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STUDY OF RETINAL VENOUS OCCLUSIVE DISEASES AND THEIR RISK FACTORS

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration among all authors. Authors VHK and SMG designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors ADP, BSJ and GG managed the analyses of the study. Author DAM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Retinal vein occlusions (RVOs) are the most common retinal vascular disease second to diabetic retinopathy and a major cause of vision loss.
Methods: The present study was done at our tertiary care center to study the role of risk factors in Retinal Venous Occlusive diseases and correlation of occurrence of lesions with various risk factors. The study objective is to study the role of risk factors in Retinal Venous Occlusive diseases.
Results: Retinal vein occlusion (RVO) is a significant cause of loss of vision. Of the two major types of RVO, Branch Retinal Vein Occlusion (BRVO) is 4-6 times more widespread than Central Retinal Vein Occlusion (CRVO) and is the most frequent type of RVO. Hyperhomocysteinemia is a significant risk factor for RVO in patients below 40 years on age. Presence of multiple risk factors increases the chances of development of RVO.
Conclusion: There is a statistically significant difference between Known cases and Newly Diagnosed cases of RVOs, showing that there is a higher risk of developing RVOs in patients.

Keywords: Central retinal vein occlusion; branch retinal vein occlusion; primary open angle glaucoma; hypertension; hyperhomocysteinemia.

1. INTRODUCTION

Retinal vein occlusions (RVOs) are the most common retinal vascular disease second to diabetic retinopathy [1] and a major cause of vision loss [2].

1.1 Classification of Retinal Venous Occlusive Diseases

- Central retinal vein occlusion (CRVO)
- Hemiretinal vein occlusion (HRVO)

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- Branch retinal vein occlusion (BRVO) [3].

In the vast majority of cases, BRVO occurs at arteriovenous crossing sites where the artery is positioned anterior to the vein [4]. Untreated RVO often results in vision impairment and significant ocular complications in a substantial proportion of patients [5,6].

2. AIMS AND OBJECTIVES

Aims: To study the role of risk factors in Retinal Venous Occlusive diseases.

Objectives: To study the risk factors associated with Retinal Venous Occlusive diseases. To study correlation of occurrence of lesions with various risk factors.

3. REVIEW OF LITERATURE

The dramatic picture of obstruction, initially described as retinal apoplexy by Liebreich (1854) and hemorrhagic retinitis by Leber (1878), was first established as a clinical entity due to thrombosis by Julius von Michel (1878) who recognized that the relatively common appearances of gross venous disturbances and profuse retinal haemorrhages were due to this cause). Hayreh reported that after any RVO in one eye, the incidence of developing a second vein occlusion in the next 4 years was 2.5% in the same eye and 11.9% in the fellow eye [7]. Before we begin with the Retinal Venous Occlusive Diseases, it is essential to understand the micro-structural anatomy of retina.

4. MATERIALS AND METHODS

Patients coming to Ophthalmology OPD of Tertiary Care Hospital, irrespective of age and sex, diagnosed with Retinal Venous Occlusive Diseases; has been selected. Detail clinical history has been noted. Detailed examination including Blood Pressure, Best corrected Visual acuity, Intraocular tension using Goldmann's Applanation Tonometer, Anterior Segment examination on and Slit Lamp Biomicroscope, as well as Gonioscopy has beendone. Posterior segment examination by Indirect and Direct ophthalmoscopy after dilatation with 0.8% Tropicamide and 5% Phenylephrine eye drops(if not contraindicated), Fundus photography; has been done. Patients with Blood Pressure more than or equal to 140/90 has been labeled as Hypertensives. Patients with intraocular pressure more than 22 mmHg, has beenevaluated further for presence or absence of glaucoma.

