A DISSERTATION ON

"A COMPARATIVE STUDY OF BLOOD FLOW VELOCITIES IN OPHTHALMIC ARTERY IN GLAUCOMA PATIENTS"

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CONTENTS

ABSTRACT

Background:

Glaucoma is a multifactorial optic neuropathy characterized by progressive damage of optic nerve fibers leading to typical optic nerve changes and field defects with or without raise in intraocular pressure. In this study Colour Doppler imaging of the retrobulbar blood vessels is done to assess the role of vascular factors in the pathogenesis of optic nerve fiber damage.

Aims and objectives:

1) To measure and compare the systolic and diastolic blood flow velocities, resistance index in Ophthalmic artery, Central retinal artery and Short posterior ciliary artery in patients with Normotensive glaucoma, untreated Primary Open angle glaucoma and normal subjects.
2) To assess the significance of vascular flow in glaucomatous optic nerve damage.
3) To correlate between optic nerve head blood flow and glaucomatous optic nerve head changes.

Methodology:

A prospective cross sectional study to assess the Peak systolic velocity, End diastolic velocity and Resistance Index using Colour Doppler imaging of the retrobulbar vessels was done in 90 subjects during the period December 2017 to June 2019. The 90 subjects were grouped as follows:

Group 1: Normotensive glaucoma- 30 patients
Group 2: Untreated primary open angle glaucoma- 30 patients
Group 3: Normal subjects- 30 controls

Results

Compared with normal group, there is significant reduction in PSV (p= 0.0005)in both Normotensive glaucoma and Primary open angle glaucoma group in all the three arteries, namely Ophthalmic artery, Central retinal artery and Short posterior ciliary artery. There is also significant reduction in EDV (p=0.0005) in both the groups in all the three arteries. Increased RI is found in all the three arteries (Ophthalmic artery, Central retinal artery and Short posterior ciliary artery) and is found to be statistically significant in the normotensive and primary open angle glaucoma group with p value of 0.0005.

Conclusion

In this comparative study of both normotensive and primary open angle glaucoma patients using Colour Doppler imaging to assess the blood flow velocities in Ophthalmic artery, Central retinal artery and Short posterior ciliary artery , it was noted that these vessels had reduced systolic and diastolic blood flow velocity and also increased resistance index . All these factors are known to contribute to the vascular compromise leading to ischemia of the optic nerve head resulting in optic nerve damage.

This study concludes that, irrespective of the intraocular pressure, vascular factors do have a role in the pathogenesis of optic nerve head changes in both normotensive and primary open angle glaucoma.

Keywords

Colour doppler imaging, normotensive glaucoma, peak systolic velocity, end diastolic velocity, resistance index

PART I

INTRODUCTION

Glaucoma is a group of disease entity with variable etiologies causing irreversible vision loss characterized by loss of neural tissue and remodeling of connective tissue elements of optic nerve head leading to characteristic optic neuropathy and varying pattern of visual dysfunction. According to World Health Organisation, Glaucoma is the second leading cause of blindness worldwide following cataract accounting to blindness in 5.1 million persons or 13.5% of global blindness.

Intraocular Pressure is one of the primary risk factors in glaucoma leading to the development and progression of glaucoma. The other risk factor is vascular dysregulation. The low ocular perfusion to optic nerve head causes ischemic changes resulting in glaucomatous optic neuropathy. A break in the auto regulation of blood supply to optic nerve head or failure of blood perfusion system to adjust to the requirements of optic nerve head is a major factor in the development and progression of nerve head changes and visual field defects.

Glaucoma has been classified based on the etiology as Primary and Secondary. Among these, the most common is Primary Open Angle Glaucoma characterized by intraocular pressure more than 21mm Hg in atleast one eye, normal and open anterior chamber angle with typical glaucomatous optic nerve head changes and visual field loss. At the other end there are patients with open, normal appearing angles with glaucomatous visual field defects and optic nerve damage inspite of normal intraocular pressure measured on all occasions. They are classified as Normotensive

glaucoma or Low tension glaucoma. Normotensive glaucoma accounts for 25-30% of all glaucoma characterized by glaucomatous optic nerve head changes and corresponding visual field defects with intraocular pressure measurements being consistently lower than 21mm Hg.

Transcranial Colour Doppler Ultrasound is a non invasive technique used to measure the blood flow velocity of intracranial blood vessels including Ophthalmic artery. It consists of a 2 MHz pulsed Doppler with a fast Fourier transformation used to analyse and derive the spectrum of returning echoes of various frequencies. Peak Systolic Velocity, End Diastolic Velocity and Resistance Index of Ophthalmic Artery, Central Retinal Artery and Short Posterior Ciliary Artery are measured to assess the blood flow of optic nerve head.

REVIEW OF LITERATURE

HISTORICAL REVIEW

1857- **Von Graefe** noted nerve head excavation without increase in intraocular pressure

1858- **Jaeger** defined the vascular etiology for both primary open angle and normotensive glaucoma.

Harris et al reported a significantly lower end diastolic velocity and higher Resistance Index in ophthalmic artery in patients with normotensive glaucoma.

Rankin et al showed a greater resistance index in central retinal and posterior ciliary arteries in patients with normotensive and primary open angle glaucoma.

Rojanapongpun et al used transcranial Doppler ultrasound and found a significant reduction of all three velocities(PSV,EDV and mean velocity) in the ophthalmic artery of patients with normotensive and open angle glaucoma

Harris et al postulated that a partially reversible vasospasm accounts for the elevated resistance to blood flow in patients with normotensive glaucoma.

Plange et al. found higher flow velocities and lesser RI and PI in SPCAs in the group of no progression.

Zeitz et al found decreased blood flow velocities in SPCA associated with glaucoma progression.

ANATOMY OF AQUEOUS HUMOUR OUTFLOW SYSTEM

Aqueous humour produced by the ciliary body passes from the posterior chamber through the pupil into anterior chamber and drains most commonly through the trabecular meshwork.

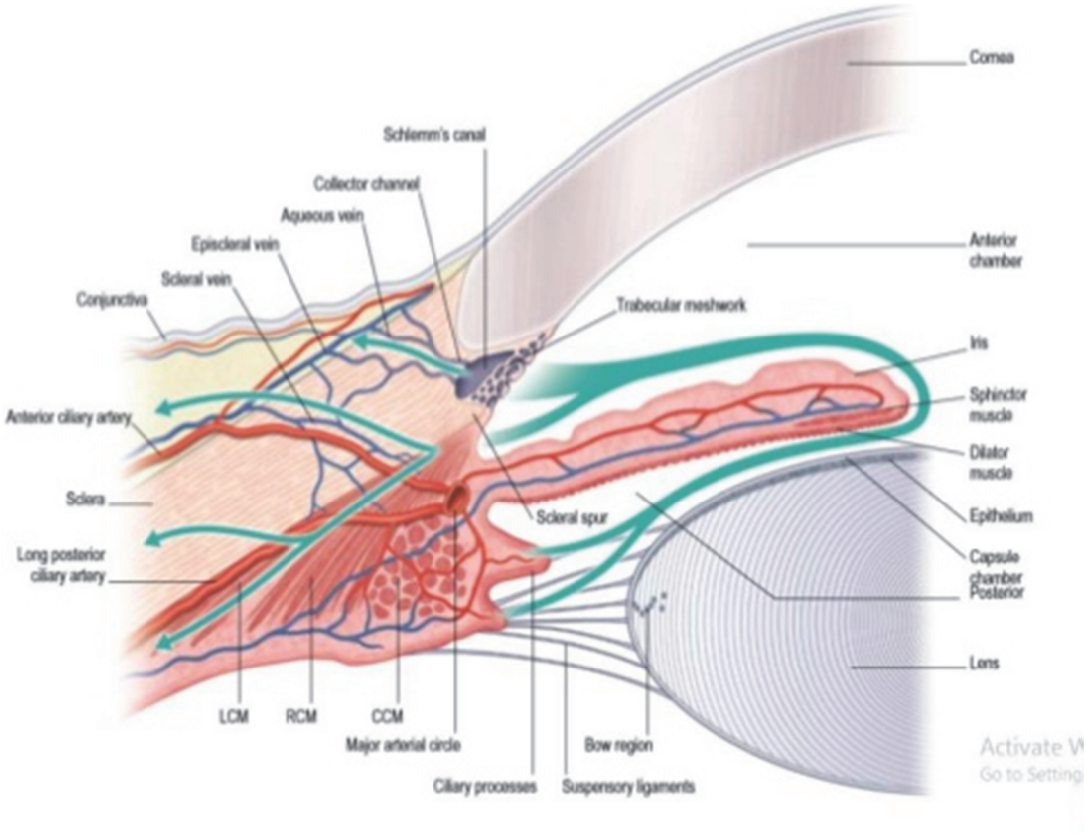


Figure 1

Anterior Chamber:

Potential space in the anterior segment of the eye bounded anteriorly by posterior surface of cornea and posteriorly by anterior surface of Iris and lens. It contains 220 µl of aqueous humour.[1]Average depth: 3.15 mm (2.6-4.4mm).Centre is deeper than the periphery. It appears deeper in Aphakia, Pseudophakia and Myopia and shallower in Hypermetropia.[2]

Posterior chamber:

Triangular in shape containing 0.6ml of aqueous.[1] Bounded anteriorly by posterior surface of Iris and part of ciliary body and posteriorly by crystalline lens and zonules.

Angle of anterior chamber:

Clinically it can be visualized by Gonioscopy.[1]

Structures forming the angle recess from posterior to anterior include:

1) Ciliary band
2) Scleral spur
3) Trabecular meshwork
4) Schwalbe's line

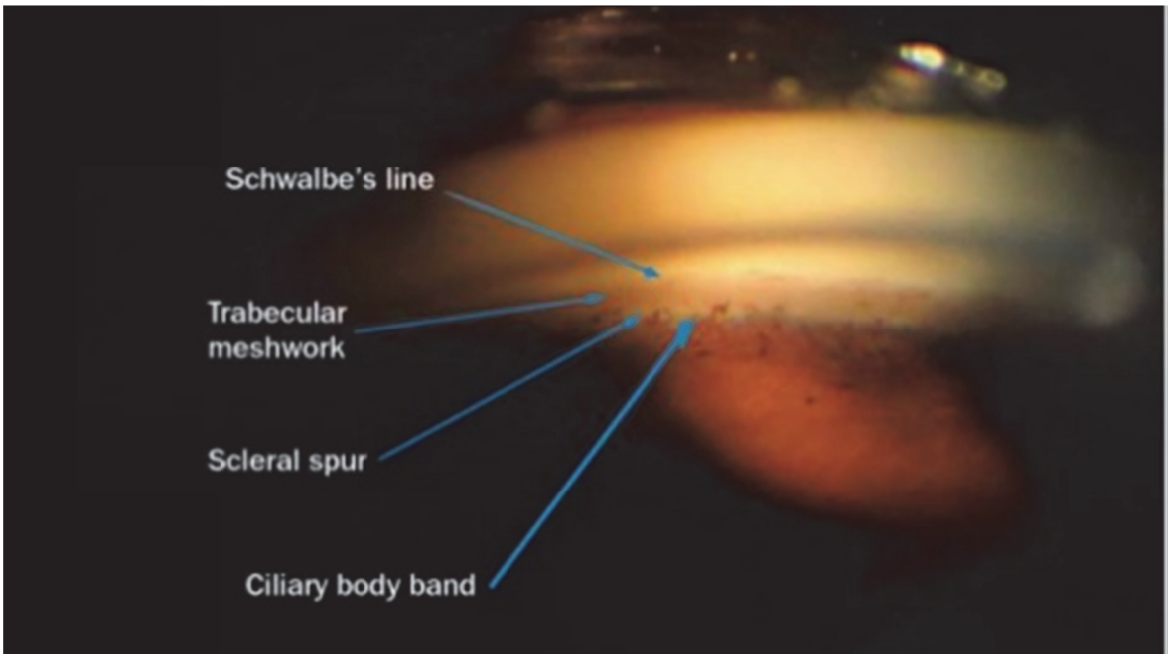


Figure 2

1) CILIARY BAND:

Dark brown band forming the posterior most part of the angle. It represents the anterior face of ciliary body between its attachment to the scleral spur and insertion of iris.

2) SCLERAL SPUR:

Wedge shaped circular ridge composed of 75-85% collagen fibres and 5% elastic fibers. It is a pale, translucent narrow strip of scleral tissue which appears as a prominent white line on gonioscopy.

3) TRABECULAR MESHWORK:

Sieve like structure made up of connective tissue lined by trabeculocytes which have contractile and phagocytic properties. It bridges the scleral sulcus and coverts it into a tube which accommodates the Schlemm's canal. Appears triangular in cross section with apex towards Schwalbe's line and base formed by Scleral spur and ciliary body. Allows the bulk flow of aqueous out of anterior chamber but prevents blood reflux into anterior chamber. Pigmentation is absent at birth which gradually develops with increasing age. It is divided morphologically and functionally into three parts:

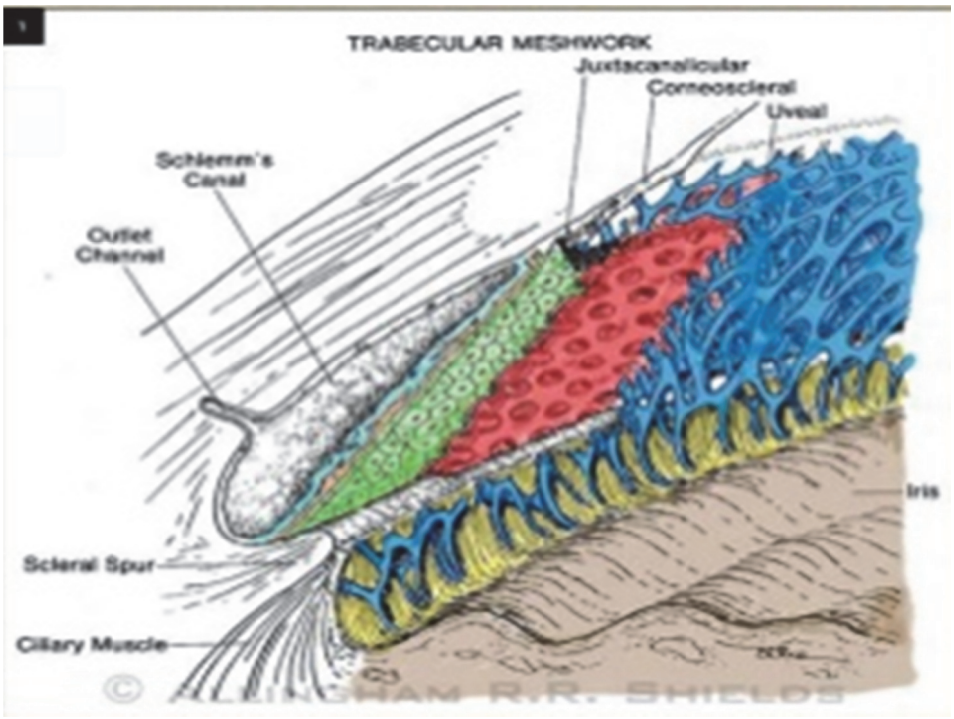


Figure 3

A) Uveal Meshwork:

Innermost part of trabecular meshwork that extends from iris root and ciliary body to Schwalbe's line. It is 2-3 layers thick containing pores with opening size between 25µ to 75µ. On electron microscopy each trabeculae is seen to have concentric layers consisting of central collagenous core, middle basement membrane and outer trabecular cells.

B) Corneo-scleral meshwork:

Large middle portion of trabecular meshwork extending from scleral spur to lateral wall of scleral sulcus. It consists of flat sheets of trabeculae with elliptical opening ranging from 5µ to 50µ. The openings become progressively smaller as they approach the Schlemm's canal. Electronic microscopic structure of each trabeculae is same as that of trabeculae of uveal meshwork[3].

C) Juxtacanalicular meshwork:

It forms the Outermost portion of trabecular meshwork. It is that portion of trabecular meshwork that forms major resistance to aqueous outflow. It consists of 2-5 layers of loosely arranged connective tissue cells, embedded in an extracellular matrix lined on either side by endothelium.[1]The outer endothelial layer of the juxtacanalicular meshwork comprises the inner wall of Schlemm's canal and the inner endothelial layer of the juxta-canalicular meshwork becomes continuous with the endothelium of corneoscleral meshwork. These endothelial cells have phagocytic properties and high level of actin with smooth muscle contractile properties.

4) SCHWALBE'S LINE:

It forms the anterior limit of drainage angle and seen as a white band in gonioscopy. Seen as fine scalloped border at the termination of descemet's membrane of cornea. Corneal wedge is used to identify Schwalbe's line.

SCHLEMM'S CANAL:

Schlemm's canal is the endothelial lined oval channel placed circumferentially in the scleral sulcus. Outer wall has numerous openings of the collector channels. It has numerous septae which passes from the collector channels to inner wall of Schlemm's canal.[4]

COLLECTOR CHANNEL:

Schlemm's canal is connected to episcleral and conjunctival veins by complex system of intrascleral channels. Two system of intrascleral system exists: a)An indirect system of numerous finer channels which forms an intrascleral plexus before

draining into the episcleral venous system and b) A direct system of large caliber vessels[4] which run a short intrascleral course and drain directly into episcleral venous system called as aqueous vein.

EPISCLERAL AND CONJUNCTIVAL VEINS:

The aqueous vessels join the episcleral and conjunctival vessels by several routes. Most aqueous vessels are directed posteriorly with most of these draining into episcleral veins, whereas few cross the subconjunctival tissue and drain into conjunctival veins.[3] The episcleral veins drain into the cavernous sinus via the anterior ciliary and superior ophthalmic veins, while the conjunctival veins drain into superior ophthalmic or facial veins via the palpebral and angular veins.

AQUEOUS OUTFLOW PATHWAY

Aqueous humour exits the eye at the anterior chamber angle by means of two pathways:

- Trabecular pathway
- Uveo scleral pathway

1) TRABECULAR PATHWAY:

It forms the major outflow pathway accounting to 75-90% of the aqueous drainage. It is the pressure dependent circulatory pathway for the aqueous draining into episcleral vascular system. Free flow of aqueous occurs from the trabecular meshwork upto the juxtacanalicular meshwork along the inner wall of Schlemm's canal where some resistance to aqueous flow occurs, hence helps in maintaining relatively stable intraocular pressure.[1]

2) UVEO SCLERAL PATHWAY:

Uveo scleral pathway accounts for 10-25% of total aqueous drainage. It forms the pressure independent pathway where the resistance to outflow occurs due to tone of ciliary muscle. Aqueous humour enters the ciliary muscle through the uveo scleral meshwork, ciliary body face and iris root. It passes posteriorly between the bundles of ciliary muscle until it reaches supra ciliary and supra choroidal spaces. It then leaves the eye through the spaces around penetrating nerves and blood vessels through sclera. Uveoscleral drainage is possible only because of pressure gradient of 2-4 mm Hg between suprachoriodal space and aqueous chamber. This pressure difference may be reversed with age or trabeculectomy causing choroidal effusion.

PHYSIOLOGY OF AQUEOUS FORMATION

Aqueous humour is produced by the non pigmented ciliary epithelium of anterior portion of ciliary body.

CILIARY BODY:

Ciliary body is the anterior portion of uveal tract located between iris and choroid. Anterior portion of ciliary body, Pars plicata is characterized by ciliary processes consisting of 70 radial ridges which forms the major site of aqueous formation. Posterior portion of ciliary body, Pars plana which is relatively flat and has pigmented inner surface and becomes continuous with the choroid at oraserrata. Ciliary body is composed of muscle, vessels and epithelium.[2]

Ciliary muscle:

Ciliary muscle consists of three types of muscle fibers:

- Outer longitudinal muscle fibers:

  Longitudinal muscle fiber gets attached to scleral spur whose contraction causes opening of trabecular meshwork and Schlemm's canal thereby increasing the aqueous outflow facility.

- Inner circular muscle fibers:

  Contraction of circular muscle fibers helps in accommodation by relaxing the lens zonules thereby increasing the axial diameter of lens and its convexity.

- Middle oblique muscle fibers:

  Contraction of oblique muscle fibers widens the uveal trabecular space.

Ciliary vessels:

Ciliary body is supplied by Major arterial circle of Iris formed by the long posterior ciliary artery(a branch of Ophthalmic artery) along with anterior ciliary artery.[3]

Ciliary epithelium:

Ciliary body is lined by two layers of epithelium.

- Outer pigmented epithelium which is composed of low cuboidal cells and become continuous with retinal pigment epithelium posteriorly.
- Inner non pigmented epithelium which is the major site of aqueous humour is continuous with the neurosensory retina posteriorly and pigmented iris epithelium anteriorly.

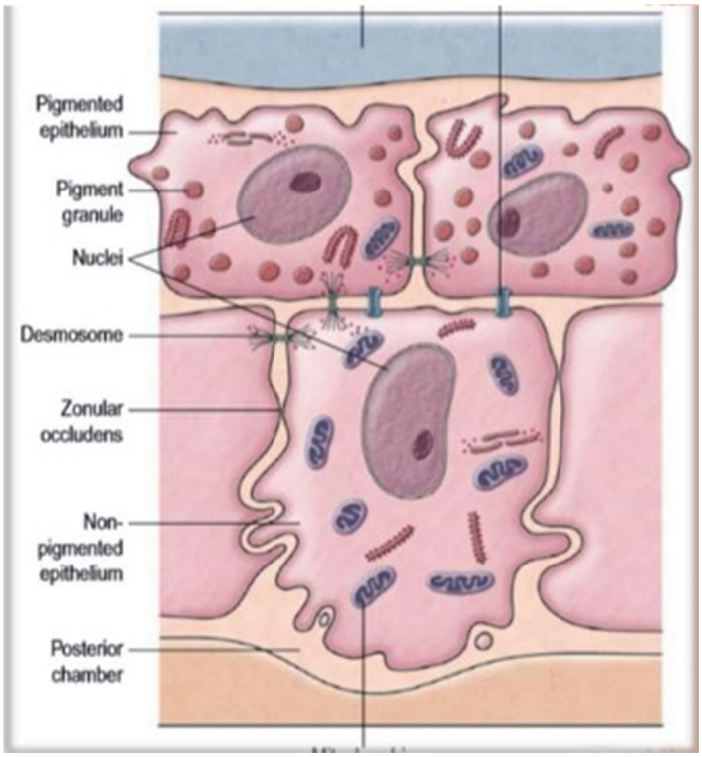


Figure 4

Aqueous humour is primarily derived from the plasma within the capillary network of ciliary processes. Three physiological processes contribute to the formation of aqueous humour and its chemical composition. These include:

- Ultra-filtration----20%
- Active transport---70%
- Diffusion---10%

ULTRAFILTRATION:

Ultrafiltration denotes the process by which fluid and its solutes crosses the semipermeable membrane under the pressure gradient. Water and water soluble substances, limited by size and charge , flow into the stroma of ciliary processes from the capillaries. As blood passes through the capillaries of the ciliary processes, about

4% of the plasma filters through the fenestrations in the capillary wall into the interstitial spaces between capillaries and the ciliary epithelium. The high concentration of colloid in the tissue spaces of ciliary processes favours the movement of water from the plasma into the ciliary stroma but retards the movements from ciliary stroma into posterior chamber.[2]

ACTIVE TRANSPORT:

Active transport or secretion is an energy dependent process that selectively moves a substance against its electrochemical gradient across a cell membrane. The majority of aqueous humour formation depends on ion or ions being actively secreted into the intercellular clefts of the non pigmented ciliary epithelium beyond the tight junctions.

