A ONE-YEAR PROSPECTIVE STUDY TO EVALUATE THE EFFICACY OF INTRAOPERATIVE SUBTENON INJECTION OF 0.01 % MITOMYCIN-C AS AN ADJUNCT TO TRABECULECTOMY IN PATIENTS ADMITTED TO SHRI BM PATIL MEDICAL COLLEGE AND RESEARCH CENTRE, VIJAYAPURA

By

DR. ARKAPRAVA RAY

Dissertation submitted to the

B.L.D.E. (DEEMED TO BE UNIVERSITY)

VIJAYAPURA, KARNATAKA

In Partial fulfilment of requirements for the degree of

MASTER OF SURGERY
In
OPHTHALMOLOGY

Under the guidance of

PROF. (DR.) REKHA R. MUDHOL
MBBS, MS, DOMS, PhD (Medical)
Professor and Head
Department of Ophthalmology

B.L.D.E. (DEEMED TO BE UNIVERSITY)
Shri B.M. Patil Medical College Hospital and Research Centre
Vijayapura, Karnataka – 586103
2024
DOI 10.5281/zenodo.15487712
https://zenodo.org/records/15487713

B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College Hospital and Research Centre
Vijayapura, Karnataka

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Date: 26/06/2024

Place: Vijayapura

Arkaprava Ray

Dr. Arkaprava Ray

Postgraduate

Department of Ophthalmology
B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College
Hospital and Research Centre
Vijayapura, Karnataka

B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College Hospital and Research Centre
Vijayapura, Karnataka

Certificate by the Guide

*This is to certify that the dissertation entitled "**A One-year Prospective Study to Evaluate the Efficacy of intraoperative subtenon injection of 0.01 % Mitomycin-c as an Adjunct to Trabeculectomy in Patients Admitted to Shri BM Patil Medical College and Research Centre, Vijayapura"** is a bonafide and genuine research work carried out by **Dr. Arkaprava Ray** under my overall supervision and guidance in partial fulfilment of the requirement for the degree of M.S. in Ophthalmology.*

Date: 26/06/2024
Place: Vijayapura

Prof. (Dr.) Rekha R. Mudhol
MBBS, MS, DOMS, PhD (Medical)
Professor and Head
Department of Ophthalmology
B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College
Hospital and Research Centre
Vijayapura, Karnataka

B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College Hospital and Research Centre
Vijayapura, Karnataka

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*This is to certify that the dissertation entitled "**A One-year Prospective Study to Evaluate the Efficacy of intraoperative subtenon injection of 0.01 % Mitomycin-c as an Adjunct to Trabeculectomy in Patients Admitted to Shri BM Patil Medical College and Research Centre, Vijayapura"** is a bonafide and genuine research work carried out by **Dr. Arkaprava Ray** under the guidance of **Prof. (Dr.) Rekha R. Mudhol** **MBBS, MS, DOMS, PhD (Medical)** Professor and Head, Department of Ophthalmology. B.L.D.E (DU)'s Shri B.M Patil Medical College, Hospitaland Research Centre, Vijayapura.*

Date: 26/06/2024

Place: Vijayapura

Prof. (Dr.) Rekha R. Mudhol
MBBS, MS, DOMS, PhD (Medical)
Professor and Head
Department of Ophthalmology
B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College
Hospital and Research Centre
Vijayapura, Karnataka

B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College Hospital and Research Centre
Vijayapura, Karnataka

Endorsement by the Principal / Head of the Institution

*This is to certify that the dissertation entitled "**A One-year Prospective Study to Evaluate the Efficacy of intraoperative subtenon injection of 0.01 % Mitomycin-c as an Adjunct to Trabeculectomy in Patients Admitted to Shri BM Patil Medical College and Research Centre, Vijayapura"** is a bonafide and genuine research work carried out by **Dr. Arkaprava Ray** under the guidance of **Prof. (Dr.) Rekha R. Mudhol** **MBBS, MS, DOMS, PhD (Medical)** Professor and Head, Department of Ophthalmology. B.L.D.E (DU)'s Shri B.M Patil Medical College, Hospitaland Research Centre, Vijayapura*

Date: 26/06/2024

Place: Vijayapura

Prof. (Dr.) Aravind V. Patil
MS (Surgery)

Principal

B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College
Hospital and Research Centre
Vijayapura, Karnataka

B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College Hospital and Research Centre
Vijayapura, Karnataka

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Date: 26/06/2024

Place: Vijayapura

Arkaprava Ray

Dr. Arkaprava Ray

Postgraduate

Department of Ophthalmology
B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College
Hospital and Research Centre
Vijayapura, Karnataka

ACKNOWLEDGEMENT

With a humble heart, I would like to begin this acknowledgement with a prayer to the Almighty God, who has given us the strength, wisdom, and grace to embark on this scholarly journey.

I am profoundly grateful to my teacher, mentor and guide, ***Prof. (Dr.) Rekha R. Mudhol****, whose unwavering inspiration, encouragement, and support have been instrumental throughout my post-graduation studies and the preparation of my dissertation. Her guidance has been invaluable, and I deeply appreciate her dedication to my academic and professional growth.*

I am deeply indebted to my esteemed Professors, ***Dr. Sunil Biradar*** *and* ***Dr Vallabha K,*** *as well as my Associate Professor****, Dr. Raghavendra K Ijeri****, whose guidance and encouragement have propelled me to new heights of professional achievement throughout my course. Their mentorship has been instrumental in shaping my academic journey, and I am forever grateful for their invaluable support and inspiration.*

My heartfelt thanks and deep gratitude to my teachers, ***Dr. Keerti Wali, Dr. Talluru Subash, Dr. Shweta Patil, Dr. Magna Mary*** *and* ***Dr. Suman D****. Without their inspiration, timely guidance, immense support, and motivation, I wouldn't have been able to complete this dissertation.*

I am grateful to ***Dr. Aravind V Patil****, Principal of BLDE (DU) 's Shri B. M Patil Medical College Hospital and Research Centre, Vijayapura, for permitting me to utilise the resources in the completion of my work. I am extremely thankful*

*to **Mr. Muragesh Mathapati** for his guidance in statistical analysis. I thank my friends and colleagues specially **Dr. Vaishnavi Patil** and **Dr. Shilpa K.** for their constant support.*

*I express my heartfelt appreciation and gratitude to my beloved parents, **Dr. Abhijit Ray** and **Mrs. Ali Ray Chakraborty,** and my beloved brother **Akashnil Ray** for their support, invaluable advice, and endless encouragement. Their boundless love and sacrifices have been the cornerstone of my journey, and I am deeply indebted to them for instilling in me the values of perseverance and determination.*

Finally, I acknowledge my heartfelt gratitude to all my patients; this study would be incomplete without their participation.

Dr. Arkaprava Ray

Postgraduate

Department of Ophthalmology
B.L.D.E. (Deemed to be University)
Shri B.M. Patil Medical College
Hospital and Research Centre
Vijayapura, Karnataka

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LIST OF ABBREVIATIONS

IOP	Intraocular pressure
MMC	Mitomycin C
IBAGS	Indiana Bleb Appearance Grading System
POAG	Primary Open Angle Glaucoma
PACG	Primary Angle Closure Glaucoma
BC	Before Christ
ONH	Optic Nerve Head
GON	Glaucomatous Optic Neuropathy
RNFL	Retinal Nerve Fibre Layer
NTG	Normal Tension Glaucoma
OHT	Ocular Hypertension
PACD	Primary Angle Closure Disease
DALY	Disability Adjusted Life Years
PCG	Primary Congenital Glaucoma
NF	Neurofibromatosis
HPG	High Pressure Glaucoma
NPG	Normal Pressure Glaucoma
PAC	Primary Angle Closure
PACS	Primary Angle Closure Suspect
IAC	Intermittent Angle Closure
CACG	Chronic Angle Closure Glaucoma
GAT	Goldmann Applanation Tonometer
NCT	Non-Contact Tonometer
CCT	Central Corneal Thickness
OCT	Optical Coherence Tomography
GCC	Ganglion Cell Complex

GLV	Global Loss Volume
FLV	Focal Loss Volume
TGF-β	Transforming growth factor-β
AC	Anterior Chamber
Nd: YAG	Neodymium-doped yttrium aluminium garnet
SCH	Suprachoroidal haemorrhage
5-FU	5-Fluorouracil
FFSS	Fluorouracil Filtering Surgery Study
Log MAR	Logarithm of the minimum angle of resolution
SICS	Small incision cataract surgery
PMMA	Polymethyl Methacrylate
SD	Standard Deviation
HbA1C	Glycated Haemoglobin
RAPD	Relative Afferent Pupillary Defect
BCVA	Best Corrected Visual Acuity

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Abstract

Background: Glaucoma, characterised by optic neuropathy and elevated intraocular pressure (IOP), is a leading cause of global blindness, affecting 3.54% of individuals aged 40 to 80. Trabeculectomy, enhanced with antimetabolites like Mitomycin C (MMC), has long been the gold standard filtering surgery for glaucoma. The conventional method of MMC application involves using soaked sponges over the subconjunctival space. However, this approach can result in complications such as blebitis and foreign-body granuloma due to residual sponges. Recent research has explored intraoperative MMC injection to improve outcomes and reduce complications. This study aims to assess the safety and efficacy of a low dose (0.1 mg/ml) of MMC administered through subtenon injection during trabeculectomy, with a follow-up period of over 6 months.

Materials and Methods: It is a prospective interventional study on patients who underwent trabeculectomy with a subtenon injection of 0.1mg/ml of Mitomycin C combined with Small incision cataract surgery with intraocular lens implantation and were followed up over 6 months. Efficacy was determined in terms of intraocular pressure reduction, bleb architecture was graded using the Indiana Bleb Appearance Grading System (IBAGS), and safety was commented upon regarding postoperative complications.

Results: Thirty patients were enrolled, with the majority having primary open-angle glaucoma (63.33%), while 36.67% had primary angle-closure glaucoma. Baseline intraocular pressure (IOP) was 31.40 (± 10.38) mmHg. It significantly reduced to 14.60 (± 3.75) mmHg on the first postoperative day, decreasing to 9.55 (± 1.57) mmHg by the 6th postoperative month ($p = 0.001$). The percentage reduction in IOP was substantial, 69.57%, by the 6th postoperative visit. Bleb morphology assessment using IBAGS revealed significant improvements in bleb height, extent, and vascularity over the 6-month follow-up ($p = 0.001$). Out of the total patients,

93.33% achieved controlled IOP without antiglaucoma medications, while 6.67% required one medication for IOP control. Complications were minimal, with transient corneal oedema in six patients and manageable postoperative hypotony in one case.

Conclusion: A sub-tenon injection of MMC effectively reduces intraocular pressure and promotes favourable bleb architecture, offering a safe and minimally complicated alternative to the conventional approach. It can be safely considered in high-risk patients as an alternate route of MMC application during trabeculectomy.

Introduction

"It's simply a tragedy that anyone today goes blind from glaucoma when it's so unnecessary."
- Willard Scott

"Glaucoma is an optic neuropathy characterised by specific structural findings in the optic disc and specific functional deficits detected by automated visual field testing, with elevated IOP recognised as a risk factor but not a defining feature". (1) Glaucoma now stands as "the second leading cause of global blindness", following cataracts, as the "World Health Organization" reported. (2) The global prevalence of glaucoma in "individuals aged 40 to 80 years" is approximately "3.54%". (3) "Primary Open-Angle Glaucoma" (POAG) is more common in "Africa at 4.20%", whereas "Primary Angle-Closure Glaucoma" (PACG) is more common in "Asia at 1.09%." As of 2013, the global estimate of individuals with glaucoma aged 40 to 80 years was 64.3 million, with projections indicating an increase to over "111.8 million by the year 2040" (3). Glaucoma management primarily focuses on reducing IOP (4,5), with the American Academy of Ophthalmology recommending an initial target of a 25% reduction from baseline in POAG. (4,6) Topical medication is the primary therapy, but issues like tolerability, insufficient IOP reduction, or adherence challenges may necessitate surgical intervention (7). Since its inception in the "mid-1960s," trabeculectomy has been the "gold standard" surgery for treating glaucoma. (7,8)

Mitomycin C is widely used in many different types of surgeries, including those for conjunctival neoplasia, cicatricial eye disease, glaucoma, pterygium, corneal refractive, and allergic eye disease. (9,10) In glaucoma surgery, notably trabeculectomy, MMC has been routinely applied for over two decades to mitigate "postoperative episcleral fibrosis, preventing bleb failure attributed to scarring." (10,11) Its impact on enhancing fibroblast density and connective tissue improves "long-term IOP control in glaucoma filtration surgery." (10–12) The traditional administration of MMC involves a "sponge soaked" in the drug applied to the subconjunctival space, adjusting concentration and exposure duration

based on the risk of failure. An alternative approach currently under investigation is the intraoperative injection of MMC, serving as an alternative to sponge application. (10)

Intraoperative MMC injection in trabeculectomy offers advantages over sponge application, generating diffuse and elevated blebs. This method may enhance long-term success without increased complications, particularly by promoting less scarring and vascularisation of the bleb. Additionally, the injection approach eliminates the need for multiple sponges, reducing the risk of retained sponges. (13) To our knowledge, there is limited research on the intraoperative injection of mitomycin C via the subtenon route, and even fewer studies have investigated the use of a lower dose of 0.1mg/ml of mitomycin C for intraoperative subtenon. To address this gap, our study is designed as a prospective interventional study to evaluate the efficacy and safety of administering a lower dose (0.1 mg/ml) of MMC through subtenon injection during trabeculectomy.

Review of literature

Historical perspective

The term “Glaucoma” originates from the Greek word “glaukos" (γλαυκῆς), tracing its linguistic roots to the 8th century BC (14). However, as per literature, the word “glaukos” may have been employed to depict an array of colours, encompassing shades such as blue, grey, and green. (15)

Before the introduction of ophthalmoscopy, any condition not visibly apparent as an external pathology was often labelled as either amblyopia or amaurosis. Glaucoma was typically identified if the pupil displayed an obscured and greenish appearance. (16)

In 1858, Stirling A. explained that the green hue in "glaucoma" was caused by light reflection in the lens, which was altered by the aqueous humour and cornea and is also observed in various conditions with dilated pupils and imperfectly transparent media.(17)

In 1965, Mailer theorised that the connection between glaucoma and green pupils might have been influenced by examinations conducted in candlelight. (18)

In 1969, Berlin and Kay proposed a progressive evolution in colour vocabulary, as published by Merrifield W in 1971, and they suggested that the Greek term “glaukos" could have been influenced by linguistic changes describing it with multiple colours like blue, grey, and green, over time. (19)

Mentioning 19th century Leffler et al. proposed a more straightforward explanation of this greenish hue, mentioning 19th-century observers who suggest that Pupil dilation, or mydriasis, makes it possible to observe the lens, which in most middle-aged patients usually shows signs of nuclear sclerosis. (14)

Drews gave an alternative explanation, linking it to “blood pigments” deposition after intraocular haemorrhage. (20)

The introduction of the ophthalmoscope revolutionised ophthalmology by enabling the visualisation of glaucoma-related excavated optic neuropathy and highlighting its relevance to amaurosis. This emphasised the shared occurrence of optic neuropathy and elevated intraocular pressure in both conditions. (14)

The ophthalmoscope era also witnessed dynamic advancements in diagnosing and treating various glaucoma types (14,15). Early filtering surgeries emerged in 1878 (21), and intraocular pressure measurement techniques like the Schiotz tonometer (1905) and Goldmann tonometer (1955) followed (22). The use of gonioscopy to visualise the anterior chamber angle was first described in 1915. (23) In the 1970s, automated perimetry made its debut. Pharmacologic agents have attempted to lower intraocular pressure, starting with eserine and pilocarpine in the 19th century and continuing with options like epinephrine, adrenergic agonists, carbonic anhydrase inhibitors, beta-blockers, and prostaglandin analogues in the 20th century. (24,25).

In tracing the historical evolution of glaucoma surgery, it is imperative to acknowledge the seminal review by Razeghinejad and Speath., who meticulously catalogued a diverse range of surgical techniques.(26) Their comprehensive work traces the roots of these procedures back to von Graefe's groundbreaking 1856 discovery of the efficacy of iridectomy for acute glaucoma (27). Subsequent notable contributions include De Wecker's introduction of sclerotomy in 1858 and innovations like cyclodialysis and ciliodestruction in 1900 and 1932, respectively. Originating in 19th-century innovations, contemporary glaucoma surgeries, particularly those introduced in the 1960s, revolve around enhancing aqueous humor outflow or reducing inflow. Trabeculectomy, a breakthrough introduced by Carins in the mid-1960s, stands out for its effectiveness, albeit with constraints. Simultaneously, non-penetrating glaucoma surgeries emerged, though universal adoption remains limited. The introduction of Molteno's shunt in the 1960s paved the way for contemporary implantable devices such as SOLX, iStent, and Ex-PRESS shunt, which predominantly emerged in 1995. (26)

Definition of glaucoma

Liu et al. described the “evolution of the definition of glaucoma traced through three distinct historical periods” (28):

1. In the year 1745, “Johann Zacharias Platner” observed that “the eyes of individuals with glaucoma were more rigid” compared to those of healthy individuals, and by the year 1830, “William Mackenzie” emphasised “the significance of elevated intraocular pressure (IOP) in diagnosing glaucoma”, thereby laying the groundwork for the initial definition of glaucoma as "a disease characterised by elevated IOP" (28).

2. In the year 1857, “von Graefe”, utilising ophthalmoscopy, observed “the pitting atrophy of the optic nerve head (ONH) in glaucoma patients” which he termed as “glaucomatous optic neuropathy (GON).” Consequently, “glaucoma” was defined as “optic neuropathy resulting from elevated IOP with characteristic signs of GON, including (a) a documented increase in the cup size of the ONH, (b) atrophy surrounding the ONH in the peripapillary area, and (c) localised wedge-shaped defects or larger diffuse defects in the retinal nerve fibre layer (RNFL)” (28).

3. In the “20th century”, the identification of “normal tension glaucoma (NTG)” and “ocular hypertension (OHT)” suggested that “elevated IOP is not necessary for glaucoma”. Rather, research suggests that GON is the primary implication of glaucoma. (28).

According to the 2020 “Preferred Practice Patterns of the American Academy of Ophthalmology”, “primary open-angle glaucoma (POAG)” is a “chronic and progressive optic neuropathy in adults, defined by the acquired atrophy of the optic nerve, loss of retinal ganglion cells and their axons, and associated with an open anterior chamber angle observed through gonioscopy” (6). According to the 2020 “Preferred Practice Patterns of the American Academy of Ophthalmology”, “primary angle-closure disease (PACD)” is defined as “the appositional or synechial closure of the anterior chamber angle, primarily due to multiple

mechanisms with pupillary block, not initially associated with elevated IOP or glaucomatous optic neuropathy but may occur acutely or chronically" (29).

Epidemiology of Glaucoma

In 2002, the "World Health Organization" officially acknowledged "glaucoma as the second leading cause of global blindness". (2) In people aged 40 to 80, the "global prevalence of glaucoma is estimated at 3.5%," with "primary open-angle glaucoma" being six times more common (3.1%) than "primary angle-closure glaucoma" (0.5%), according to Jonas et al. (2017) (30). In 2013, an "estimated 64.3 million individuals aged 40–80" were affected by glaucoma, and projections by Tham et al. suggest an "increase to 111.8 million by 2040" (31). Lin et al. outlined the global burden of glaucoma, revealing significant diversity in age-standardized DALY rates, varying from 0.58 to 42.5 per 100,000, with Mali exhibiting the highest rate, followed by Ethiopia, Botswana, Niger, and Libya [Figure 1] (32).

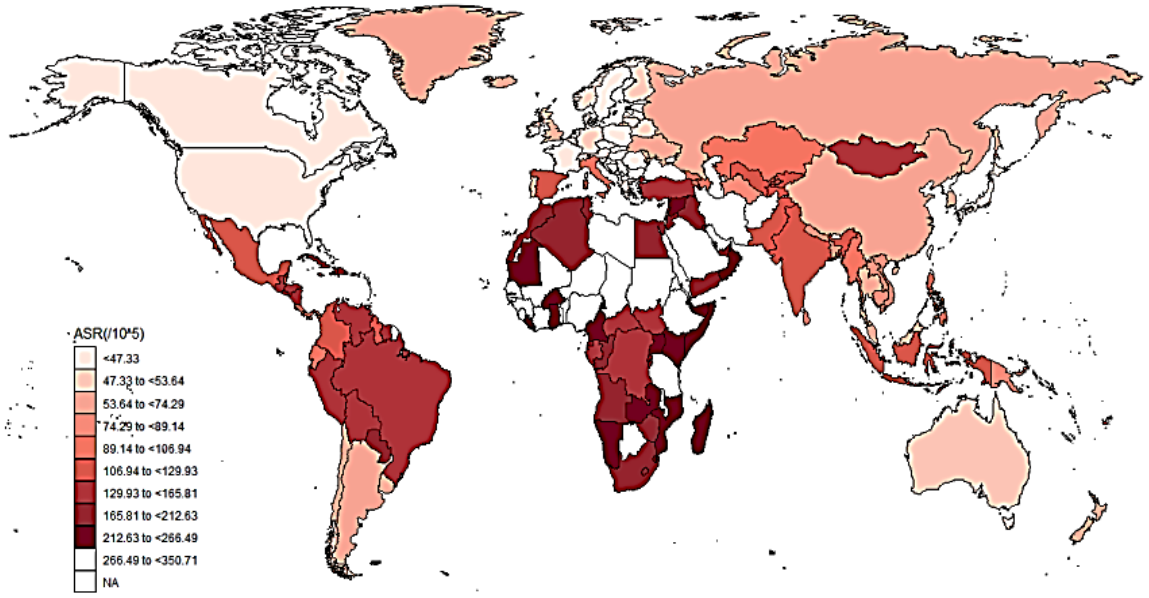


Figure 1: The burden of glaucoma across the globe. Source: Picture courtesy Lin et al.: "The Global Burden of Glaucoma: Findings from the Global Burden of Disease 2019 Study and Predictions by Bayesian Age–Period–Cohort Analysis" (32)

As reported by George et al., the “burden of glaucoma” in India is substantial, affecting around “11.2 million individuals aged 40 and older”. Of these, “6.48 million are estimated to have primary open-angle glaucoma”. At the same time, “2.54 million are affected by primary angle-closure glaucoma”, with a “potential risk for primary angle-closure disease in 27.6 million individuals” (33).

The Aravind Comprehensive Eye Survey (34) in southern India, involving “5150 individuals aged 40 and older,” revealed a glaucoma prevalence of 2.6%, with “primary open-angle glaucoma” accounting for 1.7% and “primary angle-closure glaucoma” at 0.5%. Alarmingly, 93.0% of individuals with “primary open-angle glaucoma” were undiagnosed, and 20.9% experienced blindness in one or both eyes, emphasising the need for early detection to mitigate the substantial burden of glaucoma-related blindness in India, comparable to rates observed in white populations.

According to the West Bengal Glaucoma Study(35)a survey of 1324 individuals aged 50 and above in rural West Bengal revealed a glaucoma prevalence increase from “2.7% in the 50-59 age group” to “6.5% in those aged 80 and above”. The age-standardized prevalence for all glaucoma was 3.4%. “Primary open-angle glaucoma” significantly surpassed “primary angle-closure glaucoma” by more than 10:1, “with only three primary angle-closure glaucoma cases identified”. West Bengal exhibited lower glaucoma prevalence than Hyderabad but comparable rates to Tamil Nadu and Dhaka, emphasising the need to prioritise detecting “primary open-angle glaucoma” in the region.

Cook et al. mentioned “primary open-angle glaucoma” (POAG) risk factors: African individuals have up to five times higher prevalence, Hispanics show an age-related increase and key factors include “age, high refractive error, thin central corneal thickness, large optic disc diameter, elevated intraocular pressure, and the relationship of blood pressure, diabetes mellitus.”

Cook et al. also mentioned primary angle-closure glaucoma risk factors, noting a higher prevalence in Mongoloid individuals, increased age, greater female susceptibility, positive family history, and a correlation with hypermetropia (farsightedness). According to their findings, these factors collectively contribute to the heightened susceptibility of individuals to develop primary angle-closure glaucoma. (1)

Surgical Anatomy and Physiology

Anatomy of the anterior chamber angle:

A. Schwalbe's Line:

"Schwalbe's line" is a critical anatomical feature marking the "most anterior extension of the trabecular meshwork" and serving as "the termination point of Descemet's membrane". In the area "anterior to the apical portion of the trabecular meshwork" lies "Zone S", characterised by a width ranging from 50-150 μm (36). This zone involves the "transition from trabecular to corneal endothelium and the thinning and termination of Descemet's membrane." Schwalbe's line is demarcated by "a discontinuous elevation resulting from the oblique insertion of limbal trabeculae into the limbal stroma", signifying the transition from the scleral curvature to the steeper corneal curvature (37). Pigment settling in this region may occur. Additionally, "secretory cells" known as "Schwalbe's line cells" are present, producing a "phospholipid material that facilitates aqueous flow" (36).

B. Trabecular Meshwork:

The "trabecular meshwork" assumes "a triangular shape with its apex at Schwalbe's line and its base at the scleral spur." Comprising a "connective tissue core surrounded by endothelium," the trabecular meshwork is anatomically divided into "three parts"(36) :.

1. The innermost part next to the aqueous humour, known as the "***Uveal meshwork***," is organised in "bands or rope-like trabeculae" (36).

2. The "***Corneoscleral meshwork***", comprised of "8–14 sheets of trabeculae perforated by elliptical openings", extends from "the scleral spur to the anterior wall of the scleral sulcus." (36).
3. The deepest layer before reaching "Schlemm's canal", known as the "***Juxtacanalicular part***", consists of the endothelium of Schlemm's canal on one side and trabecular endothelium on the other. The loose connective tissue between the two layers provides resistance to aqueous outflow (36).

On gonioscopy, it is seen as a pigmented band anterior to the scleral spur and is functionally divided into two parts: (37)

1. The "**anterior part"** extends from "Schwalbe's line to the front edge of Schlemm's canal," playing a role in a lesser level of aqueous outflow.
2. The "**posterior part"** comprises the remaining meshwork and serves as "the primary site of aqueous outflow," particularly the segment adjacent to Schlemm's canal. It is the functional part of the trabecular meshwork.

C. Schlemm's Canal:

Schlemm's canal is a 360-degree endothelial-lined channel with an average diameter of 190 to 370 μm. (36) Exhibiting properties of vascular endothelium, it may appear as a single channel or occasionally branch into a plexus-like system. The diameter of the canal lumen is influenced by intraocular pressure, varying from absent at high pressure to very large at low pressure.

D. Scleral Spur:

The "scleral spur" protrudes from "the inner aspect of the anterior sclera and is attached to the trabecular meshwork anteriorly and the sclera and longitudinal portion of the ciliary muscle posteriorly." Contraction of the "ciliary muscle pulls the scleral spur posteriorly"

(36). On gonioscopy, a “white line between the ciliary body band and functional trabecular meshwork” is seen (37).

E. Ciliary Body Face:

The visible part of the ciliary body in the anterior chamber is called the ciliary body face, and the width of this portion varies according to the level of iris insertion. It usually has a larger width in myopes and a smaller width in hypermetropes. During gonioscopy, its colour is perceived as “grey or dark brown” (37).

Aqueous humor dynamics

Aqueous humor dynamics involve the intricate processes of both production and outflow, which are vital for maintaining ocular health.

The epithelium of the pars plicata utilises passive and active secretion to produce aqueous humor. In this process, a high-protein filtrate is transported by active solute transport through the dual-layered ciliary epithelium and into the stroma of the ciliary processes through fenestrated capillaries. Water enters the posterior chamber passively due to the osmotic gradient that results from it. Secretion is regulated by the sympathetic nervous system, which is mediated by beta-2 and alpha-2 receptors. This process depends heavily on enzymatic activity, especially that of carbonic anhydrase (37).

Aqueous outflow occurs when fluid passes through the pupil and into “the anterior chamber from the posterior chamber”. Three routes allow fluid to leave the eye: trabecular outflow (90%), which involves the flow through “the trabeculum into the Schlemm canal and episcleral veins”; uveoscleral drainage (10%), which drains fluid from the ciliary body, choroid, and sclera through the venous circulation; and via the iris, which allows for the drainage of some fluid. Since trabecular outflow is pressure-sensitive, the outflow is enhanced

when intraocular pressure (IOP) rises. These dynamic processes are crucial for maintaining intraocular pressure balance and preventing conditions like glaucoma. (36,37)

Anatomy of the optic nerve head

The “terminal portion of the optic nerve” that is most directly impacted by elevated intraocular pressure is known as the “optic nerve head (ONH)”. The ONH is located approximately “4-5 mm from the fovea (in emmetropic eyes) and extends from the surface of the retina to the myelinated segment of the optic nerve, which starts just behind the sclera beyond the lamina cribrosa”. It is situated somewhat superiorly in a nasal direction. The axons are arranged into about 1000 fascicles within the “optic nerve head” (37):

1**. Retinal Nerve Fiber Layer**: Situated as the innermost part of the “optic nerve head”, the “surface nerve fibre layer” marks the point where nerve fibres come “into direct contact with the vitreous”. At its posterior limit, after completing a 90-degree turn, nerve fibres reach the choroid level. The “anterior limit of the scleral ring” defines the “peripheral edge of the nerve fibre layer” (37).

2. **Prelaminar Region:** Also known as “the anterior portion of the lamina cribrosa”, “the prelaminar region” is an indistinct segment of axons surrounded by the outer retina, choriocapillaris, and choroid. This layer exhibits a higher astroglial component compared to the surface layer (37).

