

Neovascular Glaucoma: Aetiology and Staging Assessment**Kundan Kumar Singh****Senior Resident, Department of Ophthalmology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India****Received: 10-01-2022 / Revised: 23-02-2022 / Accepted: 17-03-2022****Corresponding author: Dr. Kundan Kumar Singh****Conflict of interest: Nil****Abstract****Aim:** To identify the most common cause and the frequent stage of presentation in patients with neovascular glaucoma.**Methods:** A prospective observational study was conducted in the Department of Ophthalmology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India for 1 year. Total 130 eyes of 120 patients who underwent ophthalmological examination and diagnosed as having neovascular glaucoma were include in this study. All patients underwent thorough ocular examination i.e., visual acuity, slit lamp bio-microscopy, intraocular pressure (IOP) measurement by Goldmannapplanation tonometry, gonioscopy with Posner 4 mirror indirect gonioscope and dilated fundus examination with +90 D lens.**Results:** The present study was conducted in 130 eyes of 120 patients out of which 110 patients had either eye involvement and 10 patients had both eyes involvement. All Patients were aged between 15-71 years with a mean of 52.84 ± 11.9 years. Out of 120 patients, 95(79.17%) were males and 25(20.83%) were females. On gonioscopic examination, most of the cases i.e., 68(56.67%) had only rubeosisiridis without involvement of the angle, 26(20%), 16 (12.31%), 9(6.92%), 7(5.38%) had neovascularization of angle (NVA) in one, two, three and four quadrants respectively. Out of 130 eyes, 69(53.07%) had diabetic retinopathy in variable severity, 16(12.31%) had inflammatory etiology, 12(9.23%) had retinal vein occlusion and 14(10.77%) had glaucoma (PXG and absolute glaucoma). There is no statistically significant difference between the mean IOP in rubeosisiridis stage and open angle stage ($P= 0.779$). 77 eyes (59.23%) had IOP < 30 mm of Hg of which 68 were in rubeosisiridis stage. 53 eyes (40.77%) had IOP > 30 mm of Hg of which 39 were in angle closure stage. IOP < 30mm of Hg was found mostly in rubeosisiridis stage and > 30 mm of Hg was found in angle closure stage.**Conclusion:** In the present study, it was found that Proliferative diabetic retinopathy is the most common cause and rubeosisiridis is the most common stage of presentation in NVG.**Keywords:** diabetic retinopathy, rubeosisiridis, Neovascular glaucoma

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Introduction

Anterior segment ischemia will lead to neovascularization of the iris and the anterior chamber angle and mainly caused by retinal ischemia and hypoxia due to an

ocular ischemic diseases as central (CRVO) or branch retinal vein occlusion (BRVO), proliferative diabetic retinopathy (PDR) and other causes include sickle cell

retinopathy, retinal embolic diseases, chronic retinal detachment and inflammatory conditions as uveitis and vasculitis.[1] Retinal ischemia is associated with production of vascular endothelial growth factor (VEGF) which enhances retinal neovascularization, iris neovascularization and in severe cases, proliferation of fibrovascular membrane in the angle of anterior chamber which will lead to elevation of IOP and neovascular glaucoma. [2] Once the diagnosis of retinal hypoxia is established, the natural history of neovascular glaucoma can be divided to four stages: pre-rubeosis stage, preglaucoma stage, open-angle glaucoma stage and angle-closure glaucoma stage. Panretinal photocoagulation has been shown to significantly reduce or eliminate anterior neovascularization and may reverse IOP elevation in the open-angle glaucoma stage. When the IOP begins to rise, medical therapy is required to control the pressure during the open-angle glaucoma stage. The mainstays of the therapy at this stage are drugs that reduce aqueous production such as carbonic anhydrase inhibitors, topical beta-blockers and alpha agonists. Although surgical intervention is often necessary, trabeculectomy alone and other shunt-tube drainage procedures for NVG are challenging because new vessels tend to recur, bleed easily, are always associated with postoperative inflammation and have higher rate of failure to control IOP. [2] Recent case series have demonstrated a role for bevacizumab in reducing rubeosis iridis and as an adjunct treatment for NVG. [2-4] The formation of new vessels is influenced by imbalance between pro-angiogenic factors (such as, vascular endothelial growth factor-VEGF) and anti-angiogenic factors (such as pigment-epithelium-derived factor). [5] VEGF plays an important role in formation of new vessels in patients with ischemic retinal diseases. [6] VEGF and insulin growth1 factors are produced by Mueller cells, retinal pigment epithelial cells,

