



Study of Risk Factors in Patients with Retinal Venous Occlusions

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Introduction

Venous obstructive disease of the retina is a common retinal vascular disorder, second only to diabetic retinopathy in incidence^[1] causing significant visual morbidity affecting quality of life of patient. Incidence of CRVO is 0.8 per 1000 persons and 4.4 per 1000 persons for BRVO in general population^[2].

The dramatic picture of obstructions of retinal veins was initially described as retinal apoplexy by Liebrich in 1854^[3]. Leber^[4] (1877) reported the first case of BRVO and called it as hemorrhagic retinitis. It was first established as a clinical entity due to thrombosis by Julius Von Michel. Koyanagi first reported the association between BRVO and AV-Crossings.

RVO most commonly affects the venous blood supply of entire retina [CRVO] or a quadrant drained by one of the branches [BRVO] less commonly superior or inferior half of retina alone is affected [HRVO]

Central retinal vein obstruction [CRVO] and branch retinal vein obstruction [BRVO] differ with respect to pathophysiology, underlying systemic associations, average age of onset, clinical course and therapy^[5]. CRVO most commonly occurs in the elderly usually above 50 years^[6,7]. Many systemic and local factors that

contribute to the thrombus formation can predispose to the development of central retinal vein occlusion, including hypertension, diabetes mellitus, hyperviscosity, hyperlipidemia, POAG, and hyperopia^[8,9].

Branch retinal vein occlusions occur three times more common than central retinal vein occlusion. Men and women affected equally, usual age of onset is 60-70 years^[10]. BRVO almost always occur at an arterio-venous crossing, where the artery and vein share a common adventitial sheath^[5,11]. Most BRVO's occur superotemporally, probably due to the highest concentration of arteriovenous crossings lied there^[12]. Most common risk factors associated with BRVO are systemic hypertension, diabetes, hyperlipidemia, glaucoma, smoking and age related atherosclerosis⁷. Antiphospholipid antibodies, elevated plasma homocysteine levels and low serum folate levels have been associated with increased risk of vein occlusion^[13,14,15].

Objectives

- 1) To study the profile of patients presenting with Retinal Vein Occlusions (Both CRVO and BRVO) who attend outpatient department of ophthalmology.

- 2) To study the association of various risk factors with retinal venous occlusions

Material and Methods

A hospital based cross sectional study was taken up by the department of Ophthalmology, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar. A total of 64 patients diagnosed with RVO during the study period (January 2017 to June 2018) were included in the study after satisfying the inclusion criteria.

Inclusion Criteria

All diagnosed cases of retinal vein occlusion with clear media for evaluation

- 1) A CRVO is defined as an eye that has retinal vein haemorrhage or evidence of retinal vein occlusion and dilated venous system in all 4 quadrants. In this study, cases of hemiretinal vein occlusion included in CRVO group.
- 2) A BRVO is defined as an eye that has retinal haemorrhage or other evidence of retinal vein occlusion and a dilated venous system in 1 quadrant or less of retina.

Patients who are willing to give informed consent.

Exclusion Criteria

- 1) Macular Edema other than vein occlusion,
- 2) Lenticular Opacity
- 3) Vitreous Hemorrhage
- 4) Patients not willing to give informed consent.

Procedure

A complete ophthalmic examination of all patients was done including visual acuity, anterior segment evaluation by slitlamp biomicroscopy, post dilated examination of fundus using indirect ophthalmoscopy and fundus photographs are taken for record of the patient and further follow up. Fundus fluorescein angiography and OCT were done as and when required.

The following Lab investigations were done.

- CBP
- FBS
- PLBS

- Lipid Profile
- Serum Homocysteine levels(if necessary)
- Carotid Doppler
- 2D Echo
- Any other investigations whenever required

Results

In this study 64 patients are diagnosed with retinal venous occlusions (both BRVO and CRVO) and they are evaluated for the risk factors which led to their disease.

Each patient is studied in respect to their age, gender and investigated for presence of hypertension, diabetes, hyperlipidemia and other systemic and ocular risk factors through various investigations.

