"A CROSS-SECTIONAL STUDY ON MEASUREMENT OF OPTIC NERVE SHEATH DIAMETER BY B SCAN IN PATIENTS WITH ESTABLISHED PAPILLEDEMA AND ITS CORRELATION WITH FRISEN'S SEVERITY GRADING"

By

DR. YUGANDHARA PATADE, M.B.B.S

Dissertation submitted to

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, CENTRE, TAMAKA, KOLAR

In partial fulfilment of the requirements for the degree of

MASTER OF SURGERY
IN
OPHTHALMOLOGY

Under the guidance of

DR. MANJULA T R

M.B.B.S., M.S.

DEPARTMENT OF OPHTHALMOLOGY

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR.

2023

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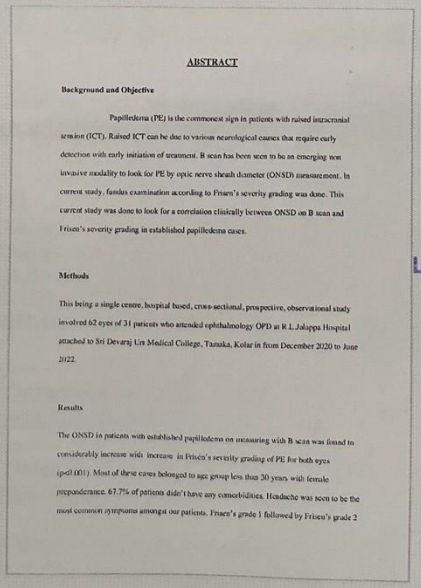

ABSTRACT

Background and Objective

Papilledema (PE) is the commonest sign in patients with raised intracranial tension (ICT). Raised ICT can be due to various neurological causes that require early detection with early initiation of treatment. B scan has been seen to be an emerging non invasive modality to look for PE by optic nerve sheath diameter (ONSD) measurement. In current study, fundus examination according to Frisen's severity grading was done. This current study was done to look for a correlation clinically between ONSD on B scan and Frisen's severity grading in established papilledema cases.

Methods

This being a single centre, hospital based, cross-sectional, prospective, observational study involved 62 eyes of 31 patients who attended ophthalmology OPD at R.L.Jalappa Hospital attached to Sri Devaraj Urs Medical College, Tamaka, Kolar in from December 2020 to June 2022.

Results

The ONSD in patients with established papilledema on measuring with B scan was found to considerably increase with increase in Frisén's severity grading of PE for both eyes ($p<0.001$). Most of these cases belonged to age group less than 30 years with female preponderance. 67.7% of patients didn't have any comorbidities. Headache was seen to be the most common symptoms amongst our patients. Frisen's grade 1 followed by Frisen's grade 2

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LIST OF ABBREVIATIONS

PE	Papilledema
ICT	Intra cranial tension
ONSD	Optic nerve sheath diameter
ICP	Intra cranial pressure
IH	Intracranial Hypertension
CVS	Cerebral venous sinus
IIH	Idiopathic Intracranial Hypertension
PPE	Pseudopapilledema
CRVO	Central Retinal Vein Occlusion
ON	Optic Nerve
CSF	Cerebrospinal Fluid
SVP	Spontaneous venous pulsation
MRI	Magnetic Resonance Imaging
ONH	Optic nerve head
LP	Lumbar puncture
CT	Computed Tomography
ICU	Intensive Care Unit
LC	Lamina Cribrosa
CRA	Central Retinal Artery
SR	Superior Rectus
MR	Medial Rectus
OA	Ophthalmic artery

ICA	Internal Carotid Artery
GCL	Ganglion cell layer
ILM	Internal limiting membrane
CNS	Central nervous system
SAS	Subarachnoid space
VA	Visual acuity
BCVA	Best corrected visual acuity
RAPD	Relative afferent pupillary defect
VEP	Visual evoked potential
EEG	Electroencephalogram
OCT	Optical Coherence Tomography
PVEP	Pattern onset visual evoked potential
fVEP	Flash visual evoked potential
ISF	Interstitial fluid
SAS	Subarachnoid space
TBI	Traumatic brain injury
ONS	Optic nerve sheath
TVO	Transient visual obscuration
TI	Thermal Index
MI	Mechanical Index
+ve	Positive

-ve	Negative
RE	Right eye
LE	Left eye
USG	Ultrasonography
DM	Diabetes Mellitus
HTN	Hypertension
RTA	Road traffic accident
CVA	Cerebrovascular accident
CKD	Chronic kidney disease
UTI	Urinary tract infection
GCS	Glasgow coma scale

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Background and Objective

Papilledema (PE) is the commonest sign in patients with raised intracranial tension (ICT). Raised ICT can be due to various neurological causes that require early detection with early initiation of treatment. B scan has been seen to be an emerging non invasive modality to look for PE by optic nerve sheath diameter (ONSD) measurement. In current study, fundus examination according to Frisen's severity grading was done. This current study was done to look for a correlation clinically between ONSD on B scan and Frisen's severity grading in established papilledema cases.

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Conclusion and interpretation

This study showed a positive correlation between ONSD measurement on B scan with Frsien's severity grades in established papilledema patients. B Scan can hence be a modality which is non invasive and less expensive when compared to other modalities by which we can detect raised intracranial tension.

Keywords: Papilledema, optic nerve sheath diameter, B Scan, Intracranial tension, Frisen's severity grading.

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INTRODUCTION

Increase of ICP can occur when there is absence of papilledema (PE), but PE cannot exist if high ICP is absent. “The term papilledema is defined as passive, non-inflammatory, hydrostatic edema of the optic nerve head secondary to high intracranial pressure (ICP).” PE is often respective and bilateral, yet might be uneven or one-sided. Increased ICP also known as intracranial hypertension (IH) may have a known or unknown cause (such as a brain tumour, meningitis), or thrombosis of the cerebral venous sinus (CVS).[1] Papilledema resulting from a variety of IH causes can occur at any age, regardless of sex, race, or ethnicity. Even though infants and very young children can have high ICP, open fontanels may prevent these patients from developing papilledema despite IH.[2] Idiopathic intracranial hypertension (IIH), on the other hand, mostly affects obese women who are in their reproductive age. In United states, 0.9 incidence in usual population and particularly females incidence of 3.5 of fifteen–forty four years of age/100,000 people/year has been assessed.[3,4] It needs to be distinguished from pseudopapilledema (PPE), which may result from hyperopia or an optic disc drusen. Inflammation inside the eye, optic neuritis, disc oedema in hypertensive patients, central retinal vein occlusion (CRVO), ischemic or compressive optic neuropathy, scleritis, and infiltrative tumours are a few more causes of optic disc enlargement. It contains red flag sign for intracranial entities, necessitating immediate diagnosis and treatment. In ischemia, inflammation, infiltration of optic nerve (ON), its compression, edema of disc unilaterally is commonly seen. However, very few cases of papilledema approximately up to 2% may be present unilaterally or very asymmetrically.[5] In such instances, ocular and orbital conditions should be looked for and investigated. [6] Cerebrospinal Fluid (CSF) opening pressure (usually between 10-25cm of H2O) is preferred considering it to be a gold standard diagnostic tool to evaluate raised ICP. High CSF-increased ICP can be caused by extensive lesions like tumor or haemorrhage, reduced CSF absorption in hydrocephalus and obstruction of venous flow, CSF production

increment in tumour of choroid plexus/pseudotumor cerebri(idiopathic).[7] Symptoms include nausea and vomiting, transient visual obscuration (when rising to stand), and headaches that are worse in the morning. It can as well result in cranial nerve palsies in which commonly abducens palsy is seen.[8] Patients should be questioned regarding their use of medications, pregnancy, and systemic diseases in patients suspected with such condition. Pupil responses of light and accomodation must be tested. In the early phases, fundoscopy reveals a halo which is C-shaped with a temporal gap. Paton's lines, which are circumferentially seen retinochoroidal folds that surrounding the disc and are typically temporal, may be present. The optic cup is obliterated, a major blood vessel's portion is obscured, and the nerve head is elevated in the late phases. Increased ICP is also suggested by the absence of spontaneous venous pulsation (SVP). The first step in confirming a papilledema diagnosis is Magnetic Resonance Imaging (MRI) to look for large lesions. Scleral flattening near the ON and a raised optic nerve head (ONH) can be observed. Lumbar puncture(LP) with opening pressure should be preferred performing whenever there is no contraindication. CSF should be sent and cytology and culture should be done.[9] Even though ICP is managed primarily for prevention of herniation and for preservation of cerebral blood flow, papilledema which is persistent may result in atrophy changes in ON and hence permanent vison loss. The etiological factors should be interpreted at the earliest. Diuretics being the main treatment line, have shown to lessen ICP by expanding CSF assimilation or reducing its production, and typically are very much endured. When medical therapy fails, surgical procedures like the creation of lumboperitoneal or ventriculoperitoneal shunts should be considered. These shunts normalize ICP by increasing CSF drainage. Optic nerve sheath fenestration can be considered to decompress nerve in certain situations where vision is at risk.[10] The severity and duration of papilledema can be categorized into four stages: early, established, chronic, and atrophic. Edema may extend beyond the ONH in the form of circumferential retinal folds

and parallel choroidal folds over the posterior pole. Established papilledema shows marked elevation of the ONH and blurring of margins, sometimes even up to 6 to 7D. Vascular signs include cotton-wool spots, engorged, tortuous venules, peripapillary splinter hemorrhages, hard exudates over the disc and the macular region, and so on. [11] There are currently no new medications that specifically treat increased ICP. A safer, quicker, and simpler method of diagnosing progressive papilledema could be developed through advancements in neuroimaging modalities. However, direct fundoscopy continues to be an essential diagnostic and treatment tool in these instances. Because of its fluid content and its superficial position, the eyeball is an excellent candidate for ultrasonography examination.[12,13] The posterior part of the eyeball's opaque region contains the echolucent vitreous. The diaphragm separates the aqueous humor-filled anterior section of the iris into two chambers. The choroid, sclera, and retina are the three layers that protect the eyeball. The biconvex transparent lens is located behind the iris. On a B-scan, the posterior segment of the vitreous is shown as a clear section, and posterior lens capsule's anterior echo is visible. Axial length of an adult eye is 24mm.[12-14] A rapid, non-invasive examination called ocular ultrasound, sometimes referred to as ocular echography or B-scan, is frequently used to assess structural integrity of eye and search for any abnormalities. Extra data can be obtained that is not promptly gotten by direct perception of visual tissues, and especially valuable in patients with conditions that prevents use of ophthalmoscopy such as huge corneal opacities, thick waterfalls or glassy drain.[15] According to recent studies, non-invasive imaging methods can be used to measure optic nerve sheath diameter (ONSD), an alternative marker for early increased ICP.[16-19] On the other hand, MRI and Computed tomography(CT)scans for ONSD measures being pricey, require more time with mobilisation of patients. For instances that require intensive care unit (ICU) and real-time ICP monitoring, ONSD assessment by ultrasonography may be a wise alternative due to its advantages of being a less expensive tool and speedy bedside process.[19,20]

AIMS AND OBJECTIVES

OBJECTIVES OF THE STUDY

1) To grade patients with established papilledema according to Frisen's severity grading.

