OCULAR MORBITIES ASSOCIATED WITH HYPERHOMOCYSTENEMIA
H. N. Sowbhagya1, Kiran Kumar L2, Minal Kothari3, Nivedhitha Nikhil4, Deepthi U. S5

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ABSTRACT: STUDY DESIGN: Retrospective study. MATERIAL AND METHODS: 49 patients of hHyc referred from various departments for ophthalmic opinion are included in the study. All cases were evaluated for anterior segment and posterior segment presentations. Field test was done for cases who had optic nerve involvement and cerebral infarcts. RESULTS: out 49 cases 25 cases had significant ocular findings mainly vascular involvements and sequelaes, like Retinal branch vein occlusion(BRVO), papillodema, visual field defects, Non arteritic anterior ischemic optic neuropathy (NA-AION) and optic disc pallor and 49%(24 patients) had no ocular findings. All cases were of moderate to intermediate hHyc and could undergo all the tests. One case with severe brain ischemia evaluated in medical casualty died. CONCLUSION: hHyc can present with varied vascular and ischemic ocular findings. Study shows the need for hHyc evaluations in all cases ocular ischemic and vascular catastrophes.

KEYWORDS: Hyperhomocystenemia, Retinal branch vein occlusion, Non arteritic anterior ischemic optic neuropathy, field defects, cerebral ischemia.

MESHTERMS: Hyperhomocystenemia, branch retinal vein occlusion, retinal ischemia, Non arteritic anterior ischemic optic neuropathy, brain infarct, optic disc pallor, optic disc edema, cerebral venous thrombosis.

INTRODUCTION: Homocysteine is a sulphur containing amino acid. It is an intermediate in the synthesis of methionine, and methyl group donor, S adenosyl methionine. It is metabolised by one of the 2 pathways remethylation or transsulfuration. Abnormalities of these lead to Hyperhomocysteinemia (hHcy). There are various causes of hHcy but mainly it is due to enzyme deficiencies – cystathionine β synthase, methionine synthase, 5-methyltetrahydrofolate reductase or vitamin deficiencies-folate, vitamin B6 or B12.1 hHcy is observed in approximately 5% of the general population and is associated with an increased risk of many disorders, including vascular and neurodegenerative diseases, autoimmune disorders, birth defects, diabetes, renal diseases, osteoporosis, neuropsychiatric disorders and cancer.1 The thrombo embolic effect of a high total plasma homocysteine level has been documented as early as 19682. In the ocular system many lines of evidence indicate that hHcy is a risk factor in a variety of disease including retinal atherosclerosis, cataract, glaucoma, exudative age related macular degeneration, macular and optic atrophy due to retinal vascular occlusions and non arteritic ischemic optic neuropathy.3

In this study we have observed the various ocular manifestations of patients with hHcy. Since retina is the window for visualization of the body’s circulation and possible to see the findings.

MATERIALS AND METHODS: This study was conducted between June 2012 and September 2014 in Kempegowda Institute of Medical Sciences and Research Centre, Bangalore India. All patients who were referred for ophthalmological opinion from the medicine, neurology and cardiology department
with hHcy were evaluated. Hyperhomocysteinemia was defined as having a serum level greater than 15μmol/L. It was further categorized as moderate, intermediate, and severe if the level was 16–30, 31–100, and more than 100μmol/L, respectively. Serum Homocysteine levels was estimated using enzymatic recycling method. Total number of hHcy subjects screened were 49. Visual acuity was tested by Snellens chart. The best corrected visual acuity was recorded. If the person could not correctly recognize the top letter of the chart, visual acuity was noted using the finger counting method. Anterior segment evaluation done using slit lamp and refraction was done by using Huwitz autorefractometer.

Intraocular pressure was recorded using Perkins tonometer. Posterior segment evaluation was done after dilating with tropicamide- phenylephrine eye drops using indirect ophthalmoscope (Keeler), 90D panfundoscopy lens and goldmann 3 mirror examinations. Visual field analysis (where possible) was done using Humphrey visual field analyser. In selected cases, we performed fluorescein angiography. Other investigations like radiological investigations such as CT, MRI, MR venogram, and lumbar puncture were reviewed from the records. Haematological workup such as lipid profile, hemogram, biochemistry and serology were reviewed.

RESULTS: 49 patients with Hyperhomocysteinemia underwent ophthalmological evaluation. Out of this 33(67%) were male patients and 16(33%) were females. The mean age group of presentation was 34.8yrs (ranging from 20yrs - 60yrs). 30 patients (61%) had moderate hHcy, 18 patients (37%) had intermediate hHcy and 1(2%) had severe hHcy. 55% of the patients had additional co morbidity like diabetes and hypertension and 45% had no co morbidity conditions. 44.8% (22 patients) presented with headache, giddiness etc, 38.7% (19 patients) presented with various visual disturbances like detective vision, field loss and 16.3% (8 patients) had no ocular symptoms. 51%(25 patients) showed ocular findings such as BRVO, papillodema, visual field defects, NA-AION and optic disc pallor and 49% (24 patients) had no ocular findings.

