DEMOGRAPHIC PROFILE OF PATIENTS WITH RETINAL VEIN OCCLUSION-AN OBSERVATIONAL STUDY

Ophthalmology

Dr Shubhratha S. Hegde MS Ophthalmology, Assistant Professor, Department of Ophthalmology, Mysore Medical College & Research Institute, Irwin Road, Mysore 570001.

Dr Asha Rani J DOMS Ophthalmology, Postgraduate, Department of Ophthalmology, Mysore Medical College & Research Institute, Irwin Road, Mysore 570001.

Dr Sandhya Dharwadkar MS Ophthalmology, Senior Resident, Department of Ophthalmology, Mysore Medical College & Research Institute, Irwin Road, Mysore 570001.

Dr D. N. Prakash* MS Ophthalmology, Associate Professor, Department of Ophthalmology, Mysore Medical College & Research Institute, Irwin Road, Mysore 570001. *Corresponding Author

ABSTRACT

BACKGROUND: Retinal Vein Occlusion(RVO) is multifactorial in causation with many systemic and ocular risk factors. The incidence of RVO has increased with increased life expectancy and increased incidence of risk factors.

AIM: This study was done to determine the demographic characteristics and risk factors in a tertiary care hospital in South India.

METHODS: 100 consecutive newly diagnosed cases of RVO were included in the study. A detailed history, complete ophthalmic examination and systemic evaluation was done.

RESULTS: The majority of the patients were aged more than 60 years(55%) with male preponderance(54%). The study also found that RVO was strongly associated with increasing age. Hypertension, dyslipidemia, diabetes mellitus, smoking and hyperhomocysteinemia were important systemic risk factors. Glaucoma was an important ocular risk factor. BRVO is the most common type of RVO.

CONCLUSION: RVO is associated with many systemic and ocular diseases. Identifying and managing these risk factors help in preventing a second attack in either eye and thereby the visual morbidity.

KEYWORDS

Retinal vein occlusion, Hypertension, Diabetes mellitus, glaucom

INTRODUCTION:

Retinal vein occlusion(RVO) is the second most common cause of visual impairment among retinal vascular diseases after diabetic retinopathy.¹⁻¹⁸ Depending on the site of occlusion, RVO is broadly classified into Central Retinal Vein Occlusion(CRVO), Hemi Retinal Vein Occlusion(HRVO), Branch Retinal vein Occlusion(BRVO) and Tributary Vein Occlusion(TVO). It is a multifactorial disease with many systemic and ocular risk factors.^{1,2} Reports suggest that 16 million people in the world are suffering from RVO.^{1,2,19} There has been an increase in the incidence of Retinal Vein occlusions due to the increasing incidence of the risk factors, sedentary lifestyle and increasing life expectancy.²⁰ Many studies are describing the demographic characteristics and risk factors of RVO in the Western population. The results from these studies cannot be extrapolated to the Indian population. Many studies have been done in India to evaluate different treatment modalities for RVO, however, there are very few studies done to determine its risk factors. This study has been done to determine the demographic profile of patients with RVO and to identify common systemic and ocular risk factors of RVO among Indian patients. By identifying and managing the risk factors we can prevent the recurrence of RVO in either eye and diminish the severity of the disease.

MATERIALS AND METHODS:

This cross-sectional observational study was conducted in the Ophthalmology Department of Mysore Medical College & Research Institute, Mysore from April 2019 to December 2019 after obtaining approval from the Institutional Ethics Committee. 100 consecutive newly diagnosed cases of retinal vein occlusion were included in the study after obtaining written consent. In patients with bilateral RVO, the type of RVO in each eye was considered an independent event. RVO was classified as Central Retinal Vein Occlusion(CRVO), Hemi Retinal Vein Occlusion(HRVO), Branch Retinal Vein Occlusion(BRVO) and Tributary Vein Occlusion(TVO).²¹ A detailed data on patient demographics, complete medical history including history of systemic diseases like Diabetes, Hypertension, Dyslipidemia, Bleeding disorders, collagen vascular disorders and history of ocular risk factors like glaucoma were noted. History of smoking, when present, was noted. Complete ophthalmic evaluation including visual acuity, slit-lamp examination, IOP, axial length measurement, and fundus examination was done. Optical Coherence

Tomography was done in patients with suspected macular involvement due to RVO. Laboratory tests including complete haemogram, blood sugar level, lipid profile were done. If relevant other tests like chest X-ray, Mantoux test, Serum Homocysteine, Toxoplasma antibody assay was advised. Systemic risk factors were treated in consultation with the concerned specialties. Macular edema, when present, was treated with IVTA, Intravitreal anti-VEGF, and/or Grid laser.

