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"Evaluation Of Homocysteine And Lipid Levels In Patients With Retinal Vein Occlusive Diseases"

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Background: Retinal vein occlusion (RVO) is the second most common retinal vascular disorder after diabetic retinopathy, causing significant visual morbidity. RVO manifests with characteristic features such as intraretinal hemorrhages, tortuous and dilated retinal veins, cotton wool spots, macular edema, and disc-edema. Systemic risk factors like older age, hypertension, diabetes mellitus, hyper-lipidemia, and coagulation abnormalities, particularly hyper-lipidemia and homocysteine in associated with RVO. Elevated homocysteine and lipid levels also contribute to vascular endothelial damage and thrombosis.

Objective: To estimate the levels of homocysteine, and lipids in patients with retinal vein occlusive diseases (RVOD).

Materials and Methods: This observational study was conducted over 12 months with 30 patients diagnosed with RVO attending the Ophthalmology department of SVRRGGH, Tirupati. Comprehensive ophthalmic and systemic histories were taken. Visual acuity, intraocular pressure, slit-lamp examination, and fundus examination were performed. Blood samples were collected after overnight fasting for estimating serum levels of homocysteine, and lipids using ELISA and chromogenic methods. Statistical analyses included unpaired t-tests and chi-square tests.

Results: The mean age of patients was 56.4 ± 13.7 years, with a slight male preponderance (53.3%). Fundus examination revealed CRVO in 20% of eyes, and BRVO in 46.7%. Elevated homocysteine levels were noted across all groups but were not statistically significant. Lipid analysis showed significantly higher LDL and total cholesterol and lower HDL in CRVO patients compared to those with IT BRVO and ST BRVO ($p<0.05$).

Conclusion: The study found elevated LDL and total cholesterol with different forms of RVOD, particularly CRVO. The role of homocysteine in RVOD, however, remains inconclusive and warrants further research.

Keywords: Retinal Vein Occlusion, Homocysteine, Lipid Levels, Central Retinal Vein Occlusion, Branch Retinal Vein Occlusion.

Introduction:

Retinal vein occlusion (RVO) is the second most common retinal vascular disease and is a common loss of vision in older patients. There are two types of RVO: Branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO).[1] The occurrence rate of vein occlusion stands at 0.7% among individuals aged 49 to 60 years, escalating to 4.6% in those aged 80 years and above. Present estimates suggest approximately 520 new cases of retinal vein occlusion (RVO) per million individuals, comprising 442 cases of branch retinal vein occlusion (BRVO) and 80 cases of central retinal vein occlusion (CRVO). RVO commonly manifests in middle-aged and older individuals, typically aged over 50 years, with an equal distribution between genders.[1,2] The global burden of people affected with RVO is calculated to be around 16.4 million adults worldwide. Many systemic risk factors were related to retinal vein occlusion with most typical association being older age, other common risk factors Hypertension, Diabetes mellitus, hyperlipidaemia, atherosclerotic cardiovascular diseases, oral contraceptive pills use among young patients, smoking and uncommon conditions like hyper-viscosity syndrome, hyperhomocysteinemia, and ocular risk factors like hypermetropia and glaucoma.[1,2] Hyperlipidaemia refers to elevated cholesterol, elevated TG or both. The problem can be due solely to hereditary factors, but more commonly it is an acquired condition. It is a common independent risk factor for occurrence RVO in adults. Total cholesterol, Triglycerides, LDL levels were raised and HDL levels were reduced in patients with retinal vein occlusion.[3] An elevated level of the amino acid, homocysteine is now generally accepted to be a risk factor for systemic vascular disease. Homocysteine appears to have a deleterious effect on vascular endothelium and may induce increased platelet aggregation and thrombosis. Levels of homocysteine may be increased by dietary habits, prescription medicines, or enzymatic mutations affecting homocysteine metabolism.[7] As retinal vein occlusion has been related to hyperlipidaemia hyperhomocysteinemia and hyper viscosity. Detection of the lipid diseases and Homocysteine levels been aimed toward preventing future occurrence of vascular occlusive events each ocular and systemic. Homocysteine, an amino acid not directly obtained from the diet, can be converted into cysteine or recycled into methionine, an essential amino acid, with the assistance of specific B vitamins. Normal homocysteine levels typically range between 5 to 15 micromol/L, with levels exceeding 15 micromol/L classified as hyperhomocysteinemia.[4-6] Elevated homocysteine levels signal a disruption in its metabolism, and such elevations have been linked to an increased risk of cardiovascular, cerebrovascular, and thromboembolic diseases. However, the evaluation and treatment of elevated homocysteine levels remain contentious due to conflicting study results regarding its impact on reducing risks for these diseases. Notably, lowering homocysteine levels has proven effective in reducing cardiovascular risks in individuals with homocystinuria, a rare genetic disorder associated with premature atherosclerotic disease.[7-9] Homocysteine levels are

typically categorized into three groups: moderate (16 to 30 micromol/L), intermediate (31 to 100 micromol/L), and severe (over 100 micromol/L). Despite these categorizations, the effects of homocysteine-lowering therapies on preventing stroke and coronary heart disease have not shown significant impacts in certain studies.[10] In this context, homocysteine and lipid levelswere estimated in patients with retinal vein occlusive diseases.

