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ORIGINAL ARTICLE

A prospective observational study to evaluate the etiology and staging of neovascular glaucoma

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ABSTRACT:

Aim: To identify the most common cause and the frequent stage of presentation in patients with neovascular glaucoma. **Materials and Methods**: A prospective observational study was conducted in the Department of Ophthalmology. Total 150 eyes of 120 patients having neovascular glaucoma in one eye or both the eyes were included in the study. All patients underwent thorough ocular examination i.e., visual acuity, slit lamp bio-microscopy, intraocular pressure (IOP) measurement by Goldman applanation tonometry, gonioscopy with Posner 4 mirror indirect gonioscope and dilated fundus examination. **Results**: The present study was conducted in 150 eyes of 120 patients out of which 110 patients had either eye involvement and 20 patients had both eyes involvement. All Patients were aged between 12-74 years with a mean of 55.47 ± 13.4 years. Out of 120 patients, 90 (75%) were males and 30 (25%) were females. The range of intraocular pressure (IOP) was 2-74 mm of Hg with mean of 28.11 ± 10.2 mm of Hg.84 (56%) presented in rubeosisiridis stage, 44 (29.33%) in angle closure stage and 22 (14.67%) in open angle stage. Out of 150 eyes, 90 (60%) had diabetic retinopathy in variable severity, 21 (14%) had inflammatory etiology, 17 (11.33%) had retinal vein occlusion and 17 (11.33%) had glaucoma (PXG and absolute glaucoma. Mean IOP angle closure stage was found to be 35.87±15.277 mm of Hg which is significantly higher than the other two stages (P = 0.000). **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: Neovascular glaucoma, Intraocular pressure, Stage

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INTRODUCTION

Neovascular glaucoma (NVG) is a severe form of glaucoma characterized by rubeosis iridis and intraocular pressure (IOP) elevation. Hypoxic disease of the retina such as diabetic retinopathy and occlusion of major retinal vessels account for more than one half of this glaucoma. Once retinal hypoxia is established the natural history of neovascular glaucoma can be divided in four stages: prerubeosis stage, preglaucoma stage, open-angle glaucoma stage, and angleclosure glaucoma stage[1]. 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 humorcausesrubeosisiridis 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] endothelin1 [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, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the patient or the relatives if the patient was not in good condition. The technique, risks, benefits, results and associated complications of the procedure were discussed with all patients.Total 150 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. The number of quadrants with new vessels in the angle were noted.
The data collected was entered in excel sheet and is analyzed using SPSS version 20.0. 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 150 eyes of 120 patients out of which 110 patients had either eye involvement and 20 patients had both eyes involvement. All Patients were aged between 12-74 years with a mean of 55.47 ± 13.4 years. Out of 120 patients, 90 (75%) were males and 30 (25%) were females. The range of intraocular pressure (IOP) was 2-74 mm of Hg with mean of 28.11 ± 10.2 mm of Hg. IOP of 2 mm of Hg was noted in 7 patients out of which 3 had chronic retinal detachment, 2 had chronic uveitis and 2 had vitreous haemorrhage with combined rhegmatogenous and tractional retinal detachment. IOP of 74 mm of Hg was noted in 4 case which had proliferative diabetic retinopathy. IOP < 10 mm of Hg IOP was noted in 40 out of 150 eyes of which 5 had chronic uveitis, 7 had retinal detachment, 24 had diabetic retinopathy in variable severity, 2 had central retinal vein occlusion and 2 underwent parsplanavitrectomy. >50 mm of Hg IOP was noted in 18 eyes outof which 6 had CRVO, 5 had PDR, 3 had PDR and VH, 3 had chronic uveitis and 1 had chronic pseudoexfoliative glaucoma.
On gonioscopic examination, most of the cases i.e., 84 (56%) had only rubeosisiridis without involvement of the angle, 28 (18.67%), 17 (11.33%), 10 (6.67%), 11 (7.33%) had neovascularization of angle (NVA) in one, two, three and four quadrants respectively. 4 cases had hyphema. In the present study, most of the patients i.e., 84 (56%) presented in rubeosisiridis stage, 44 (29.33%) in angle closure stage and 22 (14.67%) in open angle stage (Table 1).

