



## STUDY OF STAGING AND MANAGEMENT OF NEOVASCULAR GLAUCOMA

<b>Prof Dr Nishat Sultana Khayoom</b>	Professor at Department of Ophthalmology, MOH, RIO, Bangalore Medical College and Research Institute, Bangalore-Karnataka
<b>Dr Anuradha A</b>	Assistant Professor, Department of Ophthalmology MOH, RIO Bangalore Medical College and Research institute, Bangalore-Karnataka.
<b>Dr. Soujanya Patil*</b>	Junior Resident, Department of Ophthalmology, MOH, RIO, Bangalore Medical College and Research Institute Bangalore -Karnataka *Corresponding Author
<b>Prof Dr Sujatha Rathod</b>	Director, Head of Institute RIO, MOH Bangalore Medical College and Research Institute Bangalore -Karnataka

**ABSTRACT**

Glaucoma is a neurodegenerative condition that affects the eye and is associated with increased intraocular pressure (IOP). When left untreated, patients may gradually experience visual field loss, and even lose their sight completely.<sup>1</sup> It is the second leading cause of blindness around the globe first being cataracts<sup>2</sup> Neovascular glaucoma (NVG) is an intractable sight-threatening disease which is extremely difficult to manage and can lead to permanent visual loss. Once the condition develops, early diagnosis and management is essential to minimize visual loss. Hence this study was undertaken to study the common risk factors and cause, clinical presentation of NVG.

**KEYWORDS :** Glaucoma, Neovascular glaucoma(NVG)

**INTRODUCTION**

Glaucoma is a neurodegenerative condition that affects the eye and is associated with increased intraocular pressure (IOP). When left untreated, patients may gradually experience visual field loss, and even lose their sight completely.<sup>1</sup> It is the second leading cause of blindness around the globe first being cataracts<sup>2</sup>. The meaning of the word glaucoma in Greek is "clouded". Glaucoma may be defined as a condition that causes progressive neuropathy in the optic field and is characterized by structural changes to the optic nerve head or optic disk. This may lead to functional changes in the patient's visual field<sup>3</sup>. The raised intraocular pressure is frequently associated but not the only risk factor associated with glaucoma. In Glaucoma, there is gradual degeneration of retinal ganglion cells (RGCs) and optic nerves axons. Retinal ganglion cells are the neuron cells of central nervous system, cell bodies of neurons are present in the interior retina and their axons are present in optic nerve. Actual Biological basis and factors contributing to the progression of glaucoma are still not fully understood<sup>4</sup>.

Depending on the underlying cause, Glaucoma can be divided into primary or secondary. Both closed and open-angle glaucoma can develop with no identifiable cause, ensuing in idiopathic or primary glaucoma. The type of glaucoma which has an identifiable result in elevated IOP, which lead to optic nerve damage is known as secondary glaucoma<sup>4</sup>. Secondary glaucomas can again be divided into open angle and closed angle forms. Some of the causes of secondary open angle glaucoma include, pigmentary glaucoma, pseudoexfoliation glaucoma, steroid induced glaucoma, lens induced like phacolytic and lens particle glaucoma, ghost cell glaucoma, haemolytic glaucoma, UGH syndrome (uveitis, glaucoma and hyphaema), Posner schlossmann syndrome, Fuchs heterochromic iridocyclitis etc. Secondary angle closure glaucoma causes include, Iridocorneal endothelial syndromes, posterior polymorphous dystrophy, fibrous ingrowth, penetrating keratoplasty, aniridia, ciliary block or malignant glaucoma, intraocular tumors, nanophthalmos, suprachoroidal haemorrhage and ciliochoroidal effusions, retrolental fibroplasia, neovascular glaucoma etc.<sup>5</sup>

