

Evaluation of Serum Homocysteine In Patients With Ischaemic Retinal Vascular Occlusive Diseases

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Abstract

Context: Homocysteine (HCy) is a sulphur containing metabolite of methionine. Elevated plasma levels of the amino acid “homocysteine” has been identified as an independent risk factor for atherosclerosis, including coronary artery disease, peripheral vascular disease, cerebrovascular disease and venous thromboembolism. Frequent ocular diseases like diabetic retinopathy, retinal vein occlusions (RVO)², retinal artery occlusion etc are of particular epidemiological importance as leading causes of blindness.

Aims

1. To assess the level of serum homocysteine in patients with retinal vascular occlusive diseases.

2. To establish relationship between serum homocysteine levels and the presenting ocular clinical conditions.
3. To establish relationship between serum homocysteine and severity of diabetic retinopathy.

Settings and Design:Hospital based cross sectional study carried out among the patients presenting to Outpatient department of Ophthalmology of Tertiary care centre.

Methods and Material:Hospital based cross sectional study conducted among patients presenting to OPD of Ophthalmology of Tertiary care centre from June 2020 to December 2020. Informed written consent was taken. Relevant history taking and examination was done.

Statistical analysis used: Frequency, Percentage, And Student t Test.

Results: Among 100 patients, 48 were male, 52 were female in the age group of 45-70 years. Of these 100 patients, 54 patients had DR, 14 pts-CRVO, 19 pts-BRVO, 5 pts-OIS, 8 pts-CRAO. Out of these 100 pts, 25 (25%) patients had elevated serum homocysteine (Sr HCy) levels. Among these 25 patients with elevated Sr HCy levels, 44% constituted patients with DR, 20% constituted patients with CRVO.

Among 54 patients who had DR, 11 patients had raised Sr HCy levels. In this, 6 patients had PDR, 2 patients - Very severe NPDR, 3 patients - Severe NPDR.

Conclusions

Elevated HCY is a risk factor for retinal vascular occlusive diseases. There is direct relationship between levels of serum homocysteine and DR. It acts not only as an independent risk factor but also a contributory factor for the severity of DR. Hence, understanding and characterizing role of HCy in the pathogenesis of vascular occlusive diseases and DR could help in identifying novel target to combat these blinding diseases. Hence it is imperative that assessment of levels of serum homocysteine is important and should be done in vascular occlusive diseases and DR.

Keywords: Hyperhomocysteinemia, Retinal vascular occlusive diseases, Serum homocysteine, vein occlusions, Diabetic retinopathy.

Introduction

Homocysteine (HCy) is a sulphur containing metabolite of methionine. Elevated plasma levels of the amino acid "homocysteine" has been identified as an independent risk factor for atherosclerosis, including coronary artery disease, peripheral vascular disease, cerebrovascular disease and venous thromboembolism. Recent studies indicate that 15 to 30 percent of patients with premature occlusive vascular disease have elevated total plasma

HCY (homocysteine) concentrations (higher than 15 $\mu\text{mol/L}$). A plasma HCY concentration exceeding 15 $\mu\text{mol/L}$ defines hyperhomocysteinemia.¹

Frequent ocular diseases like diabetic retinopathy, retinal vein occlusions (RVO)², retinal artery occlusion etc are of particular epidemiological importance as leading causes of blindness. The most common risk factors are arterial hypertension (65%), diabetes mellitus (25%), valvular diseases of the heart (25%), and carotid artery stenosis or plaques (45%).³ Rare causes are arteritis & vascular spasm³. However, these factors do not fully explain the etiological relationships in all cases of vascular occlusions. Few studies show relationship between serum homocysteine levels and retinal vascular diseases. However, the information available on the role of elevated homocysteine in occurrence of these diseases is limited.