In the small spaces between the epithelial cells, the secreted ion or ions create sufficient osmotic forces that attracts water into the spaces. Water soluble substances of larger size or greater charge are actively transported across the non pigmented epithelium. Current evidence suggests that the paired Na/H and Cl/HCO transports Na/Cl from the stroma into the cell.[3] Main ion to be actively transported across the non pigmented epithelium include Sodium, Chloride, Bicarbonate. Active transport of Na+ plays a key feature in the formation of aqueous humour. Active of transport of water occurs through aquaporin channels in the basolateral membrane of non pigmented epithelium.

DIFFUSION:

Diffusion is the process by which the substances move across the membrane along its concentration gradient. As aqueous humour passes from the posterior

chamber into the anterior chamber, sufficient diffusional exchange with surrounding tissues occur so that the aqueous in the anterior chamber resembles plasma more closely than the posterior aqueous humour. Aqueous humour provides glucose, amino acids, oxygen and potassium to the surrounding tissues and removes carbon dioxide, lactate and pyruvate.

BLOOD AQUEOUS BARRIER:

The blood aqueous barrier consists of all of the barrier to the movement of substances from the plasma into the aqueous humour. It is formed by the tight junctions between the apical portions of the cells of non pigmented epithelium of ciliary body and also by the tight junctions between the endothelial cells of iris capillary. In some situations (eg: intraocular infection), a breakdown of blood aqueous barrier is clearly therapeutic because it brings mediators of cellular and humoural immunity to the interior of eye. In other situations (eg: some forms of uveitis and following trauma), the breakdown of the barrier is inappropriate and favours the development of complications such as cataract and synechiae formation. This barrier is not absolute, as medium sized water soluble substances may penetrate it but at a much slower rate. Lipid solubility greatly facilitates ability of substance to penetrate blood ocular barrier.[6,8]

STEPS OF AQUEOUS FORMATION:

Formation of stromal pool:

It is the first step in the formation of aqueous humour. By ultra filtration, most substances pass across the stroma between the pigment epithelium cells before

accumulating behind tight junctions of non pigmented epithelium. Protein is left in the filtrate because of the fenestrated nature of ciliary capillaries.

Active transport of stromal infiltrate:

The net effect of ion transport system located in the pigmented and non pigmented ciliary epithelium are:

- Low level of sodium in both epithelial cell layers.
- High level of potassium and ascorbate.
- Control of intracellular pH

Passive transport across non pigmented ciliary epithelium:

Active transport across non pigmented ciliary epithelium results in osmotic and electrical gradient. To maintain the balance of osmotic and electric forces, water, chloride and other small plasma constituents move into posterior chamber by ultra filtration and diffusion.

Composition of aqueous humour of anterior and posterior chamber differs because of constant metabolic interchange during intraocular course and diffusional exchange across iris is a significant factor, since iris vessels are permeable to anions.[6] The striking differences are bicarbonate in posterior chamber is higher because the freshly secreted fluid has a much higher concentration and due to diffusion into the vitreous and into the blood from iris and decomposition by the acids formed by the lens and cornea metabolism, its level decreases in the anterior aqueous. Chloride concentration in the newly formed aqueous is lower because diffusion of chloride

from the blood raises the chloride level in anterior chamber. Ascorbate concentration of posterior chamber is higher because diffusion of ascorbic occurs in anterior chamber.

FACTORS AFFECTING AQUEOUS HUMOUR FORMATION:

- **Diurnal fluctuation:** Aqueous flow is higher in the morning than in the afternoon. The rate of aqueous formation during sleep is approximately one half the rate upon first awakening.
- **Age and sex:** Appears to be similar in males and females. There is a reduction in aqueous formation with age, particularly after 60 years. Decline in aqueous production occurs at a rate of about 3.2% per decade in adults.
- **Intraocular pressure:** Aqueous humour formation increases or decreases to the changes in intraocular pressure.
- **Neural control:** Stimulation of cervical sympathetic chain decreases aqueous humour formation.

FACTORS AFFECTING INTRAOCULAR PRESSURE:

Normal intraocular pressure is defined as that pressure that does not lead to damage of optic nerve head. This cannot be expressed in precise numerical terms, such that all eyes do not respond the same to given pressure levels.[1]

Three main factors determining intraocular pressure include :

- Rate of aqueous humor formation
- Resistance to aqueous outflow across trabecular meshwork
- Episcleral venous pressure

Factors causing long term influence on Intraocular Pressure:

1. **Genetics**: The IOP appears to be under hereditary influence within the general population, through a polygenic, multifactorial mode of inheritance.[4]

2. **Age**: There is an increase in IOP with increasing age due to changes occurring in the extracellular matrix of the ageing eye.

3. **Gender**: IOP is equal between the sexes in the age group of 20-40years. In older age groups, there is apparent increase in mean intraocular pressure with age is greater in women.[2]

4. **Refractive error**: A positive correlation exists between intraocular pressure with both axial length of the globe and increasing degrees of myopia.

5. **Ethnicity**: Blacks have higher intraocular pressure than whites.

Factors causing short term influence on intraocular pressure:

1. **Diurnal variation**: The intraocular pressure is being subject to cyclic fluctuations throughout the day. The reported mean amplitude of daily fluctuation of intraocular pressure ranges from approximately 3mm Hg to 6 mm Hg. An increase in amplitude greater than 10 mm Hg is generally considered significant.[1]Many people have their peak pressures in the morning hours, but others have in the afternoon, in the evening or during sleep. The primary clinical importance of measuring diurnal IOP variation is to avoid the risk of missing an elevation in intraocular pressure with single readings. The

intraocular pressure is being recorded 6 times during the day at fourth hourly intervals and the graph is plotted connecting all points. No peak exceeding 21 mm Hg confirms the diagnosis of normal tension glaucoma.

2. **Postural variation**: The intraocular pressure increases from sitting to the supine position with reported average differences of 0.3-6 mm Hg in glaucoma patients**.** Positional increase in intraocular pressure is high in normotensive glaucoma patients.
3. **Exertional influence**: Prolonged exercise such as running lowers the intraocular pressure. Valsalva maneuver increases the intraocular pressure by increasing the episcleral venous pressure.
4. **Lid movement**: Blinking has been shown to increase the intraocular pressure.
5. **Intraocular pathology**: Anterior uveitis and retinal detachment are associated with a reduced IOP due to associated choroidal detachment.
6. **Systemic disorders**: Systemic hypertension and hyperthermia causes increased intraocular pressure. Hyperthyroidism is associated with lower intraocular pressure and hypothyroidism with increased intraocular pressure. Diabetes is associated with higher intraocular pressure than the normal population.[6,7,8]
7. **Environmental conditions**: Cold exposure causes reduction in intraocular pressure.
8. **Anaesthetic agents**: General anaesthetics causes reduction in intraocular pressure. Certain drugs like Ketamine and Succinyl choline cause transient rise in intraocular pressure.

9. **Others**: Alcohol and Heroin causes decrease in intraocular pressure whereas LSD and corticosteroids causes raise in intraocular pressure.

ANATOMY OF OPTIC NERVE HEAD:

Optic nerve head is defined as the distal portion of the optic nerve that is directly susceptible to intraocular pressure elevation. The optic nerve head extends anteriorly from the retinal surface to the myelinated portion of the optic nerve that begins just behind the sclera, posterior to lamina cribrosa. The term disc and papilla are frequently used when referring to the portion of optic nerve head that is clinically visible by ophthalmoscopy.[1]It is the optic nerve head and nerve fiber layer containing retinal ganglion cell axons that are most clearly associated with glaucomatous vision loss.

The optic nerve head comprises the nerve fibers that originate in the ganglion cell layer of the retina and converge upon the nerve head from all points in the fundus. At the surface of the nerve head, these retinal ganglion cell axons bend acutely to exit the globe through a fenestrated scleral canal called the lamina cribrosa. In the nerve head, the axons are grouped into approximately 1000 fascicles or bundles and supported by astrocytes. The surface area of optic disc ranges from 2.69± 0.70 mm^2 and that of optic cup ranges from 0.73± 0.59 mm^2.[5] The shape of optic disc is vertically oval whereas that of optic cup is horizontally oval. The neuroretinal rim is broadest at the inferior pole, followed by superior, nasal and temporal pole (ISNT rule). Deviation from this pattern denotes glaucomatous damage.

The cup area had stronger correlation with the disc area than the rim area, suggesting that correction for disc size may be more important for cup area than for rim area. There is also a positive correlation between the optic disc size and the thickness of the peripapillary retinal nerve fiber layer. The diameter of the nerve expands to approximately 3mm just behind the sclera, where the neurons acquire a myelin sheath. The optic nerve head is also the site of entry and exit of the retinal vessels. This vascular system supplies some branches to the optic nerve head, although the predominant blood supply for the nerve head comes from the ciliary circulation.

The optic nerve head may be divided into four portions from anterior to posterior:

Surface Nerve Fiber Layer

The innermost portion of the optic nerve head is composed predominantly of nerve fibers.This layer contains 94% retinal ganglion cell axons and 5% astrocytes. The axonal bundles acquire progressively more interaxonal glial tissue in the intraocular portion of the nerve head as this structure is followed posteriorly.

Prelaminar Region

The prelaminar region is also called the anterior portion of the lamina cribrosa. The predominant structures at this level are nerve axons and astrocytes, with a significant increase in the quantity of astroglial tissue.

Lamina Cribrosa Region

This portion contains fenestrated sheets of scleral connective tissue and occasional elastic fibers. Astrocytes separate the sheets and line the fenestrae, and the fascicles of neurons leave the eye through these openings.

Retrolaminar Region

This area is characterized by a decrease in astrocytes and the acquisition of myelin that is supplied by oligodendrocytes. The axonal bundles are surrounded by connective tissue septa. The posterior extent of the retrolaminar region is not clearly defined.

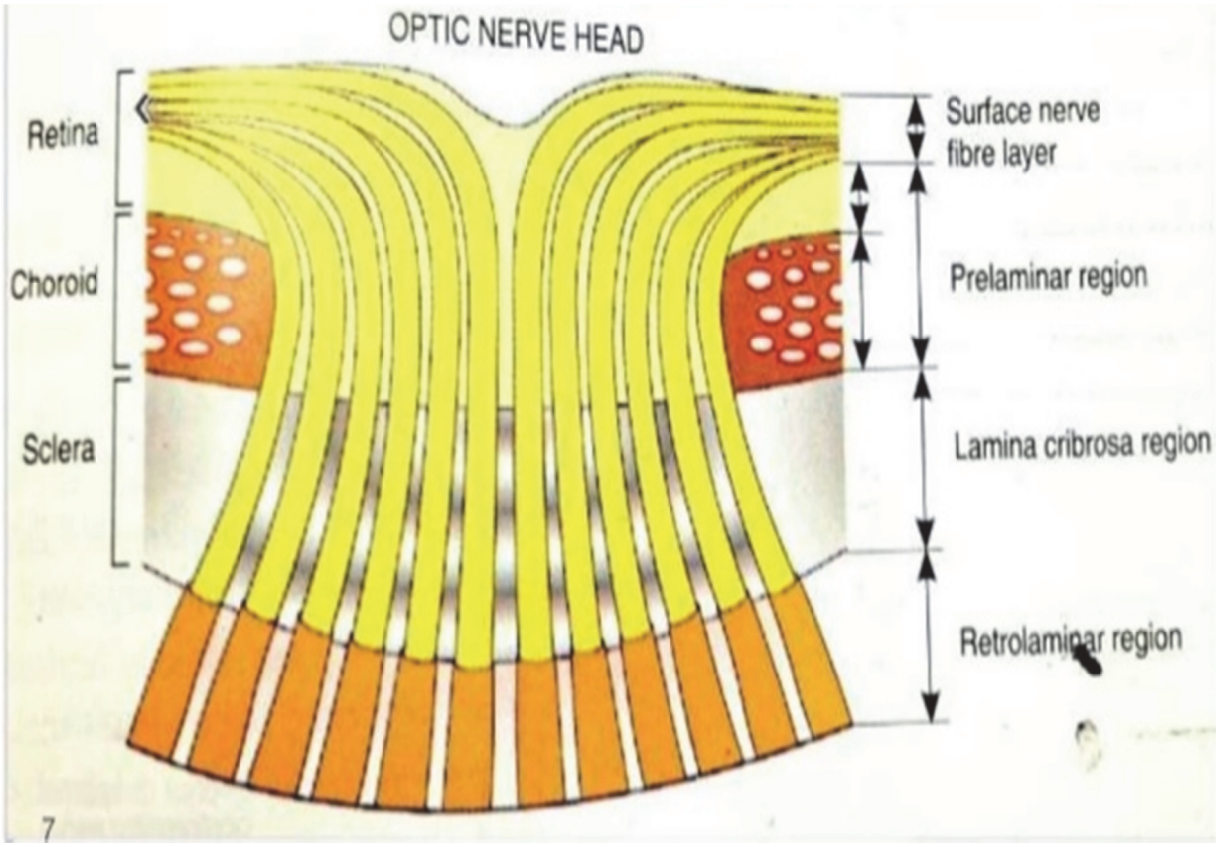


Figure 5

Peripapillary retina:

Retinal nerve fiber layer is seen as striations in the light reflexes from the bundles of nerve fiber commonly seen with red free light either on direct ophthalmoscope or on fundus camera. Retinal nerve fiber layer is seen better at the posterior pole in the peripapillary region where they reach a critical thickness especially at the vertical poles of optic nerve head.[21]

Grey crescent:

Grey crescent is seen within peripheral tissues of optic nerve head. Scleral lip is seen peripheral to the gray crescent. It is often bilateral and it is usually located along the temporal or inferotemporal disc margin. Grey crescent is due to internal extension of Bruch's membrane in the peripapillary scleral ring.

Zone beta:

Zone beta is seen between peripheral neuroretinal rim and zone alpha. It represents a retraction of retinal pigment epithelium from the disc margin due to atrophy of retinal pigment epithelium. Sclera and large choroidal vessels are visible due to RPE atrophy. It is more frequent and more extensive in patients with Primary Open Angle Glaucoma and Normotensive Glaucoma. Location and extent of zone beta atrophy correlates with visual field loss. It indicates that the area has poor perfusion.[2]

Zone alpha:

Zone alpha is better detected at the temporal disc margin. On the inner side, it is bounded by zone beta or peripapillary scleral ring and on the outer side by retina. It

is seen as irregular hyperpigmentation and hypopigmentation. It is due to parapapillary crescent of retinal pigment epithelium irregularity close to margin of Bruch's membrane. It is present in almost all eyes.[2]

BLOOD SUPPLY OF OPTIC NERVE HEAD:

Arterial Supply

Posterior ciliary artery circulation is the main source of blood supply to the optic nerve head, except for the nerve fiber layer which is supplied by the retinal circulation. The blood supply in the optic nerve head has a sectoral distribution. The four divisions of the optic nerve head correlate roughly with a four-part vascular supply.[10]

The surface nerve fiber layer is mainly supplied by arteriolar branches of the central retinal artery, which anastomose with vessels of the prelaminar region and are continuous with the peripapillary retinal and long radial peripapillary capillaries. The temporal region may also be supplied by one or more of the ciliary-derived vessels from the posterior ciliary artery circulation in the deeper prelaminar region, which may occasionally enlarge to form cilioretinal arteries.[13] The cilioretinal artery, when present, usually supplies the corresponding sector of the surface layer.

The prelaminar and laminar regions are supplied primarily by short posterior ciliary arteries, which form a perineural, circular arterial anastomosis at the scleral level, called the circle of Zinn-Haller. Branches from this circle penetrate the optic nerve to supply the prelaminar and laminar regions and the peripapillary choroid. The circle is not present in all eyes, in which case direct branches from the short posterior

ciliary arteries supply the anterior optic nerve. The peripapillary choroid may also minimally contribute to anterior optic nerve .[14]

The retrolaminar region is supplied by both the ciliary and retinal circulations, with the former coming from recurrent pial vessels. Medial and lateral perioptic nerve short posterior ciliary arteries anastomose to form an elliptical arterial circle around the optic nerve, which has also been referred to as the circle of Zinn-Haller. This perioptic nerve arteriolar anastomosis, which supplies the retrolaminar optic nerve, was found to be complete in 75%.[10] The central retinal artery provides centripetal branches from the pial system and frequently, but not always, gives off centrifugal vessels.

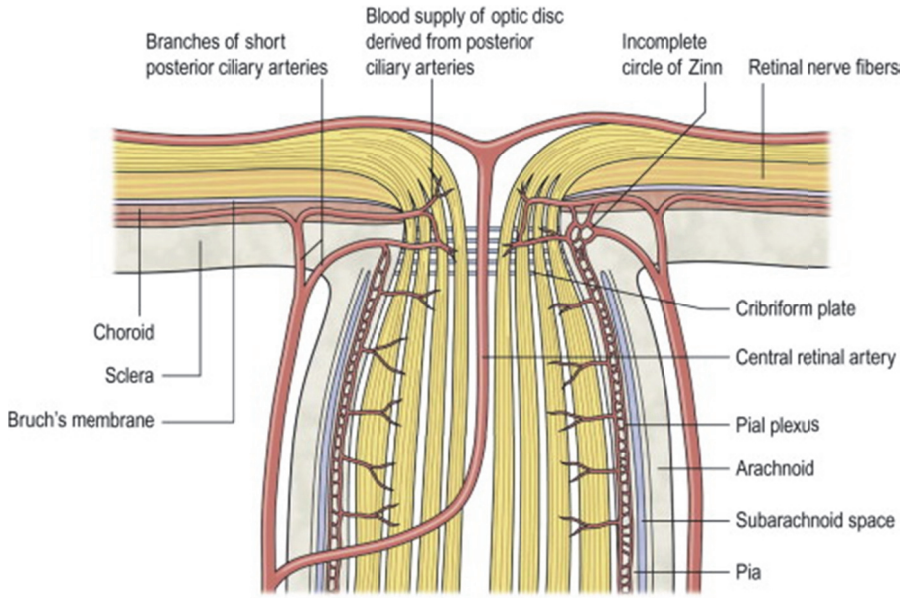


Figure 6

Continuity between small vessels from the retrolaminar region to the retinal surface has been observed, and the optic nerve head microvasculature is said to represent an integral part of the retina-optic nerve vascular system.

Capillaries

Although derived from both the retinal and ciliary circulations, the capillaries of the optic nerve head resemble more closely the features of retinal capillaries than of the choriocapillaris. These characteristics include (a) tight junctions, (b) abundant pericytes, and (c)non fenestrated endothelium. They do not leak fluorescein and may represent a nerve-blood barrier, supporting the concept of the retina-nerve vasculature as a continuous system with the central nervous system. The capillaries decrease in number posterior to the lamina, especially along the margins of the larger vessels.[19]

Venous Drainage

The venous drainage from the optic nerve head is almost entirely through the central retinal vein, although a small portion may occur through the choroidal system. Occasionally, these communications are enlarged as retinociliary veins, which drain from the retina to the choroidal circulation, or cilio-optic veins, which drain from the choroid to the central retinal vein.

PATHOGENESIS OF OPTIC NERVE HEAD CHANGES:

The pathogenesis of glaucomatous optic neuropathy has been attributed to various theories depending on the cause. The various theories include:

The **Mechanical Theory** was proposed by Muller in which the intraocular pressure above the threshold level of optic nerve head resistance distorts the lamina cribrosa leading to backward bowing, stretching and compression of laminar plates and elongation of pores. This results in compression of axonal fibers thereby resulting

in axoplasmic flow stasis leading to death of the axons and glaucomatous optic neuropathy.[19]

Role of intracranial pressure and trans lamina cribrosa pressure difference:

Pressure on anterior part of optic nerve is influenced by intracranial pressure. The lamina cribrosa serves as a barrier between high pressure intraocular space and low pressure retrobulbar CSF space. This difference in pressure is called as trans lamina cribrosa pressure difference. The importance of this pressure difference is:

a) Retinal and choroidal venous blood flows through CSF space, hence increased CSF pressure leads to increased incidence of choroidal thickening and retinal vein occlusion.[13,24]
b) Thin lamina cribrosa as in myopia is associated with steep translamina cribrosa pressure difference that leads to glaucomatous damage.

The **Vasogenic or Ischemic Theory** was proposed by Von-Jaeger. According to this, increased intraocular pressure leads to intraneural ischemia due to decreased optic nerve head perfusion. Optic nerve head perfusion depends on three factors:

1) Blood pressure
2) Intraocular pressure
3) Auto regulatory mechanism

Intraocular pressure fluctuations causes vascular dysregulation which is worse than reduced circulation due to stable elevated intraocular pressure. This leads to reperfusion injury causing death of retinal ganglion cells. The fall of perfusion

pressure causes obliteration of vessels first in the pre laminar and postlaminar region. The pre-laminar and post-laminar region blood flow and the choroid lack the ability of autoregulation.[10]

Neurochemical Theory explains the cause of glaucomatous neurodegeneration. The substances causing degeneration include reactive oxygen species, nitric oxide, excitatory amino acids, caspases, tumour necrosis factor alpha, metalloproteins and neurotrophins. Unstable ocular perfusion, unstable oxygen supply and dysregulation of auto regulation leads to oxidative stress resulting in release of reactive oxygen species within the axons of retinal ganglion cells. Mitochondrial and muller cell dysfunction also leads to imbalance between reactive oxygen species production and detoxification. This imbalance leads to the apoptosis of retinal ganglion cells.

