Original Article

# HYPERHOMOCYSTEINEMIA, A BIOCHEMICAL TOOL FOR ISCHEMIC VEIN OCCLUSION DURING ACUTE PHASE

Bassam Mubarik*, Muhammad Adrees** , Iftikhar Ahmad***.
*Assistant Professor, Department of Ophthalmology Madinah Teaching Hospital Faisalabad.
**Assistant Professor, Department of Medicine, Allied Hospital Faisalabad.
*** Assistant Professor, Department of Ophthalmology, DHQ Hospital Faisalabad.

## ABSTRACT:

The purpose of study was to differentiate ischemic central retinal vein occlusion from non ischemic central retinal vein occlusion using homocysteine level as a biochemical marker during early stage of the disease.

**METHOD:** Fasting plasma homocysteine level was measured in 50 patients with unilateral ischemic central retinal vein occlusion and compared with a total of 50 age matched patients with non ischemic central retinal vein occlusion patients and 50 age matched healthy control subjects.

**RESULTS**: Homocysteine level was found significantly increased in ischemic vein occlusion(27.1mmol/l)as compared to non ischemic vein occlusion (14.6 mmol/l) and control (12.8mmol/l) subject.(P< .05)

**KEYWORDS:** Homocysteine, ischemic vein occlusion, non ischemic vein occlusion, central retinal vein occlusion.

## INTRODUCTION:

Retinal vein occlusion is one of the most common causes for sudden loss of vision. It is second only to diabetic retinopathy in causing retinal loss of vision[1]. In central retinal vein occlusion obstruction takes place at lamina cribrosa or proximal to it where central retinal vein runs out of eye[2]. CRVO is of two-types, ischemic and non ischemic, depending upon intact capillary beds. Both types have different prognosis and different treatment options[3]. Pathogenesis of central retinal vein occlusion is explained by Vischow's triad which states that three factors are involved in thrombus formation and occlusion of vein. These factors include vessel wall damage, stasis of blood flow and hypercoagubility[4]. Central retinal artery and vein share a common adventitial sheath posterior to lamina cribrosa where at arteriovenous crossing artery can compress central retinal vein due to atherosclerotic changes and result in central retinal vein occlusion[5]. Damage to retinal vessel wall from atherosclerosis and compression causes blood flow changes in vein causing stasis, thrombosis and resultant occlusion[6]. Non ischemic type is more common. It is 75% of all cases of central retinal vein occlusion. Presentation of disease is with sudden loss of vision or loss of field of vision. Ischemic central retinal vein occlusion causes more rapid loss of vision. There are four functional tests for diagnosis of ischemic central retinal vein occlusion including visual acuity, relative afferent pupillary defect, visual field and electroretinography. Two other testes are fundus fluorescein angiography and OCT for

*Corresponding Author:*
Bassam Mubarik.
Assistant Professor, Department of Ophthalmology Madinah Teaching Hospital Faisalabad.
Email: basimmubarik77@gmail.com

differentiating ischemic and non ischemic vein occlusion. None of these tests however have 100% sensitivity or specificity during early acute stage and therefore none of these tests is considered gold standard[7].Moreover previously no biochemical marker is available as is homocysteine level. Homocysteine is a sulphar containing non protein amino acid which is a product of methionine which is included in our diet. It acts as a methyl group donor during biochemical body reactions. When a methyl group is donated S-adenosyl homocysteine is formed which is then converted to homocysteine.

Homocysteine is either metabolized to cystathione through transsulfuration pathway requiring vitamin B6 or it converts back to methionine by vitamin B 12 andfolate requiring transmethylation[8].Hyperhomocysteinemia can also occur due to many causes like deficiency of enzyme cystathione beta synthetase and methyltetrahydrofolate reductase. Mild hyperhomocysteinemia can be caused by impaired function of enzymes in a transmethylation pathway sometimes associated with deficiency of vitamin B 12 and folic acid[9].

It has been established that hyperhomocysteinemia is an independent risk factor in central retinal vein occlusion[10,11].The study was performed to evaluate whether hyperhomocysteinemia can be used as a biochemical marker to diagnose ischemic central retinal vein occlusion at an early stage.

## MATERIALS AND METHODS:

It was a case control study. It was carried out in one year duration. It was performed at Eye Department Madina Teaching Hospital Faisalabad. Patients with ischemic or non ischemic retinal vein occlusion without any other local or systemic diseases were selected for the study. Patients with any other confounding condition like liver disease, renal disease, recent cardiovascular or cerebrovascular conditions, thyroid disease, diabetes, hypertension, hyperlipidemia, glaucoma were excluded from the study. Patients who were controls were also selected according to same inclusion and exclusion criteria. Informed consent was taken from all participants. Institutional ethical committee approved the study.