3. **Laminar Region:** There are fenestrated sheets of scleral connective tissue with intermittent elastic fibres in the laminar region. Astrocytes separate these sheets and line the fenestrae, allowing the fascicles of neurons to leave the globe through these openings (37).

4. **Retrolaminar Region:** Myelin supplied by oligodendrocytes doubles the thickness in the retrolaminar area, which is characterised by a decrease in astrocytes. The posterior boundary of the retrolaminar region is not well defined, and axonal bundles are surrounded by connective tissue septa (37).

The distribution of the artery supply to the optic nerve head is sectoral. The main supply of the surface nerve fibre layer comes from the arteriolar branches of the central retinal artery; branches of the posterior ciliary circulation, especially in the temporal region, also contribute. Short posterior ciliary arteries supply the prelaminar and laminar regions, which form the circle of Zinn-Haller at the scleral level. Both ciliary and retinal circulation supply the retrolaminar region; ciliary vessels originate from recurrent pial vessels. The central retinal vein's branches carry out the majority of the optic nerve head's primary venous drainage. However, notable choroidal collaterals are also important, and retinociliary shunts can disrupt retinal circulation (37)

Classification of Glaucoma

In 2017, the "European Glaucoma Society published Guidelines for Glaucoma" in which they mentioned a well-organized classification of glaucoma as mentioned below (38):

I. **Primary congenital forms / Childhood Glaucomas**

a. Primary Congenital glaucoma (PCG): From birth to > 2 years of life

- Neonatal or newborn onset (0 – 1 month)
- Infantile onset (> 1 month until 24 months)
- Late onset or late recognised (> 2 years)
- Spontaneously non-progressing cases with normal IOP but signs of PCG present

b. Late-onset childhood open-angle glaucoma / Early juvenile: Onset > 2 months to puberty

c. Secondary childhood glaucoma

1. **Glaucoma associated with non-acquired ocular anomalies:** "Axenfeld-Rieger anomaly, Peters anomaly, ectropion uvea, congenital iris hypoplasia, aniridia, persistent fetal vasculature, oculodermal melanocytosis (Nevus of Ota), posterior polymorphous dystrophy, microphthalmos, micro-cornea, and ectopia lentis."

2. **Glaucoma associated with Non-acquired Systemic disease or syndrome: "**Chromosomal disorders such as Trisomy 21 (Down syndrome), connective tissue disorders (Marfan syndrome, Weill-Marchesani syndrome, and Stickler syndrome), metabolic disorders (Homocystinuria, Lowe syndrome, and mucopolysaccharidoses), and phacomatoses including neurofibromatosis (NF-1, NF-2), Sturge-Weber syndrome, Klippel-Trenaunay-Weber syndrome, Rubinstein-Taybi syndrome, and congenital rubella."
3. **Glaucoma associated with acquired conditions**: "Uveitis, trauma (including hyphema, angle recession, and ectopia lentis), steroid-induced conditions, and tumours (both benign and malignant)."
4. **Glaucoma following childhood cataract surgery**

II. Primary open-angle glaucoma:

a. Primary open-angle glaucoma:

- Primary Open-Angle Glaucoma / High-pressure Glaucoma (POAG / HPG)
- Primary Open-Angle Glaucoma / Normal pressure Glaucoma (POAG / NPG)

b. Primary Juvenile Glaucoma

c. Primary Open-Angle Glaucoma Suspect

d. Ocular Hypertension

III. Secondary open-angle glaucomas

a. Secondary open-angle glaucoma:

1. **Secondary Open-Angle Glaucoma caused by Ocular Disease:** "Pseudoexfoliative glaucoma, pigmentary glaucoma, lens-induced open-angle glaucoma, glaucoma associated with intraocular haemorrhage, uveitic glaucoma, neovascular glaucoma, glaucoma due to intraocular tumours, and glaucoma associated with retinal detachment."
2. **Open-angle glaucoma due to ocular trauma**

b. **Iatrogenic secondary Open-Angle Glaucoma: "**Glaucoma due to corticosteroid treatment and secondary open-angle glaucoma resulting from ocular surgery and laser procedures."

c. **Secondary Open-Angle Glaucoma caused by Extrabulbar diseases: "**Glaucoma caused by increased episcleral venous pressure"

IV. Primary angle closure (PAC)

a. Primary Angle-closure Suspect (PACS)

b. Acute Angle Closure (AAC)

c. Intermittent Angle-Closure (IAC)

d. Chronic Angle-Closure Glaucoma (CACG)

e. Status Post-Acute Angle-Closure Attack

V. Secondary angle closure

a. **Secondary Angle-Closure with pupillary block**

b. **Secondary Angle-Closure with anterior pulling mechanism without the pupillary block: "**Neovascular glaucoma, iridocorneal endothelial syndrome, posterior polymorphous dystrophy, epithelial and fibrous ingrowth after anterior segment surgery or penetrating trauma, inflammatory membrane, and aniridia."

c. **Secondary Angle-Closure with Posterior Pushing mechanism without a pupillary block:** "Aqueous misdirection, iris and ciliary body cysts, intraocular tumours, silicone oil or other tamponading fluids or gas implanted in the vitreous cavity, uveal effusion, stage 5 retinopathy of prematurity, and congenital anomalies that can be associated with secondary glaucoma."

Diagnosis of glaucoma

According to Sun X and Dai Y's works, precise assessment is the cornerstone of effective glaucoma management. The primary components of an accurate glaucoma evaluation include intraocular pressure measurement, anterior chamber angle evaluation, changes in the optic nerve head, and visual field abnormalities. (39)

Intraocular pressure assessment

In 2002, Ocular Hypertension Treatment Study, Gordon M emphasised that "elevated IOP is a major risk factor for glaucoma and that reduction of IOP is the only clinically proven therapeutic approach to arrest the progression of glaucoma". (40)

IOP can be measured directly and indirectly. The direct approach is an invasive one in which true internal IOP is measured with the help of implanted sensors. While in more commonly used indirect methods, IOP measurement depends upon its relationship with parameters like applanation and alteration of corneal radius of curvature. (39,41)

Below is a review of several commonly utilised tonometers:

A. Goldmann Applanation Tonometer: (GAT)

GAT is based on the modified Imbert-Fick principle and is considered the "gold standard" for measuring IOP. GAT is performed under topical anaesthesia after applying fluorescein dye in the tear film. (39). It is not affected by ocular rigidity, but corneal thickness, curvature, and tear film can interfere with IOP recordings with GAT. (42) GAT is suitable for patients in sitting positions, but the "Perkins tonometer" is a handheld version of GAT that can be used with patients in both sitting and lying positions. (39)

B. Schiotz tonometer:

Schiotz tonometer has been used in clinics since 1905 and is based on the principle of indenting the eyeball through gravitational pressure. It determines IOP by measuring corneal

indentation depth using a metal plunger and converting it to mm of Hg via a line scale on the instrument. (39) The Schiotz tonometer requires calibration and sterilisation prior to use, and ocular rigidity and corneal curvature well interfere with IOP measurement. (43)

C. Noncontact tonometer: (NCT)

NCT uses air puff to indent a fixed point in the central cornea. It then measures the time it takes to receive reflected light from the flattened corneal surface and converts it into an IOP measurement. It doesn't require anaesthesia, is non-invasive, and is simple to operate. However, data in eyes with higher or lower IOP is more biased. (39)

D. Rebound tonometer:

A 4 to 8-mm probe is used by the rebound tonometer to strike the cornea; the voltage in the bounced probe is subsequently converted into a digital signal. Anaesthetic is not needed, and the cornea is not applanated (39).

Factors influencing the measurement of Intraocular pressure:

- **Central corneal thickness (CCT):**

  Normal eyes have a CCT of almost 545 μm, and glaucoma risk is increased in those with thin CCT. IOP readings may be influenced by the CCT. For correcting applanation IOP measurements for CCT, no standard validated nomogram is available (39,42).

- **Corneal topography:**

  A study by Damji et al. reported a statistically significant correlation between IOP readings and corneal curvature with a correlation coefficient of r = 0.1788, and he also noted a 0.34 mmHg change in IOP with one diopter change in corneal curvature.(42)

- **Ocular rigidity:**

In hypermetropia, ocular rigidity is high, and in myopia, it is lower and can cause a change in IOP measurement value.(39)

- **Tear film:**

Tear film can affect IOP recordings in the range of 2 to 4.15 mmHg, as per the reports mentioned by Sun X and Di Y, but it can be avoided by using NCT and rebound tonometer.(39)

Gonioscopy:

Anterior chamber angle evaluation is done using gonioscopy. Indirect gonioscopy uses a mirror in a gonioprism to reflect light rays, while direct gonioscopy uses the anterior curvature of the goniolens to negate the critical angle. (37)

Sun X et al. (2017) suggested using a 1 mm beam in a dark room with sufficient illumination, with the patient facing straight ahead when describing the gonioscopy procedure. They mentioned the importance of comparing static and indentation gonioscopy findings to differentiate between permanent synechiae and reversible appositional angle closure. (44)

Different angle grading systems:

- **Shaffer angle grade:**

It is a more commonly used grading system describing the extent to which the "angle of the anterior of the chamber" is open (45).

Table 1: Shaffer angle grading system. Source: Shaffer et al. (46)

Grade	Angle width	Description	Risk of closure
4	45° – 35°	Wide open	Impossible
3	35° - 20°	Wide open	Impossible
2	20°	Narrow	Possible
1	≤ 10°	Extremely narrow	Probable
Slit	Slit	Narrowed to slit	Probable
0	0°	Closed	Closed

- **Scheie system of angle grading:** Scheie's angle grading system (1957), in which larger numbers signify narrower angles and also similarly graded angle pigmentation (23,45).
- **Spaeth's classification system:** As per the Sun and Dai's description of Spaeth's angle classification system, it includes mainly the extent of iris insertion, angle width, and peripheral iris structure. (39)

Assessment of anterior chamber depth:

- **Central anterior chamber depth:**

  Allingham et al. cite the work of Makabe R (1989), mentioning a weak correlation between the angle width and central anterior chamber depth.(37,47)

- **Peripheral anterior chamber depth:**

  Van Herick et al. mention the greater diagnostic value of Peripheral anterior chamber width, and they also describe a slit-lamp technique and grading for assessing peripheral anterior chamber depth by comparing it with the thickness of the adjacent cornea.(37,48)

Assessment of optic nerve head and retinal nerve fibre layer (RNFL)

As per Sun and Dai (2019), monitoring optic disc and RNFL alteration are the mainstay in the management of glaucoma, with clinical examination by ophthalmoscopy and fundus photography still being gold standard modalities but having the advantage of being a subjective method.(39)

- **Morphology of glaucomatous optic atrophy as seen on fundoscopy:**

  Allingham et al. categorised glaucomatous optic nerve head changes into 3 categories: Disc patterns in glaucomatous optic atrophy, vascular signs and peripapillary changes. (37)

  There can be four different disc patterns of glaucomatous optic disc as per Allingham et al.(37) :

  - There can be "focal atrophy", usually with polar or focal notching. A sharpened rim is produced as it progresses towards the edge of the disc, and no neural rim is left. (37,49)

- A less common condition called “concentric atrophy” is the expansion of the cup in concentric circles, usually directed either superotemporally or inferotemporally at the beginning. After that, it moves in a circumferential direction in the direction of the poles; this process is called temporal unfolding. (37)
- In the early cases, the deepening of the cup may be the predominant pattern, and according to Portney G’s photogrammetric analysis, this occurs only when the lamina is not initially exposed (50). In their respective research, Spaeth G. et al. and Read R. et al. described “overpass cupping," characterised by a deepened cup where vessels initially bridge over the cup before collapsing into it. (49,50)
- Pallor/cup discrepancy is observed in “glaucomatous optic atrophy”, where the cup may advance more quickly than the pallor.(37)
- If the disease is not controlled adequately, then there can be advanced glaucomatous cupping, which is a state of total cupping clinically described as a “white disc with loss of all neuroretinal rim, vessels bending at the margin” and an “extreme posterior displacement of lamina cribrosa” histologically which was called as “bean pot cupping” by Spaeth G et al.(37,49)

Vascular signs of glaucomatous disc atrophy, as described by Allingham et al., are mainly optic disc haemorrhages like splinter haemorrhages seen at the optic disc margin, which tends to come and go and in advanced cases, there can be tortuosity of vessels at the disc margin. (37) According to reports by Hendrickx K. et al., disc hemorrhages are more common in normal-tension glaucoma than in other variations. (51)

Peripapillary changes can be attributed to pigmentary disturbances and can be seen in other conditions and normal eyes, making it a more nonspecific finding. There can be a thin, uniform light band at the disc margin called a “peripapillary halo”, the incidence of which is higher in glaucoma, as per reports of Wilensky and Kolker.(37,52)

Peripapillary atrophy involving both the alpha and beta zones is more frequent in glaucoma, as per Buus and Anderson , and it correlates with quadrants having more rim loss (37,53,54).

- **The role of ocular coherence tomography (OCT) in identifying RNFL defects and changes in the optic disc:**

OCT helps diagnose glaucoma and monitor the disease over the long term.(55,56) Software in Spectral-domain OCT devices can analyse acquired images and compare them with normative databases to generate a colour-coded report with green indicating normal data lying within the range of 5^{th} to 95^{th} percentile, yellow depicting the borderline value within the 1st to 5th percentile range and red indicating data outside normal limits which is less than 1^{st} percentile.(39)

The "RNFL protocol" provides "total RNFL thickness", "average thickness of sections by clock hours", and "average thickness of superior and inferior hemispheres" in a wheel-like format. (39) "Total ganglion cell complex (GCC) thickness", which includes "macular RNFL, ganglion cell layer, inner plexiform layer, and superior and inferior GCC thickness", is provided by the GCC protocol. Additionally, it has "global loss volume" (GLV) and "focal loss volume" (FLV) parameters that show the average and focal GCC loss over the whole GCC map and are comparable to the total and pattern deviation maps used in visual fields. (57,58)

Many studies have shown that RNFL thickness measurement is a significantly better parameter for pre-perimetric glaucoma (39), and quantitative measurement of structural damage helps monitor disease progression over time(Mwanza & Budenz, 2016). As per Zhang X et al. (2017), GCC is better than RNFL in detecting progression from early to advanced stages of glaucoma.(60)

Assessment of visual field defects:

Perimetry has been used for a long time to measure the differences in light sensitivity in different parts of the visual field in order to identify and quantify any defects as well as to monitor the progression of glaucoma. (39)

Allingham et al. categorised visual field loss in glaucoma into peripheral loss, localised loss due to RNFL defects, generalised and central depression of field and temporal sector defect.(37)

Peripheral defects in the visual field boundaries, such as “peripheral nasal steps”, “vertical steps”, and “temporal sector defects”, are commonly linked with scotomas in the central arcuate area. However, peripheral defects might be the only noticeable abnormality in certain patients with early glaucomatous visual field loss.(37,61–63)

When ganglion cells and their axons sustain structural damage, it can result in partial or total loss of function in the affected area. The initial damage typically causes localised defects in the visual field, especially focal defects, because of the loss or impairment of retinal nerve fibre bundles, which are indicative of the retinal topography of these fibres. (37)

Bjerrum scotomas are described by Harrington (1965) as an arcuate visual defect that extends nasally for 10 to 20 degrees, originating from the blind spot and arcing above or below fixation to the “horizontal median raphe” (64). These arcuate retinal nerve fibres often manifest initially as one or more localised defects or “paracentral scotomas”, especially in the superior half, which correlates with early glaucomatous damage in the inferior and superior temporal poles of the optic nerve head. (37,64,65) Typically, there is a shallow paracentral depression that grows larger and denser until it forms a central absolute defect encircled by a relative scotoma. (66–68) Sometimes, the arcuate defect tapers to a point called a “Seidel scotoma”. An “Arcuate or Bjerrum scotoma” is created when defects grow and merge together to form an arching scotoma that fills the entire arcuate area. A “double arcuate (or ring) scotoma” could develop with further progression. (69) There is a relationship between the size

of the scotoma and the rate of visual field loss; larger scotomas are probably going to enlarge more quickly.(70)

Leblanc R et al. and Allingham et al. discussed the loss of retinal nerve fibres, which frequently happens unevenly in the upper and lower parts and results in a “step-like defect” where the nerve fibres converge along the median raphe. This can result in a “superior nasal step” more frequently due to greater defects above the horizontal midline, though “inferior nasal steps” are not uncommon, reflecting the somewhat higher involvement of the superior field in early glaucoma stages. (37,61)

In the initial phases of glaucoma, central vision is typically preserved, but localised damage to the fixation point may occasionally affect the central visual field, and in such cases, visual functions like acuity and colour vision may show abnormalities, necessitating differentiation from macular disorders.(37) While some studies indicate that early glaucoma may present with purely diffuse loss, others challenge this notion, proposing that generalised depression in glaucoma is uncommon and suggesting alternative causes such as “media opacity, miosis, or retinal dysfunction” for diffuse loss of perimetric sensitivity.(37,71–73)

Treatment of Glaucoma

While there are numerous treatment options for glaucoma, there isn’t a single, widely recognised gold standard for managing the condition. (37,39) Reducing IOP to the target level where additional damage is unlikely and preserving good vision while maximising quality of life are the two main objectives in order to stop the disease from progressing. (37,39,74)

As mentioned by Harasymowycz P et al., this target IOP should be individualised and should be evaluated routinely to consider the disease stage, life expectancy, risk factors, and socioeconomic circumstances of the patient, and the treatment like medications, lasers or surgery should be tailored to the patient-centric way. (75)

Kass MA et al. (2002) conducted the Ocular Hypertension Treatment Study with the aim of determining whether topical anti-glaucoma medications can postpone or prevent the

onset of primary open-angle glaucoma in patients suffering from ocular hypertension. A total of 1636 participants with ocular hypertension were randomly assigned to one of two groups: one group was administered topical IOP lowering medications, while the other group received no treatment and was monitored for a period of five years. It was determined that patients with ocular hypertension could delay or avoid primary open-angle glaucoma by using topical anti-glaucoma medications. (76)

Heijil A. et al. (2002) conducted the Early Manifest glaucoma trial, which investigated the impact of medication-assisted IOP lowering on the progression of open-angle glaucoma over a 6-year follow-up period. The study found that the treatment group experienced a delay in progression when compared to the no-treatment group. (77)

Medication intended to reduce IOP can be broadly divided into two categories. The first category consists of drugs that decrease the production of aqueous humor, like carbonic anhydrase inhibitors, β-adrenergic blockers, and α2-adrenergic agonists. The second category of agents includes those that improve aqueous humor drainage via the uveoscleral pathway (prostaglandin analogues) or the conventional pathway (cholinergic agents, rho kinase inhibitors). (39)

Figure 2: Chronology of introducing antiglaucoma drugs over time as Groves N (2020) published in Ophthalmology Times (78)**.**

YEAR	DRUG CLASS
1877	Cholinergic agonists
1897	Crystalline alkaloids
1904	Osmotic agents
1948	Adrenergic antagonists
1954	Carbonic anhydrase inhibitors
1955	Adrenergic agonists
1978	β-adrenergic inhibitors
1987	α-adrenergic agonists
1995	Carbonic anhydrase inhibitors
1995	Adrenergic agonist prodrug
1996	Prostaglandin analogs
2017	Rho kinase inhibitors

Table 2: Summary of topical anti-glaucoma agents as mentioned by Wagner I et al. in 2022 (79)

Class	Drugs	Adverse reactions	Contraindication
Prostaglandin analogues	▪ Bimatoprost ▪ Latanoprost ▪ Tafluprost ▪ Travoprost ▪ Unoprostene ▪ Latanoprostene Bunod	▪ Eyelash growth ▪ Iris darkening ▪ Keratitis ▪ Conjunctival pigmentation ▪ Uveitis	▪ Hypersensitivity
Cholinergic agents	▪ Pilocarpine ▪ carbachol	▪ Myopia ▪ Angle closure ▪ Cataract ▪ Retinal detachment	▪ Miosis ▪ Bradycardia ▪ Retinal detachment ▪ Asthma ▪ Inflammatory eye disease
Carbonic anhydrase inhibitors	First generation (Systemic) ▪ Acetazolamide ▪ Methazolamide ▪ Dichlorphenamide	▪ Renal calculi ▪ Stevens-Johnson syndrome ▪ Serum electrolyte imbalance	▪ Allergy to sulfa drugs ▪ Sickle cell disease
	Second generation (Topical) ▪ Brinzolamide ▪ Dorzolamide	▪ Corneal edema ▪ Metallic taste	▪ Allergy to sulfa drugs ▪ Sickle cell disease
Beta-adrenergic antagonist	Non-selective: ▪ Carteolol ▪ Levobunolol ▪ Metipranolol ▪ Timolol ß1 – selective: ▪ Betaxolol	▪ Congestive heart failure ▪ Exercise intolerance ▪ Hypotension ▪ Bronchospasm ▪ bradycardia	▪ Cardiovascular disease ▪ Asthma ▪ Diabetes mellitus ▪ Chronic obstructive pulmonary disease
Alpha adrenergic agonist	▪ Apraclonidine ▪ Brimonidine	▪ Hypotension ▪ Fatigue ▪ Allergic ▪ Conjunctivitis	▪ Monoamine oxidase inhibitor therapy
Rho-kinase inhibitors	▪ Netarsudil	▪ Keratitis ▪ Conjunctival haemorrhage ▪ Corneal verticillate	▪ None
Hyperosmotic agent	▪ Glycerol ▪ Mannitol ▪ Isosorbide	▪ Congestive heart failure ▪ Renal failure ▪ Nausea ▪ Vomiting ▪ Headache	▪ Cardiovascular disease ▪ Renal failure

Glaucoma Surgeries

Allingham et al. stated that the biggest mistake in managing glaucoma is to continue different drug combinations with target IOP not being achieved instead of shifting to laser or incisional surgeries(37) He also explained the indications of surgery being unable to achieve target IOP with medical therapy, progressive glaucomatous damage on maximum therapy and inability to tolerate or comply with antiglaucoma medication. (37)

As per the collaborative initial glaucoma treatment study (CIGTS) by Janz N et al. (2001), they evaluated the safety and efficacy of medical versus surgical treatment in newly diagnosed glaucoma or early glaucoma, and they concluded a similar outcome in both treatment groups. (80)

Wound healing in filtering surgeries

Four phases of wound healing—clot, proliferation, granulation, and collagen—were described by Yamanaka O et al. and Allingham et al. when discussing incisional surgeries for filtration performed in glaucoma (37,81).

1. **Clot phase**: Soon after the incision, blood vessels narrow, blood cells and elements leak, inflammatory cells are released, and eventually, blood elements clot to a fibrin-fibronectin matrix (37,82,83).
2. **Proliferation phase:** In the phase of proliferation, monocytes, macrophages, and fibroblasts migrate towards the clot, which has been studied for a long and has been explained in many animal studies (37). Miller M et al. described fibroblast migration from episcleral and subconjunctival tissue in rabbits. (84) Desjardins D et al. explained fibroblast proliferation along walls of limbal fistula in a monkey model by day six. (85) To track the progression of cellular proliferation in monkeys, Jampel et al. employed titrated thymidine as a marker of cell division. They found that the detection peaked on day five and decreased after day eleven (86). Li J et al. described angiogenesis as occurring in this phase. (87)

3. **Granulation phase**: The granulation phase then sets in when fibroblasts start to produce fibronectin, collagen and glycosaminoglycans, forming a fibrovascular connective tissue in the lining of the fistula called granulation tissue which in the rabbit model was described at day three by Miller M et al. and in monkey model at day 10 by Desjardins D et al. (37,85)
4. **Collagen phase:** In the collagen phase, fibroblasts initially generate procollagen, which converts into tropocollagen by two weeks post-surgery and by some months, it organises into mature collagen. (37,88) The amount of collagen in the wound is modulated by its amount of degradation, which is governed by the matrix metalloproteinases. (89,90)

The primary reason why glaucoma filtering surgery fails is frequent scarring of the filtering bleb as a result of fibroblasts producing excess collagen. However, bleb failure is multifactorial, involving unique characteristics of the glaucomatous eye and various phases of wound healing. Growth factors necessary for tissue repair, including transforming growth factor-β (TGF-β), are found in aqueous humor, which typically inhibits fibroblast proliferation. The postoperative alterations in aqueous humor can promote fibroblast proliferation, potentially affecting bleb success. Additionally, factors like age, ethnicity (African heritage), and long-term use of topical glaucoma medications influence wound healing. While histologic studies show conflicting results regarding age and ethnicity's direct influence, long-term topical medication use, especially combinations, may increase surgery failure risk. Strategies like preoperative corticosteroid use have shown promise in improving success rates by mitigating subclinical inflammation and conjunctival changes due to medication use. (37)

Glaucoma filtering surgeries:

Three categories of filtering processes are known: Full-thickness fistulas, in which the fistula extends to the full thickness of the limbal tissue; Partial thickness fistulas are covered by scleral flaps and non-penetrating surgeries. (36,37)

I. Full-thickness fistula procedures:

Sclerotomy was one of the earliest types of full-thickness fistula procedures described by LaGrange in 1960, involving the creation of a direct opening of limbal tissue by excision of tissue from the anterior lip of full-thickness limbal incision (37,91). Later on, Iliff and Hass described a posterior lip sclerotomy, which gained popularity. (92)

Elliot demonstrated a glaucoma filtration procedure known as trephination in which, with the help of a small trephine, a fistula was made just behind the corneolimbal junction. (93) Sugar modified it by placing the trephine more posteriorly, and it was popularised as limbo scleral trephination(37,94).

Scheie described a procedure of thermal sclerotomy, in which after making a limbal incision, electrocautery was to retract wound edges, creating a fistula, which became popularised as the Scheie procedure (95).

II. Trabeculectomy:

Full-thickness filtering surgeries had excessive aqueous filtration, complicating into prolonged shallow anterior chamber leading to synechiae, corneal decompensation and cataracts. In order to get around this, Sugar developed a concept in 1961 of covering the fistula with a partial thickness scleral flap. Carins popularised this technique in 1968, which has since been referred to as a Trabeculectomy. Since then, it has been the most popular glaucoma surgery (37).

III. Non-penetrating procedures:

Commonly performed non-penetrating filtering procedures nowadays are deep sclerotomy and canaloplasty, with a success rate between 45 % and 69 %. (96) In deep sclerotomy, Shaarawy T et al. reported a complete success rate of 34.6%, and in deep sclerotomy with collagen implant, 63.4% after 48 hours. (97)

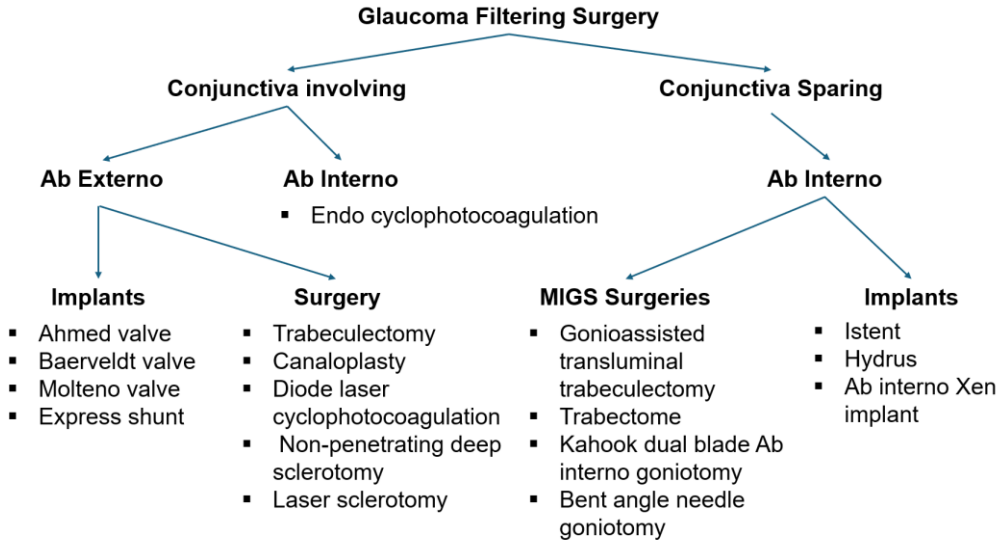


Figure 3: Different types of glaucoma filtration surgeries. Image reproduced with permission from Rao A & Cruz R (2022) (98)

Routes of aqueous outflow in trabeculectomy:

Shields M, in 1980, studied aqueous outflow using fluorescein angiography in post-trabeculectomy eyes with functional blebs, and he reported that the primary route of filtration was around the margins of the scleral flap. (99)

Benedikt O described alternative mechanisms for aqueous outflows, such as cyclodialysis, occurring when the fistula extends beyond the scleral spur and the drainage of aqueous through newly formed aqueous veins or lymphatics. (100)

Allingham et al. described five outflow pathways in trabeculectomy (37). One major route is the outflow through the cut ends of Schlemm's canal, where the aqueous humor exits through the ends of this crucial drainage structure, which helps lower intraocular pressure.

Cyclodialysis also provides an additional pathway for aqueous humor drainage by directly connecting the anterior chamber and the suprachoroidal space. Furthermore, filtration through outlet channels in the scleral flap provides another mechanism for aqueous humor to exit the eye, contributing to pressure reduction. Moreover, the filtration process extends to the connective tissue substance within the scleral flap, allowing for the permeation and outflow of aqueous humor. Lastly, filtration also occurs around the margins of the scleral flap(37).

