ejpmr, 2024, 11(4), 233-248

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW EXPLORING THE DYNAMIC OF AQUEOUS HUMOR AND GLAUCOMA: OPEN & CLOSE ANGLE PERSPECTIVE

Namrata Srivastava*[1], Dr. Mahesh Chandra[2] and Dr. Nitesh[3]

[1]Department of Optometry ERA University of Allied Health Science, Lucknow, Uttar Pradesh, India.
[2]Dr.Shushila Tiwari Hospital and Govt. Medical College, Haldwani, Uttarakhand, Himachal Pradesh.
[3]Department of Ophthalmology Satya Eye Hospital and Research Institute, Kanpur, Uttar Pradesh.

***Corresponding Author: Dr. Namrata Srivastava**

Department of Optometry ERA University of Allied Health Science, Lucknow, Uttar Pradesh, India.

Article Received on 20/02/2024 **Article Revised on 10/03/2024** **Article Accepted on 30/03/2024**

ABSTRACT

Glaucoma is a complex group of eye diseases characterized by optic nerve damage, leading to irreversible blindness, and is the second leading cause of blindness globally. It is also known to be multifactorial in origin with genetic and biological risk factors, although fundamental causes remain unknown for many types of glaucomatous. This study aims to explore the dynamics of aqueous humor and glaucoma classification, focusing on open-angle and angle-closure glaucoma. The research design involves a comprehensive literature review of glaucoma classification, anterior chamber dynamics, and clinical examination methods. Findings reveal that open-angle glaucoma is asymptomatic and leads to gradual vision loss, while angle-closure glaucoma presents as an acute phase with rapid pressure rise. The anterior chamber of the eye is filled with aqueous humors, which has physiological importance for asymptomatic management. The dynamics of the anterior chamber concern the ciliary body, the trabecular meshwork, and the uveoscleral pathway for the absorption.Clinical examination methods includes tonometry, gonioscopy, and optic nerve head examination. Treatment options include medications, laser surgery, and operating surgeries, each with associated side effects. The study has implications for understanding the pathophysiology of glaucoma and optimizing treatment strategies.

KEYWORDS: Glaucoma, Aqueous humor, Open-angle glaucoma, Angle-Closure glaucoma, Clinical examination, Treatment options.

INTRODUCTION

Glaucoma is a heterogeneous group of eye diseases characterized by optic nerve damage which leads to irreversible blindness. it is also known to be multi-factorial in origin with genetic and biological risk factors, although fundamental causes remain unknown for many types of glaucoma. Still, it is the second leading cause of blindness in the world. Worldwide it affects approximately 70 million people and alone in the USA its count is around more than 2 million.[1,2]

The anterior chamber of the eye is filled with aqueous humour has physiological importance for glaucoma management.[3] The importance of Intra Ocular Pressure is to inflate the eye for maintaining its proper shape and optical properties of the globe. It provides nourishment to the avascular components of the anterior chamber including the cornea and lens. Glaucoma has concerned the optic neuropathy which causes irreversible vision loss.[4-7]

Aqueous humour is a transparent medium in both chambers and constitutes an important optical component of the eye.[8] Production, secretion, and reabsorption is the vital process of aqueous humour in the anterior chamber and the Imbalances between them lead to increased intraocular pressure and optic nerve damage.[5,6]

An elevated intraocular pressure above the normal physiologic range of 12 to 21 mmHg.is indicated for glaucoma and it happens either due to the increased resistance and decreased outflow of aqueous humouror increased production, finally optic nerve compression withthe hindrance of oxygen and nutrition supply takes place.[5,9,10]

Classification of Glaucoma

Glaucoma is a group of different conditions associated with optic neuropathy and visual field defects. The raised IOP (Normal range is 11 to 21 mm Hg.) and normal range of IOP may have concern to the glaucoma. The raised IOP without glaucomatous damage is termed

ocular hypertension while the normal range of IOP with optic disc changes and visual field defectsis termed as normal tension glaucoma (NTG) or low-tension glaucoma.

Glaucoma may be developmental or acquired and its etiological classification concludes two terms primary and secondary glaucoma. In primary glaucoma,IOP elevation is not associated with other ocular or systemic disorders but in secondary glaucoma, it becomes secondary to the systemic/ocular disorder. Primary glaucoma has a bilateral genetic base while secondary glaucoma may beuni or bilateral with developmental, genetic and acquired factors.

According to the mechanism of aqueous flow and its aetiology, glaucoma is divided into the following-

1. Primary glaucoma

A. Open-angle glaucoma

It is the commonest asymptomatic type of glaucoma. The eye gradually does not drain aqueous therefore intraocular pressure builds and damages the optic nerve. Theearly stages arewithout warning signs because the blind spots develop in peripheral vision which is not noticed until the damage is quite severe. This is why glaucoma is called the silent thief of sight.[11]

Normal tension glaucoma (NTG)or low-tension glaucoma shows a normal range of IOP. As many as 1 in 3 people have optic nerve damage even when eye pressure is normal or not very high. This type is more common among people of Asian descent or Asian Americans. Ocular hypertension also shows normal IOP without any morphological changes/damage. Ocular hypertension (OHTN) expresses itself as reduced trabecular and uveo-scleral outflow with normal aqueous production.[6,7]

Normal tension glaucoma and ocular hypertension glaucoma, both are considered for glaucoma suspected but the case of ocular hypertensionis counted asa higher risk.

B. Angle-closure glaucoma

It is known as Primary angle-closure glaucoma (PACG), narrow-angle glaucoma or angle-closure, this rare type often comes in the acute phase with the angle narrowing between the iris and cornea. If the pupil dilates quickly and becomes large then drainage canals prevent aqueous flow to rise pressure. Theiris interferes with the route of the aqueous flow or the morphological disturbances at the angle, therefore drainage gets blocked and is known as angle closure/closed angle/narrow-angle glaucoma.

If the drainage angle is blocked completely then pressure rises very fast and is known as acute glaucoma attack. This is considered a true emergency that led to blindness. Before the stage of complete blockage of angle called chronic angle-closure glaucoma.

Signs of acute angle-closure glaucoma concludes sudden blur vision, severe ocular pain,headache, nausea, vomiting and rainbow/coloured rings/halos around lights

2. Secondary glaucoma

A. Secondary open-angle glaucoma.

B. Secondary angle-closure glaucoma.

3. Developmental glaucoma or Congenital glaucoma/childhood/infantile/pediatric glaucoma has concerns for Babies, born with drainage canals which could not properly develops in the womb.

4. Pigment dispersion syndrome/pigmentary glaucoma led to pigment dispersal from the iris followed by the closure of the angle. The symptoms conclude halos and blurry vision.[8]

Anterior Chamber

The anterior chamber (AC) is an angular space, anteriorly bounded by the posterior surface of the cornea (endothelium), posteriorly to the anterior surface of the iris and laterally to the part of the ciliary body, from here to the anterior of the crystalline lens is called posterior chamber, so between both the chambers iris becomes suspended and both the spaces are filled with the aqueous humour. If the trabecular meshwork does not absorb aqueous properly, intraocular pressure is raised which give harm to the optic nerve simultaneously, which is known as glaucoma.[13]

The anterior chamber depth of the eye varies between 1.5 mm to 4.0 mm, (average 3.0 mm). It becomes shallower at an older age, in childhood and in hypermetropic eyes, but ifthe depth decreases below 2.5 mm, the risk for angle closure glaucoma also increases. The total space contains about 0.25 ml of the aqueous humour.[13]

The chamber depth decreases with age along with its volume capacity, although it increases in myopic eyes. During accommodation chamber depth slightly decreases. The term angle is the area between the iris and the surface of the trabecular meshwork, its standard reading is 20 to 45 degrees and below 20 degrees it is termed a narrowangle.[14]

Dynamics of Aqueous Humour

The dynamics of aqueous humour concern the ciliary body for the aqueous formation and the trabecular meshwork and the uveoscleral pathway for the absorption. Diffusion, ultrafiltration and active secretion involve in aqueous humour formation while absorption of aqueous takes place through passive flow via trabecular meshwork (75%) and the uveoscleral pathway (25%).[3]

The trabecular meshwork is the main site of outflow resistance and one of the theory says, glycosaminoglycan deposition obstructs the aqueous humour outflow through the trabecular meshwork, whereas another theory saysdeposition of proteins (cochlin) obstruct the aqueous humour outflow through the trabecular meshwork.[4]

The uveoscleral outflow pathway becomes independent of the intraocular pressure although this pathway decreases with age.

Its circulation becomes higher in the morning than at night (circadian rhythm) and its flow generates resistance called intraocular pressure of an average of approximately 15mmHg.[5] Aqueous humour is produced by the ciliary body via a multistep process closely correlating with systemic vascular blood flow.