retinal capillary pericytes, endothelial cells and ganglion cells. [7] Accumulation of Insulin growth-1 factor in aqueous humor causes rubeosis iridis and later the formation of adhesions between cornea and iris block the aqueous humor drainage. [8] VEGF concentration decreases after the regression of new vessels. [9] The non-pigmented ciliary epithelium is the major site of synthesis of VEGF in patients with NVG. [10] Increased Interleukin-6 was noted in the aqueous of patients with NVG secondary to central retinal vein occlusion.[11] Studies have shown increased levels of basic fibroblast growth factor (bFGF), [12] transforming growth factor-beta1 and beta 2, [13] nitric oxide, [14] endothelin [15] and free-radicals such as the superoxide [16] in the aqueous humor of patients with NVG. Normal iris vessels have nonfenestrated endothelial cells with tight intercellular junctions whereas new vessels are thin walled without muscular layer or supporting tissue. New vessels show basement membrane changes, gaps and fenestrations in the endothelial cells on electron microscopy. [17, 18] The new vessels are mostly accompanied by a fibrovascular membrane consisting of proliferating myofibroblasts.[19]

Material and Methods

A prospective observational study was conducted in the Department of Ophthalmology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India for 1 year.

Methodology

Total 130 eyes of 120 patients who underwent ophthalmological examination and diagnosed as having neovascular glaucoma were include in this study. All patients underwent thorough ocular examination i.e., visual acuity, slit lamp bio-microscopy, intraocular pressure (IOP) measurement by Goldmannapplanation tonometry, gonioscopy with Posner 4 mirror indirect gonioscope and dilated

fundus examination with +90 D lens. Neovascularization of iris (NVI) was identified as tuft of new vessels on iris mostly at the pupillary margin in an undilated state, presence of ectropionuveae, hyphema was also observed. A single tonometer used throughout the study and IOP was measured by a single person throughout the study. Indirect ophthalmoscopy or B-Scan was done in eyes with hazy media due to corneal edema and/or dense cataract. Gonioscopy was done to identify new vessels and to grade the angle As open or closed.

Statistical analysis

The data collected was entered in excel sheet and is analyzed using SPSS version 25.0. Descriptive variables were given with frequency (percentage) or mean (standard deviation). The association of various variables like Cause of NVG with stage of NVG and stage of NVG with IOP were analyzed using appropriate parametric and non-parametric tests like chi-square test (p-value) and ANOVA- test

Results

The present study was conducted in 130 eyes of 120 patients out of which 110 patients had either eye involvement and 10 patients had both eyes involvement. All Patients were aged between 15-71 years with a mean of 52.84 ± 11.9 years. Out of

120 patients, 95(79.17%) were males and 25(20.83%) were females. The range of intraocular pressure (IOP) was 3-67 mm of Hg with mean of 31.04 ± 12.1 mm of Hg. IOP of 2 mm of Hg was noted in 15 patients out of which 6 had chronic retinal detachment, 5 had chronic uveitis and 4 had vitreous haemorrhage with combined rhegmatogenous and tractional retinal detachment. IOP of 72 mm of Hg was noted in 8 case which had proliferative diabetic retinopathy. IOP < 10 mm of Hg IOP was noted in 44 out of 130 eyes of which 7 had chronic uveitis, 8 had retinal detachment, 23 had diabetic retinopathy in variable severity, 3 had central retinal vein occlusion and 3 underwent parsplanavitrectomy. >50 mm of Hg IOP was noted in 20 eyes out of which 7 had CRVO, 4 had PDR, 4 had PDR and VH, 3 had chronic uveitis and 2 had chronic pseudoexfoliative glaucoma.