Table 1: Stage of NVG

Stage of NVG	n	%
Angle closure stage	44	29.33
Open angle stage	22	14.67
Rubeosisiridis	84	56
Total	150	100.0

Table 2: Causes of NVG

Cause	N=150	%
Chronic RRD	3	2
DR	90	60
Glaucoma	17	11.33
Inflammation	21	14
S/P PPV	2	1.33
Vein occlusion	17	11.33

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 150 eyes, 90 (60%) had diabetic retinopathy in variable severity, 21 (14%) had inflammatory etiology, 17 (11.33%) had retinal vein occlusion and 17 (11.33%) had glaucoma (PXG and absolute glaucoma) (Table 2).

Table 3: Mean IOP in three stages of NVG

Stage of NVG	Mean IOP (mm of Hg)
Angle closure stage	35.87±15.277
Rubeosis iridis	22.95±14.725
Open angle stage	22.87±17.586

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=0.879).94 eyes (62.67%) had IOP < 30 mm of Hg of which 61 were

in rubeosisiridis stage. 56 eyes (37.33%) had IOP > 30 mm of Hg of which 31 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*= 0.114), 90 eyes (60%) had diabetic retinopathy in variable severity, of these 48, 25 and 17 were in rubeosisiridis, angle closure and open angle stage respectively.

DISCUSSION

Neovascular glaucoma (NVG) is a form of secondary glaucoma characterized by formation of new vessels and proliferation of fibrovascular tissue on iris and in the angle. Slit lamp examination can reveal new vessels on iris, ciliary injection, corneal edema due to increase in IOP, anterior chamber reaction and ectropion uvea due to contraction of the fibrovascular membrane on the iris. 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 vesselsare not present on iris. Initially, the anterior chamber angle is open on gonioscopy but later, new vessels appear in the angle andin 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 150 eyes of 120 patients out of which 110 patients had either eye involvement and 20 patients had both eyes involvement. All Patients were aged between 12-74 years with a mean of 55.47 ± 13.4 years. Out of 120 patients, 90 (75%) were males and 30 (25%) were females which is comparable to the study done by Vasconcelloset al. [21] in which 46.16 % of the patients were between 60 and 79 years of age.

In the present study, 112 (74.67%) had hypoxic and ischemic changes in retina like diabetic retinopathy, vein occlusion, chronic retinal detachment and S/P PPV and 21 (14%) had inflammatory diseases like uveitis, vasculitis and eales disease. 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. 90(60%) PDR is the most common cause of NVG in the present study and Vein occlusion 11.33% . 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-epitheliumderived 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 2 case who underwent pars planavitrectomy had developed NVG. Surgical intervention like pars planavitrectomy 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 vitrectomywhere oxygen reaches the ischemic retina faster leading severe iris hypoxia.[27] In our study 11 cases (7.33%) 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 neovascularization.[28,29] In the present study 3 (2%) had developed NVG due to chronic retinaldetachment. Studies described NVG can develop rarely due to ischemia caused by chronic RD. In our study, most of the cases presented in rubeosisiridis stage followed by angle closure stage and open angle stage. In the present study, most of the patients i.e., 84 (56%) presented in rubeosisiridis stage, 44 (29.33%) in angle closure stage and 22 (14.67%) 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 edema32.In the present study, the mean IOP in angle closure stage was found to be 35.87±15.277mm of Hg which is significantly higher than the other two stages (P = 0.000).

CONCLUSION

Neovascular laucoma is a severe form of secondary glaucoma most commonly because of diseases causing retinal ischemia. So, early diagnosis and prompt treatment of the underlying retinal pathology can prevent neovascular glaucoma. In the present study, it was found that Proliferative diabetic retinopathy is the most common cause and rubeosisiridis is the most frequent stage of presentation in NVG.

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