Material & Method

Observational Study was conducted for 12 months from 2023 -2024 with the approval of IEC Lr.No154/2023 dated 18/04/2023. Patients attending the department of Ophthalmology, were included. 30 cases of retinal vein occlusion were taken as sample size by simple randomised sampling method .All the patients diagnosed with Retinal vein occlusion withage group of >18 years who give written and informed consent are included.

Subjects having proliferative diabetic retinopathy with vitreous hemorrhage were excluded Subjects with retinal pathologies similar to RVO like diabetic retinopathy, Eales disease, radiation retinopathy also excluded. Patients with glaucoma or other local factors predisposing to thrombosis, renal dysfunction(serum creatinine> 2mg/dl), malignancy, intake of vitaminB12/B6, folate and medication known to influence plasma concentration such as fibrates, methotrexate, trimethoprim, estrogens, carbamazipines, phenytoin and tricyclic antidepressants and having opaque/hazy media were excluded.

Study Method:

In this study, patients of >18 years of age who diagnosed to have RVO on routine fundus examination and having complain of sudden painless blurring of vision were evaluated. Brief history of all patients including chief complain, origin, duration and progression of symptoms, associated systemic illness and their treatment were noted. The patient's history of ocular surgery was also determined. V/A assessment was done for distance and nearby using Snellen's visual acuity charts. IOP was measured by using Goldmann applanation tonometry. Slit lamp examination done for anterior segment evaluation to look for neovascularisation of iris (NVI) and angles (NVA) Fundus examination by 20D was done. The findings of fundus examination were recorded in terms of types of retinal vein occlusion and location of it. Confirmatory test of Fundus photograph, FFA was taken. A blood sample was taken from each participant after an overnight fast for estimation of serum homocysteine, lipid, levels using ELISA and chromogenic method respectively.

Before collecting data, all subjects are briefed about the purpose of study and informed written consent was obtained. Subjects were given the right to withdraw consent at any stage any investigations done during study was done free of cost**.** The study does not cause any financial burden to the patient.

Results

Present study included total 30 patients fulfilling inclusion criteria. The mean age of the patients was found to be 56.4±13.7yrs.

Table 1: Showing mean age of patient

	Mean	Standard Deviation
Age	56.4	13.7

Table 2: Showing gender distribution

		Count	Column N %
sex	F	14	46.7%
	M	16	53.3%

Among them 53.3% were male and 46.7% were female patients with marginal male preponderance.

Table3: Showing the BCVA in both eye

		Count	Column N %
BCVA right	6/12	7	23.3%
	6/18	3	10.0%
	6/24	3	10.0%
	6/36	3	10.0%
	6/6	6	20.0%
	6/60	1	3.3%
	6/9	7	23.3%
BCVA left	6/12	2	6.7%

	6/18	3	10.0%
	6/24	3	10.0%
	6/36	6	20.0%
	6/6	5	16.7%
	6/9	11	36.7%

Anterior segment was showing the IMSC in 33.3% on right eye and 30% in left eye. Pseudophakia present in 23.3% in right eye and 26.7% in left eye.

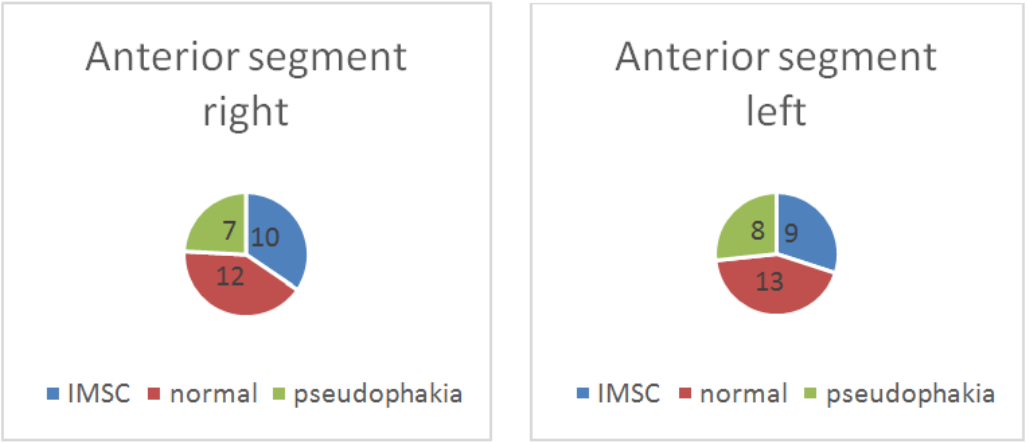

Figure 1: Showing the distribution of anterior segment findings of right eye and Left eye.

