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An observational study to assess the etiology and staging of neovascular glaucoma

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Abstract

Aim: The aim of the present study was to identify the most common cause and the frequent stage of presentation in patients with neovascular glaucoma.

Methods: The present study was a prospective observational study, 120 eyes of 10- patients who underwent ophthalmological examination and diagnosed as having neovascular glaucoma in one eye or both the eyes were included in the study for the period of one year.

Results: The present study was conducted in 120 eyes of 100 patients out of which 90 patients had either eye involvement and 15 patients had both eyes involvement. All Patients were aged between 14-84 years with a mean of 57.59 ± 12.6 years. Out of 100 patients, 80 (80%) were males and 20 (20%) were females. In the present study, most of the patients i.e., 60 (50%) presented in rubeosis iridis stage, 36 (30%) in angle closure stage and 24 (20%) in open angle stage. Out of 120 eyes, 78 (65%) had diabetic retinopathy in variable severity, 15 (12.5%) had inflammatory etiology, 12 (10%) had retinal vein occlusion and 12 (10%) had glaucoma (PVG and absolute glaucoma). 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 rubeosis iridis stage and open angle stage ($P = 0.950$).

Conclusion: In the present study, it was found that Proliferative diabetic retinopathy is the most common cause and rubeosis iridis is the most frequent stage of presentation in NVG.

Keywords: Neovascular glaucoma, proliferative diabetic retinopathy, rubeosis iridis, open angle stage, Angle closure stage

Introduction

Neovascular glaucoma (NVG) is a serious complication of a variety of ocular and systemic conditions. Neovascularization is the formation of abnormal blood vessels in an abnormal location triggered by an imbalance of anti-angiogenic and proangiogenic factors caused by retinal ischemia^[1]. NVG accounts for 3.9 to 9.2% of all new glaucoma diagnoses^[2-4].

The incidence of NVG varies depending on the etiology of retinal ischemia. For central retinal vein occlusion (CRVO) the reported incidence is 16%^[5], for proliferative diabetic retinopathy (PDR) 21.3%^[6], for central retinal artery occlusion (CRAO) 14.5%^[7], and ocular ischemic syndrome (OIS) 12.9%^[8], respectively. Carotid artery obstructive disease and fistulas are additional, extra ocular vascular causes of retinal ischemia^[9]. Early recognition and treatment of NVG are imperative to prevent aggressive evolution with severe vision loss and intractable pain that can require enucleation within a few months^[10]. NVG also carries a poor prognosis for general health: remarkably, the expected lifespan of patients with NVG decreased by 52% compared to an age-correlated normal population, which corresponds to 6.5 years. In diabetics with NVG, the expected lifespan was reduced even more significantly by 72% (5.1 years in this subgroup)^[11].

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)^[12]. VEGF plays an important role in formation of new vessels in patients with ischemic retinal diseases^[13]. VEGF and insulin growth- 1 factors are produced by Mueller cells, retinal pigment epithelial cells, retinal capillary pericytes, endothelial cells and ganglion cells^[14]. 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^[15]. VEGF concentration decreases after the regression of new vessels^[16]. The non-pigmented ciliary epithelium is the major site of synthesis of VEGF in patients with NVG^[17].

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Increased Interleukin-6 was noted in the aqueous of patients with NVG secondary to central retinal vein occlusion [18]. Studies have shown increased levels of basic fibroblast growth factor (bFGF), [19] transforming growth factor-beta1 and beta 2, [20] nitric oxide, [21] endothelin- 1 [22] and free-radicals such as the superoxide [23] 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 [24, 25]. The new vessels are mostly accompanied by a fibrovascular membrane consisting of proliferating myofibroblasts [26].

The aim of the present study was to identify the most common cause and the frequent stage of presentation in patients with neovascular glaucoma.

Materials and Methods

The present study was a prospective observational study, 120 eyes of 10- patients who underwent ophthalmological examination and diagnosed as having neovascular glaucoma in one eye or both the eyes were included in the study for the period of one year. Patients were explained about the study and informed consent for the same was obtained. Relevant detailed medical and ocular history were obtained from all the patients.

All patients underwent thorough ocular examination i.e., visual acuity, slit lamp bio-microscopy, intraocular pressure (IOP) measurement by Goldmann applanation 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 noted. 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 was noted.

Statistical analysis

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

Table 1: Patient details

Variables	N%
Gender	
Male	80 (80)
Female	20 (20)
Eyes involved	
One eye	90
Both eyes	15

The present study was conducted in 120 eyes of 100 patients

out of which 90 patients had either eye involvement and 15 patients had both eyes involvement. All Patients were aged between 14-84 years with a mean of 57.59±12.6 years. Out of 100 patients, 80 (80%) were males and 20 (20%) were females.

Table 2: Stage of NVG

Stage of NVG	N%
Angle closure stage	36 (30)
Open angle stage	24 (20)
Rubeosis iridis	60 (50)
Total	120 (100)

In the present study, most of the patients i.e., 60 (50%) presented in rubeosis iridis stage, 36 (30%) in angle closure stage and 24 (20%) in open angle stage.

Table 3: Causes of NVG

Causes of NVG	N%
Chronic RRD	2 (1.66)
DR	78 (65)
Glaucoma	12 (10)
Inflammation	15 (12.5)
S/P PPV	1 (0.84)
Vein occlusion	12 (10)
Total	120 (100)

Out of 120 eyes, 78 (65%) had diabetic retinopathy in variable severity, 15 (12.5%) had inflammatory etiology, 12 (10%) had retinal vein occlusion and 12 (10%) had glaucoma (PXG and absolute glaucoma).

Table 4: Mean IOP in three stages of NVG

Stage of NVG	Mean IOP (mm of Hg)
Angle closure stage	36.53±16.259
Rubeosis iridis	23.65±15.857
Open angle stage	23.08±18.472

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 rubeosis iridis stage and open angle stage (P= 0.950).

Discussion

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 [27]. 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 [28].

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 vessels are not present on iris. 120 eyes of 100 patients were included in the present study out of which 90 patients had either eye involvement and 15 patients had both eyes involvement. 44.8% of patients were in the age group of 60 – 80 years which is comparable to the study done by Vasconcellos *et al.* [29] in which 46.16% of the patients were between 60 and 79 years of age.

In the present study, 93 (77.5%) had hypoxic and ischemic changes in retina like diabetic retinopathy, vein occlusion, chronic retinal detachment and S/P PPV and 15 (12.5%) had inflammatory diseases like uveitis, vasculitis and eales disease. It is comparable to the study done by Vancea PP *et al.* [30] which states that 81% had NVG secondary to ischemic retinal changes and in another study done by Haefliger IO *et al.* [31] 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.²⁷ 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 [32, 33].

In Rubeosis iridis 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. Rubeosis may be severe with hyphema, anterior chamber reaction, conjunctival congestion and corneal edema [34]. In the present study, the mean IOP in angle closure stage was found to be 36.53 ± 16.259 mm of Hg which is significantly higher than the other two stages ($P = 0.000$).

Conclusion

Neovascular glaucoma 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 rubeosis iridis is the most frequent stage of presentation in NVG.

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