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Original Research Article

A study of evaluation of various risk factors of retinal vein occlusion

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ABSTRACT

Introduction: Retinal vein occlusions have a characteristic, although somewhat variable, appearance with intraretinal hemorrhage, cotton – wool spots, tortuous and dilated retinal veins, retinal edema and occasionally optic disc swelling. There are three distinct types of RVO: branch retinal vein occlusion (BRVO), central retinal vein occlusion (CRVO), and an anatomical variant of CRVO, namely, hemiretinal vein occlusion (HRVO). Intraocular steroid treatments and macular or scatter panretinal photocoagulation are also employed to manage vision loss from, and complications of, RVO.

Aims and Objectives: To study the various systemic & ocular risk factors of RVO and the prevalence of RVO (BRVO & CRVO).

Materials and Methods: This hospital based study was conducted on all RVO patients attending the OPD of Department of Ophthalmology, RNT Medical College, Udaipur.

Results: The prevalence of RVO (0.77%), BRVO (0.52%) and CRVO (0.11%) which increased with increasing age. More common in 56-65 years males. The major risk factor associated with RVO was systemic hypertension. There is a significant link between diabetic mellitus, serum homocysteine levels, and hyperlipidemia. RVO is linked to smoking, coronary artery disease, use of OCP, and vascular occlusive disease. Macular edema was resolved and vision was significantly improved after intravitreal Anti-VEGF injections.

Conclusion: To sum up, it is important to focus on modifiable risk factors like smoking, hyperlipidemia, systemic diseases like: hypertension and diabetes which are found to be associated with increased risk of developing RVO and also look into preventable aspect of the disease.

1. Introduction

Retinal venous obstruction (RVO) was first established as a clinical entity due to thrombosis by Julius Von Michel" (1878).[1] There are three distinct types of RVO: branch retinal vein occlusion (BRVO), central retinal vein occlusion (CRVO), and an anatomical variant of CRVO, namely, hemiretinal vein occlusion (HRVO). Retinal vein occlusions have a characteristic, although somewhat variable, appearance with intraretinal hemorrhage, cotton – wool spots, tortuous and dilated retinal veins, retinal edema and occasionally optic disc swelling.

The diagnosis is based on the fundoscopic finding of retinal vein dilatation in association with retinal hemorrhages and cotton-wool spots. The pathology can involve the entire venous system or can be limited to a branch of the central retinal vein. The findings are present segmentally in BRVO, in either the superior or inferior two quadrants in HRVO and in all quadrants of the fundus in CRVO.[2] Retinal venous obstructions are multifactorial in origin and no single factor on its own causes the occlusion. A whole host of local and systemic factors acting in different combinations and to different extents may

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produce the vascular occlusion.[2,3] At present, the efforts to improve visual acuity in retinal venous obstruction have been disappointing and a better understanding of various predisposing factors and pathophysiology assumes a lot of importance in the prevention and in the development of newer treatment modalities. If it is not treated it can lead to various ocular complications and hence prevention and treatment is important.

Improvement or spontaneous resolution can occur in patients with RVO. Improvement is usually associated with the development of adequate collateral blood flow. In BRVO, capillaries extending across the median raphe dilate, helping to compensate for the compromised venous drainage. In CRVO, small vessels that normally connect the retinal circulation to the choroidal circulation near the optic nerve head expand, resulting in the undulating appearance of optociliary shunt vessels. These mechanisms redirect venous drainage to the choroid, vortex veins, and superior and inferior ophthalmic veins in the orbit, bypassing the occluded central retinal vein. Chronic, untreated venous occlusive disease commonly leads to development of retinal microvascular changes characterized by microaneurysms, telangiectasias and macular edema.[4,5]

Anti-vascular endothelial growth factor (VEGF) drugs are mainstay of RVO treatment. Best visual acuity outcomes are achieved by administering anti-VEGF treatment immediately upon diagnosis of RVO-related macular edema. Anti-VEGF treatment also suppresses neovascular complications of RVO. Intraocular steroid treatments and macular or scatter panretinal photocoagulation are also employed to manage vision loss from, and complications of, RVO.[4,5]

2. Aims and Objectives

To study the various systemic & ocular risk factors of RVO and the prevalence of RVO (BRVO & CRVO) of patients attending the OPD of Ophthalmology department at R.N.T. Medical College, Udaipur.