Glymphatic theory:

Altered lamina cribrosa in glaucoma mechanically interferes with glymphatic flow thereby decreasing elimination of neurotoxic substances. Accumulation of neurotoxic substances leads to glaucomatous optic neuropathy.

Characteristics of Glaucomatous Optic Atrophy

Glaucomatous damage results in characteristic signs involving

a) The optic nerve head
b) The peripapillary retina
c) The retinal nerve fiber layer

1. FOCAL ATROPHY

The inferotemporal neural rim area is smaller than the superotemporal area so that the vertical cup disc ratio is more than horizontal cup disc ratio. The focal atrophy of the neural retinal rim often begins as a small discrete defect usually in the inferotemporal quadrant which has been called as the polar notching or focal notching or pit like changes. The temporal rim is typically involved after the involvement of superior and inferior poles, with the nasal quadrant being the last to be involved.

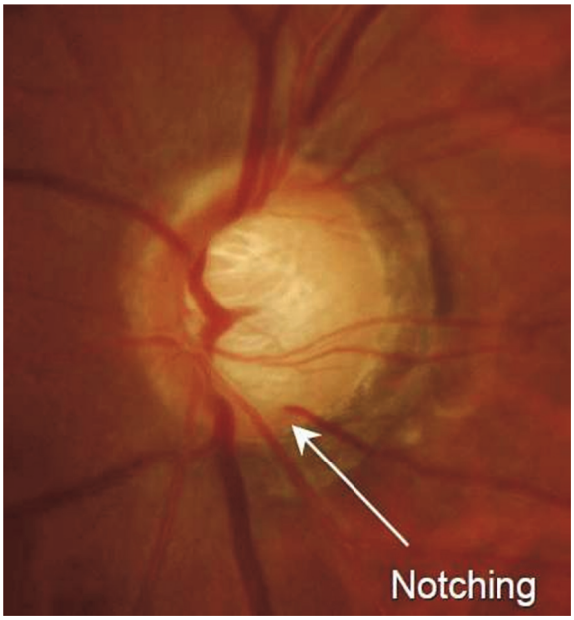


Figure 7

2. CONCENTRIC ATROPHY

Glaucomatous disc damage less commonly results in concentric enlargement of the optic cup with retention of round shape of the cup more often directed inferotemporally or superotemporally. Loss of neuro retinal rim usually begins temporally and then progresses circumferentially towards the poles which is called as

temporal unfolding. It is difficult to distinguish concentric atrophy from physiologic cup, hence it is important to compare the cup in the fellow eye and to study serial photographs for evidence of progressive change.[3,7]

3. DEEPENING OF THE CUP

Exposure of the underlying lamina cribrosa demonstrated by the deepening of the cup seen as the grey fenestra of the lamina is called as the laminar dot sign.

4.PALLOR CUP DISCREPANCY

In early stages of glaucomatous optic atrophy, enlargement of cup progresses ahead of area of pallor. This pattern differs from other types of optic atrophy in which area of pallor is more than the enlargement of the cup. It is important to differentiate area of cupping from area of pallor either by examining the optic disc with stereoscopic techniques or by seeing the kinking of blood vessels at the cup margin. Saucerization refers to a pattern of early glaucomatous change in which diffuse shallow cupping extends to the disc margin with retention of a central pale cup. Focal saucerization refers to more localized shallow sloping cup usually in inferotemporal quadrant. The retention of normal neural rim colour in the area of focal saucerization is known as tinted hollow. As the glaucomatous process continues, this is replaced either by grayish hue known as shadow sign.

5. ADVANCED GLAUCOMATOUS CUPPING

If the progression of glaucomatous optic neuropathy is not arrested by appropriate measures to reduce intraocular pressure, the end result is advanced

cupping which is seen clinically as a white disc with complete loss of neuroretinal rim and bending of all vessels at the margin of the disc. This has been called as bean pot cupping, because the cross section on histological specimen reveals extreme posterior displacement of the lamina cribrosa with undermining of the disc margin.

Vascular Signs of Glaucomatous Optic Atrophy

a. SPLINTER HEMORRHAGES :

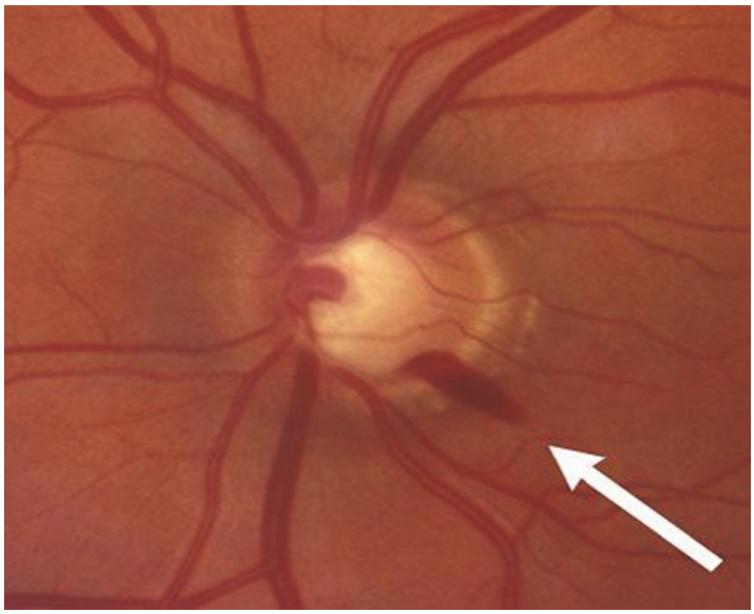


Figure 8

These are present near the disc margin of the optic nerve head and are a common feature of optic nerve damage in glaucoma. They occur more commonly in patients with normal tension glaucoma. First described by Bjerrum in 1899. They are located in the pre laminar area of the optic disc in the superficial retinal layer. They have a waxing and waning course so that they are seen in one visit and disappear in the next, and to be seen in the next visit in the same or another location.[7]The most common location is the inferotemporal quadrant, most often seen in the early to

middle stages of glaucoma. Although not pathognomic sign of glaucoma, splinter haemorrhage are a significant finding as they often precede nerve fiber defects, polar notching and visual field defects. Risk factor of development of disc haemorrhage appears to be a thin neuroretinal rim. They are also seen in conditions in patients with diabetes, pseudoexfoliation and increased vertical cup. It should be viewed as a sign of glaucoma progression.

b. BARING OF THE CIRCUMLINEAR VESSEL:

In most of normal optic nerve head , one or two blood vessels may curve to outline a portion of the physiological cup. With glaucomatous enlargement of the optic cup, these circumlinear vessels may be barred from the margin of the cup. This sign is not pathognomic of glaucoma but it's presence in glaucoma suspect patients is associated with visual field loss.

c. NASALISATION OF VESSELS

Nasalization is the nasal displacement of the retinal vessels on the optic disc is not pathognomic sign of glaucoma.

d. BAYONETING OF THE VESSELS

If a retinal vessel crosses the sharpened rim , it will cause bending at the edge of the optic disc creating the bayoneting sign.

Retinal nerve fiber bundle defects:

The loss of axonal bundles in glaucoma lead to loss of neural rim tissue and visible defects in retinal nerve fiber layer. These defects appear as dark stripes or

wedge shaped defects in peripapillary region and diffuse loss of retinal striations. They often follow disc haemorrhages and correlate highly with visual field defects and lost neural rim tissue. They are also seen in many neurological disorders, ocular hypertension. Diffuse nerve fiber defects occur in following order of decreasing frequency: Chronic open angle glaucoma > ocular hypertension > normotensive glaucoma. These defects either localized or diffuse may be the initial sign of glaucomatous disc damage.

VISUAL FIELD LOSS IN GLAUCOMA

PERIPHERAL LOSS

Defects along the peripheral boundaries of the visual field (i.e., peripheral nasal steps, vertical steps, and temporal sector defects) are most often found in association with scotomas in the more central arcuate area, although in some patients with early glaucomatous visual field loss, peripheral defects may be the only detectable abnormality. In the initial diagnosis, however, a peripheral field defect, usually a nasal step, may be the only abnormality detected by automated perimetry.

LOCALIZED NERVE FIBER LAYER DEFECTS

In glaucoma, structural damage to ganglion cells and their axons causes partial or complete functional loss in the area of damaged cells. The glaucomatous process typically causes initial damage to one or more axon bundles, creating a localized visual field defect. Focal defects, due to loss or impairment of retinal nerve fiber bundles, constitute the most definitive early evidence of visual field loss from

glaucoma. The nature of the nerve fiber bundle defects relates to the retinal topography of these fibers.

1)Arcuate Defects

Bjerrum described an arcuate visual defect called as arcuate scotoma starts from the blind spot and arches above or below fixation, or both, to the horizontal median raphe, corresponding to the arcuate retinal nerve fibers. Early visual loss in glaucoma commonly occurs in this arcuate area, especially in the superior half. Occasionally, the early arcuate defect may connect with the blind spot and taper to a point in a slightly curved course, which has been referred to as a Seidel scotoma. As the isolated defects enlarge and coalesce, they form an arching scotoma that eventually fills the entire arcuate area from the blind spot to the median raphe, which is called an arcuate or Bjerrum scotoma. With further progression, a double arcuate (or ring) scotoma develops. The rate of visual field loss correlates with the size of the scotoma, in that, the larger the scotoma, the more rapidly it is likely to enlarge. Although the arcuate defect is probably the most reliable early form of glaucomatous field loss, it is not pathognomonic.

2)Nasal Steps

A step like defect is frequently created where the nerve fibers meet along the median raphe. Because the superior field is involved somewhat more frequently than the inferior portion in the early stages of glaucoma, the nasal step more often results from a greater defect above the horizontal midline, which is referred to as a superior nasal step. Unequal contraction on the peripheral side of the defect, due to loss of

corresponding bundles of peripheral arcuate nerve fibers, produces a defect called the peripheral nasal step of Ronne. Nasal step appears to be a common defect in acute and early chronic angle-closure glaucoma .

3)Vertical Step

A stepwise defect along the vertical midline, referred to as a vertical step or hemianopic offset, is a less common feature of glaucomatous field loss. The defect more often appears on the nasal side of the vertical midline . It has been suggested that a small peripheral step at the vertical midline should arouse suspicion of glaucoma only if the defect is located temporally.

GENERALIZED AND CENTRAL DEPRESSION OF THE VISUAL FIELD

Although defects related to loss of retinal nerve fiber bundles are the most familiar visual field changes induced by glaucoma, and central vision is typically one of the last regions to be totally lost, mild central and diffuse reduction in the visual field occurs even in the early stages of glaucoma. The mechanism is pressure-induced damage with diffuse nerve fiber loss. Central vision is typically preserved in the early course of glaucoma, but rarely it may be affected by a localized damage involving the fixation point.

CONCENTRIC CONTRACTION

Generalized reduction in the visual field may become manifest as a decrease in sensitivity for specific retinal locations or as a concentric constriction of the visual field, both of which precede other detectable glaucomatous field defects. Isopter

contraction, as an early field defect of glaucoma, is often more marked in the nasal field, which has been called “crowding of the peripheral nasal isopters”.

ENLARGEMENT OF THE BLIND SPOT

Enlargement of the blind spot, due to depression of peripapillary retinal sensitivity, is also considered to be an early glaucomatous field change.

NORMOTENSIVE GLAUCOMA

Normotensive glaucoma is characterized by open, normal appearing anterior chamber angle with glaucomatous optic nerve head and visual field damage despite pressure that have never been documented above 21 mm Hg in the absence of any contributing ocular or specific systemic disorders. The low tension glaucoma is a monomer because intraocular pressure is usually at the upper end of the normal range. Prevalence of normotensive glaucoma is most common in Japanese population. Most common in females with Male: Female ratio of 1:2. According to Beaver Dam Eye study, prevalence of normotensive glaucoma increases from 0.2% in 43- 54 years of age to 1.6% in 75 years. Positive family history is seen in 5%-40% of persons with normotensive glaucoma.

Even with normal intraocular pressure, glaucomatous damage occurs because this pressure is too high for the eye to cause the damage. This occurs because of less support due to poor development of laminar architecture. Axonal loss occurs years before noticeable alterations in visual fields.[15]Prognosis is worse in females, patients with migraine or peripheral vascular disease. Neurological evaluation is done in case of pale disc without typical cupping, suspicious neurological pattern of visual field or

one that progresses unexpectedly. During 2-10 year follow up with 4-6 months interval, progression is seen in 40-60% of eyes in a step wise manner.

Differentiating feature of Normotensive glaucoma:

a) Neuroretinal rim is usually thinner at inferior and inferotemporal quadrants.
b) Optic disc splinter haemorrhage is usually more prevalent suggesting vascular disease as a risk factor. Its presence indicates progression or poor control of intraocular pressure.
c) Halo or crescent around the disc due to the absence of retinal pigment epithelium. Optic disc cupping is worser in the region of the crescent.
d) Acquired optic disc pits are more common due to focal loss of neuroretinal rim shown as localized excavation of lamina cribrosa.
e) Retinal nerve fiber defects are usually localized, deeper and closer to fixation usually within 5° of fixation.
f) Visual field defects are deeper and have localized scotomas. Increase in area and depth remains in constant proportion in normotensive glaucoma whereas in high tension glaucoma there is increase in area initially and later in depth.
g) Eyes with asymmetric intraocular pressure will have visual field loss worser in eyes with high intraocular pressure.[18]

Clinical presentation:

Resembles primary open angle glaucoma except for elevated intraocular pressure. Associated with wide diurnal variation usually with nocturnal spikes and

postural fluctuations in intraocular pressure. Classified into four types based on the morphology of optic disc

1) **Focal ischemic:**

This involves focal loss of neuroretinal rim characterized by notching in the superior or inferior pole and associated with localized dense arcuate field defects. This focal notching is usually associated with peripapillary atrophy or choroidal sclerosis. It is caused by vascular dysregulation.

2) **Myopic glaucomatous:**

Tilted or obliquely placed disc with loss of neuroretinal rim in superior or inferior pole associated with temporal myopic crescent.

3) **Senile sclerotic:**

Saucerised shallow cup with gentle sloping sides characterized by moth eaten appearance. Usually associated with cardiovascular risk factors and systemic atherosclerosis.

4) **Glaucomatous with generalized enlargement of optic cup:**

Uniformly enlarged round cup with no localized loss of neuroretinal rim.

Based on the progression, they are classified into two types:

1) **Non progesssive:**

Usually associated with transient episode of vascular shock. Observation and follow up is adequate with intervention needed once progression is noted.

2) **Progressive:**

Most common form associated with chronic vascular insufficiency of optic nerve head.

DIFFERENTIAL DIAGNOSIS:

PSEUDOGLAUCOMA:

Large physiological cupping

Congenital

Optic nerve anomalies-pits and oblique insertion

Autosomal dominant optic atrophy

Acquired

Ischemic optic neuropathy

Orbital mass leading to atrophy

Branch retinal vein occlusion

HIGH PRESSURE GLAUCOMA:

Inaccurate tonometry leading to false low reading

Variable intraocular pressure due to diurnal variations

Previous elevation of intraocular pressure

History of trauma

Steroid induced glaucoma

Pigmentary glaucoma

Chronically intermittent angle closure

Chronic primary open angle glaucoma

SPECIAL FORMS OF GLAUCOMA:

Shock induced optic neuropathy

Hemodynamic crisis

Optic neuritis

ASSOCIATED RISK FACTORS

Reduced blood flow in the blood vessels supplying the optic nerve head is considered to be a risk factor in the progression of glaucoma especially normotensive glaucoma.[14] Blood flow depends on various factors like systemic blood pressure, intraocular pressure, vascular resistance of the blood vessels and its autoregulatory mechanism. Viscosity and coagulability of blood constituents also have effects on tissue perfusion. Vascular disease causes reduction of optic nerve resistance to pressure induced damage in glaucoma. Local optic nerve blood flow abnormalities causes associated functional deficits in visual fields. Also concomitant changes of nocturnal blood pressure and intraocular pressure may affect the perfusion to optic nerve head.

The risk factors are classified as

1. Pressure independent factors
2. Pressure dependent factors

PRESSURE INDEPENDENT FACTORS

Abnormal blood flow

Systemic hypotension

Abnormal blood coagulability

Optic nerve damage due to above factors include ischemia, interruption of rapid orthograde and retrograde axonal transport, increased free radicals, trigerring of apoptosis and collapse of support provided by lamina cribrosa.

Abnormal blood flow:

The diameter of the blood vessel supplying the optic nerve is affected by vasospasm and its association with normotensive glaucoma describes the pathogenesis of damage in case of migraine and peripheral vascular disease. This leads to increased resistance in blood vessels leading to decreased perfusion of optic nerve head thus contributing to the optic neuropathy. These patients also have diffuse cerebral ischemia in neuroimaging.

Systemic hypotension:

Greater nocturnal decrease and lower level of diastolic blood pressure plays an important role in perfusion pressure of optic nerve head. 24 hour ambulatory blood pressure monitoring is necessary in these patients to assess the deteriorating visual

fields and those on anti hypertensives. Hence in these patients night dose of anti hypertensives should be avoided.[17]

Abnormal coagulability profile:

Hypercoagulability states with activation of coagulation pathway and increased red cell aggregability leads to decreased blood flow resulting in decreased perfusion. This is assessed by laser Doppler velocimetry.

Other factors:

Other factors affecting the perfusion of optic nerve head include

- Hypotensive shock with episodes of severe blood loss and associated cardiovascular risk factors.
- Carotid artery occlusive disease
- Focal arteriolar narrowing around optic nerve head
- Increased vascular resistance of ophthalmic artery
- Sleep apnoea

PRESSURE DEPENDENT FACTORS:

Although intraocular pressure remains normal, it is a risk factor in the development and progression of the disease process. Hence therapeutic reduction of intraocular pressure is necessary to slow the rate of progression.

Autoregualtion of blood flow:

Regulation of blood flow in a tissue occurs when condition changes so that the alterations are made to ensure that the blood flow is appropriate and adequate to the needs. Auto regulation is a physiological response in which mechanical or chemical factors within a tissue influence the blood flow within that tissue. This is done by altering the tone in blood vessel and thereby changing the resistance to blood flow. Variations in autoregulation is responsible for the individual variation in the susceptibility of the optic nerve head to varying degrees of intraocular pressure. Inadequancy in the autoregulation of blood flow leads to ischemia of optic nerve when intraocular pressure is elevated. This is deficient in patients with glaucoma making the optic nerve circulation susceptible to intraocular pressure.[10]

The increased intraocular pressure challenges the circulation in optic nerve head by elevating the venous pressure at the exit point from the eye thereby resulting in vascular compromise. But in normal persons, circulation of optic nerve head is maintained due to autoregulation. Autoregulation is effective upto 30mm Hg and partially effective upto 40mm Hg in normal subjects. Deficient or variation in autoregulation is the pathogenesis in glaucoma.

The role of arteries and veins in regulation of blood flow is extensively studied. Capillaries also contribute the regulation of blood flow by means of contractile unit called pericytes. These pericytes are found in abundant quantity in optic nerve and retina responsible for maintaining the tone of blood vessels by its contractile properties.

Microvascular autoregulation:

Local physical or chemical condition affects the contractile cell either directly or indirectly through the release of local hormone produced by endothelium in response to local circumstances. Microvascular autoregulation occurs by adjusting the vascular tone of blood vessel in response to local conditions. Regulation of vascular tone is important in view of maintaining the control of capillary intraluminal pressure and tissue pressure by adjusting the volume of blood that enters or leaves the tissue per unit of time. These adjustments are made by means of shear stress, stretch and by signs of metabolic state of the tissue.

Myogenic autoregulation:

Myogenic autoregulation is response to physical stimulus and metabolic regulations to chemical conditions of the environment.

Metabolic autoregulation:

Blood flow to optic nerve head increases when eyes see a flickering light due to increased metabolic needs of the optic nerve. Likewise conditions like hyperoxia, hypoxia and hypercapnia induce a regulatory change of blood flow in the optic nerve and retina without any change in the transmural pressure of the arteries or perfusion pressure.In tissues with autoregulation, flow is adjusted according to the metabolic needs of the tissues by means of precapillary sphincter and by changes in the resistance of the capillaries. In glaucoma the pericytes become less responsive to the metabolic changes thereby affecting auto regulation. Auto regulation becomes inadequate in patients with concurrent vascular conditions like hypotension and

atherosclerosis. The ability of the blood vessels to dilate in a vasospastic vessel seen in conditions like Migraine also leads to decreased perfusion of optic nerve head.

Central corneal thickness

Central corneal thickness alters the measured intraocular pressure. Increased central corneal thickness causes falsely raised intraocular pressure whereas decreased thickness causes falsely low intraocular pressure. Hence measurement of intraocular pressure is important before diagnosing glaucoma.

EVALUATION OF NORMOTENSIVE GLAUCOMA

Normotensive glaucoma is usually diagnosed by abnormal disc appearance in absence of elevated intraocular pressure. This leads to delay in the diagnosis with advanced glaucomatous damage. Diurnal curve measurements to rule out pressure spikes is necessary in diagnosis of normotensive glaucoma.

Other routine investigations like gonioscopy, measurement of central corneal thickness, fundus examination with +90 D lens, visual field examination by automated perimetry.

Fundus fluorescence angiography shows diffuse and focal hypofluorescence of disc.

OPTICAL COHERENCE TOMOGRAPHY:

Optical coherence tomography is a non invasive cross sectional diagnostic imaging modality that uses low coherence infrared diode laser to produce a highly accurate structural representation of the retina and the posterior segment tissues.

Peripapillary retinal nerve fiber layer analysis is the most commonly used scanning modality in the diagnosis and management of glaucoma. Other modalities include ganglion cell analysis, OCT angiography and anterior segment OCT.[38]

Spectral Domain OCT is an ultra high speed system that acquires depth profiles at a wavelength of 840nm at the speed of 10,000 to 30,000 scans per second with higher axial resolution of 5μm when compared to Time domain OCT with axial resolution of 10 μm. Swept Source OCT applies short cavity swept laser instead of diode laser with increasing imaging depth by using wavelength of 1050nm. High resolution imaging of deep structures like choroid and lamina cribrosa are easily measured.[35]

Peripapillary retinal nerve fiber layer

Peripapillary retinal nerve fiber layer assessment is the quantitative and objective method to detect the generalized and focal nerve fiber defects. The results are compared with the normative data. It is used in the detection of early cases and also in follow up to assess the progression of the disease process.

