperhomocysteinemia has been considered as a risk factor for atherosclerotic peripheral vascular disease (PVD).

Free Homocysteine in Hyperhomocyteinemia, responsible for pathological effect on vasculature .By various proven mechanism, it induce endothelial dysfunction and enhance growth of vascular smooth muscles, which in turn contribute the atherosclerotic process. It also increases platelet aggregation and macrophage scavenging.

The study analyses Homocysteine levels in patients who have been operated for extremity ischemia due to vascular disease. The patients were compared on the basis of his age, sex, Homocysteine levels and smoking duration, surgical options and its complications.

It has been found that patient with hyperhomocysteinemia has increase risk of PVD.

The initial observation that linked homocysteine to vascular diseases were made by McCully, in which total plasma homocysteine was 50 times more than the normal 1.

There have been many studies linking the presence of hyperhomocysteinemia with coronary artery disease and vascular disease 2, 3.

There are however not many studies which try to evaluate the severity of peripheral vascular disease and its outcome in relation to the hyperhomocysteinemia levels.

Our study is an attempt to evaluate the same in a cross section of Indian population.

MATERIAL AND METHODS

Ours was a prospective, single centre study of 100 patients, which took place in Dhiraj hospital from January 2016 to December April 2018. All 100 patients underwent vascular surgery in our centre for PVD.

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

Detailed history of the patient was taken on admission with respect to presenting complaints, associated risk factors. Patient's CT angiography was evaluated.

Homocysteine levels of all the patients was analysed in the pre operative period. The condition of vessels was analysed with the help of CT angiography report. Post operative recovery was assessed by hand held colour Doppler and condition of limbs .

Post operative mortality as well as gangrenous and ischemic status of the limb were also 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

We had 100 patients of peripheral vascular disease of which10 patients had bilateral iliac artery involvement. 37 patients had bilateral superficial femoral artery (SFA) involvement. 6 patients had bilateral popliteal artery involvement. 30 patients had unilateral SFA affected.10 patients had axillary artery involvement. 6 patients had unilateral radial artery involvement. While one patient had unilateral iliac and popliteal involvement.

We had 82 men in our study and 18 women. Peripheral vascular disease was more common in men in our study (Figure 1). However there is no significant association of Hyperhomocyteinemia with gender.

We found a significant increase in homocysteine levels with age and also the severity of disease.

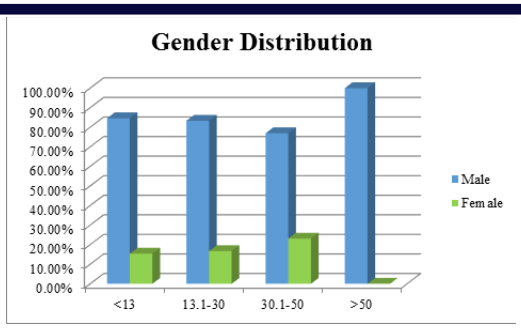

Figure 1

Homocystine Level	Age Group _Code								
	< 30		31 - 50		51 - 70		> 70		
<13	3	23.08%	5	38.46 %	4	30.77 %	1	7.69 %	13
13.1-30	4	6.67%	23	38.33 %	25	41.67 %	8	13.3 3%	60
30.1-50	0	0.00%	8	30.77 %	15	57.69 %	3	11.5 4%	26
>50	0	0.00%	0	0.00 %	1	100.0 0%	0	0.00 %	1
Total	7	7.00%	36	36.00 %	45	45.00 %	12	12.0 0%	100

78 patients of our study group were smokers. 74% of them had been smoking for longer than 10 years.

Hyperhomocysteinemia is significantly associated with smoking with a p value of 0.152. (Figure 2)

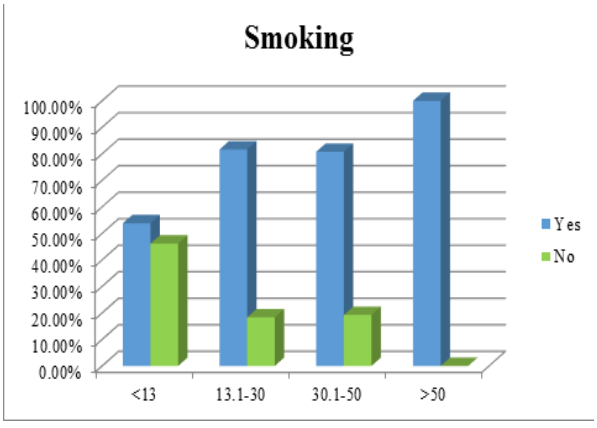

Figure 2

There was no significant relation between hypertensive status and hyperhomocysteinemia. There was also no statistically significant relationship of hyperhomocysteinemia and diabetes mellitus.