Initially, blood enters the ciliary processes, which propels ultrafiltrate from the blood into the ciliary interstitial space via a pressure gradient. Next, the ciliary epithelium transports plasma components from the basal to the apical surface to synthesize aqueous humour and transport it into the posterior chamber.

The systemic blood flow via the ciliary artery, ultrafilters with Passive diffusion in the ciliary interstitial space through a pressure gradient in the ciliary process of the ciliary body (blood-aqueous barrier). The aqueous humour production is independent of the systemic blood pressure, having a minimal association, because of the fixed rate of 4% filtration of plasma.[5,9,10]

Production of Aqueous humour takes place at the epithelium of the ciliary body with the rate of 2-3 microliters per minutewith diurnal variations viz. high aqueous humour flow in the morning and low flow in the evening. the composition concludes organic and inorganic ions, carbon dioxide, amino acids, carbohydrates, glutathione, and water.[5,7,9]

Along with the nourishment, it removes waste products, blood, macrophages and other debris from the anterior chamber and trabecular meshwork as well. Low levels of antioxidants in aqueous humour are present in glaucomatous eyes and become a reason antioxidants in aqueous humour are present in glaucomatous eyes.[15,16]

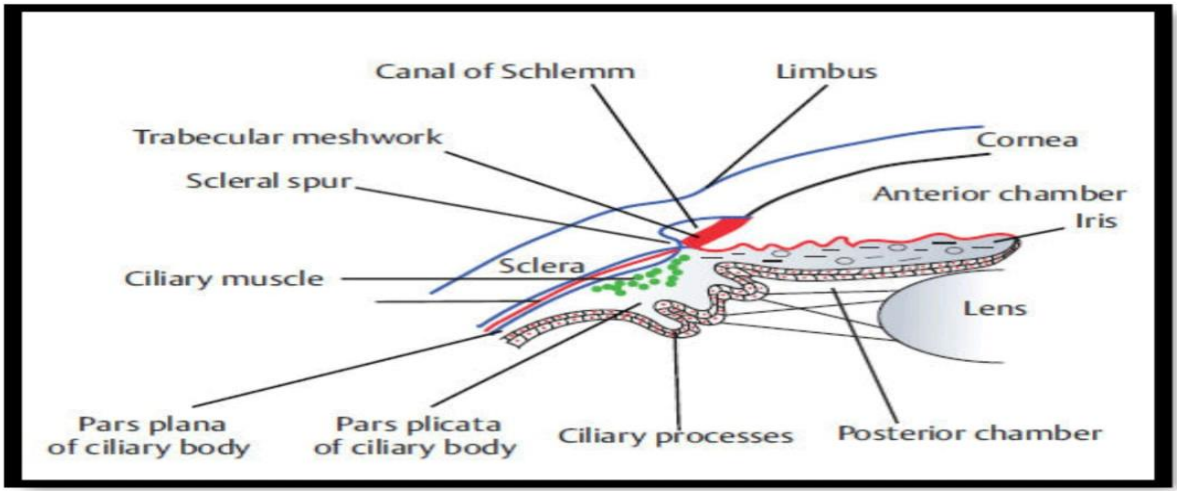


Fig. 1: Dynamics of Aqueous Humour.

Limbus is the adjoining area of the cornea & sclera, its inner surface has an indentation known as the scleral sulcus concluded with a sharp posterior margin known as the scleral spur, which prevents the collapse of Schlemm's canalwith the help of the ciliary muscle. The ciliary body attaches to the scleral spur and makes a triangular structure. The inner and anteriormost portion of this structure called *pars plicata,* is in the ciliary processes.[17] The posterior part of the ciliary body, known as pars plana, the flatter inner surface joins the choroid at the oraserrata.[18]

Schlemm's canal is a very soft tube-like structure and on its origin, it consistsof a sieve-like structure called trabecular meshwork which bridges over the scleral sulcus. rarely Schlemm's canal could be like a plexus rather than a discrete canal.Schlemm's canal often collapses at raised intraocular pressure and it reopened by a pull on the scleral spur created by longitudinal ciliary muscle fibre so Cholinergic drugs are used to facilitate this mechanism.

Towards the sclera Schlemm's canal has 25-30 aqueous collector channels further subbranches into intra-scleral and deep scleral plexi and aqueous outflow reaches from trabecular meshwork to theepiscleral veins which further drain into the ophthalmic veins to move in the general circulations.

The trabecular meshwork is a spongy, sieve-like tissue, pale tan to darkbrown, varying with pigmentation and is darker posteriorly. It is divided into-

1. Uveoscleral meshwork is the innermost area of the trabecular, characterised by the large pores and thick band of connective tissue take starts from the iris root and extends upto the Schwalbe's line.
2. Corneoscleral meshwork is characterised by the elliptical pores which reduce in size towards the Schlemm's canal. It covers the middle-most extended area of the trabecular, continuing from the scleral spur to the anterior wall of the scleral sulcus.
3. Juxtacanalicular meshwork also known asthe cribriform layer borders the canal of Schlemm,

single-layered amorphous tissue, assumed that it provides maximum resistance to outflow of the aqueous humor.

Schwalbe's line is a ridge-like structure at the adjoining area of the trabecular meshwork and Descemet's membrane at the posterior of the cornea.[14]

The unconventional pathway contributes 25-40% of total aqueous outflow, with the following channels

1. **Orbital vasculature** through diffusion into the episclera and sclera.
2. **The Uveovortex pathway** involves fluid absorption through the choroid and passed into the vortex vein.
3. **The uveo-lymphatic pathway** involves drainage into lymphatic vessels within the ciliary body, contributing up to 25-40% of total aqueous outflow.[6,19]

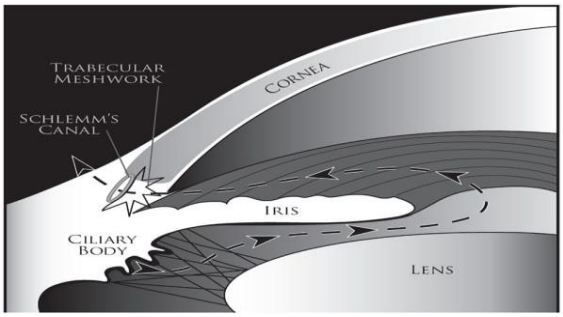


Figure 2: Conventional outflow.

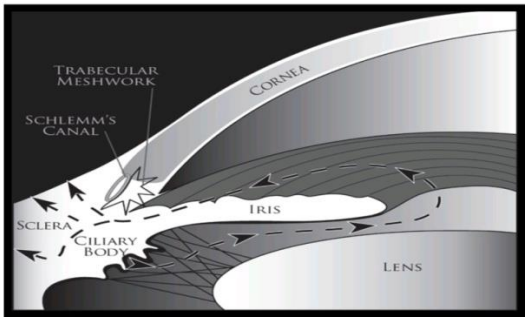


Figure 3: uveoscleral outflow.

The unconventional pathway shows resistance due to the ciliary muscle tone. pilocarpine, increases ciliary tone so outflow decreases, and atropine, decreases ciliary tone so outflow increases.[6,19,20]

Clinical Examination[21]

The following are the important investigation

1. Tonometry
2. Gonioscopy
3. Optic nerve head examination
4. Visual field examination
5. Retinal nerve fibre layer examination

2. Gonioscopy

To explain the morphology of the angle of the anterior chambergonioscopy is used. Two types ofcontact lenses are used for gonioscopy namedgonioscope and are of two types

1. Direct (direct view of angle) - Koeppe lens and Barkan lens.
2. Indirect types (provides opposite angle image) - Goldmann single mirror, Goldmann 3-mirror lens, and Zeiss 4-mirror lens.

