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Estimation of protein C and lipid levels in patients with retinal vein occlusive diseases

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Abstract

Background: Retinal vein occlusion (RVO) is the second most common retinal vascular disorder after diabetic retinopathy, causing significant visual morbidity. It results from the obstruction of the retinal venous system, affecting either the central retinal vein or branch retinal veins. RVO manifests with characteristic features such as intraretinalhemorrhages, tortuous and dilated retinal veins, cotton wool spots, macular edema, and disc edema. Systemic risk factors like older age, hypertension, diabetes mellitus, hyperlipidemia, and coagulation abnormalities, particularly deficiencies in Protein C (PC) are associated with RVO. And contribute to vascular endothelial damage and thrombosis.

Objective: To estimate the levels of Protein C 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, lipids and Protein C 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%. Significantly lower Protein C levels were found in patients with CRVO and BRVO ($p<0.05$).. 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 significant associations between lower Protein C levels and elevated LDL and total cholesterol with different forms of RVOD, particularly CRVO. These findings suggest that monitoring and managing Protein C and lipid levels could be crucial in understanding and

mitigating the progression of RVOD.

Keywords: Retinal Vein Occlusion, Protein C, , Lipid Levels, Central Retinal Vein Occlusion, Branch Retinal Vein Occlusion.

Introduction

Retinal vein occlusion (RVO) is the second commonest sight threatening Retinal vascular disorder after diabetic retinopathy that is related to visual morbidity.[1] RVO Is an obstruction of the retinal blood vessel system, and will involve the central retinal vein or A branch retinal vein. Attainable causes are external compression or diseases of the vein wall like vasculitis. RVO are often divided into two primary classes, branch RVO (BRVO) And central RVO (CRVO), depending on the positioning of occlusion, with BRVO Occurring more usually than CRVO.[2] Retinal vein occlusion have a characteristic, though some variable features like Intra retinal hemorrhages, tortuous expanded retinal veins, cotton wool spots, macular, retinal edema and disc edema.[3] The mean age at onset is around 65 years, and this disorder affects 2.1/1000 patients aged 40 years or older and 5.4/1000 patients more than 64 years.The global burden of people affected with RVO is calculated to be around 16.4 million adults worldwide. The prevalence of BRVO and CRVO is 4.42 and 0.8 per one thousand persons and it increased with age however doesn't differ with gender.[4] Central retinal vein occlusion and Hemi retinal vein occlusion were believed to be results of a blood clot within the central retinal vein at or posterior to the lamina cribrosa. Arteriosclerosis of the neighboring central retinal artery that causes turbulent venous blood flow and leading to endothelial tissue injury. Branch retinal vein occlusion occurs at an arteriovenous crossing, wherever the artery and vein share a typical membrane sheath called common adventitial sheath.[5] 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.[5,6]

PC is vitaminK-dependent anticoagulant proteins anddownregulating mechanism of the bloodcoagulation cascade.Hereditary and acquired deficiencies of protein C (PC) are important.Risk factors of thrombosis and were reported in association with retinal vein occlusion, especially in young patients.[7–9] 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.[8] As retinal vein occlusion has been related to hyperlipidaemia and hyper viscosity. Detection of the Protein C and lipid levels been aimed toward preventing future occurrence of vascular occlusive events each ocular and systemic. As per that the objective of the study was to estimate protein C and lipid levels in patients with retinal vein occlusive diseases.

Material & Method

This is a hospital based observational study conducted in department of ophthalmology in one year from the date of approval of ethical and scientific committee A total of 30 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 in the Department of Ophthalmology, SVRRGGH, Tirupati, and Written informed consent was taken from all the patients.

Inclusion criteria:

All the patients diagnosed with Retinal vein occlusion with age group of 18years and above

2. Patients having history of previous known attacks of RVO

3.Patients who are willing to participate in the study.

4. All Patients who are willing to give written and informed consent.

Exclusion criteria:

1.Patients having proliferative diabetic retinopathy with vitreous hemorrhage

2.Patients with retinal pathologies similar to RVO like diabetic retinopathy,Eales disease, radiation retinopathy.

3. Patients with glaucoma or other local factors predisposing to thrombosis, renal dysfunction (serum creatinine > 2mg/ dl) ,malignancy, intake of vitamin B12/B6 , folate .