Table 1 showing the distribution of patients according to diagnosis:

DIAGNOSIS	No. of patients	Percentage
CRVO	20	31.3%
BRVO	44	68.7%
Total	64	100%

Figure 1 showing the distribution of patients according to diagnosis:

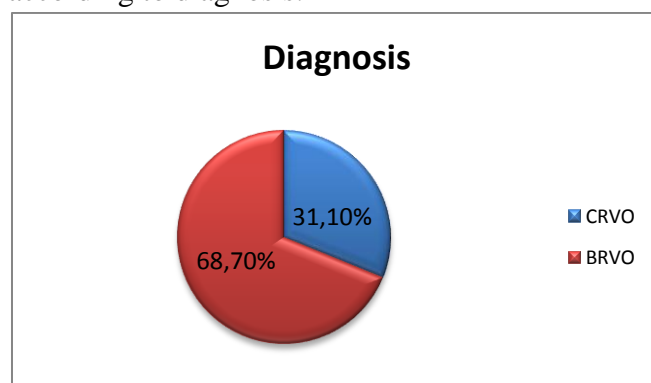
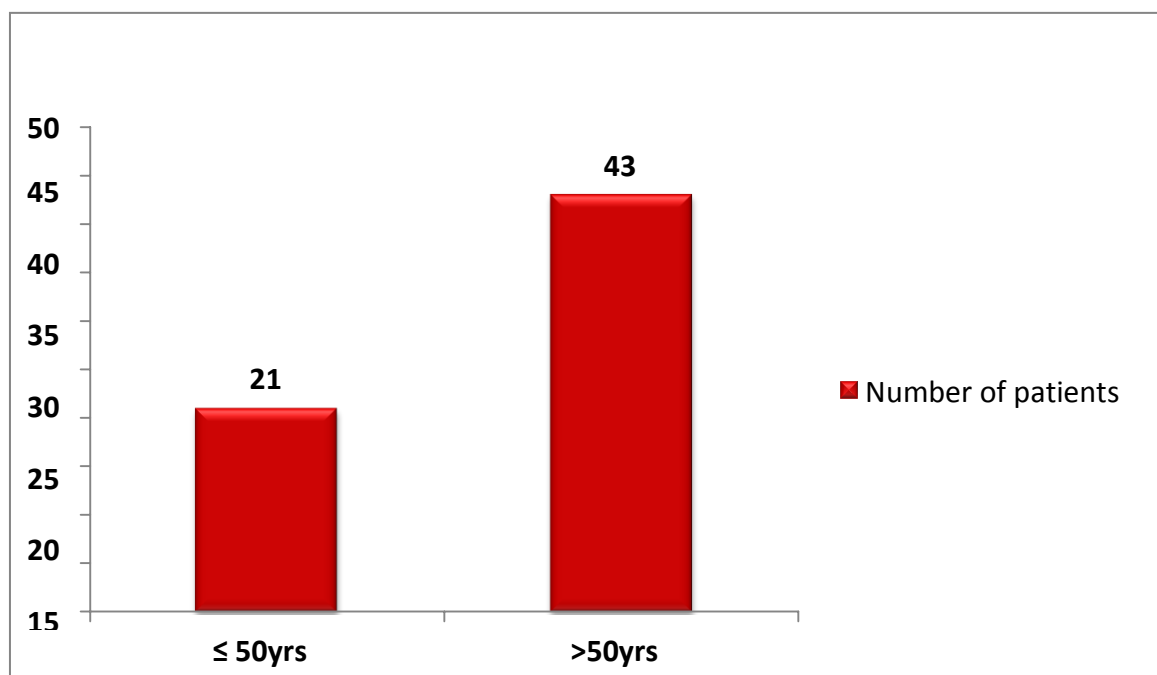


Table 2 showing Age wise distribution of study population

The study population consists of 64 patients with retinal venous occlusions. Patients observed with RVO below age group 50 are 21(32.8%) and above 50yrs are 43 (67.2%). Mean age of study population is 56.11 ± 13.36 . Hence the majority of patients are above 50yrs.