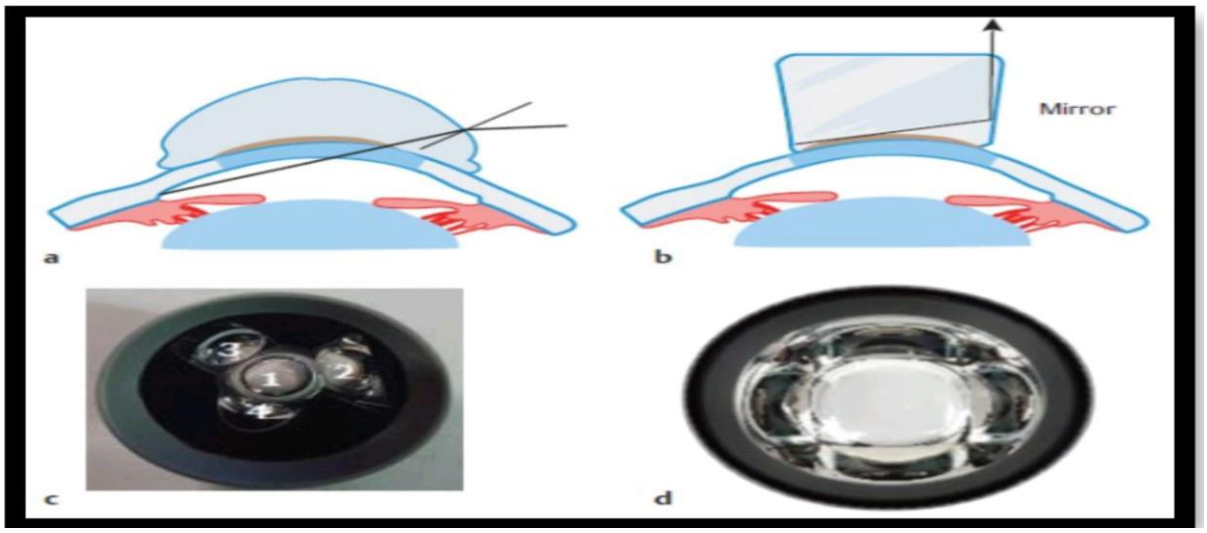


Figure 4: Types of goniolenses. (a) Koeppelens (b) Goldmann single-mirror lens. (c) Goldmann three-mirror lens. (d) Zeiss lens.

Goldmann 3-mirror lens is used widely and has a coupling surface area diameter of about 12 mm., consisting of two mirrors for the fundus examination and the remaining one for the angle examination. Before putting it over the cornea topical anaesthesia is applied and then a viscous solution is filled in Goldmanngonioscopeto couple it withthe cornea. The central lens gives an image of the posterior pole, while

the largest mirror at an angle of 73 degrees gives an image of the equator. The 67-degree mirror gives an image of Ora serrata, the angle of the anterior chamber is observed by 59 degrees. It can be used for laser trabeculoplasty.

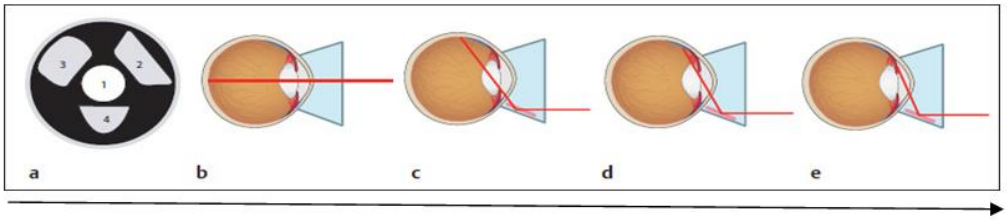


Figure: 5 (a)-Goldmann three-mirror lens (b)- Posterior pole image(c)-Equator image(d)-Ora serrata (e)- Angle of anterior chamber.

In Zeiss 4-mirror lens, every angle quadrant is observed by the opposite mirror. A coupling fluid is also not requiredhere and it hasa diameter of about 9 mm. It couldn't stabilize the globe hence laser trabeculoplasty can't be done but indentation gonioscopy can be done by this lens.

PURPOSE

1. **Diagnostic** – angle width estimation with the state of angle structure.
2. **Surgical** – to check the angle during trabeculoplasty and goniotomy.

Principal[22]

Slit lamp could not help directly with the assessment of the angle due to the phenomenon of total internal reflection, although the eyes with keratoconus, keratoglobus, high myopia and the indentation of the limbusshow angle structures uncommonly through the direct view in distorted image pattern.

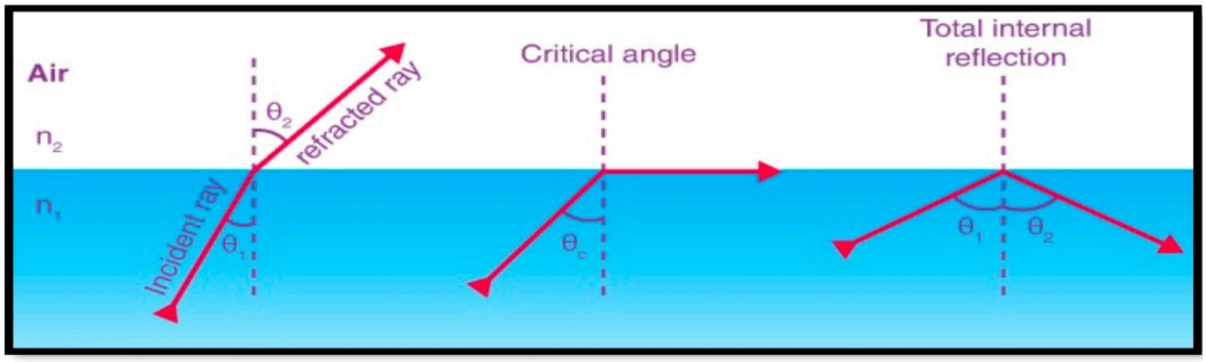


Figure: 6 - Assessment of the angle

The role of the gonioscope is to overcome the problem of total internal reflection. The light from the adjoining area of the iris and cornea goes to tear air interface with a shallow angle to reflect into the eye (total internal reflection) and again it reflects towards the cornea if at an angle more than 46 degrees(critical angle) then trabecular meshwork will show its morphology.

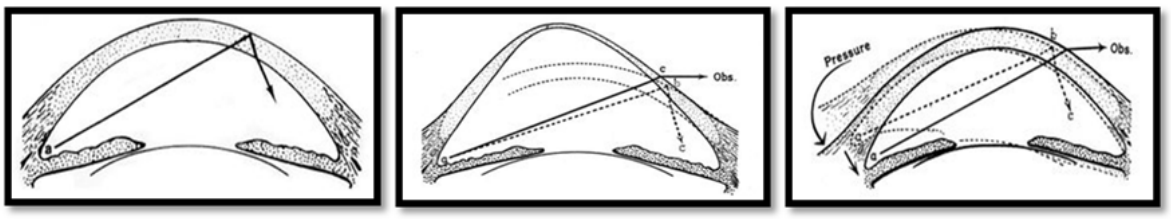


Fig a: TOTAL INTERNAL REFLACTION **Figb: KERATOCONUS** **Figc: INDENTATION OF LIMBUS**

Figure 7: Role of the gonioscope.

Indentation Gonioscopy

It has a concern with the narrow-angle followed by the indentation over the cornea thus aqueous move towards the angle due to the shift of the peripheral iris.

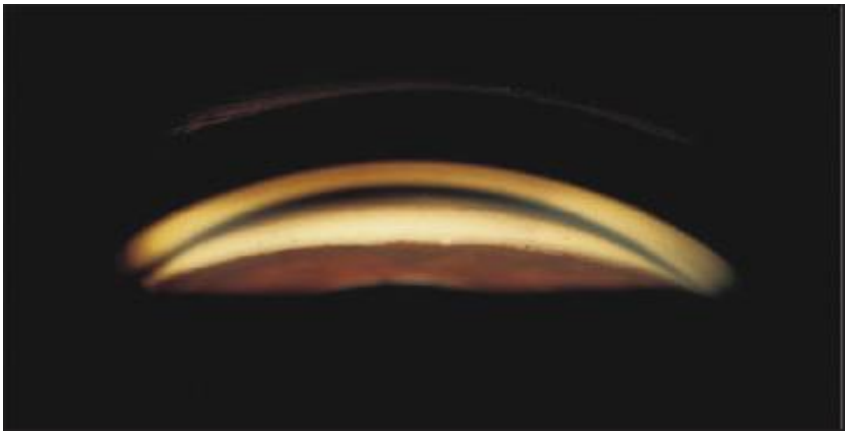


Figure: 8: ***Indentation Gonioscopy.***

What to Observe by Gonio Lens

The observation is made layer by layer from the root of the iris to the cornea in the following manner-

1. The anterior-medial surface of the ciliary body is named the ciliary body band with an existence of grey to dark brown colour.
2. The scleral spur is seen as a white band between the ciliary body and trabecular meshwork.
3. The trabecular meshwork is exhibited as pigmented faintly.
4. The Schwalbe line is seen as a bright white line.

The scleral spur is a very important landmark for the application of laser trabeculoplasty. The laser shots posteriorly to the scleral spur tend to the uveitis and with early rise in IOP and peripheral anterior synechiae (PAS) takes place.