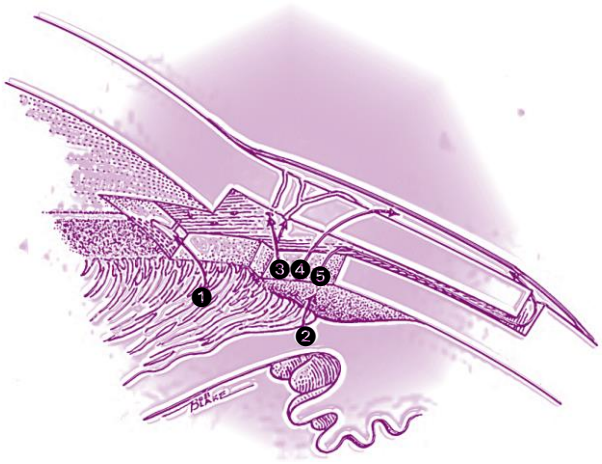


Figure 4: Routes of aqueous outflow in trabeculectomy as described by Allingham et al. 1. Outflow through cut ends of Schlemm's canal. 2. Cyclodialysis. 3. Filtration through "outlet channels in the scleral flap". 4. Filtration through the scleral flap's connective tissue substance. 5. Filtration around the scleral flap's edges (37)**.**

Indications of Trabeculectomy:

- **Inability to achieve target IOP control through medical therapy alone:**

  Trabeculectomy is indicated for glaucoma patients who are unable to achieve target IOP control through medical therapy alone. Despite the availability of various medications, some patients experience significant side effects or find the medication regimen cumbersome and difficult to adhere to, especially the elderly. Medications can cause ocular discomforts, such as stinging, redness, irritation, and dry eyes, as well as systemic side effects like bronchial asthma, particularly with beta-blockers. Additionally, over half of patients on beta blockers may need to change their medication or add another drug

within five years due to diminishing effectiveness. These challenges with medical management make trabeculectomy a necessary option for preventing disease progression (101–103).

- **Poor compliance with medical therapy:**

  Compliance with medical therapy is another critical factor influencing the decision to perform trabeculectomy. Successful glaucoma management relies heavily on the patient's adherence to their prescribed drug regimen, but studies show that many patients struggle with this, especially when multiple medications are required. Forgetfulness, a lack of motivation due to the absence of immediate vision improvement, and socioeconomic barriers such as poverty and illiteracy can all lead to poor compliance. This non-adherence can result in uncontrolled IOP, making surgical intervention through trabeculectomy necessary to prevent further optic nerve damage and vision loss. Furthermore, patients who live in remote areas with limited access to medical care may also benefit from trabeculectomy, as it reduces the need for frequent medical visits (104–106).

- **Management of intraocular pressure fluctuations:**

  The management of intraocular pressure fluctuations is also a key indication for trabeculectomy. Regardless of the patient's baseline IOP level, the severity of their glaucoma, or demographic characteristics like race and sex, diurnal variations in IOP have been found to be a significant risk factor for the progression of glaucoma. Medical therapies often result in peaks and troughs in IOP, which can be detrimental to the optic nerve. Trabeculectomy provides a more stable and less turbulent IOP control, reducing these fluctuations and offering better long-term protection for the optic nerve. This makes it a crucial procedure for patients with significant IOP variability who remain at high risk for disease progression despite medical treatment (107,108).

- **Chronic closed-angle disease,** where an iridectomy is considered insufficien**t** (109).
- **Primary open-angle glaucoma** (109).

- **Low-inflow glaucoma**, where after standard filtration surgery, persistently flat anterior chambers may be anticipated (109).

However, trabeculectomy often yields poor results in secondary glaucoma, making the procedure relatively contraindicated in these cases (109).

Surgical technique of trabeculectomy

❖ **Anaesthesia:**

In trabeculectomy, anaesthesia can range from general anaesthesia, reserved for children or uncooperative adults, to various local anaesthesia techniques. Retrobulbar injections with anaesthetics like lidocaine, bupivacaine, and mepivacaine provide deep anaesthesia, though they carry risks such as retrobulbar haemorrhage and optic nerve injury. Epinephrine can enhance the effects of these anaesthetics but may reduce optic nerve perfusion, complicating vascular occlusions. Peribulbar, subtenon, and subconjunctival anaesthesia are alternatives, with subtenon anaesthesia requiring less anaesthetic volume and causing less postoperative pain. Topical anaesthesia can be combined with other techniques for more extensive surgeries (37).

❖ **Tractional sutures:**

A successful trabeculectomy necessitates good surgical exposure, which frequently calls for the use of traction sutures. The two main methods are the “clear cornea traction sutures” and the “superior rectus traction sutures”. In the “superior rectus traction suture”, the globe is rotated downward, and a 4-0 silk suture is passed through the conjunctiva and around the superior rectus muscle, attaching it to the surgical drape. This procedure may result in a conjunctival hole or subconjunctival haemorrhage. The “clear cornea” technique involves passing a 7-0 polyglactin or silk suture into the cornea, attaching it to the drape over the cheek, which most surgeons prefer despite potential corneal and anterior chamber distortion (37).

❖ **Conjunctival flap:**

Since scarring of the filtering bleb at the external ostium is the most common cause of failure in filtering procedures, preparing the conjunctival flap is an important step in the process. Because the limbus is wider at the 12 o'clock position, some surgeons prefer this position for the flap; others, however, choose one of the superior quadrants, leaving the adjacent quadrant open in case future surgery is required. Because of the increased risk of endophthalmitis, inferior quadrant placement—which was previously used when the superior quadrants were scarred from previous surgeries—is now avoided (37).

Conjunctival flaps can be either limbus-based or fornix-based. Traditionally, limbus-based flaps, where the fornix was initially cut, were commonly used. However, many surgeons now prefer fornix-based flaps, especially for trabeculectomy (37,110). Research comparing these methods shows comparable success rates, whether used alone or in conjunction with cataract surgery (37,111,112). Some studies report better pressure control and more diffuse blebs with fornix-based flaps, while others indicate slightly better postoperative IOP control with limbus-based flaps (37,110,113). Notably, a retrospective study found cystic leaking blebs only in eyes with limbus-based flaps (114).

❖ **Scleral flap:**

Trabeculectomy involves outlining the margins of the scleral flap adjacent to the corneolimbal junction with light cautery, followed by partial-thickness scleral incisions. Originally, Cairns described a 5 × 5 mm square flap, but variations in size and shape have since been developed. A lamellar flap, hinged at the limbus, is dissected forward until at least 1 mm of the bluish-grey zone of the peripheral cornea is exposed, with the flap thickness generally being one-half to two-thirds of the scleral thickness (37).

As the thickness of the scleral flap increases, its rigidity and resistance to lifting also increase, resulting in less aqueous humor flow and a smaller pressure drop. For trabeculectomy, half-thickness flaps (about 250 μm thick) are generally recommended.

Thinner flaps can facilitate more aqueous humor flow, but they must not be too thin to avoid risks such as dehiscence or uncontrolled low IOP (115).

- **Fistula creation:**

The fistula creation begins by entering the anterior chamber with a knife behind the scleral flap hinge and widening the incision with scissors or a knife to about 0.5 mm of the scleral flap margins. Radial incisions are extended posteriorly for 1 mm on either side of the initial incision, and the deep limbal tissue flap is reflected to visualise the angle structures and excised along the scleral spur using a Kelly punch (37). A block of tissue 1.5 to 2.5 mm wide is removed just anterior to the scleral spur (36)

- **Peripheral iridectomy:**

A peripheral iridectomy is usually carried out following fistula preparation to prevent the peripheral iris from obstructing the ostium during trabeculectomy. To prevent blockage, the iridectomy should extend past the margins of the sclerectomy. Complications like inflammation, hyphema, and iridodialysis may arise, and it is crucial to ensure the incision is not made too close to the iris root to avoid substantial bleeding. Some surgeons opt not to perform an iridectomy in pseudophakic patients or during combined trabeculectomy and cataract surgery when the anterior chamber is deep and the risk of iris incarceration is minimal (37). Some studies indicate comparable postoperative vision and IOP control, regardless of whether an iridectomy is performed (37,116).

- **Scleral flap closure:**

After a peripheral iridectomy, the scleral flap is approximated with 10-0 nylon sutures. The closure method varies among surgeons; some prefer a loose approximation with two sutures at the posterior corners to promote filtration, while others opt for tighter closure to prevent hypotony and a flat anterior chamber. Optimal closure achieves mild-to-moderate resistance to aqueous flow to maintain anterior chamber depth, which is

particularly crucial when using adjunctive antifibrosis agents due to the higher risk of excessive filtration and hypotony (37,117).

Most surgeons prefer tighter scleral wound closure with the option for postoperative laser suture lysis using an argon or diode laser. Alternatively, releasable sutures, which can be removed at the slit lamp, are used. Effective techniques for releasable sutures exist, and the scleral flap can be tested for adequate flow resistance before closing the conjunctival flap by injecting a balanced salt solution into the anterior chamber via a paracentesis (37,118,119).

- **Conjunctival closure:**

Ensuring a watertight closure of the conjunctival flap is crucial in filtering procedures to prevent persistent flat blebs or anterior chambers, which can hinder the proper development of the filtering bleb. Fine absorbable sutures like 10-0 polyglycolic acid or polyglactin on a tapered, vascular needle are preferred to minimize leakage and tissue reaction. For limbus-based flaps, a tight closure can be achieved with a running suture with close bites or a double running closure involving Tenon tissue and conjunctiva. Alternatively, interrupted sutures may be used to close the Tenon capsule before running closure, especially when antifibrosis agents are used. For fornix-based flaps, a running suture along the limbus or single interrupted sutures at the ends of the flap can provide adequate closure. A balanced salt solution or viscoelastic solution may be injected into the anterior chamber after suturing the scleral flap and closing the conjunctival flap to ensure proper flow and demonstrate watertight closure. Some surgeons also use fluorescein to check for leaks at the end of the procedure (37).

Modifications in the technique of trabeculectomy:

- **Variations of scleral flap:** In addition to square flaps, some surgeons opt for triangular, semicircular, or trapezoidal shapes for the scleral flap during trabeculectomy, with no significant difference noted in long-term success rates. Techniques to influence

postoperative filtration include varying the thickness of the flap, where thinner flaps may offer greater filtration and lower intraocular pressure. Other modifications involve applying light cautery to the lateral margins of the flap, omitting sutures for the scleral flap, or excising the distal portion of the flap. However, these techniques are generally older and should be avoided when adjunctive antifibrosis agents are used. Some surgeons suggest placing the amniotic membrane under the scleral flap and suturing it with 10-0 nylon to prevent postoperative adhesion of conjunctiva and sclera in high-risk patients. Another variation is the scleral tunnel technique, similar to phacoemulsification, where the sides of the tunnel are incised with scissors to create the flap (37,120–125).

- **Variations of fistulising technique:** Cairns's Conventional technique was modified by Watson by initiating the dissection at the posterior over the ciliary body, detaching it from the underlying structure, and removing it at the Schwalbe line. Alternative techniques for creating a fistula under a scleral flap include trephinations, sclerotomies, thermal sclerotomies, and carbon dioxide laser sclerotomies. Most surgeons employ a Kelly Descemet membrane punch or a Crozafon–De Laage punch to excise limbal tissue from the posterior edge of the initial incision beneath the scleral flap (37,126–131).
- **Modifications in eyes with previous intraocular surgery:** The fornix-based conjunctival flap is advantageous for eyes with prior intraocular surgery involving the conjunctiva, such as during cataract surgery (37,110). In these situations, the conjunctiva often adheres tightly to the episclera near the limbus, making a limbus-based flap difficult. Fornix-based flaps should have their lateral edges sutured to promote posterior drainage. An anterior vitrectomy may be needed if there is loose vitreous in the anterior chamber or at the iridectomy site. (132)Although nonpenetrating trabeculectomy was once recommended for glaucoma in aphakia, early results from the Tube Versus Trabeculectomy (TVT) study indicate that glaucoma drainage devices are a better option (133,134).

Role of Mitomycin C in trabeculectomy and different routes of application

Chen C, in 1983, reported that mitomycin C enhances the efficacy of trabeculectomy to reduce IOP in eyes with a high likelihood of failure. (135) Tenon capsule fibroblasts were subjected to tissue culture after exposure to MMC by Jampel H, who came to the conclusion that there was a total inhibition of fibroblast proliferation. This finding was consistent with Madhavan H et al. (136,137).

Ramakrishna R et al. (1993) conducted a pilot study to study the efficacy and safety of topical Mitomycin C in Trabeculectomy in the southern Indian population, and they reported postoperative IOP control in 93.4% without additional antiglaucoma medications over a follow-up period of 18 weeks with no reported serious complications. (138)

In their study, Stone R et al. (1998) investigated the effectiveness of 0.3 mg/ml mitomycin C in trabeculectomy patients with titrated exposure times. They came to the conclusion that patients with a high failure rate should receive an exposure time of four to five minutes at this concentration (139).

Bindlish R et al. (2002) conducted a long-term study of 5 years to examine the results and complications of using MMC in soaked sponges during trabeculectomy and concluded that it reduces IOP significantly over 5 years but has a high incidence of delayed hypotony. (140)

Velpandian et al. (2008) evaluated the transconjunctival penetration of 0.4 mg/ml MMC applied via soaked sponges over intact conjunctiva for 3 minutes and observed its absorption into Tenon's tissue. They concluded that Mitomycin C permeates into subconjunctival tissue following its application over conjunctiva for 3 minutes, suggesting its potential utility as an alternative to subconjunctival application in trabeculectomy(141).

Al-Shahwan S et al. (2005) and Khamar M et al. (2019) discussed the complications of the conventional method of mitomycin C application in soaked sponges, and they reported

incidences of foreign body granuloma secondary to retained MMC-soaked sponge fragments and blebitis due to leftover MMC soaked sponges. (142,143)

Lee E et al. in 2008 demonstrated a “novel technique” of intra-tenon injection of 0.15 ml MMC having varied concentrations between 0.2 to 0.5 mg/ml intraoperatively during trabeculectomy using a 23-gauge needle. At follow-up over 12 months, it proves to be an effective technique with IOP reduction to less than 21 mmHg in 86%(144)

Maheshwari D. et al. (2020) compared the traditional method of using soaked sponges with the use of subtenon injection of 0.4 mg/ml MMC. After a year, the Subtenon injection group demonstrated similar efficacy and safety to the sponge application, with 90.5% of the injection group achieving complete success compared to 87% in the sponge group. (145)

Shih E and Chen Yin (2023) conducted a comparison between conventional 0.2 mg/ml MMC-soaked sponge augmented trabeculectomy and two-stage intra-tenon injections of 0.1 mg/ml. In the first stage, the injection group received an intra-tenon injection of 0.01% MMC; four hours later, trabeculectomy was performed in the second stage. At a one-year follow-up, both methods significantly decreased intraocular pressure and medication use, with no discernible differences in complications. (146)

Systems of grading Bleb:

I. Indiana Bleb Appearance Grading System [IBAGS]

The IBAGS was developed by Cantor et al. in 2003 to provide a standardised, objective method for assessing the appearance of filtering blebs, facilitating a better correlation between filtration surgery outcomes and clinical morphology (147). It utilises a set of photographic standards from the Glaucoma Service at Indiana University, including slit lamp images for grading "bleb height, extent, vascularity, and leakage (using the Seidel test)". "Fifty-one" clinical bleb photographs were evaluated by three glaucoma subspecialists in a masked manner using this scale, and it demonstrated high interobserver agreement [Figure5] (147).

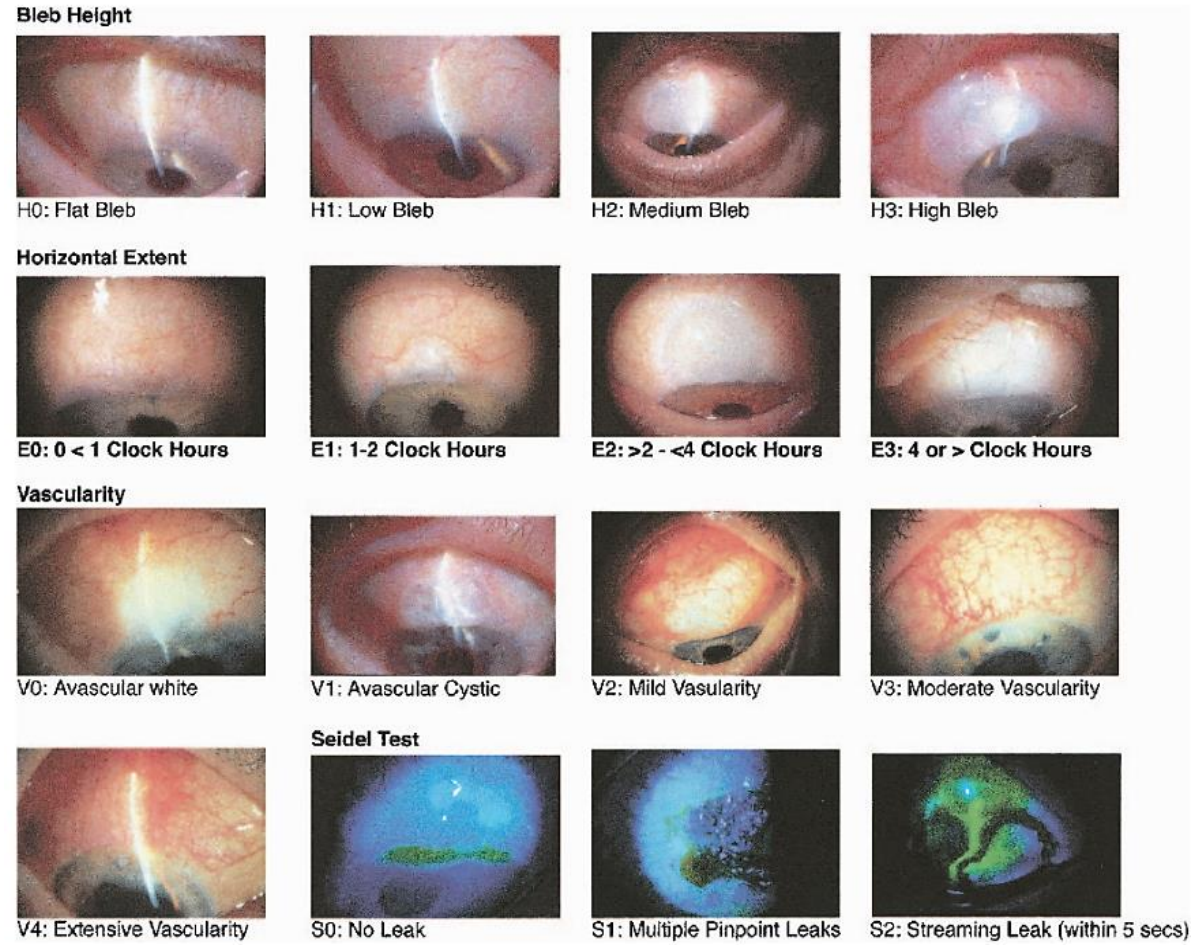


Figure 5: Photographic standards used in IBAGS to assess parameters like height (H0–H3), extent (E0–E3), vascularity (V0–V4), and leakage graded with the Seidel test (S0– S2). Image courtesy: Cantor et al. (147)

II. Moorfield bleb grading system

As described by Wells et al., this system assesses bleb morphology through four parameters: “bleb wall thickness”, “bleb height”, “proportion of diffuse area to total bleb area”, and “total bleb width”. The entire bleb was characterised as the “region where aqueous drainage separated the conjunctiva from the sclera”. In “mixed morphology blebs”, demarcated areas were delineated as “central bleb portions separated by fibrous subconjunctival tissue or contour changes”. These blebs typically exhibit both demarcated and diffuse parts, with demarcated areas clinically termed as "cystic" (thin-walled) or "encysted" (with thick walls) (148) .

For evaluating bleb vascularity, Wells et al. graded it in three distinct areas: non-bleb conjunctiva, bleb edge conjunctiva, and central bleb. Non-bleb conjunctiva, situated more than 2 mm from the bleb edge, typically encompasses the inferior conjunctiva. In contrast, the bleb edge conjunctiva, defined as a 2-mm-wide strip immediately adjacent to the bleb, includes regions with clear separation from the sclera or any demarcated zones in mixed morphology blebs. Finally, the central bleb area was assessed for vascularity [Table 2] (148).

Table 3: Criteria for Moorfields bleb grading system. Source: Wells et al. (148)**.**

Vascularity criteria	**Definition**	**Range**	**Normal**
Non-bleb conjunctiva	≥ 2mm from bleb edge	1-10	3
Bleb edge conjunctiva	2 mm border at demarcation or edge	1-10	3
Bleb centre conjunctiva	Centre of bleb	1-10	3
Morphology criteria	**Definition**	**Range**	**Normal**
Wall thickness	The thinnest part of the bleb (1 = visible hole)	1-10	3
Bleb elevation	Relative to normal conjunctival contour	1-10	3
Diffuse %	Percentage of the bleb that is diffuse	1-10	-
Width (mm)	Maximum width of bleb	1 to more than 10 mm	-

Complications of trabeculectomy:

Trabeculectomy provides a surgical guarded fistula, which is a non-physiological aqueous outflow pathway and is not devoid of complications. (149).

- **Intraoperative complications:** Intraoperative complications can be related to anaesthesia, conjunctival flap handling, scleral flap creation, and intraoperative bleeding (150):

1. **Complications related to anaesthesia:**

   Anticoagulant therapy should be stopped preoperatively to reduce hemorrhagic risks (151). Acute retrobulbar haemorrhage is a common complication associated with local anaesthesia and can jeopardise optic nerve blood flow in advanced glaucoma, so 2% lignocaine without adrenaline is preferred in such cases (149,152).

   In a comparison of topical and retrobulbar anaesthesia for trabeculectomy conducted by Zabriskie NA et al., both techniques gave the patient excellent analgesia and were equally effective (153).

   In a different study, Carrillo MM et al. compared sub-Tenon's anaesthesia for trabeculectomy with lidocaine 2% jelly and found that surgeon satisfaction and patient comfort were comparable in both groups (154).

2. **Complications related to conjunctival handling:**

   “Conjunctival buttonholes or tears” are significant complications despite their small size, often resulting from poor visualisation and improper instrument use. Gentle handling of the conjunctiva with non-toothed forceps is crucial. Limbus-based flaps offer watertight closure but are prone to tears, while fornix-based flaps provide better exposure but are leak-prone. Immediate identification and repair of buttonholes using appropriate sutures are essential to prevent complications like hypotony, shallow anterior chamber, and bleb scarring (149,155–157).

3. **Complications related to Scleral flap:**

   Scleral flap complications arise from incorrect flap thickness. To prevent tears during superficial dissection or premature entry during deep dissection, proper dissection is essential. If a tear occurs, it must be repaired by suturing the anterior limbal tissue or by making a new flap. Larger scleral flaps tend to produce more diffuse blebs, though flap shape's impact on surgical outcomes remains inconclusive (149).

4. **Complications related to Intraoperative bleeding:**

   Intraoperative bleeding can be in the form of mild conjunctival bleeding, scleral bleeding and suprachoroidal haemorrhage. Direct pressure is usually applied to control scleral bleeds in the scleral flap, while mild conjunctival haemorrhage is temporary and resolves on its own. (149). Suprachoroidal haemorrhage, though rare, is a severe complication associated with factors like higher preoperative IOP and longer axial length (158). Progressive anterior chamber shallowing, loss of red reflex, pain onset even under anaesthesia, and a dark posterior segment mass are indicators of suprachoroidal haemorrhage, which requires immediate flap closure and intravenous mannitol (149).

❖ **Postoperative and bleb-related complications:**

Postoperative care significantly influences the outcome of trabeculectomy. Patients should avoid strenuous activities and use prescribed topical steroids and cycloplegics with each visit to perform IOP measurement, Anterior Chamber (AC) depth assessment, and bleb evaluation. Low-lying, diffuse, with less vascularity, cystic changes, IOP in the lower teens, a well-formed AC, and tight conjunctival closure are the characteristics of an ideal bleb. Deviations may indicate early postoperative complications (149).

- **Early postoperative complications:**

1. ***High IOP and deep anterior chamber:***

   Tight wound closure can frequently be the cause of high IOP with deep AC, and gonioscopy may be necessary to rule out sclerotomy site obstruction by fibrin, blood, vitreous, iris, or Descemet's membrane. Management includes digital pressure, removing releasable sutures, or laser suture lysis, with further intervention if episcleral scarring occurs (149). Bleb encapsulation, or Tenon's cyst, typically arises within two to four weeks post-surgery, presenting as a tense bleb with few microcysts, raising IOP. Temporary IOP reduction is managed with aqueous suppressants, and persistent cases may need needling with antimetabolites or surgical intervention (159).

2. ***High IOP and shallow anterior chamber:***

   Aqueous misdirection, suprachoroidal haemorrhage (SCH), or pupillary block can all cause high IOP and shallow AC. Pupillary block responds to laser or surgical iridectomy, while aqueous misdirection requires aqueous suppressants, cycloplegics, or surgical options like Nd: YAG (Neodymium-doped yttrium aluminium garnet) laser or pars plana vitrectomy. SCH, marked by abrupt pain, nausea, and vision loss, is managed with steroids or surgical drainage post-liquefaction (149).

3. ***Low IOP and shallow anterior chamber with flat bleb:***

   Low IOP with shallow or flat AC and flat bleb can result from conjunctival wound leaks or serous choroidal detachment, with management ranging from conservative measures to surgical intervention (149).

4. ***Low IOP and shallow anterior chamber with elevated bleb:*** Low IOP with shallow or flat AC and elevated bleb from excessive filtration usually goes away

on its own, but in more severe cases, cycloplegia, pressure patches, or surgical deepening of the AC may be necessary (160).

- **Late postoperative complications:** Late complications following trabeculectomy primarily stem from long-term changes in bleb characteristics. Antifibrotic medications like 5-FU and MMC can help lower target IOP, but they also raise the risk of "endophthalmitis", "blebitis", "chronic hypotony", and "bleb leaks". (149).

  1. ***Chronic hypotony:***

     An IOP of "less than 5 mmHg" that lasts longer than "three months" is known as "chronic hypotony". It can cause "hypotony maculopathy", which is characterised by "choroidal folds and retinal striae without oedema", as well as reduced visual acuity. (160,161). Young age and myopia caused by reduced scleral rigidity are risk factors (149). Although outcomes are frequently unpredictable, non-surgical treatments like soft contact lenses, cryotherapy, autologous blood injection, and argon laser treatment to the bleb can be tried (162–164). To restore IOP and vision function, surgical revision may be required, which includes either closing the scleral flap or applying a scleral patch graft (165).

  2. ***Bleb leaks:***

     Antimetabolite-supplemented trabeculectomies frequently cause leaking blebs, which can occur in 1.8–10% of cases. After three to five years, the Fluorouracil Filtering Surgery Study (FFSS) Group reported a 7% rate of leaking blebs (166). Small leaks that are identified by Seidel's test may be healed with conservative measures like "soft contact lenses", "aqueous suppressants", and "antibiotics". Larger or unresponsive leaks might need to be surgically repaired or repaired using "cyanoacrylate glue", "fibrin tissue glue", or "autologous blood injection". Surgical options aim to eliminate the leak, resolve hypotony, and maintain filtration (149).

3. ***Symptomatic blebs:***

   Symptomatic blebs have been associated to “nasal or large blebs” that extend to the cornea. These blebs are usually tolerated but may cause discomfort. Initial treatment for the symptoms, including a foreign body sensation and blurred vision, involved topical lubricants. Surgery to remodel the bleb and lower its height, such as compression sutures, may be necessary if the symptoms are persistent. External revision with needling using antimetabolites or internal revision with laser for sclerotomy obstruction are the two main management strategies for late bleb failure, which is mainly caused by fibrosis at the “conjunctival and episcleral interface or sclerotomy obstruction”. Repeat glaucoma surgery may be necessary if these measures fail (149,166).

4. ***Blebitis and bleb-related endophthalmitis:***

   Thin-walled blebs, especially with antimetabolite use, increase the risk of infections that can spread to the anterior chamber (AC) and vitreous cavity, with onset varying from days to years post-surgery. Risk factors include “myopia, releasable sutures, respiratory infections, inferior limbus blebs, unguarded filtration surgery, and diabetes mellitus”. (149,167) Infections can lead to severe visual impairment, with reported incidences of up to 6% for blebitis and 7.5% for endophthalmitis (168). Common pathogens include Streptococcus, Staphylococcus, and Haemophilus influenzae. Symptoms include ocular pain, blurred vision, and tearing. Examination may reveal a milky bleb, bleb leak, hypopyon, and vitreous reaction (149). Stages of infection range from “blebitis” (Stage I) to “AC involvement” (Stage II) to “vitreous involvement” (Stage III) (166). For Stage I blebitis, intensive antibiotic therapy usually results in a better prognosis.

Materials and Methods

Study design:

This prospective interventional study involved a series of trabeculectomies with mitomycin C combined with small incision cataract surgery and intraocular lens implantation over a period of one and a half years, from September 2022 to August 2023, at the Department of Ophthalmology, Shri B.M. Patil Medical College, Hospital, and Research Centre, Vijayapura. The study included thirty participants who met the inclusion criteria.

Inclusion criteria:

1. Patients aged above 25 years.
2. Patients having “primary open-angle glaucoma”, “primary angle-closure glaucoma”, “pseudoexfoliation glaucoma”, or “normal-tension glaucoma” are not effectively managed by anti-glaucoma medications.
3. Clinically significant cataract

Exclusion criteria

1. History of prior ocular surgery and conjunctival manipulation.
2. Ocular or systemic comorbidities, such as “immunodeficiency”, “connective tissue disease”, and “uncontrolled diabetes”, that may affect the surgical procedure and study results.