Optic nerve head

Evaluation of optic nerve head by spectral domain OCT uses protocol of 193 B scans centered on optic nerve head covering an area of 6 mm^2. The various parameters measured include disc and rim area(mm^2), cup disc ratio, vertical cup disc ratio, cup volume(mm^3).

Retinal ganglion cell layer

Fifty percent of the retinal ganglion cells reside in the macular area. Assessment of macular retinal ganglion cell helps in early detection of glaucoma even before retinal nerve fiber layer defects are detected. Hence macular retinal ganglion cell layer is found to be superior or equivalent to assessment of retina nerve fiber defects.

Lamina cribrosa

Lamina cribrosa remains an area of interest in the pathogenesis of glaucoma. Imaging of lamina cribrosa by enhanced depth imaging or swept source OCT shows parameters like morphology, posterior displacement, thickness and focal defects of lamina cribrosa.

OCT angiography

OCT angiography is used to assess the peripapillary blood flow velocity in glaucoma patients to assess the perfusion of optic nerve head.

Anterior segment OCT

Anterior segment OCT measures the anterior chamber structures quantitatively and qualitatively.

HEIDELBERG RETINAL TOMOGRAPH

Heidelberg Retinal Tomograph detects worsening in optic neuropathy before it is reflected on the visual field.It is divided into 6 sectors-superonasal, superotemporal, nasal, temporal, inferonasal, inferotemporal to assess the early signs of glaucoma progression. These sectors are related to thicker retinal nerve fiber layer.

It compares rim area to the predicted rim area for a given disc area and age. It is termed as normal when it falls within 95% confidence interval, borderline if it falls within 95-99.9% and abnormal if it is outside the normal limits which is >99.9% confidence interval. Detection of progression is by Moorfield linear regression analysis.[32,35]

COLOUR DOPPLER IMAGING:

Colour Doppler imaging is a non invasive technique based on back scattering of ultrasound by formed elements in blood vessels used in quantitative measurement of blood flow velocity.[11] It uses simultaneous B scan and Doppler imaging to identify and locate orbital blood vessels like Ophthalmic artery, Central Retinal Artery, Posterior ciliary artery, Central retinal vein, Superior ophthalmic vein and vortex vein. By this technique, pulsatile blood flow velocity is measured but accurate diameter of the vessels cannot be calculated. Hence volume blood flow cannot be measured.[14]

Optic nerve head perfusion is directly related to retrobulbar circulation which is easily accessible to ultrasound. This makes colour Doppler imaging a potential tool for diagnosing early changes in vascular flow related to glaucoma. Doppler effect results in frequency shifts whose measurements is used to assess the blood velocity.[11]

Colour Doppler imaging visualizes the flow within the vessels. Sample volume is placed over the centre of vessel and to set the angle it is placed parallel to the vessel. This makes in accurate quantification of flow characteristics of vessels. Sample volume depth is set at about 4 mm for ophthalmic artery. A sample gate of < 2 mm is placed at the centre of the detected vessel to image the spectral pattern. Blood

flow towards the transducer is arterial and viewed as red, whereas away from the transducer is venous and viewed as blue.

Peak systolic velocity, end diastolic velocity and resistance index are the parameters measured using this technique. Peak systolic velocity is obtained by taking the velocity reading at the peak of spectral wave pattern, whereas end diastolic velocity is measured at the wavetrough. Resistance index is calculated by Pourcelot's formula which is

RI=(Peak systolic velocity- end diastolic velocity)/ Peak systolic velocity.

Resistance index is the most reproducible parameter having the advantage over others because it includes both systolic and diastolic velocity. Ophthalmic artery, central retinal artery and short posterior ciliary artery provides evidence of influence of vascular factors in the pathogenesis of glaucomatous optic neuropathy.[22] Ophthalmic artery is the main source of blood supply to optic nerve. Central retinal artery is the main source to retina and short posterior ciliary artery along with small contributions from plial vessels also suppies optic nerve. Hence these vessels show the blood supply conditions of optic nerve head and retina.

The technique begins with the identification of optic nerve as a hypoechoic central band in B scan mode. This is used as a reference place for Doppler study of ocular vesssels. Ophthalmic artery is identified nasally and superior to optic nerve soon it crosses the optic nerve. The flow velocity waveform is similar to that of Internal carotid Artery showing high maximum peak systolic flow and low diastolic flow velocity. A dicrotic notch due to aortic valve closure.[25]

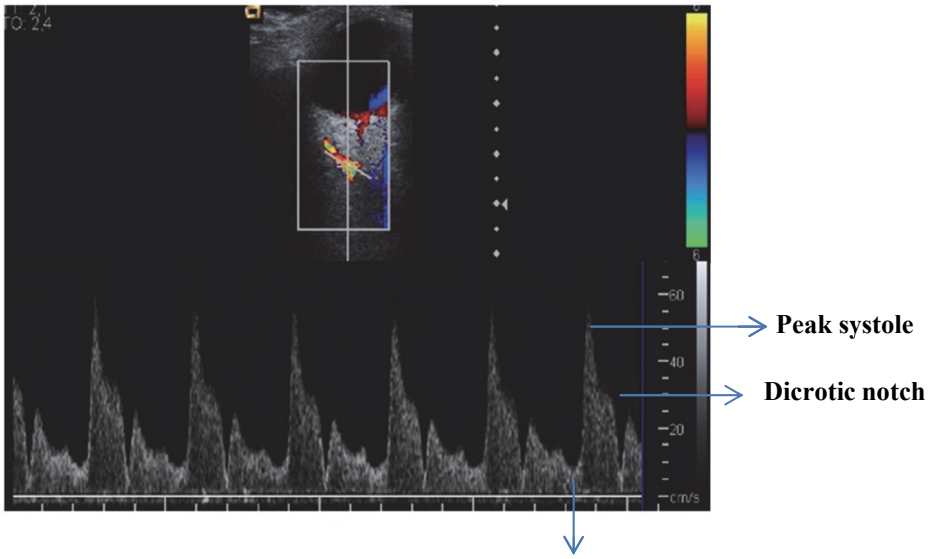


Figure 9

Central retinal artery enters the inferior surface of optic nerve about 12mm behind the globe. It has a straighter course in optic nerve having close approximation with central retinal vein. These lie immediately adjacent to each other with artery on the nasal side and vein on the temporal side.[26,27] It is identified next to central retinal vein in hypoechoic central band of conal region. The waveform of central retinal artery has a pulsatile flow with steep systolic peak suggestive of high resistance distal vascular bed.

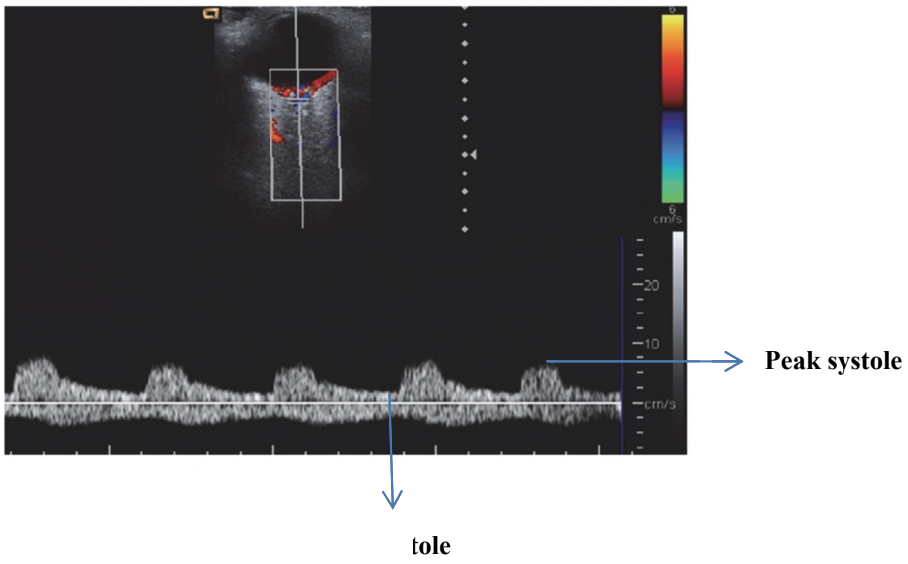


Figure 10

Posterior ciliary artery both nasal and temporal lying on each side of optic nerve in the posterolateral aspect of papilla.[28,29] The plane should be anterior as possible to reduce noise from choroid. The difficulty faced is, it is difficult to identify individual short posterior ciliary artery due to its small caliber and because of its direction variable insonation angles are required. This leads to wide variability in its measurement. The obtained waveform is from the mass effect of bundle of vessels rather than from the individual vessels. The waveform is similar to central retinal artery but with sharper peak systolic velocity.[45]

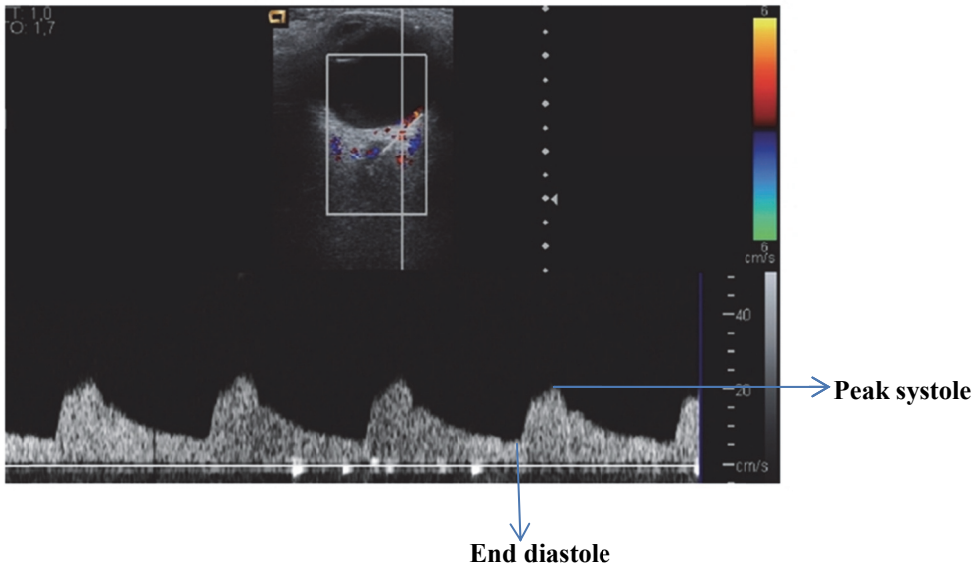


Figure 11

TREATMENT OF NORMOTENSIVE GLAUCOMA

Before starting treatment, diurnal fluctuation of intraocular pressure should be noted to confirm that their pressure is consistently below 21mm Hg and are staying within target level while on treatment. Reduction of intraocular pressure by 25-30% from the baseline IOP is necessary in case of normotensive glaucoma to prevent

progression and to maintain a stable visual field. If the baseline IOP is in high teens, reduction of intraocular pressure to a level of 15mm Hg and in case of baseline IOP in mid teens reduction of intraocular pressure to 10-12 mmHg is necessary to hault the progression. If progression in visual field or retinal nerve fiber defect is seen eventhough the intraocular pressure is maintained within the target level during day time, nocturnal elevation of intraocular pressure should be suspected.[32,35]

Collaborative Normal Tension Glaucoma study is done to determine if lowering the intraocular pressure causes decreased progression in normotensive glaucoma.140 patients were randomized to have treatment(medical/ surgical) or to have no treatment. The untreated eyes had 35% chance of progression when compared to 12% in treated group. Hence it concluded that reduction in intraocular pressure reduces progression.[32,35]

Medical treatment:

Intraocular pressure reduction is important in patients with normotensive glaucoma to prevent progression. In patients with nocturnal dip in blood pressure, lowering the intraocular pressure at night is necessary to maintain perfusion pressure to optic nerve head. This is done by IOP lowering drugs. These include:

Latanoprost, a prostaglandin analog is a potential drug for achieving adequate IOP reduction by increasing the uveoscleral outflow.

Calcium channel blockers increase the blood flow by causing vasodilation of blood vessels supplying optic nerve head. However peripheral vasodilatation lowers

the optic nerve perfusion pressure and actually worsen the disease process in patients with impaired optic nerve head blood flow contributing to damage.

In addition to reducing intraocular pressure, neuroprotection of the anti glaucoma medications also helps in stabilizing the disease process.eg; Betaxolol causes increased blood circulation around optic nerve.

Laser trabeculoplasty:

By medical treatment target intraocular pressure cannot be achieved easily. Hence Laser trabeculoplasty is tried in patients with progressive disease despite maximum tolerated medical therapy.

Filtering surgery:

Filtering surgeries like trabeculectomy with antifibrotic agents like Mitimycin C or 5-flourouracil is effective in maintaining the target intraocular pressure. The rate of visual field progression was significantly slowed in surgically treated group compared to untreated or with other modalities. Maintaining a target intraocular pressure by <12 mm Hg by surgery is found to be effective in preventing progression. Complications like post operative hypotony is seen, hence surgical management is reserved for cases with progression of visual field.

PART II

AIM OF THE STUDY

To compare the retrobulbar blood flow velocities in Normotensive glaucoma, untreated Primary open angle glaucoma with normal subjects by using Colour Doppler Imaging.

OBJECTIVES:

1) To measure the systolic and diastolic blood flow velocities, resistance index in Ophthalmic artery, Central retinal artery and Short posterior ciliary artery in patients with Normotensive glaucoma, untreated Primary Open angle glaucoma and normal subjects.
2) To assess the significance of vascular flow in glaucomatous optic nerve damage.
3) To correlate between optic nerve head blood flow and glaucomatous optic nerve head changes.

MATERIALS AND METHOD

SOURCE OF DATA:

Patients admitted in the Department of Ophthalmology, Government Mohan Kumaramangalam Medical college Hospital, Salem between December 2017 and June 2019.

A prospective cross sectional study was done to measure the retrobulbar blood flow velocities in the following group of patients(30 subjects in each group):

GROUP 1: Normotensive glaucoma

GROUP 2: Untreated primary open angle glaucoma

GROUP 3: Normal subjects

Peak systolic velocity, End diastolic velocity and the Resistance Index of Ophthalmic artery, Central retinal artery and short posterior ciliary artery were measured by means of Colour Doppler Imaging.

METHODOLOGY:

Data collection was carried out after getting ethical committee approval and informed consent was obtained from all participants.

A thorough history was taken regarding defective vision, field defects , frequent change of glasses, diabetes, hypertension, hypotension, myocardial infarction ,any significant blood loss, migraine, Raynaud's phenomenon, tobacco or alcohol intake.

Family history of glaucoma, any previous ocular surgeries, history of steroid intake in any forms was also recorded.

Visual acuity was assessed with Snellen chart. Ocular examination of both eyes were done with slit lamp biomoicroscope to detect any features of secondary glaucoma. Intraocular pressure was measured using Goldmann Applanation Tonometer and diurnal phasing was done to categorise patients as normotensive glaucoma and primary open angle glaucoma. Angle grading was done according to Shaffer's grading system. Fundus examination was done using +90 D lens and optic disc changes were noted. Visual field examination was done using Humphrey Field analyser using 24-2 strategy. Blood pressure and lipid profile was done for all patients.

Colour Doppler imaging was done with a 6-12MHz linear high frequency probe in the Department of Radiology. The examination was performed by a single experienced radiologist to avoid inter observer variation. Patient was placed in supine position with eyes closed and looking straight and also the pupils were not dilated. The ultrasound transducer was applied with coupling gel over the closed upper eyelid. Optic nerve head is identified by grey scale images in B scan mode. The sample gate is placed at the centre of the detected vessel to image the spectral pattern.

INCLUSION CRITERIA:

1) Patients above 40 years of age.
2) Either sex.
3) Patients with typical glaucomatous optic disc changes and visual field defects with normal intraocular pressure in case of Normotensive glaucoma.
4) Newly diagnosed untreated Primary open angle glaucoma patients.
5) Normal subjects as control.

EXCLUSION CRITERIA:

Subjects with:

1) Secondary open angle glaucoma
2) Angle closure glaucoma.
3) History of steroid intake.
4) History of migraine or peripheral vascular disease.

Figure 12

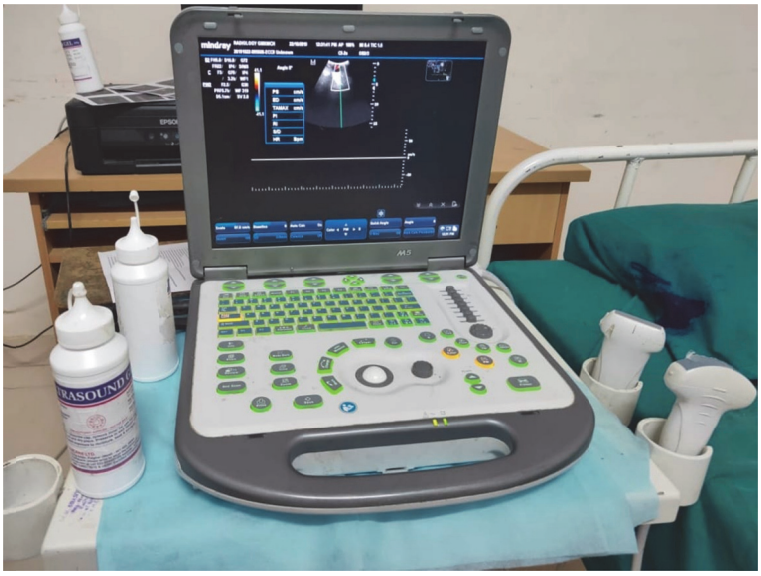
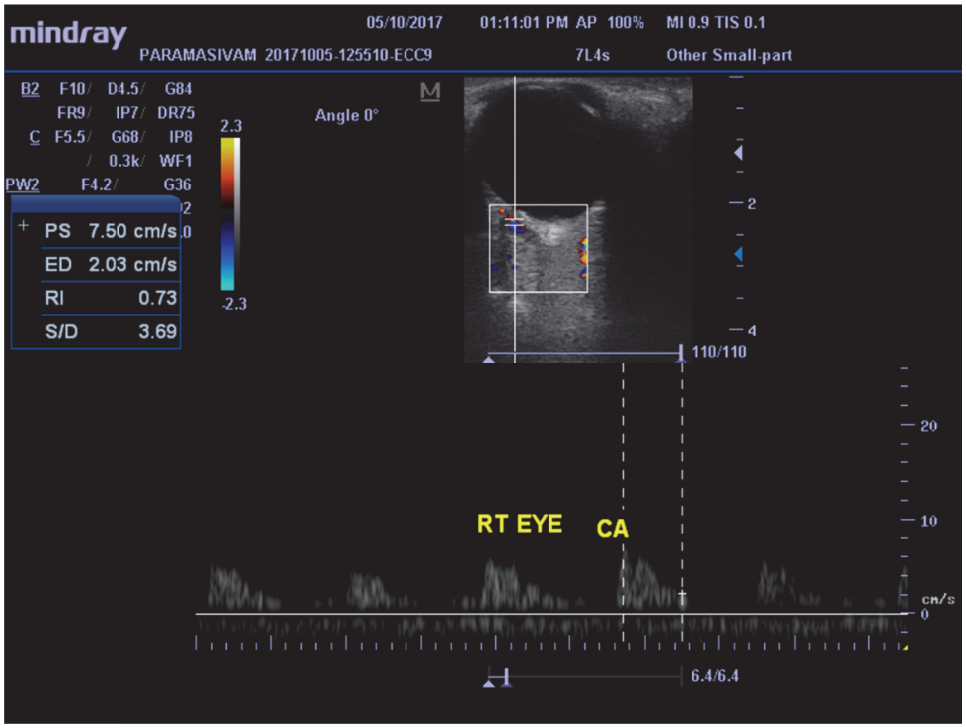
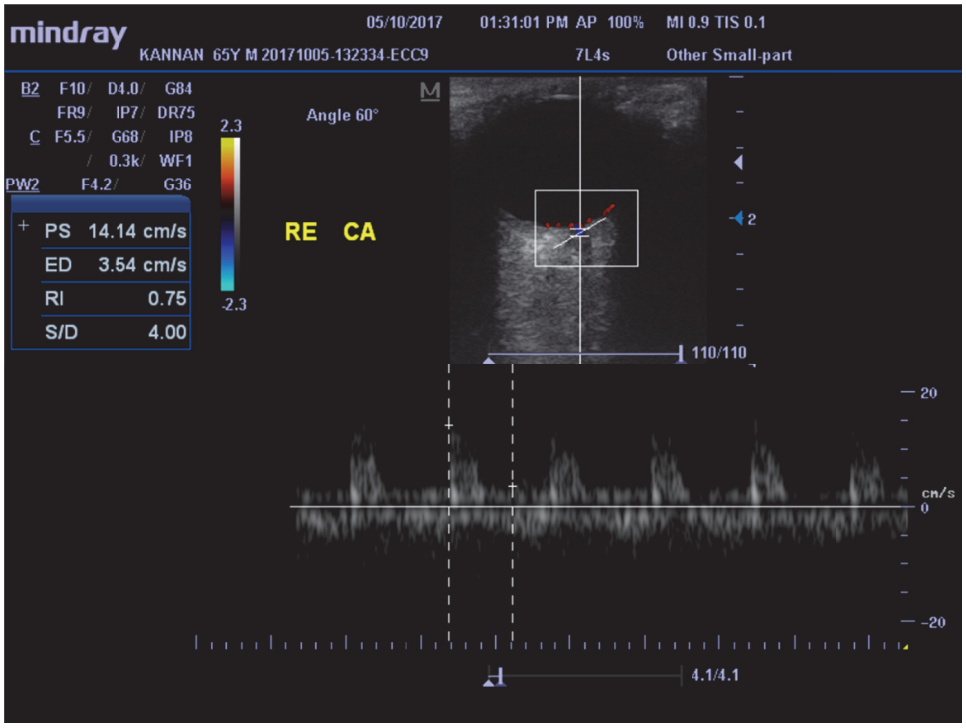
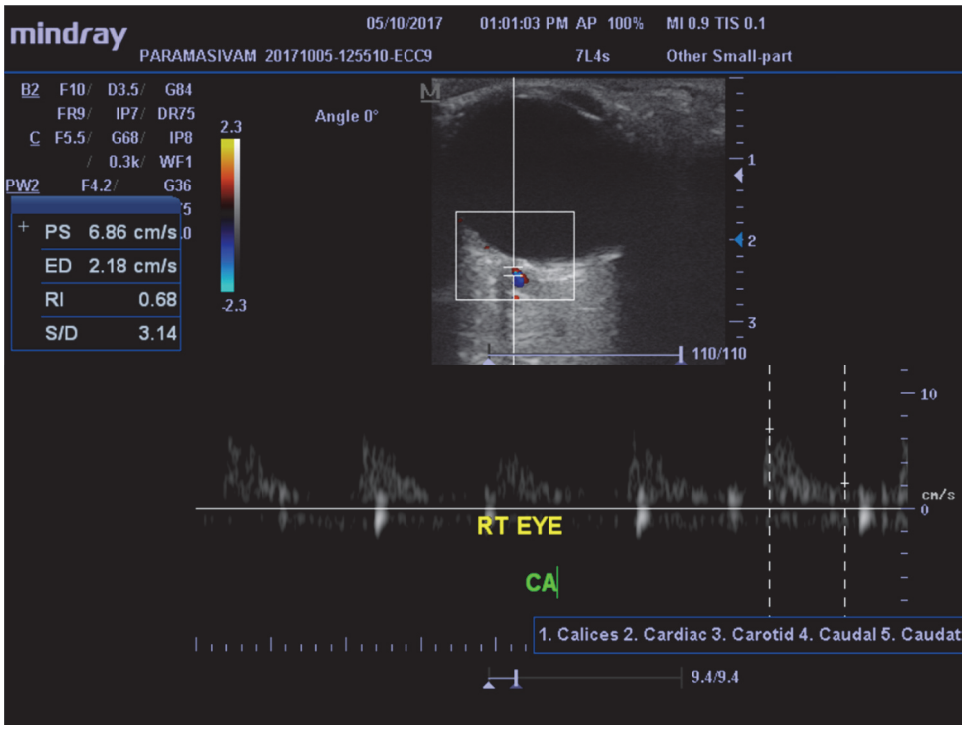