Grades of Angle Width

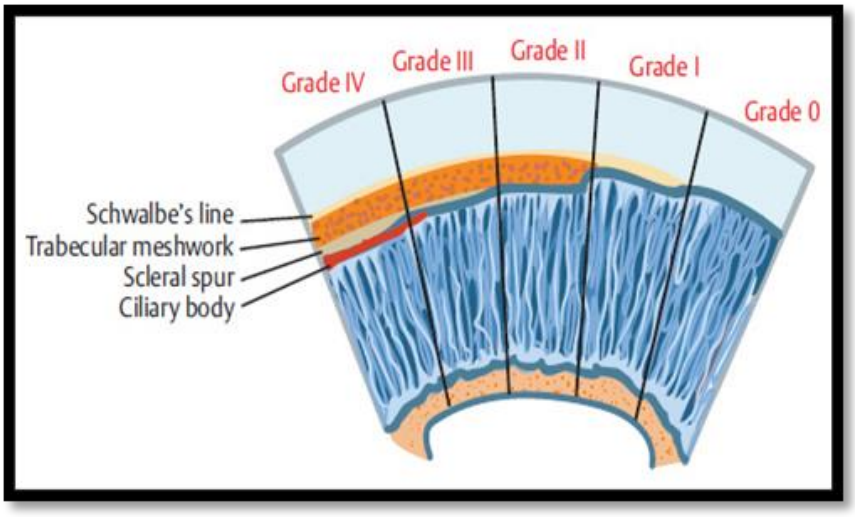


Fig: 9: Digramatic depiction of various angle structures.

Angle width depends on the related structures and is analysed by the following system-

1. Shaffer system
2. Scheie system
3. Spaeth system

Table 1: Shaffer's System of Grading the angle width.

GRADES	ANGLE WIDTH	VISIBLE STRUCTURES	ANGLE TYPE	INTERPRETATION
IV	35–45 degree	▪ Ciliary body ▪ Scleral spur ▪ Trabecular meshwork ▪ Schwalbe's line	Wide open-angle	Impossible angle closure
III	20–35 degree	▪ Scleral spur ▪ Trabecular meshwork ▪ Schwalbe's line	Open-angle	Impossible angle closure
II	10–20 degree	▪ Trabecular meshwork ▪ Schwalbe's line	Moderately narrow-angle	Unlikelyangle closure possible
I	0–10 degree	▪ Schwalbe's line	Very narrow angle	High risk angle closure
0	0	Invisible structure (Irido-corneal contact)	Closed angle	Indentation gonioscopyshould apply to confirm synechiaeclosure.

The Shaffer grading system has 4 grades (4 to 0) for angle and zero represents the severe impact of the disease. It is used most commonly and has concernswith the

1. Angle (between the iris and trabecular meshwork) width measurement in degree
2. Different anatomical structures
3. Types of the angle
4. Clinical interpretation.

3.Optic Nerve Head Examination

ONH is part of the optic nerve that extends from the retina to the scleral surface and on ophthalmoscopic examination for ONH discand papilla (the elevated area around the periphery of the disc) terms are frequently used and the total area of ONH, which is seen from the anterior side is called a disc, inside the middle of that area the optic cup is a central, depressed, pallor area of the disc (ONH) either havea partial or complete absence of axons. The bottom of the disc is formed by lamina cribrosa. An orange-red colourarea between the outer edge of the cup and the disc marginis calleda neuroretinal rim (NRR).

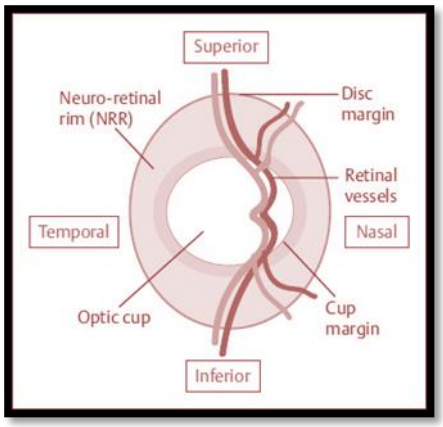


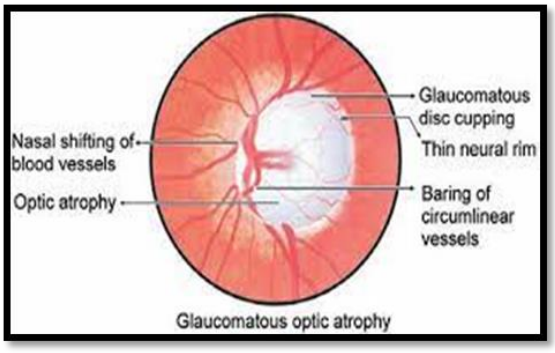
Fig. 10: Optic Nerve Head.

The thickness of the neuroretinal rim varies with the area, in sequenced descending order inferior rim, superior rim, nasal rim and temporal rim (ISNT), thatis why the cup becomes horizontally oval almost in normal eye and vertical orientation is checked for any glaucomatous changes.

The contour is checked at the adjoining area of the optic cup and neuroretinal rim, and pallor colour is checked at the optic cup while an enlarged cup may consider for normal physiological cupping. Theblood vessels take entry through the nasal-sided edge of the cup and theirbending is observed at the optic disc margin.

Thediameter of the optic cupabout the disc is called optic disc ratio (CDR)and is expressed as the difference of the disc diameter in both the meridians.

1. Standard CDR is 0.3
2. If both eyes have a CDR ratio difference > 0.2 considered suspicious.
3. If the vertical CDR is greater than the horizontal, considered glaucoma, otherwise,the standard eye has a horizontal CDR greater than the vertical.



Some of the important signs are used

1. Deepening of a cup (cupping)leads to the visibility of the lamina cribosa which gives dot-like existence (lamellar dot sign) due to loss of nerve fibres,

initially becomes diffuse and shallow, and later on extends upto the disc margin with pale colour. Total cupping is also known as bean pot cupping.

2. The bayonetting sign shows advanced glaucomatous cupping where the loss of total neural rim is found with the sharp turning of the vessels backwards and again emerges at the disc margin like a bayonet of a rifle.
3. Baring of circumlunar blood vessels is a sign of rim thinning, which may be found in various optic disc heads as physiologic cupping, where one or two vessels curve to outline the area at the superior and inferior margin called circumlunar vessels, which bared at the cup margin, therefore, lie on the floor of the optic cup.
4. Disc haemorrhages (splinter haemorrhages) are found ontheir common site, an inferior-temporal region, characterized by the flame-shape structure at the nerve head, which crosses the disc margin and extendsupto the Nerve FibreLayer. Such haemorrhagesare found with Normotensive Glaucoma and patients who have glaucoma along with diabetes, and hypertension, and patients using aspirin. This sign is indicated for the progression of glaucoma.

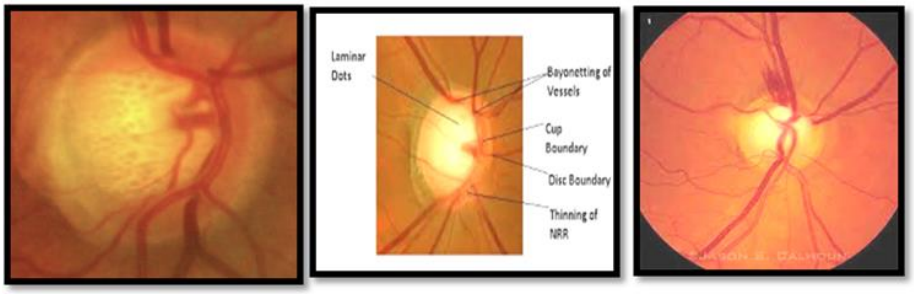


Fig. 11: Optic Disc Cupping.

4.Visual Field Analysis and Scotoma

The term *skótos* (greek) means darkness. An eye has an inactive area about the vision, in its visual field due toa blind spot, has a resemblance to a scotoma, because of the absence ofphotoreceptor cells and gives exit to the optic nerve composed of retinal ganglion cell axons. A scotoma meansa partial alteration in the visual field having concern for the partial or complete degeneration of the visual acuity.[23]

Scotoma may develop due to some pathology or disease related to the retina, optic nerve and visual cortex, its size and shape may also vary. The small scotoma at the macular reason has severe disability while at the periphery larger scotoma shows no visual disturbances.[24]

The relative diseases are retrobulbar neuritis (demyelinating disease), a disorder of the nerve fibre layer in the retina, macular degeneration, hypertension and vascular blockage of the retina and optic nerve, stroke and brain injury, methyl alcohol, ethambutol and quinine toxicity, nutritional deficiencies, Scintillating scotoma in migraine, tumours related to the pituitary gland are very important for the bilateral scotoma named bitemporal paracentral scotoma, due to the compression of the optic chiasm, severe preeclampsia due to pregnancy-induced hypertension have similarity with the increased intracranial pressure due to malignant hypertension also causes scotoma. Antibiotic streptomycin (aminoglycoside) also causes scotoma.[25,26]

The retina is subdivided vertically into temporal and nasal halves (raphe) and horizontally into superior and inferior halves (raphe) at the fovea. The retinal nerve fibre bundles never crosse the horizontal meridian and get defective due to the damage of ganglion cell axons at and around the optic nerve head.