Statistical Analysis:

All the statistical methods were carried out through the SPSS Version 20 for Windows. Descriptive data were expressed as Mean, Standard deviation, Frequency, Percentage. For inferential statistics, the Chi-square test and One-way sample 't' test were used.

RESULTS:

Of the 100 patients enrolled, 55(55%) were aged >60 years. (table 1) male preponderance was noted with male to female ratio being 54:46. (table 2). Bilateral involvement was not found in any patient. BRVO was the more common type of RVO. (fig.1) Hypertension, dyslipidemia, diabetes mellitus, and smoking were found to be important systemic risk factors. Hyperhomocysteinemia was seen in 8(8%) patients. Smoking was noted in 45(45%) patients. More than one risk factor was seen in 84(84%) patients. The metabolic syndrome which is defined as the presence of coexisting hypertension, Diabetes, and dyslipidemia, was noted in 16(16%) of patients. Glaucoma was the important ocular risk factor for with statistically significant association with RVO ($p=0.05$). It was noted in 12 patients. Shorter axial length was seen 7 patients and retinal vasculitis in 8 patients but their association with RVO was statistically insignificant. ($p=0.1$) Most of the patients came with the symptom of diminished vision(81%). The diagnosis was incidental in 19(19%) patients. In CRVO, 11(61 %) patients had Non-ischemic type at the time of presentation. (fig.2) In BRVO, the superotemporal branch was the most commonly involved (64.3%). Macular edema was noted in 66(66%) of the patients with RVO in our study.

Table 1: Age Distribution Of RVO Patients.

AGE in Years	CRVO	HRVO	BRVO	TVO
31-40	2	-	02	-
41-50	6	-	08	04
51-60	1	-	20	-

61-70	3	04	24	02
>70	6	02	14	-

Table 2: Gender Distribution Of RVO Patients

RVO TYPE	MALE(no.)	FEMALE(no.)	TOTAL(no.)
CRVO	10	08	18
HRVO	04	02	06
BRVO	36	34	70
TVO	04	02	06
TOTAL	54	46	100

Table 3: Risk Factors Of RVO

RISK FACTORS	CRVO	HRVO	BRVO	TVO	Total	p-value
HYPERTENSION	04	02	42	02	50	0.01
IHD	03	01	12	-	16	0.05
DM	04	02	22	04	32	0.05
DYSGLYPIDEMIA	06	04	22	02	34	0.01
SMOKING	08	04	33	-	45	0.05
GLAUCOMA	04	02	06	-	12	0.05
SHORT AXIAL LENGTH	04	01	02	-	07	0.1
RETINAL VASCULITIS	02	-	06	-	08	0.1
HYPERHOMOCYS TEINEMIA	02	-	06	-	08	0.05

Table 4: Distribution Of Macular Edema

RVO type	No. of cases with macular edema(%)
CRVO	10 (55)
HRVO	06 (100)
BRVO	46 (65)
TVO	04 (67)

Figure 1: Distribution Of RVO Types **Figure 2: Types Of CRVO** **Figure 3: Distribution Of Types Of BRVO****DISCUSSION:**

RVO is considered the disease of the elderly with advancing age as an important risk factor. According to Kolar P¹, Hayreh SS²¹, O'Mahoney PR¹¹, Beijing Eye study²⁶, in about 50% of the cases of RVO the age of onset is over 65 years.²¹ In our study, most of the patients in every category of RVO except TVO were aged > 60 years. BRVO is considered the disease of middle age and the elderly.^{25,27} Similarly a significant number of patients with BRVO were also in the age group of 41-60 years. TVO was found in the younger age group and unlike other types of RVO, the pathology involved is not arteriosclerosis but focal phlebitis.⁴ In keeping with findings from similar previous studies, it

