Haematological and Vascular Abnormalities in Hyperhomocysteinemia: A Study of 50 Cases

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Abstract

The rising trend of vascular and haematological abnormalities seen in different age groups of population is attributed to various modifiable and non-modifiable risk factors like Diabetes, Hypertension, Dyslipidemia, Smoking, Obesity, Sedentary Life Style, Age, Genetic Predisposition, Chronic Alcohol Consumption. Apart from all these risk factors, certain other factors play a very significant role in causing vascular and haematological abnormalities which can be modified to improve the morbidity and mortality outcomes. Hyperhomocysteinemia is being a leading cause of many vascular and haematological abnormalities & is a modifiable risk factor. So, one should keep in mind the role of homocysteine while evaluating the cases of vascular and haematological abnormalities.

Keywords: Anemia, Homocysteine, Vascular events.

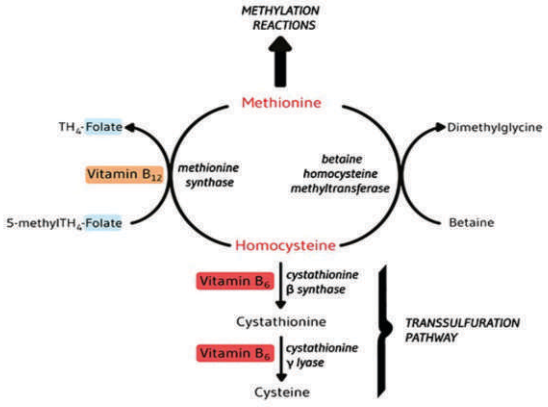
Introduction:

Homocysteine is a sulfur containing nonprotein aminoacid and an intermediate in the methionine metabolism. The fate of homocysteine is decided by either remethylation to methionine or trans-sulfuration to cysteine.[1] Vitamin B 12 , Folate and Vitamin B 6 play a major role in homocysteine metabolism as enzyme co-factors in various reactions. A normal level of homocysteine in blood is <15 micromoles/litre.[2] More than 15 micromoles/ litre is called Hyper homocysteinemia. Severity of the disease is classified into three categories. [2,3]

Moderate	:	15-30 micromoles/litre
Intermediate	:	30-100 micromoles/litre
Severe	:	>100 micromoles/litre

Homocysteinemia per se does not cause any symptoms, but the associated hypercoagulable state, and the Vitamin B12 and Folic acid deficiency in hyperhomocysteinemia are responsible for the symptoms and features. Homocysteine has effects on vascular endothelium, platelets, coagulation factors that predisposed to thrombosis. Endothelial dysfunction can be induced in a normal individual when hyperhomocysteinemia is induced transiently. Affected patients are at lifelong risk of thrombo-embolic phenomenon, which are at a major cause for mortality. Venous and arterial occlusions in small or large vessels are seen. [3]

Figure 1 : Homocysteine Metabolism



Homocysteine is methylated to form the essential amino acid methionine in two pathways. The reaction of homocysteine remethylation catalyzed by the vitamin B_{12}-dependent methionine synthase captures a methyl group from the folate-dependent one-carbon pool (5-methyltetrahydrofolate). A second pathway requires betaine (N,N,N-trimethylglycine) as a methyl donor for the methylation of homocysteine catalyzed by betaine homocysteine methyltransferase. The catabolic pathway of homocysteine, known as the transsulfuration pathway, converts homocysteine to the amino acid cysteine via two vitamin B_6 (PLP)-dependent enzymes. Cystathionine β synthase catalyzes the condensation of homocysteine with serine to form cystathionine, and cystathionine is then converted to cysteine, α-ketobutyrate, and ammonia by cystathionine γ lyase. *TH_4-Folate, Tetrahydrofolate.*

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Aims and Objectives:

To correlate between elevated levels of homocysteine and vascular and haematological abnormalities in different age group of population.

Methodology:

This observational and cross sectional study was done on sample unit of 300 patients attended at tertiary care centre in Ahmedabad during a period of 6 months from March 2020 to September 2020. Detailed clinical history, laboratory investigation, radiological investigations related to the symptoms were done in all patients.

Inclusion criteria: Age>15 years and <60 years patients having vascular and haematological abnormalities after excluding the below mentioned criteria. Patients were further screened to check the homocysteine levels and the patients with elevated homocysteine levels were included in the study.

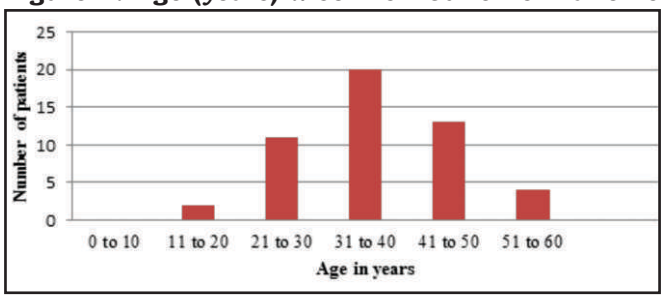
Exclusion criteria: Established causes of vascular or haematological abnormalities like Diabetes, Hypertension, Dyslipidemia, Smoking, Obesity, Genetic Predisposition, Chronic Alcohol Consumption, Hypercoaguable Disorders, CKD, Patients taking supplementation of Vitamin B12 and Folic Acid.

