"ONE YEAR CROSS - SECTIONAL STUDY TO EVALUATE HYPERTENSION AND HYPERLIPIDEMIA AS RISK FACTORS IN RETINAL VEIN OCCLUSION PATIENTS AT KLES DR. PRABHAKAR KORE CHARITABLE HOSPITAL & MRC, BELGAUM ."

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This is to certify that the dissertation entitled **"A ONE YEAR CROSS-SECTIONAL STUDY TO EVALUATE HYPERTENSION AND HYPERLIPIDEMIA AS RISK FACTORS IN RETINAL VEIN OCCLUSION PATIENTS AT KLES DR. PRABHAKAR KORE CHARITABLE HOSPITAL & MRC, BELGAUM"** is a bonafide research work done by **REG. NO.BK0111002.**

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LIST OF ABBREVIATIONS

RVO - Retinal Vein Occlusion

CRVO - Central Retinal Vein Occlusion

BRVO - Branch Retinal Vein Occlusion

ICRVO - Ischemic Central Retinal Vein Occlusion

NICRVO - Non Ischemic Central Retinal Vein Occlusion

STBRVO - Superotemporal Branch Retinal Vein Occlusion

ITBRVO - Inferotemporal Branch Retinal Vein Occlusion

SNBRVO - Superonasal Branch Retinal Vein Occlusion

INBRVO - Inferonasal Branch Retinal Vein Occlusion

MBRVO - Macular Branch Retinal Vein Occlusion

IHRVO -Ischemic Hemiretinal Vein Occlusion

NIHRVO - Non Ischemic Hemiretinal Vein Occlusion

HTN - Hypertension

DM - Diabetes Mellitus

BMI - Body Mass Index

KFT - Kidney function tests

ESR -Erythrocyte Sedimentation Rate

IOP -Intra-ocular pressure

ABN - abnormal

ABSTRACT

Background

Retinal Vein Occlusions are reported to be the second most common vascular cause of ocular morbidity after Diabetic Retinopathy. Various systemic and ocular risk factors have been found to be associated with retinal vein occlusions. The stress is more on systemic parameters like advanced Age, Hypertension, Hyperlipidemia, Diabetes, Smoking, Obesity, Systemic Vasculitides, Thrombophilic conditions, which all contribute to changes in vasculature all over the body, and also to pathogenesis of retinal vein occlusions.

Objective

- To study Hypertension and Hyperlipidemia as risk factors in Retinal vein occlusion patients.
- To study Co-existing risk factors like Age, Diabetes Mellitus,Obesity, Smoking and abnormalities in haemogram, IOP and Axial length in Retinal vein occlusion patients.

Methodology

The present one year cross sectional study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of January 2012 to December 2012. 40 patients who met the inclusion criteria were included in the study. Detailed history regarding the risk factors was obtained. Slit lamp biomicroscopy, direct and indirect ophthalmoscopy with fundus photography was carried out. Blood investigations were done.

Results

Mean age of the patients was 60.25±11.7 with more males than females. Hypertension was the most common risk factor seen in 77.5% of patients. 40% of patients were diabetic, 30% had hyperlipidemia and 55% of patients were smokers. Risk factor profiling of the patients was also done. Most of the patients had multiple risk factors, predominantly atherosclerotic ones.

Conclusions

Present study supports a multifactorial etiology of RVO, with predominance of atherosclerotic factors, rather than pointing towards a singular risk factor.

Keywords

Retinal vein occlusion, Atherosclerotic risk factors, hypertension

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INTRODUCTION

Retinal vein occlusion is the second most common retinal vascular disease following diabetic retinopathy.[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).

In 1885 Liebrich first described retinal vein occlusion and called it "retinal apoplexy"[2]. Julius Von Michel[3] established it as a clinical entity resulting from thrombosis in 1878. Leber in 1877 gave the first description of branch retinal vein occlusion and called it "hemorrhagic retinitis"[4]. Duke – Elder[5] accurately summarised the state of knowledge on retinal vein occlusion in 1967 when he stated: "Since that time (Von Michel's) the condition has been the subject of almost continuous research but nevertheless, even today, many points both in the aetiology and its intimate mechanism of the obstruction are still unelucidated."

The overall incidence of RVO in large population based studies varies depending on age and the study. In the latest report of The Beaver Dam Eye Study[6], the 15-year cumulative incidences of BRVO and CRVO were 1.8% and 0.5%, respectively. In the Blue Mountains Eye Study (BMES), done in Australia, the ten year incidence of RVO was 1.6% in the older population.[7]

Pooled data from these two large studies also showed that the risk of cardiovascular related mortality in patients having RVO is double that of matched controls.[8]

Central retinal vein occlusion is also associated with significant decrease in Vision – Related Quality of Life (QOL), much like diabetic retinopathy.[9]

Retinal venous occlusive disease typically occurs at an arteriovenous crossing in BRVO or at the lamina cribrosa in CRVO and HRVO. Retinal vein occlusions have a characteristic, although variable, appearance with intraretinal hemorrhage, cotton wool spots, tortuous and dilated veins, retinal edema and, occasionally, optic disc swelling. These findings are present segmentally in BRVO, in either the superior or inferior quadrant in HRVO, and in all quadrants of the fundus in CRVO. Vision loss can vary from minimal or no vision loss to complete blindness. Causes of vision loss with RVO include macular edema, macular nonperfusion, epiretinal membrane, dense intraretinal hemorrhages, vitreous hemorrhage, neovascular glaucoma (NVG), or tractional retinal detachment (TRD). Timely intervention can reduce the incidence and severity of these complications. Many systemic diseases are risk factors for RVO development. Recognition and treatment of an underlying systemic disease can benefit the patient visually and improve overall health.[10]

Many earlier studies determined to calculate prevalence of RVO depict association of various risk factors with development of RVO. However we studied patients of RVO for the risk factor profile and elaborated each of the risk factor considered in the study in detail. Although many studies on this subject have been done abroad, studies in Indian populations are sparse.

This study will contribute to the available Indian scientific literature on the subject and will pave way for more detailed epidemiological and interventional studies in the future.

OBJECTIVE

- **PRIMARY** - To study Hypertension and Hyperlipidemia as risk factors in Retinal Vein Occlusion patients.

- **SECONDARY** - To study Co-existing risk factors like

  SYSTEMIC -Age, Diabetes Mellitus, smoking, Obesity, Haemogram, Kidney function test in Retinal vein occlusion patients.

  OCULAR –Intra Ocular Pressure and Axial length.

REVIEW OF LITERATURE

In their large case-control study, Hayreh SS et al[11] studied and investigated 1090 consecutive patients with retinal vein occlusions. The combined group of patients with CRVO and patients with HRVO had a higher prevalence of arterial hypertension (p<.0001), peptic ulcer (p<.0001), diabetes mellitus (in ischemic type only, p<.0001), and thyroid disorder (p<.0001) when compared to the US white control population, the patients with BRVO had a greater prevalence of arterial hypertension (p<.005), cerebrovascular disease (p=.007), chronic obstructive pulmonary disease (p=.012), peptic ulcer (p<.0001), diabetes (in age less than 45 only, p=.0005), and thyroid disorder (p=.003) compared with US white population. There was no significant difference in prevalence of any systemic disease between CRVO and HRVO. A significantly greater prevalence of arterial hypertension (p=.025) and diabetes mellitus (p=.011) was present in ischemic CRVO compared with nonischemic CRVO. Similarly arterial hypertension (p=.0002) and ischemic heart disease (p=.048) were more prevalent in major BRVO than in macular BRVO. The investigators concluded that, 'a variety of systemic disorders may be present in association with different types of retinal vein occlusion and in different age groups. The presence of a particular associated systemic disease does not imply a cause – effect relationship.'

O'Mahouney et al[12] in a large meta-analysis of pooled data of 2,916 cases and 28,646 controls from 21 studies done worldwide showed that both hypertension (Odds ratio [OR], 3.5; 95% confidence interval [CI], 2.5-5.1) and hyperlipidemia (OR, 2.5; 95% CI, 1.7-3.7) were significantly associated with any form of RVO; the association was less pronounced for diabetes mellitus (OR, 1.5;95% CI, 1.1-2.0).

Similar results were found in cases with central RVO and branch RVO. They concluded that hypertension and hyperlipidemia are common risk factors for RVO in adults, and diabetes mellitus is less so.

In another large study, Cheung et al[13] studied a multi ethnic cohort of 6,147 patients from 6 U.S. communities. They found that the independent risk factors associated with RVO were hypertension (OR 2.06; 95% CI: 1.18, 3.59), older age (OR 1.34, 95% CI: 1.00, 1.81, per decade increase), less education (OR 4.08, 95% CI: 2.20, 7.54), hypertriglyceridemia (OR 1.98; 95% CI: 1.10, 3.56), renal dysfunction (OR 1.85; 95% CI: 1.01, 3.39) and the presence of retinal arteriovenous nicking (OR 4.01; 95% CI: 2.06, 7.81) and focal arteriolar narrowing (OR 4.38; 95 CI:1.44,13.34).

RVO was not significantly associated with direct measures of subclinical atherosclerosis (e.g., carotid intima media thickness and coronary artery calcium scores) or markers of inflammation (e.g. C-reactive protein, interleukin-6), and endothelial dysfunction (e.g., soluble intercellular adhesion molecule-1) or coagulation (e.g., D-Dimer). They concluded that, 'The prevalence of RVO is similar across different racial/ethnic groups. In the general population, RVO is associated with hypertension, dyslipidemia and renal dysfunction, but not with atherosclerotic disease, systemic inflammation and hematological abnormalities.'

Wong et al[14] studied pooled data from the Atherosclerosis Risk in Communities & Cardiovascular Health studies to examine the associations of retinal vein occlusion and arteriolar emboli with cardiovascular disease. They found that after adjusting for age, retinal vein occlusion was associated with hypertension (OR, 2.96; 95% CI, 1.43-6.14), systolic blood pressure (BP) (OR, 4.12; 95% CI, 1.40-12.16), diastolic BP (OR, 2.64; 95% CI, 1.07-6.46), carotid artery plaque (OR, 5.62;

95% CI, 2.60-12.16), body mass index (OR, 3.88; 95% CI, 1.23-12.18), plasma fibrinogen (OR, 3.29; 95% CI, 1.08-10.02), arteriovenous nicking (OR, 4.09; 95% CI, 2.00-8.36), and focal arteriolar narrowing (OR, 5.17; 95% CI, 2.59-10.29).

The Eye Disease Case-Control Study Group[15] found that an increased risk of CRVO was present in persons with systemic hypertension, diabetes mellitus, and open-angle glaucoma. Risk of CRVO decreased with increasing levels of physical activity.

In women, risk of occlusion decreased with use of postmenopausal estrogens and increased with higher erythrocyte sedimentation rates. Cardiovascular disease, electrocardiographic abnormalities, history of treatment of diabetes mellitus, higher blood glucose levels, lower albumin-globulin ratios, and higher alpha-globulin levels were associated with increased risk only for ischemic CRVO.

While studying BRVO[16], the group concluded that an increased risk of branch retinal vein occlusion was found in persons with a history of systemic hypertension, cardiovascular disease, increased body mass index, glaucoma and higher serum levels of alpha 2-globulin. Risk of branch retinal vein occlusion decreased with higher levels of alcohol consumption and high-density lipoprotein cholesterol. Their data suggested a cardiovascular risk profile for patients with branch retinal vein occlusion and indicated that 50% of patients with branch retinal vein occlusion may be attributable to hypertension.

In their studies on HRVO, the Eye Disease Case-Control Group compared the risk factor associations with all 3 types of RVOs[17] and found that systemic hypertension and history of diabetes mellitus were associated with increased risk of

HRVO. Glaucoma history was associated with all three types of retinal vein occlusion. They concluded that 'patients presenting with retinal vein occlusion should be evaluated for cardiovascular disease, diabetes, and glaucoma.'

A recent study done in an Asian population in Singapore by Lim et al[18] showed that there was no significant gender difference in RVO prevalence. RVO was associated with higher systolic blood pressure (age-adjusted odds ratio (OR) per SD increase 1.54, CI 1.02 to 2.31), ocular perfusion pressure (OR per SD increase 1.49, CI 1.03 to 2.16), a history of angina (OR 5.18, CI 1.49 to 18.0) and heart attack (OR 4.26, CI 1.47 to 12.3), and higher total cholesterol (OR per SD increase 1.55, CI 1.07 to 2.24) and LDL (OR per SD increase 1.47, CI 1.02 to 2.12) cholesterol levels.