secondary glaucoma, characterized by the development of neovascularization of the iris, elevated intraocular pressure (IOP) and, in many instances, poor visual prognosis. In the past, it used to be referred to as congestive glaucoma, rubeotic glaucoma or diabetic hemorrhagic glaucoma<sup>6</sup>. In 1963, Weiss and colleagues, proposed the term NVG<sup>7</sup>. NVG is associated with the development of a fibrovascular membrane on the anterior surface of the iris and iridocorneal angle of anterior chamber<sup>8</sup>. Invasion of the anterior chamber by a fibrovascular membrane at the beginning impede aqueous outflow in an open-angle phase and thereafter contracts to give rise to secondary angle closure glaucoma with synechial and high IOP<sup>9</sup>. Although NVG is also associated with a large number of uncommon ocular diseases, the majority of the diseases responsible for NVG are diabetic retinopathy, ischemic central retinal vein obstruction (CRVO), and ocular ischemic syndrome. Other rare causes are chronic intraocular inflammations, intraocular tumours, long-standing retinal detachment and central retinal artery occlusion<sup>5</sup>.

The diagnosis of NVG is clinical and requires detailed patient's history and a complete ophthalmological examination. Patients may be asymptomatic, especially when the IOP rise occurs gradually, or they can present with symptoms such as low vision, ocular pain and photophobia. In the early stages, clinical findings can be subtle, requiring the ophthalmologist to maintain high index of suspicion in case of conditions that are commonly associated with NVG such as diabetic retinopathy, central retina vein occlusion or ocular ischemic syndrome<sup>10</sup>

Regardless of progress in the medical and surgical treatment of glaucoma, the visual outcome for patients with NVG remains deprived. Visual prognosis will only be improved with the early noticing of NVG by high indicator of cautious and the prompt initiation of therapy that specifically targets the underlying disease process. Hence this study was undertaken to study the common risk factors, cause and stages clinical presentation of NVG.

**MATERIALS AND METHODOLOGY**

Prospective Observational study conducted between

Neovascular glaucoma (NVG) is a potentially blinding

February 2021 to August 2022 in glaucoma clinic of Minto Ophthalmic hospital, RIO Bangalore Medical College and Research Institute. Study was conducted after taking appropriate ethical clearance from the Institutional Ethical Committee of BMCRI.

50 patient were included after meeting the inclusion criteria (Patient willing to give informed consent, Patients with clinical diagnosis of Neovascular glaucoma) and patients not willing to give informed consent

Age less than 18years

All Other forms of secondary glaucoma

Unavailability for follow up were excluded.

- After obtaining informed consent, history and a detailed slit lamp ocular examination was done. Visual acuity checked using Snellen's chart, IOP measured by Goldman applanation tonometer, Detailed anterior segment examination assesses using slit lamp biomicroscope. A careful examination for neovascularization of iris was done for all the patients. Gonioscopy was performed using Sussman 4 mirror with special emphasis on neovascularization of angle structures and dilated fundus examination with +20, +78. +90D lens.
- B scan was done in eyes with hazy media due to corneal edema and/or dense cataract

Data was analysed using Statistical Package for the Social Sciences (SPSS) trial version. For descriptive statistics-mean, standard deviation, percentage and proportion wherever applicable was be used. Chi square test was used to check the association of categorical variable. A value of  $p \leq 0.05$  was considered to be statistically significant.

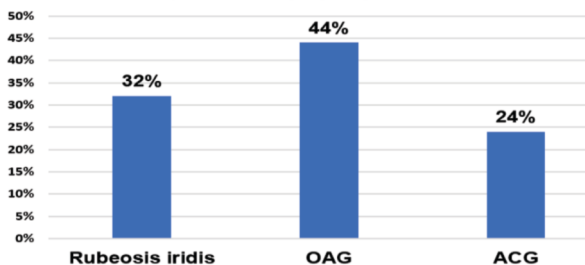
Treatment depending upon the staging and the underlying cause, different treatment modalities were assessed. Medical management like carbonic anhydrase inhibitors (oral and topical), beta-blockers, and alpha-2 agonists, VEGF inhibitors and surgical management like pan retinal photocoagulation, trabeculectomy with antimetabolites, Glaucoma draining devices, cyclophotocoagulation were noted. The postoperative stay was monitored for any complications.