Preoperative evaluation

Before participant enrolment, we explained the necessity of the surgical procedure and its potential consequences. Informed consent was acquired in the vernacular language, with a witness present. A thorough preoperative assessment was done, which involved obtaining a detailed patient history encompassing demographics, present and past ocular and systemic conditions, prior ocular surgeries, family history of glaucoma, and personal habits. A detailed ocular examination was conducted using a slit lamp (Model number: AIA-11-5S-L; Appasamy

Associates). The refractive status evaluation was done, where visual acuity was measured and documented in Log MAR (Logarithm of the minimum angle of resolution). Baseline intraocular pressure was measured using the Goldmann applanation tonometer (Model number: AATM 5001; Appasamy Associates) and diurnal variation of IOP was also documented wherever required to establish the diagnosis, for which IOP was measured every three hours over 24 hours. Gonioscopy using a four-mirror goniolens (Model number MIPL/14; Opticlear Ophthalmic Lenses) was performed and was graded using "Shaffer's anterior chamber angle grading system" (169). Peripheral anterior chamber depth was graded as per the "van Herick grading system". (48) The Humphrey Field Analyzer (Model number 740i; Zeiss) was used for automated perimetry and 24-2 program was used with a SITA strategy. Both binocular indirect ophthalmoscopy (Model number: AIO-7; Appasamy Associates) and slit lamp biomicroscopy with a 90 D lens (Model number: V90C; Volk) were used to examine the fundus, optic nerve head and the baseline cup disc ratio was recorded.

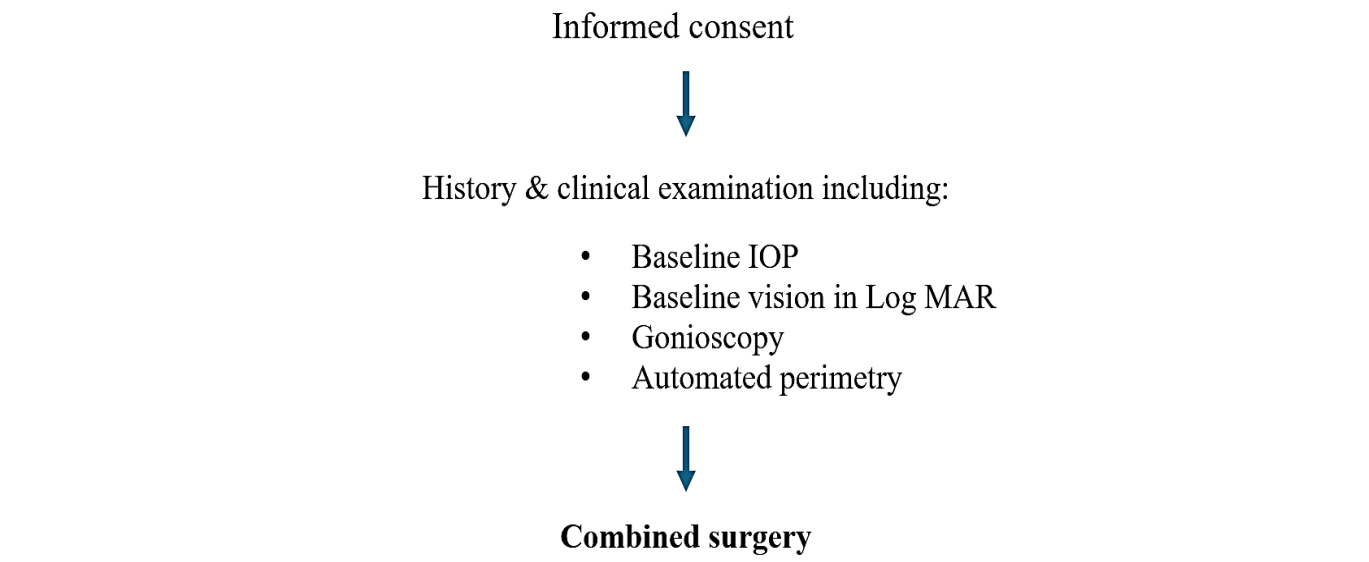


Figure 6: Flowchart depicting study protocol.

Surgical procedure:

A single experienced surgeon performed all the surgeries. In all cases we performed Trabeculectomy combined with Small incision cataract surgery (SICS) augmented with low dose (0.1 mg/ml) sub-tenon injection of MMC under local anesthesia. To prepare the mitomycin C solution, we mixed 2 mg mitomycin C with 5 ml of sterile water for injection. To make 0.1 mg/ml of mitomycin C, we took 0.1 ml of this solution and diluted it with 0.3 ml of 2% lignocaine in a 1 ml tuberculin syringe. We discarded 0.3 ml of the solution and considered only 0.1 ml for injection.

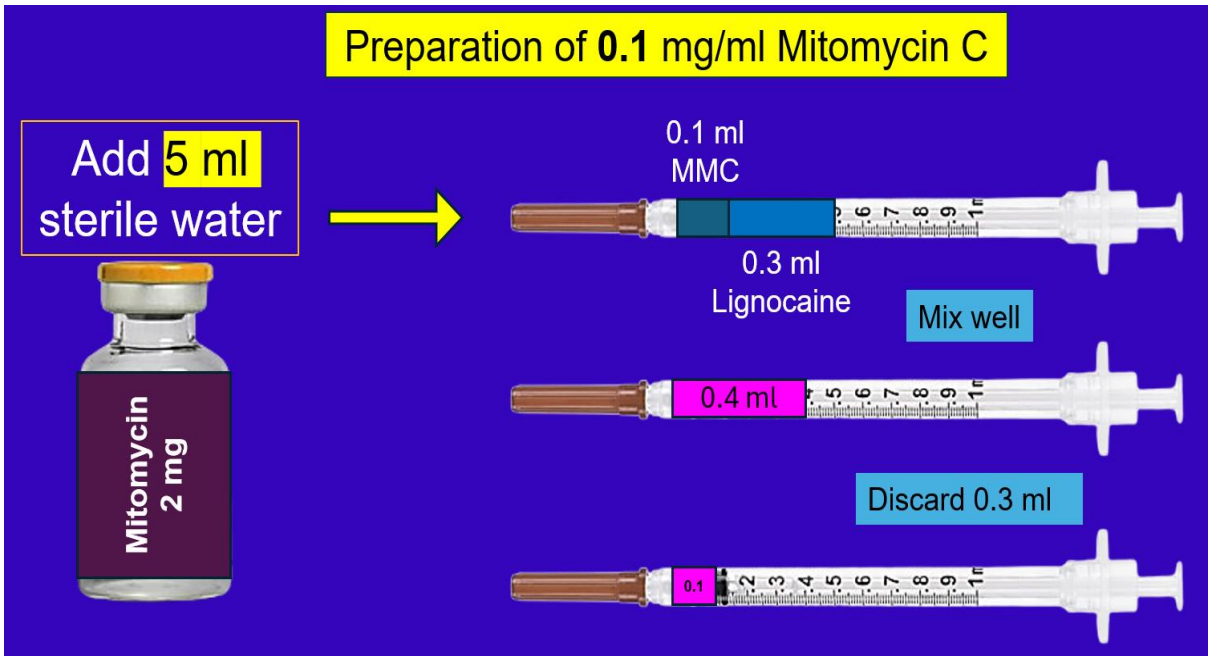


Figure 7: Preparation of 0.1 mg/ml MMC.

Prior to surgery, all patients had an intravenous infusion of 20% mannitol at a dose of 1g/kg of body weight while having their blood pressure monitored. A 5 ml solution containing a 1:1 blend of 2% lignocaine and 0.5% bupivacaine, plus 5 IU/ml of hyaluronidase without adrenaline, was injected into the peribulbar region to produce local anaesthesia. Mitomycin C was injected 8 mm distal to the 12 o'clock limbus using a 26-gauge needle containing 0.1 ml of 0.1 mg/ml. Then, it was massaged away from the limbus to spread the Mitomycin C [Figure 8]. A Thorough wash was given with 30 ml of 0.9% normal saline.

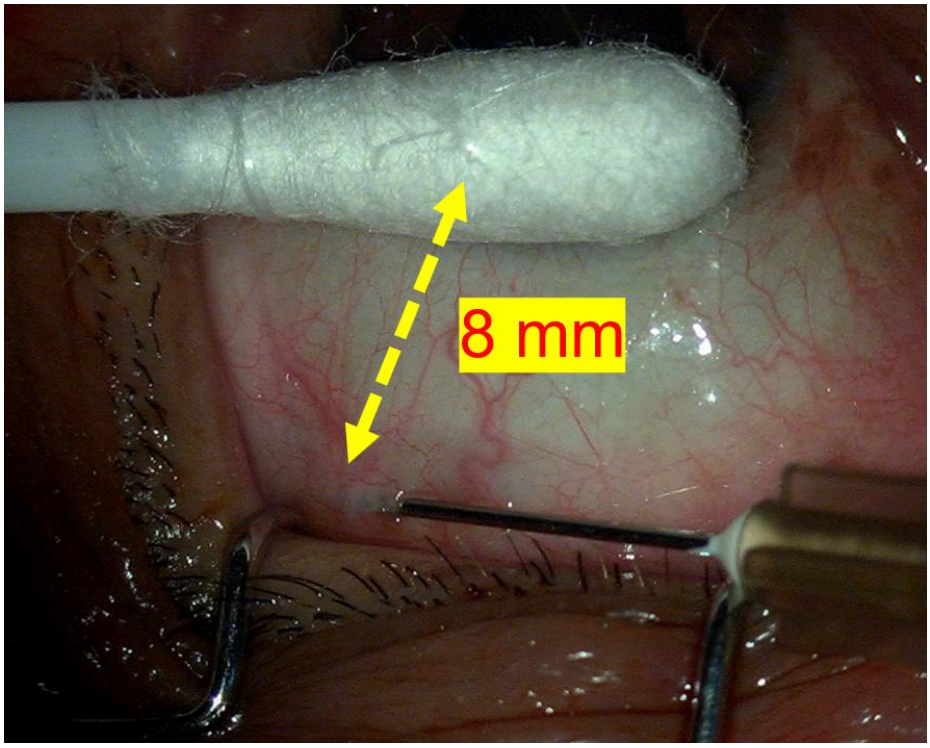


Figure 8: Site of subtenon injection of 0.1 mg/ml MMC. 8 mm away from the limbus.

A superior rectus bridle suture was taken for traction and exposure with a 2-0 silk suture. Fornix-based conjunctival peritomy and light wet field cautery were done. We raised a 3 mm × 4 mm scleral flap. A 5.5 mm scleral incision was given adjacent to the scleral flap, and a sclerocorneal tunnel was constructed with the help of a crescent knife [Figure 9].

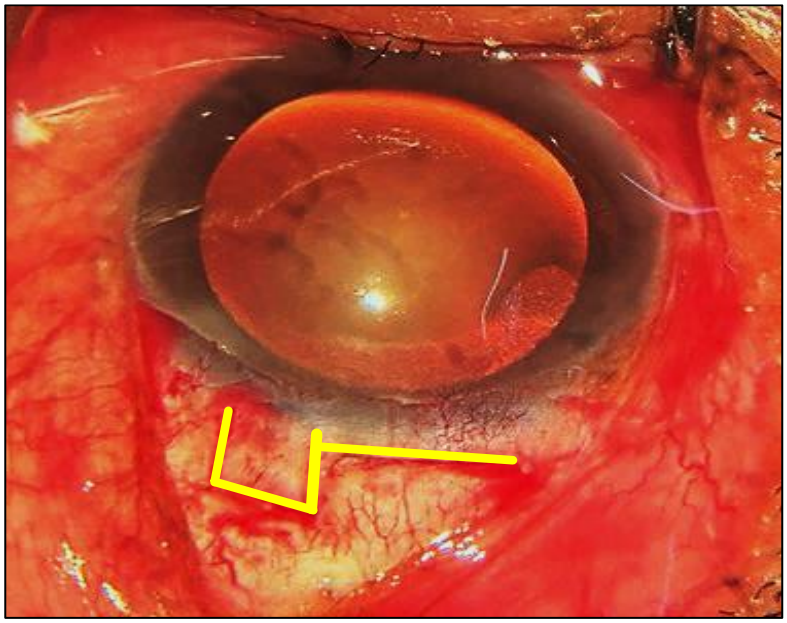


Figure 9: Surgical incision marked in yellow

After that, a conventional small incision cataract surgery was performed. Through a side port made at the 9 o'clock position, continuous curvilinear capsulorhexis was done with the help of a cystotome. After entering through the scleral tunnel using a 2.8 mm keratome, hydro dissection was performed, and the nucleus was prolapsed into the anterior chamber. Then, it was delivered out by sandwiching it between a wire Vectis and sinskey hook. Cortical wash was given with Simcoe irrigation and aspiration cannula. A rigid Polymethyl Methacrylate (PMMA) posterior chamber intraocular lens (Appalens 209, Appasamy Associates) was implanted in the capsular bag [Figure 10].

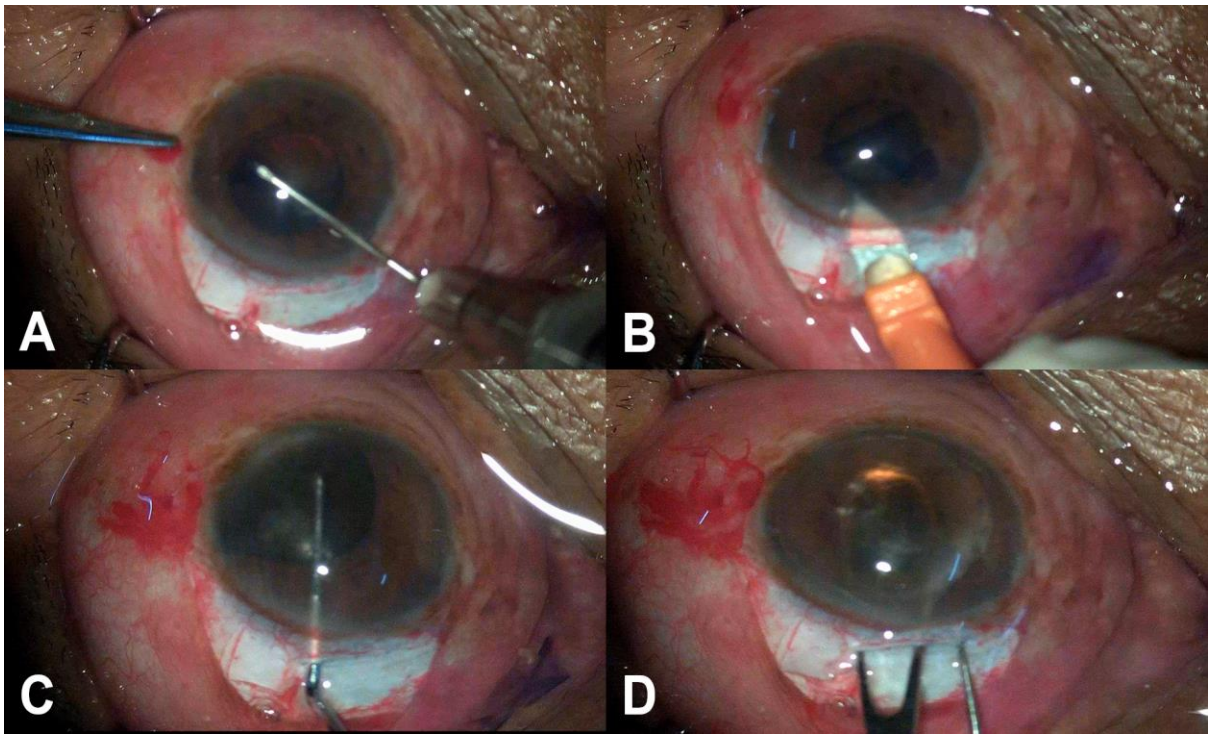


Figure 10: Surgical steps of cataract extraction. A: Continuous curvilinear capsulorhexis. B: Sclerocorneal tunnel entry with 2.8 mm Keratome. C: Nucleus prolapsed into the anterior chamber. D: Nucleus delivery with wire vectis.

A paracentesis was carried out using an 11-number surgical blade underneath the scleral flap. Using Kelly's Descemet membrane punch, a trabeculectomy was then performed to remove a small portion of the trabecular meshwork. Following the trabeculectomy, a peripheral surgical iridectomy was performed, which involved making a small opening in the iris adjacent to the

trabeculectomy ostium to prevent blockage of the new drainage pathway. This step is crucial to ensure that aqueous humor can flow freely from the anterior chamber to the sub-Tenon's space, thereby reducing intraocular pressure. The scleral flap was repositioned and secured in place with four 10-0 monofilament nylon sutures. After confirming a well-maintained anterior chamber, the conjunctiva was closed using two interrupted 8-0 vicryl sutures [Figure 11].

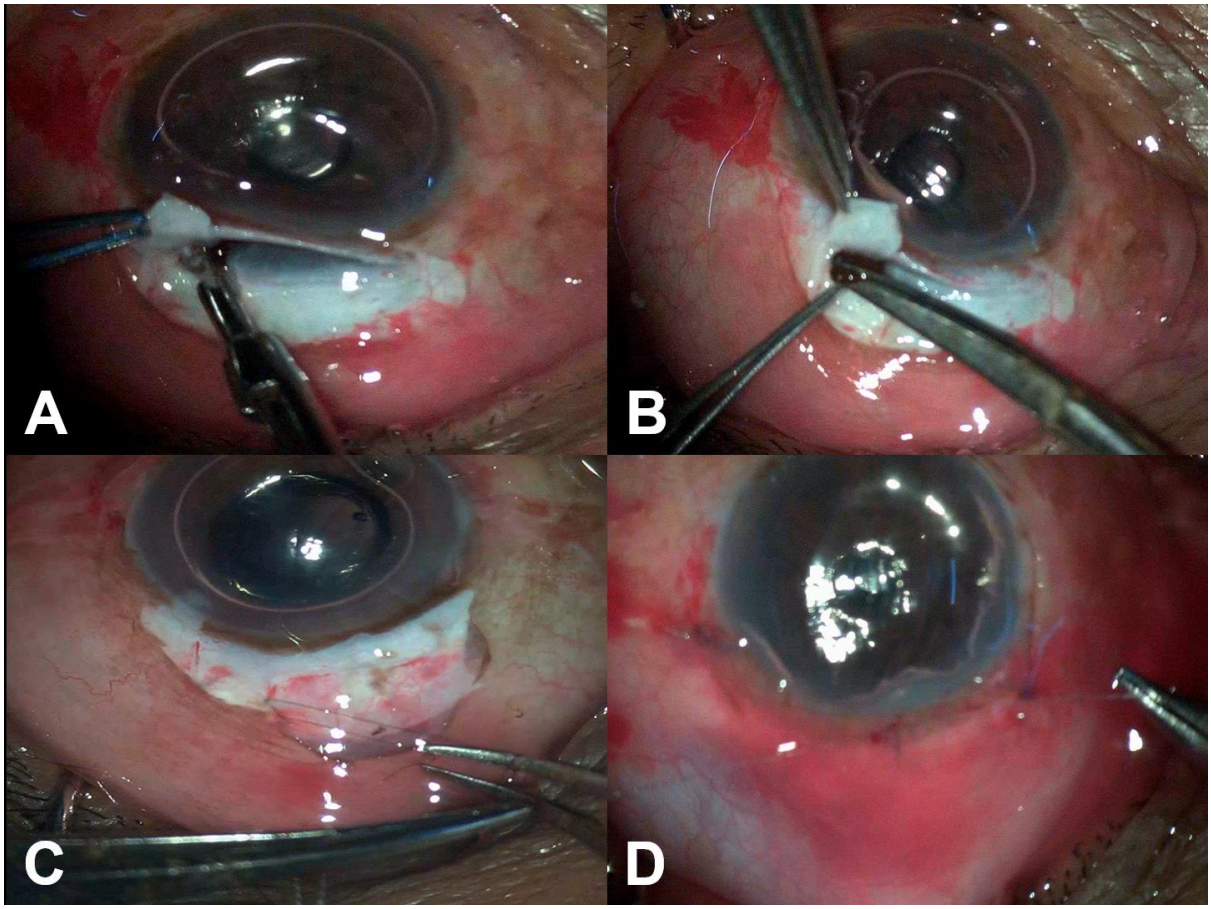


Figure 11: Steps of trabeculectomy. A: Sclerostomy done with Kelly's punch. B: Surgical peripheral iridectomy. C: Scleral flap suturing with 10-0 nylon. D: Watertight suturing closure of conjunctiva with 8-0 vicryl.

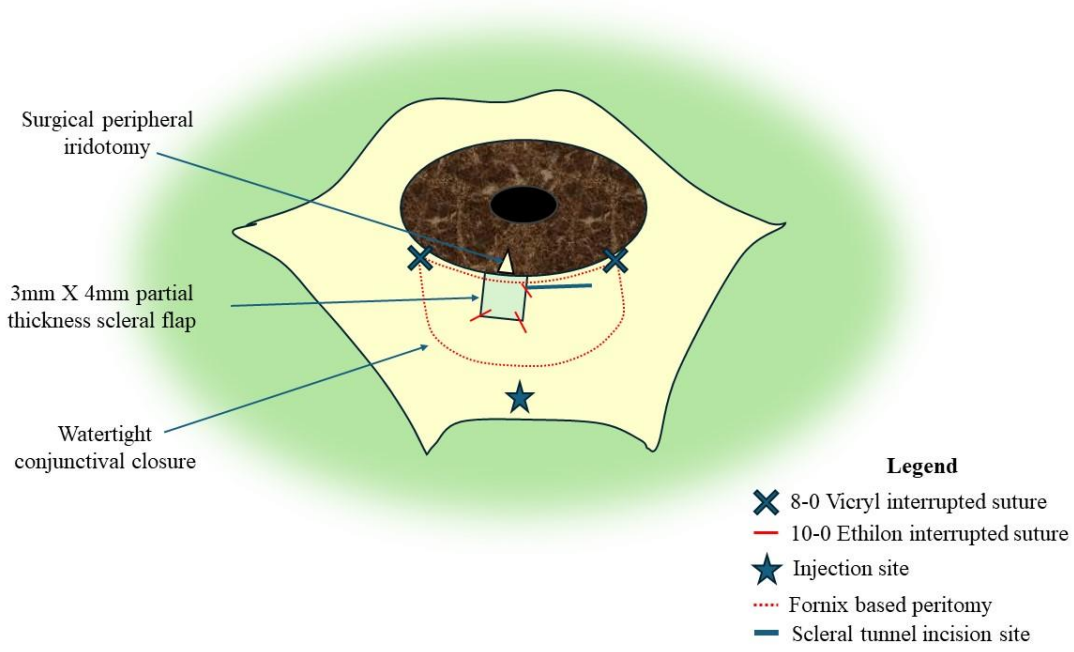


Figure 12: Surgical site schematic diagram.

Postoperative evaluation and outcome measurement:

Data was collected on the first day, one week, one month, three months, and six months following surgery. Visual acuity was measured and quantified in Log MAR; Intraocular pressure was measured using a Goldmann applanation tonometer (Model number: AATM 5001; Appasamy Associates), and bleb grading was done using the Indiana Bleb Appearance Grading System including bleb extent, height and vascularity was graded in all visits (147). Anterior chamber depth was assessed using Spaeth's clinical classification of shallow anterior chamber. (36) Documentation of any complications, such as bleb leaks, hypotony (characterised by intraocular pressure less than 6 mm Hg), infection, and corneal oedema/haze, was undertaken. And use of any antiglaucoma medications were also noted at every follow-up.

The criteria for surgical success were clearly defined. Complete success was characterised by postoperative IOP ranging from more than 6 mm Hg to 18 mm Hg, achieved without the necessity for antiglaucoma medications or interventions. In cases where additional anti-glaucoma medications were required postoperatively to achieve IOP ranging from more

than 6 mm Hg to 18 mm Hg, the outcome was categorised as qualified success. However, the outcome was considered a failure if the postoperative IOP remained higher than 18 mm Hg, even after taking additional anti-glaucoma drugs.

Statistical analysis:

To achieve a “power of 99%” for detecting a “difference in the proportion” of sub-Tenon Injection Success rate at 6th-month follow-up, with a baseline success rate of 82.5% (145), “G*Power ver. 3.1.9.4 software” is used for sample size calculation. Based on this, the study was assigned a sample size of 30.

All data was tabulated in the master chart using “Microsoft Excel version 365”. “Descriptive variables” were expressed in “frequency (percentage) or mean with standard deviation (SD)”. The association between categorical variables like Visual acuity in Log MAR and intraocular pressure during postoperative follow-ups was assessed using the “Friedman test”. The “Mann–Whitney U test” was employed to determine significant differences in IOP reduction between the open-angle and closed-angle groups post-surgery. Statistical significance was defined as a “P value of less than 0.05”. The statistical analysis was carried out utilising “IBM SPSS Statistics 29.0”.

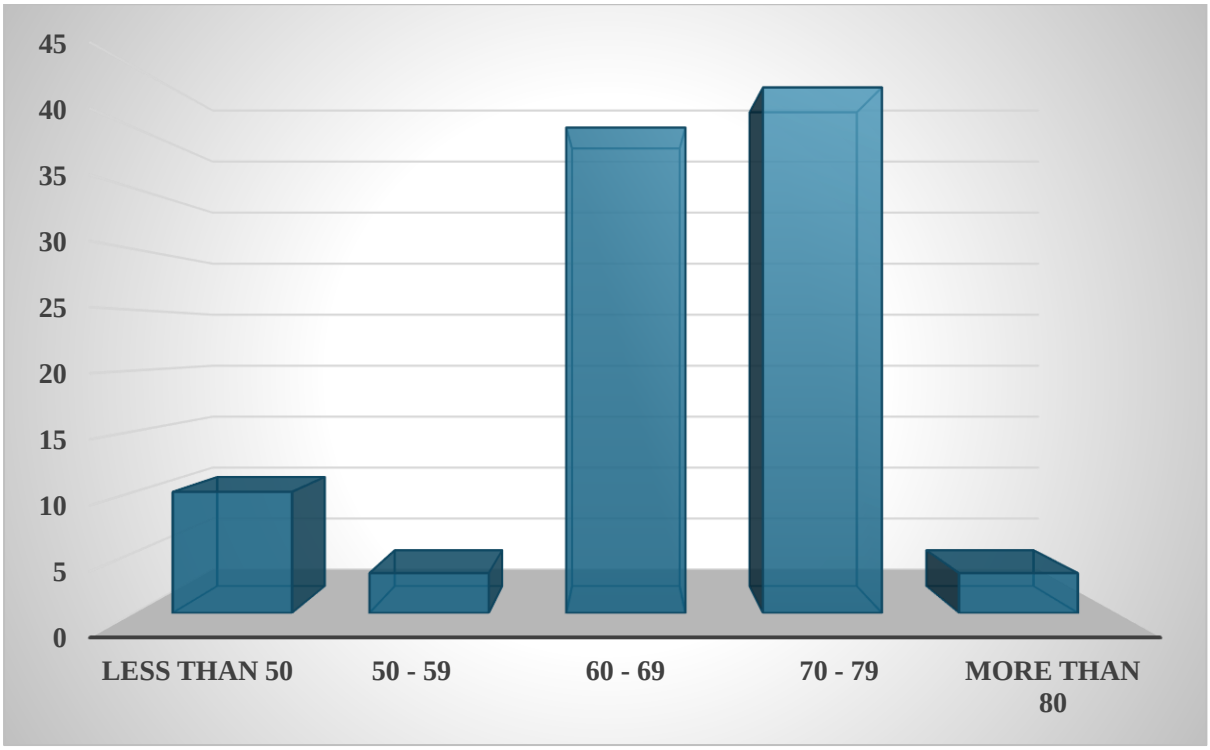
Ethical perspective:

The study received ethical approval from the committee responsible for overseeing research adherence to ethical guidelines. Their endorsement, granted under Order number BLDE (DU)/IEC/685/2022-23, dated 30th August 2022 [Appendix III], adhered strictly to the principles outlined in the Helsinki Declaration (170).

Results

Table 4: Age distribution of patients

Age (in Years)	No. of Patients (n)	Percentage (%)
Less than 50	3	10.0
50 - 59	1	3.3
60 - 69	12	40.0
70 - 79	13	43.3
More than 80	1	3.3
Total	30	100

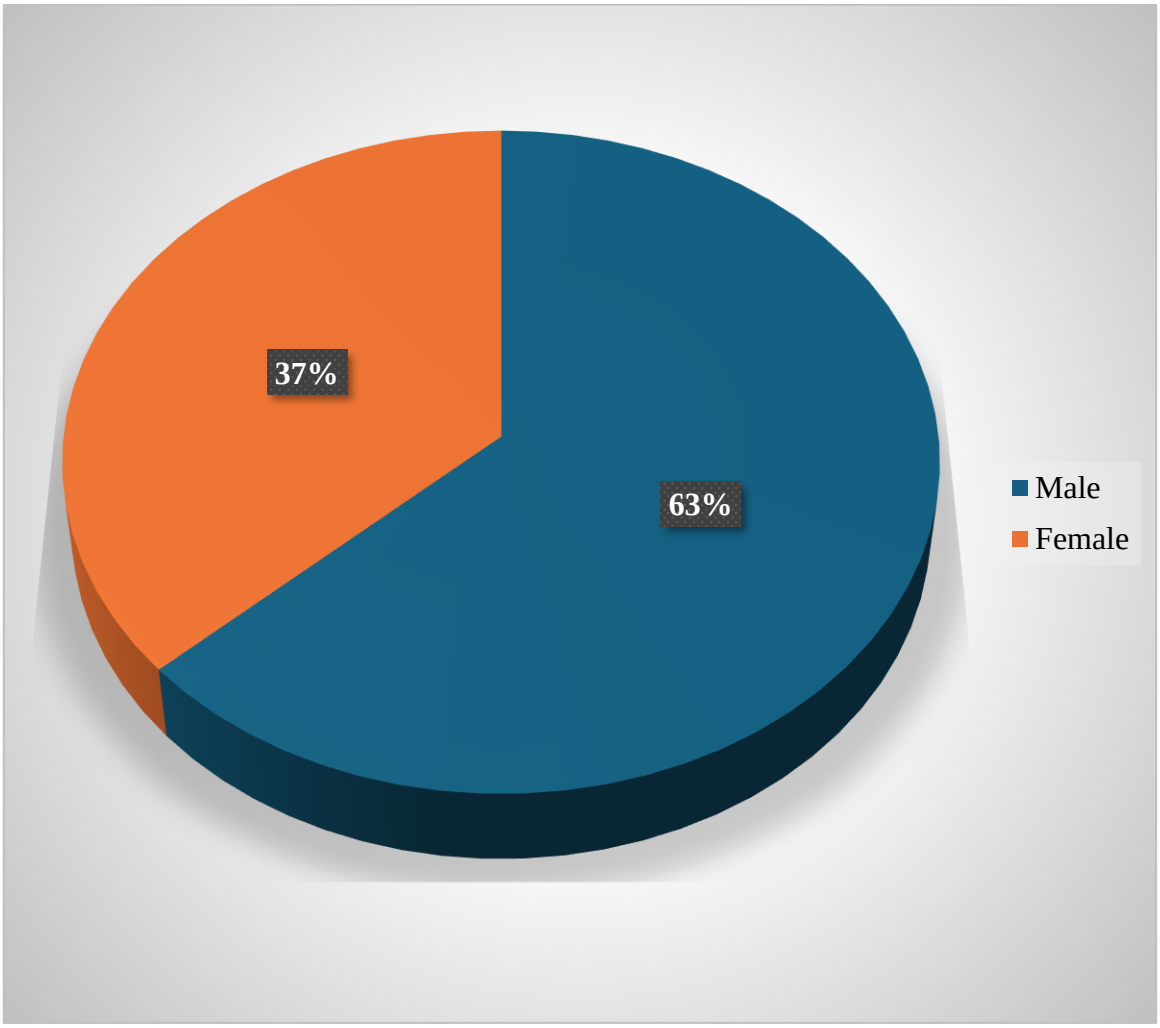


Graph 1: Bar graph showing the age distribution of patients.