Figure 13

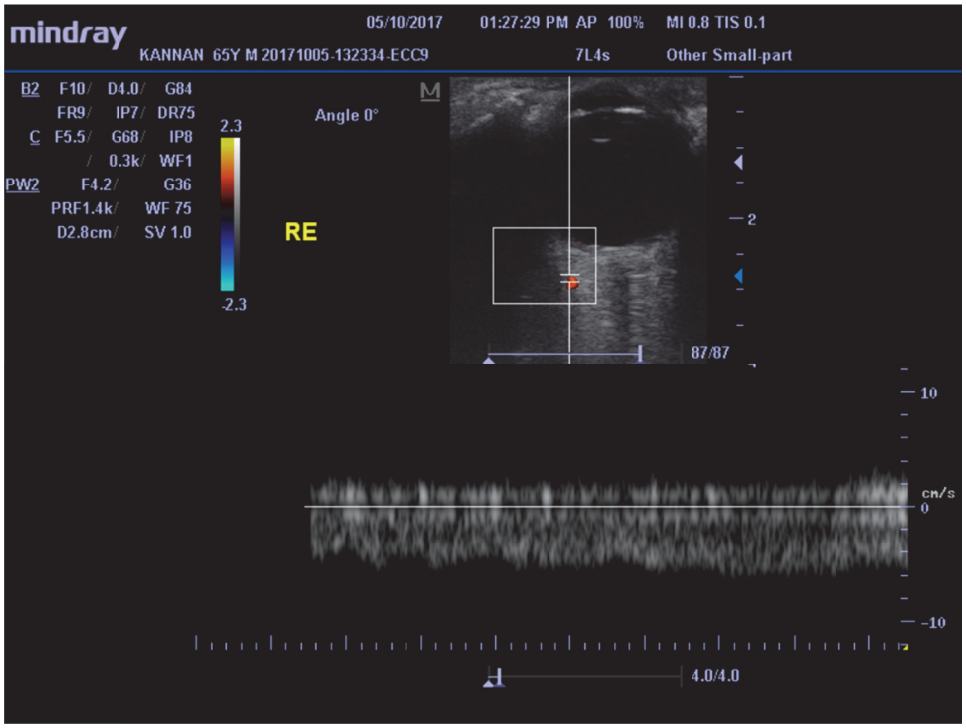
Colour Doppler Imaging showing the data of blood flow velocity in Central Retinal Artery







Colour Doppler Imaging showing the data of blood flow velocity in Ophthalmic Artery



BLOOD FLOW VELOCITY- NORMAL VALUES:

	Peak systolic velocity(cm/sec)	End diastolic velocity(cm/sec)	Resistance Index
Ophthalmic artery	38-48	13-19	0.6-0.7
Central Retinal artery	11-14	4-6	0.6-0.7
Short posterior ciliary artery	12-15	5-7	0.5-0.7

Peak systolic velocity and End diastolic velocity below the normal in all these arteries with Resistance Index of more than 0.7 denotes reduced blood flow to optic nerve head.

STATISTICAL ANALYSIS:

The collected data were analyzed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference in the multivariate analysis the one way ANOVA with Tukey's Post-Hoc test was used .To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value 0.05 is considered as significant level.

RESULTS

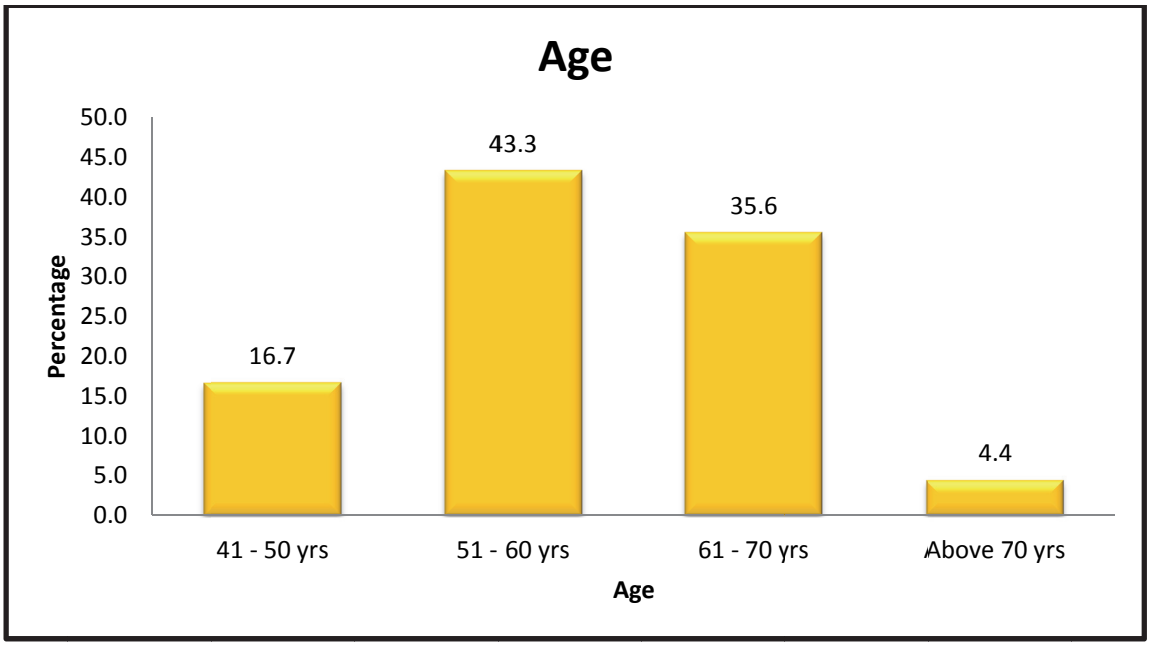
A) AGE:

Of the total 90 patients(30 in each group),43.3% of the study population are between 51- 60 years of age. This age group had the maximum number of patients (39 patients).

TABLE 1: Comparison of age among the study population

Age	Frequency	Percent
41 - 50 yrs	15	16.7
51 - 60 yrs	39	43.3
61 - 70 yrs	32	35.6
Above 70 yrs	4	4.4
Total	90	100.0

CHART 1: Age distribution of the study population



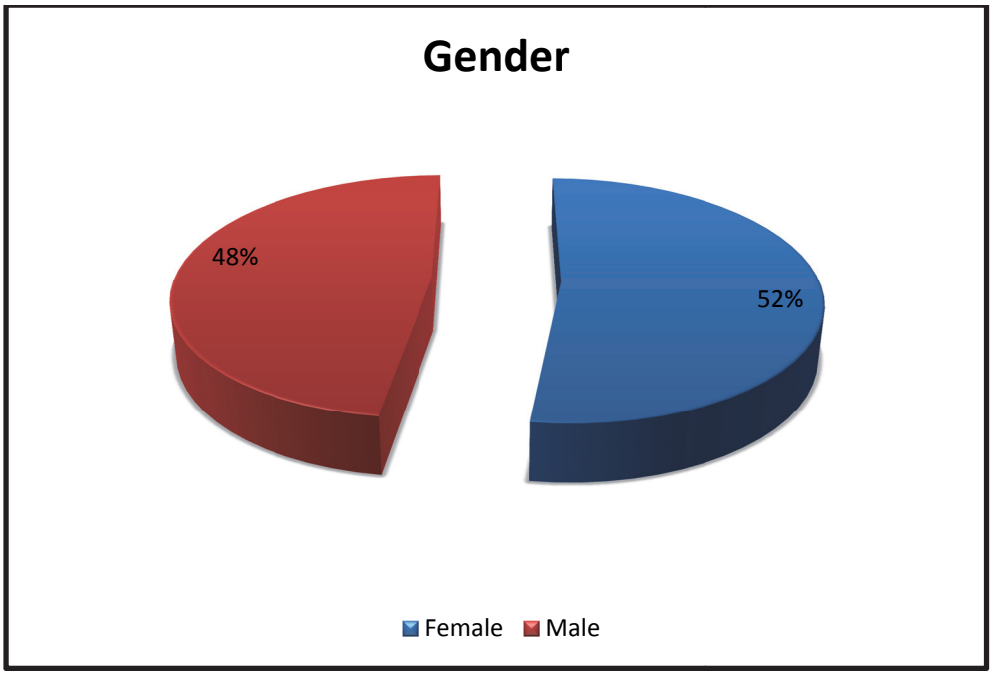
B) SEX:

Among the study population, presentation of glaucoma occurred most common in females contributing to 52.2% of the total.

TABLE 2: Sex distribution of the study population

SEX		
	Frequency	**Percent**
Female	47	52.2
Male	43	47.8
Total	90	100.0

CHART 2: Sex distribution of the study population



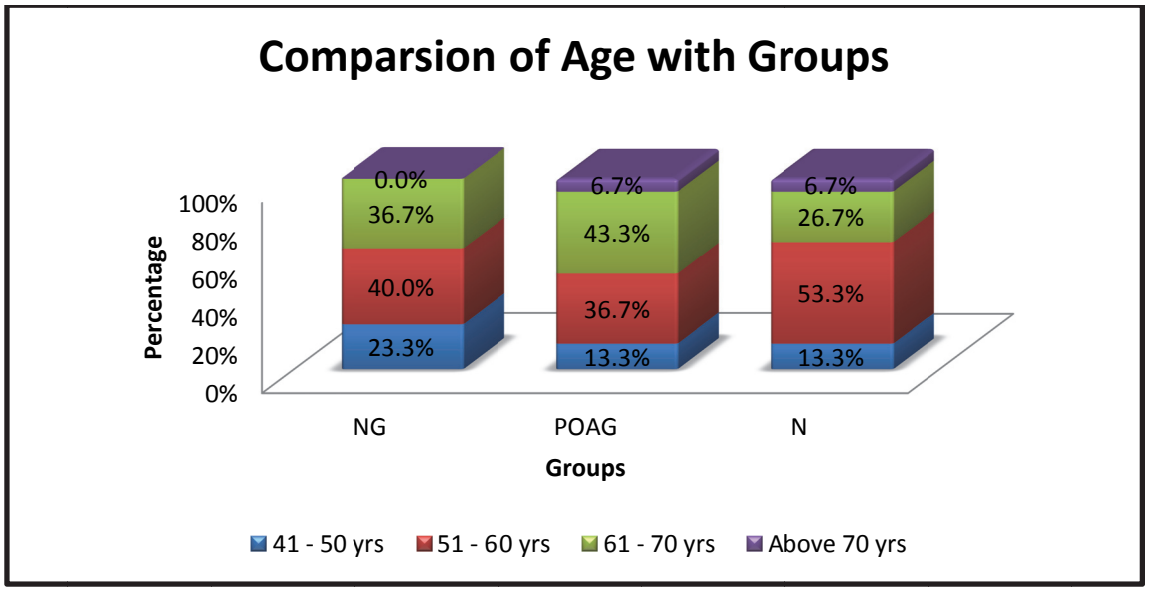
C) AGE COMPARISON IN DIFFERENT GROUPS:

The most common age group with normotensive glaucoma is 51-60 years contributing to 40% of the group. Primary open angle glaucoma occurred most commonly between 61-70 years accounting to 43.3%. Control group is most common between 51-60 years. There is no statistical significance of the disease in relation to the age in the different groups of the study population.(p>0.05)

TABLE 3: Comparison of age with different groups

Comparsion of Age with Groups								
			Groups			Total	□ 2 - value	P-value
			NG	POAG	N			
Age	41 - 50 yrs	Count	7	4	4	15	5.464	0.486 #
		%	23.3%	13.3%	13.3%	16.7%		
	51 - 60 yrs	Count	12	11	16	39		
		%	40.0%	36.7%	53.3%	43.3%		
	61 - 70 yrs	Count	11	13	8	32		
		%	36.7%	43.3%	26.7%	35.6%		
	Above 70 yrs	Count	0	2	2	4		
		%	0.0%	6.7%	6.7%	4.4%		
Total		Count	30	30	30	90		
		%	100.0%	100.0%	100.0%	100.0%		
# No Statistical Significance at P>0.05 level								

CHART 3: Comparison of age with different groups



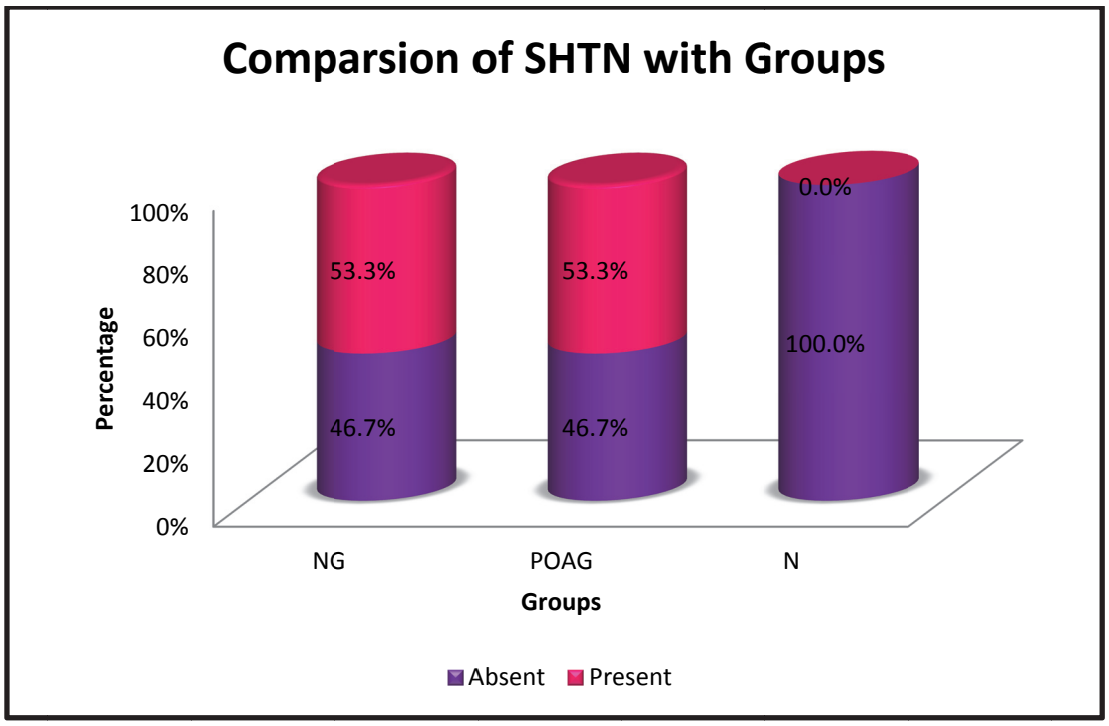
D) COMPARISON OF SYSTEMIC HYPERTENSION IN EACH GROUP

The association of systemic hypertension with glaucoma is statistically significant($p<.0.01$) in our study group. The incidence of systemic hypertension is 53.3% in both normotensive glaucoma and primary open angle glaucoma.

TABLE 4: Association of systemic hypertension in glaucoma

Comparsion of SHTN with Groups								
			Groups			Total	□ 2 - value	P-value
			NG	POAG	N			
SHTN	Absent	Count	14	14	30	58	24.828	0.0005 **
		%	46.7%	46.7%	100.0%	64.4%		
	Present	Count	16	16	0	32		
		%	53.3%	53.3%	0.0%	35.6%		
Total		Count	30	30	30	90		
		%	100.0%	100.0%	100.0%	100.0%		
** Highly Significant at P < 0.01 level								

CHART 4: Comparison of systemic hypertension in glaucoma



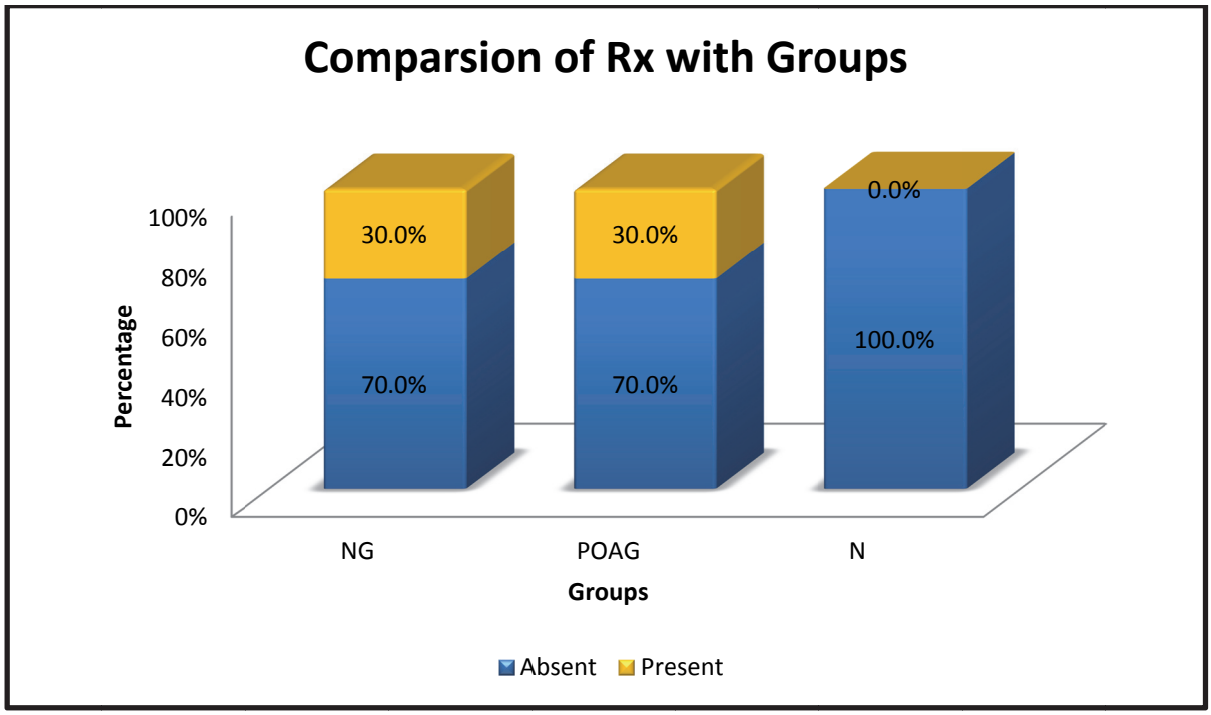
E) PREVALENCE OF GLAUCOMA IN COMPARISON WITH TREATMENT OF HYPERTENSION:

Prevalence of glaucoma is noted to be common in hypertensive patients without treatment and is found to be statistically significant($p<0.01$). 70% of patients in normotensive and primary open angle glaucoma are hypertensives but not on any medications.