2) To correlate optic nerve sheath diameter measurement by B scan with Frisen's severity grading.

REVIEW OF LITERATURE

EMBRYOLOGY OF OPTIC NERVE (ON)

The origin of ON is the neural ectoderm. The optic stalk appears between gestational period of 22 and 28 days and it develops within it. The optic vesicle and forebrain cavity are connected by the optic stalk. [21] It has two layers: ganglion cell axons forms the inner and outer layer comprises of neuroglial supporting cells. Neuroepithelial cells, like astrocytes and oligodendrocytes, begin to multiply at 8 weeks of pregnancy and take part in development of ON's connective tissue along with its myelination. Myelination begins in the center and continues to reach the lamina cribrosa(LC) at birth or immediately after that.[22]

ANATOMY AND PHYSIOLOGY OF ON

Nerve cell layer of retina is made up of ganglion cell axons. The axons of the ganglion cells are supplied by central retinal artery (CRA), and they are normally not myelinated. Progressing 90 degrees later, they enter the optic plate. They are arranged as ON here. Optic disc is nourished by a circle of small ciliary artery branches called Circle of Zinn. Additionally, optic disc blood supply is also contributed by peripapillary arteries. The ON comprises of fibers that are almost about 1.2 million with various diameters that range between 0.7-10μm. Larger fibers originate from peripheral retina, whereas smaller fibers support central vision.[23] The fibers of the macular retina are deeper in the ON's center compared to superficial fibers belonging to peripheral retina. The length of ON is approximately 6cm and further can be divided into 4 parts anatomically: intracanalicular(6–10mm), intracranial(10–16mm), intraocular(0.7–1mm), and intraorbital(30mm). The intraocular portion is divided into prelaminar and laminar sections by the LC.[24] It is essential to note that this section of the nerve does not have any myelin. The LC serves like a barrier which prevents oligodendrocytes, so they don't cause myelination of optic nerve in its intraocular part since they cause myelination of nerves.[25] The ON is myelinated and dural

sheath surrounds it and CSF surrounds beyond the LC. The ON's orbital part is surrounded by extraocular muscles. Due to the adhesion of the ONS to superior rectus(SR)muscle and also to medial rectus(MR)muscle, optic neuritis-related eye movement pain is caused by inflammation of ON. Ophthalmic artery(OA), primary branch of internal carotid artery(ICA) frames fundamental supply of intra-orbital division of ON and intra-canalicular division of ON. In intracanalicular section, the OA travels through ON's dura sheath. The OA, anterior communicating, inferior cerebral, and internal carotid arteries supply the intracranial ON division. The optic chiasm is formed by the joining of 90% of the ON fibers from each side, and the rest of the fibers which are about 10% project to areas that control pupillary responses.[25]

OPTIC NERVE HEAD (ONH) ANATOMY

ON is a one-of-a-kind feature because it is the only tract that can be seen clinically using direct ophthalmoscopy and is encompassed by cerebrospinal fluid.[26] Central scotoma and the centrocaecal scotoma are both present in ON disorder because the ONH is produced by axons of the ganglion cell layer(GCL), with the papillomacular bundle accounting for approximately 90% of this contribution. The extension is from disc to sphenoid bone's optic canal.

4 parts of ON :

(a) Intra-ocular

(b) Intra-orbital

(c) Intra-canalicular

(d) Intra-cranial portions.[27]

For purposes of description, intraocular optic nerve is further subdivided into:

(i) Surface nerve fiber layer region

(ii) Prelaminar area

(iii) LC region

(iv) Retrolaminar area.

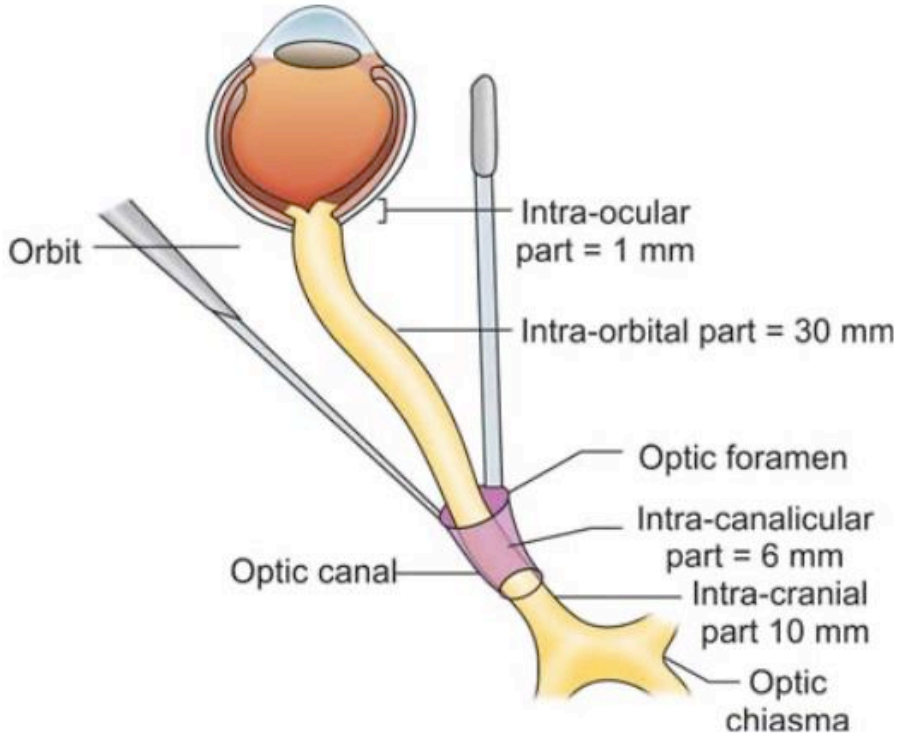

Figure 1: Portions of the ON

(a) Intra-ocular part : The optic disc appears in the eye after passing through the choroid and sclera. The ONH's intraocular portion which measures around diameter of 1.5mm on an average and approximately grows to 3millimeters just behind the sclera and here neurons begin to gain the myelin sheath.[28-30] ONH may be divided as follows from anterior to posterior (Figure 2) :

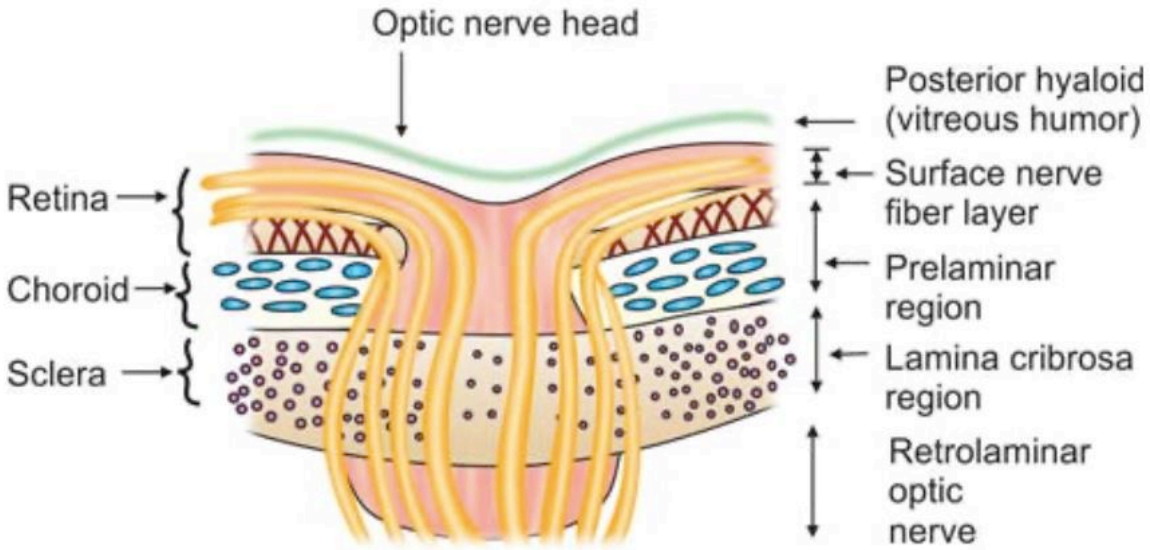

Figure 2 : ONH Divisions

(i)Surface nerve fiber layer

It is basically made out of bundles of axons, for example nerve fibers of the retina around 94% which unite on the disc and astrocytes. The Elschnig's internal limiting membrane which is a thin astrocytes layer separates the optic disc from vitreous which is then continuous with internal limiting membrane (ILM) of retina which covers disc.

(ii) Prelaminar region

This part of the ON just distal to the ONH where neurons and a larger number of astroglial tissues are the most common structures. The Jacobie border tissue separates this section of the ON from choroid.

(iii) LC

It's a structure that looks like a fibrillar sieve and which is formed of connective tissue sheets that are fenestrated as well as lined by glial tissue. Through these fenestrations, bundles of fibers from the ON exit the eye. Border tissue of Elschnig is made up of rim of connective tissue that is collagenous and glial cells that connect the choroid, sclera and ON fibers.

(iv) Retrolaminar region

The axons in this region of the ON acquire a myelin sheath that is supplied by oligodendrocytes, making it distinctive. As it travels through sclera, the ON's diameter nearly doubles, from 1.5 to 3.0 mm.

At this point, about two-thirds of the interstitial cells are oligodendrocytes, which are responsible for making the myelin that covers the axons. Schwann cells in peripheral nerves perform the same function.

Relevance: Instead of being compared to peripheral nerves, the ON is thought to be similar to white matter tracts of the brain. The ON is more susceptible to Central nervous system (CNS) tract diseases like multiple sclerosis because of this composition.

(b) Intra-orbital part :

From the back of the eyeball to the optic foramina, the intra-orbital portion of the ON runs. This part is somewhat sinous that allows for the expansion of optic nerve during eye movements.

The following points are significant in relation to the ON's intra-orbital portion:

1. Meninges (dura, arachnoids, and pia mater) surround the optic nerve's intra-orbital portion. Subarachnoid space ends at the point where the ON enters the globe and wraps around it into the orbit. However, it continues intracranially posteriorly. The pial sheath separates the nerve into fasciculi by sending septa, which carry the capillaries.

2. Vein that goes with the CRA crosses the subarachnoid space (SAS) to enter the nerve on its inferomedial side, approximately 10 millimeters from the eyeball.