Among 30 participants, 13 (43.3%) were in the age group 70 – 79 years, 12 (40.0%) were between 60 – 69 years, 3 (10.0%) were less than 50 years of age, 1 (3.3%) was between 50 – 59 years of age and 1 (3.3%) aged more than 80 years [Table 4; Graph 1].

Table 5: Gender distribution of patients

Gender	No. of Patients (n)	Percentage (%)
Male	19	63.30
Female	11	36.70
Total	30	100

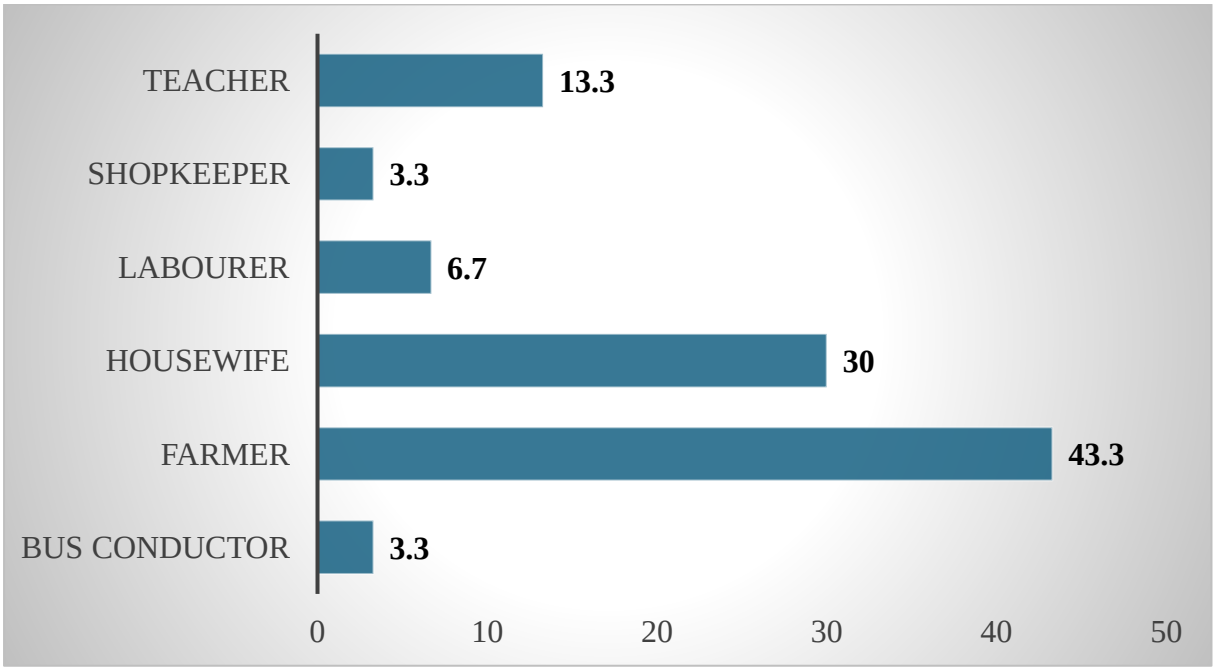


Graph 2: Pie chart showing gender distribution among participants.

Among the 30 participants, 19 (63.30%) were male and 11 (36.70%) were female [Table 5; Graph 2].

Table 6: Distribution of occupation among patients

Occupation	No. of Patients (n)	Percentage (%)
Bus conductor	1	3.3
Farmer	13	43.3
Housewife	9	30.0
Labourer	2	6.7
Shopkeeper	1	3.3
Teacher	4	13.3
Total	**30**	**100.0**

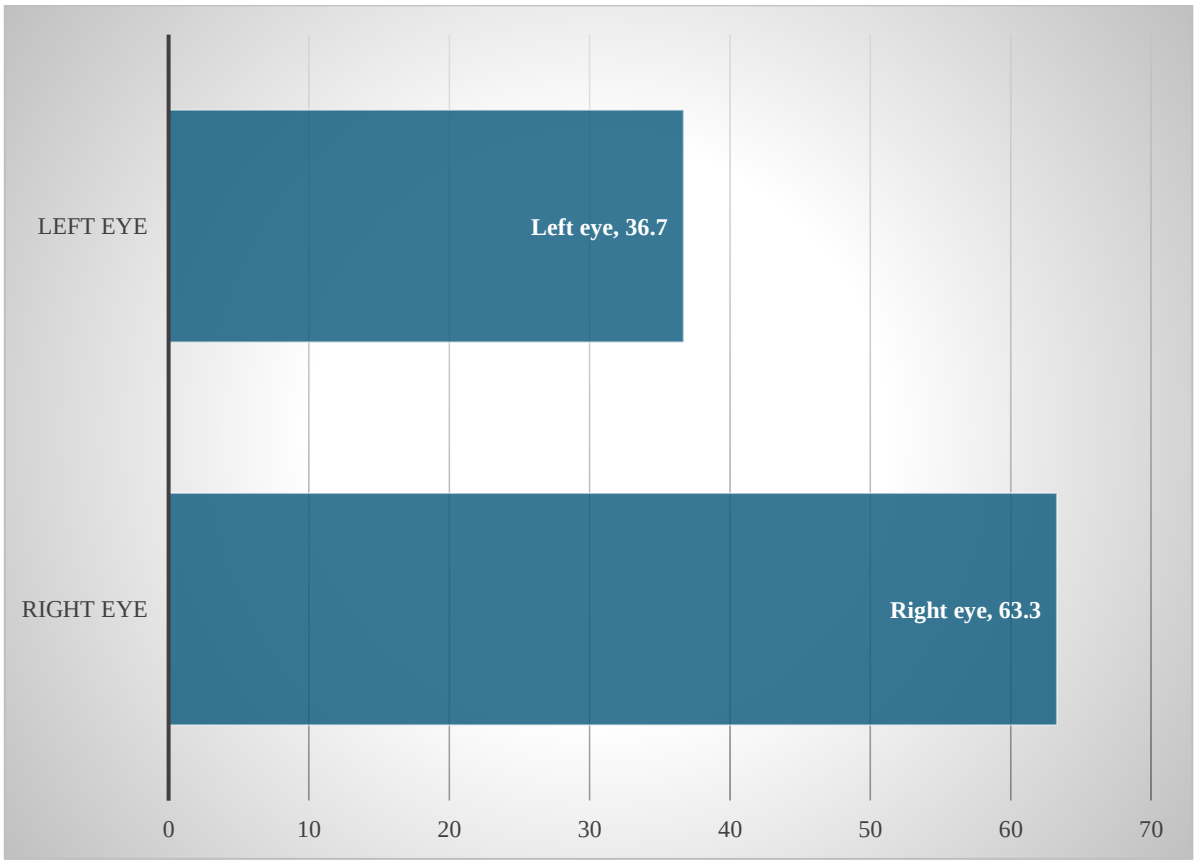


Graph 3: Bar graph showing percentage distribution as per occupation.

Among all the participants, 13 (43.3%) were farmers, and 9 (30%) were housewives. The remaining 8 (26.7%) were schoolteachers, labourers, shopkeepers, and bus conductors [Table 6; Graph 3].

Table 7: Laterality of eye considered for surgery.

Eye Considered	No. of Patients (n)	Percentage (%)
Right eye	19	63.30
Left eye	11	36.70
Total	30	100

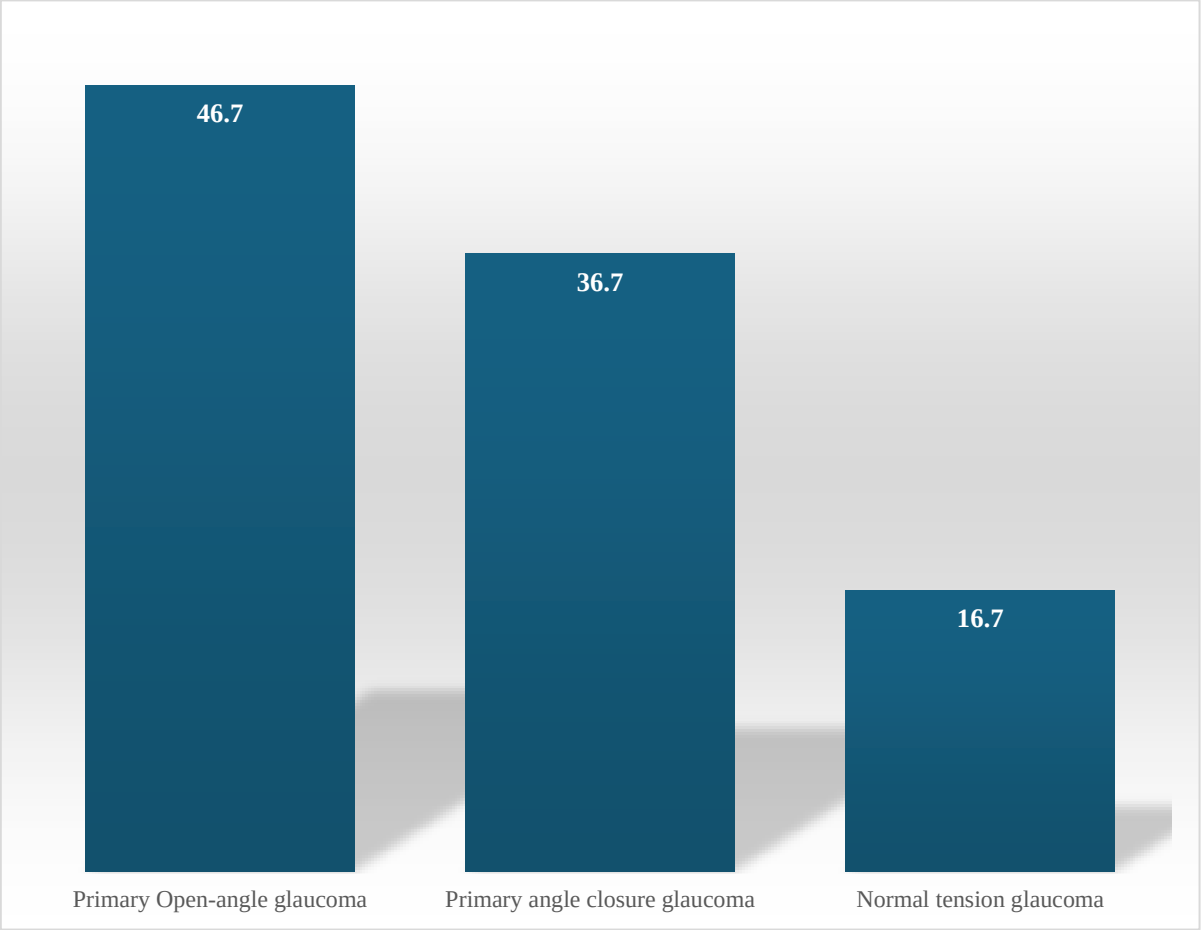


Graph 4: Bar graph showing the percentage distribution of laterality of the eye.

Among all 30 eyes operated, 19 (63.3%) were right eye and 11 (36.7%) were left eye [Table 7; Graph 4].

Table 8: Distribution of diagnosis

Diagnosis	No. of Patients (n)	Percentage (%)
Primary Open-angle glaucoma	14	46.70
Primary angle closure glaucoma	11	36.70
Normal tension glaucoma	5	16.70
Total	30	100



Graph 5: Bar graph representing the distribution of diagnosis.

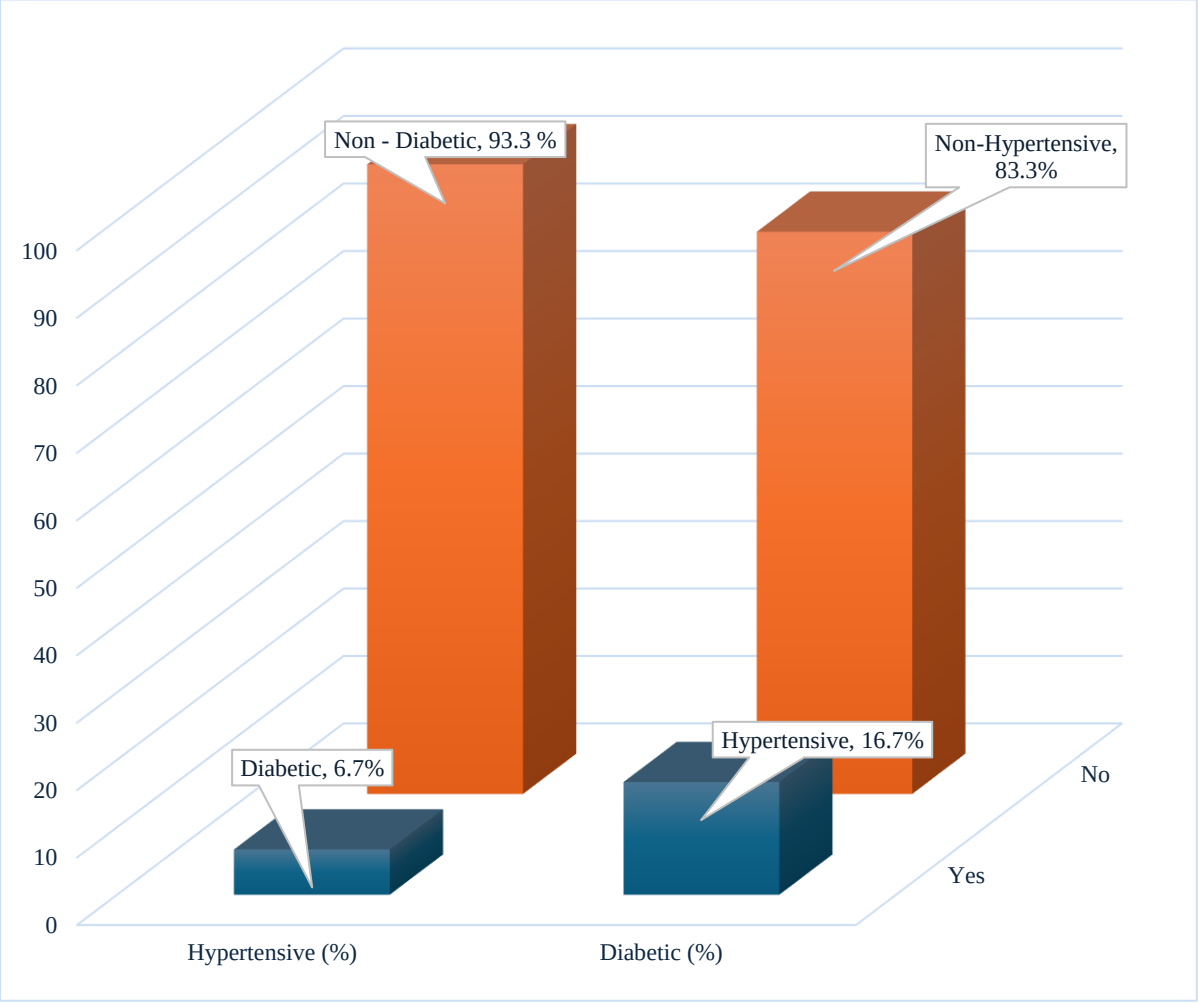
Among all 30 eyes, 14 (46.7%) had primary open-angle glaucoma, 11 (36.7%) had primary-angle closure glaucoma, and 5 (16.7%) had normal tension glaucoma.

Table 9: Distribution of diabetes among participants

Diabetic	No. of Patients (n)	Percentage (%)
Yes	2	6.7
No	28	93.3
Total	30	100

Table 10: Distribution of hypertension among participants

Hypertensive	No. of Patients (n)	Percentage (%)
Yes	5	16.7
No	25	83.3
Total	30	100



Graph 6: Bar graph showing the distribution of diabetes and hypertension.

Among all participants, 2 (6.7%) were diabetic and 5 (16.7%) were hypertensive [Table 9 and 10; Graph 6].

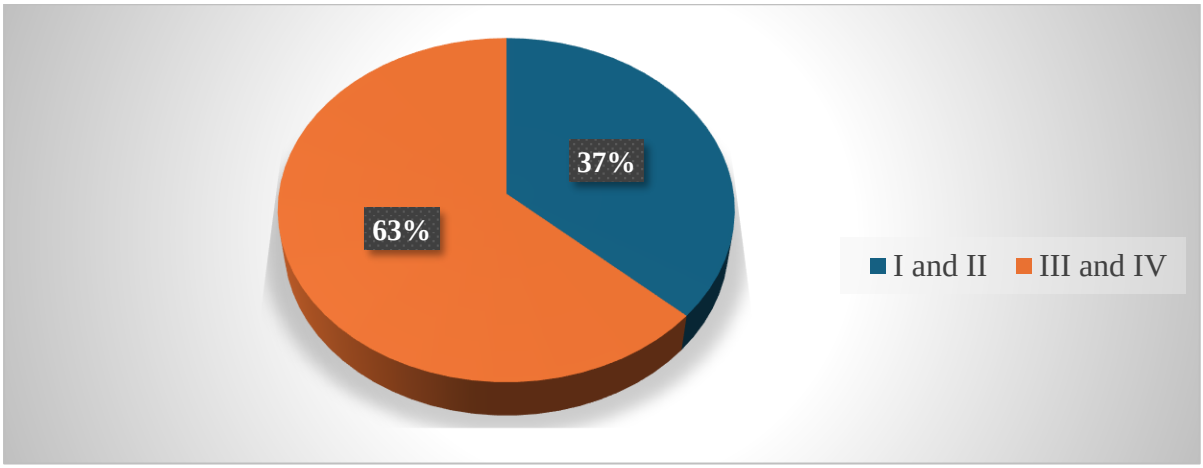
Table 11: Baseline values of Vision, IOP and Cup disc ratio

Pre-operative parameters	Mean	Standard deviation
Visual acuity (in Log MAR)	1.11	0.32
IOP (in mmHg)	31.40	10.38
Cup disc ratio	0.75	0.12

During the preoperative evaluation, the Mean visual acuity in Log MAR (±SD) was 1.11 (±0.32). Baseline Mean Intraocular pressure (±SD) was 31.40 (±10.38) mm Hg, and the mean Cup disc ratio (±SD) was 0.75 (±0.12) [Table 11].

Table 12: Distribution of participants as per Shaffer grading of anterior chamber angle.

Gonioscopic grading (Shaffer grading)	No. of Patients (n)	Percentage (%)
I and II	11	36.70
III and IV	19	63.30
Total	30	100

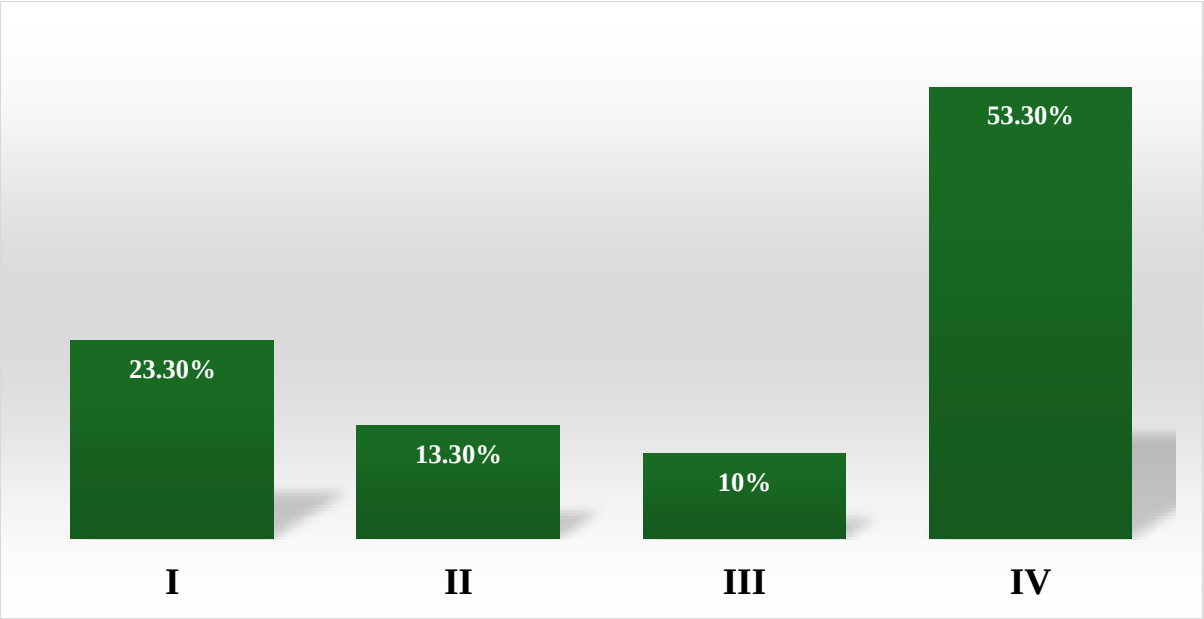


Graph 7: Pie chart representing the distribution of patients according to Shaffer grading of the angle of the anterior chamber.

Among all participants,19 (63.3%) had a Shaffer grading of I and II, while 11 (36.7%) had a Shaffer grading of III and IV (Table 12; Graph 7).

Table 13: Distribution of peripheral anterior chamber depth as per van Herick grading system

Von Herick grading of peripheral anterior chamber depth	No. of Patients (n)	Percentage (%)
I	7	23.30
II	4	13.30
III	3	10.00
IV	16	53.30
Total	30	100

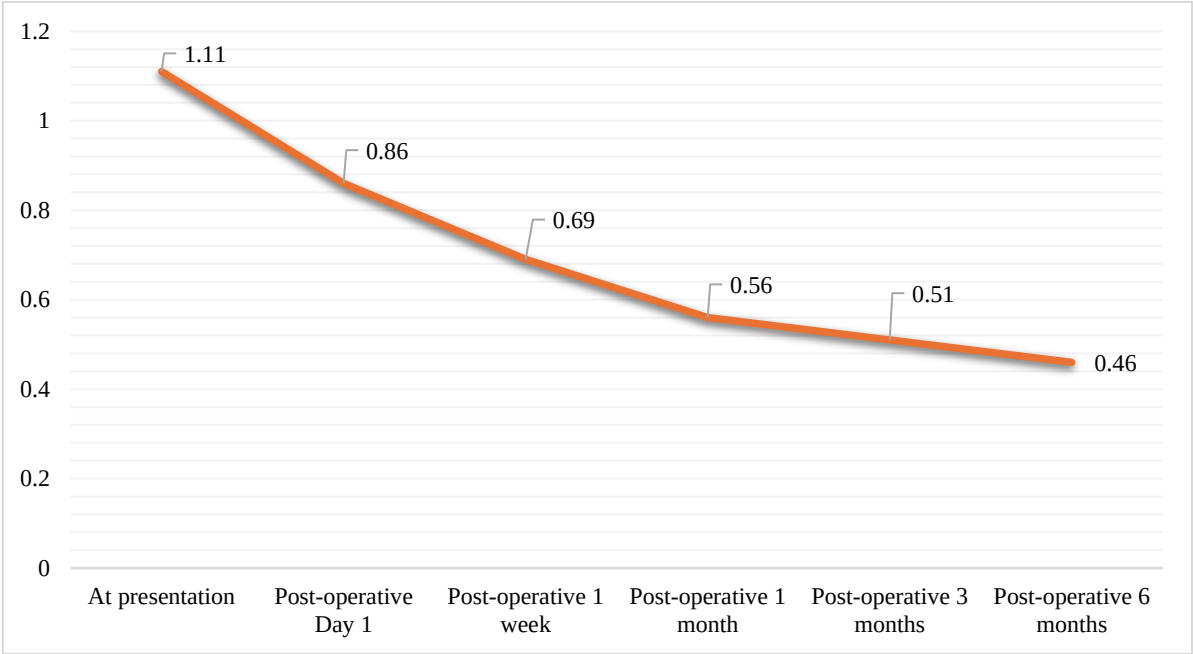


Graph 8: Bar graph showing the distribution of peripheral anterior chamber depth among participants using von Herrick grading.

Among 30 participants, 16 (53.3%) had von Herrick peripheral anterior chamber depth of grade I, 7 (23.3%) had grade I, 4 (13.3%) had grade II and 3 (10.0%) had grade III [Table 13; Graph 8]

Table 14: **Visual acuity in Log MAR over follow-ups**

Visual acuity over Follow-ups	Mean	SD	Friedman Test	P value
At presentation	1.11	0.32	116.67	***0.001****
Post-operative Day 1	0.86	0.26		
Post-operative 1 week	0.69	0.30		
Post-operative 1 month	0.56	0.31		
Post-operative 3 months	0.51	0.33		
Post-operative 6 months	0.46	0.33		

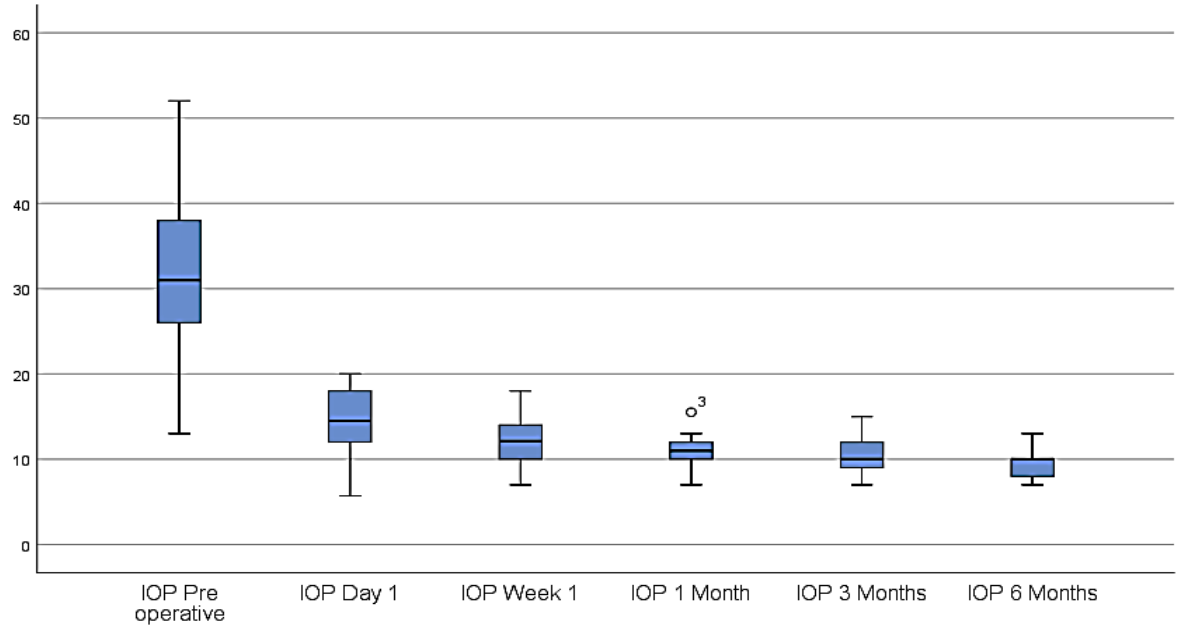


Graph 9: Mean visual acuity in Log MAR over follow-ups as represented in this line graph.

The mean visual acuity in Log MAR (±SD) at presentation was 1.11 (±0.32). On the first postoperative day, it improved to 0.86 (±0.26). In the first week, first month, third month, and sixth month, mean visual acuity was 0.69 (±0.30), 0.56 (±0.31), 0.51 (±0.33) and 0.46 (±0.33), respectively. Mean Visual acuity significantly improved over the follow-ups, with a p-value of 0.001 estimated using the Friedman test [Table 14; Graph 9].

Table 15: Mean IOP (± Standard deviation) over follow-ups.