Pathomechanism of raised serum homocysteine induced vascular occlusive disease includes direct toxicity to endothelial cells, synergistic interaction between homocysteine & lipoproteins, various platelet abnormalities-increased adhesiveness, decreased survival and increased thromboxane A activity, promotes the clotting cascade via inactivation of protein C, activation of coagulation factor V, increased vascular smooth muscle proliferation and inhibition of thrombomodulin.¹

In diabetic retinopathy (DR), the role of homocysteine is that it is toxic to the vascular endothelium and therefore it induces thrombosis and hence may play a vital role in aggravating the hypoxic status such as that seen in diabetic retinopathy by further closure of the capillary bed⁴. Therefore, elevated homocysteine may act as pathogenetic link through which the various risk factors may exert their deleterious effect on retinal vascular

endothelium.⁵Hence we intend to assess the role of serum homocysteine in the occurrence of various retinal vascular occlusive diseases and also its relationship in severity in DR.

Subjects and Methods

A cross sectional study was conducted in 100 patients diagnosed with retinal vascular occlusive diseases visiting the outpatient department of Ophthalmology, HIMS Teaching Hospital, Hassan during the study period of June 2020 to December 2020. Informed consent was taken from all patients included in the study.

Patients with significant diabetic retinopathy (severe, very severe, proliferative DR with or without maculopathy), retinal vein occlusions (central, branch, tributary vein occlusions), retinal artery occlusions (central, cilioretinal artery occlusions), patients presenting with ocular ischaemic syndromes were included in the study. Patients with pre-existing systemic hyperviscosity syndromes and hypercoagulable conditions, pre-existing ocular diseases like glaucoma, inflammatory vasculitis and pre-existing systemic autoimmune disease were excluded from the study.

Patients fulfilling the inclusion criteria were recruited into the study. The aims and objectives of the intended study were properly explained to the patients and informed written consent was taken. Ophthalmic examination was done as follows: Visual acuity, Best corrected visual acuity using Snellen's chart, Intraocular pressure measurement with Perkin's tonometer, detailed slit lamp examination and slit lamp biomicroscopy using 90D lens & indirect ophthalmoscopy using 20D lens. FFA, fundus photographs & OCT were done. History of systemic diseases like diabetes mellitus, hypertension, hyperlipidaemia, cardiovascular disease and duration

was taken. Routine investigations like CBC, RBS, ESR, lipid profile, BP measurement were done. Cardiovascular examination was done. All patients underwent serum analysis of fasting homocysteine levels. Venous blood samples were drawn from patients and all examinations were performed at 8.00 h after an overnight fast.⁵ The machine used for serum homocysteine assay was ARCHITECT homocysteine.

Results

The study was conducted on 100 patients diagnosed with retinal vascular occlusive diseases. We measured fasting serum homocysteine levels in these patients.

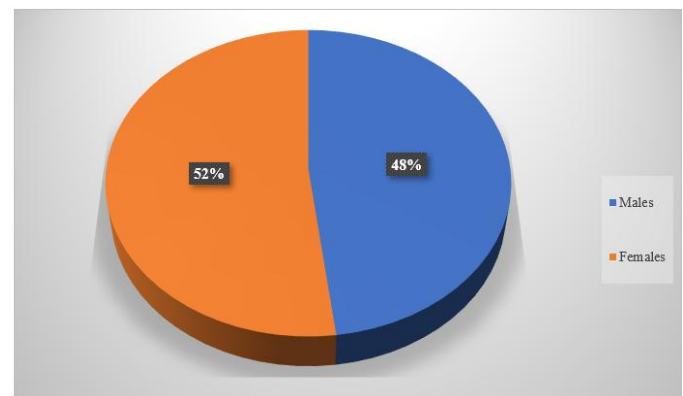


Figure 1: Gender distribution

Among 100 patients 48 were male, 52 were female in the age group of 45-70 years, mean age-57.5 years.