4.Patients having opaque/hazy media

Comprehensive ophthalmic and systemic histories were taken. Visual acuity was measured using Snellens visual acuity chart, intraocular pressure measured by using Goldman applanation tonometry. Slit lamp examination done for anterior segment evaluation to look for neovascularisation of iris (NVI) and angles (NVA) and fundus examination were performed by using 20D was done. The findings of fundus examination were recorded in terms of types of retinal vein occlusion and location of it and the Confirmatory test through Fundus photograph,(FFA).Blood samples were collected after overnight fasting and sent to Multi Dispilinary Research Unit(MRU), S.V.MedicalCollege,Tirupathi for estimating serum levels ofProtein Cusing ELISA and chromogenic methods and serum lipid profile .

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: Comparison of the Protein C, protein S and homocysteine among the fundus findings

		Fundus examination						Chi-square (p-value)
		CRVO		IT BRVO		ST BRVO		
		Count	N %	Count	N %	Count	N %	
Protein C	Low	5	83.3%	8	100.0%	10	62.5%	4.37 (0.05)*
	Normal	1	16.7%	0	0.0%	6	37.5%	

	High	0	0.0%	0	0.0%	0	0.0%	

On comparison of the markers with fundus changes, there is significant lower protein C level in patients with CRVO, IT BRVO and ST BRVO. ($p<0.05$) there is higher level of homocysteine among the all three group patients. However this finding was not statistically significant.

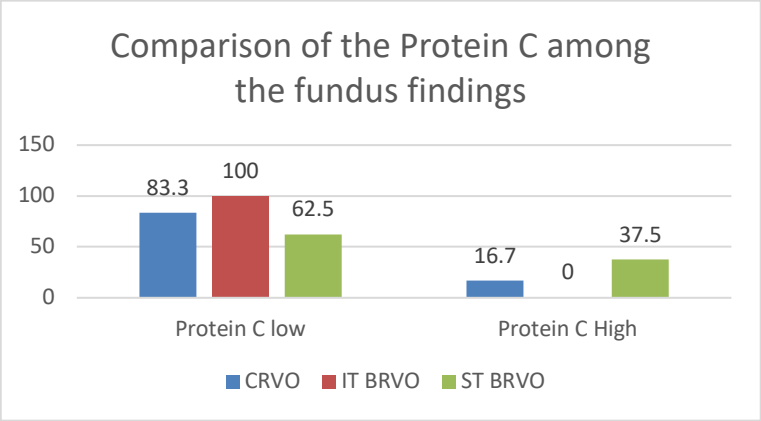

Figure 1: Comparison of the Protein C among the fundus findings

Table 2: Comparison of the lipid profile parameters with fundus examination findings

		Fundus examination						Chi-square (p-value)
		CRVO		IT BRVO		ST BRVO		
		Count	N %	Count	N %	Count	N %	
LDL	Normal	0	0.0%	4	50.0%	8	50.0%	5.00
	High	6	100.0%	4	50.0%	8	50.0%	(0.05)*
Cholesterol	Normal	0	0.0%	4	50.0%	9	56.3%	5.82
	High	6	100.0%	4	50.0%	7	43.8%	(0.05)*
HDL	Low	6	100.0%	4	50.0%	6	37.5%	6.89
	Normal	0	0.0%	4	50.0%	10	62.5%	(0.01)*

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.($p<0.05$)

