ORIGINAL RESEARCH

To evaluate the etiology and staging of neovascular glaucoma (NVG) and to assess intraocular pressure (IOP) across different stages of the disease

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ABSTRACT
Background: 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.**Material and Methods:** A prospective observational study was conducted in the Department of Ophthalmology, involving 130 eyes from 110 patients diagnosed with NVG. Detailed ocular examinations were performed, including visual acuity, slit-lamp biomicroscopy, IOP measurement using Goldmannapplanation tonometry, and gonioscopy to assess the angle status. Neovascularization of the iris (NVI) and associated complications, such as hyphema, were noted. Fundus examination and, when necessary, B-scan ultrasonography were used to visualize the retina in cases of corneal opacity. **Results:** Of the 110 patients, 70 were male (63.64%) and 40 were female (36.36%). Most patients were between 40-50 years of age (27.27%), followed by those in the 30-40 and over 50-year age groups (22.73% each). The stages of NVG were classified into angle closure stage (38.46%), open angle stage (30.77%), and rubeosisiridis stage (30.77%). Diabetic retinopathy was the leading cause of NVG, accounting for 38.46% of cases, followed by retinal detachment (15.38%) and vein occlusion (15.38%). The mean IOP was 30.15 mm Hg (SD 5.12) in the angle closure stage, 24.85 mm Hg (SD 4.58) in rubeosisiridis, and 18.30 mm Hg (SD 3.45) in the open angle stage.**Conclusion:** NVG predominantly affects middle-aged to elderly individuals, with diabetic retinopathy being the leading cause. As NVG progresses, intraocular pressure increases, with the highest levels observed in the angle closure stage. Early diagnosis and intervention are crucial to managing NVG and preventing severe visual impairment, particularly in diabetic patients.

Keywords: Neovascular glaucoma, intraocular pressure, diabetic retinopathy, angle closure, ocular examination.

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 rubeosisiridis and as an adjunct treatment for NVG.[3]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). VEGF plays an important role in formation of new vessels in patients with ischemic retinal diseases.[4] VEGF and insulin growth1 factors are produced by Mueller cells, retinal pigment epithelial cells, retinal capillary pericytes, endothelial cells and ganglion cells.Accumulation of Insulin growth-1 factor in aqueous humorcausesrubeosisiridis and later the formation of adhesions between cornea and iris block the aqueous humor drainage.[5] VEGF concentration decreases after the regression of new vessels. The non-pigmented ciliary epithelium is the major site of synthesis of VEGF in patients with NVG. Increased Interleukin-6 was noted in the aqueous of patients with NVG secondary to central retinal vein occlusion. Studies have shown increased levels of basic fibroblast growth factor (bFGF), transforming growth factor-beta1 and beta 2,nitric oxide, endothelin[1] and free-radicals such as the superoxidein 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.[6] New vessels show basement membrane changes, gaps and fenestrations in the endothelial cells on electron microscopy. The new vessels are mostly accompanied by a fibrovascular membrane consisting of proliferating myofibroblasts.

AIM AND OBJECTIVES

The aim of this study was to evaluate the etiology and staging of neovascular glaucoma (NVG) and to assess intraocular pressure (IOP) across different stages of the disease.

MATERIAL AND METHODS

A prospective observational study was conducted in the Department of Ophthalmology,Department of Opthalamology, Rama Medical College Hospital and Research Centre, Hapur, Uttarpradesh, India,andSantosh Medical College & Hospital Ghaziabad, NCR Delhi, India, following the acquisition of informed consent from all patients or their relatives if the patient was unable to provide consent due to their medical condition. The procedure, along with its associated risks, benefits, and potential complications, was thoroughly explained to all participants. The study included 130 eyes from 110 patients diagnosed with neovascular glaucoma. The duration of study was from April 2019 to March 2020.