3. Materials and Methods

This observational, descriptive cross-sectional hospital based study was conducted in Department of Ophthalmology, RNT Medical College, Udaipur during the period of one and a half year from June 2020 to December 2021 on All RVO patients attending the OPD of Ophthalmology department.

3.1. Sampling technique

Non probability, purposive sampling was done.

3.2. Sample size

All patients reporting to OPD, Ophthalmology department within study duration, eligible according to inclusion criteria & gave written or verbal informed consent were included in the study after taking proper ethical clearance from Institutional Ethics Committee.

3.3. Inclusion criteria

All diagnosed cases of BRVO & CRVO satisfying the study criteria, presenting to or referred to Ophthalmology department at RNT Medial College and Hospital Udaipur, from June 2020 to December 2021 were included in the study.

3.4. Exclusion criteria

Patients with ocular conditions that would affect visual acuity (dense corneal &lens opacities, amblyopia) were excluded. Patients with poor view of the fundus were excluded from the study.

Thorough medical history and general examination of the patient was carried out to rule out the presence of any systemic disease predisposing to a vein occlusion. A detailed ocular history which included history of previous ocular disease and the treatment was elicited.

Baseline investigations were carried out: such as Complete blood count (CBC), Random & Fasting Blood Sugar levels, HbA1c, Lipid profile, Serum Urea, Creatinine, Electrolytes, ESR, Blood VDRL for Syphilis etc.

Ocular examination at initial presentation included the following: Best corrected visual acuity; IOP: Goldman applanation/ Non contact tonometer/Schiotz tonometer; Pupillary reaction; Slitlamp biomicroscopy; Direct/Indirect ophthalmoscopy; OCT Pre Injection (Anti VEGF/Triamcinolone) & post injection; Visual fields.

Patients were followed up every month for a minimum period of 6 months.

3.5. Statistical analysis

A pre tested structured questionnaire was filled and data was entered in the Excel sheet. Quantitative & qualitative variables were analyzed on SPSS version 16.0. Qualitative variables were expressed as proportions while mean & standard deviation were used for quantitative variables. Relevant statistical tests were used for calculation of p values. These include both parametric & non parametric tests like paired t test, ANOVA, chi square test.

4. Results

Around 62.5% had ST BRVO, 15% Non-ischemic CRVO, 12.5% IT BRVO, 5% Macular BRVO and ischemic CRVO respectively.(Figure 1)

67.5% are hypertensives among the study participants. 45% are having hyperlipidemia among the study participants. 45% are diabetes among the study participants. 7.5% are having CAD among the study participants. 20% of the study participants are smokers. 5% of the study participants have vascular occlusive events. 62.5% of the study participants had raised serum homocysteine levels. 53% of the study participants had OCP. (Table 1)

CMT at presentation is about 565.05±206.11, at 1 month 431.90±176.05 and at 6 months 261.33±103.00.(Figure 3)

97.5% had macular edema 2 5% had NVI/NVG 7 5% had vitreous hemorrhage (Table 2)

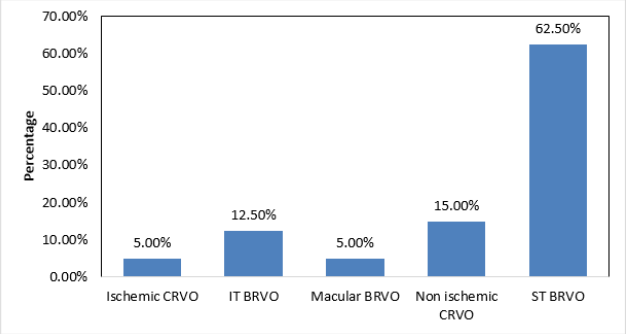

Fig. 1: Distribution of type of RVO among the study participants (N=40)

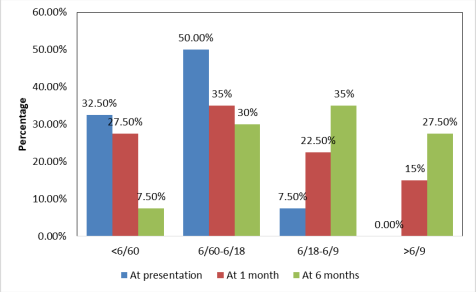

Fig. 2: Distribution of BCVA among the study participants (N=40)