Age in groups	Number of patients	Percentage
≤ 50 yrs	21	32.8%
>50 yrs	43	67.2%
Total	64	100%

Figure 2 showing Age wise distribution of study population**Table 4** Distribution of study population according to their gender

The study population consists of 38 (59.4%) males and 26 (40.6%) females. Hence from this study venous occlusions are more common in males compared to females

GENDER	Number of patients	Percentage
Males	38	59.4%
Females	26	40.6%
Total	64	100%

Figure 3: Distribution of study population according to their gender

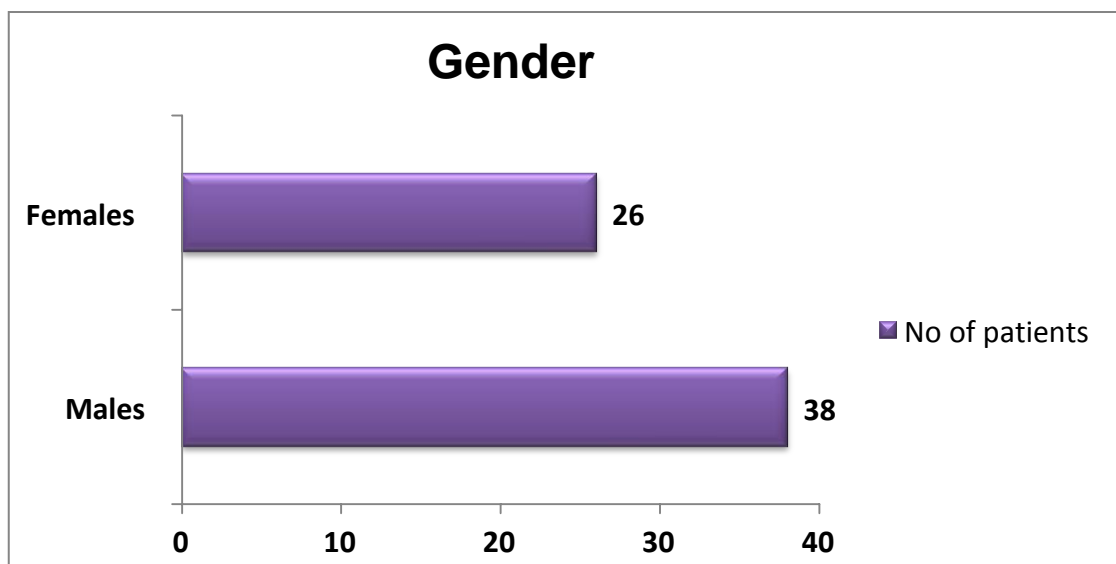
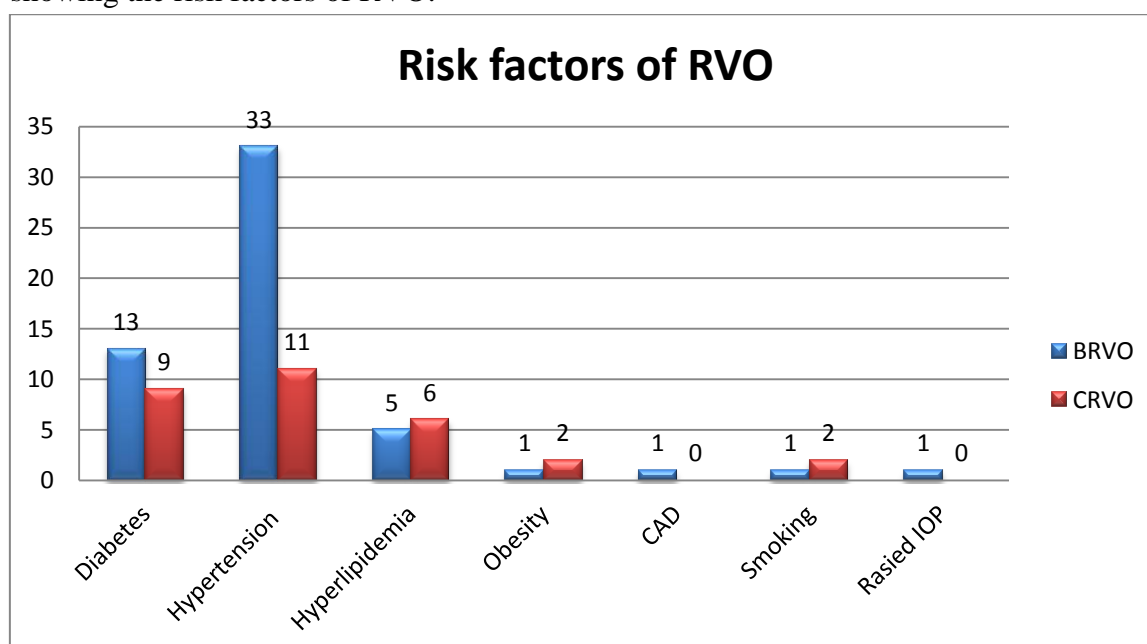