ANATOMY OF RETINAL VEINS

EMBYOLOGY –

The development of the vascular system of the eye and orbit is complex. Many vessels are transitory, that is arising and regressing in response to the changing needs of the embryonic eye[19]. The terminal portion of the ophthalmic artery invades the embryonic fissure of the human eye at about the 5mm stage of the embryo. The fissure closes between the fifth and seventh week. The vessel remains in the optic cup and becomes the hyaloid artery.[20] In the third trimester the hyaloid system atrophies.[19] Central retinal artery and vein are the remnants of the hyaloid vessels. Ida Mann[21] describing the development of central retinal vessels has reported that from the 3rd month of intrauterine life onwards, there are always two trunks of the central retinal vein (CRV) in the optic nerve, one on either side of central retinal artery. One of the 2 CRV trunks usually disappear just before birth. Hayreh in his study on anatomy of central retinal artery also reported CRV with two trunks in the anterior part of the optic nerve.[22] Dual trunked CRV is a congenital anomaly in 20.5% of eyes in the general population as reported by Chopdar.[23]

GROSS ANATOMY -

The CRV is formed on the optic nerve head by the union of the retinal venous tributaries. The vein runs on the lateral side of the central retinal artery in the axial part of the nerve, in a fibrous envelope in common with the artery or separated by it by axon bundles. At times two veins enter the nerve head and unite within the substance of the nerve. This reflects the embryonic origins of the vein as two venous channels at the third month of intrauterine life. The vein receives tributaries from the

retina, the optic nerve head at all levels, the pia and from the posterior central vein. It joins the orbital plexus of veins, to drain into the superior or inferior ophthalmic vein, and/or cavernous sinus directly. Because of these multiple connections blockage of the blood flow in the cavernous sinus will not block blood flow in the central retinal veins, though it may impede it.[24]

The branch retinal veins more or less follow the pattern of the arterioles. A vein may run parallel to the corresponding artery for a short distance but they almost never run next to each other. The normal A:V ratio is 2:3 and this applies to CRV also. The larger retinal vessels lie in the inner-most portion of the retina close to the inner limiting membrane; retinal glial cells, mainly astrocytes, extend over large areas in close relationship with retinal vessel walls. Astrocytes constrain the retinal vessels and maintain their integrity. At the arteriovenous (A-V) crossing sites, the deeper vessels may indent the retina down to the outer plexiform or outer nuclear layer.[25]

When two vessels cross, the artery usually lies anterior (vitriad) to the vein, and the two vessels share a common adventitial coat. Many more A-V crossings occur temporally than nasally because the nasal vessels assume a much straighter course. The crossings are important because they represent the most common site of branch retinal vein obstructions. The retinal veins drain into the CRV, which also acts as a major efferent channel for vessels of the optic nerve. Near the disc the retinal veins are approximately 150µm in diameter.[26]

HISTOLOGY-

Retinal veins have extremely thin walls and slightly larger lumen than the corresponding arteries. The structure of the CRV is simpler than that of the central

retinal artery. The continuous endothelium lies on a basement membrane. Outside this is a layer of smooth muscle or pericyte and media is represented by a separation of occasional smooth muscle cells from basement membrane. There is neither an internal nor an external elastic lamina. A connective tissue adventitia is present.[24]

CLASSIFICATION RETINAL VEIN OCCLUSION –

A. HAYREH S.S CLASSIFICATION OF RVO-

Hayreh S.S has recognized 6 distinct clinical entities of RVO[27]:

1. Central retinal vein occlusion (CRVO), consisting of:
    a) Non-ischemic CRVO (or venous stasis retinopathy)
    b) Ischemic CRVO (or hemorrhagic retinopathy)
2. Hemi-central retinal vein occlusion (HCRVO): This also consists of:
    c) Non-ischemic HCRVO (or hemi-venous stasis retinopathy)
    d) Ischemic HCRVO (or hemi-hemorrhagic retinopathy)
3. Branch retinal vein occlusion (BRVO): This consists of:
    e) Major BRVO
    f) Macular BRVO

B. COATS CLASSIFICATION-

Coats was the first to suggest that patients with CRVO fall into 2 groups based on clinical appearance & prognosis[28]:

1. Patients with dramatic 'blood and thunder' ophthalmoscopic appearance, loss of vision and poor prognosis.

2. Patients with mild ophthalmoscopic changes, generally good visual acuity and good prognosis.

C. MAGARGAL'S CLASSIFICATION-

Magargal and colleagues[29] felt that venous occlusion is a spectrum of disease with capillary non-perfusion ranging from little if any ischaemia to marked ischaemia and that the amount of ischemia is roughly correlated with the development of neovascular complications. They have subdivided CRVO into 3 groups based on an estimate of the percentage of the obstructed area that is non-perfused or the **"Ischaemic Index"** on FFA.[10] These groups are:

1. Non-ischaemic or hyper-permeable

2. Ischaemic

3. Indeterminate

D. CVOS CLASSIFICATION-

The Central Vein Occlusion Study (CVOS)[30] classified CRVO on the basis of capillary non-perfusion seen on Fundus Fluorescein Angiography (FFA) as:

1. Perfused – less than 10 disc areas of capillary nonperfusion.

2. Nonperfused – 10 or more disc areas of capillary nonperfusion.

3. Indeterminate – perfusion cannot be assessed.

E. BRVO CLASSIFICATION -[31]

1. Major BRVO which may be further subdivided as follows:
    - First order temporal branch at the optic disc
    - First order temporal branch away from the disc but involving branches to the macula
2. Minor macular BRVO – involving only a macular branch.
3. Peripheral BRVO not involving the macular circulation .

PATHOGENESIS –

A good understanding of pathogenesis of a disease is absolutely fundamental to a scientific grasp of the clinical features of the disease and its logical management. Like all ocular vascular occlusive disorders, all types of RVO are multifactorial in origin and usually no single factor on its own causes the occlusion.[27]

CENTRAL RETINAL VEIN OCCLUSION –

The pathogenesis of CRVO is still not completely understood. Numerous theories have been presented over the years without consensus. Hayreh has suggested that nonischemic CRVO occurs after occlusion of retinal venous flow, while ischemic CRVO develops after occlusion of venous and arterial flow. His studies were based on animal models with occlusion of the retinal vessels at their entry into the optic nerve.[32-34]

However other experimental and pathologic studies did not support this theory. Fujino and coworkers[35] found that more anterior obstruction of the central retinal vein alone produced a picture similar to an ischemic CRVO. Later Hayreh also outlined the same finding.[27]

In a large histopathologic series, Green and co-investigators supported the hypothesis that thrombus formation is the primary event in CRVO.[36] They found fresh or recanalized thrombus in the region of lamina cribrosa in 28 of 29 eyes enucleated after CRVO.

The reason that thrombus formation tends to occur in the region of the lamina cribrosa is unknown. The close anatomic association of the central artery and vein, as well as the narrowing of the central retinal vessels as they pass through the lamina cribrosa, may contribute to turbulent flow and thrombus formation.[37]

Klein and Olwin[38] postulated the following 3 occlusive mechanisms in retinal vein occlusions:

1. External compression of CRV
2. Haemodynamic disturbances
3. Primary venous wall disease

1. EXTERNAL COMPRESSION OF CRVO.

Ischemic CRVO

In ischemic CRVO, the site of occlusion is most probably in the region of lamina cribrosa or immediately posterior to it. Senile degenerative changes in the wall

of CRA and CRV result in marked narrowing of the artery and compression of the vein by the sclerosed artery[39]. Sclerotic changes in the lamina cribrosa also contribute to external compression of CRV. This leads to endothelial proliferation and further stagnation and thrombosis in the CRV. In patients with these predisposing changes, a fall of systemic blood pressure during sleep would finally complete the thrombotic process. In these eyes, there is a marked rise of venous pressure because the site of CRVO is in the region of the lamina cribrosa or immediately behind that, with only a few small collaterals left to drain away the blood.[27] The effect of nocturnal hypotension is discussed below under the sub-heading of haemodynamic factors.

Any other ocular condition causing compression of the central retinal vein might equally be involved in the pathogenesis of occlusion. Such potential conditions include glaucoma, optic nerve haemorrhage, papilledema and drusen of the optic nerve head.[40]

Non-ischemic CRVO

81% of patients with CRVO belong to this category[41]. The major difference in these eyes is that the site of occlusion in this type is neither in the lamina cribrosa nor in the adjacent retrolaminar region but further back. The severity of the retinopathy would depend on the site of occlusion. The further back the occlusion, the milder the retinopathy because of the availability of more and more collateral channels.[27]

2.HEMODYNAMIC FACTOR-

Haemodynamic disturbances on the arterial side play an important role in the development of this thrombosis as suggested by Hayreh.[42] This is because blood flow in the retinal vessels depends upon the perfusion pressure,

Perfusion Pressure = Mean Arterial Pressure – Venous Pressure

The mean arterial pressure (MAP) is further defined as,

MAP = 1/3 (systolic BP – diastolic BP) +diastolic BP

Where BP stands for blood pressure. Venous stasis caused by external compression and endothelial proliferation causes rise in venous pressure proximal to the site of thrombosis, fall in perfusion pressure and sluggish circulation.

A fall in systemic arterial blood pressure would further lower the perfusion pressure. Nocturnal hypertension causes precipitous fall in perfusion pressure during sleep[42]. This may convert a partial thrombosis to complete thrombosis because of poor, sluggish circulation during sleep. The fact that many CRVO patients wake up with poor vision strongly suggests that nocturnal arterial hypotension plays an important role as the final insult in precipitating CRVO in persons who are susceptible.

Some of these patients experience transient recurrent thrombosis of the CRV. The explanation for these episodes of amaurosis fugax is that, as the thrombus progresses to completely occlude the CRV, it causes sudden stoppage of blood flow in the retinal vascular bed leading to transient ischemia of the retina and associated visual loss. This sudden stoppage of venous outflow would also result in sudden rise in the blood pressure to the arterial level in retinal vascular bed proximal to the site of CRV thrombus. Since it is a fresh thrombus, it cannot withstand this high sudden arterial blood pressure, and it pops out, resulting in restoration of retinal circulation and normal visual function. A gradual and progressive increase in size of the throm-

bus in the CRV and nocturnal arterial hypotension for many hours during sleep then finally, one day, produce permanent irreversible occlusion of CRV.

In eyes with ischemic CRVO, the retina also suffers from focal or more extensive ischemia, usually of a recurrent transient nature. With retinal ischemia there is also ischemic capillaropathy.

As the BP returns to normal or even to hypertensive levels during waking hours there is restoration of retinal circulation, though it remains sluggish. Consequent rise in intraluminal pressure in ischemic capillaries ruptures the weakened capillaries and produces extensive retinal haemorrhages[27].

It is also well-established that CRVO is significantly more common in patients with raised intraocular pressure (IOP) and glaucoma[43,44]. The pressure in the CRV at the optic disc depends upon the IOP, the former being always higher than the latter to maintain blood flow. A rise of IOP would produce retinal venous stasis and sluggish venous outflow. Morphologic studies of the optic nerve, in experimentally produced glaucomatous neuropathy by chronic IOP elevation in rhesus monkeys, showed that as compared to age matched controls, there was marked thickening of the fibrous tissue envelope and narrowing of the central retinal vessels.[45]

CRVO associated with Cilioretinal artery occlusion:

A major cause of serious visual loss in non-ischemic CRVO is the development of associated cilioretinal artery occlusion. During CRVO, blood pressure in the entire capillary bed transiently rises to the level of CRA blood pressure. B.P. within the cilioretinal arteries and choroidal vascular bed being lower than in the CRA, the cilioretinal arteries cannot pump blood into a high pressure

retinal capillary bed resulting in physiological block in the cilioretinal artery circulation. Within a day or two with the development of venous collaterals by CRV in the optic nerve the blood pressure in the retinal vascular bed falls and results in almost normal filling of the cilioretinal artery once again. However, in the mean time the retina supplied by the cilioretinal artery has usually been damaged irreversibly by ischemia resulting in visual loss.[27]

The severity of retinal ischemia in the area supplied by the cilio-retinal artery and associated visual loss depends upon the length of time elapsed before the circulation was re-established.[27]

Conversion of non-ischemic to ischemic CRVO

The gradual extension of the thrombotic process in the CRV towards the optic disc eliminates the available collaterals and would convert non-ischemic to ischemic CRVO. In elderly patients marked nocturnal arterial hypotension may cause precipitous fall in perfusion pressure and may convert a non-ischemic to ischemic CRVO.[45]

HEMICENTRAL VEIN OCCLUSION-

Its pathogenesis is similar to CRVO. Usually one of the 2 trunks of CRV is involved. HRVO occurs when a branch of the CRV becomes occluded at or near the optic disc or when one of the branched of a dual-trunked CRV becomes occluded in the anterior part of the optic nerve. Occasionally, however, both trunks may be involved - presumably due to site of occlusion being in the main trunk of CRV after the union of the two trunks, and this on routine examination would appear to be ordinary CRVO. It may be that occlusion of one of the two trunks has a non-ischemic

pattern and occlusion of the second trunk an ischemic pattern; this is presumably determined by the location of the site of occlusion in the two trunks and the number of available collaterals in each trunk.[27]

ROLE OF RHEOLOGICAL FACTORS-

Thrombus formation at the site of damaged endothelium is due to aggregation of platelets and fibrin formation. Conversion of fibrinogen to fibrin involves a cascade of reactions involving a large number of clotting factors. To prevent in vivo coagulation, there is the anti-coagulant system. Injury to the endothelium, by any means, alters the balance between the coagulation and anticoagulation systems and results in thrombosis. It has been postulated that imbalance between the various systems involved in the cascade of coagulation can cause thrombosis[46]. Retinal vein occlusions have been associated with various abnormalities of the clotting and the fibrinolytic systems, high plasma viscosity, high hematocrit, high plasma homocysteine, etc. These factors are later discussed individually.