was found that the prevalence of RVO increased with age.^{1,4,6,10,12,16,19,26}

This may be because of increased arteriosclerosis and increased incidence of ocular and systemic risk factors with age (eg: glaucoma, hypertension)¹⁹ in our study, males were more commonly affected than females in all types. similar male preponderance was noted by Kolar P^{1,10}, Rehak J²⁹ Thapa et al.³⁰ Hayreh SS found that all categories of RVO, except BRVO, were more common in men than in women.^{21,23,25,31} Ip M et al⁶, Lauri M et al¹³ and Mitchell P et al³² found that there is no difference in the prevalence of RVO between males and females. RVO was unilateral in all the cases included in our study. Morris R, in his major review, reported that about 10% of CRVO and 5-6% of BRVO are bilateral at diagnosis.⁷ Right eye was more commonly involved in our study. In the Beaver Dam study, the prevalence of RVO was similar in both eyes.²⁷ Hayreh SS also found that except BRVO which was more common in the right eye, all other types of RVO had no difference in involvement between two eyes.²¹ BRVO was the most common type of RVO. This is in accord with the other similar studies.^{1,2,6,10,14,19,21,26,29,30} In our study, Hypertension, Ischemic heart disease, Diabetes Mellitus, smoking and Hyperhomocysteinemia were the important risk factors for the development of RVO. A similar result was recorded by Thapa et al³⁰ Hayreh SS^{23,25}, Kolar P^{1,10} and Yau et al¹⁵. In the Beaver Dam study, RVO was found to have a strong association with hypertension and smoking, but not with cardiovascular disease and altered serum lipid levels.²⁷ Metabolic syndrome has been noted as a strong risk factor for the development of RVO in our study. In the meta-analysis done by Kolar P, a strong association has been found between metabolic syndrome and RVO.¹ Among the Indian studies, a similar study done by Archana K found that hypertension was an only significant risk factor for RVO.²⁰ Hyperhomocysteinemia was found as an independent risk factor for RVO by Kolar P¹, Beijing eye study group²⁶, Janssen et al²⁸ Rehak J²⁹, Glueck et al³³, Cahill et al³⁴, Trello M et al³⁵. A statistically significant association was found between Hyperhomocysteinemia and RVO in our study. But a case-control study done by Di Capua et al³⁶ and Mc Gimpsey et al³⁷ found no correlation between RVO and homocysteine levels. Moreover, 5-7% of normal people do have elevated plasma homocysteine and it has not been proven that lower plasma homocysteine levels can reduce the risk of RVO.^{4,38} Among ocular risk factors, our study demonstrated a statistically significant association between RVO and glaucoma. Glaucoma was found to be an important risk factor in all types of RVO except TVO. Hayreh SS et al²¹ and Roger S et al¹⁹ found that glaucoma was associated with CRVO and HCRVO, but had no role in the pathogenesis of BRVO. Kolar P¹ and Yin X39 in their meta-analysis have found that glaucoma has a role in the development of RVO. Keren S et al¹⁷, Sperduto RD et al⁴⁰, Thapa R et al³⁰ and Mitchell P et al³² also found an association between RVO and glaucoma. No correlation was found between shorter axial length and RVO. Similar results were noted in Beaver Dam study.²⁷ Beijing eye study²⁶, Kumar SV³ and Thapa et al³⁰ found the shorter axial length to be associated with BRVO. No association was found between vasculitis and RVO. This result is in discordance with the findings of Kolar P¹ Beaver Dam study²⁷ and Hayreh SS⁴¹. Diminution of vision was the most common presenting symptom in our study. Macular edema is the most common cause of visual impairment in RVO.⁴ The diagnosis was incidental in 19% of the patients. This emphasizes the importance of regular eye examination in patients with risk factors for RVO. In BRVO, the superotemporal branch was most commonly involved. This is proposed to be due to an increased number of AV crossings in that quadrant and increased symptoms as fovea is involved.^{2,5,21,25,27,30} Because of their asymptomatic nature, the nasal BRVO is less diagnosed and reported. These findings are in concordance with the result from many other similar studies.^{2,3,9,10,12,18,25-27,30} In CRVO, 50% (9/18) of the patients were aged less than 60 years. CRVO, which is considered a disease of the elderly, is now increasing in younger individuals. Similar to other studies, most of the patients (61%) had a Non-ischemic type of CRVO at the time of presentation.^{10,23,31,42} Hayreh et al found that 81% of the patients belonged to this category initially.^{8,21} Macular edema was found in 66% of the patients with RVO in our study. Macular edema was detected in 37% of all RVO eyes in Beijing eye study.²⁶

CONCLUSION:

The burden of RVO is increasing with the increase in the life expectancy of the people and increasing incidence of risk factors. Since RVO is associated with many systemic and ocular risk factors, early detection, and proper control of these risk factors, have a major role to play in prevention. Emphasis should also be laid on periodic eye examination in patients having these risk factors for early detection

and management of RVO.