**RESULTS:**

**1. Staging Of Glaucoma**

In this study, among 50 cases, 44% presented in Open angle Glaucoma stage, 32% in rubeosis iridis, 24% presented in Angle closure Glaucoma stage. Maximum number of patients (44%) presented in open angle Glaucoma stage.

**Graph no.1- staging of glaucoma**



**2. Distribution according etiology of NVG**

Etiology*	No. of Patients	Percentage
PDR	19	38
CRVO	10	20
BRVO	4	8
CRAO	1	2
UVEITIS	8	16
POAG	3	6
PACG	2	4
PXFG	1	2
UGH	1	2

POSTRD	1	2
Total	50	100

- \*PDR- Proliferative diabetic retinopathy
- CRVO- Central retinal vein occlusion
- BRVO- Branch retinal vein occlusion
- CRAO- Central retinal artery occlusion
- POAG- Primary open angle glaucoma
- PACG – Primary angle closure glaucoma
- PXFG- Pseudo exfoliation glaucoma
- UGH- Uveitis- glaucoma- hyphaema
- Post RD- post radiation surgery

**3. Distribution according to different treatment modalities**

Table no.2. shows different treatment modalities given to our patients. Majority (34%) of the patients were treated by cyclocryotherapy followed by medical therapy only in 32% and 28% were treated with pan retinal coagulation. 2% needed GDD, 2% needed anti VEGF and rest 2% of the patients were treated with anti-VEGF.

Treatment	No. of Patients	Percentage
MEDICAL	16	32
PRP	14	28
TRAB	01	2
GDD	01	2
ANTI VEGF	01	2
CYCLO CRYO	17	34
total	50	100

**4. Different treatment modalities in Rubeosis iridis group**

In the present study, out of 16 patients of rubeosis iridis, more than half of them were managed by medical treatment alone and 37.5% by pan retinal photocoagulation and 6.25% patients were given anti-VEGF. PRP and Anti-VEGF were combined with medical treatment.

N= 16

Treatment	No. of Patients	Percentage
PRP	6	37.5
MEDICAL	9	56.25
ANTI VEGF	1	6.25
CYCLO CRYO	-	-
Total	16	100

**5. Different treatment modalities in OAG group**

N=22

Treatment	No. of Patients	Percentage
PRP	8	36.36
CYCLO CRYO	9	40.91
MEDICAL	3	13.63
GDD	1	4.55
TRAB	1	4.55
Total	22	100

Out of 22 patients who presented in Open angle Glaucoma stage, 36.36% patients underwent pan retinal photocoagulation, 40.91% underwent cyclo cryo, 13.63% were given medical treatment alone. GDD was inserted in 1 patient and trabeculectomy was done in only 1 patient. Thus, patients presenting in Open angle stage were managed mostly with PRP and cyclo cryo.

**6. Different treatment modalities in ACG group**

Treatment	No. of Patients	Percentage
Cyclo cryo	8	66.67
MEDICAL	4	33.33
TRAB + AM	-	-
total	12	100

Out of 27 patients who presented in angle closure stage, majority of them (66.67%) were managed by cyclo cryo and rest 33.33% were treated by medical treatment alone as they presented with very advanced stages with PL negative. So, trabeculectomy was not done in none of the ACG group in our study.

**7. Comparison of visual acuity at presentation and final visual outcome**

Visual acuity	At presentation	Final visual outcome
>6/60	3 (6%)	7 (14%)
≤6/60	47 (94%)	43 (86%)
Total	50 (100%)	50 (100%)

At the end of the study, after treatment and follow up, out of 50 patients, maximum i.e, 43 (86%) patients had vision ≤6/60 and only 7 (14%) had final vision >6/60. This shows poor vision even after treatment of glaucoma.