3.PRIMARY VENOUS DISEASE-

This may be degenerative, inflammatory or traumatic. Degenerative venous disease occurs in hypertensive and diabetic retinopathies, inflammatory occlusions may be due to periphlebitis caused by behcet's disease, sarcoidosis, Eales disease etc. These are more likely in young adults with non-ischemic CRVO. Inflammatory occlusions are more common in tributaries as compared to main veins. Trauma can cause direct concussive injury to venous vessel wall and can lead on to venous occlusion.

In young persons, all the available evidence suggests that phlebitis of the CRV is responsible for thrombosis[27]. CRVO due to phlebitis has been given different eponyms including "papillophlebitis," "retinal vasculitis," "mild retinal and papillary vasculitis" and "optic disc vasculitis-type 2".

PATHOGENESIS OF BRVO-

Koyanagi[47] in 1928 first reported the association between BRVO and arterio-venous crossing, and now it is well established that site of occlusion in BRVO is invariably at the arterio-venous crossing. A number of studies[48-51] have reported that at the site of occlusion in BRVO, the retinal arteriole lies anterior to the occluded vein in 93%-100% of cases. It is also well-known that BRVO is seen more commonly in the temporal than nasal part of the retina, and of the temporal retina more frequently in the superior than inferior quadrant. The arterio-venous crossings have been shown to be more frequent in the supero-temporal quadrant than elsewhere[51,52] and situated closer to the optic disc in the supero-temporal than infero-temporal quadrant.[52]

The clinical picture and fluorescein angiographic studies in BRVO do show the site of obstruction to blood flow in the retinal vein at the arteriovenous crossing. From this clinical information it would seem logical to assume that the sclerotic retinal arteriole probably compresses the accompanying vein because of a common thickened, adventitial and glial sheath; however, histopathological studies[53,54] have failed to confirm this view.

Moreover, the very low incidence of BRVO inspite of the very high incidence of anterior location of the arteriole at the arterio-venous crossing in patients with arteriosclerosis and hypertension clearly indicates that, in the multifactorial etiology

of BRVO, factors other than simple anatomical arrangement must play important roles.

In addition, focal phlebitis is a well known cause of BRVO, e.g., in toxoplasmic chorio-retinitis and retinal vasculitis. Similarly, BRVO is seen in dysproteinemias, sickle cell disease and other hematologic disorders. Unlike CRVO and HCRVO, glaucoma and raised IOP play little role in the pathogenesis of BRVO.[27]

RISK FACTORS FOR RETINAL VEIN OCCLUSION-

As described above, RVO has a multifactorial etiology and pathogenesis. A large multitude of factors have been found to be associated with the disease. They can be divided into ocular and systemic risk factors.

OCULAR RISK FACTORS-

1. **Glaucoma and raised IOP**.

Many large studies have linked CRVO and raised IOP or glaucoma[15,55]. An increased cup-to-disc ratio has also been found to be a significant predictor of incident RVO[55]. Another study of 450 cases of RVO found that optic cup (OC) and optic nerve-sited RVO without optic nerve head swelling(ONHS) are associated with raised IOP and may share a common management strategy aimed at controlling ocular pressure. Glaucomatous optic disc cupping, in contrast, seems to be important in the OC-sited RVO group only. Intraocular pressure, primary open angle glaucoma (POAG), and glaucomatous optic disc cupping do not significantly seem to contribute to the development of RVO at an AV crossing or when the occlusion occurs within the optic nerve in association with ONHS.[44] This suggests that presence of high IOP

and POAG are important local risk factors for the development of CRVO and HRVO but are not so significant for BRVO[27].The mechanism whereby glaucoma or raised IOP may predispose to RVO has been described above.

Most of the studies used IOP in the fellow eye for data collection and analysis as it has been commonly observed that, immediately after CRVO, the IOP is typically slightly lower than the fellow eye.[56]

2. Axial length

Another proposed local risk factor for development of RVO is a shorter axial length. It has been postulated that eyes with shorter axial length have smaller lamina cribrosa and a narrower scleral canal through which the central retinal vein and artery could pass, causing physical blockage in the vein which predisposes to thrombus formation.

Many studies concluded that a shorter axial length is seen with eyes having RVO, when compared to either the unaffected fellow eye or a control group[57-59]. Some studies have used presence of hyperopia in RVO to imply a shorter axial length.

Other studies found no significant association[60]. Few studies have shown that shorter axial length has significant association with CRVO but not BRVO[61,62]. Another study found shorter axial length to be significantly associated with BRVO.[63]

To summarise, the association of hyperopia and axial length with RVO awaits further research, preferably in large multi-ethnic studies.

SYSTEMIC RISK FACTORS-

Systemic work up is a vital part of the examination process for a patient with RVO, particularly if no risk factor is known. Many of the risk factors are treatable diseases that, if left untreated, can result in high morbidity and mortality.

HYPERTENSION-

A high blood pressure (BP) on presentation or a history of hypertension (HTN) is the most common systemic risk factor associated with all kinds of RVOs. All studies evaluating for systemic risk factors have found HTN to be significantly associated with RVO. The Eye Disease Case Control Studies recommend treatment of hypertension to prevent development of RVO.[15-17]

HTN is currently classified into the following categories by the The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure[64]

Blood Pressure Classification	SBP mmHg	DBP mmHg
Normal	<120	and <80
Prehypertension	120–139	or 80–89
Stage 1 Hypertension	140–159	or 90–99
Stage 2 Hypertension	≥160	or ≥100

SBP, systolic blood pressure; DBP, diastolic blood pressure

Hypertension is an increasingly important medical and public health issue. The prevalence of hypertension increases with advancing age to the point where more than half of people aged 60–69 years and approximately three-fourths of those 70 years of age and older are affected.[65]

The combined effect of arteriosclerosis caused by chronic HTN and transient nocturnal hypotension in HTN patients, especially those who take antihypertensive medications at bedtime, are thought to play an important role in pathogenesis of RVO.[27]

DIABETES MELLITUS-

Presence of Type 1 or Type 2 Diabetes Mellitus (DM) contributes to the total picture of atherosclerosis and retinal microvasculopathy.

Most of the studies that implicate DM as a risk factor have also found HTN, hyperlipidemia and other atherosclerotic risk factors to present along with DM. A study with 63 patients with BRVO found that there was greater prevalence of insulin resistance as measured by the oral Glucose Tolerance Test (GTT)[66]. Another study did not find a significant difference in HbA1c values and diabetic microvascular complications (retinopathy and proteinuria) between diabetics and non-diabetics having RVO.[67]

HYPERLIPIDEMIA-

Another risk factor for atherosclerosis which is often found in patients having RVO is hyperlipidemia.[12,13,18] Dyslipidemia is also a risk factor for recurrence of CRVO.[68] Various studies have used various aspects of the lipid profile as markers for hyperlipidemia.

HYPERHOMOCYSTEINEMIA-

Hyperhomocysteinemia appears to be one of the most common and significant thromobophilic risk factors for development of RVO. It has also been found to be a risk factor for recurrence of CRVO.[68]

Homocysteine is a naturally occurring amino acid in the body and is required in several reactions that occur within the cells. Although the exact mechanism(s) by which hyperhomocysteinaemia causes thrombosis are unknown, it has been shown to be directly toxic to endothelial cells, impair thrombomodulin expression, directly activate factor V and inhibit protein C activation[69-71]. The causes for hyperhomocysteinemia are genetic mutation, vitamin B6 and folate deficiencies, certain medications, and kidney disease. Hyperhomocysteinemia can be treated by folate and Vitamin B12 supplementation[10]. Few studies have found significant associations between homocysteine levels and all types of RVO.[70,72-76] However, there is no convincing data yet that decreasing homocysteine levels with vitamin supplementation will reduce the risk of RVO.[75,76]

THROMBOPHILIC RISK FACTORS-

In addition to hyperhomocysteinemia, certain hematologic abnormalities are risk factors for RVO especially in young adults[10]. The body normally maintains an elegant balance between thrombosis and fibrinolysis. When the coagulation cascade is activated, both the intrinsic and extrinsic pathways help in the conversion of prothrombin to thrombin. Thrombin has many different roles in regulating thrombosis other than the production of fibrin from fibrinogen. In particular it binds with thrombomodulin which in the presence of protein S converts inactive protein C to an

active form. Activated protein C binds to and inhibits the procoagulant action of activated factor V and factor VIII. Thus people deficient in protein S or protein C are prone to thrombosis. Anti-thrombin III (ATIII) is a serine protease inhibitor which not only inhibits thrombin generation but also other coagulation factors. Deficiency of ATIII also results in an increased risk of thrombosis.[77]

Protein C is a naturally occurring anticoagulant. **Activated protein C resistance** is the most common identifiable cause of systemic venous thrombosis[78]. This inheritable condition is transferred in an autosomal dominant pattern. While systemic levels of protein C are normal, the usual anticoagulation response is abnormal leading to increased thrombosis[10]. In 1994 a single point mutation in the factor V gene was identified and called Factor V Leiden.[79] This was demonstrated to be responsible for the poor anticoagulant response. The factor V Leiden mutation affects factor V, rendering it resistant to inactivation by protein C, which is a thrombophilic effect.[80]

A simplified diagram of the coagulation and anticoagulation systems is described below.

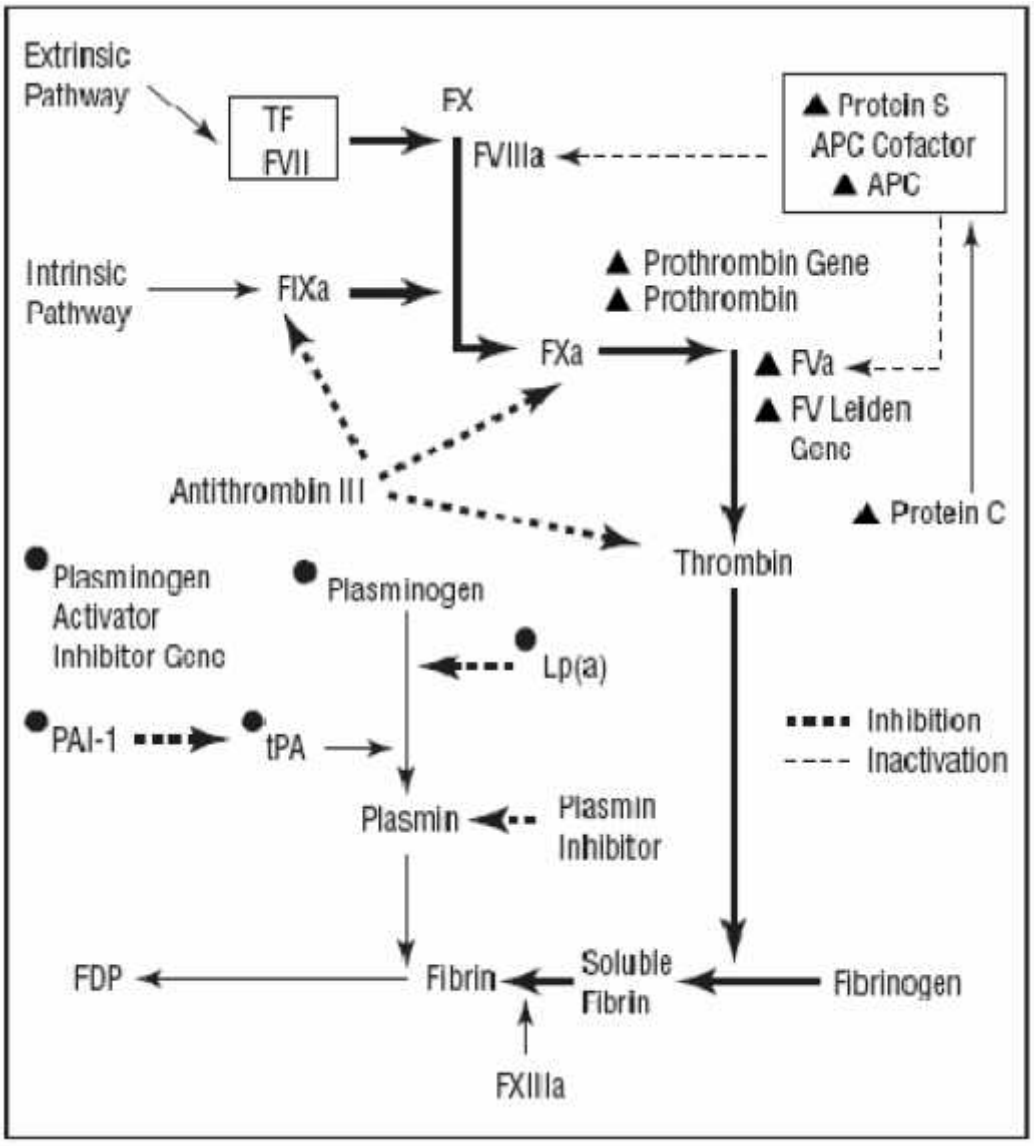

Figure: Thrombosis and fibrinolysis[46]. Clotting factor X (**FX**) is the final common pathway for all coagulation. Solid black circles indicate hypofibrinolysis; Solid triangles - thrombophilia; **TF** - tissue factor; **FVII** - factor VII; **FVIIIa** - activated form of factor VIII; **APC** - activated protein C; **FIXa** - activated form of factor IX; **FXa** - activated form of factor X; **FV** - factor V; FVa - activated form of factor V; **Lp(a)** - lipoprotein(a); **PAI-1** - plasminogen activated inhibitor 1; **tPa** - tissue plasminogen activator; and **FXIIIa** - activated form of factor XIII.