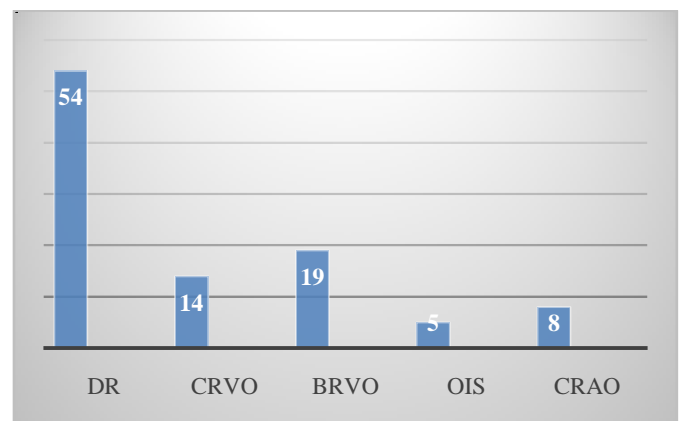


Figure 2: Distribution of each pathological condition among 100 patients included in the study Among the 100 patients, 54 patients had Diabetic retinopathy

(DR), 14 had central retinal vein occlusion (CRVO), 19 had branch retinal vein occlusion (BRVO), 5 had ocular ischaemic syndrome (OIS), 8 had central retinal artery occlusion (CRAO)

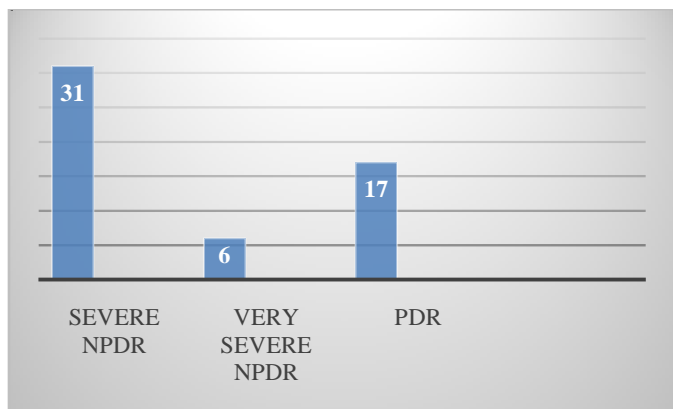


Figure 3: DR grading among 54 DR patients.

Among 54 patients, 31(57.4%) had severe NPDR, 6(11.1%) patients had very severe NPDR and 17(31.4%) patients had PDR.

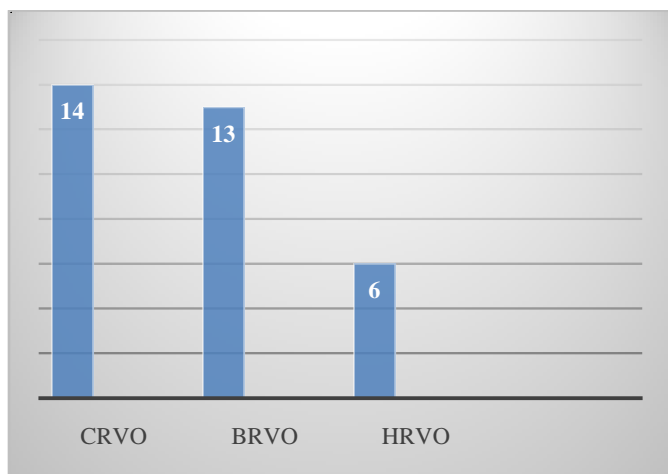


Figure 4: Distribution among retinal vein occlusions.

Out of the 33 retinal vascular occlusion patients, 14(42.4%) patients had CRVO, 13(39.3%) patients had BRVO and 6(18.1%) patients had hemiretinal vein occlusion (HRVO)

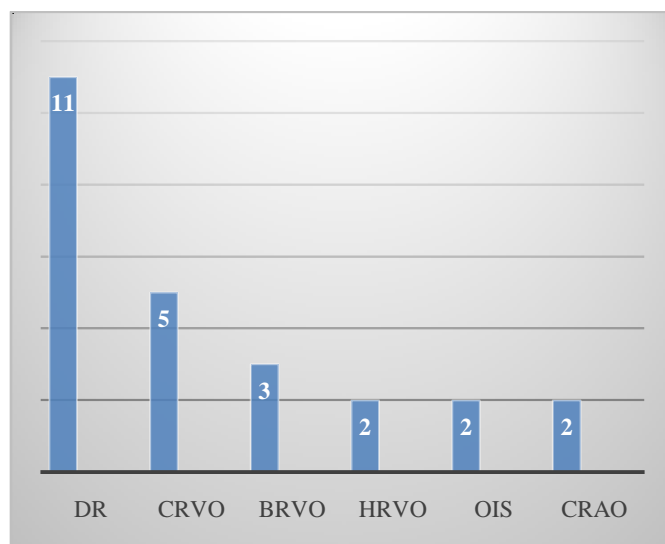


Figure 5: Distribution among 25 patients who had elevated serum homocysteine.