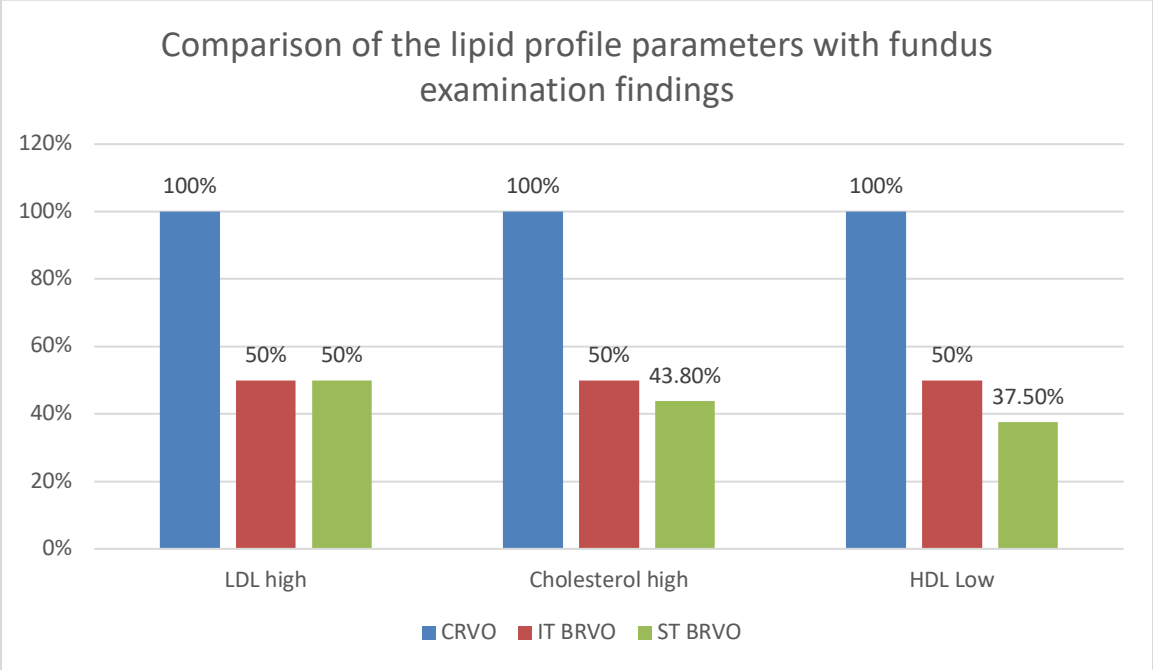

Figure 2: Comparison of the lipid profile parameters with fundus examination findings

Discussion

Retinal vein occlusive diseases (RVO) are significant causes of vision impairment and blindness, characterized by the blockage of retinal veins leading to ischemia and hemorrhagic retinopathy. RVO primarily encompasses central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO), each with distinct clinical manifestations and risk profiles. Various systemic factors such as hypercoagulability,anddyslipidemia, have been implicated in the pathogenesis of RVO, suggesting an intricate interplay between hemostatic and metabolic abnormalities.

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.

In study by Napal JJ et al., included 170 patients (93 men and 77 women; average age 68 ± 11 years) and 170 controls (80 men and 90 women; average age 67 ± 10 years). Peripheral retinal vein occlusion (RVO) was observed in 113 cases. 70 In another study by Liu Q et al., out of 50 patients, 14 (28%) had positive test results at the onset of CRVO.

On comparison of the markers with fundus changes, there is significant lower protein C level in patients with CRVO, IT BRVO and ST BRVO. ($p<0.05$) .On assessment of the fundus examination with lipid profile, there is significant higher mean level of LDL and cholesterol and low HDL in patients with CRVO when compared to IT BRVO and ST BRVO.($p<0.05$)

In concordance to present study Lahiri K et al., documented with Patients with retinal vein occlusion (RVO) exhibited significantly elevated levels of, total cholesterol, triglycerides, LDL cholesterol, and

VLDL cholesterol, along with significantly decreased levels of HDL cholesterol compared to control subjects ($P < 0.001$).

In the context of Central Retinal Vein Occlusion (CRVO), the roles of Protein C, Protein S, and homocysteine are critical due to their involvement in coagulation and vascular health. Reduced levels of Protein Cwhich is essential anticoagulants, contribute to a hypercoagulable state that increases the risk of thrombosis in the retinal veins, thereby playing a significant role in the development of CRVO. Lower levels of these proteins impair the anticoagulant pathways and endothelial function, making retinal veins more susceptible to occlusion.

The study underscores notable correlations between reduced Protein C levels and elevated lipid levels with various forms of Retinal Vein Occlusive Disease (RVOD). These findings suggest that monitoring and managing Protein C and lipid levels could be crucial in understanding and potentially mitigating the progression of RVOD.

Conclusion

This study examined Protein C, 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 significantly lower Protein C levels in all RVOD types, suggesting its potential role in disease pathogenesis. 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. These results highlight the importance of monitoring Protein C and lipid levels in RVOD,

The study highlights significant associations between reduced Protein C levels and elevated lipid levels with different forms of RVOD. The findings underscore the potential importance of monitoring and managing Protein C and lipid levels in patients with RVOD to better understand and mitigate the disease progression.

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