Some studies have found increased incidence of activated Protein C resistance in patients with RVO who were younger than 50 years as compared to the general population[81,82]. Factor V Leiden has been suggested as risk factor for development of CRVO in patients younger than 60 years[83,84]. However other studies have not supported this notion.[85-87]

Lupus anticoagulant factor, also known as anticardiolipin antibody, is a circulating immunoglobulin that may cause mild prolongation of coagulation studies, especially partial thromboplastin time, but paradoxically is associated with thrombosis. Patients with this factor test positive on Venereal Disease Research Laboratory (VDRL) testing[10]. Presence of these antibodies causes the **antiphospholipid syndrome**, a condition that can either be idiopathic or secondary to another condition such as systemic lupus erythematosus, infection or pregnancy[77]. Systemic manifestations of the disease include retinal vein, retinal artery, and choroidal occlusions as well as spontaneous abortions and systemic occlusions[10,88]. A significantly higher incidence of this condition has been found to be present in CRVO[89-91] and BRVO[90,91] by some studies. Some others did not find a significant presence of these antibodies.[92,93]

For many of these thrombophilic disorders, the required treatment is anticoagulation or agents that reduce platelet aggregation. But ironically, antithrombotic therapy, in the form of aspirin and warfarin use has also been found to be risk factor for CRVO.[94]

Two recent published reviews analysing hypercoagulable states and retinal vein occlusions concluded that extensive testing for thrombophilias is not warranted

in the vast majority of patients with central retinal vein occlusion. Older patients with any of the common vascular risk factors do not require thrombophilic screening.[95]

However, when tests for common cardiovascular risk factors for RVO are negative, evaluation for potential coagulation disorders may be indicated, particularly in young patients and in patients with bilateral RVO, a history of previous thromboses or a family history of thrombosis.[96]

INCREASED PLASMA VISCOSITY-

Plasma viscosity can be increased by either an increase in formed elements in the blood, such as red or white blood cells, or by an abnormality of serum protein[45]. Increased plasma viscosity in RVO has been reported to play a role in CRVO pathogenesis.[97,98] It has been found to be significantly higher in patients with BRVO[99]. High packed cell volumes or hematocrit are associated with high viscosity. High hematocrit has been found to be associated with CRVO[97] and BRVO[99]. There are case reports of CRVO with multiple myeloma[100] and Waldestrom's macroglobulinemia.[101]

Many other anecdotal case reports have described RVO in many other systemic conditions like Grave's disease[102], Crohn's disease[103], oral contraceptives[104,105], sarcoidosis[106], syphilis[107], pulmonary tuberculosis[108], carotid cavernous fistula[109,110], hepatitis B vaccination[111], HIV[112], renal failure[98], and systemic lupus erythematosus.[113]

In conclusion, a whole host of local and systemic factors acting in different combinations and to different extents may produce the vascular occlusion. In such a multifactorial scenario in various types of RVO, a particular factor or combination of

factors may be present in one case and not in another, or a factor may play a major role in one and only a subsidiary one in another. Moreover, the role of the various factors may vary, with some as predisposing factors and others as precipitating ones in one group and vice versa in another.[27]

DIFFERENCES BETWEEN ISCHEMIC AND NON- ISCHEMIC CRVO-

While the diagnosis of CRVO is not difficult, the main problem is differentiation of non-ischemic from ischemic CRVO. This differentiation is crucial in the correct management of CRVO because non-ischemic CRVO (NICRVO) is a comparatively benign condition but ischemic CRVO (ICRVO) is often associated with serious blinding complications. Various clinical tests used for the differentiation can be divided into morphological and functional tests.

FUNCTIONAL TEST-

These are visual acuity, visual fields plotted with Goldmann perimeter, relative afferent pupillary defect (RAPD) and electroretinography (ERG).

1. Visual Acuity

The visual acuity findings in both types of RVOs are summarised below[114]. Visual acuity of 6/120 or worse in ischemic CRVO gave the best sensitivity (91%) and specificity (88%) during the first 3 months of CRVO in differentiation of ischemic from non-ischemic CRVO. Thus, if the visual acuity during the acute phase of CRVO is better than 6/120, it is in all likelihood a non-ischemic CRVO (in 88%), but the opposite is not necessarily true.

Since visual acuity is influenced by the various types of macular lesions (e.g., edema, hemorrhages, cystic changes and ischemia), it can be markedly reduced even when the rest of the retina may be non-ischemic and functioning normally. If the media is hazy due to cataract or vitreous opacities, or there are optic nerve lesions or macular degeneration or amblyopia, then visual acuity does not give reliable information[27]

Visual Acuity	NICRVO	ICRVO
Better than 6/60	58%	1.7%
Less than 6/120	19.1%	93.3%

2. Perimetry:

Visual field plotting with a Goldmann perimeter is far more helpful in differentiation of the two types of CRVO than a standard 30° automated perimeter. This is because the latter provides information about the central field only and not the peripheral fields extending up to 70-80°.[114]

3. Relative afferent pupillary defect (RAPD)

This simple test is a highly useful and reliable functional test in differentiation of ischemic from non-ischemic CRVO. The RAPD is recorded in log units of neutral density filters.

The sensitivity and specificity of the RAPD for detection of ischemic CRVO are 88% and 90%, respectively, when RAPD of > 0.70 log units of neutral density

filters is used as a cutoff; and 80% and 97%, respectively, when RAPD > 0.90 log units is used as a cutoff.

RAPD has many advantages over fluorescein fundus angiography and ophthalmoscopy, including the following[27]:

a. RAPD gives reliable information (with much higher sensitivity and specificity) at the earliest stages of CRVO and throughout the course of the disease. The duration of the CRVO appears to have no statistically significant influence on RAPD.

b. RAPD provides reliable information in spite of hazy media.

c. RAPD (like the other functional tests) can detect conversion of non-ischemic to ischemic CRVO very early (within days), when morphological tests usually give little indication.

d. It is a non-invasive test, easy to perform as a part of routine eye examination, inexpensive, readily available and objective.

RAPD, however, like other tests, has limitations, including the following[27]:

a. To test for RAPD, it is essential to have a normal fellow eye, and normal optic nerves and pupils in both eyes, therefore this test cannot be performed on eyes using miotics or other drops affecting the pupils, nor when there is any optic nerve disorder in either or both eyes, nor when the fellow eye is abnormal.

b. The amount of RAPD is influenced by the size of central scotoma because it is modified more by the number of retinal ganglion cells involved than by the area of the retina[115].

Thus, a patient with a large, dense central scotoma associated with marked macular edema due to non-ischemic CRVO would show a larger RAPD than otherwise expected.

4. Electroretinography (ERG)

This is also an objective functional test. The parameter with the best sensitivity (80-90%) and specificity (70-80%) in such a differentiation was the amplitude of the b-wave (both photopic and scotopic)[115]. ERG has the same advantages as RAPD except that it is not so easy to perform during a routine eye examination, requires expensive equipment, and is not as readily available. However, it has a distinct advantage over RAPD testing in that it does not require a normal fellow eye, normal pupils or normal optic nerve.

If the information provided by ERG (i.e. b-wave amplitude of 60% of the normal mean value in both photopic and scotopic ERG) is combined with that provided by RAPD (> 0.70 log units), it was helpful in differentiating 97% of the CRVO cases.[115]

MORPHOLOGICAL TEST-

These consist of: ophthalmoscopy and fluorescein fundus angiography. Ophthalmologists almost universally use ophthalmoscopic and fluorescein angiographic appearances to evaluate and manage CRVO and to differentiate ischemic from non-ischemic CRVO.

1. Ophthalmoscopy

There is virtually a continuous evolution of ophthalmoscopic lesions in CRVO. The following findings are commonly used to differentiate ICRVO & NICRVO:

a) **Retinal hemorrhages:** These are an invariable finding in CRVO. The most diagnostic feature of hemorrhages in CRVO is their location in the peripheral retina, seen best on indirect ophthalmoscopy. The only ophthalmoscopic parameter to show reasonable sensitivity (81-84%) and specificity (72-74%) in differentiation of the two types of CRVO was the presence of more extensive hemorrhages in posterior retina in ischemic CRVO than in non-ischemic CRVO during the first 3 months of the disease only; and there was no statistically significant difference between the two types of CRVO in the amount of retinal hemorrhages after that period[114]. However, the hemorrhages vary markedly not only from eye to eye (in both ischemic and non-ischemic CRVO) but also with time since onset.

For example, in eyes with ischemic CRVO, although there are usually extensive hemorrhages during the early stages of disease, there may be minimal hemorrhages during its very early phase (i.e., within a day or so after the onset), increasing in severity over the following days and weeks, and starting to resolve after about 6 months. Non-ischemic CRVO associated with extensive retinal hemorrhages is not a rarity.[27]

b) **Cotton-wool spots:** These represent focal inner retinal ischemic spots and are constantly evolving. Cotton-wool spots, which have always been regarded as diagnostic of ischemic CRVO, did not show high enough sensitivity and specificity to help in differentiating the two types of CRVO, since non-ischemic CRVO can also have some cotton-wool spots.[114]

2. FUNDUS FLUORESCEIN ANGIOGRAPHY (FFA)

For differentiation of ischemic from non-ischemic CRVO, retinal capillary obliteration is the fundamental information required from angiography. The characteristic features seen are a delay in arteriovenous transit time, blocked fluorescence due to hemorrhages, and retinal capillary non-perfusion. Factors associated with risk of neovascularisation include an arteriovenous transit time of more than 20 seconds[116] and presence of capillary non-perfusion.[117]

There are no definite criteria for assessing the risk of neovascularisation, however, the Central Vein Occlusion Study used 10 disc diameters of non-perfusion as its cut-off for predicting risk.[30]

However, during the early stages of CRVO, angiography has many serious limitations in providing this information, including the following: (a). Fluorescein angiography fails to provide the required information on the retinal capillary non-perfusion in at least one third of the patients[114] due to extensive retinal hemorrhages, poor quality angiograms (from hazy media, poor circulation, inadequate pupil dilation) or inability to perform angiography.(b). Even when retinal capillaries are satisfactorily seen on fluorescein angiograms, the findings may be misleading because: i) Retinal capillary obliteration is a progressive phenomenon. Available evidence indicates that it takes at least 3-4 weeks, often longer, after the development of ischemic CRVO, for retinal capillaries to be obliterated[118] so that if a patient is seen during the first 2-3 weeks after the onset of ischemic CRVO, fluorescein angiography may show perfectly normal filling of the retinal capillaries inspite of retinal ischemia. Some eyes with mild ischemic CRVO may develop slowly progressive retinal capillary obliteration many months or even years after the onset of CRVO. Under these circumstances, the initial observation of normal retinal capillary

perfusion may mislead one into believing that this is non-ischemic CRVO when it is in fact ischemic. ii) It is well established that in various retinopathies associated with retinal capillary obliteration, e.g., diabetic retinopathy, ischemic CRVO, BRVO and others, the retinal capillary obliteration starts first in the peripheral retina and then slowly progresses towards the posterior pole.

Therefore, standard fluorescein fundus angiography covering usually only the central 30°, and rarely 60°, of the posterior pole (i.e. optic disc and macular region) may provide no information about the peripheral retina. Sampling by a standard 30° (sometimes even with a 60°) angiography may reveal almost normal capillary perfusion at the posterior pole when in fact the retina may have extensive peripheral retinal capillary obliteration[27]. (iii) Even if there are perfectly satisfactory angiograms, there can be problems in their evaluation. Welch and Augsburger[119] studied reproducibility and accuracy of eight retinal specialists in assessing the extent of retinal capillary nonperfusion on fluorescein angiography in CRVO and found that the proportion of agreement with the correct classification was less than 60% for all the specialists.