REFERENCES:

- Kolar P. Risk factors for central and branch retinal vein occlusion: a meta-analysis of published clinical data. *J Ophthalmol*. 2014;724780.
- Li J, Paulus YM, Shuai Y, Fang W, Liu Q, Yuan S. New Developments in the Classification, Pathogenesis, Risk Factors, Natural History, and Treatment of Branch Retinal Vein Occlusion. *J Ophthalmol*. 2017;2017:4936924. doi:10.1155/2017/4936924
- Kumar S. (2017). Clinical study of branch retinal vein occlusion. *International Journal Of Clinical Trials*, 4(4), 191-195.
- Morris R. Retinal vein occlusion. *Kerala J Ophthalmol* 2016;28:4-13
- Johnston RL, Brucker AJ, Steinmann W, Hoffman ME, Holmes JH. Risk factors of branch retinal vein occlusion. *Arch Ophthalmol*. 1985;103:1831-2.
- Ip M, Hendrick A. Retinal Vein Occlusion Review. *Asia Pac J Ophthalmol (Phila)*. 2018;7(1):40-5.
- Schmidt-Erfurth U, Garcia-Arumi J, Gerendas BS, et al. Guidelines for the Management of Retinal Vein Occlusion by the European Society of Retina Specialists (EURETINA). *Ophthalmologica*. 2019;242(3):123-62.
- Blair K, Czyz CN. Central Retinal Vein Occlusion. [Updated 2020 Mar 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK525985/>
- Cochran ML, Mahabadi N, Czyz CN. Branch Retinal Vein Occlusion (BRVO) [Updated 2019 Aug 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK535370/>
- Kolar P. Definition and Classification of Retinal Vein Occlusion. *International Journal of Ophthalmic Research*. 2016. 2. 124-29.
- O'Mahoney PR, Wong DT, Ray JG. Retinal vein occlusion and traditional risk factors for atherosclerosis. *Arch Ophthalmol*. 2008;126(5):692-9.
- Buddy R, Elliott D. Evaluation and Management Of Retinal Vein Occlusion. (2004, November 15) Retrieved from <https://www.reviewofophthalmology.com/article/evaluation-and-management-of-retinal-vein-occlusion>.
- Lauri M, Chen E, Looman M, Gallagher M. The burden of disease of retinal vein occlusion: a review of the literature. *Eye (Lond)*. 2011;25(8):981-8.
- Esmaili DD, Boyer DS. Recent advances in understanding and managing retinal vein occlusions. *F1000Research* 2018, 7:467 retrieved from <https://doi.org/10.12688/f1000research.12886.1>
- Yau JW, Lee P, Wong TY, Best J, Jenkins A. Retinal vein occlusion: an approach to diagnosis, systemic risk factors, and management. *Intern Med J*. 2008;38(12):904-10.
- Karia N. Retinal vein occlusion: pathophysiology and treatment options. *Clin Ophthalmol*. 2010;4:809-16.
- Keren S, Loewenstein A, Coscas G. Pathogenesis, prevention, diagnosis, and management of retinal vein occlusion. *World J Ophthalmol* 2014; 4(4): 92-112
- Sankaranarayanan RP, Padmavathi P, Nova S, Vaikkakara S. Study on clinical profile of patients with retinal vein occlusion. *J. Evolution Med. Dent. Sci*. 2017;6(51):3885-9
- Rogers S, McIntosh RL, Cheung N, et al. The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia. *Ophthalmology*. 2010;117(2):313-9.
- Archana K, Radhika M. Baseline Characteristics and Risk Factors for Retinal Vein Occlusions. *International Journal of Contemporary Medical Research*. 2019;6(3):13-16
- Hayreh SS. Retinal vein occlusion. *Indian J Ophthalmol* 1994;42:109-32
- Hayreh SS. Classification of central retinal vein occlusion. *Ophthalmology*. 1983;90(5):458-474.
- Hayreh SS, Zimmerman MB. Fundus changes in central retinal vein occlusion. *Retina*. 2015; 35(1):29-42.