Ophthalmic examination including visual acuity, relative afferent pupillary defect, FFA and fund us examination of both eyes were performed and used for diagnosis of ischemic and non ischemic central retinal vein occlusion. Venous blood samples were taken during fasting condition. Anticoagulant was added and centrifuge was done for plasma. Plasma homocysteine level was determined with enzymatic method in a semiautoanalyser with a reagent kit. Statistical analysis ANOVA was performed by using R 3.4.1 for comparing results.

## RESULTS:

Based on inclusion and exclusion criteria 150 patients were selected. For Ischemic CRVO patients 25 males and 25 females were selected. A total of 50 age and sex match non ischemic CRVO and a total of 50 age and sex matched healthy control people were selected. The mean age of ischemic CRVO patients was 62 plus minus 10 years. The mean age of non ischemic and healthy control were 65 plus minus 10 years and 60 plus minus 10 years respectively.

**Table 1:**
**baseline features of study population.**

| | Male | Female | Mean age in years |
|---|---|---|---|
| Ischemic CRVO | 25 | 25 | 62±10 |
| NON ISCHEMIC CRVO | 30 | 20 | 65±10 |
| Control | 30 | 20 | 60±10 |

**Table 2:**
**Mean and SD**

| Patients | Ischemic CRVO | Non ischemic CRVO | Control |
|---|---|---|---|
| Homocysteine(mmol/l) | 27.100±5 | 14.580±5 | 12.780 ±2 |

After using the ANOVA the F-value and P-Value are respectively 606.56 and 0.0000. P-Value is very small so the results are significant. Plasma homocysteine levels were statistically significantly higher in patients with ischemic CRVO, followed by non ischemic CRVO as compared to control group because in ischemic CRVO group mean value is higher than the other two groups.

## DISCUSSION:

Prognosis of ischemic CRVO is extremely poor due to ischemia of macula. Rubeosisiridis develops in approximately 50% of eyes usually between 2 and 4 months of diagnosis (100 day glaucoma)and there is high risk for glaucoma. Retinal neovesseles develop in 5% of CRVO patients. Patients with ischemia should be seen monthly for six months to detect anterior segment neovesseles. Subsequent review should continue for up to two years to detect significant ischemia and macular edema. In non ischemic form conversion to ischemic form takes place in 15% of cases in four months and in 34% cases within 3 years. In cases that do not become ischemic, prognosis is reasonably good with return of vision to normal or near normal in about 50% of cases. It is always essential to diagnose ischemic or non ischemic type of CRVO during early acute phase because of different diagnosis and different treatment of both conditions[3].

In one study Lahri KD et. al. studied level of homocysteine and found that level of homocysteine increased in retinal vein occlusion in comparison with healthy people.[12] Homocysteine is believed to cause damage to vascular endothelium by disturbing supply of nitrous oxide[13]. Homocysteine is also believed to change in various thrombotic factors causing a mitogenic effect on arterial smooth muscle cells.[14] Albumin , fibronectin, transthyretin, and factor V have now been identified as molecular targets for homocysteine[15].

Formation of homocysteine thiolactone which is a metabolite of homocysteine is considered to be responsible for toxic effects of homocysteine in humans. It is said to cause damage to endothelial cells[16]. Higher level of homocysteine in ischemic CRVO cases may suggest that there is role of homocysteine as active biochemical agent during acute phase of disease[17].

We conclude from this study that raised homocysteine level may be regarded as a biochemical marker for diagnosis of ischemic CRVO during acute early phase of disease.

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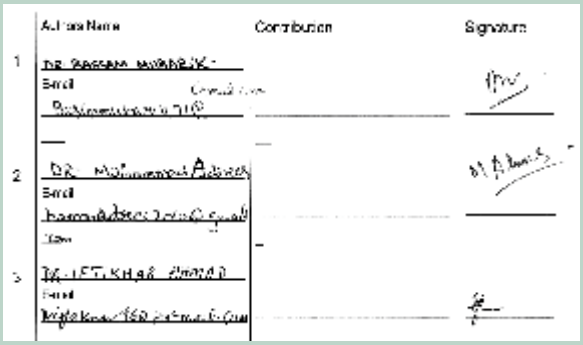


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After Revision

When Imam Ali was asked about Faith in Religion, he replied that the structure of faith is supported by four pillars endurance, conviction, justice and jihad.

***Hazrat Ali (Karmulha Wajhay)***