In conclusion, none of the above 6 tests have 100% sensitivity and specificity in differentiating the two types of CRVO during the early acute phase, so that no one test can be considered a "gold standard". The 4 functional tests proved to be overall much superior to the two morphologic tests in differentiating ischemic from non-ischemic CRVO: with RAPD most reliable in uniocular CRVO.[114]

METHODOLOGY

This was a one year cross sectional study conducted in the Department of Ophthalmology from January 2012 to December 2012 to study hypertension and hyperlipdemia and also other systemic and ocular risk factors in patients with retinal vein occlusion.

SOURCE OF DATA – All patients diagnosed with retinal vein occlusions attending ophthalmic OPD and IPD at KLES Dr. Prabhakar Kore Hospital and MRC, Belgaum were included in the study. The procedure and investigations were explained to the patients and informed written consent was taken.

Method of collection of data-

Study Design- Cross- sectional study

Sample Size-40

Taking 64% Prevalence of major risk factor i.e Hypertension in Retinal Vein Occlusion

$n=4pq/d^2$

p=64

q=36

d=15%(Absolute Error)

95% confidence

Sample Size = 41~40

Duration:

One year.-1st JAN 2012 –31st DEC 2012

A total of 40 patients who fulfilled the following inclusion criteria were included in the study.

Inclusion criteria:

- Patients who are detected as having any type of Retinal Vein Occlusion on fundus examination in the OPD.
- Old cases of Retinal Vein Occlusion, treated or untreated.
- Cases referred to KLE's Hospital and MRC Belgaum, diagnosed with Retinal Vein Occlusion

Exclusion criteria:

1. Retinal Vein Occlusion secondary to vasculitis . For e.g. Eales' disease, sarcoidosis etc.

Methodology:

All patients who satisfied any one of the inclusion criteria formed the subjects of the study. The patients were enrolled in the study and informed consent was taken by the investigator.

1. Demographic parameters such as age, sex, occupation and address were noted.
2. Detailed history was obtained with emphasis on-

- Pattern and duration of visual loss.

- Transient visual disturbance, if any

- Patient was enquired regarding history of Hypertension, Hyperlipidemia, Diabetes mellitus, Cardiovascular diseases, smoking ,ocular diseases and other risk factors such as any form of blood dyscrasias .

- The treatment History was also noted.

3. Thorough family and personal history was obtained

4. Visual acuity was measured by Snellen's Chart and best corrected visual acuity was given.

5. A complete anterior segment examination was done under slit Lamp biomicroscopy.
6. Detailed Fundus examination was done with Direct and Indirect Ophthalmoscopy.
7. Fundus photography was taken in the retina clinic.
8. Fundus Fluorescein Angiography(FFA) was done only in patients who gave consent for the procedure and those who were fit for the procedure.
9. BP was recorded by manual sphygmomanometer(average of 3 reading) in the right arm supine position and was graded as follows.

Category	'Systolic' Pressure in mmHg	'Diastolic' Pressure in mmHg
Stage I	140-159	90-99
Stage II	>160	>100

10. Weight in kilograms and Height in meters was measured (for calculating Body Mass Index – BMI)
11. IOP measurement of both eyes was done by Schiotz Tonometry
12. Axial Length measurement was done of both eyes by A-scan ultra-sonography.

All the measurements were made by the same observer and using the same instrument.

Following Laboratory investigations were done:

1. Blood Glucose (fasting).
2. Complete Lipid Profile.
3. Complete Blood Counts .
4. Erythrocyte Sedimentation Rate (ESR).
5. Blood urea and serum creatinine.

STATISTICAL METHOD

Distribution of demographic, clinical pattern and risk factor profile were noted. Comparison of hypertension and smoking in the combined group of CRVO and HCRVO with BRVO was calculated using chi square test. Comparison of axial length between the affected and unaffected eye was done using the student t test.

DISCUSSION

Retinal vein occlusion is the second most common retinal vascular disease following diabetic retinopathy. Many systemic and ocular diseases are risk factors for the development of retinal vein occlusion. In the present study we studied patients of retinal vein occlusion for the risk factor profile and elaborated each of the risk factor in detail.

The present study included 40 patients of RVO who met the inclusion criteria.When the age distribution was studied in 40 patients, the youngest patient was of 35 years and the oldest was of 90 years. The mean age of the studied population was 60.27 ± 11.7 years. This was similar to the Hisayama study[122] in which the mean age of RVO patients was 67 ± 7 years.

Ning Cheung et.al[13] in their study showed that prevalence of RVO increases with age. Prevalence of atherosclerotic risk factors also increases with age with most of people being affected after the 6th decade of life. Increased age may reflect the cumulative effects of many factors leading to the development of RVO.

Though the prevalence of RVO is equal in both sex, few studies have shown the prevalence to be more in men. In the present study the prevalence of BRVO was seen in 60% of males as compared to 40% female and also in the combined group of CRVO and HCVO the distribution was seen as 73% of males and 27% of female. This was similar to the Hisayama study[122] .

Finding from most of the studies[50-51] show that BRVO, most frequently involves the superotemporal quadrant. This may be due to the more frequent A-V

crossing in the supero-temporal quadrant and proximity of A-V crossing to the disc[27]. The superotemporal quadrant vein occlusion causes a greater macular edema than RVO elsewhere, and are more symptomatic leading to presentation bias. In our study, almost equal number of patients with incident BRVO, occurred in superotemporal and inferotemporal quadrant.

FFA was done in 16 patients and macular ischemia was seen in 10/16 patients. Superotemporal BRVO was seen in 28% patients, Inferotemporal BRVO in 32% patients and 3% of cases occurred outside the temporal quadrant. This was similar to that seen in the Blue Mountains study.

22% of patients had CRVO and 5% of patients had HCVO.

Atherosclerotic risk factors cause sclerotic changes in the structures adjacent to the Central retinal vein, and secondary endothelial proliferation in it (within the optic nerve), causing narrowing of the lumen of the central retinal vein. This produces circulatory stasis and thrombus formation leading to the occlusion. Also, hemodynamic disturbances on the arterial side play a role in the development of the thrombosis[27].

Atherosclerotic changes and arterio-venous crossing of retinal branch vessels play an important role in development of BRVO. Sclerotic retinal arterioles compress the accompanying vein because of a common thickened, adventitial and glial sheath[27].

In this study it was found that, among the patients with RVO, 78%(31/40) had hypertension . This was similar to that found by Hayreh et al[11] in their study. The Eye Disease Case-Control studies[15-17] also found a similar prevalence in all 3 types of RVOs – CRVO, HRVO and BRVO. These studies recommended treatment of

hypertension as a strategy to prevent RVO. All other studies have also reported a highly significant prevalence of hypertension (HTN) in RVO patients[11-18].

An important fact found in this study was the high percentage (47.5%) of previously undiagnosed or unknown hypertensives. No other study comments on this aspect. All major studies have been done in western developed countries where patient awareness and a good health care infrastructure combine to screen, diagnose and treat HTN early. In a developing country like India, the primary health care infrastructure and national health programmers still focus on killer, communicable diseases. In a rural community like ours, preventive health aspects like screening and early detection are practically non-existent. This may account for the finding that a majority of the patients having high B.P, are diagnosed as HTN only after they present to the ophthalmologist with an RVO. Another finding in the study was equal number of stage I and stage II hypertensives. This shows that prevalence of RVO was seen equally in both stages of hypertension.

Studies have shown strong and known association of hypertension and related focal arteriolar abnormalities with RVO. Retinal arteriolar signs such as arteriovenous nicking and focal narrowing represents established microvascular damage caused by long standing elevated blood pressure[7]. In the present study, according to the arteriosclerotic grading system, 55% (22/40) of patients had grade II arteriosclerotic changes (A-V crossing changes). Among these 22 patients 46% had Gunn's sign ,36% had Salu's sign and 18% had Bonnet's sign. This indicated that hypertensive patients who develop Gunn's sign have to be followed carefully for the development of retinal vein occlusion.

In the present study, the prevalence of diabetes mellitus is 40% (16/40). This was almost similar to that found by Hayreh et al[11] done in Iowa, USA. Of these diabetic patients, 35% were diagnosed as having diabetes after presenting with RVO at our hospital. It again reflects poor patient awareness and below par motivation of the health care providers .All patients who were diabetics were also hypertensives.

Many studies'[13,18] have shown associaion between RVO and hyperlipidemia . In the present study the prevalence of hyperlipidemia in patients with RVO was 30%(12/40) which was similar to other studies. However it was less compared with the prevalence of hypertension . A meta-analytic study by O'Mahoney et al showed 2.5times higher risk of retinal vein occlusion in patients with hyperlipdemia[12].

Another contributor to atherosclerosis is Smoking/ tobacco chewing which was seen in 57.5% of the patients of total patients with RVO, which was similar to The Eye Disease Case-Control Group[15-17] in which the prevalence of smoking was found to have significant association with RVO. The Beaver Dam study[6] has shown association of RVO with smoking. This may, in part, be explained by the inflammatory stimulus and atherosclerotic changes seen in smoking.

Among the 22.5%(9/40) non hypertensive patients 56%(5/9) of patient were smokers and 34%(3/9) had deranged lipid profile attributing smoking and hyperlipdemia as risk factors for RVO after HTN .

In the sample, 9 (24%) patients were smokers who were also hypertensive and diabetics, 7 (18%) others were smokers and hypertensives, This may depict that patients with multiple risk factors may have an increased risk of developing RVO.

The study done by Hayreh et al[11] showed a greater prevalence of arterial hypertension in BRVO patients when compared with the combined group of CRVO and HCVO (P=<.0001). In the present study, the prevalence of hypertension in both the groups was the same and no such association was seen (p=0.44) .

Similarly in Hayreh et al[11] study, the prevalence of smoking was greater in BRVO patients when compared with the combined group of CRVO and HCVO. In the present study, there was no difference in prevalence between the two groups.

In our study 52.5%(21/40) patients had BMI more than 25 which was in agreement with other studies like The Eye Disease Case-Control Studies[15-17]and that done by Wong et al[14],which showed Body Mass Index (BMI) could be associated with RVO.

Hematologic abnormalities can produce stagnation of the flow in the vein and result in thrombus formation in susceptible eyes. When haematological testing was performed to evaluate the complete hemogram, we found hemogram deranged in only one patient (anemia). Though few studies have suggested an association between RVO and blood viscosity as measured by hematocrit[97,99], no large studies have proven this association. Another reason for why hemotological evaluation proved to be of less usefulness, was that we could not examine the complete coagulation profile of patients as was done in many other studies.

In the study done by Cheung et al[13], the incidence of abnormal KFT was marginally higher in patients with RVO. In the Beaver Dam Eye Study persons with elevated creatinine levels were shown to have 60% higher risk of RVO. RVO and nephropathy are both closely related to hypertension, and one may expect this

association to be due to concomitant damage to the renal and retinal vasculature. However In the present study only one patient had abnormal KFT in the form of increased serum urea and creatinine.

Erythrocyte Sedimentation Rate (ESR) was found to be higher in 28% of RVO patients. This was in accordance with that found with Appaiah et al[121]. The Eye Disease Case-Control Study[15] found that an increased ESR was significant in women only. When a gender analysis of ESR positive patients was done, no such finding was noted. However ESR being an easily available and routinely done test, may be performed in all patients with RVO to look for signs of systemic inflammation. Whether this influences the current management of RVO, is a subject of further interventional studies.

In the present study, 35% (14/40) patients had abnormal disc findings which included glaucomatous disc, neovascularisation of disc(NVD) or disc odema, among which 1 patients was found with glaucomatous disc , and 2 patients with NVD and Most of the others had disc edema and /or hyperaemia.

Hayreh et al in his study showed raised IOP in patients with RVO. In the present study 15%(6/40)patients had increased IOP. The Blue mountain eye study did not find significant association between retinal vein occlusion and IOP during the 10 year follow up study.

As reported by Kumar et al[58] and others[57,59], we also found a shorter axial length to be a highly significant factor for the development of RVO. A hyperopic refraction and a shorter axial length have been thought to predispose to development of RVO, due to presence of a smaller scleral canal and narrow available passage for

the central retinal vessels. But when diseased and non-diseased eyes of same patient were compared with respect to axial length in unilateral cases, it was found that there was no significant disparity. This means, that if a shorter axial length is a risk factor then the other eye may also be predisposed to develop RVO in the future which should alert the ophthalmologist.

In the present study, 5(12.5%) patients had hypertension and 5(12.5%) had smoking as the only risk factor. 7(17.5%) patients were hypertensive as well as smokers and 2 (5%) had diabetes and hypertension together. Maximum number of patients 9(22.5%) suffered from diabetes, hypertension and were smokers also. Risk factor profile of most of our subjects suggests a multifactorial etiology rather than pointing towards a singular risk factor in particular.

In this study we have made a sincere effort to describe risk factors in patients with RVO, however our sample size was limited. Due to the cost factor involved, other risk factors could not be studied. In the current study the risk factor were described in detail and our finding matched with many other similar studies that had given these associations and had a control group.