3. The ON is in close approximation and surrounded by the annulus of Zinn and the 4 rectus muscles near the optic foramen (FIGURE 3). [11]

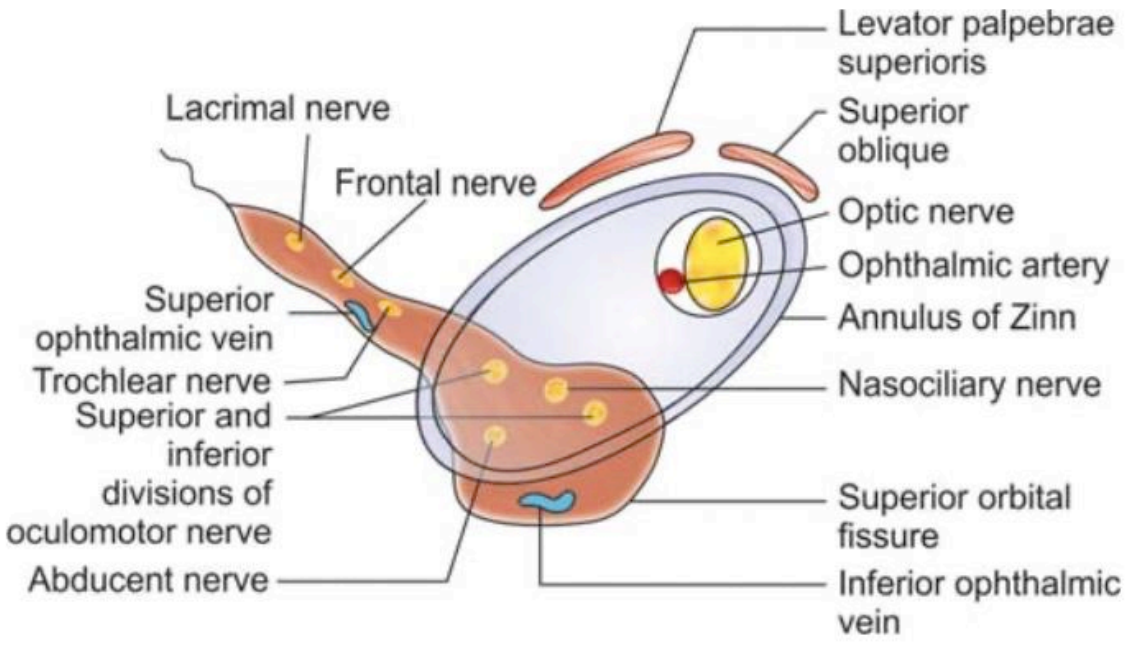

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Figure 3 : Annulus of Zinn and recti muscles surrounding the ON.

Relevance: This close proximity of the structures around the ON accounts for symptom complex of orbital apex syndrome that is characterized by proptosis, painful ophthalmoplegia (third, fourth, sixth nerve palsy) and loss of vision.

- Some fibers of the SR and MR muscles adhere to ON close to the optic foramen. Retrobulbar neuritis is characterized by painful ocular movements as a result of this.
- Prior to entering the eyeball, ON is surrounded by long and short posterior ciliary nerves and arteries.
- Between ON and LR muscle are divisions of oculomotor, nasociliary, sympathetic, abducent nerves, as well as ciliary ganglion.

From the lateral to medial, ON is crossed superiorly by OA, superior ophthalmic vein and nasociliary nerve.

(c) Intra-canalicular part :

This component has a length of about 5-7 mm. Together with the meningeal sheaths, this section of the optic nerve has very little room for expansion. Intra-canalicular portion of ON is frequently affected in majority of traumatic optic neuropathies. In contrast to the intra-orbital portion, the intra-canalicular portion of the ON has no space to expand, so any edema there can result in compression.

Relations of the Intra-canalicular Part :

Ophthalmic artery: In the dural sheath, it crosses ON inferiorly from the medial going to the lateral side. At orbital end of the canal, it exits the sheath.

Sinuses sphenoidal and posterior ethmoidal: A thin bone lamina separates these, which are located medially to it. This portion of the bone is very thin, especially in children, which is why patients with sinusitis frequently develop optic neuritis.

(d) Intra-cranial part :

This is the optic nerve's most proximal 10 mm before it joins the chiasma. It is in close proximity to internal carotid vessels and cavernous sinus. It is covered in pia mater, but when it enters the optic canal, it is covered in arachnoids and dural sheaths. The ICA follows it from below to lateral. Below the ON, the ICA becomes OA. This section of ON is connected to anterior perforated substance, the medial olfactory tract root and anterior cerebral artery on the superior side. [11]

Functional Organization of the Axons in ON

Retinotopy segregation, which refers to the topographic connection of ON fibres to retinal location, increasingly disappears as axons enter the nerve, notably between axons originating from superior and inferior retinas. It is still well defined, though, both at the ONH and close to the chiasma. There is only moderate retinotopy in the early ON section.[31] After decreasing distally[32,33], the retinotopy is then directed for eventual nasal decussation close to the chiasma.[34] According to the description, macula fibres are located in temporal region not far from ONH. Nasal retina's fibres are found in nasal region of the disc, whereas superior and inferior arcuate retina's fibres are found in superior and inferior poles, respectively (FIGURE 4). Superior and inferior retinal fibres (superotemporal arcuate and superonasal radiating fibres, respectively) occupy superior and inferior parts of nerve, while macular fibres occupy a more central location in the more proximal portion of ON.

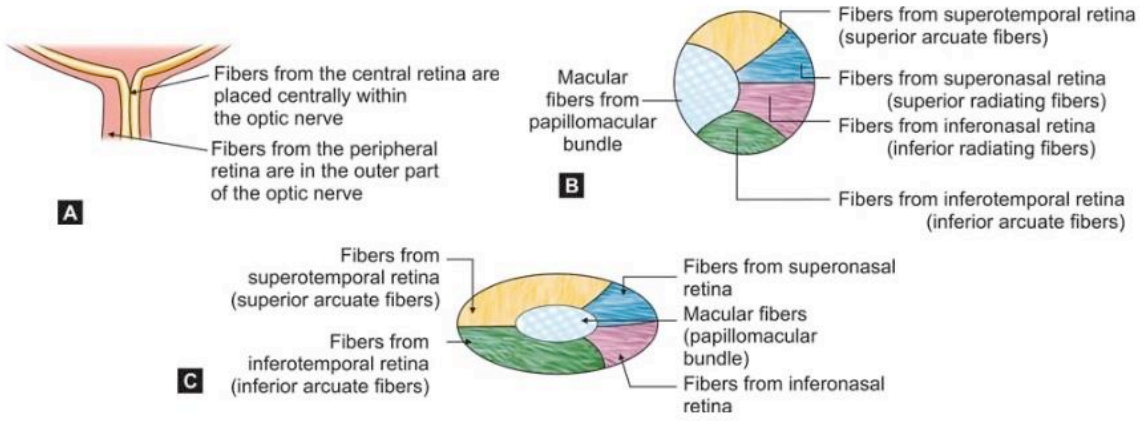


Figure 4 :Arrangement of fibers of retina

BLOOD SUPPLY OF OPTIC NERVE

1.Intra-ocular part of ONH:

Surface nerve fibre layer region

- Major supply:by retinal arterioles capillaries
- Occasionally:Cilioretinal artery from ciliary derived vessel.[27]

Prelaminar region

- Vessels of ciliary region

LC area

- Short posterior ciliary arteries
- Arterial circle of Zinn

Retrolaminar region

- Ciliary and retinal circulation
- Centripetal branches from pial plexus

2. Intra-orbital

Periaxial supply

- OA, long posterior ciliary arteries, lacrimal artery and CRA before entering the ON.

Axial supply

- CRA (intra neural branch).
- Central collateral arteries from CRA.

3.Intra-canalicular

- Pial plexus (OA)

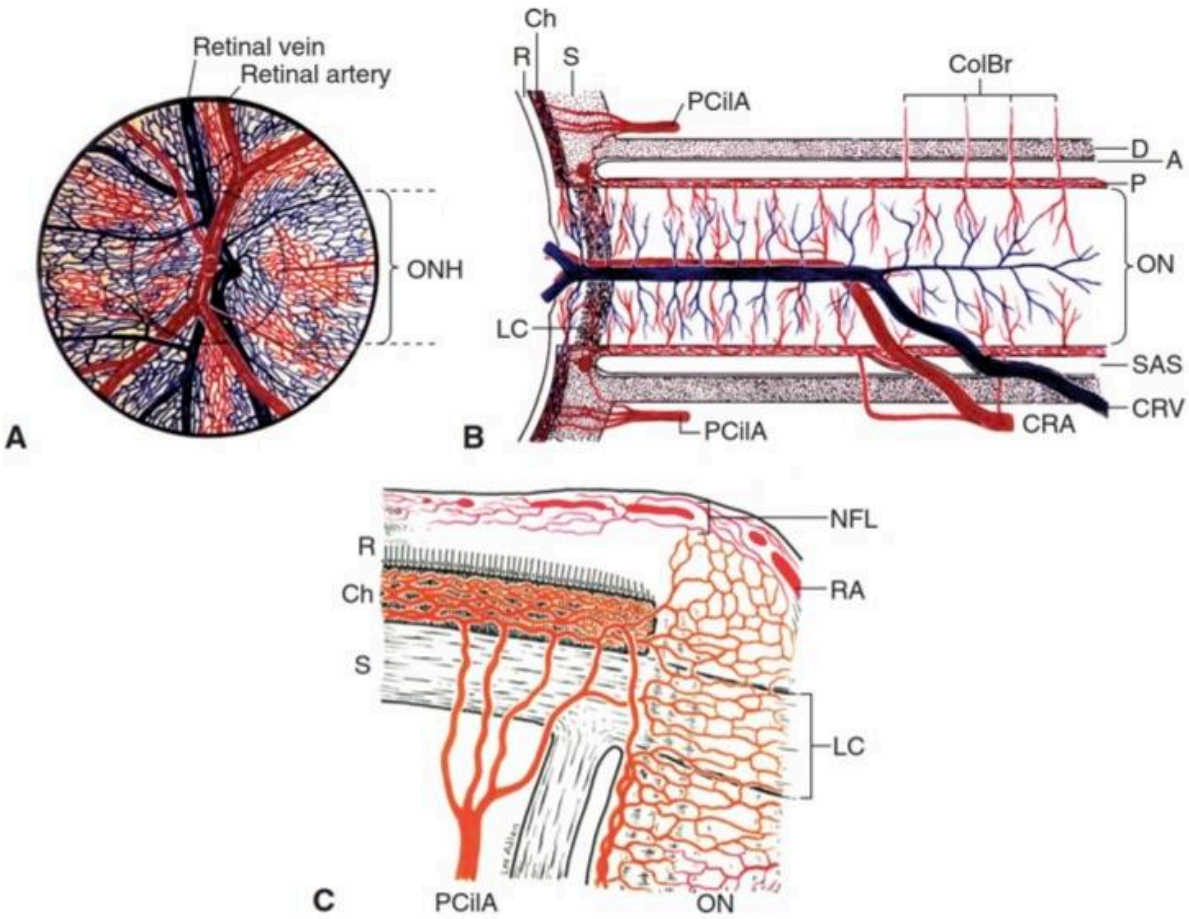
4. Intra-cranial

Pial plexus

- ICA (direct and indirect branches)
- anterior cerebral artery
- OA
- Anterior communicating artery

VENOUS DRAINAGE OF OPTIC NERVE

- **ONH** : central retinal vein (mainly).[27]
- **Orbital part** by peripheral pial plexus
- **Intracranial part** : Pial plexus draining to anterior cerebral and basal vein



A=arachnoid; Ch=choroid; ColBr=collateral branches; D=dura; LC=lamina cribosa; NFL=superficial nerve fiber layer of the ONH; ON=optic nerve; P=pia; PCilA=posterior ciliary artery; R=retina; RA=retinal arteriole; S=sclera; SAS=subarachnoid space.