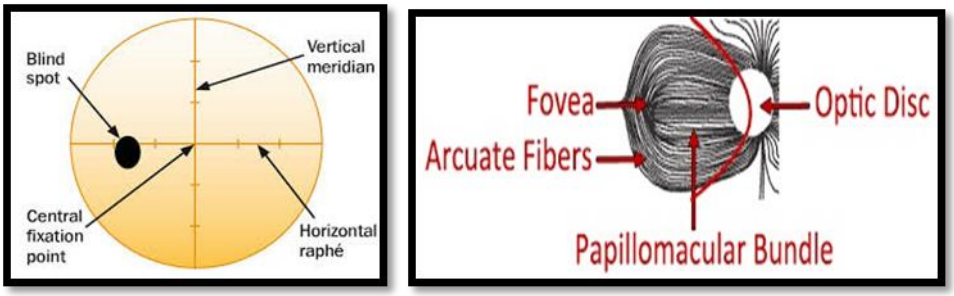


Fig. 12: Retinal Nerve FibreChanges in Condition of demyelinating disease.

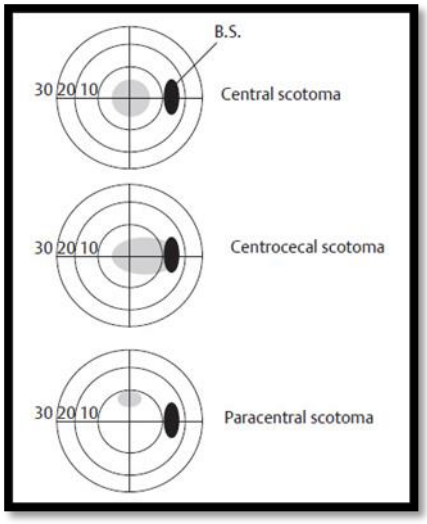
Important points

1. Papillomacular bundles are those running from the macula to ONH.
2. An arcuate is formed around the papillomacular bundles by the fibres which run from the temporal side to ONH.
3. Fibres from the nasal side to ONH run straight are called radial fibres.

NFB FIELD DEFECT[21]

The anatomy of RNFL and the location of damaged nerve fibres are the essential factors for the main three types of field defect-

1. Papillomacular bundle defects,
2. Arcuate NFB defects and
3. Nasal NFB defects



Nerve Fibre Bundle visual field defect follows the horizontal meridian, especially in the nasal portion of the visual field with the tendency to exhibit in the Bjerrum area (within 10 to 20 degrees from the fixation point).

1. PAPILLOMACULAR BUNDLE DEFECT[12]

In advance glaucoma central island of the visual field remains unaffected, although relative scotomas are as follows-

1. Central scotoma involves the defect over the central fixation area.
2. Centrocecal scotoma is the defect involving the area from the central scotoma (central fixation area) to the blind spot.
3. Paracentral scotoma is the isolated visual field defect within the 10 degrees with the time it increases upto the absolute defect.

2. ARCUATE DEFECT[21]

An arcuate defect for glaucoma develops first and among them, lower arcuate fibres involve first compared to the upper arcuate as the superior-temporal and the inferotemporal area of the ONH becomes weaker because they are oriented large pores and thinner connective tissue at the lamina cribrosa.

If the visual field and optic disc have no change but arcuate defects are still present then it may be due tojuxtapapillary retinochoroiditis and retinal artery occlusions (chorioretinal disease), Drusen of ONH, papillitis and colobomas (ONH disease) and pituitary adenoma and optic chiasmatic arachnoiditis (anterior optic nerve lesions).

Some of the important defects related to the arcuate defects are

1. The Arcuate (bjerrum) scotoma starts from the blind spot to the surrounding macula along the horizontal raphe in an arch pattern and never crossesthe horizontal raphe. It may involve either one (arcuate scotoma) or both the arcuate (double arcuate or ring scotoma).
2. Seidel scotoma develops when paracentral scotoma joins to the blind spot to form a sickle shape scotoma and its concavity faces the macula.
3. Roenne nasal step is the defect at the nasal field, where asymmetric nerve fibre loss is found around the horizontal meridian.

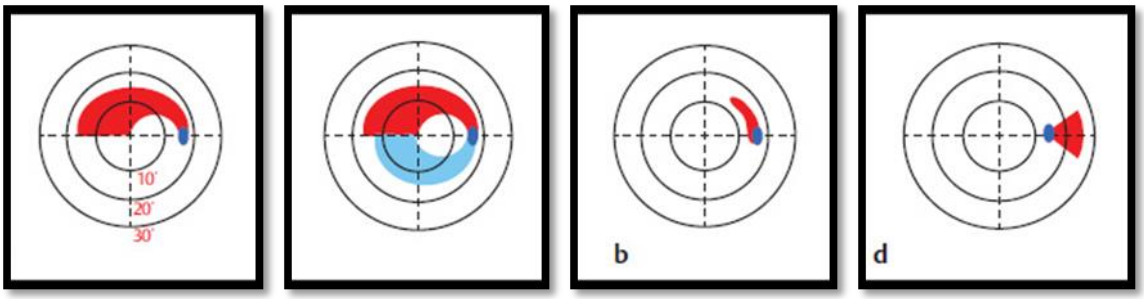
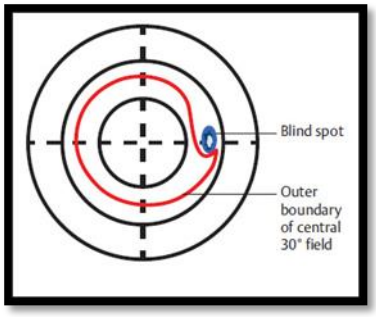


Fig. 12.01. Arcuate nerve fibre bundle (NFB) defects. (a) Arcuate (Bjerrum) scotoma. (b) Seidel scotoma. (c) Double arcuate (ring) scotoma with nasal step. (d) Temporal sector defect.

3. RADIAL FIBRE (NASAL NERVE FIBRE) DEFECT:[21] Suchfibres represent wedge-shaped temporal scotoma arising from the blind spot which extends from the centre of the macula to the temporal retinal periphery.



OTHER VISUAL FIELD DEFECTS[21]

1. Double arcuate scotoma forms tubular vision to form constriction of the visual field and it has concerns to glaucoma, retinitis pigmentosa (RP), and central retinal artery occlusion (CRAO).
2. In early glaucomastages, enlargement of blind spotisseen although it is not a confirmed sign because it may occur in optic nerve or retinal disorders too.
3. Baring of the blind spot is also not a confirmed sign of glaucoma as it becomes associated with lens opacities, miosis, or the ageing process but sometimes during perimetry results show a vertical elongation of scotoma including constriction of the central visual field and exclusion of the blind spot.

5. RETINAL NERVE FIBRE LAYER EXAMINATION[27]

RNFL means the axons of the ganglion cells within the innermost retina and they grouped at the optic disc to form the neuroretinal rim (NRR). Its importance isto eliminate Glaucomatous Optic Neuropathy.

RNFL is formed by the expansion of the fibres of the optic nerve; it is thickest near the optic disc, gradually diminishing toward the oraserrata. Patients with retinitis pigmentosa have abnormal thinning of the RNFL which correlates with the severity of the disease. However, the thickness of the RNFL also decreases with age and not visual acuity.[28,29]

RNFL analysis is made by OCT. At the start of the test, the following three important data should be entered carefully, otherwise, they produce suspicious interpretation results

