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Original Research Article

SERUM HOMOCYSTEINE LEVELS IN RETINAL VEIN OCCLUSIONS

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ABSTRACT

Background: Hyperhomocysteinemia has been implicated in various cardiovascular and cerebrovascular diseases and is now being explored for its potential impact on retinal vasculature. Elevated homocysteine levels can damage the endothelium, the inner lining of blood vessels, leading to endothelial dysfunction. **Aims and Objective:** To study the Serum levels of Homocysteine in Retinal Vein Occlusions.

Materials and Methods: The present study was undertaken on 160 patients. The patients enrolled in this study were divided into the following groups: Group A: This group served as the study group and comprised of 66 patients of retinal vaso-occlusive disease. Group B: This group served as healthy control group and comprised of age and gender matched normal 60 patients. Group C: This group served as the sick control group and comprised of 34 patients, sick controls who either have diabetes or hypertension or both but, without retinal vaso occlusive disease.

Results: The mean serum homocysteine was highest in study group (19.60±1.29 µmol/dl). followed by sick control group(15.995±0.637µmol/dl) and least in healthy control group (13.16±0.65µmol/dl).

Conclusions: The mean serum homocysteine was highest in study group followed by sick control group and least in healthy control group.

Keywords: Retinal Vein Occlusions, Hyperhomocysteinemia.

INTRODUCTION

After diabetic retinopathy, Retinal Vein Occlusion is the second most frequent retinal vascular disease. According to studies conducted in general populations, its prevalence ranges from 5.2 to 16 per 1,000 people. Retinal Vein Occlusion (RVO) is more frequent in men than in women, and it is more common in those over 65, with Branch Retinal Vein Occlusion (BRVO) being four times more prevalent than Central Retinal Vein Occlusion (CRVO).[1]

Retinal Vaso occlusive diseases, are among the leading causes of vision impairment and blindness worldwide.[2] Hyperhomocysteinemia has been implicated in various cardiovascular and cerebrovascular diseases and is now being explored for its potential impact on retinal vasculature. Elevated homocysteine levels can damage the endothelium, the inner lining of blood vessels, leading to endothelial dysfunction.[3] Elevated levels of homocysteine, an amino acid derived from methionine metabolism, have been associated with endothelial dysfunction, increased platelet aggregation, and thrombus formation, all of which can contribute to vascular occlusion.[4]

This damage results in reduced nitric oxide (NO) availability, a key regulator of vascular tone and health, causing vasoconstriction and promoting a pro-thrombotic state. Homocysteine can induce oxidative stress and inflammatory responses within the vascular system. It promotes the production of reactive oxygen species (ROS), which further damage the endothelium and promote inflammation, exacerbating vascular occlusion. High homocysteine levels enhance platelet aggregation and coagulation, increasing the risk of thrombus formation. Thrombi can obstruct retinal veins or arteries, leading to ischemia and subsequent retinal damage.[5]

Hyperhomocysteinemia is an independent risk factor for thrombovascular disorders, however it is unclear whether the mildly elevated amino acid content is the causal agent or only a marker for the illness.[6]

This study aims to study the Serum levels of Homocysteine in Retinal Vein Occlusions.

MATERIALS AND METHODS

The present study was undertaken on 160 patients, who presented to the Retina service and the Ophthalmology Outpatient Department of Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh.

Design: Cross sectional case control study

Ethics committee clearance: Approval was obtained from the institutional ethics committee

Consent: All the Tenets of the Declaration of Helsinki were followed. A well informed written consent for ocular examination and blood sampling was taken from all the patients enrolled in the study.

Exclusion Criteria

1. Patients taking Vitamin or other supplements
2. Patients taking drugs that can affect levels of homocysteine

Inclusion Criteria: Individuals diagnosed as case of Retinal vaso-occlusive diseases is in the study group. The patients enrolled in this study were divided into the following groups:

Group A: This group served as the study group and comprised of 66 patients of retinal Vaso-occlusive disease.

Group B: This group served as healthy control group and comprised of age and gender matched normal 60 patients.

Group C: This group served as the sick control group and comprised of 34 patients, sick controls who either have diabetes or hypertension or both, but without retinal Vaso occlusive disease.

Each patient was subjected to a though history taking and a very meticulous ocular and systemic examination.

Blood Sample Collection: Venipuncture was used to obtain the fasting blood samples without application of any tourniquet (to avoid minimal chances of haemolysis) from cubital fossa of either arm after cleansing the site with spirit swab. The blood samples were collected in Plain vials and Serum was prepared by centrifugation and stored in Eppendorf tube at -80°C for later use.