Figure 5 : Schematic representation of vascular supply to ON and ONH

Figure A shows intra-ocular view of ONH

Figure B shows lateral view of ONH

Figure C shows sagittal view of ONH

The CRA is only present in capillaries of anterior intraorbital ON and nerve fibre layer. All levels of capillary beds empty into central retinal vein.

Pupillary Light Reflex

Pupillary light reflex's afferent limb is the optic nerve. A signal is transmitted to ganglion cells of retina when light enters eye and then photoreceptors are activated. While temporal retinal fibres convey signal to ipsilateral pretectal nucleus, nasal retinal fibres carry it to the contralateral pretectal nucleus. When neurons in Edinger-Westphal nucleus are bilaterally activated by fibres from both pretectal nuclei, efferent limb of reflex is started. The ciliary ganglion is innervated by axons of preganglionic parasympathetic neurons, which travel peripherally along oculomotor nerve. Short ciliary nerves are formed by the ciliary ganglion's postganglionic parasympathetic axons. Miosis is caused by the sphincter pupillae contraction by the short ciliary nerves. Both side pretectal nuclei and Edinger-Westphal nuclei activation results in pupillary constriction in ipsilateral eye, known as the direct response, and that in the contralateral eye, known as the consensual response, when one eye is stimulated with light. [35]

ASSESSMENT OF OPTIC NERVE FUNCTION

Evaluation of several aspects are used to assess optic nerve function. These boundaries ought to be assessed in each quiet with thought optic neuropathy. Additionally, optic neuropathies can be assessed with the help of electrophysiological testing. Since papilledema can mimic many other optic nerve related conditions, it is essential to evaluate in a broader spectrum.

VISUAL ACUITY(VA)

VA, a crucial function of ON, is a significant predictor of vision function. In order to rule out refractive errors, best-corrected visual acuity (BCVA) should be measured. Doctor can foresee a refractive defect when pinhole viewing leads to an improvement in eye acuity.

With test letters, Snellen acuity is evaluated (optotypes). When viewed from a specified distance, they are designed to have a 5 min arc angle. A patient with a 20/40 Snellen acuity (6/12in m) can see 20/40 line clearly from 20 feet away, which is unlike a normal person.

COLOR VISION

In contrast to BCVA, ON diseases, particularly optic neuritis, may have a significant impact on color vision. However, visual acuity and color vision typically suffer concurrently in macular disease. Dyschromatopsia, or color vision impairment, can also persist in optic neuropathy even after visual acuity is restored.

Monocular color vision testing is used. Pseudoisochromatic color plates are readily available and frequently utilized for color vision evaluations. Congenital dyschromatopsia can be identified in males with bilateral, symmetric colour vision impairment. The Farnsworth-Munsell 100-hue test has the most information. Its use is restricted to specialised therapeutic settings since it requires 85 coloured discs and is time consuming to operate.

CONTRAST SENSITIVITY

A stronger contrast makes it simpler to perceive the optotype. By increasing the contrast between the illumination and the black letters, reading is made simpler. Snellen acuity prototypes are projected at close to 100% contrast, which facilitates resolution by the visual system. However, 20/20 vision is not always a sign of good vision because inadequate contrast sensitivity can seriously impair visual quality. because seeing 100% contrast every day is uncommon. Pelli-Robson contrast sensitivity letter has rows of identically sized letters, however there is less contrast when there are three letters in a row. Test subject must watch progression of progressively lower contrast sinusoidal gratings. Amblyopia, posterior

subcapsular cataracts, and optic neuropathy are a few of illnesses to reduced contrast sensitivity. In clinical practise, contrast sensitivity testing is seldom ever done.

PUPILLARY EXAMINATION

Pupillary testing makes it simple to identify ON abnormalities, especially when looking for a relative afferent pupillary deficiency (RAPD). Typically, a light source focused on one pupil generates symmetrical pupillary constriction on the same side and another sides(direct and consensual reaction). Whenever ON in 1 eye is damaged or inflamed more than in other, a RAPD is seen in the eye that is more afflicted. In other words, the light will cause bilateral pupillary constriction if it is directed at the eye that is unaffected by the disease. The impaired signal conduction along the ON, however, will cause a bilateral pupillary dilatation if the light is directed at the affected eye.

The absence of RAPD often suggests normal optic nerves in both eyes or bilateral symmetric optic neuropathy. Patients who have severe retinal dysfunction, such as a detached retina, an ischemic central retinal vein occlusion, an occluded CRA, are at risk for RAPD.

VISUAL FIELD

The varied patterns of vision loss can be described, quantified, tracked, and located using a visual field defect test. There are numerous methods for assessing the visual field. The technique is chosen based on level of detail necessary and patient's compliance. A fundamental test that should be possible at patient's bedside or in centre gives a general assessment of visual fields is confrontation visual field testing. The examiner stands one meter away from the patient. One eye is covered, and patient is instructed to fix other eye on the examiner's nose. Patient is then asked to name numbers that are on examiner's fingers at midpoint of each of 4 quadrants of each eye. For thorough evaluation, perimetry is utilised to

measure the visual field. The two principal types of perimetry are static and dynamic. Static stimuli in visual field testing activate and deactivate at different locations within visual field area being examined. In kinetic testing, an isopter is made by connecting all points with the same sensitivity to a specific stimulus.

VISUAL EVOKED POTENTIALS (VEP) for ON FUNCTION ASSESSMENT

The VEP is an electrical response to a light stimulus that is predominantly recorded from the visual cortex. Its functionality has evolved since its introduction in the 1930s.[36] Ciganek (1961) was 1st to describe an electroencephalography (EEG) response in humans to stimulus of flashlight. One of the first clinical trials of VEP on patients with optic neuritis was carried out by Halliday and colleagues.[37,38] VEP continues to play a crucial complementary role to other tests such as MRI and optical coherence tomography (OCT) as it provides an objective and repeatable assessment of visual function.

VEP is recorded using occipital-mounted electrodes and often monocular stimulation.

The most often employed stimuli are reversed black-and-white checkerboard pattern, pattern-onset visual evoked potential (PVEP), and flash visual evoked potential (fVEP). Due to fVEP's limited sensitivity and considerable intersubject variability, PVEP is recommended in the majority of clinical sittings. Patients with substantial media opacity, reluctant patients, and infants all frequently undergo fVEP. The pattern-onset VEP is favoured because the PVEP is significantly reduced in individuals with fixation instability (nystagmus) as a result of retinal image motion's impact stimuli's effectiveness.[38]

To ensure more uniformity in results among electrophysiology labs, International Society of Clinical Electrophysiology of Vision (ISCEV) has standardised testing process for both stimulus conditions.[39]

CEREBROSPINAL FLUID (CSF)

The clear, proteinaceous fluid known as CSF is found in the spaces surrounding the CNS of mammals. It is a marvel with many facets, supporting the nervous system throughout the organism's lifespan. At any given time, the average adult circulates approximately CSF of 150mL. The ventricular part adds up to generally 17% of the all out liquid volume, remainder of which is in the cistern and SAS. CSF formation occurs at 0.3–0.4mL/min rate; corresponding to 430–530mL/day and 18-25mL/hour, respectively.[40] The conventional theory holds that cardiac pulsations and pulmonary respiration exert forces that cause CSF to flow. For centuries, people have known about CSF's existence. One of the 1st people to describe the fluid surrounding the brain as water was Hippocrates. [41] The steady creation of liquid was estimated, however anatomists couldn't portray, nor pinpoint, the method for creation. Choroid plexus which is a CSF source wasn't known until Cushing published "Studies on the Cerebro-Spinal Fluid" (1914).[42] Soon after, Dandy carried out experiment: ablation of choroid plexus in a dog of 1 lateral ventricle was done and then obstruction of the foramen leading into 3rd ventricle was done; he found that ventricle removed and cleared of CSF would implode, while the ventricle which wasn't controlled expanded.[43] This prompted conviction that choroid plexus is fundamental producer of CSF. "According to original theory of CSF production, the choroid plexus epithelium produces 75% of all CSF, with the remaining 25% coming from other CNS structures like the ependymal wall, cerebral parenchyma, and interstitial fluid (ISF)." [44]

Production of Cerebrospinal fluid

In 1st stage, across endothelium of capillaries that is fenestrated plasma is filtered passively into choroidal interstitial space as a result of osmotic pressure gradient that exists amongst 2 surfaces during CSF secretion from any of 4 choroid plexuses.[45] Ultrafiltrate is then actively transported into ventricular spaces across choroidal epithelium. New findings regarding choroid plexus being primary source of CSF production shed light on an alternative hypothesis proposed by Oreskovic and Klarica on CSF production. CSF formation is viewed as an active process that is unaffected by ICP in their proposed new working theory. The CSF formation rate and rate of absorption of CSF must be equal in healthy physiological conditions. Due to the fact that formation and absorption take place in distinct parts of system, they speculate that this could also apply to flow rate. To them, it follows logically that if there is to be constant volume of CSF, CSF secretion is what propels flow and circulation.[46] The new idea adopts a more methodical approach and focuses on Virchow-Robin spaces, which are located between points where cerebral vasculature enters CNS through the pia mater and descends from the subarachnoid region.[47] Even if the serum is hypotonic, it's noteworthy to notice that changes in osmolarity can be extremely abrupt and that CSF volume flow can recover to basic.[48]

Movement and Absorption of CSF

Following production, CSF is normally moved through ventricular system with help from concurrently beating ciliated ependyma.[49] CSF travels to 3rd ventricle through foramen of Monro from lateral ventricles. Through Sylvius aqueduct, it then enters 4th ventricle. The CSF may enter SAS via foramens of Luschka laterally or Magendie medially from 4th ventricle. By passing through Magendie foramen, spinal SAS is filled in. CSF enters the SAS above cerebral cortex and cisterns' SAS through Luschka foramen. New theories on the production

of CSF are comparable to theories of absorption. According to research conducted on ovine and rabbit models, cervical lymphatics may also significantly absorb CSF.[45] CSF that does not resorb through arachnoid granulations may travel two different routes to the cervical lymphatics. 1st is along exiting cranial nerves' SAS.[45,50] This gives CSF a direct way to go to the extracranial lymphatics from cisterns. Virchow–Robin space, which is potential space surrounding arteries and veins that penetrate brain parenchyma, is 2nd pathway through which CSF may travel to lymphatics.[51] CSF may be shunted to the ISF or enter the Virchow–Robin space if it is not absorbed through the classical pathway. If CSF enters ISF, eventually reentering of it in SAS, the Virchow–Robin space, or the bloodstream. Depending on the cardiac pulsations forces and pulmonary respiration forces, CSF either will reenter the SAS or reabsorbed by cervical lymphatics from Virchow–Robin space. Since the arachnoid granulations are not fully formed at birth, the infants' more powerful venous plexus on the dura's inner side is required for CSF absorption.[52,53] Despite being less developed, dural venous plexus is nevertheless assumed to have role in absorption. Filling of dural venous plexus parasagitally has been demonstrated in animal models and adult and fetal cadaver dissections using intradural injections.[54-56] The precise mechanism of CSF uptake is still a mystery.[53]

