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Original research article

To Determine the Most Common Aetiology and Stage of Neovascular Glaucoma: A Prospective Study

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Abstract

Aims: 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, M.G.M. Medical College & Hospital, Jamshedpur, Jharkhand, India for 18 months. 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 Goldmann applanation tonometry, gonioscopy with Posner 4 mirror indirect gonioscope and dilated fundus examination.

Results: On gonioscopic examination, most of the cases 74 (61.67%) presented in rubeosis iridis stage, 29 (24.16%) in angle closure stage and 17 (14.17%) in open angle stage Out of 120 eyes, 75 (62.5%) had diabetic retinopathy in variable severity, 16(13.33%) had inflammatory etiology, 13 (10.83%) had retinal vein occlusion and 13 (10.83%) had glaucoma (PXG and absolute glaucoma). 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 = 0.0001). Whereas there is no statistically significant difference between the mean IOP in rubeosis iridis stage and open angle stage (P= 0.749). 75 eyes (62.5%) had IOP < 30 mm of Hg of which 55 were in rubeosis iridis stage. 45 eyes (37.5%) had IOP > 30 mm of Hg of which 27 were in angle closure stage. IOP < 30mm of Hg was found mostly in rubeosis iridis 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=0.17), 75 eyes (62.5%) had diabetic retinopathy in variable severity, of these 40, 20 and 15 were in rubeosis iridis, angle closure and open angle stage respectively.

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

Keywords: diabetic retinopathy, IOP, rubeosis iridis

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] According to the Federal Statistical Office of Germany, NVG's age-specific incidence in Germany in the age group from 45 to 64 years is 8 per 100,000. It increases to 24 per 100,000 in subjects older

than 64 years.[5] The incidence of NVG varies depending on the etiology of retinal ischemia. For central retinal vein occlusion (CRVO) the reported incidence is 16%[6], for proliferative diabetic retinopathy (PDR) 21.3%[7], for central retinal artery occlusion (CRAO) 14.5%[8], and ocular ischemic syndrome (OIS) 12.9%[9], respectively. Carotid artery obstructive disease and fistulas are additional, extra ocular vascular causes of retinal ischemia.[10] 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.[11] 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).[12] Studies have shown increased levels of basic fibroblast growth factor (bFGF), 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 non fenestrated 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, M.G.M. Medical College & Hospital, Jamshedpur, Jharkhand, India for 18 months, 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 120 eyes of 100 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 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 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.

Statistical analysis

The data collected was entered in excel sheet and is analyzed using SPSS version 25.0. Descriptive variables were given with frequency or mean. 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 120 eyes of 100 patients out of which 80 patients had either eye involvement and 20 patients had both eyes involvement. All Patients were aged between 15-69 years with a mean of 54.37 ± 11.4 years. Out of 100 patients, 71 (71%) were males and 29 (29%) were females. The range of intraocular pressure (IOP) was 2-75 mm of Hg with mean

of 27.01 ± 8.2 mm of Hg. IOP of 2 mm of Hg was noted in 10 patients out of which 4 had chronic retinal detachment, 3 had chronic uveitis and 3 had vitreous haemorrhage with combined rhegmatogenous and tractional retinal detachment. IOP of 70 mm of Hg was noted in 5 case which had proliferative diabetic retinopathy. IOP < 10 mm of Hg IOP was noted in 30 out of 120 eyes of which 4 had chronic uveitis, 6 had retinal detachment, 16 had diabetic retinopathy in variable severity, 2 had central retinal vein occlusion and 2 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, 4 had chronic uveitis and 1 had chronic pseudoexfoliative glaucoma.

On gonioscopic examination, most of the cases 74 (61.67%) presented in rubeosis iridis stage, 29 (24.16%) in angle closure stage and 17 (14.17%) in open angle stage (Table 1).

Table 1: Stage of NVG

Stage of NVG	n	%
Angle closure stage	29	24.16
Open angle stage	17	14.17
Rubeosis iridis	74	61.67
Total	120	100.0

Table 2: Causes of NVG

Cause	**N=120**	**%**
Chronic RRD	2	1.67
DR	75	62.5
Glaucoma	13	10.83
Inflammation	16	13.33
S/P PPV	1	0.83
Vein occlusion	13	10.83

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 120 eyes, 75 (62.5%) had diabetic retinopathy in variable severity, 16(13.33%) had inflammatory etiology, 13 (10.83%) had retinal vein occlusion and 13 (10.83%) 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	34.77±13.27
Rubeosis iridis	21.85±12.72
Open angle stage	21.77±15.58

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 = 0.0001). Whereas there is no statistically significant difference between the mean IOP in rubeosis iridis stage and open angle stage (P= 0.749). 75 eyes (62.5%) had IOP < 30 mm of Hg of which 55 were in rubeosis iridis stage. 45 eyes (37.5%) had IOP > 30 mm of Hg of which 27 were in angle closure stage. IOP < 30mm of Hg was found mostly in rubeosis iridis 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= 0.17), 75 eyes (62.5%) had diabetic retinopathy in variable severity, of these 40, 20 and 15 were in rubeosis iridis, 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 vessels are 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 120 eyes of 100 patients out of which 80 patients had either eye involvement and 20 patients had both eyes involvement. All Patients were aged between 15-69 years with a mean of 54.37 ± 11.4 years. Out of 100 patients, 71 (71%) were males and 29 (29%) 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, Out of 120 eyes, 75 (62.5%) had diabetic retinopathy in variable severity, 16(13.33%) had inflammatory etiology, 13 (10.83%) had retinal vein occlusion and 13 (10.83%) had glaucoma (PXG 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 cases are secondary to inflammatory diseases like chronic uveitis and intraocular neoplasms. Out of 120 eyes, 75 (62.5%) had diabetic retinopathy in variable severity, 16(13.33%) had inflammatory etiology, 13 (10.83%) had retinal vein occlusion and 13 (10.83%) had glaucoma (PXG and absolute glaucoma). 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 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 7 cases (5.83%) 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 2 (1.67%) had developed NVG due to chronic retinal detachment. Studies described NVG can develop rarely due to ischemia caused by chronic RD. 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., 74 (61.67%) presented in rubeosis iridis stage, 29(24.16%) in angle closure stage and 17 (14.17%) in open angle stage. 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.In the present study, the mean IOP in angle closure stage was found to be 34.77±13.27mm of Hg which is significantly higher than the other two stages (P = 0.0001).

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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