CONCLUSION

In the present study a detailed evaluation of the risk factors for RVO was carried out and risk factor profiling of the RVO patients was done.

The pathogenesis of retinal vein occlusion is multifactorial process and there is no single risk factor that causes RVO. Some risk factors predispose an individual or an eye to develop retinal vein occlusion and others act as an adjuvant to the final insult to produce a clinically evident disease .

In the multifactorial etiological scenario of retinal vein occlusions, systemic factors like hypertension, diabetes, smoking , hyperlipidemia etc play an important role. An extensive laboratory work up to look for risk factors is not useful in all cases. Public health measures for prevention, early diagnosis and proper treatment of these conditions may help prevent retinal vein occlusions, and also reduce the morbidity and mortality due to these diseases in the population.

SUMMARY

- One year cross-sectional study was done to evaluate hypertension and hyperlipdaemia as risk factors in patients with retinal vein occlusion was studied at KLES Dr Prabhakar Kore Hospital and MRC , Belgaum. Other risk factors like Diabetes Mellitus , smoking, obesity, ocular factor were also studied .

- A total of 40 retinal vein occlusion patients fulfilling the inclusion criteria were included in the study .

- Mean age of patients was 60.27±11.7 years. 65% were males and 35% were females. There were more number of males in the present study.

- Hypertension was the most common risk factor seen in 77.5% of the patients. A majority of the hypertensive patients were hitherto unknown hypertensives. 55% of patients had grade II atherosclerotic changes with majority having gunn's sign.

- Diabetes mellitus was seen in 40% of the patients. Of these diabetic patients , 35% were diagnosed as having diabetes after presenting with RVO at our hospital. Hyperlipidaemia was seen in 30% of patients. 58% of patients were smokers.

- Another risk factor found in patients with retinal vein occlusion in this study is raised ESR, seen in 28% of patients.

- Among the ocular risk factors, there was no significant difference between axial length of the affected and unaffected eye, neither was any increased intraocular pressure noted in eyes with RVO.

- An abnormal kidney function tests and a deranged hemogram was seen in a very few of our patients.

- In the present study, 5(12.5%) patients had hypertension and 5(12.5%) had smoking as the only risk factor. 7(17.5%) patients were hypertensive as well as smokers and 2 (5%) had diabetes and hypertension together. Maximum number of patients 9(22.5%) suffered from diabetes, hypertension and were smokers also.

- Present study supports a multifactorial etiology of RVO, with predominance of atherosclerotic factors, rather than pointing towards a singular risk factor.

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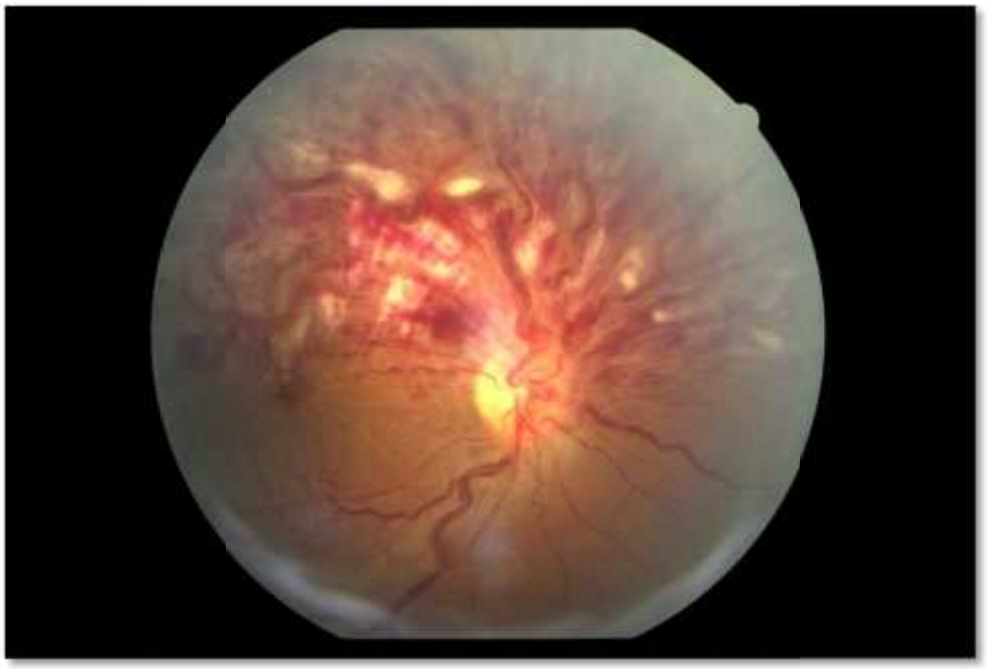


Figure 1. HEMICENTRAL VEIN OCCLUSION

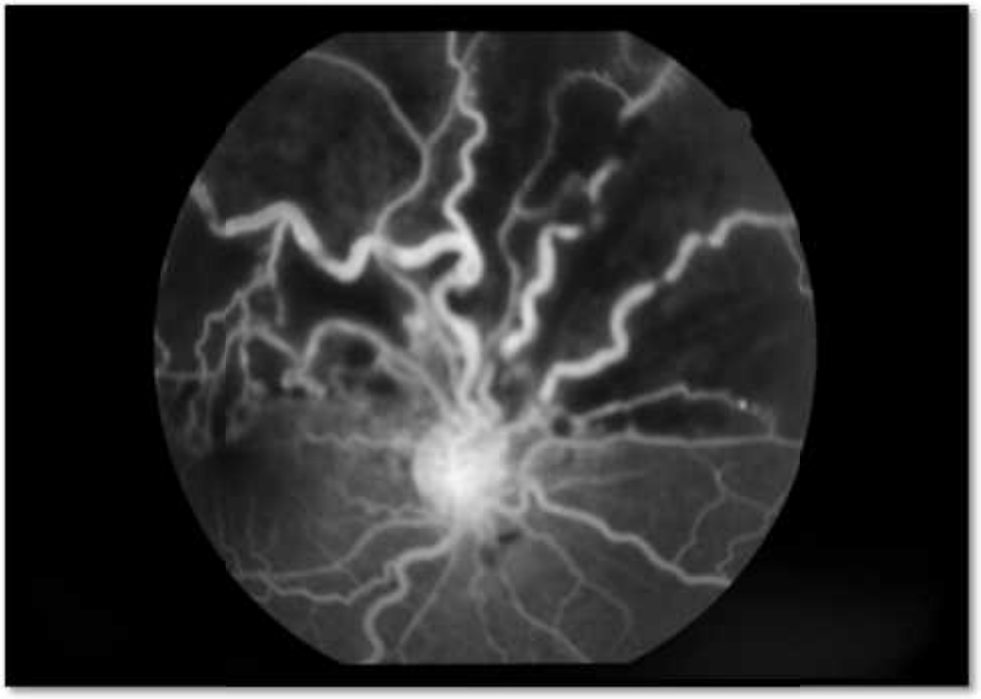


Figure 2. FFA OF PATIENT WITH HEMICENTAL VEIN OCCLUSION SHOWING AREAS OF NON- PERFUSION.

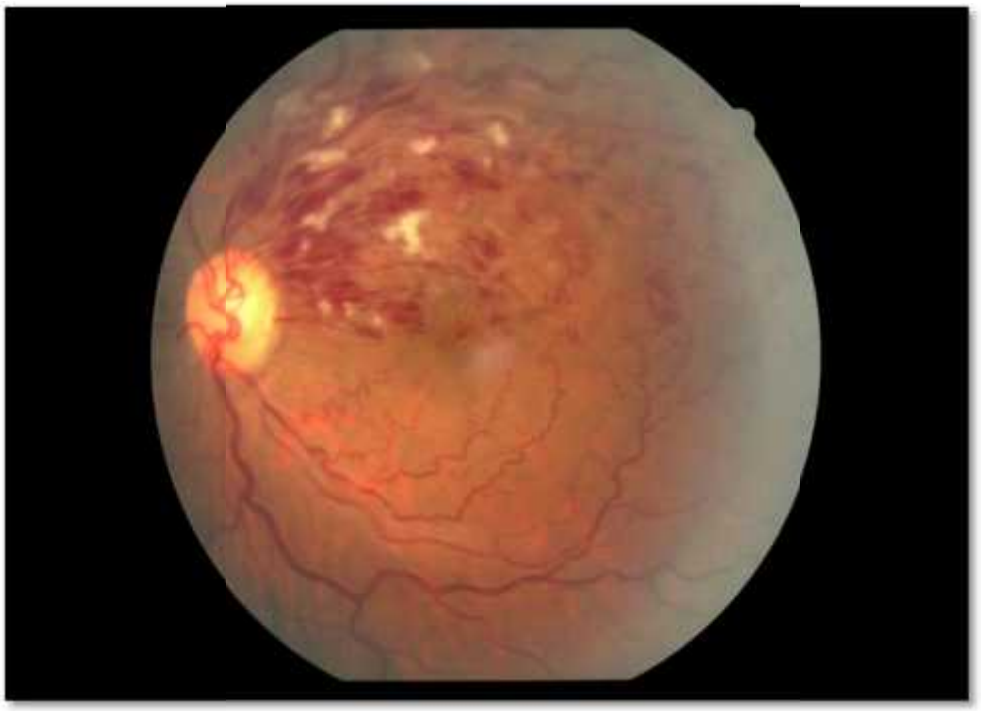


Figure 3. SUPEROTEMPORAL BRANCH RETINAL VEIN OCCLUSION

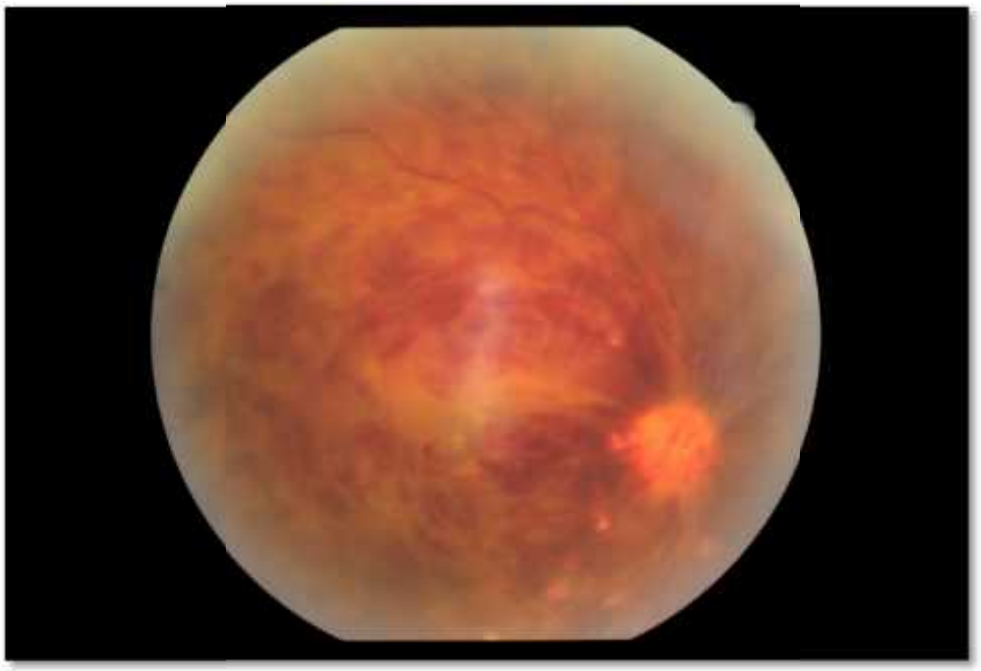


Figure 4. ISCHAEMIC CENTRAL RETINAL VEIN OCCLUSION

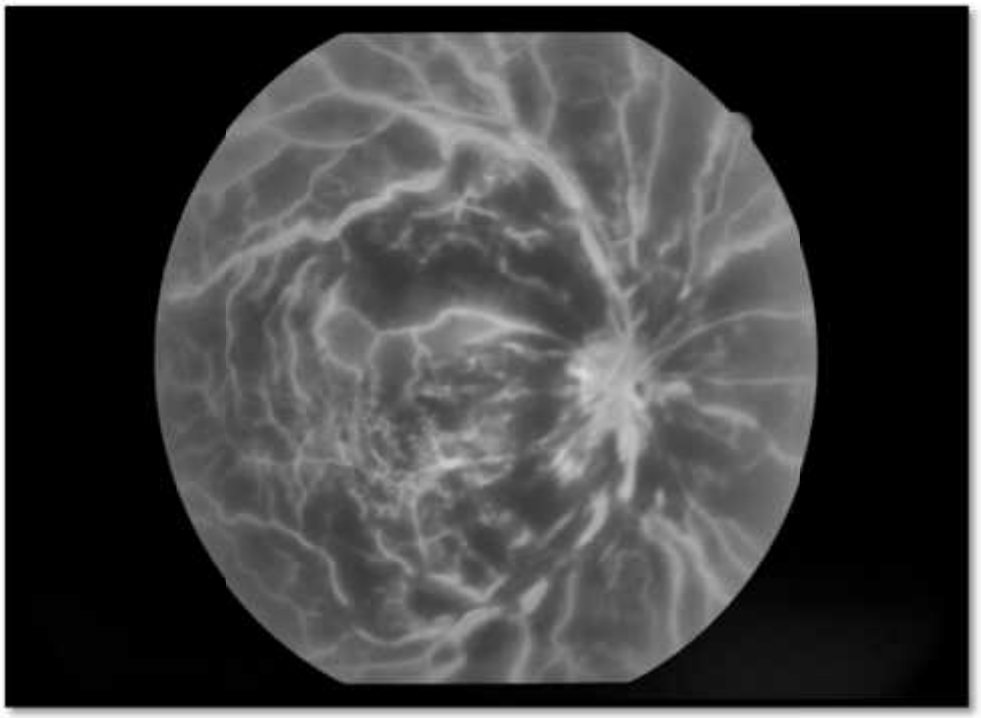


Figure 5. FFA OF ISCHEMIC CENTRAL RETINAL VEIN OCCLUSION SHOWING AREAS OF NON PERFUSION.