The Pathophysiology of CSF

Disruptions in homeostasis of CSF can cause either excessive production or reduced CSF absorption, both of having the potential to cause diseases. Any obstruction of the ventricular system can cause an increase in ICP, which can lead to a series of abnormalities in brain.[57] Obstructive hydrocephalus frequently presents with tumours, intraventricular hemorrhages and congenital webs.[58] An inflammatory response is triggered by infection, meningitis, and subarachnoid hemorrhage. This response results in an obstruction of arachnoid granulations

due to scarring, which in turn reduces CSF absorption and disrupts CSF homeostasis. Ventriculomegaly can occur as a result of loss of neurons, ischemia, following craniectomy or traumatic brain injury patient (TBI).[59,60] The ON is surrounded by all 3 meningeal layers and, as a result, is continuous with brain's SAS making it a central nervous system component with limited regenerative capacity. The mechanical theory, which proposed that high ICP caused compression of subarachnoid portion of the central retinal vein, resulting in disc edema due to venous obstruction, was challenged when electron microscopy was introduced. Using electron microscopy, it was discovered that optic disc edema in PE was primarily intra-axonal and affected axoplasmic energy-dependent transport. Optic disc edema is the swelling of the axons and the leakage of cellular contents into extracellular space of disc caused by stasis of intra-axonal fluid. Vascular telangiectasias, nerve ischemia, and venous obstruction and dilation are all secondary effects of reduced axon perfusion. [61]

THE OPTIC NERVE SHEATH (ONS)

Optic disc oedema was initially described by Von Graefe in 1860.[62] Hayreh researched it in 1964 by raising ICP with the aid of balloons that were inflated and positioned in subdural region of rhesus monkeys. According to this study, development of an optic disc oedema requires a rise in CSF in ONS.[63] Relationship between ONSD and rising ICP have been studied through many studies.[64–69]

ONS anatomy:

ON is white matter tract in CNS stretching all the way to orbit and completely surrounded by CSF along the way.[70] On the 22nd day, it begins at diencephalic neural fold and travels anteriorly and laterally along optic canal before entering orbit.[71] It's around 4mm in diameter and 40–50mm long. It is enclosed by an ONS, which is then surrounded by an SAS filled

with CSF. 0.4mm is the thickness of ONS. The SAS, a blind ending region that encircles the ON, is between 0.1 and 0.2 mm wide and contains roughly 0.1 ml of CSF.[70,72] Since it is believed that CSF communicates among various compartments of CSF, any substantial ICP change will be reflected in the ONS diameter.[73,74,75] ONS is dural sheath that begins at optic canal and travels to sclera with ON.[71] Division is into 3 segments:

a) Intra-cranial: Dura invaginates here to allow for the creation of the faliciform ligament at the sphenoid planum. This is the shortest portion. The ligament protects the dorsal surface of ON even though it is not completely anchored to the bone.

b) Intra-canalicular: The ONS leaves base of skull through optic canal, where it travels obliquely in a direction laterally and ventrally. Carotid-oculomotor membrane is made up of dural coating of clinoid process is in touch with ONS. Here, OA and ICA's primary intracranial branch begin. After passing through optic canal, the artery joins orbit.

c) Intra-orbital: Annular ligament, where several recti muscles attach, is formed in part by the dense ONS that is present in this area. It is surrounded by adipose tissue, which facilitates eye movement. OA, superior ophthalmic vein, cranial nerve IV, frontal nerve, and nasociliary nerve all pass via the orbital region of the ONS.

Understanding the structure of the ONS as well as the CSF communication between ONS and intracranial space is necessary to comprehend ONS' reaction to rises of ICP. The CSF, which is created by choroid plexus, communicates with cisterns and SAS, including SAS around ONS. CSF movement between different segments is communicated by SAS of bulbar part of ON, which is a dense system of fine trabeculae and septa arranged in a reticular form.[72,75] Additionally, this is the portion of the SAS closest to the nerve that is the widest and ends blindly behind globe. Here, CSF travels freely between SAS of ON and intracranial SAS,

reversing its path back to where it can be reabsorbed.[76, 77] CSF flow may be inconsistent as a result of this complicated system.[72] An elevation in ICP is primarily transmitted to SAS surrounding ON, resulting in ONS distension. Normal axoplasmic flow around the ON is then disrupted as a result of this pressure, causing papilloedema. [74,72] The ONS has a larger SAS and is wider near the eyeball, which gives useful information about where the ONSD should be measured. [65,75,72]

Optic nerve sheath diameter:

In their "Descriptionio anatomica oculi humani," published in 1780, Zinn and Weisberg established the ONS, which is a dura mater extension that covers the ON and extends to the back of eye.[78] It was hypothesized that the optic nerve sheath's subarachnoid fluid's direct continuation with intracranial compartment's subarachnoid fluid was the cause of this startling discovery. A leptomeningeal sheath covers ON, which is part of the CNS. The dural covering expands as ICP rises, pushing CSF toward tiny rim of the SAS between sheath and nerve. Nerve sheath's anterior portion, behind the globe, shows these changes more clearly. ONSD responds dynamically to changes in ICP, just like it does to any physiological change.[79] ONS begins to widen at a distance of 3mm from globe, but beyond that distance, presence of arachnoid trabeculations prevents the ONS from expanding. As a result, ON may protrude or flatten the posterior globe and the ONS may distend as a result of CSF collection in perineural space due to increased ICP.[80] Optic disc edema caused by increased ICP, also known as PE, is a sign that potentially life-threatening conditions like intracranial masses, cerebral venous thrombosis, cranial injuries, subarachnoid hemorrhages, meningitis, and idiopathic intracranial hypertension (IIH) require immediate medical attention.[81] For a correct diagnosis, the patient's clinical history and ophthalmological findings are essential. Axoplasmic flow stasis, caused by increased ICP in the ONS, causes edema of the ONH's axons.[82,83] PE typically manifests bilaterally, but it can also manifest unilaterally or

asymmetrically.[81,8,84] Long-term PE can cause severe permanent vision loss.[85] ONH elevation, unclear optic disc margins, venous congestions, hemorrhages, exudates, and choroidal/retinal folds are all possible signs of PE on ophthalmoscopy. [86] Ophthalmoscopy is a common diagnostic procedure for optic disc edema; however, its accuracy is dependent on the severity of PE and clinician's expertise.

It can be particularly challenging to accurately diagnose subtle PE. Due to the overlap of ophthalmic signs (such as disc elevation and blurry margins) in both PPE and PE, it is easy to confuse them with pseudopapilledema (PPE), a group of benign conditions that mimic disc edema and include ONH drusen, nasally elevated nerves, and crowded hyperopic discs. Headaches, nausea, vomiting, pulsatile tinnitus, transient visual obscuration and diplopia, among other systemic and ocular symptoms seen with elevated ICP and PE, are not always present in patients with PPE. In acute PE, abnormal VA, reaction of pupils, colour vision, or field defects (other than enlarged blind spots) are uncommon.[81] In contrast, patients with PPE may have unrelated headaches, visual disturbances, or visual field defects that further complicate a clinician's decision-making. [87,88] In patients with PPE, ancillary tests like optical coherence tomography (OCT), orbital ultrasound and fluorescein angiography have been used to enhance accuracy of diagnosis to avoid ordering a costly and sometimes invasive neurological work-up. This study aims to assess diagnostic capabilities of orbital ultrasound in patients with PE. [89-93]

Pathophysiology of papilledema :

Since Türck and Coccius independently described PE in 1853, numerous theories have been advanced regarding the underlying pathophysiology. [94] In the middle of the 1800s, Türck (1853) and Von Graefe (1860) proposed that in patients with cerebral tumors, venous stasis of the cavernous sinus caused by increased ICP would mechanically cause a stagnation of

blood flow in retinal veins, causing disc edema.[94,95] In 1898, Deyl proposed that in PE, central retinal vein, which pierces SAS in its course, becomes occluded as pressure in the perioptic SAS increases, thus leading to hyperemia and edema of ON.[96] Many contradictory theories, both mechanical and non-mechanical in nature, existed without experimental support. It was not until 1960's that Hayreh conducted a series of anatomical and physiological studies in human cadavers and rhesus monkeys to understand the mechanism of PE.[97] In 1965, Hayreh cauterized central retinal vein where it meets ONS in six rhesus monkeys to investigate the role of central retinal vein compression.[98, 99] Upon anatomical examination, Hayreh discovered that SAS between the ON and its sheath is largest immediately behind the globe and narrowest in region of optic canal.[97] Because cutting open retrobulbar ONS (sheath fenestration) in rhesus monkeys prevented the development of disc edema when the ICP was elevated, he also established that successful transmission of the raised intracranial CSF pressure to ONS is a prerequisite for the development of optic disc edema. Using stereoscopic color fundus photography and fluorescein angiography, Hayreh documented the progression of PE in rhesus monkeys.[82, 100] On stereoscopic fundus photography, the first notable finding was elevation (swelling) of optic disc at lower pole, followed by superior, disc and then temporal disc. The next sign was a blurring of disc margin, followed by it's hyperemia and late vascular changes like microaneurysms, hemorrhages, capillary dilation, and venous engorgement. Hayreh claims that, in comparison to fluorescein angiography, which looks for vascular changes later in the process, stereoscopic fundus photography was much more effective at detecting early optic disc edema. This suggests that vascular changes are a byproduct of optic disc swelling. To gain a deeper understanding of pathogenesis of PE, Tso and Hayreh also carried out a series of histopathological studies on rhesus monkeys. [83] At first, they used light microscopy to confirm that prominent axonal swelling in optic disc surface and anterior part of prelaminar

region was a major factor for PE and believed it to be responsible for the edema seen on ophthalmoscopy. After that, they demonstrated blood vessel leakage in prelaminar and laminar cribrosa regions, posterior to nerve fiber layer, by injecting horseradish peroxidase intravenously. They came to the conclusion that optic disc edema is caused by both blood vessel fluid leakage and axonal swelling. Ultimately, Tso and Hayreh infused tritiated leucine intravitreously and noticed through autoradiographs of ONH that stasis of axoplasmic flow is principally reason for axonal swelling. [101] As a result, Hayreh came to the conclusion that PE's pathogenesis is primarily mechanical. The axoplasmic flow stasis that results from the elevated CSF pressure first spreads to the perioptic SAS, swelling nerve fibers and causing disc edema. Secondarily, the ONH's swelling compresses venules, causing vascular changes like fluid leakage and venous stasis. Optic disc edema is caused by extracellular fluid leakage from region's blood vessels and swollen axons in the presence of elevated ICP.

Frisén's severity grading

The modified Frisén scale uses the optic nerve appearance via ophthalmoscopy to assess the degree of PE [9, 102]. The hallmark sign of grade I is C-shaped halo that has temporal gap, grade II shows a circumferential halo, grade III is obscuration of one or more segments of major blood vessels leaving disc, grade IV is obscuration of major blood vessel on disc, and grade V is complete vessel obscuration. Since its introduction in 1982, the papilledema standard has been the six-stage Frisén grading system.[9] Neuro-ophthalmologists assess visible components of optic disc and peripapillary retina using direct funduscopic inspection or digital colour fundus pictures in clinical practise. Degree of optic disc swelling is then determined by grading it on a scale of 0 to 5. Grade 0 denotes normality, grades 1 and 2 imply mild swelling, grades 3 denote moderate abnormalities, and grades 4 or 5 indicate a serious condition in which the optic disc starts to atrophy.[9] Despite Frisen grading scheme's broad

use in clinical and research contexts, its main drawbacks include poor consistency, intra- and inter-observer variability, cumbersome processing steps, specialised knowledge with variational results.[102-105] Consequently, modified variants of the Frisén grading system have been used quite a bit. By evaluating crucial aspects at various phases, Scott and colleagues[102] altered original Frisen scale scheme in order to increase the systematic dependability on identifying severe papilledema. Ecbegaray and colleagues[103] proposed an automated feature-classifying approach for predicting Frisén scale grades using fundus photographs with blood vessel, peripapillary texture, and disc margin obscuration features. This approach was designed to reduce intra- and inter-observer variability and speed up processing. Even while the most recent fundus cameras may produce images with high definition and in full colour, this imaging method is still essentially only capable of 2D images. As a result, it is challenging to directly examine and measure the volumetric information of the optic disc. Stereoscopic fundus photographs could be used to indirectly reconstruct 2 dimensional into 3 dimensional information.