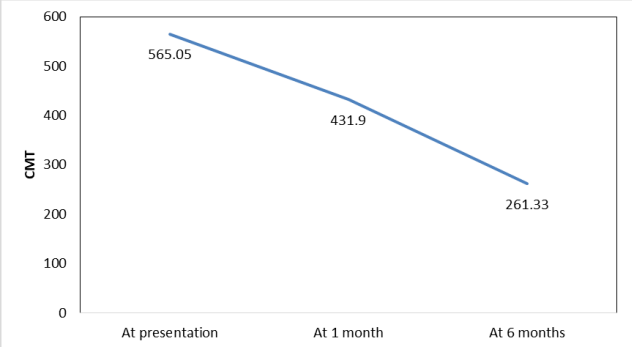

Fig. 3: Distribution of CMT among the study participants (N=40)

Table 1: Distribution of hypertension among the study participants (N=40)

	Frequency	Percentage
Hypertension	27	67.5
Hyperlipidemia	18	45.0
Diabetes	18	45.0
CAD	3	7.5
Smoking	8	20
Vascular occlusive events	2	5
Serum homocysteine (Raised)	25	62.5
OCP	9	53

Table 2: Distribution of macular edema among the study participants (N=40)

	Frequency	Percentage
Macular edema	39	97.5
NVI/NVG	1	2.5
Vitreous hemorrhage	3	7.5%

5. Discussion

5.1. Prevalence

As per the data obtained from hospital records, mean foot drop of patients attending ophthalmology clinic, is 32310 individuals. Out of these individuals meeting our inclusion criteria of the median age are 17,321. For age specific prevalence calculation, SPSS V 16.0 was used along with procurement in statcalc software version 3.04 with these variables for age specificity, the prevalence obtained for midyear population attending ophthalmology clinic in MBGH is as stated below:

RVO- 0.77%, BRVO- 0.52%, CRVO- 0.11% which is concordant with the study done by Song et al in which the global prevalence of RVO, BRVO, and CRVO in adults aged 30-89 years was 0.77 percent, 0.64 percent, and 0.13 percent.

5.2. Type of RVO

In our study, amongst 40 study participants with RVO, 32 patients had BRVO and 8 had CRVO giving a ratio of 4:1. In a population-based study in patients with retinal vein occlusion conducted by David R, Zangwill L et al, the frequency of BRVO to CRVO was 3.2:1 which is in concordance with our study.[6]

Amongst all study participants, 62.5% had Supero-temporal BRVO, 15% had Non-ischemic CRVO, 12.5% had Infero-temporal BRVO, 5% had Macular BRVO and ischemic CRVO respectively which was different than the previous study conducted by Ponto et al[7] which showed BRVO in 16.8%, HRVO in 8.2% and CRVO in 50%.

Hypertension contributed as one of the major systemic risk factors for RVO contributing to 67.5% which is in

concordant with studies observed by Mahoney et al, and Lim et al.[8,9] This was also similar to previous study by Ponto et al.[7] which showed hypertension in 68.5% patients. Another study by Stem et al showed hypertension in 88.9% patients having CRVO.[7,10] Sperduto et al Wong et al study stated that systemic hypertension is a risk factor linked to RVO.[11,12] Song et al in a meta analysis stated hypertension as the biggest risk factor associated with RVO.[13]

Previous studies done by Lim et al linked retinal vein occlusion to hyperlipidemia.[9] Paul Mahoney et al study stated hyperlipidemia as the most common risk factor in adults for RVO after hypertension.[8] A study conducted by Liu et al found hyperlipidemia in 42% cases with RVO. The results are in concordance with our present study where hyperlipidemia is seen in 45% of patients with RVO.[14]

In the present study, 45% participants had diabetes mellitus which in in contrary to the previous study done by Ponto et al which showed diabetes in 6.5% patients.[7] This could be attributed to the smaller sample size, regional epidemiology of the present study. Another study by Stem et al showed diabetes in 42.9% patients having CRVO and Hayreh et al, Wang et al also showed preponderance of diabetes mellitus and established a link between diabetes mellitus and risk of RVO, especially CRVO.[10,15,16] According to the present study, diabetes mellitus can be attributed as a risk factor for the occurrence of RVO.