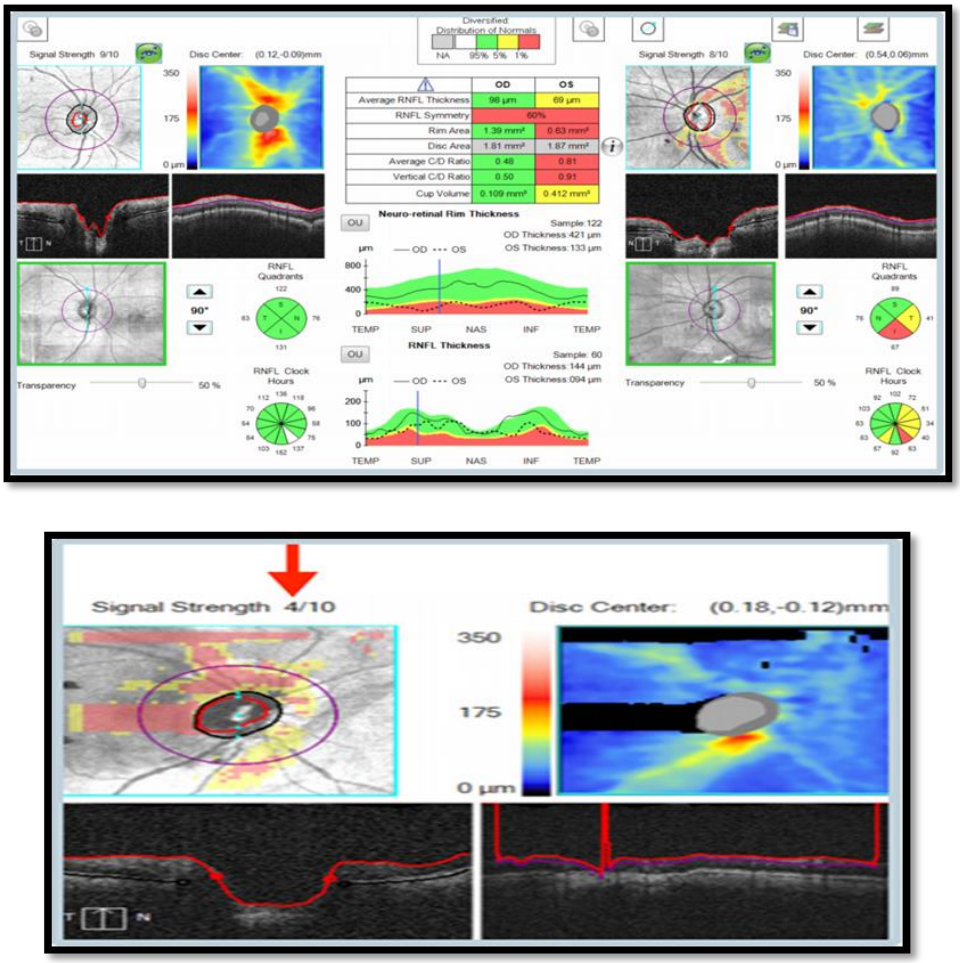
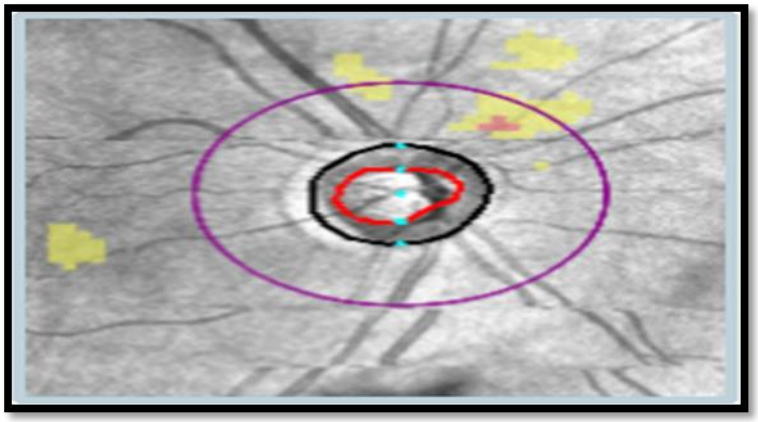


Fig. 12.02: Retinal Nerve FibreLayer (RNFL) defects.



1. An Accurate Date of Birth, as it correlates with the controlled group.
2. Signal Strength is the score which gives the intensity of the captured signal by the OCT. Low score signal strength is called segmentation error which leads to the incorrect calculation for the thickness parameter due to the misplacement of the retinal layer.
3. Movement Artifact produces if the eye is misaligned usually on the horizontal scale of the map.

STATISTICAL ANALYSIS

The finding of thecurrent patient is correlated with the preloadeddatabase of many other normal individuals to determine it. Thisis considered as the standard of care. There are two different statistical aspects-

1. Age-Matched Controls
2. Population Bell Curve

AGE-MATCHED CONTROL

The analysis of NRR, RNFL and GCC (ganglion cell complex) is made by the appropriate correlation of age-matched control group, it becomes an inbuilt large control database(details of normal patients) of the machine and achieved by the clinical research for the different age groups.

Above mention tissues get degenerate with age, therefore it is necessary to correlate it with age-related tissue loss or real glaucomatous change.

BELL CURVE

Same-age group patients may have match either similar, thinner or thicker profile to the preloaded clinical data so the bell curve facilitates the easiest identification of the thickness profile in the following colour form-

1. Green represents 95% chancesfor normal as compared to the age-matched controls.
2. Yellow represents relatively thin witha 5% chance towards the normal.
3. Red represents relatively thin with a1% chance towards normal.
4. White represents relatively thicker than 95% of the normal.

The mentioned colour code used for thethickness map of RNFL and GCC denote the actual measurement of the RNFL and GCC and the deviation map of RNFL and GCC denote statistical analysis to compare it with the age-matched controls.

During the OCT scan the RNFL thickness is measured on thousands of locationsacross the entire scan within the circular cut-out area of about 3.47-mm and known as the RNFL Circular Tomogram. The Circular Tomogram is displayed in the following name-

1. RNFL Thickness Map
2. RNFL Deviation Map
3. RNFL Tabular Data
4. RNFL Pie Charts
5. RNFL Graph

RNFL THICKNESS MAP

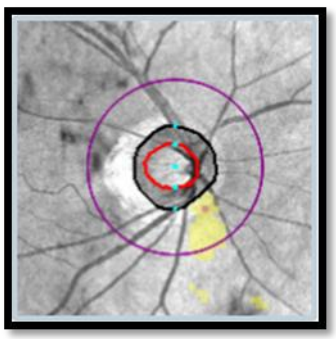
The thickness of the RNFL is measured over thousands of points and plotted on a map through the colours. Warm colours, like red and white represents relatively thicker areas andcool colours, like green and blue, represent relatively thinner areas of the RNFL.

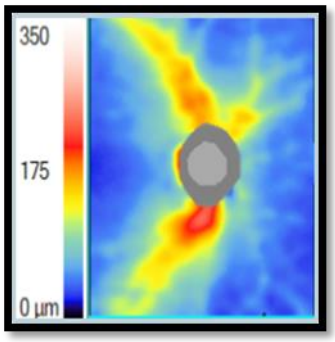
Typically, a normal, nonglaucomatous eye has an RNFL thickness of 80 microns or greater. An eye with an average RNFL thickness of 70 to 79 is suspicious for glaucoma. An average thickness of 60 to 69 is seen in less than 5% of the normal population and implies glaucoma.[30]

The superior and inferior portions of the scan have thick areas in the normal study.

RNFL DEVIATION MAP

	OD	OS
Average RNFL Thickness	88 µm	87 µm
RNFL Symmetry	95%	
Rim Area	1.28 mm²	1.11 mm²
Disc Area	2.04 mm²	1.97 mm²
Average C/D Ratio	0.60	0.65
Vertical C/D Ratio	0.54	0.62
Cup Volume	0.221 mm³	0.268 mm³





This representsa statistical plot and compares the patient's RNFL to acontrol group of age.The thinnest area is called a static anomaly and is marked with a yellow or red colour while normal limits have no impression.

TABULAR DATA

This statistically significant table consists of various details with the different colour codes in the backgroundfora statistically well-defined comparison group. At the same time in the table, it is defined for the right and left eye. An asymmetry of the RNFL between both eyes is a common feature of early-onset Glaucoma. The grey colour represents no comparison group for the obtained patient data.

1. Average RNFL Thickness		5. Average C/D Ratio
2. RNFL Symmetry		6. Vertical C/D Ratio
3. Rim Area		7. Cup Volume
4. Disc Area		

AVERAGE RNFL THICKNESS

Across the circular tomogram, diffuse changes in the average thickness are shown in numbers with the colour code. An important issue is the number, which can not estimate smaller changes along with the clinical significance but the colour code is most relevant.

RNFL SYMMETRY

It is also measured by the circular tomogram, the asymmetry between the eyes is considered a strong chance for the early stage of glaucoma, and statistical significance can be confirmed by the colour coding.

RIM AREA

It represents the area of the neuroretinal rim which refers to the neural tissue between the disc and the cup and becomes comparable to the age-matched control data.

DISC AREA

It represents the area of the disc and is used for the cup-disc ratio. The bigger the disc will have a large cup and vice versa.

AVERAGE C/D RATIO

It represents the cup-to-disc ratio. The clinical research concludes OCT shows a higher value than that of clinical estimation.

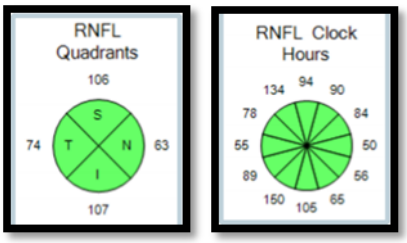
VERTICAL C/D RATIO

This is An importantestimation of the single-point cup-to-disc ratio. The early glaucoma disease indication is to affect vertical poles first.

CUP VOLUME

It gives detail about the volume of the cup, about the cup-to-disc ratio.The rim area (NRR), disc area and cup volume give a combined measurement for the cup-to-disc or C/D ratio.