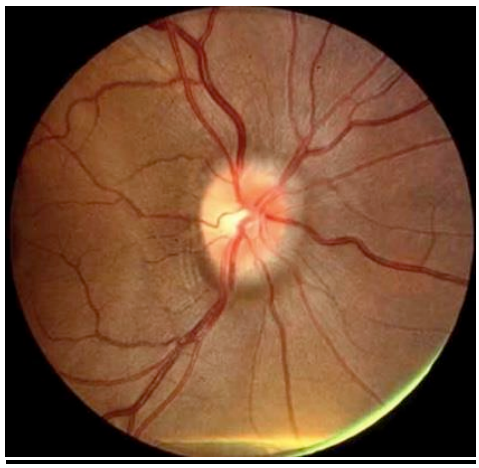


Figure 6 : Grade I : C-shaped halo with temporal gap.

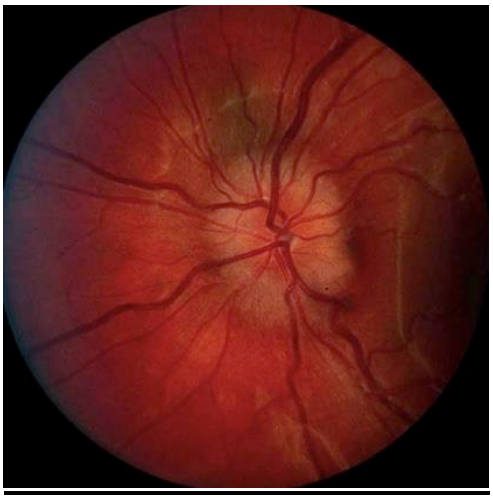


Figure 7 : Grade II : Halo becomes circumferential

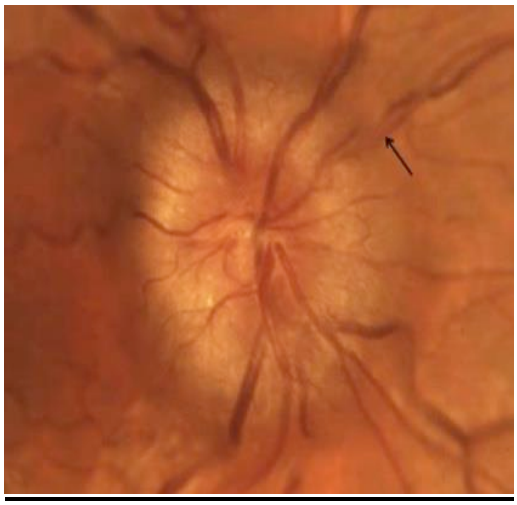


Figure 8 : Grade III : Loss of major vessels as they leave the disc (arrow).

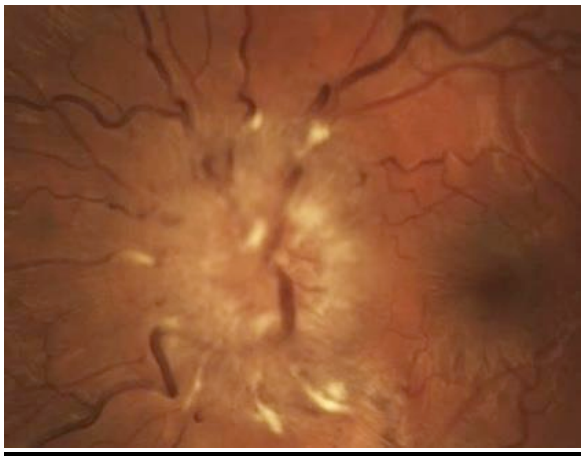


Figure 9 : Grade IV : Loss of major vessels on disc.

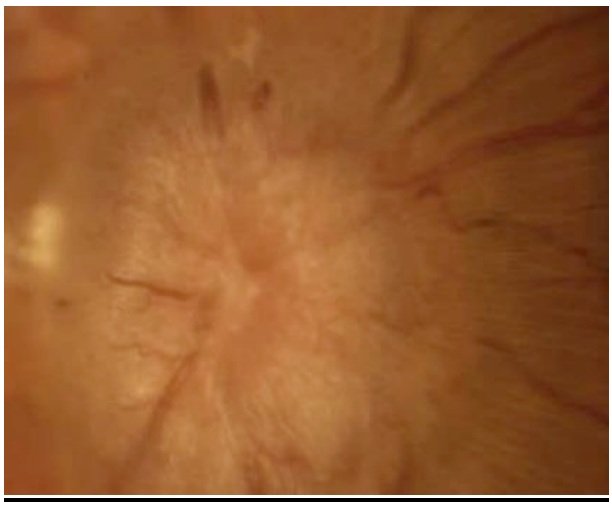


Figure 10 : Grade V : Criteria of grade IV with partial or total obscuration of all vessels of disc. [119]

Symptoms of Elevated ICP

1) Headaches

Headaches are most common presenting symptom (84-94% patients).[106, 107] Headaches typically occur daily, are diffuse and might be so severe in nature that they may awaken the patient during sleep or exist with nausea [108]. Headaches as a non-specific sign can cause problems when they present in a patient with PPE. Kovarik and co (2015) reported 25 out of 34 pediatric patients referred for suspected PE had headaches, and 26 of them were determined to have PPE [109].

2) Transient visual obscurations (TVOs)

These are episodes of transient blurring or loss of vision. TVOs in PE typically occur for less than 30 seconds and may be associated with postural changes. Transient ischemia of ON is thought to contribute to TVOs in both PE and PPE.[110]

3) Pulsatile Tinnitus

Pulse synchronous tinnitus, described as a whooshing sound, occurs in 52-58% of patients with elevated ICP and is useful in diagnosing PE [106, 107]. The pathophysiology is not fully understood, but some postulate that it is due to alterations in the cerebral vasculature.

4) Other symptoms

Retrobulbar pain, diplopia, and visual loss have also been reported in patients with elevated ICP[111]. Sixth cranial nerve becomes vulnerable to the effects of elevated ICP as it passes over petrous portion of temporal bone. Sixth nerve palsy, found in 10-20% of patients with

elevated ICP, can cause horizontal diplopia.[108] ON can also be affected if ICP is not controlled causing vision loss secondary to atrophy of ON.[86]

Transorbital Ultrasound

History and overview

Although it was recognized in the 1940s that medical diagnostic ultrasound imaging had potential, it wasn't until the 1970s that it truly piqued interest of researchers and developed into a crucial diagnostic tool.[112] Modern ultrasound is portable, easier for usage and sophisticated, providing high image quality.[113] Transorbital ultrasound of ON and dural sheath encompassing it, was spearheaded by Ossoinig (1970's) utilizing A-scan procedure. By describing shift in reflectivity between ON and ONS, he was able to identify the structures using ultrasound.[114] Later, Ossoinig described about how ICP and the fluid around the ON are related.[115] Numerous groups conducted patient and cadaver studies to confirm this, revealing linear relationship between ICP and SAS surrounding nerve. Additionally, the bulbous ONS dilates when ICP rises.[115-118] Hansen and Helmke (1994), described current technique of ONSD measurement using a B-scan technique.[73] It was also noted that as ICP rises, ONS's bulbous portion expands. Using gelatin injected into the SAS of postmortem ON specimens, they continued their investigation into the best location for ONSD measurement. In support of Liu's observation on cadavers, these researchers demonstrated that maximal increase in diameter occurred 3mm behind ONH as opposed to 10mm.[117, 65] These authors also talked about how easy it is to reproduce this method for scanning the ONSD in clinical practice.[65,119] Since this pioneering work in the 1990s, the B-scan technique has improved with modern high frequency transducers that provide better penetration and image quality. A number of authors have studied this method and use of ONSD measurement as a non-invasive method for diagnosing raised ICP.[120-122] Orbital ultrasound measures ONSD, which

increases with increase in ICP, to aid in PE diagnosis. Neuro-intensive care doctors have been using B scans to measure the ONSD in recent years because they are relatively simple to use. They got correlation of the larger ONSD with higher ICP in patients who have had invasive ICP monitoring.[18, 68, 123] The retro-bulbar portion of the ONS in humans, which is only surrounded by fat in orbit, rapidly expands in response to CSF pressure elevation transmitted from intracranial SAS, as shown by postmortem and in vivo studies.[65, 119] It is interesting to note that standardized A-scan procedures serve as the foundation for the well-known method in the field of ophthalmic ultrasonography for detecting fluid around the retrobulbar optic nerve. Dr. Ossoinig first described standardized echography in the early 1970s. Standardized A-scan is the most accurate way to measure ONSD with ultrasound, and it includes a special S-shaped amplifier and a calibration for tissue sensitivity.[66,114] He also introduced the 30° test to distinguish between solid or infiltrative optic nerve lesions like meningioma and glioma and an enlarged ONSD caused by increased subarachnoid CSF. The 30° test is carried out by comparing the A-scan measured ONSD at primary gaze to that at 30° lateral gaze when an enlarged ONSD is observed. Redistribution of increased amount of CSF over a larger area is thought to be the cause of a reduction in the ONSD's width at lateral gaze. ONSD has been shown to decrease by 25% to 30% when a lot of fluid is present. [124, 125] In both children and adults, the A-scan has been shown to be useful in distinguishing between PPE and PE.