TABLE 5:Prevalence of glaucoma in comparison with treatment of hypertension

Comparsion of Rx with Groups								
			Groups			Total	χ^2 - value	P-value
			NG	POAG	N			
Rx	Absent	Count	21	21	30	72	11.25	0.004 **
		%	70.0%	70.0%	100.0%	80.0%		
	Present	Count	9	9	0	18		
		%	30.0%	30.0%	0.0%	20.0%		
Total		Count	30	30	30	90		
		%	100.0%	100.0%	100.0%	100.0%		
** Highly Significant at P < 0.01 level								

CHART 5: Prevalence of glaucoma in comparison with treatment of hypertension



F) COMPARISON OF LIPID PROFILE IN EACH GROUP

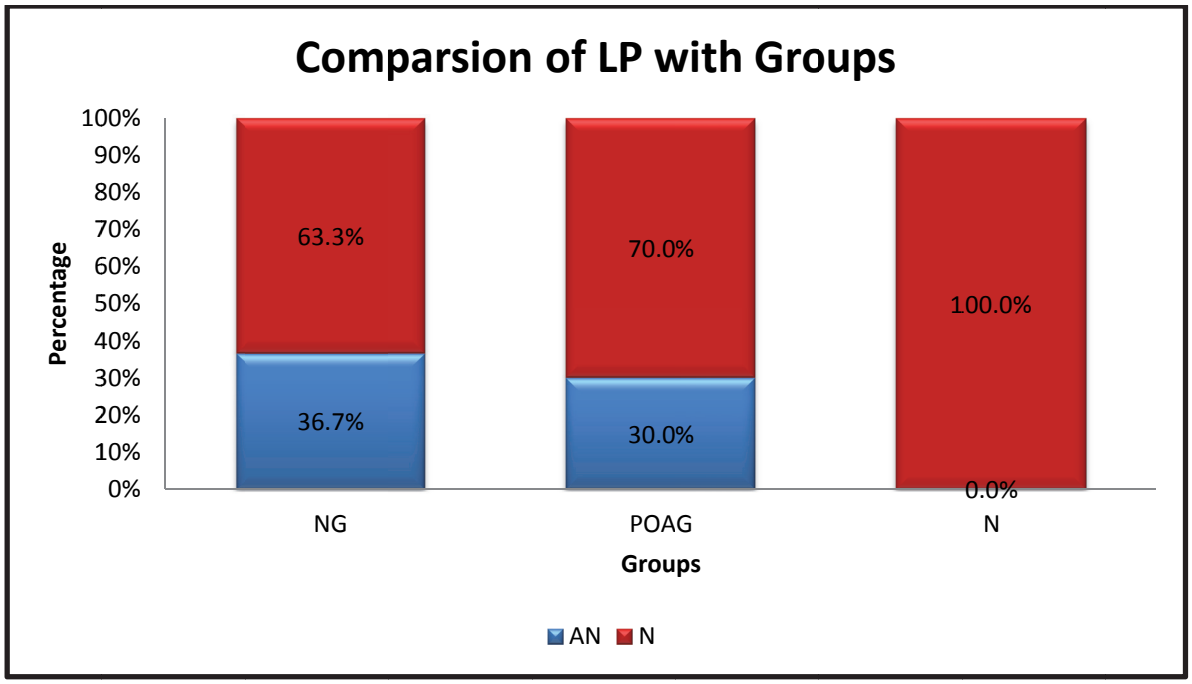
The association of glaucoma with abnormal lipid profile is statistically not significant in both normotensive glaucoma and primary open angle glaucoma.

The prevalence of normotensive glaucoma with abnormal lipid profile is 36.7% and that of primary open angle glaucoma is 30%.

TABLE 6: Comparison of lipid profile in each group

Comparsion of LP with Groups								
			Groups			Total	□ 2 - value	P-value
			NG	POAG	N			
LP	AN	Count	11	9	0	20	13.24	0.001 **
		%	36.7%	30.0%	0.0%	22.2%		
	N	Count	19	21	30	70		
		%	63.3%	70.0%	100.0%	77.8%		
Total		Count	30	30	30	90		
		%	100.0%	100.0%	100.0%	100.0%		
** Highly Significant at P < 0.01 level								

CHART 6: Comparison of lipid profile in each group



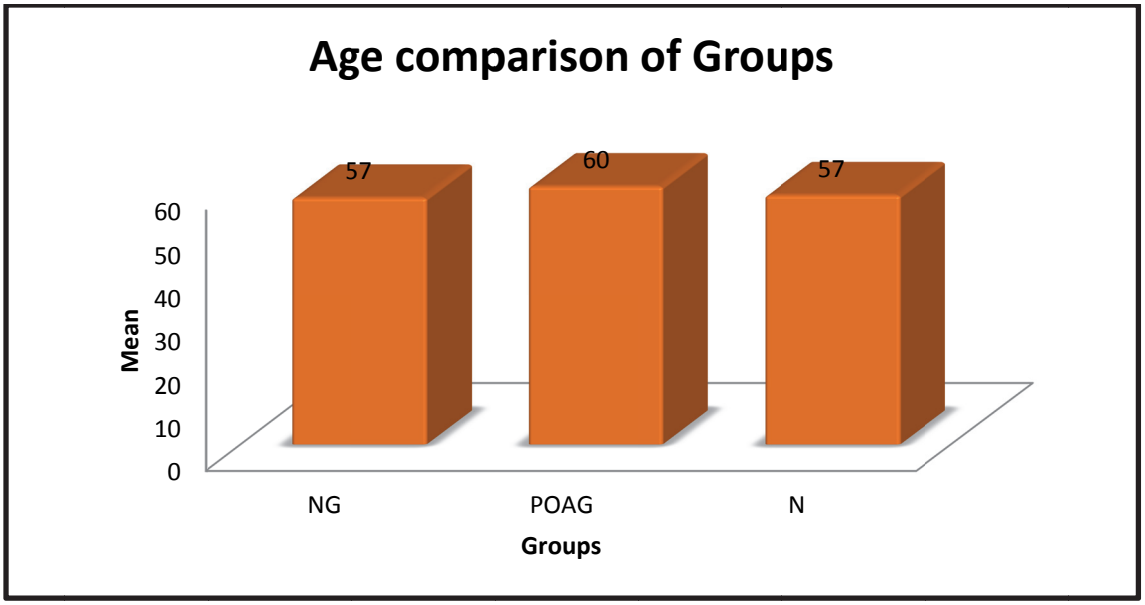
G) MEAN DISTRIBUTION OF AGE IN EACH GROUP:

The mean age group in case of Normotensive glaucoma is 57 years and that of Primary open angle glaucoma is 60 years.

TABLE 7: Mean distribution of age

Comparison of Groups with Oneway ANOVA							
Age	**N**	**Mean**	**S.D**	**Minimum**	**Maximum**	**F-value**	**P-value**
NG	30	57	7	43	69		
POAG	30	60	8	47	73		0.372 #
N	30	57	7	45	72	0.999	
# No Statistical Significance at P>0.05 level							

CHART 7: Mean distribution of age



H) COMPARSION OF IOP AND CD RATIO WITH EACH GROUP:

The mean IOP in Normotensive patients is 16.27± 2.10 mm Hg. The mean IOP in POAG group is 26.8±2.59 mm Hg. The mean value of C:D ratio in normotensive patients is 0.68±0.12 and that of primary open angle glaucoma patients is 0.64±0.09.

TABLE 8:Comparsion of IOP and CD ratio with each group

Comparison of IOP and CD with Groups with Oneway ANOVA								
		N	**Mean**	**S.D**	**Minimum**	**Maximum**	**F-value**	**P-value**
IOP	NG	30	16.27	2.10	11.5	19.5	344.11	0.0005 **
	POAG	30	26.80	2.59	22.5	33.0		
	N	30	13.97	1.07	12.0	16.5		
CD	NG	30	0.68	0.12	.45	.85	156.16	0.0005 **
	POAG	30	0.64	0.09	.50	.85		
	N	30	0.32	0.03	.30	.40		
** Highly Significant at P < 0.01 level								

CHART 8: Comparsion of IOP with each group

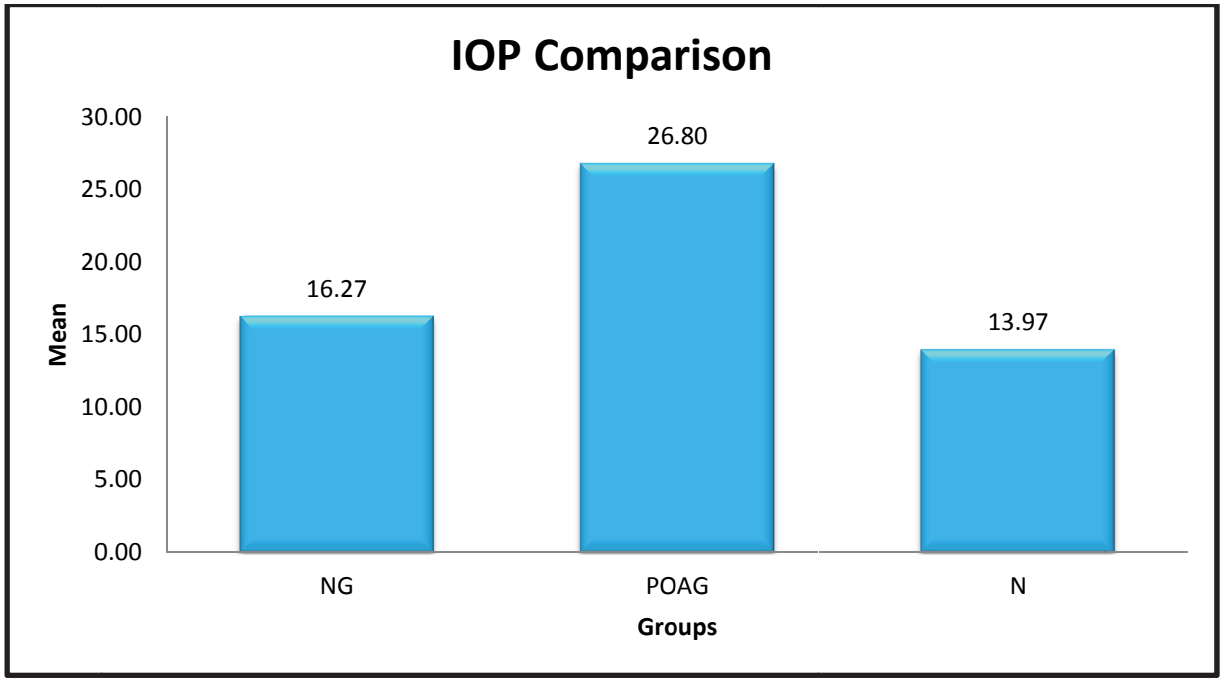
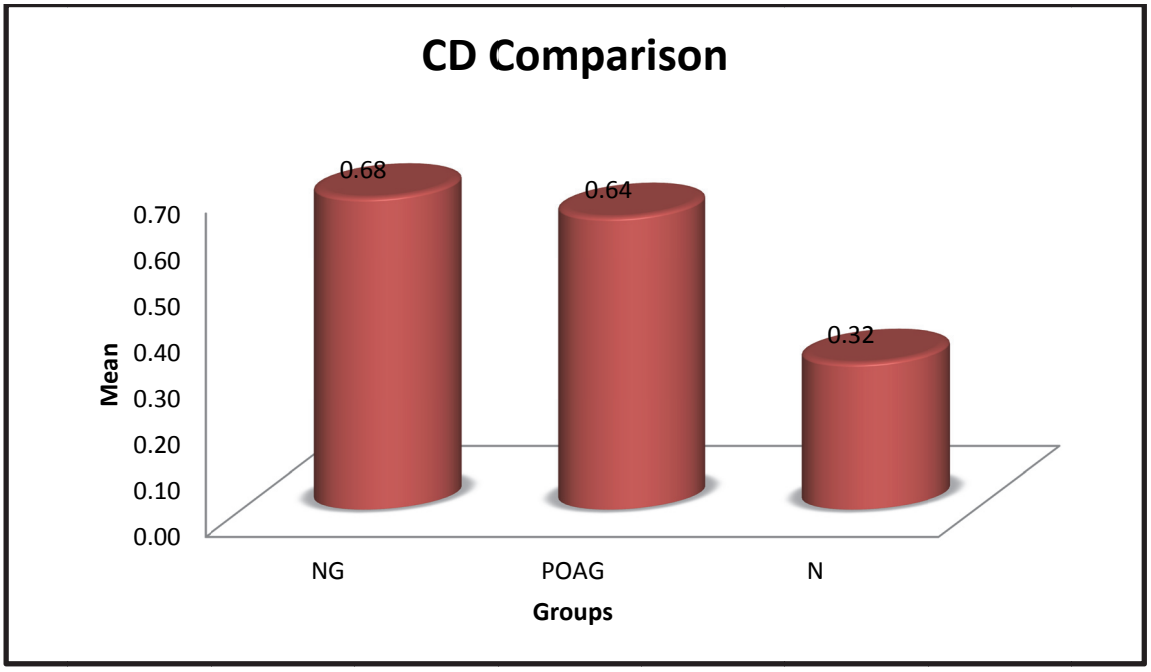


CHART 9: Comparsion of CD Ratio with each group



I) COMPARISON OF VARIABLES IN OPHTHALMIC ARTERY OF EACH GROUP:

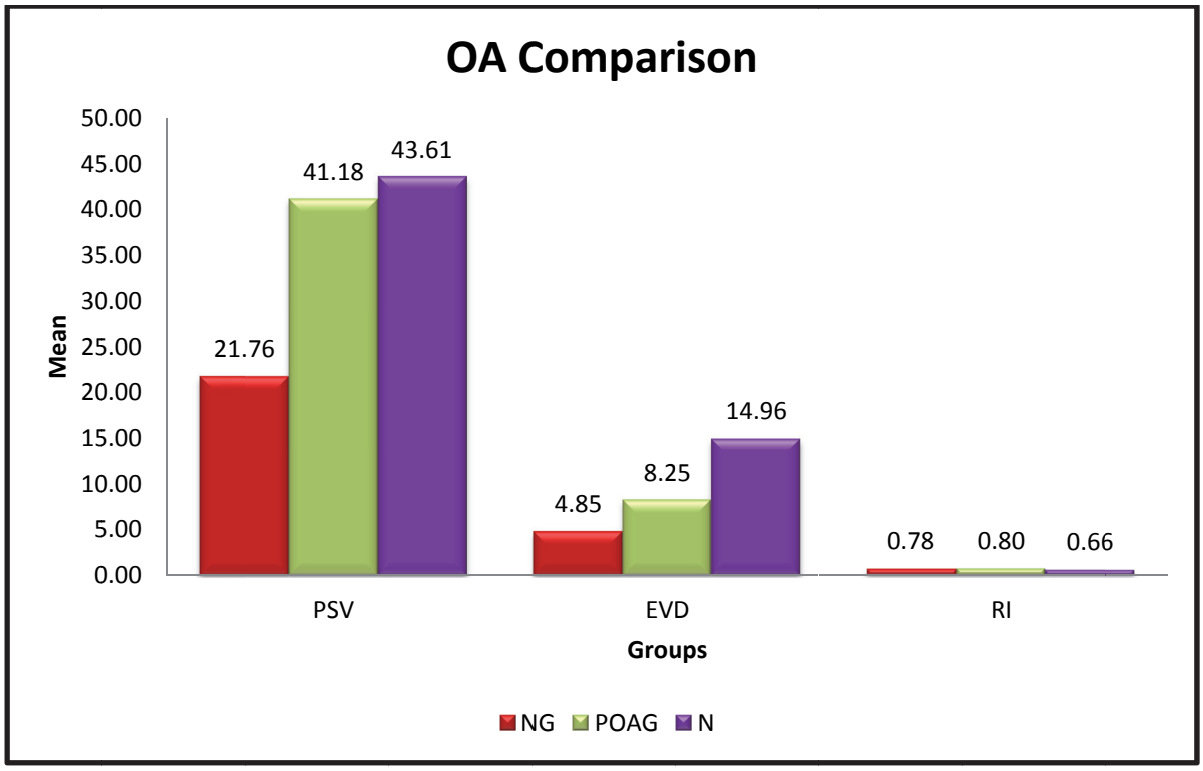
The mean value of PSV in Ophthalmic artery of Normotensive patients is 21.76 ±0.85 cm/sec , in Primary open angle glaucoma is 41.18±2.36 cm/sec and that of normal subjects is 43.61±0.99 cm/sec. The mean value of EDV in ophthalmic artery of Normotensive patients is 4.85±0.76 cm/sec, in Primary open angle glaucoma is 8.25±1.02 cm/sec and that of normal subjects is 14.96±0.42 cm/sec. The mean value of RI in ophthalmic artery of Normotensive patients is 0.78±0.03, Primary open angle glaucoma is 0.8±0.03 and that of normal subjects is 0.66±0.01. These variables are comparable and are found to be statistically significant($p<0.01$).

TABLE 9:Comparison of variables in ophthalmic artery of each group

Comparison of with Groups with Oneway ANOVA								
		N	Mean	S.D	Minimum	Maximum	F-value	P-value
OA PSV	NG	30	21.76	0.85	20.38	23.66	1772.49	0.0005 **
	POAG	30	41.18	2.36	36.50	46.84		
	N	30	43.61	0.99	41.39	45.63		
OA EDV	NG	30	4.85	0.76	3.40	6.00	1334.6	0.0005 **
	POAG	30	8.25	1.02	6.90	10.80		
	N	30	14.96	0.42	14.22	15.81		
OA RI	NG	30	0.78	0.03	.72	.84	230.03	0.0005 **
	POAG	30	0.80	0.03	.70	.84		
	N	30	0.66	0.01	.63	.68		
** Highly Significant at P < 0.01 level								

Multiple Comparisons							
Dependent Variable			Mean Difference	Std. Error	Sig.	95% C.I	
						LB	UB
OA PSV	NG	POAG	-19.42233*	.40224	0.0005 **	-20.3815	-18.4632
		N	-21.84633*	.40224	0.0005 **	-22.8055	-20.8872
	POAG	N	-2.42400*	.40224	0.0005 **	-3.3831	-1.4649
OA EDV	NG	POAG	-3.40433*	.19923	0.0005 **	-3.8794	-2.9293
		N	-10.11467*	.19923	0.0005 **	-10.5897	-9.6396
	POAG	N	-6.71033*	.19923	0.0005 **	-7.1854	-6.2353
OA RI	NG	POAG	-.01833*	.00708	0.030 *	-.0352	-.0015
		N	.12133*	.00708	0.0005 **	.1045	.1382
	POAG	N	.13967*	.00708	0.0005 **	.1228	.1565
** Highly Significant at P < 0.01 level and * Significance at P < 0.05 level							

CHART 12: Comparison of variables in ophthalmic artery of each group



J) COMPARISON OF VARIABLES IN CENTRAL RETINAL ARTERY OF EACH GROUP:

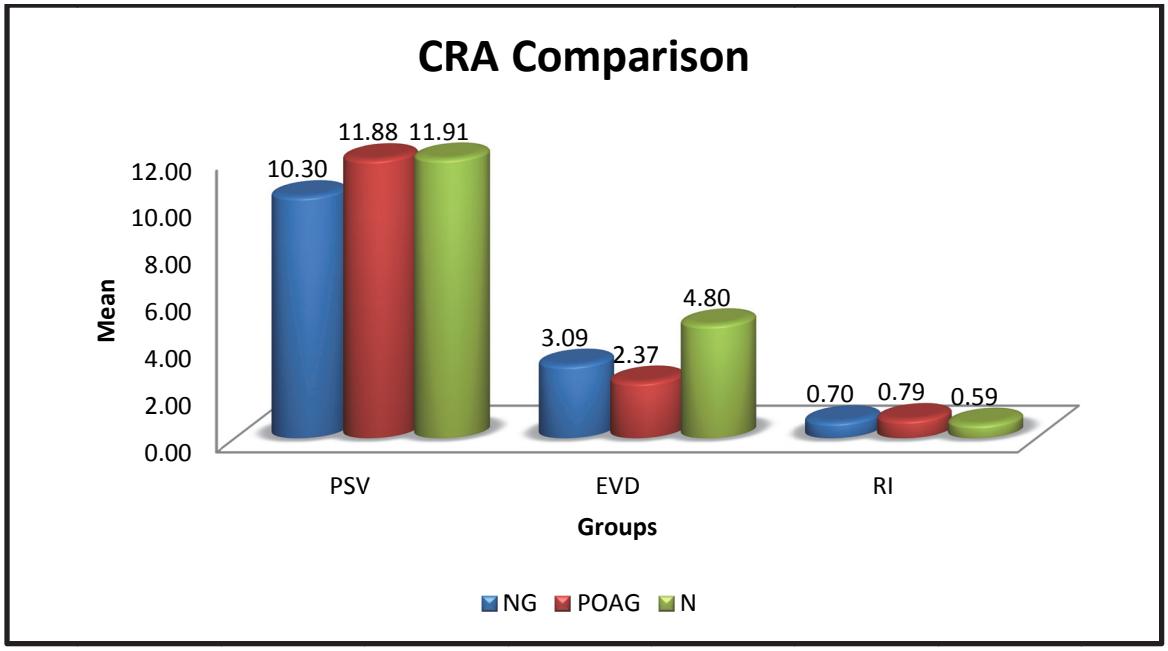
The mean value of PSV in Central retinal artery of Normotensive patients is 10.3 ±0.4 cm/sec, in Primary open angle glaucoma is 11.88±0.54 cm/sec and that of normal subjects is 11.91±0.39 cm/sec. The mean value of EDV in Central retinal artery of Normotensive patients is 3.09±0.17 cm/sec, in Primary open angle glaucoma is 2.37±0.21 cm/sec and that of normal subjects is 4.80±0.36cm/sec. The mean value of RI in Central retinal artery of Normotensive patients is 0.7±0.02, Primary open angle glaucoma is 0.79±0.04 and that of normal subjects is 0.59±0.03. These variables are comparable and are found to be statistically significant($p<0.01$).