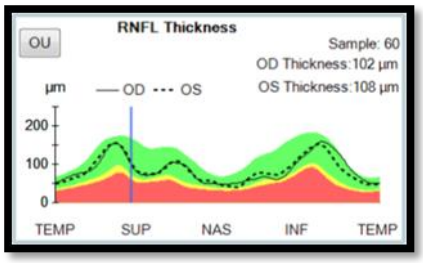
RNFL PIE CHART



Each detail has two different types of the RNFL Circular Tomogram in the form of Pie Charts for the same eye for the statistical interpretation to express the numerical and colour-coded data in different ways.

First Pie Chart expresses itself as quadrant pies in four quadrantsfor the diffuse changes and the second expresses for the focal changes in the clock-hour pies. Both the data limits presume for glaucoma.

RNFL GRAPH



The RNFL Circular Tomogramrepresents a graphical plot with colourimetric curves to determine the statistical significance of each point. There are two different peaks in the graph

1. Blunt Peaks
2. Shift Peaks

The graphical curve has a thin segment then known as blunted peak and is not a marker of statistical significance.

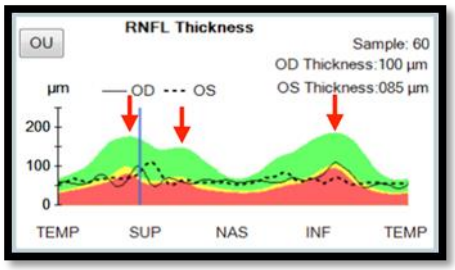


Figure 12.03BLUNT PEAK.

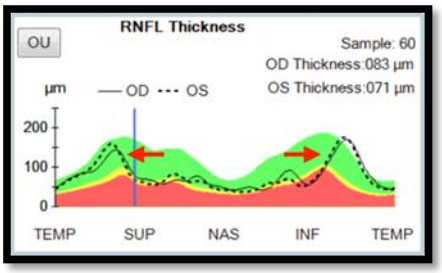
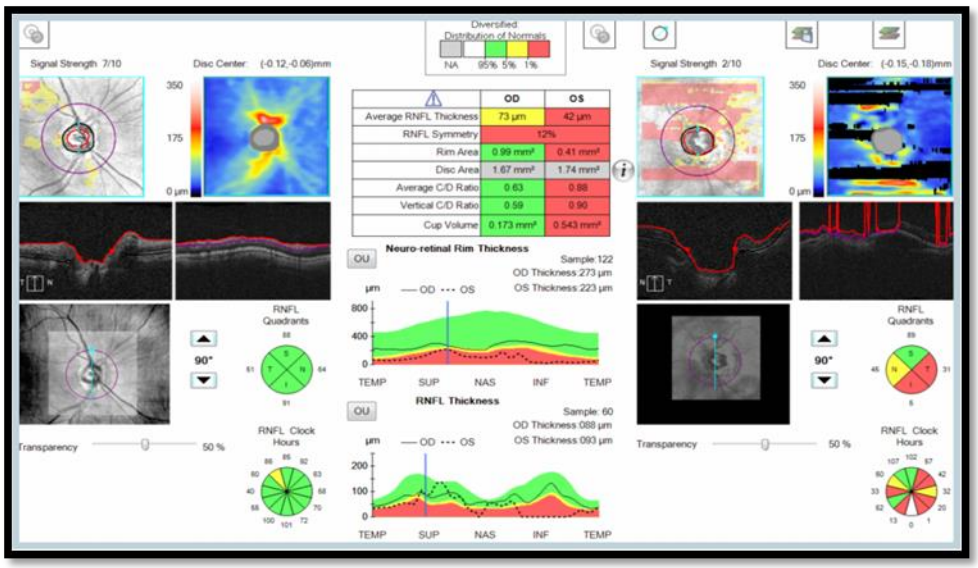


Figure 12.04 SHIFTED PEAK.

If the graphical curve appears normal in height and shape withoutalignment with the typical display called a shifted peak. Often it happens due to tilted optic nerve or any morphological changes in anatomy and the spectrum is filled with the green colour for normal impression. So it should not be considered normal or even though if the colour changes take place to express any anomaly again it should not be considered abnormal.

FALSE POSITIVE – RED DISEASE

If the OCT reporting has many red boxes in the statistical analysisdenotedas a false positive OCT scan. Thus misinterpretation will give rise to a wrong classification or Glaucoma Suspect for an individual havinga normal visual field.



TREATMENT

Glaucoma is usually controlled by eyedrops through the lowering of eye pressure. It is maintained either by reducing the production of aqueous or increasing the drainage at the angle. Following are the side effects of the drugs used to treat the glaucoma

1. Stinging or itching
2. Red Eyes or change in eye colour/red skin or colour change around the eyes
3. Changes in pulse rate, heartbeat, breathing
4. Changes in energy level
5. Dryness in mouth and eyes, blurred vision
6. Eyelash growth

Medicines, laser treatment, and surgery are well effective for lowering IOP but all the treatments never work equally on every individual.

GLAUCOMA TREATMENT[31,32]

ALPHA-ADRENERGIC AGONISTS

Such medicines reduce production and increase the outflow of the aqueous humour but they produce Side effects like blurred vision, fatigue, and increased heartbeat rate and blood pressure. Some of them are

1. Apraclonidine (Iopidine)
2. Brimonidine (Alphagan)
3. Epinephrine (Gluaconand Epifrin)
4. Dipivefrin (Propine)

BETA-BLOCKERS

These drugs reduce aqueous humour production and fluid flow rate in the eye. The side effects of these drugs include low blood pressure, reduced heart rate and shortness of breath. The following are the drugs-

1. Timolol (Timoptic XE, Ocumeter and Timoptic)
2. Levobunolol (Betagan)
3. Carteolol (Ocupress)
4. Metipranolol (OptiPranolol)
5. Betaxolol (Betoptic)

BIODEGRADABLE DRUG DELIVERY IMPLANT

Durysta™ is a biodegradable eye implant injected directly into the anterior chamber, that includes bimatoprost (prostaglandin) for the reduction of the IOP. Mostly used for individuals having ocular hypertension or open-angle glaucoma. This implant therapy is not for re-administered for the second time. The most common side effect is redness, pain, light sensitivity, subconjunctival haemorrhage, dry eye, irritation, blurry vision, iritis, and headache.

CARBONIC ANHYDRASE INHIBITORS

They are available in drop and tablet form to reduce the production of the aqueous. The side effects of oral administration include stinging, loss of appetite and taste changes, secondary effects are including depression, stomach problems, and weight loss, and there is an increased risk of serious anaemia and kidney stones with long-term use.

1. Dorzolamide (Trusopt)
2. Brinzolamide (Azopt)
3. Acetazolamide (Diamox)-an oral medication
4. Methazolamide (Neptazane)-an oral medication

MIOTICS (CHOLINERGIC AGENTS)

This type of drug constricts the pupil thus aqueous drainage flow increases. The side effects conclude with irritation, allergy, an increased risk of myopia and cataracts. Other side effects are dermatitis, urinary incontinence, lung congestion, and changes in heartbeat. Such drugs are

1. Pilocarpine (Isopto Carpine, Pilocar, and Pilopine HS ointment)
2. Echothiophate (Phospholine Iodide)

PROSTAGLANDIN ANALOGS

The property of this drug is vasodilation, so it reduces eye pressure by increasing the outflow of the aqueous. The side effects include sensitivity and irritation in fluctuation mode, sometimes the colour of the eye shifted to darken, sunken eyes and eyelash growth.Some of the drugs are

1. Tafluprost ophthalmic solution (Zioptan™)
2. Latanoprost (Xalatan)
3. Bimatoprost (Lumigan)
4. Travoprost (Travatan)
5. Unoprostone isopropyl ophthalmic solution (Rescula)
6. Latanoprostene bunod ophthalmic solution (Vyzulta™)
7. Latanoprost preservative-free formulation (Iyuzeh™)

Vyzulta (latanoprostenebunod) is a modified class of medications used once a day to treat glaucoma.

RHO KINASE INHIBITORS

Netarsudil ophthalmic solution (Rhopressa) is a RHO Kinase inhibitor that reduces the pressure by increasing the aqueous outflow. The side effects may include eye redness, stinging and corneal deposits.