Figure 6. FUNDUS PHOTOGRAPH BEING TAKEN IN THE 'RETINA CLINIC'.

Figure 7. SLIT-LAMP BIOMICROSCOPY

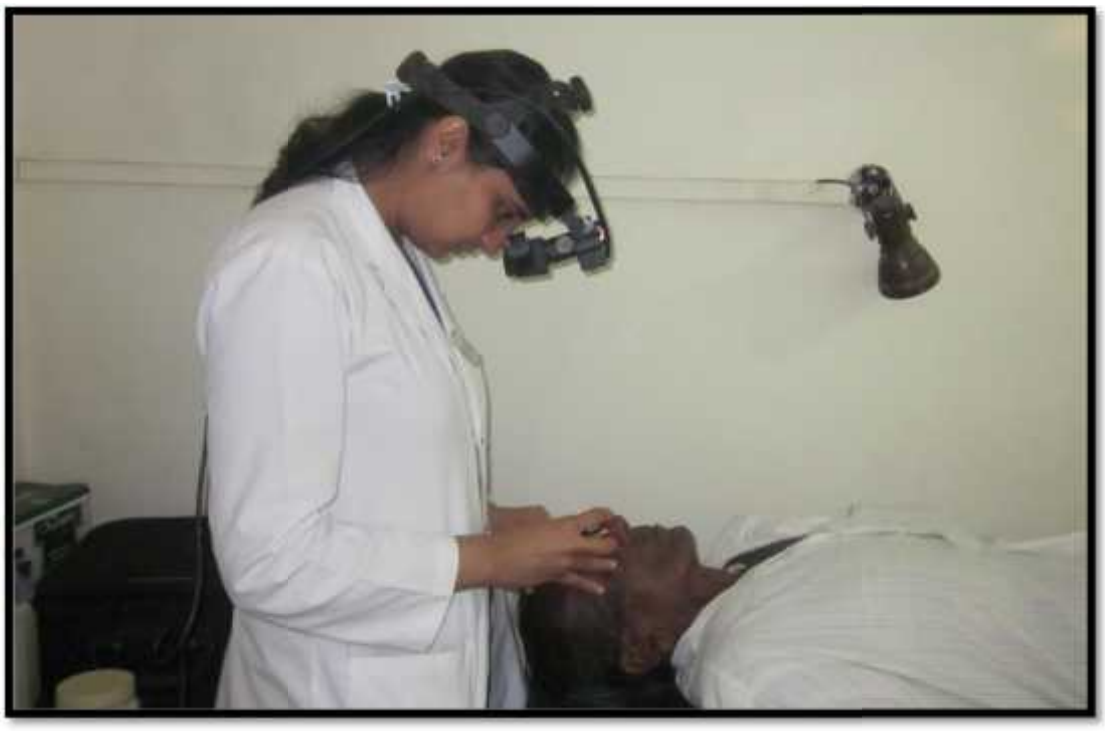


Figure 8. INDIRECT OPHTHALMOSCOPIC EXAMINATION

ANNEXURE II

CONSENT FORM

INFORMED CONSENT DOCUMENT

ID NO: | | | | | |

Consent for participation in a study titled **"HYPERTENSION AND HYPERLIPIDAEMIA AS RISK FACTORS IN RETINAL VEIN OCCLUSIONS PATIENTS –ONE YEAR CROSS – SECTION SYUDY**

Principal Investigator (PI) – REG. NO.BK0111002.

You are requested to be a subject in a research study title-" **HYPERTENSION AND HYPERLIPIDAEMIA AS RISK FACTORS IN RETINAL VEIN OCCLUSIONS PATIENTS –ONE YEAR CROSS – SECTION SYUDY**

conducted between January 2012 and December 2012. Dr ----------, a post graduate student in Department of Ophthalmology at J.N. Medical College, Belgaum, is the principal investigator of this study, under the guidance of Dr. S B Patil, Professor, Department of Ophthalmology, J.N. Medical College, Belgaum.

Introduction and Purpose of the study:

Retinal vein occlusion risk factors are on the rise, therefore the prevention, diagnosis and

management of the final disease is also bound to become a significant issue.The present study aims to describe the risk factor profile of the patients presenting with retinal vein occlusions seeking care in our hospital.

Notwithstanding its methodological limitations, it may pave way for more detailed analytical and experimental studies later.

Procedures involved:

Patients fulfilling the inclusion criteria for retinal vein occlusion, either admitted in the Ophthalmology ward or attending the out patient clinic of KLES Prabhakar Kore Charitable Hospital and MRC, will be asked to participate. If you agree to participate in this study, you will be asked to answer some questions pertaining to your present ailment, relevant past and family history. After this a local anesthetic solution will be applied to your eyes. The intra ocular pressure will be measured by placing an applanation tonometer on your cornea. A probe will also be placed on your cornea and the axial length of your eyeball will be measured. After this 3 ml of blood will be collected under strict aseptic precautions and subjected to various tests. FFA will be done as and when required.

Fluorescein, 5ml of 10%solution will be injected intravenously and photographic surveillance of the passage of Fluorescein through the retinal and choroidal circulation will be seen.

Risks and benefits:

Slight and tolerable amount of pain will be experienced when the blood is drawn, but there will be no other risk to you by participating in this study. The results of this study may help us assess the risk factors for retinal vein occlusion.

Alternative:

Your participation in this study is totally a voluntary decision. If you choose not to participate, it will not affect the care given to you during your present admission or your future relationship with KLES Dr. Prabhakar Kore Charitable Hospital & MRC. You are free to discontinue at any time and for any reason.

Privacy and confidentiality:

Confidentiality will be maintained. You will be given a special ID number and the same will be used for study purpose. Only Dr. ---------- will have access to the information.

Institutional/Sponsors policy:

In the unlikely event of any procedure related complication, you will be treated in the KLES Prabhakar Kore Charitable Hospital and MRC free of cost.

Financial incentives for participation:

You will not be offered any financial incentives / remuneration for participating in the research.

Authorization to publish results:

When the results of the research are to be published or discussed in conferences by the PI, no information will be disclosed that will reveal your identity.

Contact information in case of any queries:

In case of any questions, you may contact Dr. P. V. Patil, Chairman of J N Medical College, Institutional Ethics Committee, J N Medical College, Ph. No. 0831 2471350

STATEMENT OF CONSENT:

I, Mr/Mrs./Ms. _____ have read / have been read to me and have completely understood the entire information given in the consent form which explains all the details of the study like the purpose, procedure involved, risks & benefits, privacy & confidentiality, incentives and the authorization to publish the results of the study. My signature in the space provided for signature below indicates that I have voluntarily agreed to participate in the study. I may withdraw my participation for any reason or may be withdrawn by the investigator from the study for any reason at any time. I am not giving up any of my legal rights by signing this consent form. I will be given a copy of this consent form.

Signature / Thumb impression of the participant

(or parent in case of minors under 18 years) _____

Name of the participant (or parent in minors): _____

Signature of the witness: _____

Name of the witness: _____

Signature of the Investigator: _____

Name of the investigator: _____

Date: _____

ANNEXURE III

PROFORMA

Patient Details

Date : / /

Name :		
Address:		
Age :	Sex:	Occupation:
IP No.:		Other details:

Chief complaints:

PRESENTING COMPLAINTS

1.Diminution of vision (tick whichever is applicable)

(1 - Right eye, 2 - Left eye, 3 - Both)

Sudden Distant progressive ive

Gradual near Non Progressive

Painful

Painless

Duration

2.Loss of Visual Field (1-yes,2-no)

If yes specify location (_____)

3.Floaters. (1- Yes, 2- No)

4.Transient Visual Disturbance (1-present, 2-absent)

5.Any others-pain, redness, watering etc. (describe)

6.H/o wearing spectacles [ ] (1 - Yes, 2 - No)

[ ] 1 - distant, 2 - near, 3 both)

If yes, Duration

PAST HISTORY

1.Previous afflictions same eye / opposite eye [ ] (1 - yes, 2 - no)

2.If yes – Nature of treatment (Nil / Drugs / Lasers / Surgery)

3.Past H/O ocular trauma / surgery [ ] (1 - yes, 2 - no)

4.Past H/O Glaucoma OR glaucoma medications [ ] 1 - yes, 2 - no)

H/O SYSTEMIC DISEASES

1. Hypertension - [ ] - yes, 2 - no)

If Yes – Duration

Treatment

2. Diabetes Mellitus – [ ] -yes,2-no)

If Yes- Duration

Treatment

3. Hyperlipidemia – [ ] -yes,2-no)

If Yes – Duration

Treatment

4.Blood diseases – Anemia, eosinophilia, leukemia, etc. [ ] (1-yes,2-no)

If Yes – Duration

Treatment

5.Cardiac diseases – Valvular heart diseases, IHD etc. [ ] -yes,2-no)

If Yes – Duration

Treatment

PERSONAL HISTORY: [ ] - yes, 2 - no)

1.Smoking

2.Alcoholism

3.Exercise

4.tobacco

FAMILY HISTORY : (1 - yes, 2 - no) If yes, specify

1.Similar affliction in the family.

2.Family H/O Hypertension

Diabetes Mellitus

Heart disease

Blood diseases

3.Family H/O Glaucoma

II) EXAMINATION

GENERAL PHYSICAL EXAMINATION

1.pulse : / minute

2.B.P: / mm of Hg

3.RR / minute

4.Pallor ☐ 1 – present, 2 – absent

5.Oedema ☐ 1 - present, 2 – absent

6.Lymphadenopathy ☐ 1 – present, 2 – absent

7.Icterus ☐ 1- present, 2 - absent

8.Clubbing ☐ 1- present, 2 – absent

9.Cyanosis ☐ 1 – present, 2 - absent

B.M.I. = Weight(in kg)/Ht^2(in metres) =

OCULAR VARIABLES	**Right eye**	**Left eye**
1.Visual acuity	☐	☐
a.With Pinhole	☐	☐
b.With spectacles	☐	☐
c.Near vision	☐	☐
2.Adenexa		
(1 - normal, 2 – abnormal. If 2 specify)	☐	☐
3.Conjunctiva		
(1 - normal, 2 - congested)	☐	☐

	Right eye	**Left eye**
Cornea		
(1 – normal, 2 – abnormal. If abnormal specify)	☐	☐
Sclera	☐	☐

(1 – normal, 2 – abnormal. If abnormal specify)

Anterior chamber

(1 – normal, 2 – shallow, 3 - deep)

Iris

(1 – normal, 2 – abnormal. If abnormal specify)

If NVS present, mention clock hour

Pupil

a. Size (1 - normal, 2 - miotic, 3 - mydriayic)

b. Shape (1 - normal, 2 - irregular)

c. Reaction (1 - present, 2 - absent)

d. Afferent papillary defect (1 - present, 2 - absent)

Lens

(1 – normal, 2 - cataractous)

Refraction correction

RE	sph	cylin	axis	sph	cyn	axis	LE

Intra-Ocular Pressure: OD OS

Axial length: OD OS

Fundus OD OS

1. Optic disc

a. Size

b. Shape

c. Margins

d. Colour

e. C:D Ratio

f. Odema ☐ ☐

(1 - present, 2 - absent)

g. Hemorrhage ☐ ☐

(1 - present , 2 - absent)

h. NVD ☐ ☐

(1 - present, 2 - absent)

2. Blood vessels (1 - present, 2 - absent)

a. Arteries

- Narrowing
  - Focal ☐ ☐
  - General ☐ ☐
- Sheathing ☐ ☐

b. Vein

- Site of obstruction
- Tortousity ☐ ☐
- Dilatation ☐ ☐
- Sheathing ☐ ☐
- A:V Ratio ☐ ☐
-