Table 4: Showing the distribution of the fundus examination findings

		Count	Column N %
Fundus examination right	CRVO	5	16.7%
	IT BRVO	5	16.7%
	Normal	12	40.0%
	ST BRVO	8	26.7%

Fundus examination left	CRVO	1	3.3%
	IT BRVO	3	10.0%
	Normal	18	60.0%
	ST BRVO	8	26.7%

Fundus on right eye showing 60% abnormal with 16.7% with CRBO, 16.7% with IT BRVO and 26.7% with ST BRVO. Similarly the left eye fundus showing the 40% abnormal results with 3.3% CRVO, 26.7% with ST BRVO and 10% wit IT BRVO. L,

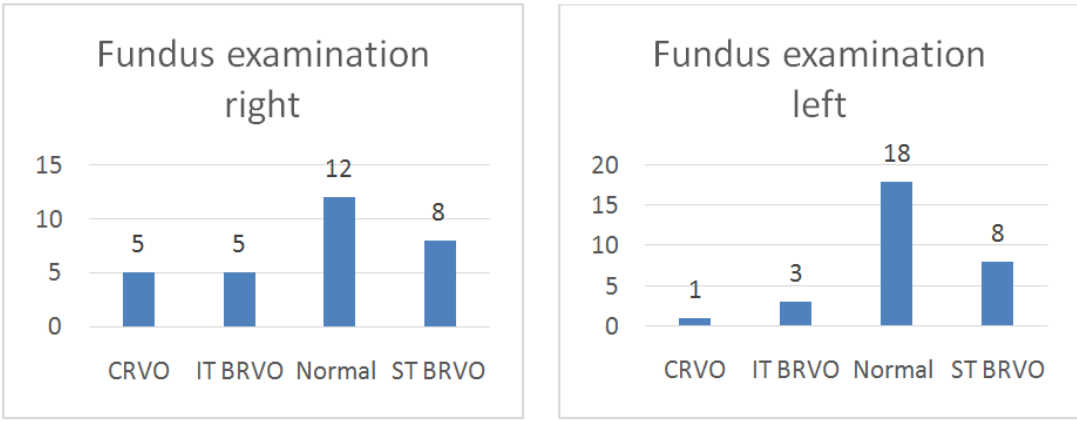

Figure.2: Showing the distribution of the fundus examination findings of right eye and left eye.

On assessment of the fundus examination with lipid profile, there is significant higher mean level of LDL and cholesterol and low HDLin patients with CRVO when compared to IT BRVO and ST BRVO.($p<0.05$)

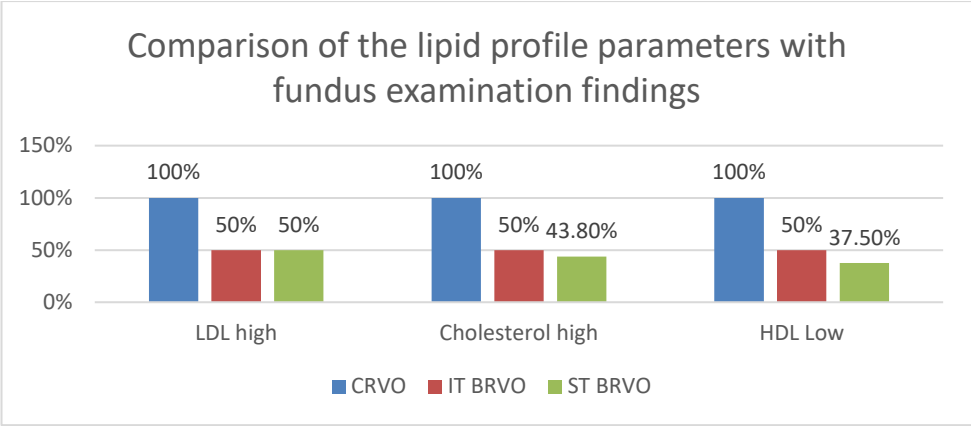

Figure.3: Comparison of the lipid profile parameters with fundus examination findings

Discussion

Present study included total 30 patients fulfilling inclusion criteria. The mean age of the patients was found to be 56.4±13.7yrs. Among them 53.3% were male and 46.7% were female patients with marginal male preponderance. Anterior segment was showing the IMSC in 33.3% on right eye and 30% in left eye. Pseudophakia present in 23.3% in right eye and 26.7% in left eye.