On gonioscopic examination, most of the cases i.e., 68(56.67%) had only rubeosisiridis without involvement of the angle, 26(20%), 16 (12.31%), 9(6.92%), 7(5.38%) had neovascularization of angle (NVA) in one, two, three and four quadrants respectively. 5 cases had hyphema. In the present study, most of the patients i.e., 68(56.67%) presented in rubeosisiridis stage, 39(32.5%) in angle closure stage and 23(19.17%) in open angle stage (Table 2).

Table 1 Demographic profile of patients

Gender	Number of patients=120	%
Male	95	79.17
Female	25	20.83
Age in years		
Below 20 years	9	7.5
20-30	23	19.17
30-40	45	37.5
40-50	29	24.17
Above 50	14	11.67

Table 2: Stage of NVG

Stage of NVG	Number eyes	%
Angle closure stage	39	32.5
Open angle stage	23	19.17
Rubeosisiridis	68	56.67
Total	130	100

Table 3: Causes of NVG

Cause	Number eyes	%
Chronic RRD	3	2.31
DR	69	53.07
Glaucoma	14	10.77
Inflammation	16	12.31
S/P PPV	2	1.54
Vein occlusion	12	9.23

Chronic Rhegmatogenous Retinal Detachment, DR – Diabetic retinopathy, Glaucoma – pseudoexfoliative glaucoma (PXG) and absolute glaucoma, Inflammation – Chronic uveitis, Vasculitis and Eales disease, S/P PPV – status post parsplanavitrectomy, Vein occlusion –

central retinal vein occlusion and branch retinal vein occlusion.

Out of 130 eyes, 69(53.07%) had diabetic retinopathy in variable severity, 16(12.31%) had inflammatory etiology, 12(9.23%) had retinal vein occlusion and 14(10.77%) had glaucoma (PXG and absolute glaucoma) (Table 3).

Table 4: Mean IOP in three stages of NVG

Stage of NVG	Mean IOP (mm of Hg)
Angle closure stage	37.32±15.124
Rubeosis iridis	24.11±15.214
Open angle stage	23.97±16.367

Compares the mean IOP in different stages of NVG. Mean IOP in Angle closure stage is significantly higher than the mean IOP in other two stages ($P = 0.000$). Whereas there is no statistically significant difference between the mean IOP in rubeosisiridis stage and open angle stage ($P = 0.789$). 77 eyes (59.23%) had IOP < 30 mm of Hg of which 68 were in rubeosisiridis stage. 53 eyes (40.77%) had IOP > 30 mm of Hg of which 39 were in angle closure stage. IOP < 30mm of Hg was found mostly in rubeosisiridis stage and > 30 mm of Hg was found in angle

closure stage. On assessing the Cause of NVG in relation to stage of NVG ($P = 0.144$), 69eyes (53.07%) had diabetic retinopathy in variable severity, of these 68, 39 and 23 were in rubeosisiridis, angle closure and open angle stage respectively.

Discussion

Neovascular glaucoma (NVG) is one of the most refractory types of secondary glaucomas commonly caused by ischemic retinal disorders such as proliferative diabetic retinopathy and central retinal vein occlusion (CRVO) characterized by neovascularization of the iris (NVI) and

the anterior chamber angle (NVA) with eventual angle closure and intractable elevation of intraocular pressure (IOP). Because of the prognosis of NVG is poor, the management should include the treatment of the underlying disease and elevation of IOP. Rubeosis can be missed in early stages as it can't be seen unless the iris is examined under high magnification in undilated stage. New vessels on iris usually appear before the appearance of new vessels in angle but in rare conditions like ischemic central retinal vein occlusion, new vessels in the angle are seen without involvement of the iris. Therefore, it is very important to perform gonioscopy even though new vessels are not present on iris. Initially, the anterior chamber angle is open on gonioscopy but later, new vessels appear in the angle and in the final stages, due to formation of fibrovascular membrane and tissue contraction synechiae can occur leading to synechial angle closure. [20]