Each patient underwent a comprehensive ophthalmological examination that included visual acuity assessment, slit-lamp bio-microscopy, and intraocular pressure (IOP) measurement using Goldmannapplanationtonometry. A single tonometer was used throughout the study, and all IOP measurements were taken by the same examiner to ensure consistency. Gonioscopy was performed using a Posner 4-mirror indirect gonioscope to examine the angle and classify it as open or closed. The number of quadrants with new vessels in the angle was also recorded. Additionally, a dilated fundus examination was

performed with a +90D lens to assess the retinal health.

Neovascularization of the iris (NVI) was defined by the presence of a tuft of new vessels on the iris, typically near the pupillary margin in an undilated state, and the presence of ectropionuveae and hyphema were noted when observed. For eyes with hazy media caused by corneal edema or dense cataract, indirect ophthalmoscopy or B-scan ultrasonography was used to visualize the retina.

Statistical analysis

The data collected during these examinations were entered into an Excel spreadsheet and analyzed using SPSS version 23.0. Descriptive variables were reported as frequency (percentage) for categorical data, and mean (standard deviation) was calculated for continuous variables.

RESULTS

The present study was conducted in 130 eyes of 110 patients out of which 90 patients had either eye involvement and 20 patients had both eyes involvement.

Table 1: Demographic parameters

Parameters	Number of Patients	Percentage (%)
Gender		
Male	70	63.64
Female	40	36.36
Age in Years		
Below 20	10	9.09
20-30	20	18.18
30-40	25	22.73
40-50	30	27.27
Above 50	25	22.73

In this study, 110 patients were included, consisting of 70 males (63.64%) and 40 females (36.36%). The age distribution shows that the majority of patients fall within the age group of 40-50 years, with 30 patients (27.27%). This is followed by patients aged 30-40 years (22.73%) and those above 50 years (22.73%). The lowest age group representation is from patients below 20 years (9.09%). This distribution indicates that neovascular glaucoma (NVG) is more prevalent in middle-aged to elderly populations, with a higher incidence in males than females.

Table 2: Stage of Neovascular Glaucoma (NVG)

Stage of NVG	Number of Eyes	Percentage (%)
Angle closure stage	50	38.46
Open angle stage	40	30.77
Rubeosisiridis	40	30.77

The stages of NVG were classified into three categories: angle closure stage, open angle stage, and rubeosisiridis. Of the 130 eyes studied, 50 eyes (38.46%) were in the angle closure stage, which represents the most advanced stage of NVG. The remaining cases were evenly distributed between the open angle stage and rubeosisiridis stage, each accounting for 40 eyes (30.77%). This distribution suggests that NVG progresses to advanced stages in a significant proportion of patients, highlighting the importance of early detection and intervention.

Table 3: Causes of Neovascular Glaucoma (NVG)

Cause	Number of Eyes	Percentage (%)
Chronic RRD	20	15.38
Diabetic Retinopathy (DR)	50	38.46
Glaucoma	15	11.54
Inflammation	10	7.69

S/P PPV	15	11.54
Vein Occlusion	20	15.38

The most common cause of NVG in this study was diabetic retinopathy (DR), which affected 50 eyes (38.46%), making it the predominant factor. Chronic retinal detachment (RRD) and vein occlusion each contributed to 20 eyes (15.38%), while glaucoma and post-surgical cases (S/P PPV) each accounted for 15 eyes (11.54%). Inflammation, as a cause of NVG, was the least frequent, affecting 10 eyes (7.69%). These findings underscore the significant impact of diabetic retinopathy as a leading cause of NVG, followed by retinal vascular occlusions and other complications, emphasizing the need for targeted screening in diabetic patients.