IOP over Follow-ups	Mean	SD	Friedman Test	P value
At presentation	31.40	10.38	104.27	***0.001****
Post-operative Day 1	14.60	3.75		
Post-operative 1 week	12.32	2.92		
Post-operative 1 month	10.89	1.90		
Post-operative 3 months	10.20	1.98		
Post-operative 6 months	9.55	1.57		

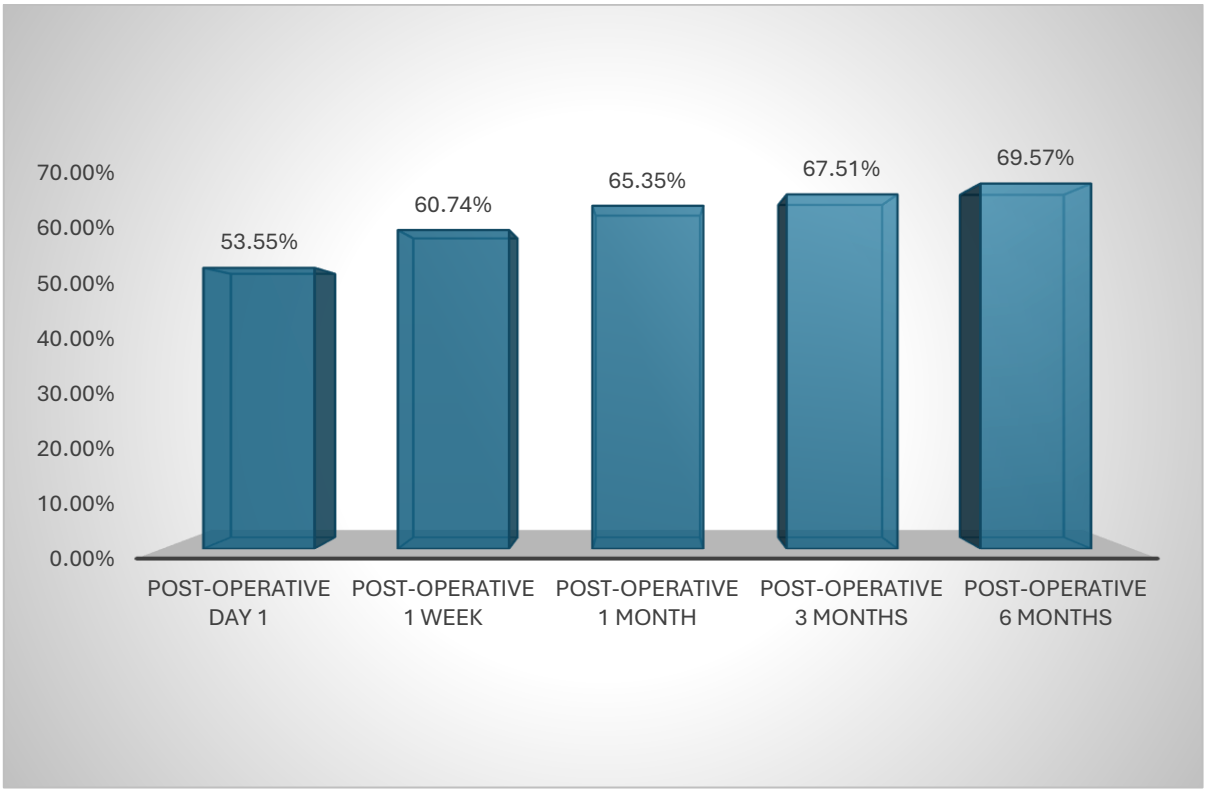


Graph 10: Box and Whisker plot depicting the reduction in IOP over follow-ups.

The mean IOP at the presentation was 31.40 (±10.38) mmHg, which reduced to 14.60 (± 3.75) mmHg on the first postoperative day. At subsequent follow-ups on the first week, first month, third month and six months, mean IOP were 12.32 (±2.92) mmHg, 10.89 (±1.90) mmHg, 10.20 (±1.98) mmHg and 9.55 (±1.57) mmHg respectively. Mean IOP was reduced significantly over all the follow-ups, with a p-value of 0.001, as estimated using the Friedman test [Table 15; Graph 10].

Table 16: Percentage reduction of IOP from preoperative value at each follow-up.

Follow-ups	Percentage reduction in IOP	Friedman Test	P value
Post-operative Day 1	53.55%	104.27	***0.001****
Post-operative 1 week	60.74%		
Post-operative 1 month	65.35%		
Post-operative 3 months	67.51%		
Post-operative 6 months	69.57%		

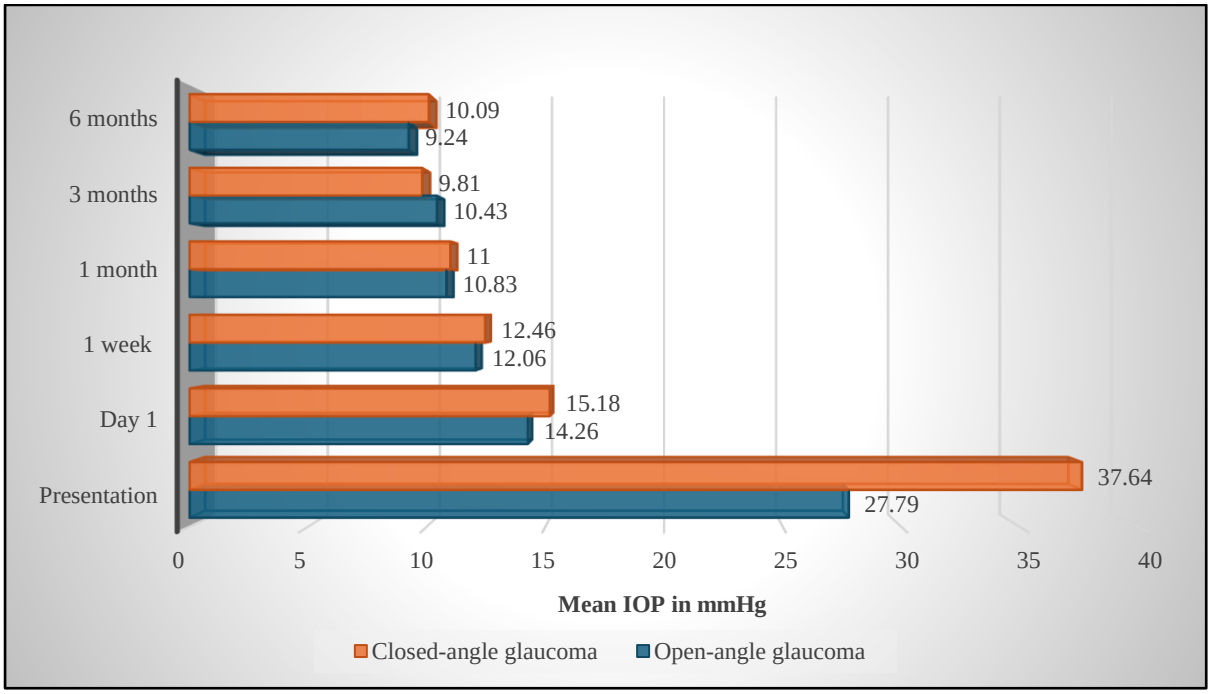


Graph 11: Bar graph showing Percentage reduction of IOP from preoperative value at each follow-up.

The percentage reduction in IOP on the first postoperative day from preoperative IOP was 53.55%. In the first week, first month, third month and sixth month, the percentage reductions in IOP were 60.74%, 65.35%, 67.51% and 69.57%, respectively. There was a significant reduction over follow-ups with a p-value of 0.001 [Table 16; Graph 11].

Table 17: Mean IOP at presentation and at each follow-up in both open-angle and closed-angle glaucoma groups.

IOP	Open-angle glaucoma (n=19)		Closed-angle glaucoma (n=11)		Mann-Whitney Test	p-value
	Mean	SD	Mean	SD		
At presentation	27.79	10.26	37.64	7.50	44.50	***0.008****
Day 1	14.26	3.94	15.18	3.49	88.50	0.497
1 week	12.06	2.64	12.76	3.44	88.50	0.497
1 month	10.83	2.03	11.00	1.73	96.00	0.735
3 months	10.43	1.99	9.81	1.99	89.00	0.525
6 months	9.24	1.56	10.09	1.51	66.00	0.103



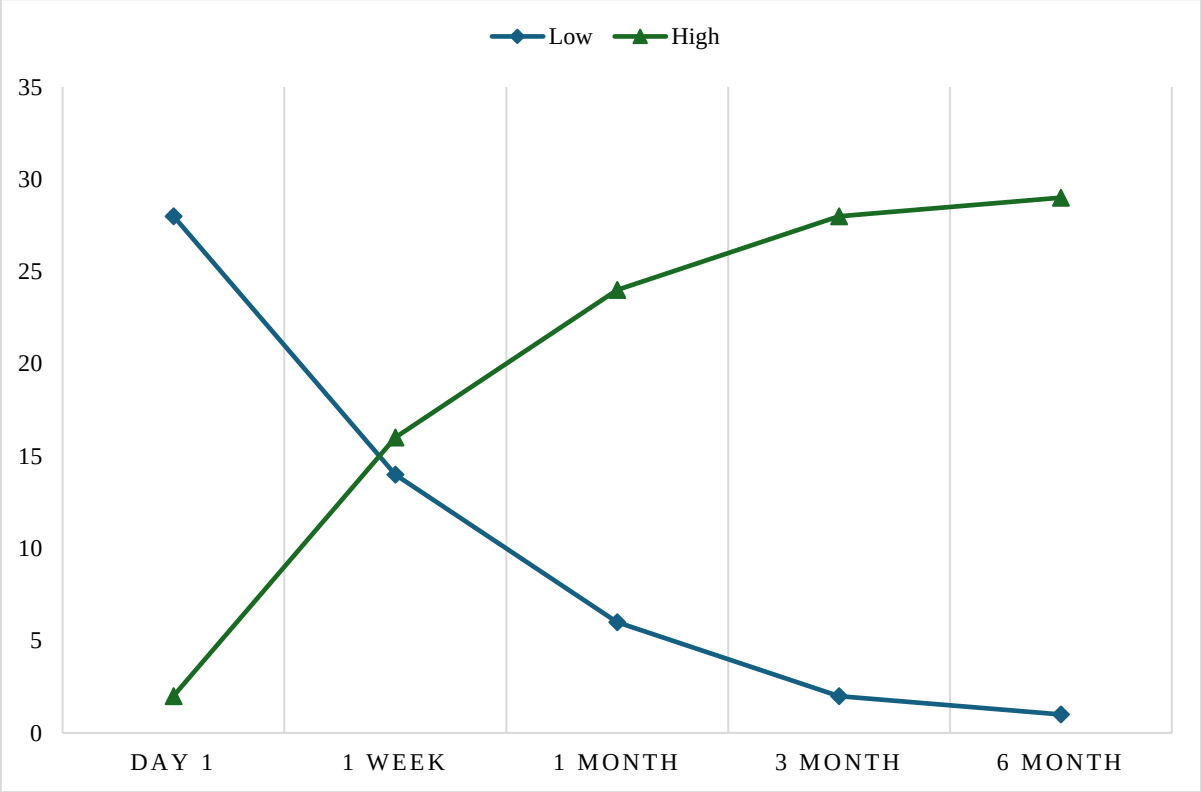
Graph 12: Bar graph comparing Mean IOP at presentation and at each follow-up in both open-angle and closed-angle glaucoma groups.

A significant difference in mean IOP was noted in the open-angle glaucoma and closed-angle glaucoma group at presentation with 27.79 (10.26) and 37.64 (7.50) in open and closed-angle glaucoma, respectively, having a p-value of 0.008 as per Mann – Whitney test. However, there was a significant difference postoperatively over the follow-ups, with mean IOP in open and closed-angle glaucoma being 9.24 (1.56) and 10.09 (1.51), respectively, having a p-value of 0.103 that is statistically not significant [Table 17; Graph 12].

Table 18 (a): Bleb height as per IBAGS over follow-ups

Bleb height	Day 1	1 week	1 month	3 month	6 month	*P value*
Low (H_0,H_1)	28	14	6	2	1	***0.001****
High (H_2,H_3)	2	16	24	28	29	
* *Cochran Q test*						

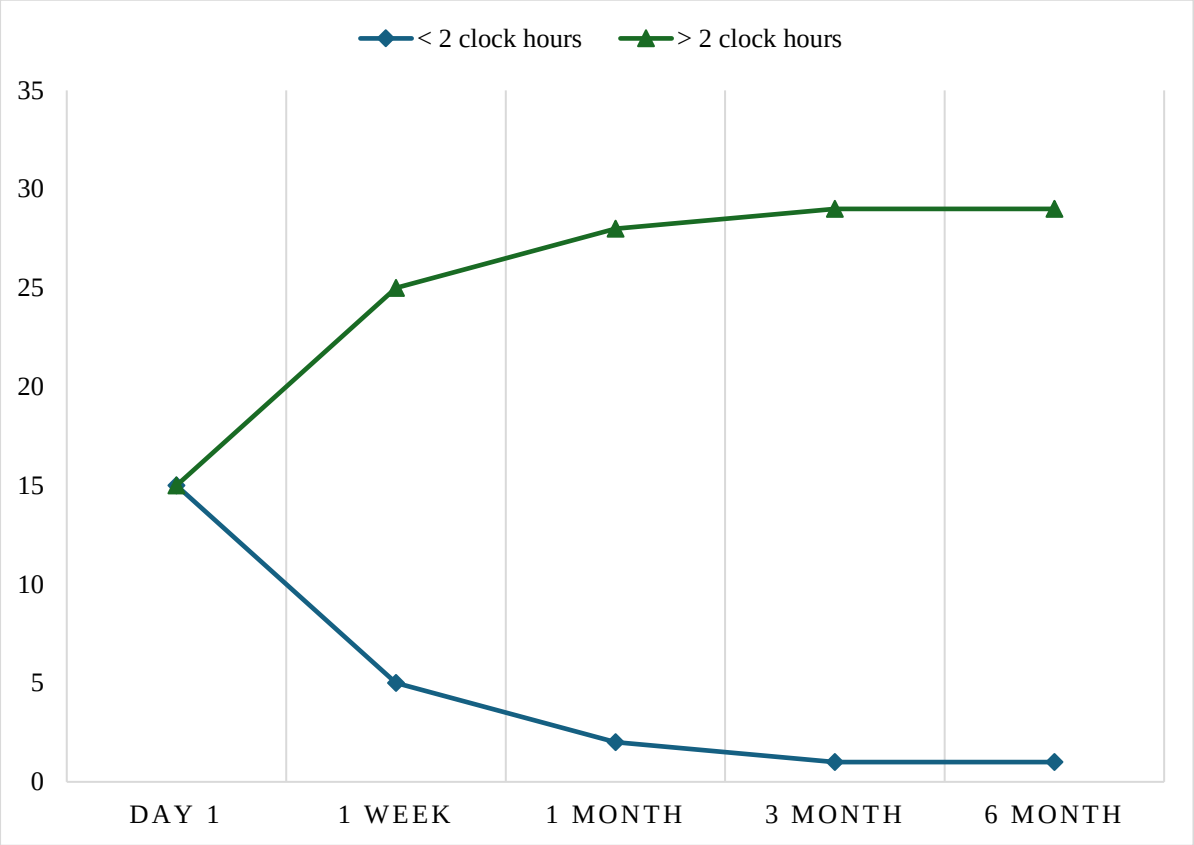
Graph 13 (a): The line graph shows the bleb height over follow-ups.



Bleb height, as assessed using IBAGS, increased over follow-ups. On day one postoperative, 28 eyes had low bleb (H_0, H_1), while 2 had a high bleb (H_2, H_3). At 1 month, 24 eyes had high bleb, and at 6 months, 29 eyes had High bleb (H_2, H_3). (p value = 0.001) [Table 18 (a); Graph 13 (a)]

Table 18 (b): Bleb extent as per IBAGS over follow-ups

Bleb extent	Day 1	1 week	1 month	3 month	6 month	*P value*
< 2 clock hours (E_0,E_1)	15	5	2	1	1	***0.001****
> 2 clock hours (E_2,E_3)	15	25	28	29	29	
** Cochran Q test*						

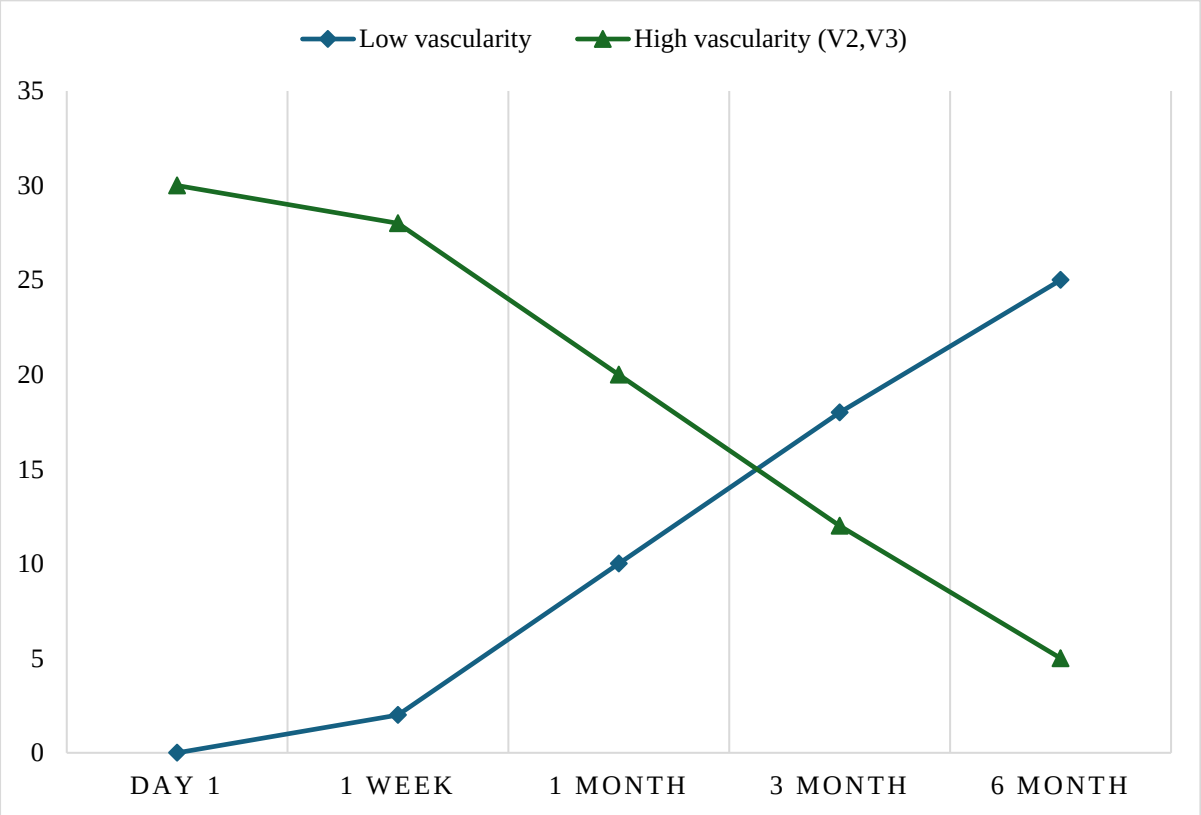


Graph 13 (b): Line graph showing bleb extent as per IBAGS over follow-ups.

Bleb extent, as assessed using IBAGS, increased over follow-ups. On day one postoperative, 15 eyes had bleb spanning less than 2 clock hours, and 15 had bleb spanning more than 2 clock hours. However, at 1 month, 28 eyes had bleb spanning more than 2 clock hours, which increased to 29 at 6 months (p value = 0.001) [Table 18 (b); Graph 13 (b)]

Table 18 (c): Bleb vascularity as per IBAGS over follow-ups

Bleb vascularity	Day 1	1 week	1 month	3 month	6 month	*P value*
Low vascularity (V_0,V_1)	0	2	10	18	25	***0.001****
High vascularity (V_2,V_3)	30	28	20	12	5	
* *Cochran Q test*						

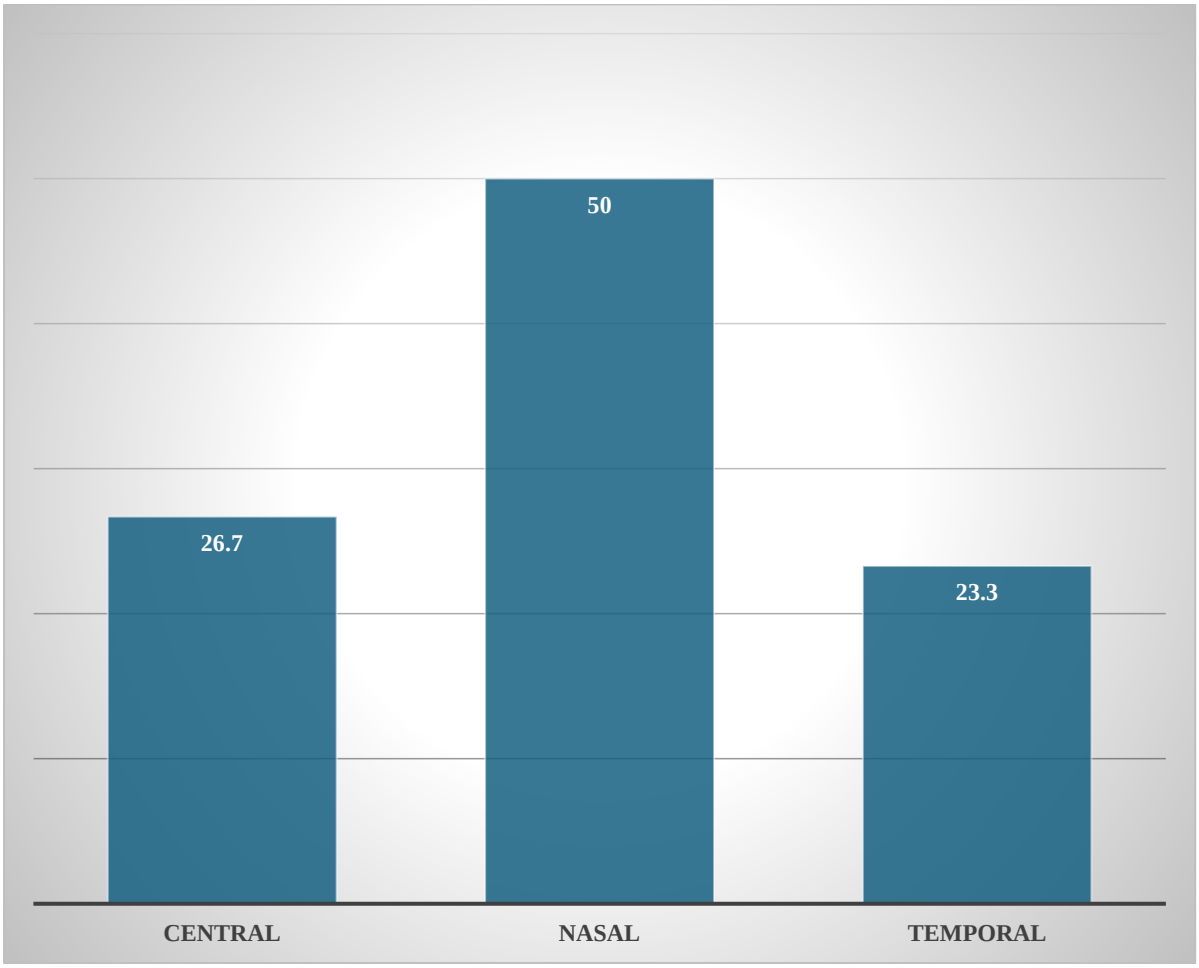


Graph 15(c): Line graph showing bleb vascularity over follow-ups.

Bleb vascularity, as assessed using IBAGS, reduced over follow-ups. In 3rd postoperative month, 18 eyes bleb had reduced vascularity bleb, and 12 still had high vascular bleb. However, by the end of 6 months, 25 eyes had bleb blebs with low vascularity. (p value 0.001) [Table 18 (c); Graph 13 (c)].

Table 19: Bleb position at last visit.

Bleb position	No. of Patients (n)	Percentage (%)
Central	8	26.7
Nasal	15	50.0
Temporal	7	23.3
Total	30	100



Graph 13: Bar graph showing bleb position at last visit.

At the 6th postoperative month, 50% of eyes had a nasal bleb, 26.7% of eyes had a central bleb, and 23.3% of eyes had a temporal bleb [Table 19; Graph 14].

Table 20: Surgical success rate

Surgical outcome	No. of Patients (n)	Percentage (%)
Complete success	28	93.33%
Qualified Success	2	6.67%
Failure	0	0
Total	30	100

The surgical outcomes showed 28 patients (93.33%) achieved complete success, 2 patients (6.67%) achieved qualified success, and there were no reported failures among the total of 30 patients studied [Table 20].

Table 21: List of Complications

Complications	No. of Patients (n)	Percentage (%)
Corneal edema	6	20%
Hypotony	0	0
Bleb leak or others	0	0
Choroidal detachment	0	0
Blebitis	0	0

In our study, we observed hypotony in one patient, and six patients had corneal oedema, which was well-managed conservatively [Table 21].

Discussion

In terms of glaucoma filtration surgery, trabeculectomy has long been considered the "gold standard", and it has undergone many evolutionary refinements. The incorporation of antimetabolites, particularly mitomycin C, has revolutionised postoperative outcomes. Traditionally, mitomycin C is soaked in sponges and applied in the subconjunctival space. However, this method has proven cumbersome, with reported incidents of lost mitomycin C-soaked sponges leading to the development of foreign body granulomas. (142,143) In recent years, exploring the sub-tenon route for mitomycin C injection has emerged as a novel approach. Over a six-month period, this study evaluates the "safety" and "efficacy" of this method using a lower dose (0.1 mg/ml). Thirty patients were enrolled, with the majority having primary open-angle glaucoma (63.33%), while 36.67% had primary angle-closure glaucoma. By the sixth month, there was a significant reduction in baseline IOP, with a 69.57% reduction from 31.40 (± 10.38) mmHg to 9.55 (± 1.57) mmHg ($p = 0.001$). Bleb morphology in terms of height, extent, and vascularity improved significantly over six months, giving diffuse, elevated and minimally vascular blebs ($p = 0.001$) with no bleb encapsulation. Most patients (93.33%) achieved controlled IOP without additional medications, while 6.67% required one medication. Complications were minimal, with transient corneal oedema in six patients and manageable postoperative hypotony in one case.

The average age of the participants in our study was 66.93 (± 10.06) years., which aligns with findings from studies conducted in southern India by Senthilkumar VA et al. and Mudhol et al., where the average age was, respectively, 69.96 (± 11.01) and 63.87 (± 7.90) years (171,172). However, this differs from the results reported by Rajendrababu S et al., where the patients were significantly younger, with a mean age of 46.41 (± 20.43) years (173), and by Gupta V et al., who found the mean age to be 53.20 (± 11.23) years (174).

Among all our participants, 63.30% were male, and 36.70% were female. This finding is consistent with studies by Senthilkumar VA et al., Majtanova N et al., Mudhol et al.,

Maheshwari D et al., and Gupta V et al., which also demonstrated a higher predilection of glaucoma in males (171,172,174–176). However, the study by Yadava U et al. showed a different trend, with a higher predilection in females, comprising 55% of the participants (177)

Multiple previous studies have discussed the impact of the profession on the development of glaucoma. Hartwig A. et al. examined the influence of occupations with increased exposure to vibration on intraocular pressure (178). Burganova AM et al. reported that glaucoma patients often face occupational risk factors such as “high neuropsychiatric tension (29.7%)”, “heavy physical labour (10.7%)”, “chemicals (6.2%)”, and “night shifts (3.9%)” (179). Little MP et al. demonstrated a relationship between low-dose occupational exposure and glaucoma, while Ahn S et al. explored the effect of light irradiance on glaucoma (180,181). In our study, 43.3% of participants were farmers, suggesting a possible increased prevalence of glaucoma among farmers due to higher sun exposure.

In our research, we evaluated the left eye in 36.7% of cases and the right eye in 63.3% of cases. This slightly differed from the findings of Majtanova N, who included the right and left eyes almost equally, at 52% and 48%, respectively (175). It also deviated from the findings of Jagannathan J, who included both the left eye (49.6%) and the right eye (50.4%) almost equally (182).

Considering the demography of southern India, we had 46.7% POAG cases and 36.7% PACG cases. This aligns with similar studies done in the southern Indian population, such as those by Ramakrishna R et al., who reported 42% POAG and 30% PACG, and Maheshwari D et al., who included 38% POAG (138,176). However, Mudhol et al., who also conducted their study in a similar demographic, reported a much higher percentage of POAG at 73.3%, compared to 13.3% for PACG (172). Their percentage of Normal Tension Glaucoma (13.3%) was similar to our study (16.7%) (172). Conversely, Rajedrababu S et al. reported a substantially lower percentage of POAG cases at 26.3%, but this can be attributed to their inclusion of only repeat trabeculectomy cases (173).

The impact of glycaemic status on intraocular pressure (IOP) has been extensively documented; Hymowitz MB et al. found an elevated mean IOP in patients with an average HbA1c of 9.0 ± 2.1 mg/dl (183). This finding is consistent with studies by Bonovas S et al., Oshitari T et al., and Pasquale LR et al. (184–186). Senthilkumar et al. reported 45.8% diabetics and 38.9% hypertensives in their study (171). However, in contrast to these findings, our study observed only 6.7% diabetics and 16.7% hypertensives, which is significantly lower than reported in previous studies.

The "mean baseline visual acuity" in Log MAR (±SD) was 1.11 (±0.32) in our study, which was inferior to the reports of Maheshwari D. et al. with 0.32 (±0.28) (176). This difference can be attributed to our inclusion of cases with significant cataract requiring surgical intervention. However, our values aligned with that of Senthikumar VA et al., who reported it to be 0.80 (±0.40), attributing it to their consideration of phacotrabeculectomy with Mitomycin C (187).