During a period of 6 months, all the cases of vascular and haematological abnormalities were evaluated for their respective causes. Required investigations like haemogram, FDP , D dimer , LFT , RFT , iron profile, vit B12, thyroid function, HbA 1C , lipid profile , ECG , 2D echo, venous and arterial doppler, MRI, USG abdomen, CXR chest were done. After reviewing these reports patients fulfilling exclusion criteria were excluded. On further investigating the cause, Homocysteine level was done and the patients fulfilling the inclusion criteria were included in the study.

Results:

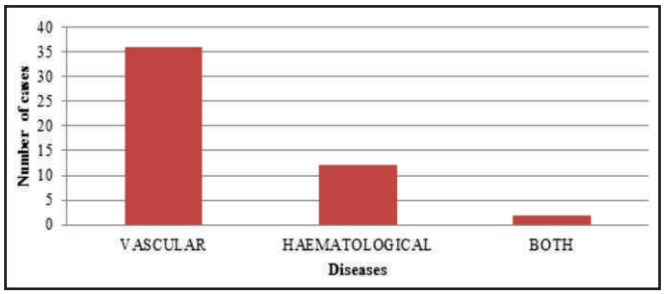
Out of sample unit of 300 cases studied, 50 cases had elevated Homocysteine levels along with vascular and haematological abnormalities. Out of 50 cases, 35 cases were males and 15 cases were females.

Figure 2: Age (years) wise Distribution of Patients



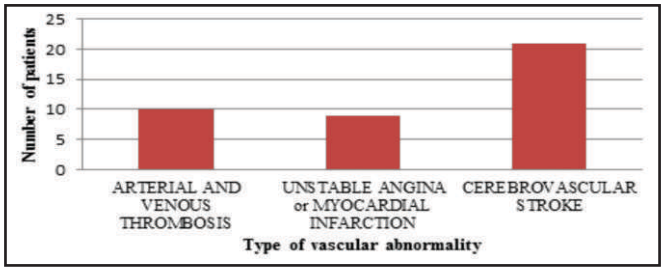
As shown in figure 2, maximum cases being 20 (40%) were from age group of 31-40 years, the rest being from other age groups.

Figure 3: Abnormality wise Distribution of Patients



As shown in figure 3, out of those 50 cases 36(72%) were associated with vascular abnormalities like cerebrovascular stroke, myocardial infarction, unstable angina, venous and arterial thrombosis and others. 12 cases (24%) were associated with vitamin B12 deficiency, folic acid deficiency and megaloblastic anemia. Rest 2 cases (4%) had features of both.

Figure 4 : Distribution of patients according to different Vascular Abnormalities



As shown in figure 4, total 10 patients were diagnose with arterial and venous thrombosis , 9 patients had unstable angina and myocardial infarction , and 21 had cerebrovascular stroke.

Data analysis :

On analysing the data of 50 cases , with the two variables being elevated homocysteine and presence of vascular & haematological abnormalities , the level of coefficient (PEARSON COEFFICIENT) calculated, turned out to be 0.205 (r value) which suggested a partial positive correlation.

Discussion:

The current study aims to establish a correlation between elevated levels of homocysteine and vascular and haematological abnormalities. Based on the data available from the study, the r value (Pearson Coefficient) turned out to be 0.205 with respect to the above two mentioned variables, suggesting a positive partial correlation. The results of the current study are in accordance to the various studies done over a period of time establishing hyperhomocysteinemia as a potential cause of thrombotic events. Present study suggested a high prevalence of vascular events associated with hyperhomocysteinemia, with cerebrovascular stroke being a leading presentation among them.[4] There is increased risk of myocardial infarction seen with the presence of elevated homocysteine levels.[5,6] Other pro coagulable events like cerebral venous sinus thrombosis,[7] deep vein thrombosis[8] are ascribed to a lesser proportion as compared to other vascular diseases. One of the common presentations is seen in around 25% percent of population[9] associated with elevated homocysteine levels is associated with haematological abnormalities likely to be Vitamin B12 deficiency, Folic acid deficiency, more commonly seen with vegetarians. [10]

Treatment:

Administration of Pyridonixe, Folic Acid, Cyanocobalmine, Betaine in standard doses helps in treating the cause, apart from medical management.

Conclusion:

Based on the data studied and the statistical correlation applied the study showed the importance of hyperhomocystinemia being one of the risk factors of the aforementioned diseases and its importance is understood in patients who do not have explainable causes of the diseases and its treatment is associated with a modifiable factor which can help in decreasing the morbidity and mortality in general population..

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