- Hayreh SS, Podhajsky PA, Zimmerman MB. A natural history of visual outcome in central retinal vein occlusion. *Ophthalmology*. 2011;118(1):119-33.
- Hayreh SS, Zimmerman MB. Fundus changes in branch retinal vein occlusion. *Retina*. 2015;35(5):1016-27.
- Zhou JQ, Xu L, Wang S, et al. The 10-year incidence and risk factors of retinal vein occlusion: the Beijing eye study. *Ophthalmology*. 2013;120(4):803-8.
- Klein R, Klein BE, Moss SE, Meuer SM. The epidemiology of retinal vein occlusion: the Beaver Dam Eye Study. *Trans Am Ophthalmol Soc*. 2000;98:133-43.
- M. C. H. Janssen, M. den Heijer, J. R. M. Cruysberg, H. Wollersheim, and S. J. H. Bredie. Retinal vein occlusion: a form of venous thrombosis or a complication of atherosclerosis? A meta-analysis of thrombophilic factors. *Thrombosis and Haemostasis*. 2005;93(6):1021-26
- J. Rehak and M. Rehak. Branch retinal vein occlusion: pathogenesis, visual prognosis, and treatment modalities. *Current Eye Research*. 2008;33(2):111-31.
- Thapa R, Paudyal G, Bernstein PS. Demographic characteristics, patterns, and risk factors for retinal vein occlusion in Nepal: a hospital-based case-control study. *Clin Exp Ophthalmol*. 2010;38(6):583-590.
- Hayreh SS, Podhajsky PA, Zimmerman MB. A natural history of visual outcome in central retinal vein occlusion. *Ophthalmology*. 2011;118(1):119-33.
- Mitchell P, Smith N, Chang A. Prevalence and associations of Retinal Vein Occlusion in Australia. The Blue Mountain Eye Study. *Arch Ophthalmol*. 1996;114:1243-7.
- Glueck, C. J., Wang, P., Hutchins, R., Petersen, M. R., & Golnik, K. Ocular Vascular Thrombotic Events: Central Retinal Vein and Central Retinal Artery Occlusions. *Clinical and Applied Thrombosis/Hemostasis*, 2008;286-294.
- Cahill MT, Stinnett SS, Fekrat S. Meta-analysis of plasma homocysteine, serum folate, serum vitamin B(12), and thermolabile MTHFR genotype as risk factors for retinal vascular occlusive disease. *Am J Ophthalmol*. 2003;136(6):1136-1150.
- Trello M, Pasca S, Damiano R, et al. Retinal vein occlusion: evaluation of "classic" and "emerging" risk factors and treatment. *J Thromb Thrombolysis*. 2010;29(4):459-64.
- Di Capua M, Coppola A, Albinetti R, et al. Cardiovascular risk factors and outcome in patients with retinal vein occlusion. *J Thromb Thrombolysis*. 2010;30(1):16-22.
- McGimpsey SJ, Woodside JV, Bamford L, et al. Retinal vein occlusion, homocysteine, and methylenetetrahydrofolate reductase genotype. *Invest Ophthalmol Vis Sci*. 2005;46(12):4712-4716.
- Fay WP. Homocysteine and thrombosis: guilt by association?. *Blood*. 2012;119(13):2977-78
- Yin X, Li J, Zhang B, Lu P. Association of glaucoma with the risk of retinal vein occlusion: A meta-analysis. *Acta Ophthalmol*. 2019;97(7):652-659. doi:10.1111/aos.14141
- Sperduto RD, Hiller R, Chew E, et al. Risk factors for hemiretinal vein occlusion: comparison with risk factors for central and branch retinal vein occlusion: the eye disease case-control study. *Ophthalmology*. 1998;105(5):765-71.
- Hayreh SS. Prevalent misconceptions about acute retinal vascular occlusive disorders. *Prog Retin Eye Res*. 2005;24(4):493-519.
- Raju VK, Abdulkader A. Central Retinal Venous Occlusion-A Clinical Study. *Kerala J Ophthalmol*. 2009; 21(2):158-62