Table 4 showing the risk factors of RVO

Parameter	BRVO	CRVO	P value
Age in years			
Less than or equal to 50	21	0	0.004
>50 years	23	20	
Gender			
Male	25	13	0.537
Female	19	7	
Other risk factors			
Diabetes	13	9	0.228
Hypertension	33	11	0.11
Hyperlipidemia	5	6	0.12
Obesity	1	2	0.175
CAD	1	0	0.26
Smoking	1	2	0.175
Rasied IOP	1	0	0.26

Figure 3 showing the risk factors of RVO:



Discussion

The discussion of association between various ocular and systemic risk factors confounding to retinal venous occlusive disease is not new. A case-control study of risk factors for retinal vein occlusions using 87 patients with vein occlusions, chosen randomly from photographic files between 1985 and 1990, and a control group of 85 subjects 38 years of age (the youngest individual in the vein occlusion group) or older, who were randomly selected from the records of two general ophthalmologists in the department. Certain risk factors for retinal vein occlusion were highly significant when subjects with retinal vein occlusion were compared with the control group. These risk factors included systemic hypertension (odds ratio [OR], 3.86; 95% confidence interval [CI], 2.08 to 7.16), open-angle glaucoma (OR, 2.89; 95% CI, 1.38 to 6.05), and male sex (OR, 2.61; 95% CI, 1.43 to 4.79). Race, presence of diabetes mellitus, history of coronary artery disease or stroke, and family history of diabetes, glaucoma, coronary artery disease, or stroke were not significant risk factors in the population studied. Logistic analysis of the risk factors showed no interactions. Risk factors for branch retinal vein occlusion and central retinal vein occlusion were identical.

Age and Gender Distribution

In this study, 43 (67%) patients of RVO are >50 years and 21 (33%) patients are <50 years. Of total 20 patients of CRVO all patients are more than 50 years and none are less than 50 years. Of total 44 patients of BRVO 23(52.3%) are more than 50 years and 21(47.7%) are less than 50 years with a mean age of 56.11+/-13.36 years. According to present study of total 44 patients of BRVO that were studied 25 (56.8%) are males and 19(43.2%) are females and of total 20 patients of CRVO 13(65%) are Males and 7(35%) are Females.

The findings of the present study can be compared with the following studies:

Hayreh et al. have observed that the most prevalent ages for CRVO development are 65

years and older, and it is more common in men than in women.

Roger et al, gave the age wise incidence of RVO.

Age [in years]	Prevalence
40 -49	1.57/1000
50-59	4.58/1000
60-69	11.11/1000
70-79	12.76/1000
>80	10.32/1000

Risk Factors

Hypertension

In the present study CRVO group 11 (17%) patients had Hypertension. In BRVO group 33(52%) patients had hypertension Previous studies have shown systemic hypertension to be a risk factor for both CRVO and BRVO.

Cugati et al (2006) noted increasing mean arterial blood pressure and atherosclerotic retinal vessels were significant predictors of incident Retinal vein obstruction.^[16] Stem et Al (2013) confirmed in their study that hypertension and vascular diseases are important risk factors for central Retinal vein Occlusion.^[17]

Diabetes Mellitus

In the present study 9(14%) patients of CRVO group and 13 (20%) patients of BRVO group had diabetes mellitus

Previous Studies have found that the frequency of diabetes was significantly increased in patients with RVO compared to normal subjects. DM is known as a risk factor for BRVO^[18]. A meta-analysis showed that, in BRVO, the odds ratio for DM is 1.1 (95% CI: 0.8–1.5)^[7]. DM was shown to be not significantly associated with BRVO as reported by other authors^[10].

Hyperlipidemia

In this study 6(9%) patients of CRVO and 5(7%) patients of BRVO had Hyperlipidemia.