**8. Comparison of final IOP with IOP at presentation**

IOP (mmhg)	At presentation	Final IOP
≤30	9 (18%)	32 (64%)
>30	41 (82%)	18 (36%)
total	50 (100%)	50 (100%)

In our study, 82% of the patients presented with high IOP >30mmhg, out of which, in 46% of the patients' fair control of IOP <30mmhg was possible whereas 36% of the patients had persistent high IOP. The statistical comparison was done using Chi-square test and it was found to be statistically significant with p=0.0005 (p<0.05 is significant).

**DISCUSSION**

Neovascular glaucoma (NVG) is an intractable sight-threatening disease which is extremely difficult to manage and can lead to permanent visual loss. Once the condition develops, early diagnosis and management is essential to minimize visual loss. NVG is a potentially blinding disease and is an ophthalmic emergency. Early diagnosis and multidisciplinary systematic approach would be needed to salvage useful vision in these eyes. Timely and appropriate treatment of underlying cause of ischemia and controlling the IOP are the keys to successful management of this condition. Increased awareness of NVG risk factors and early detection of retinal ischemia can improve the prognosis of NVG. Hence this study was undertaken to study the stage and management of NVG

**Clinical staging of glaucoma**

S.N	Clinical staging	Gomez G et al12	Therese Y et al13	AlRubaie K15	Present study
1	Pre rubeosis	12.26	4	-	-
2	Rubeosis iridis	-	-	-	32
3	Open angle	38.69	18	29.5	44
4	Angle closure	49.05	56	44.2	24
5	Undetermined angle	-	-	26.3	-

The above discussion table shows the different clinical staging of glaucoma at the time of presentation. A retrospective chart review was performed by AlRubaie K<sup>15</sup> evaluating the eyes of patients with a diagnosis of NVG at King Khaled Eye Specialist Hospital (KKESH), Riyadh, Saudi Arabia (from January 2002 to December 2012). The anterior chamber angle was open in 176 (29.5%) eyes and a synechial closure was present in 264 (44.2%) eyes. The angle status was undetermined in 157 (26.3%) eyes due to poor visualization. Therese Y et al<sup>13</sup> study included 181 eyes of 162 patients diagnosed with NVG.

This was a retrospective cohort study conducted at an eye center of a tertiary, urban, government hospital. Most of the eyes (n=101 or 56%) were in the closed angle stage of NVG and were phakic (n=148 or 82%).

In a study conducted by Gomez G et al<sup>14</sup> It is noteworthy that 49% of 473 eyes had NVG stage 3 and 55% were blind at baseline. These observations suggest that majority of the patients with neovascular glaucoma presented at later stages. However, in the present study, 32% presented in pre-

glaucomatous stage and 44% had open angle and 24% had closed angle glaucoma. This discrepancy may be due to difference in inclusion of patients of pre-glaucomatous stage and varying possibility being early seeking of health care by our patients.

**Treatment modalities**

S.N	Treatment modality	Tolba et al14	Na Liao et al11	Present study
1	PRP	2.78	17.5	28
2	TRAB+AM	9.56	4.9	2
3	GDD	10.75	72.0	2
4	ANTI VEGF	20	-	2
5	MEDICAL			32
6	CYCLO CRYO or Laser	57	5.6	34

The above table shows different treatment modalities done in cases of NVG. In a study conducted by AlRubaie K et al<sup>15</sup> which was retrospective study aimed to present the outcomes of the therapeutic interventions for neovascular glaucoma (NVG) between 2002 and 2012 for 10 long years at a tertiary eye hospital in Saudi Arabia, following findings were discussed. Retinal laser photocoagulation was considered the main treatment for the underlying disease. Traditionally, retinal ablation by laser and/or cryotherapy has been the first line of treatment for NVG. There is strong evidence that pan retinal photocoagulation is the treatment of choice for the prevention of the development of NVG if retinal ischemia is a factor - level A recommendation by the American Academy of Ophthalmology. Intravitreal bevacizumab alone and in the combination with retinal laser was administered to 11.2% and 5.5% of the patients in the study, respectively. These predominantly included advanced cases. The role of antiangiogenic agents in the treatment of the ischemic components of NVG has been established<sup>16,17</sup>. It has been shown to induce rapid resolution of iris and iridocorneal angle vessels as demonstrated angiographically. The effect has been observed after both intravitreal and intracameral administration<sup>16,17,18</sup>. In one more study the majority of patients received intravitreal injections. While PRP provides a more permanent reduction of the ischemic angiogenic stimulus, bevacizumab-induced regression of iris neovascularization is often temporary and recurrence is possible.<sup>19,20</sup>