TABLE 10: Comparison of variables in Central retinal artery of each group

Comparison of with Groups with Oneway ANOVA								
		N	**Mean**	**S.D**	**Minimum**	**Maximum**	**F-value**	**P-value**
CRA PSV	NG	30	10.30	0.40	9.90	11.55	126.31	0.0005 **
	POAG	30	11.88	0.54	11.28	14.04		
	N	30	11.91	0.39	11.20	12.80		
CRA EDV	NG	30	3.09	0.17	2.75	3.45	668.39	0.0005 **
	POAG	30	2.37	0.21	1.89	2.80		
	N	30	4.80	0.36	4.32	5.65		
CRA RI	NG	30	0.70	0.02	.65	.74	302.34	0.0005 **
	POAG	30	0.79	0.04	.70	.84		
	N	30	0.59	0.03	.53	.64		
** Highly Significant at P < 0.01 level								

Multiple Comparisons							
Dependent Variable			Mean Difference	Std. Error	Sig.	95% C.I	
						LB	UB
CRA PSV	NG	POAG	-1.58000*	.11593	0.0005 **	-1.8564	-1.3036
		N	-1.61100*	.11593	0.0005 **	-1.8874	-1.3346
	POAG	N	-.03100	.11593	0.961 #	-.3074	.2454
CRA EDV	NG	POAG	.71600*	.06822	0.0005 **	.5533	.8787
		N	-1.71133*	.06822	0.0005 **	-1.8740	-1.5487
	POAG	N	-2.42733*	.06822	0.0005 **	-2.5900	-2.2647
CRA RI	NG	POAG	-.09233*	.00796	0.0005 **	-.1113	-.0733
		N	.10333*	.00796	0.0005 **	.0843	.1223
	POAG	N	.19567*	.00796	0.0005 **	.1767	.2147
** Highly Significant at P < 0.01 level and # No Significance at P>0.05 level							

CHART 11: Comparison of variables in Central retinal artery of each group



K) COMPARISON OF VARIABLES IN SHORT POSTERIOR CILIARY ARTERY OF EACH GROUP:

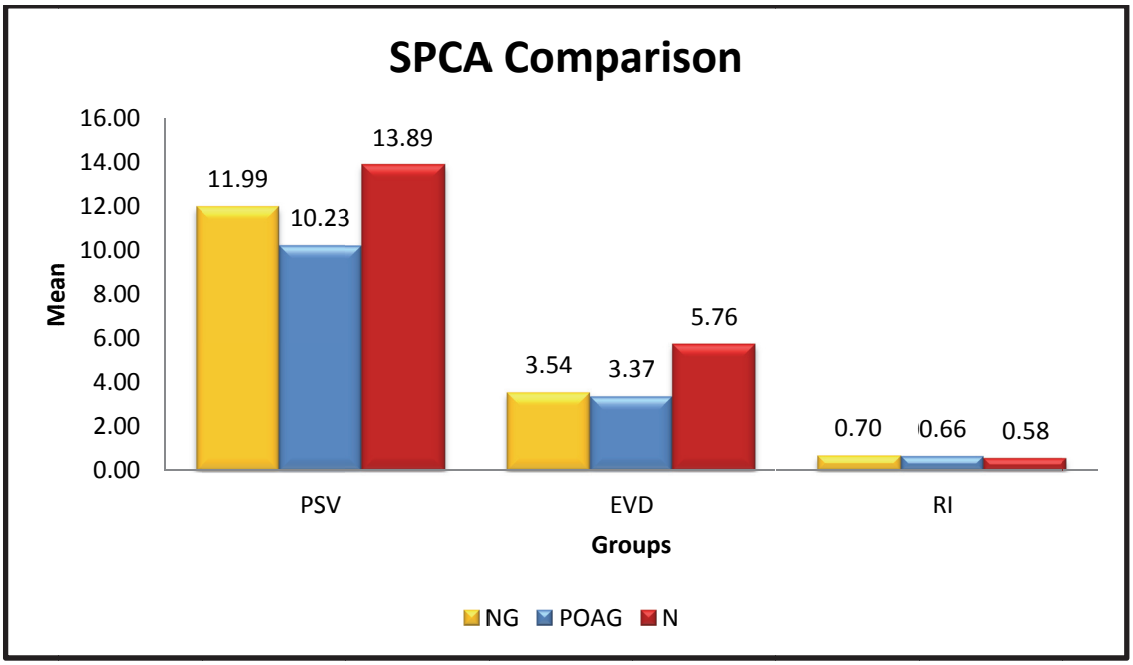
The mean value of PSV in Short posterior ciliary artery of Normotensive patients is 11.99 ±0.45 cm/sec , in Primary open angle glaucoma is 10.23±0.64 cm/sec and that of normal subjects is 13.89±0.81 cm/sec. The mean value of EDV in Short posterior ciliary artery of Normotensive patients is 3.54±0.38 cm/sec, in Primary open angle glaucoma is 3.37±0.26 cm/sec and that of normal subjects is 5.76±0.33cm/sec. The mean value of RI in Central retinal artery of Normotensive patients is 0.7±0.04, Primary open angle glaucoma is 0.66±0.04 and that of normal subjects is 0.58±0.03. These variables are comparable and are found to be statistically significant ($p<0.01$).

TABLE 11: Comparison of variables in Short posterior ciliary artery of each group

Comparison of with Groups with Oneway ANOVA								
		N	Mean	S.D	Minimum	Maximum	F-value	P-value
SPCA PSV	NG	30	11.99	0.45	11.09	12.77	236.4	0.0005 **
	POAG	30	10.23	0.64	9.33	11.45		
	N	30	13.89	0.81	12.89	15.48		
SPCA EDV	NG	30	3.54	0.38	2.99	4.43	498.9	0.0005 **
	POAG	30	3.37	0.26	2.95	4.00		
	N	30	5.76	0.33	4.93	6.49		
SPCA RI	NG	30	0.70	0.04	.62	.76	76.1	0.0005 **
	POAG	30	0.66	0.04	.57	.73		
	N	30	0.58	0.03	.53	.68		
** Highly Significant at P < 0.01 level								

Multiple Comparisons							
Dependent Variable			Mean Difference	Std. Error	Sig.	95% C.I	
						LB	UB
SPCA PSV	NG	POAG	1.75767*	.16837	0.0005 **	1.3562	2.1591
		N	-1.90233*	.16837	0.0005 **	-2.3038	-1.5009
	POAG	N	-3.66000*	.16837	0.0005 **	-4.0615	-3.2585
SPCA EDV	NG	POAG	.17933	.08439	0.091 #	-.0219	.3806
		N	-2.21367*	.08439	0.0005 **	-2.4149	-2.0124
	POAG	N	-2.39300*	.08439	0.0005 **	-2.5942	-2.1918
SPCA RI	NG	POAG	.03533*	.00997	0.002 **	.0116	.0591
		N	.11967*	.00997	0.0005 **	.0959	.1434
	POAG	N	.08433*	.00997	0.0005 **	.0606	.1081

CHART 12: Comparison of variables in Short posterior ciliary artery of each group



OBSERVATION

1) A one way analysis of variance was done using ANOVA with Post- Hoc test which showed no significant difference among the three groups in age (p= 0.486).

2) Chi square test is used to find the significance which showed significant difference in association with systemic abnormalities like systemic hypertension (p=0.005) and abnormal lipid profile (p=0.001).

3) Significant association is found between patients with glaucoma and patients with hypertension who were not on any medications(p=0.004).

4) Comparing IOP with different group showed significant difference among two groups with p value of 0.0005. The mean IOP in Normotensive patients is 16.27± 2.10 mm Hg. The mean IOP in POAG group is 26.8±2.59 mm Hg.

5) Statistically significant difference is found in C:D ratio between the two glaucoma groups(p=0.0005). The mean value of C:D ratio in normotensive patients is 0.68±0.12 and that of primary open angle glaucoma patients is 0.64±0.09.

Blood flow velocities

6) Compared with normal group, there is significant reduction in PSV (p= 0.0005)in both Normotensive glaucoma and Primary open angle glaucoma group in all the three arteries, namely Ophthalmic artery, Central retinal artery and Short posterior ciliary artery.

7) There is also significant reduction in EDV (p=0.0005) in both the groups in all three arteries.

8) Increased RI is found in all the three arteries (Ophthalmic artery, Central retinal artery and Short posterior ciliary artery) and is found to be statistically significant in the normotensive and primary open angle glaucoma group with p value of 0.0005.

LIMITATIONS

- Only small group of patients were studied.
- Central corneal thickness was not measured in any of the patients.

CONCLUSION

In this comparative study of both normotensive and primary open angle glaucoma patients using Colour Doppler imaging to assess the blood flow velocities in Ophthalmic artery, Central retinal artery and Short posterior ciliary artery, it was noted that these vessels had reduced systolic and diastolic blood flow velocity and also increased resistance index . All these factors are known to contribute to the vascular compromise leading to ischemia of the optic nerve head resulting in optic nerve damage.

It was also noted that the incidence of glaucoma was high in patients with systemic abnormalities like systemic hypertension and dyslipidemia.

This study concludes that, irrespective of the intraocular pressure, vascular factors do have a role in the pathogenesis of optic nerve head changes in both normotensive and primary open angle glaucoma.

BIBLIOGRAPHY

1. The glaucoma 2nd edition, Ritch ,Robert, Shields, M.Bruce,Krupin,Theodore; 1996
2. Becker- Shaffer's diagnosis and therapy of glaucomas,6th edition,1989 :
3. Chandler and Grant's glaucoma: L.Epstein, Rand R, Allingham, Joel S.Shuman, fourth edition, 1997
4. Clinical Anatomy of the eye ,2nd edition, Richard S.Snell, MichaelA.Lemp
5. The glaucomas – concepts and fundamentals , TarekM.Eid, George L.Spaeth
6. Duane;s Clinical Ophthalmology Glaucoma surgeries, Volume 6; William Tasman , Edward A Jaeger, Joseph Caprioli
7. Principles and practice of Ophthalmology ; third edition,Volume 2; Daniel M.Albert, Frederick A. Jakobeic
8. Duke –Elder. Sir.Volume III Glaucomas
9. D. G. Bedi, D. S. Gombos, C. S. Ng, and S. Singh, "Sonography of the eye," American Journal of Roentgenology, vol. 187, no. 4, pp. 1061–1072, 2006
10. S. S. Hayreh, I. H. Revie, and J. Edwards, "Vasogenic origin ofvisual field defects and optic nerve changes in glaucoma," British Journal of Ophthalmology, vol. 54, no. 7, pp. 461–472, 1970.
11. N. Plange, M. Kaup, A. Weber, A. Harris, K. O. Arend, and A.Remky, "Performance of colour Doppler imaging discriminating normal tension glaucoma from healthy eyes," Eye, vol. 23, no. 1, pp. 164–170, 2009.

12. A.Harris, H. S.Chung, T. A. Ciulla, and L.Kagemann, “ Progress in measurement of ocular blood flow and relevance to our understanding of glaucoma and age-related macular degeneration, ” Progress in Retinal and Eye Research, vol. 18, no. 5, pp. 669–687, 1999.

13. Flammer J, Orgu¨ l S. Optic nerve blood-flow abnormalities in glaucoma. ProgRetin Eye Res 1998; 17(2): 267–289.

14. Doppler imaging in evaluation of optic nerve blood supply in normal and glaucomatous subjects. Int Ophthalmol.1992;16:273-276. 25. Galassi F, Nuzzaci G, Sodi

15. Anderson DR. Normal Tension Glaucoma Study. Collaborative normal tension glaucoma study. CurrOpinOphthalmol. 2003; 14:86–90.

16. Fuchsj¨ager-Mayrl G, Wally B, Georgopoulos M, et al. Ocular blood flow and systemic blood pressure in patients with primary open-angle glaucoma and ocular hypertension. Invest Ophthalmol Vis Sci. 2004;45:834–839.

17. Garh¨ofer G, Fuchsj¨ager-Mayrl G, Vass C, Pemp B, Hommer A, Schmetterer L. Retrobulbar blood flow velocities in open angle glaucoma and their association with mean arterial blood pressure. Invest Ophthalmol Vis Sci. 010;51:6652–6657.

18. Anderson DR. Normal-tension glaucoma (Low-tension glaucoma). Indian J Ophthalmol. 2011;59Suppl(Suppl1):S97–S101. doi:10.4103/0301-4738.73695

19. Anderson DR. Glaucoma, capillaries, and pericytes: 1. Blood flow regulation. Ophthalmologica. 1996;210:257–62.

20. Mozaffarieh M, Flammer J. Chapter 5. London: Current Medical Group; 2008. Pocket Reference to Ocular Blood Flow and Glaucomatous Optic Atrophy.

21. Anderson DR. Correlation of the peripapillary anatomy with the disc damage and field abnormalities in glaucoma. Doc OphthalmolProc Ser. 1983;35:1–10.

22. Fatima Jimenez-Aragon, Elena Garcia-Martin, Raquel Larrosa-Lopez, Jose M. Artigas-Martín, PilarSeral-Moral, and Luis E. Pablo, "Role of Color Doppler Imaging in Early Diagnosis and Prediction of Progression in Glaucoma," BioMed Research International, vol. 2013, Article ID 871689, 11 pages, 2013.

23. J. Flammer, S. Orgül, V. P. Costa et al., "The impact of ocular blood flow in glaucoma," Progress in Retinal and Eye Research, vol. 21, no. 4, pp. 359–393, 2002.

24. K. Yaoeda, M. Shirakashi, A. Fukushima et al., "Relationship between optic nerve head microcirculation and visual field loss in glaucoma," ActaOphthalmologicaScandinavica, vol. 81, no. 3, pp. 253–259, 2003.

25. N. Plange, M. Kaup, A. Weber, A. Harris, K. O. Arend, and A. Remky, "Performance of colour Doppler imaging discriminating normal tension glaucoma from healthy eyes," Eye, vol. 23, no. 1, pp. 164–170, 2009.

26. N. Akcar, N. Yildirim, B. Adapinar, T. Kaya, and I. R. Ozkan, "Duplex sonography of retro-orbital and carotid arteries in patients with normal-tension glaucoma," Journal of Clinical Ultrasound, vol. 33, no. 6, pp. 270–276, 2005.

27. F. Galassi, A. Sodi, F. Ucci, G. Renieri, B. Pieri, and M. Baccini, "Ocular hemodynamics and glaucoma prognosis: A Color Doppler Imaging Study," Archives of Ophthalmology, vol. 121, no. 12, pp. 1711–1715, 2003.

28. P. Calvo, A. Ferreras, V. Polo et al., “Predictive value of retrobulbar blood flow parameters in glaucoma suspects,” Investigative Ophthalmology & Visual Science, vol. 53, no. 7, pp. 3875–3884, 2012

29. O. Zeitz, P. Galambos, L. Wagenfeld et al., “Glaucoma progression is associated with decreased blood flow velocities in the short posterior ciliary artery,” British Journal of Ophthalmology, vol. 90, no. 10, pp. 1245–1248, 2006.

30. A. Martínez and M. Sánchez, “Predictive value of colour Doppler imaging in a prospective study of visual field progression in primary open-angle glaucoma,” ActaOphthalmologicaScandinavica, vol. 83, no. 6, pp. 716–722, 2005.

31. E. Hodapp, R. K. Parrish, and D. R. Anderson, Clinical Decisions in Glaucoma, The CV Mosby, St Louis, Mo, USA, 1993.

32. A. Ferreras, A. B. Pajarín, V. Polo, J. M. Larrosa, L. E. Pablo, and F. M. Honrubia, “Diagnostic ability of heidelberg retina tomograph 3 classifications: glaucoma probability score versus moorfields regression analysis,” Ophthalmology, vol. 114, no. 11, pp. 1981.e1–1987.e1, 2007.

33. E. J. Boote, “Doppler US techniques: concepts of blood flow detection and flow dynamics,” Radiographics, vol. 23, no. 5, pp. 1315–1327, 2003

34. T. H. Williamson and A. Harris, “Ocular blood flow measurement,” British Journal of Ophthalmology, vol. 78, no. 12, pp. 939–945, 1994.

35. S. Miglior, M. Guareschi, E. Albe', S. Gomarasca, M. Vavassori, and N. Orzalesi, “Detection of glaucomatous visual field changes using the Moorfields regression analysis of the Heidelberg retina tomograph,” American Journal of Ophthalmology, vol. 136, no. 1, pp. 26–33, 2003.

36. A. Heijl, M. C. Leske, B. Bengtsson, L. Hyman, B. Bengtsson, and M. Hussein, “Reduction of intraocular pressure and glaucoma progression: results from the early manifest glaucoma trial,” Archives of Ophthalmology, vol. 120, no. 10, pp. 1268–1279, 2002.

37. M. C. Leske, A. Heijl, L. Hyman, B. Bengtsson, L. Dong, and Z. Yang, “Predictors of long-term progression in the early manifest glaucoma trial,” Ophthalmology, vol. 114, no. 11, pp. 1965–1972, 2007.

38. R. S. Harwerth, L. Carter-Dawson, F. Shen, E. L. Smith III, and M. L. J. Crawford, “Ganglion cell losses underlying visual field defects from experimental glaucoma,” Investigative Ophthalmology and Visual Science, vol. 40, no. 10, pp. 2242–2250, 1999.

39. C. A. Johnson, P. A. Sample, L. M. Zangwill et al., “Structure and function evaluation (SAFE): II. Comparison of optic disk and visual field characteristics,” American Journal of Ophthalmology, vol. 135, no. 2, pp. 148–154, 2003.

40. S. J. A. Rankin, B. E. Walman, A. R. Buckley, and S. M. Drance, “Color Doppler imaging and spectral analysis of the optic nerve vasculature in glaucoma,” American Journal of Ophthalmology, vol. 119, no. 6, pp. 685–693, 1995.

41. M. T. Nicolela, S. M. Drance, S. J. A. Rankin, A. R. Buckley, and B. E. Walman, “Color Doppler imaging in patients with asymmetric glaucoma and unilateral visual field loss,” American Journal of Ophthalmology, vol. 121, no. 5, pp. 502–510, 1996.

42. H. J. Kaiser, A. Schoetzau, D. Stümpfig, and J. Flammer, “Blood-flow velocities of the extraocular vessels in patients with high-tension and normal-tension primary open-angle glaucoma,” American Journal of Ophthalmology, vol. 123, no. 3, pp. 320–327, 1997.

43. H. Birinci, M. Danaci, I. Oge, and N. D. Erkan, “Ocular blood flow in healthy and primary open-angle glaucomatous eyes,” Ophthalmologica, vol. 216, no. 6, pp. 434–437, 2002.

44. J. Neméth, R. Kovács, Z. Harkányi, K. Knézy, K. Sényi, and I. Marsovszky, “Observer experience improves reproducibility of color Doppler sonography of orbital blood vessels,” Journal of Clinical Ultrasound, vol. 30, pp. 332–335, 2002.

45. A. Harris, T. H. Williamson, B. Martin et al., “Test/retest reproducibility of color Doppler imaging assessment of blood flow velocity in orbital vessels,” Journal of Glaucoma, vol. 4, no. 4, pp. 281–286, 1995.

46. G. K. Kouvidis, A. Benos, G. Kyriakopoulou, G. Anastopoulos, and D. Triantafyllou, “Colour Doppler ultrasonography of the ophthalmic artery: flow parameters in normal subjects,” International Angiology, vol. 19, no. 4, pp. 319–325, 2000.

PATIENT CONSENT FORM

STUDY TITLE:

"A COMPARATIVE STUDY OF BLOOD FLOW VELOCITIES IN OPHTHALMIC ARTERY IN GLAUCOMA PATIENTS"

DEPARTMENT OF OPHTHALMOLOGY, GMKMCH SALEM

PARTICIPANT NAME : AGE : SEX: I.P. NO :

I confirm that I have understood the purpose of surgical/invasive procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the possible complications that may occur during and after medical/ surgical procedure. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to participate in this study for various surgical/invasive procedures and their outcomes.

Time :

Date : Signature / Thumb Impression Of Patient

Place : Patient's name:

Signature of the Investigator : _____

Name of the Investigator _____

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு:

கண்நீர் அழுத்த நோயில் கண்தமனியின் ரத்தஓட்ட வேகம் பற்றிய ஒப்பிட்டு ஆய்வு

பெயர் : தேதி :

வயது : உள்நோயாளி எண் :

பாலினம் : ஆய்வு சேர்க்கைஎண் :

இந்த ஆய்வின் நோக்கம் மற்றும் விவரங்கள் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. இவ்வாய்வில் இருந்து நான் எந்த நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எனக்கு எந்த பாதிப்பும் இல்லை என்பதையும் தெளிவாக புரிந்து கொண்டேன்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆய்வின் போதோ என்னுடைய பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டார்கள் என்பதையும் அறிந்து கொண்டேன்.

இந்த ஆய்வில் எவ்வித நிர்பந்தமும் இன்றி எனது சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகின்றேன்.

நான் சுயநினைவுடனும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் சேர்த்துக்கொள்ள சம்மதிக்கின்றேன்.