Table 4: Mean IOP (Intra ocular pressure) in Stages of Neovascular Glaucoma (NVG)

Stage of NVG	Mean IOP (mm of Hg)	Standard Deviation (SD)
Angle closure stage	30.15	5.12
Rubeosisiridis	24.85	4.58
Open angle stage	18.30	3.45

The mean IOP was measured in three stages of NVG. In the angle closure stage, the mean IOP was 30.15 mm Hg with a standard deviation (SD) of 5.12, indicating a high pressure associated with advanced NVG. In the rubeosisiridis stage, the mean IOP was 24.85 mm Hg with an SD of 4.58, while the open angle stage had a mean IOP of 18.30 mm Hg with an SD of 3.45. The results demonstrate a trend of increasing IOP as NVG progresses, with the angle closure stage showing the highest levels of intraocular pressure, reflecting the severity of the condition in this advanced stage

DISCUSSION

The demographic results of this study, where NVG predominantly affected males (63.64%) and individuals in the 40-50 age range (27.27%), are consistent with previous studies. Hayreh et al. (2013) observed a similar gender disparity in NVG patients, with males more commonly affected, likely due to their higher prevalence of risk factors such as diabetes and retinal vascular diseases.[7] Furthermore, Kwon et al. (2014) also found that NVG is more prevalent in middle-aged to elderly populations, with the incidence rising sharply after the age of 40. This age distribution aligns with the current study's findings, suggesting that NVG is largely a disease of older adults, with fewer cases in younger individuals.[8]In this study, 38.46% of eyes were in the angle closure stage, with the remaining cases evenly divided between open angle stage (30.77%) and rubeosisiridis (30.77%). These results correspond to the findings of Guan et al. (2015), who noted that NVG often progresses from rubeosisiridis to angle closure, with patients presenting in more advanced stages due to delayed diagnosis.[9] Similarly, Lim et al. (2016) reported that a significant portion of patients with NVG had already reached the angle closure stage by the time of diagnosis, highlighting the aggressive nature of this condition. Early intervention in the open angle stage can significantly reduce the risk of progression to more severe stages, underscoring the importance of regular screening, especially in high-risk populations.[10]Diabetic retinopathy (DR) was the most common cause of NVG in this study, accounting for 38.46% of cases. This finding is in line with prior studies, such as those by Takihara et al. (2014), who found DR to be the leading cause of NVG, responsible for nearly 40% of cases. Chronic retinal detachment (RRD) and vein occlusion were also significant contributors, each affecting 15.38% of eyes.[11]Amini et al. (2016) similarly identified vein occlusion as a major cause of NVG, often secondary to ischemic processes in the retina. The current study's results emphasize the strong association between diabetic retinopathy and NVG, which has been consistently reported across multiple studies. These findings reinforce the need for aggressive management of diabetic retinopathy to prevent NVG development.[12]The mean IOP in the angle closure stage was 30.15 mm Hg, with an SD of 5.12, which is consistent with the findings of Mauri et al. (2013), who reported similarly elevated IOP levels in NVG patients at the advanced angle closure stage.[13] The current study also found that IOP was lower

in the rubeosisiridis stage (mean IOP of 24.85 mm Hg, SD 4.58) and open angle stage (mean IOP of 18.30 mm Hg, SD 3.45), which aligns with Cheung et al. (2014), who noted that IOP tends to increase as NVG progresses, reflecting the worsening obstruction of aqueous outflow. Elevated IOP in NVG is a critical factor leading to optic nerve damage, and controlling IOP is paramount in preventing further vision loss.[14]The distribution of NVG stages in this study mirrors that of Luo et al. (2015), who found a similar proportion of patients presenting in advanced stages.[15] The relationship between diabetic retinopathy and NVG has been well established in studies such as Saad et al. (2016), which reported a nearly identical prevalence of NVG caused by DR. This study's findings also echo the importance of early detection and management of retinal conditions to prevent NVG progression, as emphasized by Lim et al. (2016).[16]

CONCLUSION

This study highlights that neovascular glaucoma (NVG) predominantly affects middle-aged to elderly individuals, with a higher incidence in males. Diabetic retinopathy emerged as the leading cause of NVG, followed by retinal vein occlusion and chronic retinal detachment. The progression of NVG to the angle closure stage is associated with the highest intraocular pressures, underscoring the importance of early diagnosis and intervention. Managing NVG in its earlier stages can potentially prevent severe visual impairment, emphasizing the need for regular screening in high-risk populations, particularly those with diabetes.

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