In the present study, 7.5% participants had CAD which is in concordance with the previous study done by Ponto et al which showed CAD in 5.4% patients.[7] Chen YY et al and Wong et al found higher prevalence of myocardial infarction and cardiovascular disease amongst patients with BRVO and CRVO which is contrary to our study which can be attributed to the descriptive design of the study and smaller sample size.[12,17]

20% participants had history of smoking. Previous study by Ponto et al showed history of smoking in 10.9% patients, was significantly considered a risk factor for RVO.[7]

5% participants had history of vascular occlusive events in the form of stroke which was lower than the previous study done by Stem et al showed history of Cerebro vascular accident in 34.5% patients, MI in 11.1%, DVT/PE in 4% patients.[10]

In Calguru D et al study, hyperhomocysteinemia was found to be a part of an essential risk factor for arteriosclerosis that caused venous occlusion.[18] In this study, 62.5% participants had raised serum homocysteine levels which were similar to a study done by Lahiri KD, Dutta J et al which showed serum homocysteine levels to be significantly high in patients with RVO.[19] The meta-analysis by Cahill et al also showed that the retinal vascular occlusion is associated with elevated plasma Hcys levels and low serum folate levels.[20]

In our study, 53% participants had taken OC pills in their reproductive period which is in concordance with Kirwan et alstudy in which the prevalence of retinal vein occlusion in female patients less than 35 years taking the OCP was 66.0%.[21]

In our study, at the time of presentation; 32.5% patients had BCVA <6/60, 50% patients had BCVA ranging between 6/60 - 6/18 and 17.5% had 6/18 - 6/9. Mean Central macular thickness at presentation was 565.05 ± 206.11. The poor visual acuity at presentation could be attributed to macular edema which was confirmed with the OCT imaging and the patients were given intravitreal Anti-VEGF injection (Bevacizumab) and repeat injections were given at a minimum interval of 4 weeks if required. In our study, repeat injections (Anti-VEGF) after first dose were required for less than 2 times in about 50% patients and more than 2 times in about 25%. Previous study by Rezar et al showed mean total injections 8 ± 6.3.[22]

At 1 month follow up after intravitreal injection: 27.5% patients had BCVA <6/60, 35% patients had BCVA ranging between 6/60 - 6/18, 22.5% had 6/18 - 6/9 and 15% had ≥6/9 which was improved but not statistically significant. (p value=0.21) while Mean CMT at 1 month post injection was 431.90±176.05 which was significantly improved. (p value <0.001)

At 6 months follow up post injection, patients with BCVA <6/60 were 7.5%, 30% had 6/60 - 6/18, 35% had 6/18 -6/9 and ≥6/9 were 27.5% which was statistically improved. (p value= 0.02)

Mean CMT at 6 months follow up post injection was 261.33±103.00 which was significantly improved (p value <0.001).

Chen et al, in a case series of 59 eyes followed up for at least 1 year found that visual acuity improved by 2 lines or more in 15%, remained stable in 56%, and decrease by 29%.[17]

McIntosh et al based on the analysis of 7 studies (159 eyes) reported the development and resolution of Macular edema over time.[23]

Hence, the visual improvement and resolution of macular edema over time was statistically important and in concordance with the previous studies.

A study by Quinlan et al showed macular edema in 89% patients which is in concordance with our study where macular edema was the most common ocular complication of RVO attributing to 97.5% patients leading to poor vision.[24]

Previous study by Quinlan et al showed vitreous hemorrhage in 18.3% patients. In our study, 7.5% patients had vitreous hemorrhage which were observed during follow up which was in lower proportion to that of previous study which could be due to lower sample size.[24]

In the present study, 2.5% of total RVO cases, 12.5% cases with CRVO and 50% with Ischemic CRVO developed

NVI/NVG.

Hayreh SS, Zimmermann et al study showed the probability of developing NVI to be 49% and NVG to be 29% in ischemic CRVO within 6 months.[15]

6. Limitations

A detailed study with a larger sample is required for analysis of risk factors. In this study, as most of the subjects presented when they had marked diminution of vision, for estimating prevalence multiple hospital based studies should be done to cover the entire region of Udaipur. Further prospective study is required to measure the risk factors among RVO Subjects.

7. Conclusion

It is concluded that it is important to focus on modifiable risk factors like smoking, hyperlipidemia, systemic diseases like: hypertension and diabetes which are found to be associated with increased risk of developing RVO and also look into preventable aspect of the disease.

8. Source of Funding

None.

9. Conflict of Interest

None.

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