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<tr>
<th>Sl no</th>
<th>Manifestation</th>
<th>No’s</th>
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<th>Comments</th>
<th>Visual fields</th>
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<tbody>
<tr>
<td>1</td>
<td>Papillodema</td>
<td>6</td>
<td>12.2%</td>
<td>2 cases were due to cerebral venous thrombosis on MR venogram.</td>
<td>4 patients had normal fields and 2 had peripheral constriction</td>
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<td></td>
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<td>1 case of Benign intracranial hypertension.</td>
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<td>3 were idiopathic.</td>
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<tr>
<td>2</td>
<td>Branch retinal vein occlusion</td>
<td>10</td>
<td>20.4%</td>
<td>Most common involved vessels were STVO followed by ITVO.</td>
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<td>3</td>
<td>Non Arteritic anterior ischemic optic neuropathy (NA-AION)</td>
<td>2</td>
<td>4.1%</td>
<td>1 patient showed arcuate field defects, 1 had inferior altitudinal defect.</td>
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<td>4</td>
<td>Temporal Optic disc pallor</td>
<td>4</td>
<td>8.2%</td>
<td>Brain infarcts most common vessel involved was MCA and PCA.</td>
<td>3 patients showed homonymous hemianopic field defects.</td>
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<tr>
<td>5</td>
<td>Normal fundus with field defects</td>
<td>3</td>
<td>6.1%</td>
<td>Brain ischemia.</td>
<td>2 showed homonymous hemianopic field defects</td>
</tr>
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</table>

2 patients with papillodema showed cerebral venous sinus thrombosis, 1 had benign intracranial hypertension features and rest 3 showed normal MRI. 7 patients showed infarctions in
the brain. Most common vessel involved was the Middle cerebral artery followed by the posterior cerebral artery. Out of 10 vein occlusions 7 had superotemporal vein occlusion and 3 had inferotemporal vein occlusion.

**DISCUSSION:** At the cellular level hHcy causes vascular endothelial damage, proliferation of the vascular smooth muscle cells, elevated lipid peroxidation leading to free radical formation. By these pathophysiological processes hHcy can produce vascular occlusion and neovascularisation. Hyperhomocysteinemia is reported as an independent risk factor for systemic and ocular vasoocclusive disorders, including nonarteritic ischemic optic neuropathy (NAION), central retinal artery occlusion (CRAO), and central retinal vein occlusion (CRVO), especially in young patients. It has been reported that as many as 17% of young patients with NAION may have isolated hyperhomocysteinemia as the risk factor.

In our study 4.1% of patients with hHcy presented with NAAION. In a study conducted in Indian subcontinent hyperhomocysteinemia was a significant independent risk factor for RVO. However severity of hHcy levels and types of RVO had no “dose response” relationship. In our study branch retinal vein occlusion (BRVO) was the most common ocular manifestation (20.4%) of hHcy. In a study done Gore A D et al in 66% of the eyes with BRVO, superior temporal retinal vein was the most common vessel involved followed by 22-43% of eyes with occlusion of major branch in inferior temporal quadrant. Increased plasma homocysteine is associated with both retinal vein and retinal artery occlusion and the elevation being greater in vein occlusion.

In a case series presented by Virendra Sachdeva et al. from LVPEI, India 4 cases of isolated abducent nerve palsy was associated with hHcy. However we did not come across any such cases.

In our study we came across 6 patients with papilloedema and hHcy, 4 of which had a normal MRI and the other 2 had cerebral venous sinus thrombosis diagnosed on MR venogram. A study done by Ida Martinelli et al. shows that hyperhomocysteinemia increases the risk of cerebral vein thrombosis by approximately 4-fold. In our study 14.3 % of hHcy had silent ischemia of the brain with ocular presentations like optic disc pallor in 4 cases, field defects in 5 cases. Elevated levels of total homocysteine (tHcy) an amino acid are an independent risk factor for silent stroke, even in healthy middle-aged adults.

**REFERENCES:**


AUTHORS:
1. H. N. Sowbhagya
2. Kiran Kumar L
3. Minal Kothari
4. Nivedhitha Nikhil
5. Deepthi U. S.

PARTICULARS OF CONTRIBUTORS:
1. Professor and HOD, Department of Ophthalmology, RGUHS.
2. Assistant Professor, Department of Ophthalmology, RGUHS.
3. Junior Resident, Department of Ophthalmology, RGUHS.
4. Junior Resident, Department of Ophthalmology, RGUHS.
5. Junior Resident, Department of Ophthalmology, RGUHS.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. H. N. Sowbhagya, No.41-42/45, Sreegurukrupa, 7th Cross, Saraswathipuram, Nandini Layout, Bangalore-560096.
E-mail: drhnsowbhagyaappaji@gmail.com

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