COMBINATION OF DRUGS

For better results sometimes combined drug effects are used. Following are the combination-

1. Dorzolamide and timolol (Cosopt®)
2. Latanoprost and timolol (Xalacom®)
3. Brimonidine and timolol (Combigan™)
4. Brinzolamide and brimonidine (Simbrinza®)
5. Netarsudil and latanoprost (Rocklatan™)

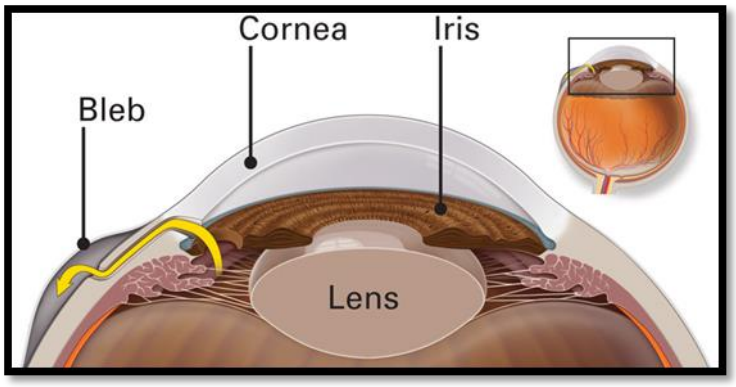
Most frequently used Combigan concludes the side effects of beta blockers and alpha agonists. Same way Simbrinza Suspension includes blurry vision, irritation, change in taste change, and dry mouth.

LASER SURGERY

There are two types of laser surgery to drain the aqueous-

Trabeculoplasty or selective laser trabeculoplasty (SLT) has concernedwithopen-angle glaucoma to make fluid flows out properly to maintainintra-ocular pressure. Iridotomy has a concern with the angle-closure glaucoma wherea tiny aperture is made in the iris to make drainage easy.

Minimally invasive glaucoma surgery (MIGS) performed through a small incision has aim to reduce intraocular pressure either by performing standalone procedures, or done along with cataract surgery if it is there. Such procedures provide a safety profile with rapid visual recovery than traditional surgery.



OPERATING SURGERIES

The procedure is applied to make a drainage channel named Trabeculectomy where a tiny flap is made in the sclera in continuation of the bleb (pocket) in the conjunctiva. The site of this procedure is made below the upper eyelid. The aqueous is absorbed in the conjunctival tissue.

Some of the drainage implants are also there having a part of the device named reservoir implanted below the conjunctiva where aqueous accumulates and is then absorbed in the conjunctival tissue accordingly. In hypermature cataract sometimes the angle becomes narrow due to the bulging of the crystalline lens, by the removal of the crystalline lens or implanting of the intraocular lens space becomes enough for the smooth aqueous flow.[12]

REFERENCES

1. Thylefors B, Negrel AD, Pararajasegaram R, Dadzie KY. Global data on blindness Bull World Health Organ 1995; 73(1): 115-21.
2. Quigley HA. Number of people with glaucoma worldwide Br J Ophthalmol 1996; 80(5): 389-93.
3. ManikGoel, Renata G Picciani, Richard K Lee, Sanjoy K Bhattacharya, Bascom Palmer Eye Institute, University of Miami, Miami, FL 33136, USA @openophthalmologyjournal.com /VOLUME /4 /PAGE/52/FULLTEXT.
4. Millar C, Kaufmn PL. Aqueous humor: secretion and dynamics In: Tasman W, Jaeger EA, Eds. Duane's foundations of clinical ophthalmology. Philadelphia: Lippincott-Raven 1995.
5. Goel M, Picciani RG, Lee RK, Bhattacharya SK. Aqueous humor dynamics: a review. Open Ophthalmol J. Sep 3 2010; 4: 52-9. doi:10.2174/1874364101004010052
6. Sunderland DK SA. Physiology, Aqueous Humor Circulation.
7. Toris CB, Koepsell SA, Yablonski ME, Camras CB. Aqueous humor dynamics in ocular hypertensive patients. J Glaucoma, Jun 2002; 11(3): 253-8. doi:10.1097/00061198-200206000-00015.
8. Hogan MH, Alvarado JA, Weddell JE. Histology of the human eye. Philadelphia: WB Saunders 1971.
9. R TCYMT. Aqueous humor dynamics. In: DC CNL, ed. Atlas of Glaucoma. Second edition ed. Informa HK; 2007; 13 – 28:chap 3.
10. Kiel JW, Hollingsworth M, Rao R, Chen M, Reitsamer HA. Ciliary blood flow and aqueous humor production. ProgRetin Eye Res., Jan 2011; 30(1): 1-17. doi:10.1016/j.preteyeres.2010. 08.001. my.clevelandclinic.org/health /diseases /4212-glaucoma
11. What Is Glaucoma? Symptoms, Causes, Diagnosis, Treatment, David Turbert, aao.org/eye-health/diseases/what-is-glaucoma, Dec. 06, 2022 en.wikipedia.org/wiki/Anterior_chamber_of_eyeball Anatomy of Anterior Chamber, Dr. Parthopratim Dutta Majumder SankaraNethralaya, Chennai, https://www.eophtha.com/posts/anatomy-of-anterior-chamber, Published Online: April 5th, 2020.
12. Ferreira SM, Lerner SF, Brunzini R, Evelson PA, Llesuy SF. Oxidative stress markers in aqueous humor of glaucoma patients. Am J Ophthalmol, Jan 2004; 137(1): 62-9. doi:10.1016/s0002-9394(03) 00788-8
13. Kaeslin MA, Killer HE, Fuhrer CA, Zeleny N, Huber AR, Neutzner A. Changes to the Aqueous Humor Proteome during Glaucoma. PLoS One, 2016; 11(10): e0165314. doi:10.1371/journal.pone.0165314.
14. Hara K, Lutjen-Drecoll E, Prestele H, Rohen JW. Structural differences between regions of the ciliary body in primates Invest Ophthalmol Vis Sci., 1977; 16(10): 912-24.
15. Ruskell GL. An ocular parasympathetic nerve pathway of facial nerve origin and its influence on

intraocular pressure Exp Eye Res 1970; 10(2): 319-0.
16. Johnson M, McLaren JW, Overby DR. Unconventional aqueous humor outflow: A review. Exp Eye Res., May 2017; 158: 94-111. doi:10.1016/j.exer.2016.01.017.
17. Fautsch MP, Johnson DH. Aqueous humor outflow: what do we know? Where will it lead us? Invest Ophthalmol Vis Sci., Oct. 2006; 47(10): 4181-7. doi:10.1167/iovs.06-0830 entokey.com/the-glaucoma
18. Principles of Gonioscopy, Wallace L M Alward MD, Reid A Longmuir MDaao.org/education /disease-review/principles-of-gonioscopy, NOV 08, 2017.
19. Fletcher, Donald C.; Schuchard, Ronald A.; Renninger, Laura W. (2012-09-01). "Patient awareness of binocular central scotoma in age-related macular degeneration". Optometry and Vision Science, 89(9): 1395–1398. doi:10.1097 /OPX.0b013e318264cc77. ISSN 1538-9235. PMID 22863789. S2CID 34805670.
20. Bilateral effects of unilateral visual cortex lesions in human", Matthew Rizzo and Donald A. Robin, Brain, 1996; 119: 951-96.
21. The role of axoplasmic transport in the pathogenesis of retinal cotton-wool spots", D. McLeod, J. Marshall, E. M. Kohner, and A. C. Bird, Br J Ophthalmol, 1977; 61(3): 177–191.
22. Possible Roles of Vertebrate Neuroglia in Potassium Dynamics, Spreading depression, and migraine", Gardner-Medwin, J. Exp. Biol. (1981), 95, pages 111-127 (Figure 4). eyecarepd.com/glaucoma-glossary
23. Desissaire, Sylvia; Pollreisz, Andreas; Sedova, Aleksandra; Hajdu, Dorottya; Datlinger, Felix; Steiner, Stefan; Vass, Clemens; Schwarzhans, Florian; Fischer, Georg; Pircher, Michael; Schmidt-Erfurth, Ursula (2020-10-01). "Analysis of retinal nerve fiber layer birefringence in patients with glaucoma and diabetic retinopathy by polarization sensitive OCT". Biomedical Optics Express, 11(10): 5488–5505. doi:10.1364/BOE. 402475. ISSN 2156-7085.
24. Oishi A, Otani A, Sasahara M, Kurimoto M, Nakamura H, Kojima H, Yoshimura N. Retinal nerve fiber layer thickness in patients with retinitis pigmentosa. Eye, 2008 Mar 14, online advance publication. PMID 18344951
25. Medeiros FA, Vizzeri G, Zangwill LM, Alencar LM, Sample PA, Weinreb RN. Comparison of retinal nerve fibre layer and optic disc imaging for diagnosing glaucoma in patients suspected of having the disease. 2008. Ophthalmology, 2008; 115: 1340-1346.
26. New glaucoma therapies improve results and reduce recovery time, Shivani Kamat, M.D.Ophthalmology, March 1, 2023, https://utswmed.org/medblog/new-treatments-for-glaucoma brightfocus.org/glaucoma /treatments.