ஆராய்சியாளர் ஒப்பம் பங்கேற்பாளர் ஒப்பம்

(அ)

இடது பெருவிரல் ரேகை

PROFORMA

A COMPARATIVE STUDY OF BLOOD FLOW VELOCITIES IN OPHTHALMIC ARTERY IN GLAUCOMA PATIENTS

Group (Tick any one)

Group-A : NORMOTENSIVE GLAUCOMA PATIENTS

Group-B : UNTREATED PRIMARY OPEN ANGLE GLAUCOMA PATIENTS

Group-C : CONTROL GROUP

PATIENT DETAILS :

Name :

Age/Sex :

IP. Number :

Ward/Unit :

Date of study :

PRE-OPERATIVE ASSESSMENT:

Detailed history

RBS

Blood pressure

Lipid profile

Visual acuity

Anterior segment examination

Intraocular pressure

Fundus imaging

Gonioscopy

Visual field assessment

Colour Doppler imaging

KEY TO MASTER CHART

S.NO	-	SERIAL NUMBER
SHTN	-	SYSTEMIC HYPERTENSION
Rx	-	TREATMENT
LP	-	LIPID PROFILE
IOP	-	INTRAOCULAR PRESSURE
C:D	-	CUP:DISC RATIIO
VF	-	VISUAL FIELDS
CDI	-	COLOUR DOPPLER IMAGING
CRA	-	CENTRAL RETINAL ARTERY
OA	-	OPHTHALMIC ARTERY
SPCA	-	SHORT POSTERIOR CILIARY ARTERY
PSV	-	PEAK SYSTOLIC VELOCITY
EDV	-	END DIASTOLIC VELOCITY
RI	-	RESISTANCE INDEX
RE	-	RIGHT EYE
LE	-	LEFT EYE

MASTER CHART

S.NO	AGE/SEX	RISK FACTOR			IOP		C:D		VF		COLOUR DOPPLER IMAGING-NORMOTENSIVE GLAUCOMA																	
											OA						CRA						SPCA					
		SHTN	Rx	LP	RE	LE	RE	LE	RE	LE	PSV		EDV		RI		PSV		EDV		RI		PSV		EDV		RI	
											RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
1	43/F	_	_	N	15	17	0.5	0.5	+	+	23	23.17	5.8	6.2	0.74	0.73	9.8	11.2	3	3	0.7	0.73	12.9	11.8	3	4.5	0.7	0.6
2	52/M	+	+	N	13	15	0.7	0.5	+	+	21.5	21.8	5.8	5.2	0.73	0.76	8.6	12.2	3	3.1	0.7	0.74	11.2	12	3.4	4	0.7	0.66
3	56/M	+	_	AN	17	16	0.6	0.7	+	+	21	22.5	5	5.9	0.76	0.74	9.5	11.9	3	3.4	0.68	0.71	12.6	11.8	3.2	3.2	0.74	0.73
4	62/F	_	_	N	12	11	0.7	0.8	+	+	22.8	23.28	6	5	0.74	0.78	9	11.2	2.5	3.1	0.72	0.72	11.6	12.78	4.5	3.25	0.61	0.74
5	51/F	+	+	N	13	15	0.6	0.7	+	+	20	21.28	4.5	5.2	0.77	0.75	10.5	10.2	2.5	3	0.76	0.7	11.7	12.5	4.12	3.75	0.64	0.7
6	49/M	+	+	AN	12	16	0.6	0.6	+	+	22.54	21.56	3.58	3.56	0.84	0.83	11	11.5	2.7	3	0.75	0.73	12.1	12.65	3.12	3.25	0.74	0.74
7	65/M	_	_	N	17	18	0.7	0.7	+	+	23.25	22.52	4.8	5.2	0.8	0.76	10.2	10.5	3.1	2.9	0.7	0.72	12.35	11.7	3.45	4.1	0.72	0.64
8	50/F	+	+	N	16	18	0.5	0.4	+	+	21.35	23.45	5.7	5.4	0.73	0.77	9.8	10.1	3.5	2.9	0.64	0.71	11.54	11.2	3.68	3.9	0.68	0.65
9	52/M	_	_	AN	11	14	0.4	0.6	+	+	22.8	21.56	3.4	5.5	0.85	0.74	10.3	9.5	3.1	2.7	0.7	0.71	12.45	11.65	3	3.98	0.75	0.65
10	53/F	_	_	AN	15	18	0.6	0.7	+	+	23.5	22.56	5.6	5.4	0.76	0.76	10.4	9.9	3.1	3.3	0.7	0.66	11.21	10.96	4.12	4.1	0.63	0.62
11	56/M	+	_	N	16	15	0.5	0.6	+	+	21.75	22.58	5.8	4.8	0.73	0.79	10.2	10.5	3.5	3.4	0.65	0.67	11.35	12.35	4.32	2.96	0.61	0.76
12	59/M	+	_	AN	18	20	0.8	0.9	+	+	23.54	20.69	4.6	5.1	0.8	0.75	9.7	10.2	2.9	3.4	0.7	0.66	12.68	12.86	3.2	3.24	0.74	0.74
13	64/F	_	_	N	17	20	0.7	0.7	+	+	21.35	21.5	5.6	5.3	0.74	0.75	9.7	10.5	2.8	3.2	0.71	0.69	12.6	12.75	3.12	3.02	0.75	0.76
14	69/M	+	+	AN	12	15	0.7	0.8	+	+	20.36	21.54	5.4	5.3	0.73	0.75	10.9	11.3	2.7	3.4	0.75	0.7	12.57	11.36	3.26	3.01	0.74	0.73
15	56/F	_	_	N	15	16	0.6	0.6	+	+	20.13	21.63	5.6	5.4	0.72	0.75	12.5	10.6	2.9	3.1	0.76	0.7	11.02	11.56	4.3	2.56	0.6	0.77

S.NO	AGE/SEX	RISK FACTOR			IOP		C:D		VF		COLOUR DOPPLER IMAGING-NORMOTENSIVE GLAUCOMA																	
											OA						CRA						SPCA					
		SHTN	Rx	LP	RE	LE	RE	LE	RE	LE	PSV		EDV		RI		PSV		EDV		RI		PSV		EDV		RI	
											RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
16	68/F	_	_	N	18	17	0.5	0.6	+	+	22.45	20.95	5.3	5.6	0.76	0.73	9.5	10.8	3.12	3.16	0.67	0.7	12.56	11.56	3.56	4.12	0.71	0.64
17	52/M	_	_	N	14	15	0.7	0.8	+	+	21.63	22.34	5.7	5.8	0.73	0.74	10.6	9.6	3.24	3.52	0.69	0.63	11.33	11.35	3.68	3.69	0.67	0.67
18	63/M	+	_	AN	16	18	0.7	0.7	+	+	20.96	20.58	5.3	6.3	0.74	0.69	10.9	10.5	2.98	3.2	0.72	0.7	11.65	12.4	3.68	2.56	0.68	0.79
19	65/F	+	+	N	13	14	0.8	0.8	+	+	20.1	21.54	4.8	4.6	0.76	0.78	9.6	10.5	3.31	3.42	0.65	0.67	11.8	11.75	4.45	4.41	0.62	0.62
20	64/F	_	_	N	16	15	0.7	0.6	+	+	20.36	22.1	4.7	4.3	0.77	0.8	11	9.5	3.21	2.98	0.7	0.68	12.03	11.2	3.12	3	0.74	0.73
21	68/M	_	_	N	18	17	0.6	0.5	+	+	22.5	21.9	4.1	4.8	0.81	0.78	10.6	9.9	2.96	2.96	0.72	0.7	11.9	11.65	4.22	4.33	0.64	0.62
22	67/F	+	+	AN	17	19	0.8	0.9	+	+	21.53	20.63	3.75	3.56	0.82	0.83	10.2	10.6	3.12	3.16	0.7	0.7	11.45	12.65	4.1	2.94	0.64	0.76
23	59/F	_	_	N	16	18	0.5	0.7	+	+	21.45	21.46	3.68	3.54	0.83	0.83	9.5	10.5	3.32	3.21	0.65	0.7	11.65	12.56	3.45	3.12	0.7	0.75
24	56/M	+	_	N	15	17	0.8	0.9	+	+	20.49	22.5	4.5	3.68	0.78	0.83	10.4	9.7	3.25	3.32	0.68	0.65	12.34	12.96	3.02	3.24	0.75	0.75
25	49/M	_	_	N	20	17	0.7	0.8	+	+	21.5	22.63	5.68	4.68	0.73	0.79	10.5	9.8	3.1	3.02	0.7	0.7	11.5	11.52	4.1	3.25	0.64	0.71
26	49/F	+	+	AN	18	20	0.8	0.8	+	+	20.45	20.3	3.68	3.57	0.82	0.82	10.2	9.6	3.65	2.96	0.64	0.69	12.69	12.84	3.45	3.6	0.72	0.71
27	52/F	+	_	AN	19	20	0.6	0.8	+	+	21.45	20.6	3.49	5.3	0.83	0.74	10	10.5	2.85	2.99	0.7	0.71	12.69	12.54	2.98	3	0.76	0.76
28	49/M	+	_	AN	17	15	0.7	0.9	+	+	21.6	19.5	4.63	3.64	0.78	0.81	10.3	9.6	3.01	3.12	0.7	0.6	11.59	11.6	2.69	3.54	0.76	0.69
29	46/F	+	+	N	19	17	0.5	0.7	+	+	21.56	22.58	3.54	3.25	0.83	0.85	10.3	9.8	3.24	2.95	0.68	0.69	11.86	11.54	3.56	3.9	0.69	0.66
30	63/M	_	_	N	18	20	0.8	0.9	+	+	23.86	23.46	4.56	5	0.8	0.78	10.6	9.7	2.91	2.85	0.72	0.7	12.95	11.3	3.1	4.1	0.76	0.63

S.NO	AGE/SEX	RISK FACTOR			IOP		C:D		VF		CDI-PRIMARY OPEN ANGLE GLAUCOMA																	
											OA						CRA						SPCA					
		SHTN	Rx	LP	RE	LE	RE	LE	RE	LE	PSV		EDV		RI		PSV		EDV		RI		PSV		EDV		RI	
											RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
1	50/M	+	_	N	28	25	0.6	0.5	+	+	47	46.4	9.8	7.45	0.79	0.83	11.23	12.35	2.13	1.96	0.81	0.84	10.6	12.3	3.12	3	0.7	0.75
2	52/F	+	_	N	31	27	0.7	0.7	+	+	45.75	36	8.5	10.3	0.81	0.71	11.65	11.52	2.53	1.25	0.78	0.89	10.9	11.8	3.1	3.4	0.71	0.71
3	47/F	_	_	N	25	23	0.5	0.6	+	+	36	37	10.3	11.3	0.71	0.69	12.67	12.36	2.86	1.98	0.77	0.83	10.2	11.96	3	3.2	0.7	0.73
4	63/M	+	+	AN	26	28	0.6	0.6	+	+	43	41.35	7.86	8.52	0.81	0.79	11.58	12.6	2.54	1.63	0.78	0.87	10.8	10.35	3.12	3.12	0.71	0.69
5	68/F	_	_	N	24	26	0.8	0.7	+	+	46.35	47.32	7.1	7.58	0.84	0.83	12.47	15.6	2.75	2.31	0.77	0.85	11.2	11.2	3.42	2.86	0.69	0.74
6	54/F	_	_	N	29	24	0.6	0.5	+	+	36.5	39.75	7.64	7.94	0.79	0.8	12.5	11.47	2.1	1.69	0.8	0.85	11.5	10.98	3.25	3.4	0.71	0.69
7	52/M	_	_	N	23	28	0.5	0.7	+	+	38.54	39.53	8.12	8.14	0.78	0.79	12.85	11.96	2.45	1.86	0.8	0.84	11.25	10.6	3.2	3.65	0.71	0.65
8	51/F	+	_	AN	34	31	0.6	0.8	+	+	41.68	43.85	7.45	8.36	0.8	0.8	12.57	11.45	2.45	2.36	0.8	0.79	9.68	10.57	2.65	3.24	0.72	0.69
9	57/M	+	+	AN	32	30	0.5	0.6	+	+	45.97	39.65	7.65	7.42	0.83	0.81	12.47	11.35	2.45	2.14	0.8	0.81	9.35	9.61	3.15	3	0.66	0.68
10	62/F	_	_	N	25	28	0.6	0.7	+	+	38	36.4	8.3	6.95	0.78	0.8	12.45	11.69	2.65	2.47	0.78	0.78	10.2	11.68	3.25	3.21	0.68	0.72
11	67/M	_	_	N	26	24	0.5	0.5	+	+	37.5	36.8	7.23	8.12	0.8	0.77	12.58	11.45	1.78	2.65	0.85	0.76	10.4	11.25	3.25	3.12	0.68	0.72
12	56/M	+	+	AN	28	29	0.6	0.6	+	+	39.56	41.32	7.65	7.55	0.8	0.81	12.68	11.45	2.45	2.35	0.8	0.8	9.68	10.24	3.12	3.05	0.67	0.7
13	49/F	_	_	N	24	21	0.6	0.5	+	+	42.35	40.65	8.65	7.1	0.79	0.82	12.68	11.57	1.94	2.65	0.84	0.77	9.36	10.25	3.25	3.12	0.65	0.69
14	54/M	+	_	AN	26	23	0.7	0.6	+	+	41.52	42.53	7.32	7.24	0.82	0.83	11.69	12.4	1.98	2.65	0.83	0.78	10.4	9.68	3.65	4.35	0.64	0.5
15	53/F	_	_	N	28	25	0.6	0.5	+	+	41.36	46.25	7.35	8.12	0.82	0.82	11.6	11.75	2.37	2.34	0.79	0.8	10.47	9.68	3.25	3.84	0.68	0.6

S.NO	AGE/SEX	RISK FACTOR			IOP		C:D		VF		CDI-PRIMARY OPEN ANGLE GLAUCOMA																	
											OA						CRA						SPCA					
		SHTN	Rx	LP	RE	LE	RE	LE	RE	LE	PSV		EDV		RI		PSV		EDV		RI		PSV		EDV		RI	
											RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
16	47/F	+	+	AN	23	27	0.5	0.8	+	+	42.31	41.32	7.23	7.55	0.82	0.81	12.3	11.68	2.4	2.54	0.8	0.78	11.2	9.8	3.24	3.51	0.7	0.64
17	64/M	+	_	N	24	23	0.6	0.5	+	+	41.36	41.9	7.45	6.95	0.81	0.83	11.9	11.24	2.4	2.6	0.8	0.7	9.2	9.5	3.24	3.51	0.64	0.63
18	73/F	+	_	N	26	24	0.7	0.6	+	+	42.5	38.12	7.1	7.12	0.83	0.81	11.65	11.41	2.4	2.3	0.8	0.8	9.6	9.64	3.61	3.57	0.62	0.62
19	66/M	+	+	N	28	28	0.6	0.6	+	+	41.5	43.25	6.85	7.21	0.83	0.83	11.3	11.4	2.3	2.65	0.7	0.7	9.32	10.5	3.68	3.84	0.6	0.63
20	72/M	_	_	N	29	29	0.7	0.8	+	+	44.2	41.56	6.95	6.85	0.84	0.83	12.6	12.7	2.3	2.41	0.8	0.8	9.35	10.25	3.68	3.57	0.6	0.65
21	68/M	_	_	N	32	34	0.8	0.9	+	+	42.8	38.56	7.23	8.12	0.83	0.78	11.95	11.65	2.84	2.65	0.76	0.77	9.65	10.25	3.69	3.84	0.6	0.6
22	70/M	+	+	N	34	27	0.9	0.8	+	+	42.35	43.15	8.6	8.96	0.79	0.79	11.4	11.32	2.3	2.14	0.8	0.8	9.67	10.25	3.65	3.84	0.6	0.6
23	54/F	+	_	AN	26	26	0.6	0.7	+	+	44.2	41.25	9.12	9.25	0.79	0.77	11.25	11.3	2.31	2.6	0.8	0.76	9.65	10.24	3.1	3.54	0.67	0.65
24	65/M	_	_	N	29	27	0.7	0.8	+	+	41.68	38.5	9.18	9.65	0.77	0.74	11.24	11.65	2.34	2.41	0.8	0.8	9.84	9.61	3.61	3.74	0.63	0.61
25	63/F	+	+	AN	27	28	0.6	0.7	+	+	40.65	39.56	8.63	8.24	0.78	0.79	11.24	11.78	2.65	2.54	0.7	0.7	9.21	9.65	3.52	3.42	0.61	0.64
26	62/M	+	+	N	26	23	0.5	0.5	+	+	41.35	39.5	8.36	8.3	0.79	0.78	11.65	11.54	2.64	2.61	0.7	0.7	9.45	9.21	3.65	3.12	0.61	0.66
27	60/F	_	_	N	24	24	0.7	0.6	+	+	39.65	41.35	8.46	9.1	0.78	0.77	11.24	11.65	2.95	2.64	0.73	0.77	9.45	10.25	3.24	3.65	0.65	0.64
28	57/F	+	+	AN	24	26	0.8	0.5	+	+	39.84	41.25	10.2	9.7	0.74	0.76	11.54	11.95	2.45	2.12	0.8	0.8	9.68	10.24	3.15	3.75	0.67	0.63
29	67/F	_	_	N	26	27	0.7	0.6	+	+	39.57	39.54	9.6	9.8	0.75	0.75	11.24	11.64	2.41	2.62	0.78	0.77	10.84	10.65	3.17	3.02	0.7	0.71
30	62/M	_	_	N	28	28	0.6	0.6	+	+	41.85	40.25	10.5	9.6	0.74	0.76	11.25	11.54	2.5	2.45	0.77	0.78	10.28	9.21	3.14	3.12	0.69	0.66

S.NO	AGE/SEX	RISK FACTOR			IOP		C:D		VF		CDI-NORMAL																	
											OA						CRA						SPCA					
		SHTN	Rx	LP	RE	LE	RE	LE	RE	LE	PSV		EDV		RI		PSV		EDV		RI		PSV		EDV		RI	
											RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
1	45/M	_	_	N	16	14	0.3	0.3	_	_	40.2	42.58	14.35	14.95	0.64	0.64	12.64	11.96	4.65	4.28	0.63	0.64	13.54	12.75	5.24	5.36	0.61	0.5
2	52/M	_	_	N	13	14	0.4	0.3	_	_	42.69	45.68	13.98	15.84	0.67	0.65	12.35	11.54	5.64	4.67	0.54	0.59	13.65	13.42	5.1	5.32	0.62	0.6
3	54/F	_	_	N	15	13	0.3	0.3	_	_	43.57	46.52	15.98	14.68	0.63	0.68	12.96	11.58	5.64	4.37	0.56	0.62	14.25	13.47	6.24	5.24	0.56	0.61
4	62/M	_	_	N	12	12	0.3	0.3	_	_	43.85	44.36	13.54	15.42	0.7	0.65	12.65	11.45	5.27	4.35	0.58	0.62	14.95	12.57	5.84	6.32	0.6	0.5
5	57/F	_	_	N	12	14	0.3	0.4	_	_	44.85	43.65	16.54	14.95	0.63	0.65	11.35	11.24	4.68	4.57	0.58	0.59	13.57	13.45	5.57	6.24	0.58	0.53
6	56/F	_	_	N	14	14	0.3	0.3	_	_	43.57	44.69	14.73	15.84	0.66	0.64	11.65	11.24	4.51	5.31	0.61	0.52	13.68	14.21	5.47	6.21	0.6	0.56
7	53/M	_	_	N	13	13	0.3	0.3	_	_	43.65	42.57	15.67	15.94	0.64	0.62	11.65	11.24	4.5	5.23	0.61	0.53	13.41	12.42	5.34	6.34	0.6	0.5
8	57/F	_	_	N	18	15	0.4	0.3	_	_	43.68	42.57	14.68	15.24	0.66	0.64	12.64	11.54	4.27	4.62	0.66	0.6	13.24	12.54	5.47	6.31	0.58	0.5
9	52/M	_	_	N	17	14	0.3	0.3	_	_	43.94	42.75	14.67	15.43	0.66	0.63	12.54	11.24	4.21	4.62	0.66	0.58	13.57	12.84	5.61	6.3	0.58	0.5
10	54/F	_	_	N	13	14	0.4	0.3	_	_	43.69	44.52	15.67	13.47	0.64	0.7	12.64	11.23	4.54	4.32	0.64	0.61	13.54	12.47	5.04	6.37	0.62	0.5
11	48/F	_	_	N	12	12	0.3	0.3	_	_	44.69	46.57	14.68	15.96	0.67	0.65	11.54	11.84	4.51	4.23	0.6	0.64	13.54	12.24	5.09	6.47	0.6	0.47
12	48/M	_	_	N	15	14	0.3	0.3	_	_	43.91	43.51	14.68	15.37	0.66	0.64	12.45	11.34	4.21	4.62	0.66	0.6	13.64	12.57	6.24	5.24	0.54	0.58
13	56/F	_	_	N	13	13	0.3	0.3	_	_	44.13	44.36	14.98	15.43	0.66	0.65	12.45	11.96	4.25	4.76	0.65	0.6	13.68	12.24	6.01	5.41	0.5	0.55
14	52/F	_	_	N	14	14	0.3	0.3	_	_	44.21	44.3	16.87	13.47	0.6	0.7	11.65	12.84	5.02	4.86	0.56	0.62	13.57	13.57	6.24	5.21	0.54	0.61
15	53/F	_	_	N	12	12	0.3	0.3	_	_	45.91	43.61	14.98	15.67	0.67	0.64	12.54	11.36	5.26	4.65	0.58	0.6	14.57	13.47	5.34	6.14	0.63	0.54

S.NO	AGE/SEX	RISK FACTOR			IOP		C:D		VF		CDI-NORMAL																	
											OA						CRA						SPCA					
		SHTN	Rx	LP	RE	LE	RE	LE	RE	LE	PSV		EDV		RI		PSV		EDV		RI		PSV		EDV		RI	
											RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
16	58/M	_	_	N	16	15	0.3	0.3	_	_	43.57	44.25	14.52	15.24	0.66	0.65	11.74	11.52	5.35	4.96	0.54	0.56	12.54	13.24	5.34	5.24	0.57	0.6
17	68/F	_	_	N	13	14	0.3	0.4	_	_	44.68	45.25	15.34	15.24	0.65	0.66	12.62	11.57	5.65	4.27	0.55	0.63	13.75	13.24	6.51	5.32	0.52	0.6
18	72/F	_	_	N	14	14	0.3	0.3	_	_	43.21	41.25	14.87	14.27	0.65	0.65	11.39	11.02	5.69	4.21	0.5	0.61	13.25	13.85	6.21	6.32	0.53	0.54
19	45/M	_	_	N	12	16	0.4	0.3	_	_	43.5	42.58	15.31	15.68	0.64	0.63	12	10.39	5.87	4.63	0.51	0.55	13.24	14.65	5.24	5.32	0.6	0.63
20	62/F	_	_	N	15	13	0.3	0.3	_	_	45.85	42.65	15.24	14.78	0.66	0.65	11.96	12.56	5.41	4.65	0.54	0.62	15.27	12.54	6.23	5.62	0.6	0.55
21	63/M	_	_	N	16	15	0.4	0.4	_	_	43.5	43.68	14.32	14.57	0.67	0.66	12.86	12.64	5.96	5.34	0.53	0.57	14.65	14.85	5.34	5.61	0.63	0.62
22	52/F	_	_	N	14	14	0.3	0.3	_	_	43.5	45.8	14.35	14.25	0.67	0.68	12.94	12.65	5.21	5.67	0.6	0.55	14.36	14.57	5.24	5.62	0.63	0.61
23	59/M	_	_	N	13	13	0.4	0.3	_	_	44.21	42.65	15.27	14.35	0.65	0.66	11.65	11.82	5.61	4.37	0.51	0.63	15.24	15.34	5.24	4.62	0.65	0.7
24	55/M	_	_	N	14	15	0.3	0.3	_	_	41.25	43.58	14.9	15.23	0.63	0.65	12.65	11.48	4.91	5.84	0.61	0.5	12.34	15.34	5.31	6.24	0.56	0.6
25	56/F	_	_	N	12	18	0.4	0.3	_	_	42.65	41.25	15.34	15.24	0.64	0.63	11.61	11.42	4.32	4.52	0.62	0.6	15.67	14.57	5.37	6.51	0.65	0.55
26	68/F	_	_	N	14	13	0.3	0.3	_	_	42.65	43.85	14.75	14.62	0.65	0.66	12.42	11.62	4.27	4.61	0.65	0.6	15.64	14.35	5.31	6.51	0.66	0.54
27	64/M	_	_	N	13	16	0.3	0.3	_	_	42.14	43.52	14.32	15.24	0.66	0.64	12.34	11.24	4.25	4.51	0.65	0.6	15.64	15.32	5.31	6.25	0.66	0.6
28	68/F	_	_	N	16	13	0.4	0.3	_	_	43.25	42.15	14.25	15.34	0.67	0.63	12.51	11.24	4.36	4.28	0.65	0.61	15.48	14.36	5.92	6.35	0.61	0.55
29	72/F	_	_	N	14	14	0.3	0.3	_	_	43.15	42.58	14.24	14.32	0.66	0.66	12.51	11.24	4.61	4.67	0.63	0.5	15.46	14.26	7.35	5.62	0.52	0.6
30	63/M	_	_	N	13	15	0.3	0.3	_	_	43.15	42.15	14.12	14.32	0.67	0.66	12.51	11.26	4.68	4.62	0.62	0.58	15.34	14.38	5.64	6.35	0.63	0.55