Laboratory investigations including Haemoglobin levels, lipid profile (Serum Cholesterol, Serum Triglyceride, Serum LDL, Serum HDL, Serum VLDL), Serum Homocysteine level, blood glucose level; would be done. Patients with Hemoglobin levels below 12.5 g/dL has been labelled as Anaemic. Patients with Serum Cholesterol >200 mg/dL, Serum Triglyceride >150 mg/dL, Serum LDL >100 mg/dL, Serum HDL <40 mg/dL, Serum VLDL .30 mg/dL ; has been considered to have Dyslipidemia. Patients with Fasting Plasma Glucose >75 mg/dL and Post-prandial Plasma Glucose >140 mg/dL has been considered Diabetics. Patients with Primary Open Angle Glaucoma, hypertensives, diabetics and those with dyslipidemia has been further classified into known cases and newly diagnosed cases. Known cases has been further classified into whose with controlled disease, and those with uncontrolled disease, Patients with Serum Homocysteine levels >4.44um/L has been considered to have Hyperhomocysteinemia. Patients addicted to tobacco consumption in any form has been divided into old cases (<10 years duration) and new cases (>10 years duration). All patients who have been diagnosed with retinal vein occlusion, irrespective of age and sex.

5. OBSERVATION AND RESULTS

Sample size was calculated with 95% confidence in interval estimation, 20% anticipated range from previous studies and 10% absolute error of margin by using formula:

$n = Z2\ \pi\ (1- \pi)\ /d2$

Where,

Z = Table Value of alpha error from Standard Normal Distribution table (1.96 for 95% confidence interval)
π = anticipated range (from previous studies)
d = the absolute precision required on either side of true value of the population proportion π
Population proportion = π = 20% = 0.2
Level of significance (alpha error) = 5%
Margin of error = d = 0.1
Confidence interval = 95 %
n = (1.96)2 X 0.20 X 0.80 / (0.1)2
Thus, minimum sample size was decided to be 60.

As shown in Table 1, there was a linear increase in the number of patients with age up to the age of 70 years. The age distribution between groups was statistically not significant as per Student t-test ($p>0.05$).

Table 1. Age distribution of patients in BRVO and CRVO groups

Age (years)	BRVO (n=49)		CRVO (n=11)		Total	
	N	%	N	%	N	%
21-30	5	10.2%	0	-	5	8.3%
31-40	6	12.2%	0	-	6	10%
41-50	5	10.2%	0	-	5	8.3%
51-60	14	28.5%	4	36.4%	18	30%
61-70	17	34.6%	5	45.4%	22	36.7%
71-80	2	4.09%	2	18.2%	4	6.7%
Total	49	100%	11	100%	60	100%
Mean ± SD	57.8 ± 12.77		65.0 ± 8.33		59.3 ± 12.37	
p value	p>0.05					

Table 2. Sex distribution of patients in BRVO and CRVO groups

Sex	BRVO (n=49)		CRVO (n=11)		Total	
	N	%	N	%	N	%
Male	17	34.7%	7	63.6%	24	40%
Female	32	65.3%	4	36.4%	36	60%
Total	49	100%	11	100%	60	100%
p value	p>0.05					

Table 3. Distribution of patients according to Co-morbidities

Co-morbidities	BRVO (n=49)		CRVO (n=11)	
	N	%	N	%
Hypertension	34	69.4%	9	81.8%
Diabetes Mellitus	30	61.2%	5	45.5%
Dyslipidemia	22	44.9%	5	45.5%
Primary Open Angle Glaucoma	8	16.3%	6	54.5%
Smoking/Mishri	16	32.6%	2	18.2%
Hyperhomocysteinemia	10	20.4%	2	18.2%

As shown in Table 2, the sex distribution of patients in BRVO and CRVO groups is characterized in Table 4 and there was no statistically significant difference between the groups as per Chi- Square test (p>0.05).