Ultrasonography of ONS

In cases of elevated ICP, ONS ultrasound has potential of replacing invasive ICP monitoring and is a bedside diagnostic procedure that is straightforward, secure, and inexpensive. Ophthalmic ultrasonography commonly use a frequency range of 5 to 10.5 MHz for assessing eye and orbit.[126] Helmke and Hansen used ultrasonography on cadavers to show that high pressure can cause sheath diameter in the region right behind the eye to expand by more than 50%.[65] This is in line

with the conclusions reached by Qayyum et al., Cammarata and colleagues and Amini and colleagues, who suggested that ocular ultrasound might be better substitute for invasive approaches for identifying elevated ICP.[127-129] The same researchers have previously used intrathecal infusion studies to show that ONSD adapts to variations in lumbar CSF pressure.[65] Similar research was done by Tamburrelli and co by showing that there is linear association between expansion of ONS and concomitant rises in ICP.[118] Beyond that, a linear relationship between expansion of the optic nerve sheath and concurrent increases in ICP is observed. These changes in the ONS occur prior to changes in the nerve becoming visible by fundoscopy. Tamburrelli and co discovered that the ONSD had an 88% sensitivity and 90% specificity for identifying an ICP >15 mmHg using 4.5mm as the cutoff for normal.[118] Past studies showed how ONSD can be used as non-invasive mode of diagnosis of elevated ICP.[120] Tayal and colleagues discovered a correlation between an ONSD of ≥ 5mm and CT results that suggested elevated ICP.[20] The use of cranial CT data indicating increased ICP was done to assess the ONSD's accuracy. Recent investigations have correlated ONSD with clinical characteristics and anomalies in CT scans, both of which serve as proxies for elevated ICP.[130] Aduayi et al. have established a better reliability of ONS ultrasonography in predicting raised ICP, by comparing ONSD with anomalies and CT findings of high ICP.[131] Ocular ultrasound, when compared to CT, demonstrates better diagnostic test accuracy in order to identify raised ICT, notably better sensitivity, for ruling out elevated ICT in low-risk groups, and high for ruling out elevated ICT in high-risk groups, according to a systematic review and meta-analysis.[132] ONSD measurements made using MRI and Bscan are correlated. Bäuerle and co. established repeatability and precision of ONSD

measurement with MRI and Ultrasonography.[133] They have suggested the fact saying this method is worth utilising as a non-invasive, bedside tool for longitudinal assessments of ONSD.[165] Shirodkar with colleagues have shown a link between the ONSD assessed by MRI and ultrasonography.[134] There are a few studies that have directly compared invasively obtained ICT and ultrasound measurements of ONSD. The normal ONSD cutoff value ranges from 5.2 to 5.9mm when measured 3mm posterior to globe. The results of increased ICT on a CT scan have also been compared to the findings of higher ICT on an ultrasound of the ONS. An ONSD cutoff of 5 millimetres, evaluated by CT scan, was revealed by a study by Qayyum and co to indicate ICP >20 mmHg. They also demonstrated that ONSD by ultrasound guidance is not only sensitive but specific diagnostic tool for analysing elevated ICT.[135]

In their investigation, Kimberly and colleagues recommended ONSD cutoff of 5mm for predicting an ICT >20mmHg.[136] An ICT >20 mmHg was predicted by an ONSD of 5.5mm in a recent research by Amini et al. having 100% sensitivity and specificity.[137] Using Codman intraparenchymal probes, Sahoo and Deepak Agrawal revealed a cutoff of 6.3mm for predicting ICP >20mmHg in patients receiving neurocritical care. [138]

Technique of measurement of ONS by transorbital ultrasound :

- It is rapid and easy process. Some general guidelines in this method help produce the optimum image quality for the ONSD. [139]
- When insonation programme is set to "tiny parts" or "superficial," a higher frequency linear array transducer requirement is there.
- Different depths for various age groups are usually changed.

- The patient is typically advised to close his or her eyes and is placed in position preferably supine and head position which is neutral.
- On the eyelid, coupling gel is placed. It serves as a conduit between the transducer and the eyelid.
- Depending on the situation, the transducer may be placed in an axial or sagittal plane, softly above the upper eyelid on the temporal side.
- The hand is stabilised, and last digit is resting on orbital ridge. On globe, the least pressure possible is recommended.
- To see the globe, lens, vitreous, and ON, beam is focused with fine movements caudally and medially.

- The ONS appears as a lateral, hypoechoic, thin line that runs parallel to the nerve on both sides.

- Small adjustments to the angulation are necessary until image is clear, in centre of monitor, and shows clearly defined lines of ONS.
- Once an ideal image has been captured, it can be saved as either a still image or a clip.
- Probe can be removed once all the photos have been captured, minimising exposure to ultrasound beam. Stored images can be measured later.
- Cursors are positioned parallel to and in centre of ON measuring 3mm posterior to papilla using calliper function.
- The diameter of the ONS is measured in 2^{nd} measurement, which is taken perpendicular to this line at 3.0mm point.

- Zoom option can be used to increase measurement accuracy.

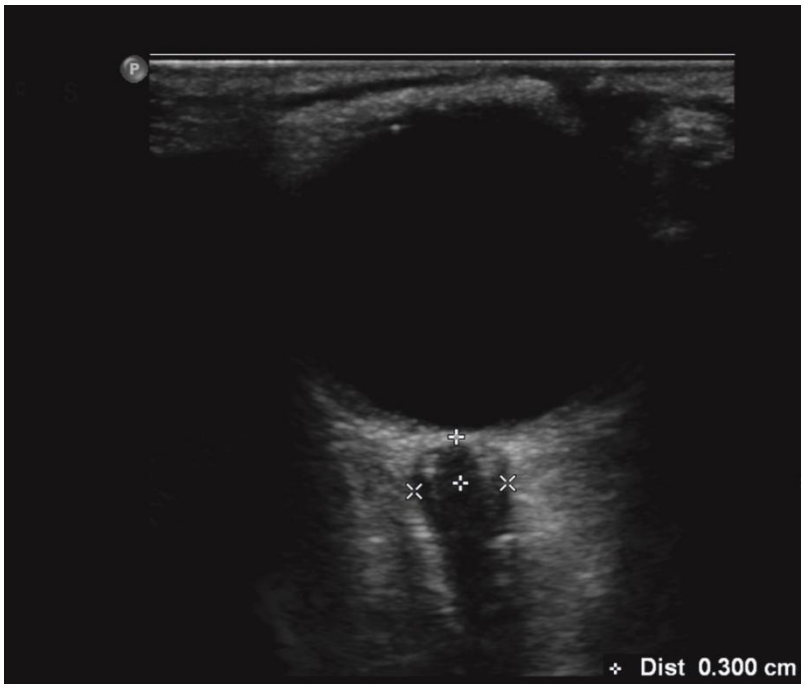


Figure 11 : Measurement of ONSD

Table 1: Pros, Cons and safety considerations:

Pros	**Cons**
Relatively cost effective	Trained operator is required to perform all the examinations.
The technique is non invasive	Error in measurements can occur due to inexperience in technique.
Equipment available in most Emergency Departments.	Thermal injury can occur due to over exposure to the ultrasound beam.
The equipment is portable	ONSD cannot be used in conditions with ocular injury/diseases of ON.
Results are rapid.	Pressure on globe should be avoided.
Technique and measurements are reproducible	There is a chance of error increasing for small measurements.
Patients tolerate it well.	
Ionising radiation is avoided.	

- Ultrasound imaging is generally considered a safer modality when used by a trained operator.
- In order to avoid thermal harm, the ultrasonic beam's interface with scanned tissue should be brief. An ultrasound image is created when sound waves are transferred through probe to tissues being scanned and are reflected from tissue interfaces. When some of this energy is absorbed, it causes a thermal shift that raises the local temperature of tissues. Long-term exposure to this radiation should be minimal by applying the ALARA principle or reducing the ultrasound output power. [140,141] "The thermal index (TI) should be set to <1.0 and the mechanical index (MI) to set <0.7, according to the recommendations of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)."
- This permits a 30-minute window of safe investigation before potential tissue damage.[142]

• On-screen guide for potential tissue heating is provided by TI. The likelihood and size of non-thermal impacts can be estimated using MI. It is advised that monitoring be periodically interrupted to reduce exposure during investigations where more acoustic output and time for monitoring are necessary.[143]

• To rationalise the use of ultrasonography as safe modality of diagnosis, the risks associated with the technology must be acknowledged.

MATERIAL AND METHODS

MATERIALS AND METHODS:

SOURCE OF DATA:

A total of 62 eyes of 31 diagnosed with established papilledema were included in this cross sectional study, visiting outpatient department of Ophthalmology at R.L.Jalappa Hospital and Research Centre, attached to Sri Devaraj Urs Medical College.

STUDY DESIGN :

Prospective cross sectional observational study.

STUDY PERIOD:

December 2020 to June 2022.

INCLUSION CRITERA:

All patients diagnosed with established papilledema.

EXCLUSION CRITERIA:

1) Patients with globe rupture

2) Patients with previous intraocular surgeries

3) Patients with previous intracranial surgeries

ETHICAL CLEARANCE:

Prior to the commencement, study was approved by Institutional Ethics and Research Committee, Sri Devraj Urs Medical College, Kolar.

INFORMED CONSENT:

All patients fulfilling selection criteria were explained about nature of study. A written informed consent was obtained from all the participants before enrolment (Annexure II and III).

METHOD OF COLLECTION OF DATA:

This study was done on the patients coming to R.L.Jalappa Hospital and Research Centre, Tamaka, Kolar.

The patients were initially clinically assessed by taking detailed history, BCVA using Snellens chart after which slit lamp examination using 90D lens for fundus examination were done. Patients were examined for established papilledema and graded according to Frisén's severity grading. Following this, the patient was taken up for B scan to measure the ONSD using 4 SIGHT ACCUTOME ultrasound unit using a 10-MHz linear probe on closed upper eyelid of supine patients with adequate aqueous gel as coupling agent. Correlation of papilledema according to Frisen's severity grading and ONSD was being done. The grading of papilledema was done as follows:

Table : 2 FRISÉN'S SEVERITY GRADE [9]

GRADE	FINDINGS
Grade 0 (Normal Optic Disc)	• Prominence of the retinal nerve fiber layer at nasal, superior, and inferior poles in inverse proportion to disc diameter. • Radial nerve fiber layer striations, without tortuosity.
Grade I (Minimal Degree of Edema)	• C-shaped halo that is subtle and grayish with a temporal gap; obscures underlying retinal details. • Disruption of normal radial nerve fiber layer arrangement striations Temporal disc margin normal.
Grade II **(Low Degree of Edema)**	• Circumferential halo Elevation (nasal border) • No major vessel obscuration
Grade III (Moderate Degree of Edema)	• Obscuration of 1 segment of major blood vessels leaving disc Circumferential halo • Elevation (all borders) • Halo (irregular outer fringe with finger-like extensions)
Grade IV (Marked Degree of Edema)	• Total obscuration on disc of a segment of a major blood vessel on disc • Elevation (whole nerve head, including the cup) Border obscuration (complete) Halo (complete)
Grade V (Severe Degree of Edema)	• Obscuration of all vessels on disc and leaving disc.

SAMPLE SIZE CALCULATION:

Sample size estimated was done based on sensitivity of Optic nerve width in detecting papilloedema was 95% when the normal Optic nerve width (ONW) was set at ≤3.0mm as reported by study done by Neudorfer M et al using below formula $n=Z_{\alpha 2)}{}^2P\hat{}(1-P\hat{})/d^2$ [91]

Where P^ is pre-determined value of sensitivity (or specificity) that is ascertained by previous published data or clinician experience/judgment and for $\alpha = 0.05$, Zα2 is inserted by 1.96.

P^ = 95% or 0.95

d = 9.5% or 0.095.

Using the above values at 95% Confidence level a sample size of 21 subjects were to be included in the study.

Considering Non response rate of 10%, 21 + 2.1 = 23.1 ≈ 24 patients to be included in the study was calculated.

STATISTICAL ANALYSIS:

The SPSS 22 version software was used to analyze data that was entered into a Microsoft Excel data sheet. Frequencies and ratios were used to represent categorical data. Mean and standard deviation were used to represent continuous data. The Kolmogorov–Smirnov test and the Shapiro–Wilk test were used to determine normality of the continuous data.