For estimation of Serum Homocysteine levels Fine Test ELISA kit was used to estimate the level of Homocysteine. The detection range of this kit is 7.813-500 pmol/ml and the sensitivity is 4.688 ng/ml. Statistical analysis was done using SPSS 28.0 for Windows software (SPSS Inc. Chicago, Illinois, USA). Using a one-way ANOVA test, Chi- square test, post hoc tukey test, the differences in the mean blood levels of homocysteine across the different groups were examined.

RESULTS

Out of 160 patients enrolled in the study 75 (46.9%) were males and 85 (53.1%) were females and the mean age was 54.62±10.53 years.

In Group A (study group), mean age of patients was 53.32±10.54 years. Out of the 66 patients enrolled in this group, 30 (45.5%) were males and 36 (54.5%) were females. There were 19 patients of CRVO and 46 patients of BRVO.

In Group B (healthy control group), mean age of patients was 56.48±10.26 years. Out of the 60 patients enrolled in this group, 30 (50.0%) were males and 30(50.0%) were females. In Group C (sick control group), mean age of patients was 53.85±10.80 years. Out of the 34 patients enrolled in this group, 15 (44.1%) were males and 19 (55.9%) were females.

All the above groups were age and gender wise matched as there was no statistically significant difference between them.

Serum Homocysteine Level in Various Groups

In the study group (Group A), mean serum homocysteine level was 19.60±1.29(µmol/dl), minimum value was 17.09(µmol/dl) and maximum value was 22.88(µmol/dl). In the Healthy control (Group B), mean serum homocysteine level was 13.16±0.65(µmol/dl), minimum value was 11.87(µmol/dl) and maximum value was 14.32(µmol/dl). In the sick control (Group C), mean serum homocysteine level and standard deviation was 15.99±0.64 µmol/dl. minimum value was 14.080(µmol/dl) and maximum value was 16.980(µmol/dl) (Table 1 and Figure 1). The mean serum homocysteine level in CRVO was 19.49±1.01(µmol/ml) and BRVO was 19.69±1.39 (µmol/ml).

The difference in mean serum homocysteine level between Group A and Group B was 6.44 (µmol/ml), between Group A and Group C was 3.607 (µmol/ml) and between Group C and Group B was 2.836 (µmol/ml) and all these differences were statistically significant (Table 2).

The analysis of serum homocysteine levels reveals highly significant differences among the groups. Study group had significantly higher serum homocysteine levels compared to Healthy Controls, with a p-value of <0.001, indicating a statistically significant difference. The 95% confidence interval for this comparison ranged from 6.035 to 6.852, demonstrating a substantial increase in serum homocysteine levels in study group compared to Healthy Controls. Similarly, study group also had significantly higher serum homocysteine levels compared to Sick Controls, with a p-value of <0.001. The confidence interval for this comparison ranged from 3.124 to 4.090, suggesting a notable increase in serum homocysteine levels in study group compared to Sick Controls. Additionally, there was a highly significant difference between Healthy Controls and Sick Controls, with a p-value of <0.001. The 95% confidence interval for this comparison ranged from

-3.328 to -2.345, indicating a substantial reduction in serum homocysteine levels in Healthy Controls compared to Sick Controls.

Table 1: Mean Serum Homocysteine Levels in Various Groups Using One Way Anova Test

S. No.	Groups	Serum Homocysteine (µmol/ml)		F- Value	P- Value
		Mean	Std. Deviation		
1	Group A (Study group)	19.60	1.29	701.141	<0.001
2	Group B (Healthy Control)	13.16	0.65		
3	Group C (Sick Control)	15.99	0.64		

Table 2: Group Wise Comparison of Mean Homocysteine Level Using Post Hoc Tukey Test

Groups	P- Value	95% Confidence Interval	
		Lower Bound	Upper Bound
Group A (Study group) vs Group B (Healthy Control)	<0.001	6.035	6.852
Group A (Study group) vs Group C (Sick Control)	<0.001	3.124	4.090
Group B (Healthy Control) Vs Group C (Sick Control)	<0.001	-3.328	-2.345