Most of the studies suggested a significant association between the CRVO and hyperlipidemia (HLD)^[9]. For any clinical presentation of RVO, hyperlipidemia was twice more common than the controls, equivalent to a pooled odds ratio of 2.5. The significant risk estimates were observed for the patients with CRVO^[9]. HLD is an established risk factor for the

atherosclerosis, and early HLD is associated with an increased arterial compliance, and later due course of the disease the arteries would become more rigid^[11]. Thus, the duration and severity of HLD may affect the extent of the atherosclerotic events in the central retinal artery, which could, in turn, affect the risk of developing the CRVO^[9].

Intraocular Pressure

In the present study one patient of BRVO had high IOP of 28mm hg on ATN. This patient appears to have CDR of 0.6 with thinning of NRR (inferior and superior) Gonioscopy showed open angles. Visual fields could not be recorded because of presence of significant media opacity (grade III nuclear cataract). Hence the patient is diagnosed as glaucoma (POAG) which accounts to the development of retinal venous occlusion in this case

It is postulated that the central retinal Vein may get compromised at the lamina cribrosa in patients with raised intraocular pressure CRVO was associated with increased intraocular pressure (IOP), primary open-angle glaucoma and ocular hypertension^[19]. There is a strong correlation between glaucoma and CRVO because of the association of optic disk cupping with distortion of the retinal vessels at the disk, predisposing the vein to occlusion^[19].

CAD

In present study out of 64 patients of RVOs only one patient had CAD and diagnosed as BRVO and none of patients with CRVO had an attack of CAD. The evidence from observational studies on the impact of RVO on vascular mortality (ie, death from vascular causes) is conflicting.

Data from a pooled cohort of the Beaver Dam Eye Study and the Blue Mountain Eye Study showed no association between RVO and cardiovascular-related (HR=1.2; 95% CI, 0.8–1.8) or cerebrovascular-related mortality (HR=0.9; 95% CI, 0.4–2.1) after adjustment for age, gender, body mass index, hypertension, diabetes, and other factors among patients of all ages.²⁹ However, in RVO patients younger than 70 years, the risk of cardiovascular mortality was twice as

high (HR=2.5; 95% CI, 1.2–5.2).²⁹ A United Kingdom hospital-based study found that, compared with the general population, RVO patients had a higher rate of mortality related to myocardial infarction.³⁰ The present study is consistent with previous studies.^[20]

CVA

In present study out of 64 patients of RVOs none of patients with CRVO and BRVO had an attack of CVA.

Cugati et al found that men with RVO are associated with a non-significant 2.3-fold higher risk of cerebrovascular mortality for all ages in a pooled cohort of two-population based studies.^[16]

Obesity

In present study out of 64 patients of RVOs only 5 patients are obese with increased BMI and 3 cases are diagnosed as BRVO and 2 with CRVO are obese.

The Eye Disease Case Control Study (EDCC) Group suggested that the increased body mass index shall be considered as a risk factor for RVO^[13]. The Group had found that the participants who rated themselves as presently above average in terms of physical activity had about 60% lower odds of CRVO than did those who rated themselves as below average (screening analysis)^[13].

Smoking

In present study out of 64 patients of RVOs only 3 patients are smokers and of these one case has CRVO and 2 patients are diagnosed as BRVO.

The association of cigarette smoking with retinal arteriolar emboli has also been reported in the Beaver Dam study^[4].

Tobacco use in any form causes arteriosclerotic changes in the blood vessel wall and may cause retinal vein occlusion due to compression. Lee et al in their study on 354 patients of BRVO found that 28 % of them were smokers.^[21] The present study does not show significant correlation between smoking and RVO.

In one study, the prevalence was found to vary by race/ethnicity and increased with age but did not differ according to gender^[4]. This provides

summary data on the prevalence of RVO and suggests that approximately 16 million people may have this condition. Research on preventive and treatment strategies for this sight threatening eye disease is needed^[4].

Conclusion

The present study concludes that increasing age and HTN are major risk factors for development of retinal vein occlusion. Diabetes and hyperlipidemia showed lesser risk next to hypertension. CVA, CAD, obesity, smoking, IOP are not statistically significant risk factors.

Conflicts of Interest: None

Source of funding: None

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