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ORIGINAL ARTICLE

To evaluate the etiology and staging of neovascular glaucoma

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ABSTRACT:

Aim: To evaluate the etiology and staging of neovascular glaucoma. **Materials and Methods**: An observational research was done at the Department of Ophthalmology. The research comprised a total of 150 eyes from 120 individuals who had neovascular glaucoma in either one or both eyes. The patients received a comprehensive ocular examination, including assessments of visual acuity, slit lamp bio-microscopy, measurement of intraocular pressure (IOP) using Goldmann applanation tonometry, gonioscopy using a Posner 4 mirror indirect gonioscope, and dilated fundus examination. **Results**: 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**: 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, IOP, Staging

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INTRODUCTION

Neovascular glaucoma (NVG) is an intense kind of glaucoma distinguished by the presence of rubeosis iridis and an increase in intraocular pressure (IOP). Hypoxic retinal diseases, such as diabetic retinopathy and blockage of major retinal arteries, contribute to almost 50% of cases of this glaucoma. After the onset of retinal hypoxia, the progression of neovascular glaucoma may be categorised into four stages: prerubeosis stage, preglaucoma stage, open-angle glaucoma stage, and angle-closure 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 research was done at the Department of Ophthalmology, after the permission of

the protocol review committee and institutional ethics committee. Following the acquisition of informed consent, a comprehensive medical history was obtained from the patient or, if the patient's condition was not favourable, from their family. All patients were informed about the methodology, potential hazards, advantages, outcomes, and related complexities of the surgery. This research included a total of 150 eyes from 120 individuals who had ophthalmological examination and were diagnosed with neovascular glaucoma. All patients received a comprehensive ocular examination, which included assessments of visual acuity, slit lamp bio-microscopy, measurement of intraocular pressure (IOP) using Goldmann applanation tonometry, gonioscopy with a Posner 4 mirror indirect gonioscope, and dilated fundus examination with a +90 D lens. Neovascularization of the iris (NVI) was detected as a cluster of newly formed blood vessels on the iris, mostly located at the edge of the pupil. This was visible without the need of dilation. Additionally, the presence of ectropionuveae and hyphema was noted. A singular tonometer was used consistently throughout the trial, and intraocular pressure (IOP) was assessed exclusively by one individual during the whole duration of the study. Indirect ophthalmoscopy or B-Scan was performed on eyes with cloudy media caused by corneal edoema and/or severe cataract.Gonioscopy was used to detect neovascularization and classify the angle as either open or closed. The presence of neovascularization in the angle was seen and quantified.

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 current investigation was carried out on 150 eyes belonging to 120 individuals, with 110 patients exhibiting involvement in one eye and 20 patients displaying involvement in both eyes. The age range of all patients was 12 to 74 years, with a mean age of 55.47 ± 13.4 years. Among the 120 patients, 90 (75%) were male and 30 (25%) were female. The intraocular pressure (IOP) ranged from 2 to 74 mmHg, with a mean of 28.11 ± 10.2 mmHg. Among the 7 patients, 3 had chronic retinal detachment, 2 had chronic uveitis, and 2 had vitreous haemorrhage with coupled rhegmatogenous and tractional retinal detachment. In all cases, an intraocular pressure (IOP) of 2 mm Hg was observed. An intraocular pressure (IOP) of 74 mmHg was observed in four cases who presented with proliferative diabetic retinopathy. The intraocular pressure is less than 10 mmHg. In 40 out of 150 eyes, intraocular pressure (IOP) was observed. Among them, 5 eyes had chronic uveitis, 7 eyes had retinal detachment, 24 eyes had varying degrees of diabetic retinopathy, 2 eyes had central retinal vein occlusion, and 2 eyes had pars plana vitrectomy. Greater than 50 millimetres of mercury In 18 eyes, intraocular pressure (IOP) was observed. Among them, 6 eyes had central retinal vein occlusion (CRVO), 5 eyes had proliferative diabetic retinopathy (PDR), 3 eyes had both PDR and vitreous haemorrhage (VH), 3 eyes had chronic uveitis, and 1 eye 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]. 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 [25]. 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. 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[26,27]. In the present study 3 (2%) had developed NVG due to chronic retinal detachment. Studies described NVG can develop rarely due to ischemia caused by chronic RD[28]. 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 edema.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

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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