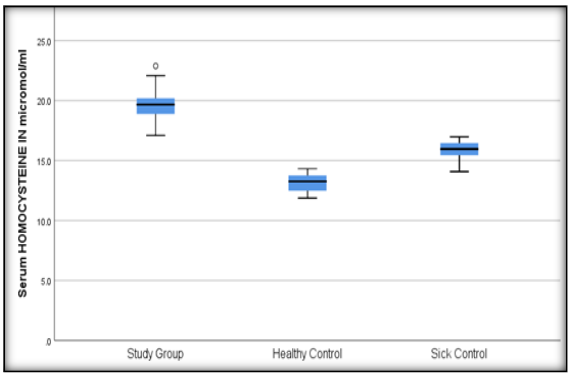

Figure 1: Box Plot Showing Serum Homocysteine Levels in Various Groups

DISCUSSION

Hyperhomocysteinemia may have a function as an independent atherogenic risk in individuals with vascular occlusive disorders.[7] A high quantity of homocysteine in the blood causes atherosclerosis by increasing oxidative stress, impairing vascular endothelial function, and inducing thrombosis.[8]

Cahill et al.,2000,[4] discovered higher homocysteine levels in hypertension and heart disease patients. Hyperhomocysteinaemia causes both venous and arterial occlusive retinal disorders.[5]

In the present study the mean serum homocysteine was highest in study group (19.60±1.29 µmol/dl) which comprised of 66 patients of retinal Vaso-occlusive disease, followed by sick control group(15.995±0.637µmol/dl) which comprised of 34 patients, who either had diabetes or hypertension or both but without retinal Vaso occlusive disease and was least in healthy control group (13.16±0.65µmol/dl) age and gender matched normal 60 patients and these differences were statistically significant.

In retinal vascular disorders, homocysteine levels are increased. A growing body of research suggests that homocysteine levels are significantly elevated in Vaso occlusive Retinal Diseases. The incidence of hyperhomocysteinemia, as reported in heterozygosity for homocystinuria, was investigated in 19 individuals who had retinal vein occlusion or retinal artery occlusion before the age of 50 years, using a standardised, oral methionine loading test. Afterload peak concentrations of homocysteine surpassed the mean level measured in normal control subjects by more than two standard deviations in four of the 19 patients (21%), two with retinal artery occlusion and two with central retinal vein occlusion, and were also within the ranges established in homocystinuria obligate heterozygotes. Researchers inferred that hyperhomocysteinemia predisposes to the development of premature retinal artery and retinal vein occlusion since the prevalence of heterozygosity for homocystinuria in the normal population is one in 70 (1.4%) at most.[5]

Biousse et al, 1997,[9] describe a 24-year-old male with bilateral central retinal vein occlusions who had previously experienced bouts of protracted transitory monocular vision loss with no evidence of vein occlusion. Extensive hematologic investigations for reasons of venous blockage were normal, elevated plasma homocysteine was found same for the patient's and his asymptomatic father's. They concluded that regardless of ophthalmoscopic appearance, impending vein occlusion should be included in the differential diagnosis of transitory monocular vision loss, and hyperhomocystinemia should be evaluated as a probable cause of retinal vein occlusion.

The mean plasma total homocysteine levels in patients with retinal vascular occlusive disease and matched healthy controls. were substantially higher than in controls (16.1 ± 8.3 vs. 8.96 ± 5.6 mol/L p).[10]

Cahill et al.,2000,[11] conducted a retrospective case-control analysis on hospitalised controls and patients with retinal artery, central retinal vein (including hemiretinal vein), and branch retinal vein occlusions. They investigated the link between disease and

increased total Homocysteine level, they defined it as a level more than or equivalent to 12 mol/l, and stated that there will be the risk of retinal vascular occlusive disease above this. They compared 87 instances of retinal vascular occlusive disease to 87 age-matched controls, comprising of 26 cases of retinal artery occlusion, 40 of cases of central retinal vein occlusion, and 21of cases of branch retinal vein occlusion. Mean total Homocysteine levels were greater in all illness groups, with a significant difference in patients with retinal artery occlusions (p= 0.032) and patients with central retinal vein occlusions (p=0.0001). When established cardiovascular risk variables were controlled for, total Homocysteine was found to be an independent risk factor for retinal vascular occlusive disease (OR-2.85, 95% CI-1.43-5.68). They reported that high total Homocysteine levels are a separate risk factor for retinal vascular occlusive disease.

Devi et al,2025,[12] in a hospital based cross sectional study reported that elevated Homocysteine is associated with a majority of cases diagnosed with RVO. However, clinical presentation is not affected by the presence or absence of Homocysteine and its severity.

CONCLUSION

High plasma homocysteine is a risk factor for retinal vascular occlusive disease so it may be useful to measure homocysteine in the management of these patients.

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