**Treatment of NVG at different stages of glaucoma-**

Majority (34%) of the patients were treated by cyclo cryo followed by medical therapy only in 32% and 28% were treated with pan retinal coagulation. 2% needed GDD, 2% needed anti VEGF and rest 28% of the patients were treated with anti-VEGF. Trabeculectomy surgery was done only in one patient as majority of the patients presented at advanced stages. Amongst the patients of rubeosis iridis, more than half of them were managed by medical treatment alone and rest by pan retinal photocoagulation. Anti-VEGF was given to only one patient. PRP and Anti-VEGF were always combined with medical treatment. Patients presenting in Open angle stage were managed mostly with PRP (36.36%) and cyclo cryo (40.91%) and only few with medical treatment alone. GDD was inserted in 1 patient and trabeculectomy was done in only 1 patient. Majority of closed angle glaucoma group patients (66.67%) were managed by cyclo cryo and rest 33.33% were treated by medical treatment alone as they presented with very advanced stages with PL negative. So, trabeculectomy was not done in none of the ACG group in our study. In the present study, filtering surgery is less

Neovascular glaucoma is a very difficult condition to manage, and visual outcome does not always follow IOP control due to the underlying ocular disease. Blindness can ensue, which may be very painful due to high intraocular pressure and inflammation.

This study has some limitations including the hospital-based study, small sample size, exclusion of many cases due to loss to follow-ups and lack of data. The short follow-up period is a further limitation. However, this study highlights the clinical profile and treatment modalities and outcome of NVG in a tertiary centre which gets maximum referrals over a long period of 2 years

## CONCLUSION

NVG seen in our tertiary centre usually presented late with advanced NVG and poor VA. Most of the patients had DR and CRVO. Better IOP control was achieved with combinations of treatment. However, a great percentage of eyes still lost vision despite aggressive measures. Aggressive screening for NVG among high-risk groups such as patients with DR and hypertension/CRVO is warranted to institute treatment at an early phase to prevent vision loss.

Various modalities of treatment are available, they have to be chosen according to aetiology and stage of presentation. Angle closure patients have been proven to have poorer prognosis and hence early surgical intervention wherever possible has to be employed. Surgical intervention is required in most of the cases, but most of them are found to have increased complications and patients must be explained about the need for continuing treatment even after surgery and prolonged follow up.

Timely and appropriate treatment of underlying cause of ischemia and controlling the IOP are the keys to successful management of this condition. Increased awareness of NVG risk factors and early detection of retinal ischemia can improve the prognosis of NVG.