In concordance to present study Lahiri K et al., documented with Patients with retinal vein occlusion (RVO) exhibited significantly elevated levels of plasma homocysteine, total cholesterol, triglycerides, LDL cholesterol, and VLDL cholesterol, along with significantly decreased levels of HDL cholesterol compared to control subjects ($P < 0.001$). A notable negative correlation was observed between homocysteine and HDL cholesterol in RVO patients ($r = -0.273$, $P < 0.029$). The study suggests that individuals with low HDL cholesterol should undergo screening for elevated homocysteine levels, as the combination of low HDL cholesterol and elevated homocysteine may have a synergistic impact on retinal circulation. Further research is warranted to investigate whether treating elevated homocysteine levels could potentially raise HDL cholesterol levels, which could serve as an important preventive and therapeutic strategy for retinal vein occlusion.[9] Findings in study by Napal JJ et al., suggest that hyperhomocysteinemia and antiphospholipid syndrome should be considered in RVO patients. Additionally, genetic thrombophilia testing should be considered in those under 50 years or without cardiovascular risk factors. Aspirin therapy is likely the preferred treatment for RVO to reduce overall vascular risk, while anticoagulation should be reserved for high-risk thrombophilia cases.[10] Moreover, systemic vascular comorbidities can compromise the integrity of endothelial cells within the central retinal vein, further predisposing individuals to CRVO. Additionally, factors contributing to a prothrombotic state, such as elevated homocysteine levels or the presence of anticardiolipin antibodies, can heighten the risk of CRVO.[11] Elevated levels of homocysteine, known as hyperhomocysteinemia, have been identified as an independent risk factor for vascular diseases, including RVO. High homocysteine levels are thought to promote endothelial dysfunction, oxidative stress, and

thrombosis, which can lead to vascular occlusions. In patients with RVO, elevated homocysteine levels may contribute to the pathogenesis by impairing vascular integrity and promoting thrombus formation. Elevated homocysteine levels can inhibit the activation of protein C, thereby reducing its anticoagulant effect. This inhibition further exacerbates the hypercoagulable state. Conversely, deficiencies in protein C or protein S diminish their ability to inhibit clot formation, enhancing the risk of thrombosis, especially in the presence of elevated homocysteine levels. Monitoring homocysteine, levels is essential in evaluating and managing patients with suspected hypercoagulability. Treatment strategies may involve anticoagulant therapy, vitamin supplementation (e.g., folate, B vitamins for homocysteine. Lifestyle modifications and dietary adjustments can also play a role in managing homocysteine levels.

Abnormal lipid levels, particularly elevated total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, have been associated with atherosclerosis and vascular diseases. Although the exact role of lipid abnormalities in RVO is less clear compared to arterial diseases, studies suggest that dyslipidemia may contribute to endothelial dysfunction and vascular inflammation, predisposing individuals to vascular occlusive events. Conversely, high levels of high-density lipoprotein (HDL) cholesterol, often considered protective against cardiovascular diseases, may exert a beneficial effect by promoting endothelial repair and reducing inflammation. The relationship between homocysteine, and lipid levels in patients with retinal vein occlusive diseases underscores the complex interplay between thrombosis, vascular endothelial function, and lipid metabolism. Monitoring these biochemical markers can provide valuable insights into the pathophysiology of RVO and help guide therapeutic strategies aimed at reducing thrombotic risk and preserving visual function in affected individuals. In the context elevated homocysteine levels, can lead to endothelial dysfunction and increased oxidative stress, further contributing to retinal vein damage and thrombosis. However, while there is some evidence linking elevated homocysteine to CRVO, its role remains less clear, with studies showing varying results, indicating a need for further research to fully understand its impact.

Conclusion

This study examined homocysteine, and lipid levels in 30 patients with retinal vein occlusive diseases (RVOD), including central retinal vein occlusion (CRVO), superior temporal branch retinal vein occlusion (ST BRVO), and inferior temporal branch retinal vein occlusion (IT BRVO). The mean patient age was 56.4 ± 13.7 years, with a slight male predominance (53.3%). Key findings include elevated homocysteine levels were observed, though not statistically significant. Lipid profiles showed significantly higher LDL and total cholesterol and lower HDL in CRVO compared to IT BRVO and ST BRVO, indicating more severe dyslipidemia in CRVO. Even though the role of homocysteine remains inconclusive, however, the role of homocysteine requires further investigation due to the lack of statistical significance in this study.

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