We reported a baseline IOP of 31.40 (±10.38) mmHg, which aligns well with Majtanova N et al. and Maheshwari D et al. Both included a higher percentage of POAG patients and reported their baseline IOP to be 32.34 (±9.45) mmHg and 29.00 (±11.92) mmHg, respectively (145,175). However, unlike our study, both of them considered a higher dose injection of MMC. Conversely, Rajendrababu S. et al., who included more PACG and secondary glaucomas, had a higher baseline IOP of 39.42 (±9.65 mmHg) (173).

Senthilkumar VA et al., who mainly focused on open-angle glaucoma, reported a "mean cup-to-disc ratio" of 0.77 (±0.1), which is similar to our finding of 0.75 (±0.12) (171). However, it's worth noting that we considered both open-angle and closed-angle glaucomas in our analysis.

Majtanova N et al. reported a "mean anterior chamber depth" of 3.20 (± 0.41) mm, which they attributed to their focus on primarily POAG and pseudoexfoliation glaucoma cases (175). In our study, 53.30% of eyes had a van Herick grade 4 peripheral anterior chamber, and upon

gonioscopy, 63.3% of eyes exhibited Shaffer grading 3 or higher. These findings correlate with our higher proportion of open-angle eyes (63.3%).

We had 46.7 % eyes with Relative Afferent Pupillary Defect (RAPD), which can well explain our consideration of moderate and severe glaucomas with a mean of 0.77 (±0.1).

Senthikumar et al. found that at six months of follow-up, the "mean baseline LogMAR Best Corrected Visual Acuity (BCVA)" of phacotrabeculectomy enhanced with 0.2 mg/dl MMC-soaked sponges was 0.80 (±0.4). (171). In our study, the "mean baseline LogMAR BCVA" was 1.11 (±0.32), which improved to 0.46 (±0.33) at 6 months. This difference can be attributed to a higher preoperative cup-to-disc ratio in our patients.

Our study demonstrates a "significant reduction" in IOP postoperatively. The "mean IOP" markedly reduced to 14.60 (± 3.75) mmHg on the first postoperative day, with a continued decline to 9.55 (± 1.57) mmHg by the 6th postoperative month. There was a significant initial reduction of 53.55% in IOP on the first postoperative day and 69.57% by six months. In contrast to our study, Gupta VP et al.(174) utilised a 0.02% Mitomycin C sub-tenon injection, observing a rise in mean IOP from 13.50 (± 5.65) to 15.17 (± 2.48) mmHg from the first postoperative day to the 6th postoperative month. However, their mean percentage reduction in IOP until the last follow-up was comparable to our findings at 68%, potentially attributed to their consideration of a higher initial mean IOP. Whereas Maheshwari D et al.(145) employed a subconjunctival injection of 0.04% MMC and achieved a significant reduction in IOP from 29.00 (± 11.92) mmHg preoperatively to 12.00 (± 6.12) mmHg at the 2nd postoperative week. However, this reduction remained stable throughout the 12-month follow-up, with the mean IOP being 12.19 (± 4.03) mmHg at the last follow-up.

Shih E and Chen Y (146) demonstrated a two-staged approach of intra-tenon injection of Mitomycin C, administered four hours before trabeculectomy, and as per their reported outcomes, IOP was reduced from baseline 33.50 ± 10.10 mmHg to 15.26 ± 6.08 mmHg at six

months follow up which was statistically significant. But in our study, we achieved a statistically significant IOP reduction to 9.55 (± 1.57) mmHg at six months. Senthilkumar VA et al. demonstrated “twin-site combined phacoemulsification and Mitomycin C augmented trabeculectomy”, and they achieved a 24.90% IOP reduction at their last follow-up, which is comparably lower than our findings of 69.57 % at last follow. However, it can be attributed to their lower baseline IOP considerations (19.80 ± 4.70 mmHg).

We observed a significant discrepancy in IOP at the presentation, with closed-angle glaucoma patients exhibiting markedly higher initial IOP (37.64 ± 7.50 mmHg) compared to those with open-angle glaucoma (27.79 ± 1.26 mmHg). Post-surgery, we observed a substantial reduction in IOP in both groups, reaching 9.24 ± 1.56 mmHg in the open-angle glaucoma group and 10.09 ± 1.51 mmHg in the closed-angle glaucoma group after 6 months. Intriguingly, at the 6-month postoperative mark, no significant difference in IOP existed between the two groups, suggesting that although an initial IOP disparity was evident, the surgical interventions effectively equalised IOP levels in both open-angle and closed-angle glaucoma patients over the 6-month follow-up period. Our finding aligned with the 6-month results reported by Maheshwari D et al. (176). However, Maheshwari D et al.(176) reported a higher success rate in open-angle glaucoma (68.8%) than in closed-angle glaucoma (55.2%) at 36 months, indicating potential long-term variations in surgical outcomes between both groups

Pakravan M et al. compared “subtenon injection of MMC” with the “conventional application using soaked sponge”. They reported the “mean bleb height, extent, and vascularity” as per IBAGS to be “2, 1.8, and 1.6”, respectively, in the “subtenon group” and “2.3, 2.1, and 1.9”, respectively, in the “conventional group”. This indicates a “more diffuse and less vascularised bleb” formation in the “subtenon injection group” at the 6-month follow-up. (188) Gupta VP et al. compared the “subconjunctival injection of MMC at the end of trabeculectomy” with the” intra-Tenon injection of MMC prior to the conjunctival peritomy”; the “extent of blebs in both groups was comparable”. Additionally, “65% of blebs in both

groups extended >4 clock hours (E3), with 35% in both groups extending >2 to <4 clock hours (E2)" (174). In our study, combining trabeculectomy with cataract surgery augmented with subtenon injection of MMC, at 6 months, we observed diffuse blebs with a larger extent, with IBAGS grading revealing 29 eyes with a high bleb, 29 with a diffuse bleb spanning > 2 clock hours, and 25 having low vascularity (Figure 4).

A low dose of mitomycin C through the sub-tenon route, as per our reports, achieved 93.33 % complete success and 6.67% qualified success. Our reports were much more convincing than the outcomes of Maheshwari D et al., who achieved an overall success of 90.5% with 52.4% "complete success" and 26.1% "qualified success" in the "subtenon injection group", and they compared it with the conventional route using soaked sponges, which achieved an overall success of 87.0%. Lee et al. compared subtenon injection in combined surgery with cataract extraction and trabeculectomy alone and reported a complete success of 86% and 90%, respectively, in both groups. (144) Quist et al. described "subtenon injection in patients of trabeculectomy with Ex-PRESS shunt" and reported "complete success" in 60.0%.(189)

Rajendrababu et al.(173) reported postoperative complications of a "high dose (0.4 mg/ml) of MMC in seven eyes" like hyphema, conjunctival buttonhole, conjunctival retraction, aqueous misdirection and kissing choroid. Maheshwari et al. compared sub-tenon injection with a soaked sponge approach of 0.2 mg/ml MMC application. They reported nine complications, all in sponges groups, and no significant complications in the injection group. In our study, we observed hypotony in one patient, and six patients had corneal oedema, which was well-managed conservatively.

Limitations of the study

1. We included a small sample size in our study.
2. We have not compared the subtenon route of mitomycin C application with other routes.

Summary

This study evaluated the safety and efficacy of using a lower dose of mitomycin C at 0.1 mg/ml over six months.

- Thirty participants were involved, predominantly male (63.3%) and aged 60-79 years (83.3%), with farmers comprising the majority (43.3%).
- The distribution of operated eyes was 63.3% right eye and 36.7% left eye, with types of glaucoma including primary open-angle (46.7%), primary-angle closure (36.7%), and normal tension (16.7%).
- Systemic comorbidities included diabetes in 6.7% and hypertension in 16.7% of participants
- Preoperative mean visual acuity was 1.11 Log MAR and mean intraocular pressure was 31.40 mm Hg.
- Postoperatively, visual acuity improved significantly to 0.46 Log MAR, and mean IOP reduced to 9.55 mm Hg with a 69.57% reduction by the sixth month.
- Bleb characteristics, such as height, extent, and vascularity, also showed statistically significant improvement achieving a diffuse and minimally vascular bleb over 6 months. At six months, 50% of eyes had nasal blebs, 26.7% had central blebs, and 23.3% had temporal blebs.
- Our study reported a 93.33% complete success rate and 6.67% qualified success.
- Minimal complications were noted, including hypotony in one patient and corneal edema in six patients, all managed conservatively without requiring revision surgery.
- Overall, the use of low dose subtenon injection of MMC is both safe and effective, achieving favourable bleb morphology and significant reduction in IOP over six months.

Conclusion

This study demonstrated a significant reduction in intraocular pressure, with most patients achieving controlled intraocular pressure without additional antiglaucoma medications, indicating a high success rate over a six-month follow-up period. Visual acuity also showed significant improvement over the follow-up period. Low dose mitomycin C administered by subtenon injection produced a desirable bleb morphology that was diffuse, avascular, and had minimal complications. It is a promising alternative to the conventional mitomycin C application method using soaked sponges. Subtenon injection of low dose mitomycin C augmented trabeculectomy is both safe and efficacious, providing significant intraocular pressure reduction, favourable bleb architecture, and minimal complications.

Appendix I

Consent form

STUDY SUBJECT CONSENT FORM

I confirm that Dr ARKAPRAVA RAY has explained the purpose of the research, the study procedure, the benefits, and the possible discomfort that I may experience in the language best understood by me. Therefore, I agree to participate as a subject in this research project and willfully consent.

_____ _____

(Participant) (Date)

_____ _____

(Witness to above signature) (Date)

ಅಧ್ಯಯನವಿಷಯಕಾನ್ಸೆಂಟ್ಫಾರ್ಮ್

ಡಾ. ಅರ್ಕಪ್ರವ ರೇ,ನನಗೆ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ, ಅಧ್ಯಯನದ ವಿಧಾನ ಮತ್ತು ಸಂಭವನೀಯ ಅಸ್ವಸ್ಥತೆಗಳು ಮತ್ತು ನನ್ನ ಸ್ವಂತಭಾಷೆಯಲ್ಲಿ ನಾನು ಅನುಭವಿಸಬಹುದಾದ ಪ್ರಯೋಜನಗಳನ್ನು ವಿವರಿಸಿದ್ದೇನೆ ಎಂದು ನಾನು ಖಚಿತ ಪಡಿಸುತ್ತೇನೆ. ಮೇಲಿನ ಎಲ್ಲಾ ವಿಷಯಗಳನ್ನು ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ನಾನು ಅದನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ. ಆದ್ದರಿಂದ, ಈ ಸಂಶೋಧನಾಯೋಜನೆಯಲ್ಲಿ ವಿಷಯವಾಗಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಗೆ ನೀಡಲು ನಾನು ಒಪ್ಪುತ್ತೇನ

(ಭಾಗವಹಿಸುವವರು) (ದಿನಾಂಕ)

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Appendix II

Case Proforma

DEPARTMENT OF OPHTHALMOLOGY
B.L.D.E UNIVERSITY'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586103

CASE PROFORMA

Case No:

Name:

Age years Sex: (1-Male 2-Female) IP no:

Address:

Contact no: /

Occupation

Date of admission: Date of Discharge:

Is the patient eligible for study? (1-Yes, 2-No):

Has informed consent been given? (1-Yes, 2-No):

SURGEON'S NAME: **PROF. (DR.) REKHA R. MUDHOL**

SURGEON'S SIGNATURE:

Chief Complaints:

1. Diminution of vision: Right Eye Duration: days/months/years
   Left Eye Duration: days/months/years.
2. Others (if any):

1

History of Present Illness: (1- Present 2- Absent)

1. Diminution of vision: ☐
2. Diplopia / Polyopia: ☐
3. Colored halos: ☐
4. Glare ☐
5. Black spots / non seeing area before eye: ☐
6. Redness: ☐
7. Watering: ☐
8. Discharge: ☐
9. Pain in eyes: ☐
10. Headache: ☐
11. H/O trauma: ☐
12. H/O wearing glasses: ☐

Past history: Present (1) or Absent (2)

1. Ocular Surgery: ☐ …….
2. Diabetes: ☐ ……
3. Hypertension: ☐ …….
4. CAD: ☐ …….
5. Others:……..

Personal History: Present (1) or Absent (2)

1. Smoking: ☐ …….
2. Alcohol Consumption: ☐ …….
3. Diet: ☐ ……...

Family History of glaucoma: ☐ (1- Present, 2- Absent)

General Physical Examination:

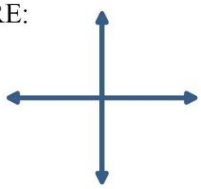
1. Built: ☐ (Well built – 1, Moderately built – 2, Poorly built – 3, Emaciated – 4)
2. Pallor: Present (1) or Absent (2): ☐
3. Icterus: Present (1) or Absent (2): ☐
4. Clubbing: Present (1) or Absent (2): ☐
5. Koilonychia: Present (1) or Absent (2): ☐
6. Cyanosis: Present (1) or Absent (2): ☐
7. Lymphadenopathy: Present (1) or Absent (2): ☐
8. Edema: Present (1) or Absent (2): ☐
9. Pulse: ☐ /minute
10. Temperature: ☐ degree Fahrenheit
11. Blood pressure: ……. /……mmHg
12. Respiratory rate: ☐ cycles per minute

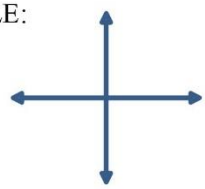
Systemic Examination: Normal (1) or Abnormal (2)

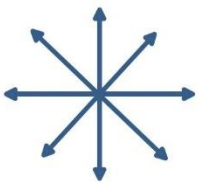
1. CNS: ☐
2. CVS: ☐
3. Respiratory system: ☐
4. Per abdomen: ☐

Ocular Examination:

- Head posture: 1 – Face turn, 2 – Head tilt, 3 – Chin lift, 4- All absent ☐
- Visual axis: 1 – Parallel, 2 – Deviated ☐
- Facial Symmetry: 1 – Symmetrical 2 – Asymmetrical ☐
- Ocular motility: 1 – Normal (N), 2 – Restricted (R) ☐

RE: 

LE: 

BINOCULAR: 

3

- Visual Acuity:

	RE	**LE**
DISTANT		
PINHOLE		
NEAR		
BCVA		

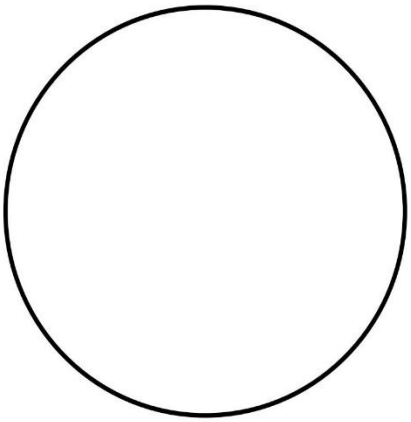
Prescription	Spherical	Cylindrical	Axis	BCVA
RE				
LE				

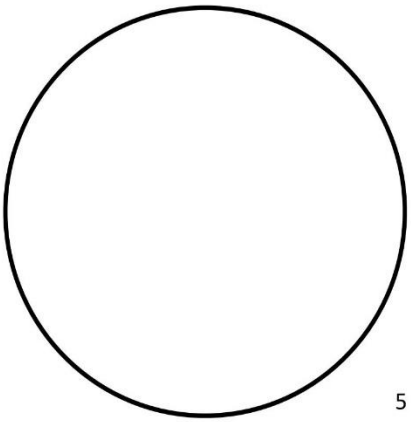
• **Conjunctiva** 1- Normal 2- Conjunctival Congestion 3- Ciliary congestion	☐	☐
• **Cornea** 1- Clear 2- Opacity	☐	☐
• **Anterior Chamber** **(**Von Herick grading)	☐	☐
• **Iris** 1- Normal colour and pattern 2- Atrophic patches	☐	☐
• **Pupil** **Shape:** **1-** Round and regular. **2-** Irregular **Reaction:** 1- Reactive 2- RAPD (Mention grade) **Pseudo exfoliation granules in margin** 1- Present 2- Absent	**Size**:……mm ☐ ☐ ☐	**Size**:……mm ☐ ☐ ☐

• **Lens:** 1- Transparent, 2- Cataractous, 3- Pseudophakia, 4- Aphakia If cataract present: 1- Immature 2- Mature 3- Hyper mature (1- Present, 2- Absent) A) Cortical cataract B) Nuclear sclerosis If present: GRADE: C) Posterior Sub capsular cataract	☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐
Lacrimal duct patency (1-Patent, 2-Regurgitation, 2A-Clear fluid; 2B-Mucopurulent; 2C- Blocked)	☐	☐

FUNDUS EXAMINATION:

Fundus	Right eye	Left eye
Media		
Disc		
Blood vessels		
Background		
Macula		





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INTRA OCULAR PRESSURE:

- At presentation: (With…….on……..…….)
  Right Eye: mmHg Left Eye: mmHg
- Diurnal IOP monitoring (**if done**):

	Right Eye	Left Eye
Maximum IOP		
Minimum IOP		
Variation of IOP		

GONIOSCOPY: Grading of angle by Shaffer's method

Right eye	Left eye
	

DIAGNOSIS:

INVESTIGATIONS

1. Random Blood Sugar: …….mg/dl
2. PERIMETRY: Right eye:
   Left eye:

Preoperative preparation: (TICK):

i. Written and informed consent taken. ☐
ii. Lignocaine sensitivity testing ☐
iii. Tab Ciprofloxacin 500mg 1 tab after dinner ☐
iv. Tab Acetazolamide 250 mg 1 tab after dinner and morning ☐
v. IV Mannitol 20% _____ m ☐

OPERATIVE PROCEDURE: TRABECULECTOMY WITH 0.01% OF MITOMYCIN-C SUBTENON INJECTION UNDER LOCAL ANESTHESIA

COMBINED WITH SICS WITH PCIOL IMPLANTATION UNDER LA (**YES** OR **NO**)

DATE OF SURGERY: ☐☐■☐☐■☐☐☐☐

OPERATING EYE: Right / Left

ANESTHESIA: Peribulbar block/ Retrobulbar block/ Topical Anesthesia

INCISION: ☐

(1-Superior, 2-Temporal, 3-Superior temporal, 4-Inferior temporal)

OPERATIVE COMPLICATION: ☐ (1- Present, 2-Absent)

Postoperative follow up.

Date	Day 1	1 WEEK	1 MONTH	3 months	6 months
A) BLEB MORPHOLOGY (INDIANA GRADING SYSTEM)					
Height H0: Flat bleb H1: Low bleb H2: Medium bleb H3: High bleb	☐	☐	☐	☐	☐
Horizontal extent E0: 0 – 1 clock hour E1: 1 – 2 clock hours E2: 2 – 4 clock hours E3: > 4 clock hours	☐	☐	☐	☐	☐
Vascularity V0: Avascular white V1: Avascular cystic V2: Mild vascularity V3: moderate vascularity V4: Extensive vascularity	☐	☐	☐	☐	☐
Seidel test S0: No leak S1: Multiple pinpoint leaks S2: Streaming leak	☐	☐	☐	☐	☐

B)TRABECULECTOMY OSTIUM 1: Patent 2: Closed	☐	☐	☐	☐	☐
C) SURGICAL IRIDECTOMY 1: Patent 2: Closed	☐	☐	☐	☐	☐
D) ANTERIOR CHAMBER DEPTH (Von Herick grading)	☐	☐	☐	☐	☐
E) IOP	☐	☐	☐	☐	☐
F) Vision Visual acuity Pinhole	☐ ☐	☐ ☐	☐ ☐	☐ ☐	☐ ☐
Signature of Guide					

Dr. Arkaprava Ray
Investigator
PG Student
Department of Ophthalmology

Prof. (Dr.) Rekha R. Mudhol
Thesis Guide
Professor
Department of Ophthalmology

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Appendix III

Institutional ethical clearance

BLDE
(DEEMED TO BE UNIVERSITY)
Declared as Deemed to be University u/s 3 of UGC Act, 1956
Accredited with 'A' Grade by NAAC (Cycle-2)
The Constituent College
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 685/2022-23 30/8/2022

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Friday, 26th August, 2022 at 3.30 p.m. in the Department of Pharmacology** scrutinizes the Synopsis of Post Graduate Student of BLDE (DU)'s Shri B.M.Patil Medical College Hospital & Research Centre from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "A ONE-YEAR PROSPECTIVE STUDY TO EVALUATE THE EFFICACY OF INTRAOPERATIVE SUBTENON INJECTION OF 0.01 % MITOMYCIN-C AS AN ADJUNCT TO TRABECULECTOMY IN PATIENTS ADMITTED TO SHRI BM PATIL MEDICAL COLLEGE AND RESEARCH CENTRE, VIJAYAPURA".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: Dr. Arkaprava Ray

NAME OF THE GUIDE: Dr. Rekha R. Mudhol, Professor, Dept. of Ophthalmology

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA
Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA
MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103, Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

Appendix IV

Colour plates

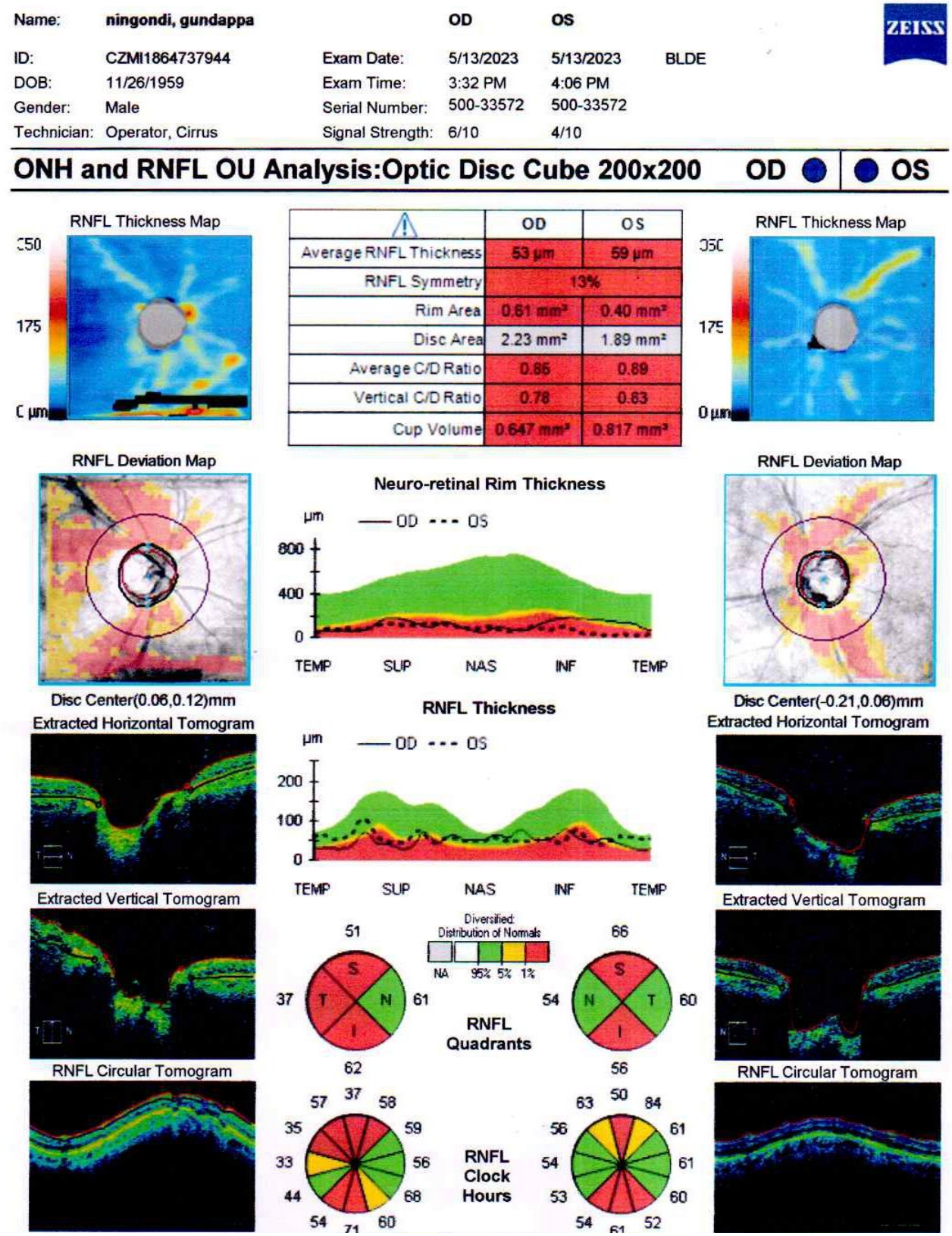

Figure 13: OCT RNFL analysis of both eyes showing RNFL loss and NRR loss.

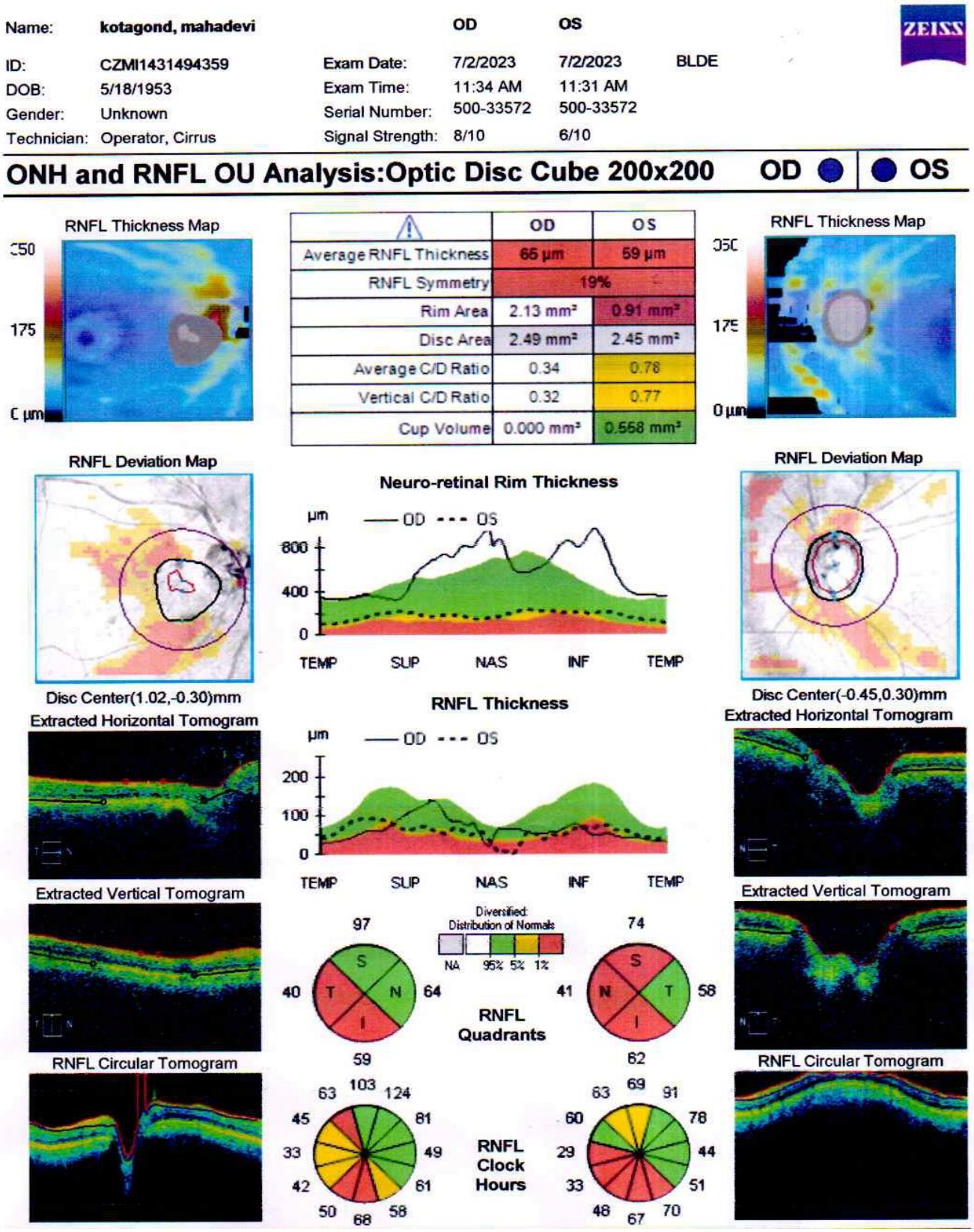

Figure 14: OCT RNFL analysis of both eyes showing RNFL and NRR thickness loss in left eye.