As shown in Table 3, 30 (69.4%) and 30 (61.2%) patients with BRVO had Hypertension and Diabetes Mellitus respectively while 22 (44.9%) and 8 (16.3%) patients had Dyslipidemia and Primary Open Angle Glaucoma respectively. 16 (32.6%) and 10 (20.4%) patients were Smokers and had Hyperhomocysteinemia. 9 (81.8%) and 5 (45.5%) patients with CRVO had Hypertension and Diabetes Mellitus respectively while 5 (45.5%) and 6 (54.5%) patients had Dyslipidemia and Primary Open Angle Glaucoma respectively. 2 (18.2%) patients each were smokers and had Hyperhomocysteinemia.

As shown in Table 4, 16 (100%) patients with BRVO and 2 (100%) patients with CRVO had smoking history of >10 years. The association of smoking with retinal venous occlusive disease was found to be statistically not significant as per Chi-Square test (p>0.05).

Table 4. Association of smoking/mishri with retinal venous occlusive diseases

Duration	BRVO (n=49)		CRVO (n=11)		p Value
	N	%	N	%	
≤10 years	0	-	0	-	p>0.05
>10 years	16	100%	2	100%	
Total	16	100%	2	100%	

Table 5. Association of single and multiple risk factors with retinal venous occlusive diseases

Parameters	BRVO (n=49)		CRVO (n=11)		p Value
	N	%	N	%	
Single Risk Factor	12	24.5%	6	54.5%	p<0.05
Multiple Risk Factors	37	75.5%	5	45.5%	

As shown in Table 5, 12 (24.5%) patients with BRVO had single risk factor while 37 (75.5%) patients with BRVO had multiple risk factors. It was observed that in patients with CRVO, 4 (36.4%) and 7 (63.6%) patients had single risk factor and multiple risk factors respectively. There is significant association of single and multiple risk factors with retinal venous occlusive diseases as per Chi-Square test ($p<0.05$).

6. DISCUSSION

The present hospital based Cohort study was undertaken to study specific risk factors for Retinal Venous Occlusive Diseases and establish causal relationship. All the patients satisfying the inclusion criteria, presenting with RVO's to Ophthalmology OPD were enrolled in the study. The sample size was sixty patients. BRVO was found in 52 eyes of 49 patients and CRVO was found in 14 eyes of 11 patients. In the present study, majority of the patients (36.7%) were in the age group of 61-70 years .There was a linear increase in the number of patients with age upto the age of 70 years. The age distribution between groups was statistically not significant as per Student t-test ($p>0.05$).

Di Crecchio L et al [8] in 2014, noted that atherosclerosis (age, hypertension) and not tHcy may be the main culprit for RVO. Among the patients with diabetes for ≤5 years, 1 patient had uncontrolled diabetes. Among the patients with diabetes for >5 years, 7 and 8 patients had controlled and uncontrolled diabetes respectively. The association of duration of diabetes with BRVO was found to be statistically not significant as per Chi- Square test ($p>0.05$).

Al Wadani F et al [9] in 2014, found risk of RVO was significantly higher in persons with hyperhomocysteinemia [difference of mean 31.62 µmol/L (95% Confidence Interval or CI 16.60-47.86), $P = 2.1 \times 10\text{-}13$]. Among cases with RVO, 12 persons had hypertension and 8 persons were having normal systolic and diastolic pressures. In control group also, 12 persons had hypertension and 8 persons showed normal blood pressure. The authors did not find any significant association of hypertension with the severity of hyperhomocysteinemia among cases with RVO [odds ratio (OR) = 2.33 (95% CI 0.37–14.6)].

7. CONCLUSION

There is a statistically significant difference between Known cases and Newly Diagnosed cases of RVOs, showing that there is a higher risk of developing RVOs in patients who are known cases of above mentioned risk factors. Serum Homocysteine is a significant risk factor below 40 years of age and level of Sr. Homocysteine are higher in the age group of patients below 40years. Hypertension is a significant risk factor. Age above 60 years, is a significant risk factor. Known case of Open Angle Glaucoma more than 5 years duration is a significant risk factor for development of CRVO. The intraocular pressure values are significantly higher in CRVO group than in BRVO group. Presence of Multiple risk factors carries a significantly higher risk of developing RVOs.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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