The present study was conducted in 130 eyes of 120 patients out of which 110 patients had either eye involvement and 10 patients had both eyes involvement. All Patients were aged between 15-71 years with a mean of 52.84 ± 11.9 years. Out of 120 patients, 95(79.17%) were males and 25(20.83%) were females which is comparable to the study done by Vasconcelos et al. [21] in which 46.16 % of the patients were between 60 and 79 years of age.

In the present study, Out of 130 eyes, 69(53.07%) had diabetic retinopathy in variable severity, 16(12.31%) had inflammatory etiology, 12(9.23%) had retinal vein occlusion and 14(10.77%) had glaucoma (PVG and absolute glaucoma). It is comparable to the study done by Vancea PP et al. [22] which states that 81% had NVG secondary to ischemic retinal changes and in another study done by Haefliger IO et al. [23] they found that the majority (97%) of cases are associated with hypoxia and retinal ischemia. The

remaining 3% cases are secondary to inflammatory diseases like chronic uveitis and intraocular neoplasms. The commonest causes of NVG are Proliferative Diabetic Retinopathy (PDR) and central retinal vein occlusion. 69(53.07%) PDR is the most common cause of NVG in the present study and Vein occlusion 12(9.23%). The formation of new vessels is influenced by imbalance between pro-angiogenic factors (such as, vascular endothelial growth factor-VEGF) and anti-angiogenic factors (such as pigment-epithelium derived factor). Studies have shown that increased levels of VEGF and decreased levels of PEDF was found in the vitreous of patients with proliferative diabetic retinopathy. [24,25] In the present study 1 case who underwent pars planovitrectomy had developed NVG. Surgical intervention like pars planovitrectomy for PDR increases the incidence of rubeosis iridis. [26] Retinal hypoxia is frequently seen in proliferative retinopathies. A portion of oxygen from the aqueous humor diffuses posteriorly towards the hypoxic retina causing the iris hypoxia. This explains the risk of rubeosis after surgery like oxygen reaches the ischemic retina faster leading severe iris hypoxia. [27] In our study 9 cases (7.5%) had NVG due to pseudoexfoliative material on iris. Studies found that pseudoexfoliative material gets deposited adjacent to the endothelial wall and causes thinning of the basement membrane, endothelial wall fenestration and reduction of lumen of the vessel thus causing iris hypoxia and ischemia leading to neovascularisation. [28,29] In the present study 3(2.31%) had developed NVG due to chronic retinal detachment. Studies described NVG can develop rarely due to ischemia caused by chronic RD. [30,31] In our study, most of the cases presented in rubeosis iridis stage followed by angle closure stage and open angle stage. In the present study, most of the patients i.e., 68(56.67%) presented in rubeosis iridis stage, 39(32.5%) in angle closure stage

and 23(19.17%) in open angle stage. In Rubeosisiridis stage most of the patients present with normal IOP and are usually asymptomatic. IOP begins to rise in Open angle glaucoma stage. In Angle closure glaucoma stage, IOP usually raises very high even up to 60 mmHg. Rubeosismay be severe with hyphema, anterior chamber reaction, conjunctival congestion and corneal edema. [32] In the present study, the mean IOP in angle closure stage was found to be 37.32 ± 15.124 mm of Hg which is significantly higher than the other two stages ($P=0.000$). [33]

Conclusion

In the present study, it was found that Proliferative diabetic retinopathy is the most common cause and rubeosisiridis is the most common stage of presentation in NVG.

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