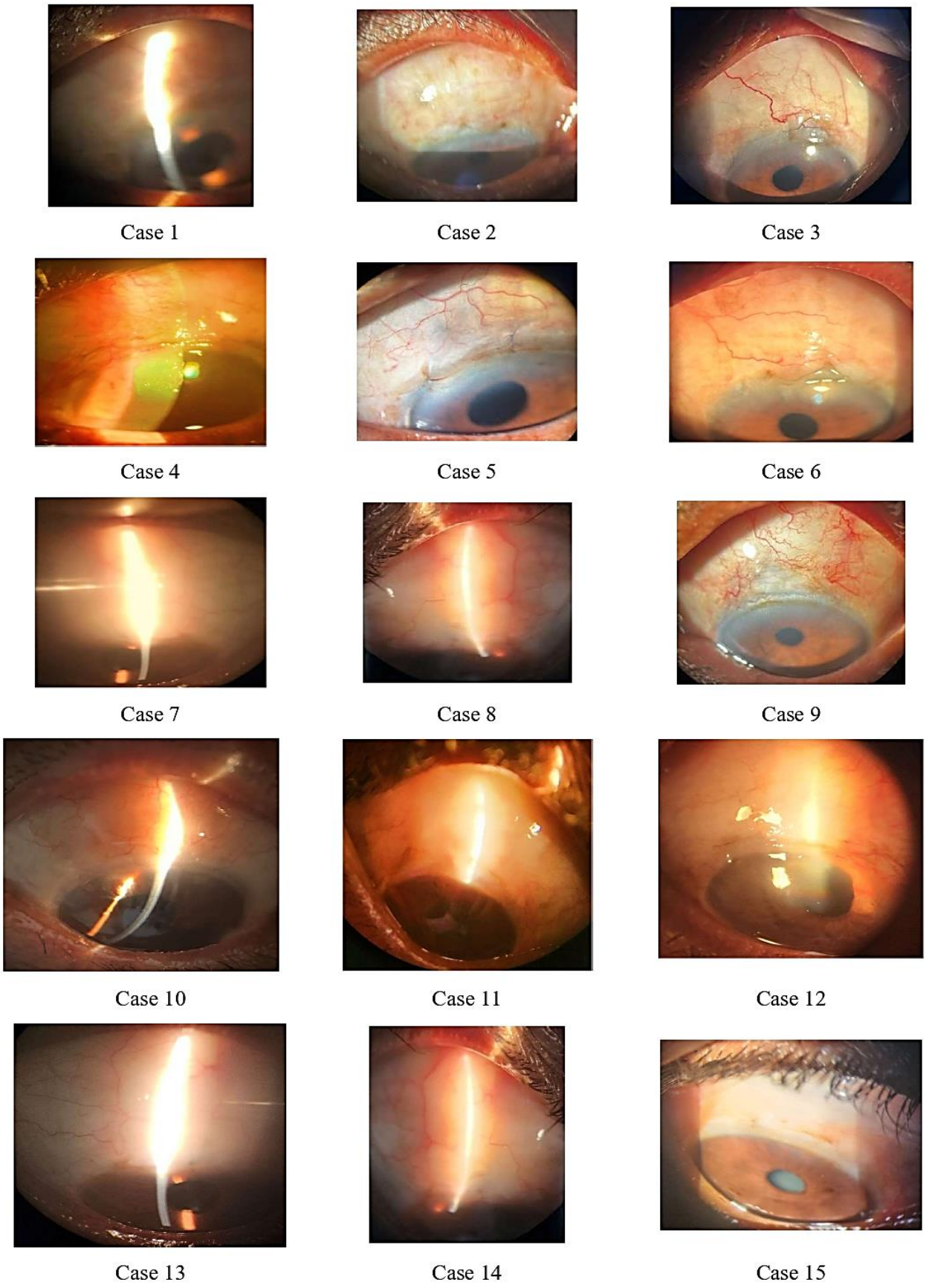

Figure 15 (a): Bleb photographs of all the cases at 6 months follow up (Case 1-15)

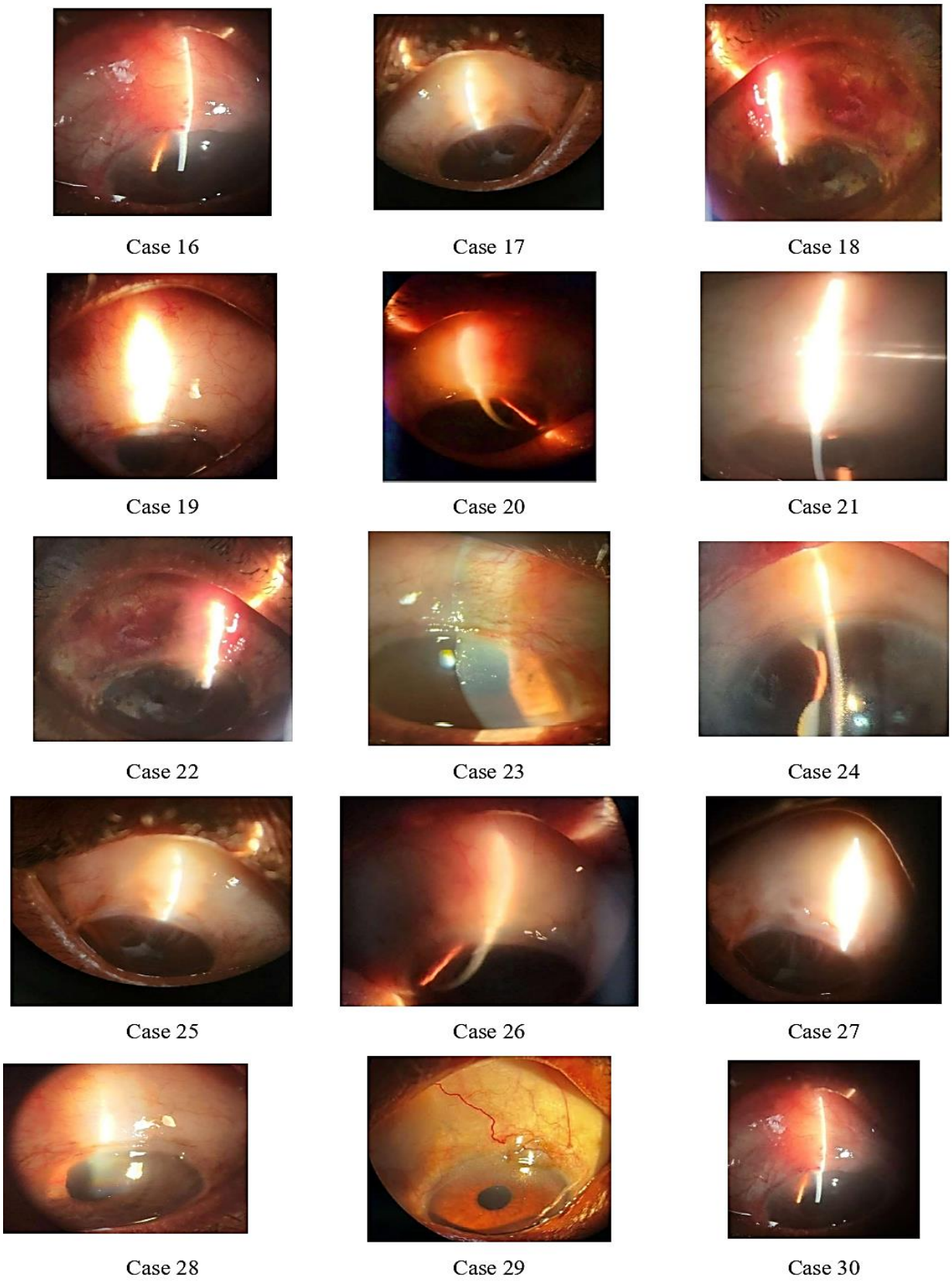

Figure 15: Bleb photographs of all the cases at 6 months follow up (Case 16 – 30)

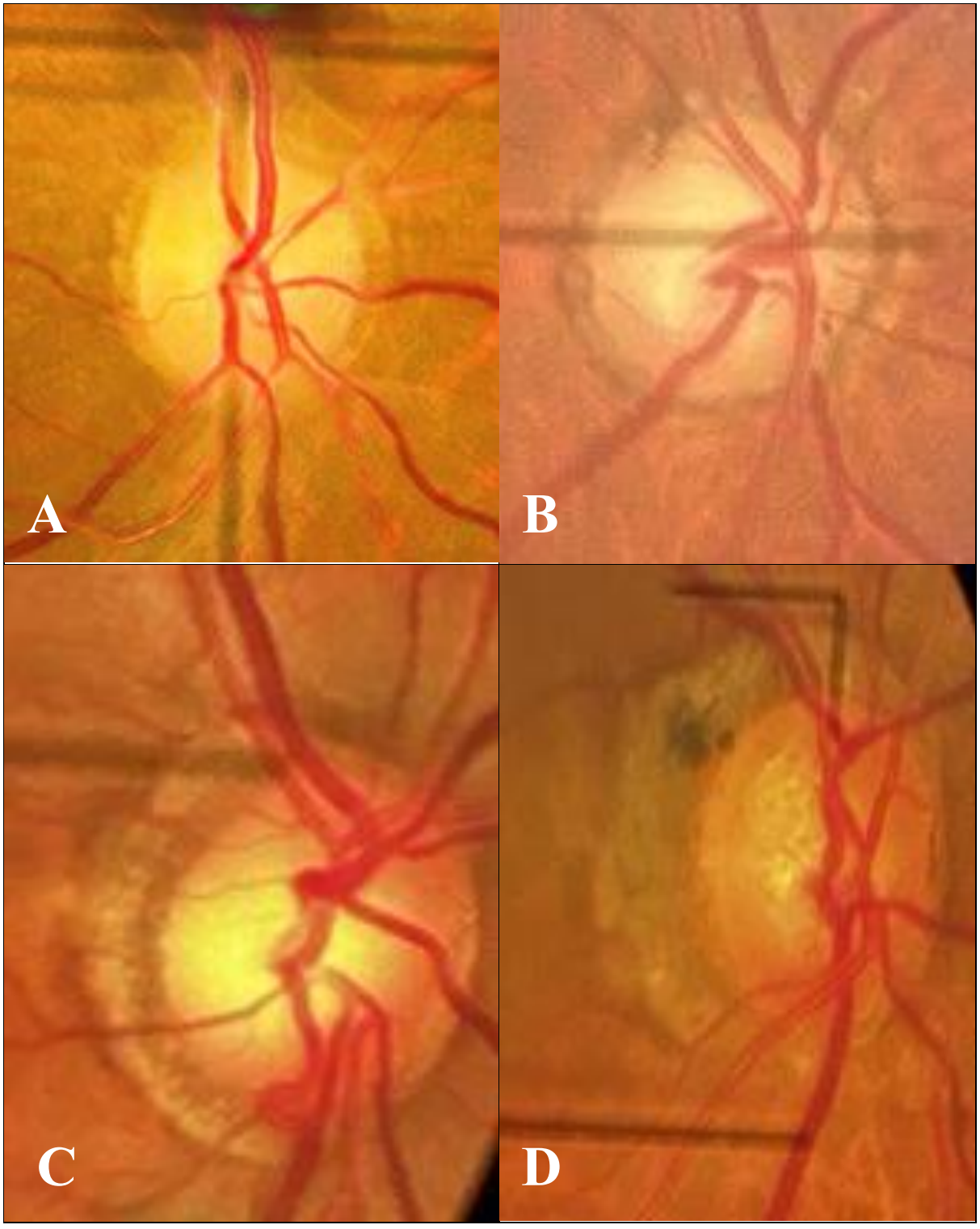

Figure 16: Optic disc photographs: A: Optic disc showing 0.8 cup : disc ratio; B: Optic disc with 0.7 cup disc ratio C: Optic disc with 0.6 cup disc ratio and a peripapillary atrophy D: Optic disc with 0.8 cup disc ratio with bipolar notching, laminar dot sign and a peripapillary atrophy involving alpha zone.

Appendix V

Master Chart

Key to Master Chart:

IP	In Patient
M	Male
F	Female
RE	Right eye
LE	Left eye
O	Open angle
C	Closed angle
POAG	Primary Open-Angle Glaucoma
PACG	Primary Angle Closure Glaucoma
NTG	Normal tension glaucoma
IOP	Intraocular pressure
AC	Anterior Chamber
CD	Cup : Disc

Case no	Name	IP number	Age	Sex	Occupation	Eye considered	Diagnosis group	Diagnosis	Diabetic	Hypertensive
1	Basanna devanagi	202249	65	M	Shopkeeper	RE	O	POAG	No	No
2	Iramma Kumbar	202534	75	F	Housewife	RE	O	POAG	No	No
3	Suglabai Maindragi	202535	75	F	Housewife	RE	O	POAG	No	No
4	Krishna Rathod	420617	66	M	Farmer	RE	C	PACG	No	Yes
5	Gollal Taluk	239954	64	M	Farmer	LE	O	NTG	No	No
6	Sharanappa Talawar	14895	40	M	Farmer	RE	O	POAG	No	No
7	Dundappa Kolhari	21460	68	M	Farmer	LE	O	NTG	No	Yes
8	Shivayogi Walikar	17725	78	M	Farmer	RE	O	NTG	No	No
9	Abdul Razak	330748	64	M	Labourer	RE	C	PACG	No	No
10	Mahadevi Kotagond	112713	73	F	Housewife	RE	O	POAG	No	No
11	Basappa Kalebag	102570	76	M	Farmer	LE	O	POAG	No	Yes
12	Gundappa Ningondi	136484	60	M	Farmer	RE	C	PACG	No	Yes
13	Chandrakant Goudar	16180	43	M	Teacher	LE	C	PACG	No	No
14	Shettavva Kamanakeri	167837	70	F	Housewife	RE	O	NTG	No	No
15	Mahadevi Kotagond	112713	73	F	Housewife	LE	O	POAG	No	No
16	Kamalabai Dotre	185574	65	F	Housewife	RE	C	PACG	No	No
17	Sadashiv Mantur	186123	59	M	Teacher	RE	C	PACG	Yes	No
18	Lakkawwa Ambiger	218321	65	F	Housewife	LE	O	POAG	Yes	Yes
19	Gundawwa Madrikar	221971	74	F	Housewife	RE	O	POAG	No	No
20	Sangappa Wali	225899	75	M	Farmer	RE	O	POAG	No	No
21	Jubeda Tambole	230058	75	F	Housewife	RE	O	POAG	No	No
22	Subhashchandra	237695	65	M	Farmer	LE	O	POAG	No	No
23	Mallangouda Patil	237621	70	M	Teacher	LE	O	NTG	No	No
24	Mallappa Goudappagol	285312	75	M	Farmer	RE	C	PACG	No	No
25	Vittal Hugar	300210	70	M	Conductor	LE	O	POAG	No	No
26	Shankar Lamani	323088	82	M	Farmer	RE	O	POAG	No	No
27	Mamtaj Begam	246929	68	F	Farmer	LE	C	PACG	No	No
28	Abdul Razak	330748	64	M	Labourer	LE	C	PACG	No	No
29	Mamtaj Begam	246929	68	F	Farmer	RE	C	PACG	No	No
30	Chandrakant Goudar	16180	43	M	Teacher	RE	C	PACG	No	No

Case no	Name	At presentation							
		Vision	IOP	Peripheral AC depth	Gonio	Pupil	Pseudoexfoliation	Cataract	CD ratio
1	Basanna devanagi	0.60	26	4	Open	Reactive	Absent	Present	0.6
2	Iramma Kumbar	1.77	30	4	Open	RAPD	Absent	Present	0.9
3	Suglabai Maindragi	1.77	28	4	Open	RAPD	Absent	Present	0.7
4	Krishna Rathod	1.3	31	2	Closed	RAPD	Present	Present	0.9
5	Gollal Taluk	1.77	19	4	Open	RAPD	Absent	Present	0.9
6	Sharanappa Talawar	1	36	4	Open	Reactive	Absent	Present	0.8
7	Dundappa Kolhari	0.77	13	4	Open	Reactive	Absent	Present	0.6
8	Shivayogi Walikar	1.77	14	4	Open	RAPD	Absent	Present	0.8
9	Abdul Razak	1.3	39	2	Closed	RAPD	Absent	Present	0.9
10	Mahadevi Kotagond	1.3	28	4	Open	RAPD	Absent	Present	0.7
11	Basappa Kalebag	1	38	3	Open	Reactive	Present	Present	0.7
12	Gundappa Ningondi	0.77	31	2	Closed	Reactive	Absent	Present	0.7
13	Chandrakant Goudar	1	52	1	Closed	Reactive	Absent	Present	0.6
14	Shettavva Kamanakeri	0.77	16	3	Open	Reactive	Absent	Present	0.6
15	Mahadevi Kotagond	0.6	36	4	Open	Reactive	Absent	Present	0.7
16	Kamalabai Dotre	1	38	1	Closed	Reactive	Present	Present	0.8
17	Sadashiv Mantur	1	48	1	Closed	RAPD	Absent	Present	0.5
18	Lakkawwa Ambiger	1	32	4	Open	Reactive	Absent	Present	0.7
19	Gundawwa Madrikar	1	28	3	Open	Reactive	Present	Present	0.8
20	Sangappa Wali	1.3	23	4	Open	RAPD	Absent	Present	0.9
21	Jubeda Tambole	1.3	37	4	Open	RAPD	Absent	Present	0.9
22	Subhashchandra	1.3	47	4	Open	RAPD	Present	Present	0.9
23	Mallangouda Patil	1	18	4	Open	Reactive	Absent	Present	0.7
24	Mallappa Goudappagol	1	42	1	Closed	Reactive	Absent	Present	0.6
25	Vittal Hugar	1	44	4	Open	RAPD	Present	Present	0.9
26	Shankar Lamani	1	15	4	Open	RAPD	Present	Present	0.9
27	Mamtaj Begam	1	38	2	Closed	Reactive	Absent	Present	0.7
28	Abdul Razak	1	28	1	Closed	Reactive	Absent	Present	0.6
29	Mamtaj Begam	1	31	1	Closed	RAPD	Absent	Present	0.8
30	Chandrakant Goudar	1	36	1	Closed	Reactive	Absent	Present	0.7

Case no	Name	Post operative Day 1								
		Vision	IOP	Bleb height	Extent	Vascularity	Seidel test	Ostium	Iridectomy	Central AC depth
1	Basanna devanagi	0.47	12	0	2	2	0	1	1	3
2	Iramma Kumbar	1	5.7	0	1	3	0	1	1	3
3	Suglabai Maindragi	0.77	12	1	1	3	0	1	1	3
4	Krishna Rathod	1	18	1	3	3	0	1	1	3
5	Gollal Taluk	1	16.3	1	1	3	0	1	1	3
6	Sharanappa Talawar	1	18	1	2	2	0	1	1	3
7	Dundappa Kolhari	0.77	13	1	1	3	0	1	1	3
8	Shivayogi Walikar	1	15	0	1	4	0	1	1	3
9	Abdul Razak	1.3	13	1	2	2	0	1	1	3
10	Mahadevi Kotagond	1	14	2	2	3	0	1	1	3
11	Basappa Kalebag	1	12	1	1	3	0	1	1	3
12	Gundappa Ningondi	1	18	1	1	3	0	1	1	3
13	Chandrakant Goudar	1	13	1	1	4	0	1	1	3
14	Shettavva Kamanakeri	1	9	1	1	2	0	1	1	3
15	Mahadevi Kotagond	0.3	10	1	2	3	0	1	1	3
16	Kamalabai Dotre	1	8	1	2	3	0	1	1	2
17	Sadashiv Mantur	0.3	20	1	2	2	0	1	1	3
18	Lakkawwa Ambiger	0.6	12	1	2	3	0	1	1	3
19	Gundawwa Madrikar	1	12	1	1	3	0	1	1	3
20	Sangappa Wali	1	18	1	1	3	0	1	1	3
21	Jubeda Tambole	1	19	2	1	3	0	1	1	3
22	Subhashchandra	1	19	1	1	3	0	1	1	3
23	Mallangouda Patil	0.3	20	1	3	3	0	1	1	3
24	Mallappa Goudappagol	0.6	16	1	2	2	0	1	1	3
25	Vittal Hugar	1	19	1	0	3	0	1	1	3
26	Shankar Lamani	1	15	1	2	2	0	1	1	3
27	Mamtaj Begam	0.47	18	1	1	2	0	1	1	3
28	Abdul Razak	1	13	1	2	2	0	1	1	3
29	Mamtaj Begam	0.77	17	1	3	2	0	1	1	3
30	Chandrakant Goudar	1	13	1	2	3	0	1	1	3

Case no	Name	1 week follow up								
		Vision	IOP	Bleb height	Extent	Vascularity	Seidel test	Ostium	Iridectomy	Central AC depth
1	Basanna devanagi	0.47	12	1	2	2	0	1	1	3
2	Iramma Kumbar	1	8	2	2	2	0	1	1	3
3	Suglabai Maindragi	0.6	15	2	1	3	0	1	1	3
4	Krishna Rathod	1	14	2	3	2	0	1	1	3
5	Gollal Taluk	1	12.2	2	2	2	0	1	1	3
6	Sharanappa Talawar	1	13	2	3	2	0	1	1	3
7	Dundappa Kolhari	0.6	9	2	1	2	0	1	1	3
8	Shivayogi Walikar	0.77	13	1	1	3	0	1	1	3
9	Abdul Razak	1.3	15	1	2	2	0	1	1	3
10	Mahadevi Kotagond	0.47	10	2	2	3	0	1	1	3
11	Basappa Kalebag	1	14	1	2	3	0	1	1	3
12	Gundappa Ningondi	0.77	14	2	1	2	0	1	1	3
13	Chandrakant Goudar	0.3	8.7	2	2	2	0	1	1	3
14	Shettavva Kamanakeri	1	10	2	2	2	0	1	1	3
15	Mahadevi Kotagond	0.3	8	1	2	2	0	1	1	3
16	Kamalabai Dotre	1	7	1	3	2	0	1	1	3
17	Sadashiv Mantur	0.3	18	2	3	2	0	1	1	3
18	Lakkawwa Ambiger	0.3	10	1	2	3	0	1	1	3
19	Gundawwa Madrikar	0.77	12	1	2	2	0	1	1	3
20	Sangappa Wali	0.77	12	1	2	2	0	1	1	3
21	Jubeda Tambole	1	15	3	2	3	0	1	1	3
22	Subhashchandra	1	18	1	2	3	0	1	1	3
23	Mallangouda Patil	0.3	10	1	3	2	0	1	1	3
24	Mallappa Goudappagol	0.6	12	1	3	2	0	1	1	3
25	Vittal Hugar	0.77	14	2	1	3	0	1	1	3
26	Shankar Lamani	0.77	14	1	2	2	0	1	1	3
27	Mamtaj Begam	0.3	16	2	2	0	0	1	1	3
28	Abdul Razak	0.6	15	1	2	2	0	1	1	3
29	Mamtaj Begam	0.3	12	2	3	0	0	1	1	3
30	Chandrakant Goudar	0.3	8.7	2	3	2	0	1	1	3

Case no	Name	1 month follow up								
		Vision	IOP	Bleb height	Extent	Vascularity	Seidel test	Ostium	Iridectomy	Central AC depth
1	Basanna devanagi	0.3	13	2	2	2	0	1	1	3
2	Iramma Kumbar	1	12	3	2	2	0	1	1	3
3	Suglabai Maindragi	0.6	15.5	2	2	0	0	1	1	3
4	Krishna Rathod	1	11	2	3	2	0	1	1	3
5	Gollal Taluk	1	13	2	2	0	0	1	1	3
6	Sharanappa Talawar	0.77	12.5	2	3	0	0	1	1	3
7	Dundappa Kolhari	0.47	8.8	2	1	1	0	1	1	3
8	Shivayogi Walikar	0.77	10	1	2	3	0	1	1	3
9	Abdul Razak	1.3	13	1	2	2	0	1	1	3
10	Mahadevi Kotagond	0.3	11	2	2	2	0	1	1	3
11	Basappa Kalebag	0.77	10	2	2	2	0	1	1	3
12	Gundappa Ningondi	0.6	12	2	2	2	0	1	1	3
13	Chandrakant Goudar	0.17	10	2	2	2	0	1	1	3
14	Shettavva Kamanakeri	0.47	8	2	2	2	0	1	1	3
15	Mahadevi Kotagond	0.3	7	2	2	0	0	1	1	3
16	Kamalabai Dotre	1	8	1	3	2	0	1	1	3
17	Sadashiv Mantur	0.3	12	2	3	0	0	1	1	3
18	Lakkawwa Ambiger	0.3	11	2	3	2	0	1	1	3
19	Gundawwa Madrikar	0.47	10	2	2	2	0	1	1	3
20	Sangappa Wali	0.77	9	1	2	2	0	1	1	3
21	Jubeda Tambole	0.77	13	3	2	3	0	1	1	3
22	Subhashchandra	1	10	2	2	2	0	1	1	3
23	Mallangouda Patil	0.17	11	2	3	2	0	1	1	3
24	Mallappa Goudappagol	0.3	12	2	3	0	0	1	1	3
25	Vittal Hugar	0.6	11	2	1	0	0	1	1	3
26	Shankar Lamani	0.3	10	1	3	2	0	1	1	3
27	Mamtaj Begam	0.3	9	2	2	0	0	1	1	3
28	Abdul Razak	0.47	13	1	2	2	0	1	1	3
29	Mamtaj Begam	0.17	9	2	3	0	0	1	1	3
30	Chandrakant Goudar	0.17	12	2	3	2	0	1	1	3

Case no	Name	3 month follow up								
		Vision	IOP	Bleb height	Extent	Vascularity	Seidel test	Ostium	Iridectomy	Central AC depth
1	Basanna devanagi	0.3	10	3	2	2	0	1	1	3
2	Iramma Kumbar	1	10	2	2	2	0	1	1	3
3	Suglabai Maindragi	0.47	15	2	2	0	0	1	1	3
4	Krishna Rathod	1	10	2	3	0	0	1	1	3
5	Gollal Taluk	1	12	2	2	0	0	1	1	3
6	Sharanappa Talawar	0.77	14	2	3	0	0	1	1	3
7	Dundappa Kolhari	0.3	9.6	2	3	2	0	1	1	3
8	Shivayogi Walikar	0.77	10	2	3	2	0	1	1	3
9	Abdul Razak	1.3	12	2	2	1	0	1	1	3
10	Mahadevi Kotagond	0.3	12	2	2	2	0	1	1	3
11	Basappa Kalebag	0.6	11	2	3	2	0	1	1	3
12	Gundappa Ningondi	0.3	11	2	3	0	0	1	1	3
13	Chandrakant Goudar	0.17	9	2	2	2	0	1	1	3
14	Shettavva Kamanakeri	0.47	8	1	3	0	0	1	1	3
15	Mahadevi Kotagond	0.3	7	2	1	0	0	1	1	3
16	Kamalabai Dotre	1	7	2	3	2	0	1	1	3
17	Sadashiv Mantur	0.17	10	2	3	0	0	1	1	3
18	Lakkawwa Ambiger	0.17	8	2	3	2	0	1	1	3
19	Gundawwa Madrikar	0.3	9.5	2	2	0	0	1	1	3
20	Sangappa Wali	0.77	11	3	2	0	0	1	1	3
21	Jubeda Tambole	0.77	10	3	3	2	0	1	1	3
22	Subhashchandra	0.77	12	2	2	2	0	1	1	3
23	Mallangouda Patil	0.17	9	2	3	0	0	1	1	3
24	Mallappa Goudappagol	0.17	8	2	3	0	0	1	1	3
25	Vittal Hugar	0.6	11	2	2	0	0	1	1	3
26	Shankar Lamani	0.3	9	1	3	0	0	1	1	3
27	Mamtaj Begam	0.17	8	2	3	0	0	1	1	3
28	Abdul Razak	0.47	12	2	2	1	0	1	1	3
29	Mamtaj Begam	0.17	8	2	3	0	0	1	1	3
30	Chandrakant Goudar	0.17	13	2	2	3	0	1	1	3

Case no	Name	6 month follow up									Bleb position at 6 months	CD ratio at 6 months
		Vision	IOP	Bleb height	Extent	Vascularity	Seidel test	Ostium	Iridectomy	Central AC depth		
1	Basanna devanagi	0.17	9	3	2	0	0	1	1	3	N	0.7
2	Iramma Kumbar	1	10	2	2	2	0	1	1	3	N	0.9
3	Suglabai Maindragi	0.47	13	2	3	0	0	1	1	3	C	0.8
4	Krishna Rathod	1	12	2	3	0	0	1	1	3	C	0.9
5	Gollal Taluk	1	11	2	2	0	0	1	1	3	T	0.9
6	Sharanappa Talawar	0.6	12	2	3	0	0	1	1	3	N	0.7
7	Dundappa Kolhari	0.3	8.6	2	3	0	0	1	1	3	C	0.7
8	Shivayogi Walikar	0.77	10	2	3	0	0	1	1	3	N	0.8
9	Abdul Razak	1.3	10	2	2	1	0	1	1	3	N	0.9
10	Mahadevi Kotagond	0.3	10	2	3	0	0	1	1	3	N	0.6
11	Basappa Kalebag	0.6	9	2	3	2	0	1	1	3	T	0.8
12	Gundappa Ningondi	0.3	12	2	3	0	0	1	1	3	C	0.8
13	Chandrakant Goudar	0.17	10	2	2	0	0	1	1	3	N	0.6
14	Shettavva Kamanakeri	0.3	7	1	3	0	0	1	1	3	N	0.6
15	Mahadevi Kotagond	0.17	8	3	1	0	0	1	1	3	T	0.7
16	Kamalabai Dotre	1	7	2	3	2	0	1	1	3	N	0.8
17	Sadashiv Mantur	0.17	11	2	3	0	0	1	1	3	C	0.6
18	Lakkawwa Ambiger	0.17	7	2	3	2	0	1	1	3	T	0.7
19	Gundawwa Madrikar	0.3	8	2	3	0	0	1	1	3	C	0.8
20	Sangappa Wali	0.6	8	3	2	0	0	1	1	3	N	0.9
21	Jubeda Tambole	0.6	9	3	2	0	0	1	1	3	N	0.9
22	Subhashchandra	0.77	9	2	2	2	0	1	1	3	T	0.9
23	Mallangouda Patil	0.17	8	2	3	0	0	1	1	3	T	0.8
24	Mallappa Goudappagol	0.17	10	2	3	0	0	1	1	3	N	0.6
25	Vittal Hugar	0.47	10	2	3	0	0	1	1	3	T	0.9
26	Shankar Lamani	0.3	9	2	3	0	0	1	1	3	N	0.9
27	Mamtaj Begam	0.17	8	2	3	0	0	1	1	3	C	0.7
28	Abdul Razak	0.17	10	2	2	1	0	1	1	3	C	0.5
29	Mamtaj Begam	0.17	10	2	3	0	0	1	1	3	N	0.8
30	Chandrakant Goudar	0.17	11	2	3	0	0	1	1	3	N	0.7

Appendix VI

Plagiarism report

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Summary

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