- A:V Nicking ☐ ☐

3.Macula (1 - Present, 2 - absent)

- FR ☐ ☐
- Odema ☐ ☐
- Hemorrhage ☐ ☐
- Exudates

Soft ☐ ☐

Hard ☐ ☐

4.Background (1 - Present, 2 - absent)

- Hemorrhage ☐ ☐
- Odema ☐ ☐
- Exudates

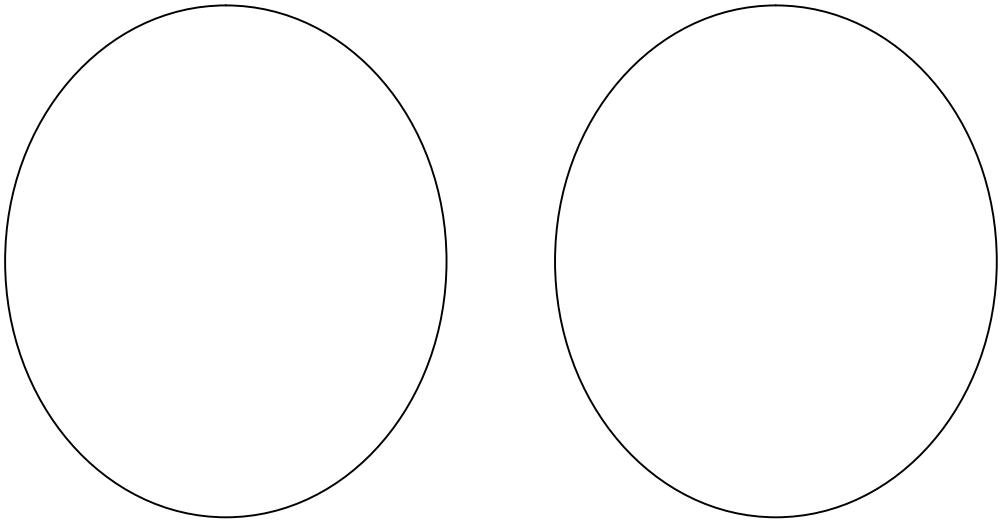
Soft ☐ ☐

Hard ☐ ☐

- NVD ☐ ☐

FUNDUS DIAGRAM:

OD OS



INVESTIGATIONS

CBC-

Lipid profile-

FBS-

ESR-

Blood urea-

Serum creatinine-

DIAGNOSIS:

KEY TO MASTER CHART

Under column Eye – OD - Right eye, OS - Left eye

Under column RVO

ICRVO – Ischemic Central Retinal Vein Occlusion

NICRVO – Non Ischemic Central Retinal Vein Occlusion

STBRVO – Superotemporal Branch Retinal Vein Occlusion

ITBRVO – Inferotemporal Branch Retinal Vein Occlusion

SNBRVO – Superonasal Branch Retinal Vein Occlusion

IHRVO – Ischemic Hemiretinal Vein Occlusion

NIHRVO – Non Ischemic Hemiretinal Vein Occlusion

Under column BCVA- Best corrected visual acuity.

CF- Counting fingers, HMCF – Hand movements close to face

Under column HTN – Hypertension

K = known hypertensive with history of using medication

UK = unknown hypertensive, no history of medication use. Detected on testing.

No = No history of medication. B.P. within normal on testing.

Under column DM – Diabetes Mellitus.

No – Not a known diabetic, T1 – Type 1 diabetic, T2 - Type 2 diabetic

Under column BMI: The numerical value is given. Units are kg/m^2.

Under column Smoking

Y = known smoker , N = No history of smoking

Under column of Ant Seg – Anterior Segment

N – normal anterior segment with normal pupillary reaction

NVI- neovacularization of iris

PI – Peripheral iridectomy

NP – Normal anterior segment with abnormal pupillary reactions

Under column - ref – Refraction

M- myopia, H- Hypermetropia, E – Emmetropia

Under column Lipids

P = deranged lipid profile on blood tests with higher values than normal

N = lipid profile with all normal value.

Under column KFT – kidney function tests

P = any higher value than normal., N = normal values.

Under column haemogram

N = Hemogram with all normal values

Hb = anemia of any type

Under column ESR – stands for Erythrocyte Sedimentation Rate

N = Normal ESR

Abnormal values are mentioned wherever detected.

Under column IOP - Intra-ocular pressure in mm of Hg

Under columns AxL-OD & AxL-OS- Axial length of right & left eye in mm.

Under column Disc – for Optic disc findings

N = normal disc, G = glaucomatous disc, NVD = Neovascularisation of the disc, DO = Disc Odema .

Under column macular involvement-

Y- involvement present

N- involvement absent

Under the column FFA- Fundus fluorescein Angiography

D- done , ND- not done

hospital no	age	sex	eye	RVO	BCVA-OD	BCVA-OS	HTN	DM	BMI	Smoking/tobacco chewing	Ant Seg-OD	Ant Seg-OS	Ref- OD	Ref- OS	lipids	haemogram	ESR	KFT	IOP-OD	IOP-OS	AxL-OD	AxL-OS	Disc	macular involvement	FFA
2067584	48	M	OD	ITBRVO	CFCF	6\6	NO	NO	20.08	Y	N	N	M	M	N	N	N	N	14.6	12.2	23.05	23.15	N	Y	D
1994240	55	M	OD	STBRVO	6\6	6\6	K-140/90	T2	26.56	N	N	N	M	M	P	N	N	N	20.6	24.4	23	23.5	N	N	D
2084294	35	M	OS	ITBRVO	6\6	6\12	UK-170/100	T2	22	N	N	N	E	M	P	N	N	N	10.2	20.6	23.15	23.5	N	N	D
2091698	63	F	OS	ITBRVO	6\6	6\60	NO	NO	25.97	N	N	N	H	H	N	N	N	N	14.6	15.9	21.69	21.8	N	Y	D
2095232	42	M	OS	IHCVO	6\6	CF-2mts	UK200/110	NO	25.41	Y	N	N	H	H	N	N	N	N	17.3	14.6	23.42	23.14	NVD	Y	ND
202850	36	F	OD	ITBRVO	6\60	6\6	UK-200/100	NO	24	N	N	N	E	E	N	N	N	N	18.2	14.6	23.07	23.11	N	Y	ND
2095416	62	F	OS	ICRVO	6\6	6\60	K-140/90	T2	25.66	N	N	NP	H	H	N	HB	41	N	14.6	14.6	22.78	22.1	O	Y	ND
2369708	54	M	OD	STBRVO	6\9	6\9	K-160/100	T2	26.76	N	N	N	H	H	P	N	N	N	17.3	14.9	23.06	23.2	N	N	D
2250963	58	F	OS	STBRVO	6\6	6\36	UK-170/100	NO	23.34	N	N	N	E	E	N	N	N	N	14.6	17.3	22.83	22.78	N	Y	ND
2257584	52	M	OS	ICRVO	6\6	6\24	UK-160/100	NO	25.66	N	N	N	H	H	P	N	N	N	17.3	15.4	23.7	23.1	O	Y	ND
2263815	55	F	OD	ITBRVO	6\18	6\9	UK-160/100	NO	25.79	N	N	N	H	H	P	N	N	N	10.2	14.6	22.96	23.22	N	N	ND
2300765	39	F	OD	NICRVO	6\6	6\6	UK-140/100	NO	23.13	N	N	N	E	E	N	N	N	N	14.6	17.3	23.33	23.16	O	N	ND
2256154	75	F	OS	SNBRVO	6\12	CF-2Mts	K-144/94	NO	26.49	N	N	N	M	M	N	N	N	N	14.6	14.6	22.93	22.03	N	N	D
2336749	54	M	OS	STBRVO	6\6	6\6	NO	NO	21.49	N	N	N	H	H	P	N	N	N	11.3	13.7	23.72	24.95	N	N	D
472589	66	M	OD	ITBRVO	6\36	6\6	UK-160/100	T2	22.43	Y	N	N	M	M	N	N	25	N	10.2	10.2	24.34	23.99	N	N	ND
2037720	60	M	OD	ITBRVO	6\36	6\9	NO	NO	26.55	Y	N	N	H	H	N	N	20	N	17.3	14.6	21.82	21.92	N	Y	ND

2066006	68	M	OD	ITBRVO	CF-2Mts	6\60	K-140/90	T2	26.7	N	N	N	H	H	N	N	N	N	14.6	14.6	23.74	23.63	N	Y	ND
484145	70	F	OD	ICRVO	CF-3Mts	PL-ve	NO	NO	26.8	N	N	NP	M	-	P	N	30	N	24.4	28	23.5	23.12	OG	Y	ND
482487	70	M	OD	ICRVO	HMCF	6\6	UK-140/90	NO	25.8	Y	N	N	H	H	N	N	N	N	14.6	14.6	23.16	23.16	O	Y	ND
482126	65	M	OS	ICRVO	6\60	CF-1Mts	UK-150/90	NO	23.5	Y	N	NVI	M	M	N	N	N	N	17.2	19.4	22.76	22.95	O	Y	ND
439188	58	F	OD	STBRVO	6\18	6\9	UK-160/100	T2	26	N	N	N	H	H	P	N	39	N	10.2	12.2	21.41	22	N	N	ND
488282	60	F	OS	ITBRVO	CF-2Mts	6\36	NO	NO	25.5	N	N	N	M	M	P	N	35	N	17.3	14.6	22.48	21.98	N	Y	ND
460024	46	M	OD	IHCVO	CF-2Mts	6\9	UK-210/120	T2	26	Y	N	N	H	H	N	N	30	N	17.3	14.6	23.25	23.12	N	N	ND
462158	65	F	OS	ITBRVO	6\18	6\60	UK-180/100	NO	23	N	N	N	M	M	N	N	N	N	14.6	15.9	22.94	23.07	N	N	ND
464607	90	M	OD	STBRVO	HMCF	6\18	UK-170/100	NO	22	N	N	N	M	M	N	N	35	N	10.2	10.2	22.16	22.75	N	Y	D
1790248	57	F	OD/OS	ITBRVO	6\9	CF-2Mts	K-156/98	T2	28	N	N	N	M	M	N	N	N	N	12.2	14.6	23.26	23.25	N	Y	D
457532	59	M	OD	STBRVO	6\9	6\36	NO	NO	25.25	Y	N	N	E	E	N	N	N	N	12.2	9.4	24.12	24.25	N	N	D
435086	70	M	OS	STBRVO	6\9	CF-3Mts	NO	NO	22	Y	N	N	E	E	N	N	35	N	17.3	17.3	24.33	24.02	N	Y	D
1921058	71	M	OD	ICRVO	CF-1Mts	6\18	UK-160/100	T2	26	Y	N	N	H	H	N	N	N	N	17.3	14.6	23.75	23.12	O	Y	D
1441881	74	M	OD	NICRVO	HMCF	6\18	K-140/90	T2	26.25	Y	PI	PI	M	M	P	N	N	N	14.6	15.9	23.54	23.61	NVD,G	N	ND
1698660	48	M	OD	STBRVO	6\9	6\12	K-150/90	NO	23.72	Y	N	N	M	M	P	N	N	N	20.3	17.3	23.54	23.61	NVD	N	D
2189725	56	M	OS	STBRVO	6\9	6\12	UK-196/100	T2	26.25	Y	N	N	H	H	N	N	N	N	17.3	15.4	22.95	21.83	N	N	ND
915694	75	M	OS	NICRVO	6\9	CF-2Mts	K-140/100	NO	23.72	Y	N	N	M	E	N	N	60	N	17.3	14.6	23.13	23.03	O	Y	ND
2193406	65	F	OS	NICRVO	6\6	6\36	K-148/90	NO	23.86	N	N	N	M	M	N	N	N	N	20.6	20.6	23.03	23.08	O	N	ND
506317	58	M	OS	STBRVO	6\9	6\9	K-150/90	N0	23.43	Y	N	N	M	M	N	N	30	N	14.6	14.6	22.93	23.28	N	N	ND
2348176	72	M	OD	ICRVO	CF-2Mts	6\9	UK-180/100	T2	24.22	N	N	N	H	H	N	N	N	N	20.8	20.8	21.76	22.7	O	Y	D
2326254	72	M	OD/OS	ITBRVO	6\12	CF-2Mts	UK-150/90	T2	23	Y	N	N	H	H	N	N	N	N	20.6	22.3	23.36	23.18	N	Y	D

2149705	51	M	OD	NICRVO	6\12	6\6	UK-140/90	T2	22	Y	N	N	M	M	N	N	N	N	17.9	18.6	22.88	23.1	O	N	ND
454051	70	M	OD	NICRVO	6\9	6\36	NO	NO	23.39	Y	N	N	H	H	N	N	N	N	14.6	14.6	23.08	23.86	O	N	ND
2351089	67	F	OD	ITBRVO	6\24	CF-2mts	K-140/90	T2	26.72	N	N	N	M	M	P	N	N	N	14.6	17.3	23	23.38	N	Y	D