72 patients in our study group underwent coronary angiogram for simultaneous cardiac status evaluation. Of these, 23 patients had normal coronary vessels.

26 patients had single vessel coronary artery disease (SVD), of these 22 patients had hyperhomocyteinemia.

14 patients had double vessel disease (DVD), Out of the 14 patients 13 had hyperhomocyteinemia.

All 4 patients who had triple vessel disease (TVD) had hyperhomocysteinemia.

One of the patients had TVD with left main coronary artery stenosis and required simultaneous coronary artery bypass surgery and Aorto bifemoral bypass grafting.

Of the 100 patients, 7 were admitted with pre-existing gangrene of the digits of the affected limbs.

We found that a greater number of patients with hyperhomocysteinemia were admitted with preoperative gangrene of the limbs, indicating severe disease. (Table 1)

Homocystine Level	Pre Op Gangrene					p value
	Yes	%	No	%		
<13	0	0.00%	13	100.00		0.001
13.1-30	3	5.00%	57	95.00%		
30.1-50	3	11.54%	23	88.46%		
>50	1	100.00%	0	0.00%		

Table -1

5 of our patients developed gangrene of the digits of operated limb and needed further intervention.

The development of post operative gangrene was also associated with hyperhomocysteinemia. We had five patients with post operative gangrene development. (Table 2)

Homocystine Level	Post Op Gangrene					p value
	Yes	%	No	%		
<13	0	0.00%	13	100.00%		0.769
13.1-30	3	5.00%	57	95.00%		
30.1-50	2	7.69%	24	92.31%		
>50	0	0.00%	1	100.00%		

Table -2

At the end of our study, 12 patients had undergone amputation for gangrene of which 7 patients had pre-existing gangrene. All patients who underwent amputation had hyperhomocysteinemia. (Table 3)

Homocystine Level	Outcome					
	Amputation	%	Death	%	Uneventful	%
<13	0	0.00%	0	0.00%	13	100.00%
13.1-30	6	10.00%	2	3.33%	52	86.67%
30.1-50	5	19.23%	2	7.69%	19	73.08%
>50	1	100.00%	0	0.00%	0	0.00%

Table 3

DISCUSSION

In our study we found that homocysteine levels were associated with an increased severity of vascular disease. Although various other factors also affect homocysteine levels like age, sex, smoking 8. it has been found that predisposition of male population to PVD is more than female 9. Hyperhomocysteinemia has been considered as a new risk factor for vascular disease. Homocysteine levels can predict the severity of peripheral vascular disease and poor outcome of treatment 6.

Further studies are required to establish the role of intervention for lowering the Homocysteine levels other then adding folic acid and its benefits in patients with peripheral vascular disease. In addition, the measurement of homocysteinemia needs to be standardised so correlation is more appropriate to disease 4.

It has been established that lowering the markedly elevated circulating homocysteine, greatly reduces cardiovascular risk 5. Supplementation of Folic acid has been shown to decrease homocysteine levels 7.

The investigations that have been published so far regarding the effects of raised homocysteine levels in plasma, on vessels and their athero-thrombotic predisposition has demonstrated with increased PVD in hyperhomocysteinemia. This was found to be true in our study as well.

In our study we have shown that higher homocysteine levels can be a risk factor in predicting the severity of PVD and poor outcomes.

LIMITATIONS

Our study is a single centre study with limited number of patients. Patients undergoing vascular procedure in emergency, collecting homocysteine sample may not be a priority.

CONCLUSION

Hyperhomocyteinemia is a risk factor for PVD and Coronary artery disease.

Preoperative evaluation of homocysteine level in patients may allow the surgeon to modify his procedure for better outcome of PVD patients.

Our study suggests that these patients might require aggressive management with bypass surgery and anticoagulants. However this requires further study to prove it conclusively.

There is need for further studies regarding precautions and protective strategies to be undertaken in patients undergoing vascular surgical procedures with hyperhomocysteinemia.

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