Among 25 patients, 11 (44%) patients had DR, 5(20%) patients had CRVO, 3(12%) patients had BRVO, 2(8%) patients had HRVO, 2(8%) had OIS and 2(8%) had CRAO.

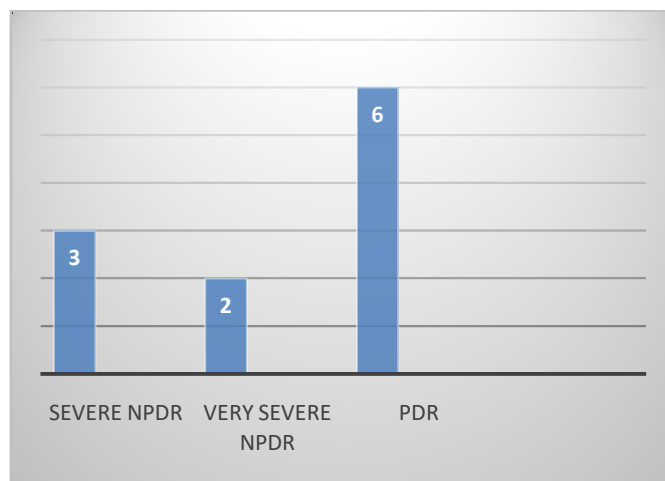


Figure 6: Elevated serum homocysteine among diabetics. Of 11 patients, 6(54.5%) had PDR, 3(27.2%) had severe NPDR and 2(18.1%) had very severe NPDR.

Discussion

Elevated homocysteine level may act as a pathogenetic link through which various risk factors may exert their deleterious effect on the progression of diabetic retinopathy⁵. Clinical and experimental evidence suggests

both direct toxicity to endothelial cells and a synergistic interaction between homocysteine and the lipoproteins. Various platelet abnormalities have also been reported including increased adhesiveness, decreased survival and increased thromboxane A activity. A prevailing hypothesis is that homocysteine promotes the clotting cascade through several actions; inactivation of protein C, activation of coagulation factor V, increased vascular smooth muscle proliferation and inhibition of thrombomodulin.¹

In our study, among 100 patients 25(25%) patients had elevated HCy levels. Out of the 33 retinal vascular occlusion patients, raised serum homocysteine was found in 5 patients with CRVO, 3 patients with BRVO and 2 patients with HRVO accounting to 10(40%) out of 25 patients with raised homocysteine levels. Also Abu El-Asrar et al reported that hyperhomocysteinemia was present in 29 (60.4%) of the patients with retinal vein occlusion and in 6 (75%) patients with retinal artery occlusion and concluded that high plasma homocysteine was a risk factor for retinal vascular occlusive disease⁶. Brown BA et al concluded that 15 of 20 patients (75%) with retinal vein occlusion disease had an elevated fasting serum homocysteine level.⁷

In our study, among 54(54%) patients who had diabetic retinopathy, serum HCy was found to be raised in patients with PDR than in severe NPDR and very severe NPDR. Similarly, Giulia Malaguarnera et al reported that higher plasma levels of homocysteine have been found in diabetics with proliferative diabetic retinopathy compared to both no proliferative DR and diabetics without retinopathy⁵. Also, Yang G et al in their study reported that 4 patients in PDR group had raised serum levels of HCy, the rate being significantly higher than that in background DR group.⁸

Among the 54 DR patients, 11(44%) patients had elevated HCy. 6 patients with PDR had elevated HCy constituting to about 24%, severe NPDR constituting to 12%, very severe NPDR to 8%. Our results are similar to the study conducted by Chong Xu et al who stated that a high homocysteinemia is common in the relationship with the incidence of DR, especially with PDR.⁹

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