## Conflict Of Interest

None declared

## REFERENCES

- Natalie Schellack, Gustav Schellack, Selente Bezuidenhout, Glaucoma: a brief review, South African Pharmaceutical journal, 2015;82(5):18-22.
- Arthur S, Cantor LB. Update on the role of alpha-agonists in glaucoma management. *Exp Eye Res.* 2011;93(3):271-283
- Fraser S, Manvikar S. Glaucoma: the pathophysiology and diagnosis. The Pharmaceutical Journal [homepage on the Internet]. 2010. c2015. Available from: [www.pharmaceutical-journal.com/learning/learning/11045043.article](http://www.pharmaceutical-journal.com/learning/learning/11045043.article)
- Shahida, Muhammad Imran Qadir. Glaucoma: Etiology, Pathophysiology and Management. *Biomed J Sci & Tech Res* 30(5)-2020. BJSTR. MS.ID.005005.
- AK Khurana textbook of ophthalmology, 7<sup>th</sup> edition, chapter 10, page no.231
- Gustavo B. Rodrigues, Ricardo Y. Abe, Camila Zangalli, Savio L. Sodre, Flavia
- Albert DM, Jakobiec FA, editors. Principles and practice of ophthalmology. 1999, Philadelphia: WB Saunders Publishers.
- Hayreh SS. Neovascular glaucoma. *Prog Retin Eye Res.* 2007;26(5):470-85.
- Shazly TA, Latina MA. Neovascular glaucoma: etiology, diagnosis and prognosis. *Semin Ophthalmol.* 2009;24(2):113-21.
- Gustavo B. Rodrigues, Ricardo Y. Abe, Camila Zangalli, Savio L. Sodre, Flavia A. Donini, Danilo C. Costa, Andre Leite, Joao P. Felix, Marcelo Torigoe, Albeiro Diniz-Filho and Homero Gusmão de Almeida; Neovascular glaucoma: a review; *International Journal of Retina and Vitreous*, (2016) 2:26, DOI 10.1186/s40942-016-0051-x.
- Na Liao, Chaohong Li, Huilv Jiang, Aiwu Fang, Shengjie Zhou and Qinmei Wang, Neovascular glaucoma: a retrospective review from a tertiary center in China, *BMC Ophthalmology* (2016) 16:14, DOI 10.1186/s12886-016-0190-8
- Lazcano-Gomez G, Soohoo JR, Lynch A, Bonell LN, Martinez K, Turati M, Gonzalez-Salinas R, Jimenez-Roman J, Kahook MY. Neovascular Glaucoma: A Retrospective Review from a Tertiary Eye Care Center in Mexico. *J Curr Glaucoma Pract* 2017;11(2):48-51.
- Angela Therese Y. Uy, MD, John Mark S. de Leon, MD, Jubaida M. Aquino, Clinical Profile and Treatment Outcomes of Patients with Neovascular Glaucoma in a Tertiary Hospital in the Philippines, *Philipp J Ophthalmol* 2021;46: 82-87
- Doaa A. Tolba, Ahmed M. Abdelrahman, Hagar Hamdy, Sara M. Esmat, Clinical characteristics and interventions in neovascular glaucoma cases: a study from the glaucoma care clinic at Cairo University Hospitals, *Delta Journal of Ophthalmology* 2021, 22:208-213
- AlRubaiie K, Albahlal A, Alzahim T, et al. (September 03, 2021) Neovascular Glaucoma Progress and Impact of Therapeutic Intervention in Saudi Arabia. *Cureus* 13(9): e17696. DOI 10.7759/cureus.17696
- Iliev ME, Domig D, Wolf-Schnurbursch U, Wolf S, Sarra GM: Intravitreal bevacizumab (Avastin) in the treatment of neovascular glaucoma. *Am J Ophthalmol.* 2006, 142:1054-1056. 10.1016/j.ajo.2006.06.066
- Olmos LC, Lee RK: Medical and surgical treatment of neovascular glaucoma. *Int Ophthalmol Clin.* 2011, 51:27-36. 10.1097%2FIIO.0b013e31821e5960
- Grisanti S, Biester S, Peters S, Tatar O, Ziemssen F, Bartz-Schmidt KU,

Tuebingen Bevacizumab Study Group: Intracameral bevacizumab for iris rubeosis. *Am J Ophthalmol.* 2006, 142:158-160. 10.1016/j.ajo.2006.02.045

- Wolf A, von Jagow B, Ulbig M, Haritoglou C: Intracameral injection of bevacizumab for the treatment of neovascular glaucoma. *Ophthalmologica.* 2011, 226:51-56. 10.1159/000327364
- Saito Y, Higashide T, Takeda H, Murotani E, Ohkubo S, Sugiyama K: Clinical factors related to recurrence of anterior segment neovascularization after treatment including intravitreal bevacizumab. *Am J Ophthalmol.* 2010, 149:964-972. 10.1016/j.ajo.2010.01.008