The correlation between 2 quantitative and qualitative variables was determined using Spearman's correlation.

Table 3 : Spearman's correlation coefficient

Correlation coefficient (r)	Interpretation (Correlation)
0-0.3	+ve weak
0.3-0.6	+ve moderate
0.6-1.0	+ve strong
0to(-0.3)	-ve weak
(-0.3)to(-0.6)	-ve moderate
(-0.6)to–(1)	-ve strong

Graphical representation of data: To create multiple kinds of graphs, including bar diagrams, pie diagrams, and scatter plots, Microsoft Word and Excel were employed.

After taking into account all the standards for statistical tests, a p value (Probability that the result is true) of 0.05 or lower was considered statistically significant.

Statistical software: Data analysis was done using statistical software MS Excel and IBM SPSS Statistics, Somers, NY, USA.

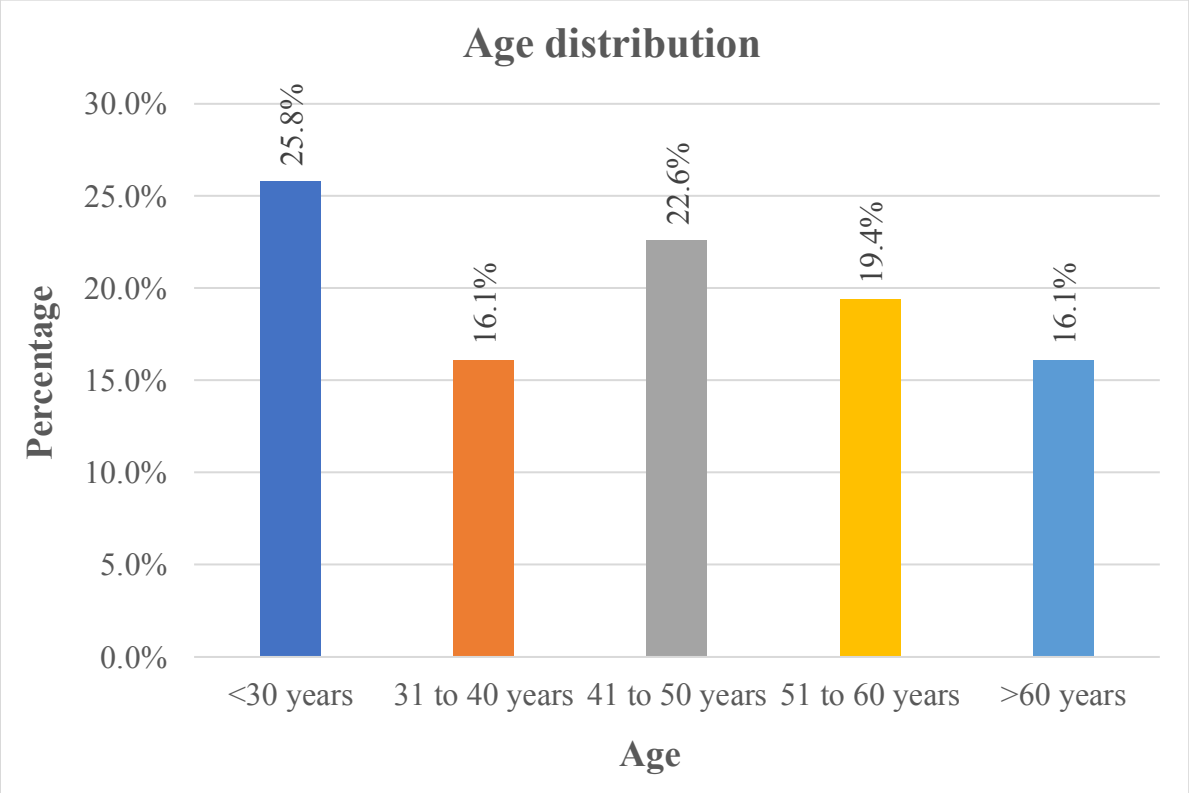
RESULTS

RESULTS:

Table 4: Age distribution of subjects

		Count	%
Age	<30 years	8	25.8%
	31 to 40 years	5	16.1%
	41 to 50 years	7	22.6%
	51 to 60 years	6	19.4%
	>60 years	5	16.1%
	Total	31	100.0%

Mean age of subjects was 45.26 ± 16.07 years. Majority of subjects were in age group, <30 years (25.8%).

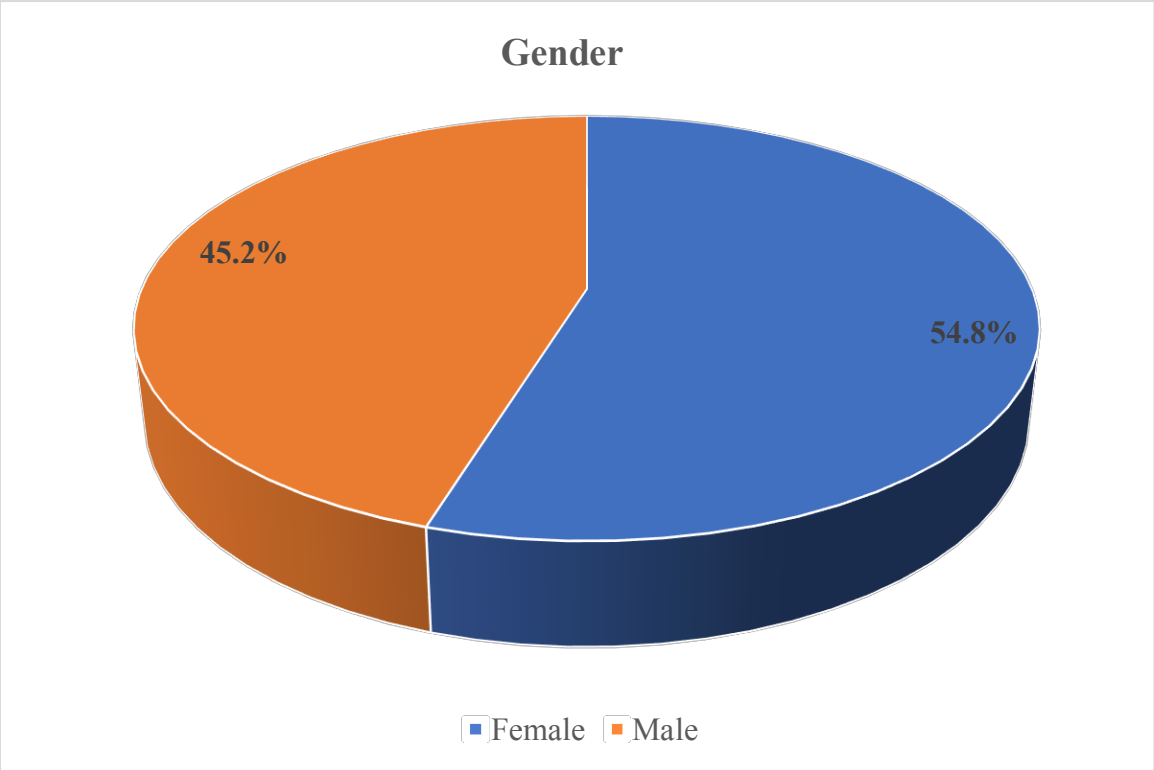


Graph 1: Bar diagram showing Age distribution of subjects

Table 5: Gender distribution of subjects

		Count	%
Gender	Female	17	54.8%
	Male	14	45.2%
	Total	31	100.0%

In the study 54.8% were females and 45.2% were males.



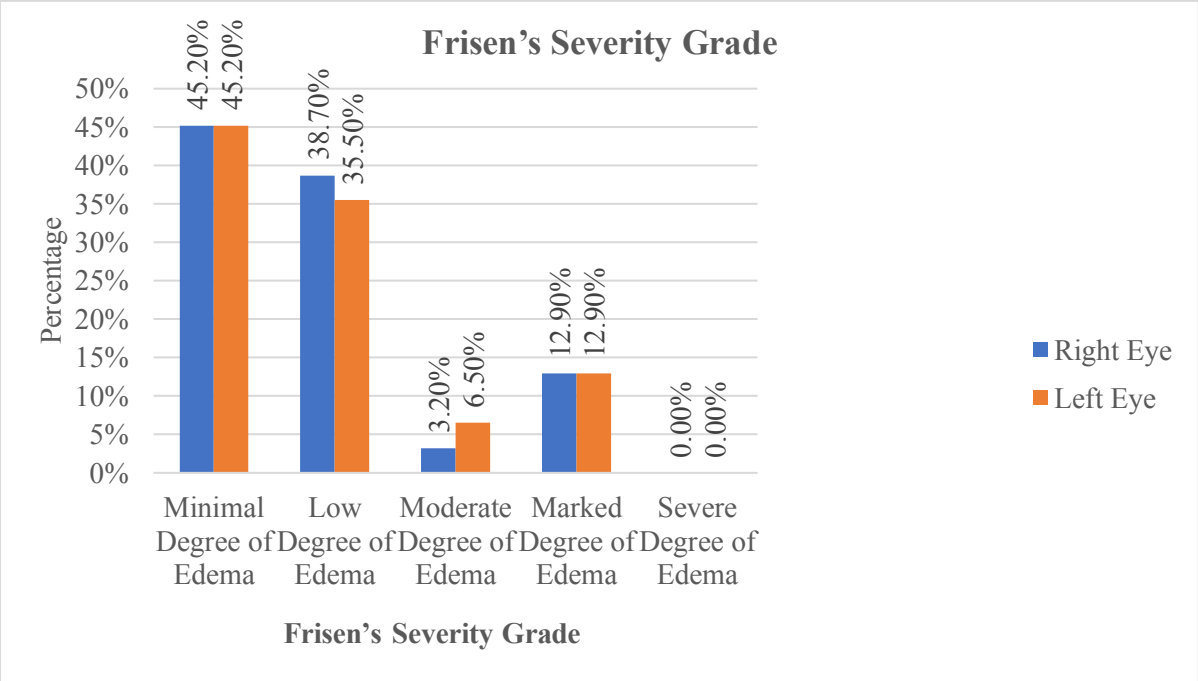
Graph 2: Pie diagram showing Gender distribution of subjects

Table 6: Frisen's Severity Grade distribution of subjects

		Count	%
Frisen's Severity Grade Right Eye (RE)	Minimal Degree of Edema	14	45.2%
	Low Degree of Edema	12	38.7%
	Moderate Degree of Edema	1	3.2%
	Marked Degree of Edema	4	12.9%
	Severe Degree of Edema	0	0.0%
Frisen's Severity Grade Left Eye (LE)	Minimal Degree of Edema	14	45.2%
	Low Degree of Edema	11	35.5%
	Moderate Degree of Edema	2	6.5%
	Marked Degree of Edema	4	12.9%
	Severe Degree of Edema	0	0.0%

Frisen's Severity Grade on Right eye was Grade 1 in 45.2%, Grade 2 in 38.7%, Grade 3 in 3.2% and Grade 4 in 12.9%.

Frisen's Severity Grade on Left eye was Grade 1 in 45.2%, Grade 2 in 35.5%, Grade 3 in 6.5% and Grade 4 in 12.9%.

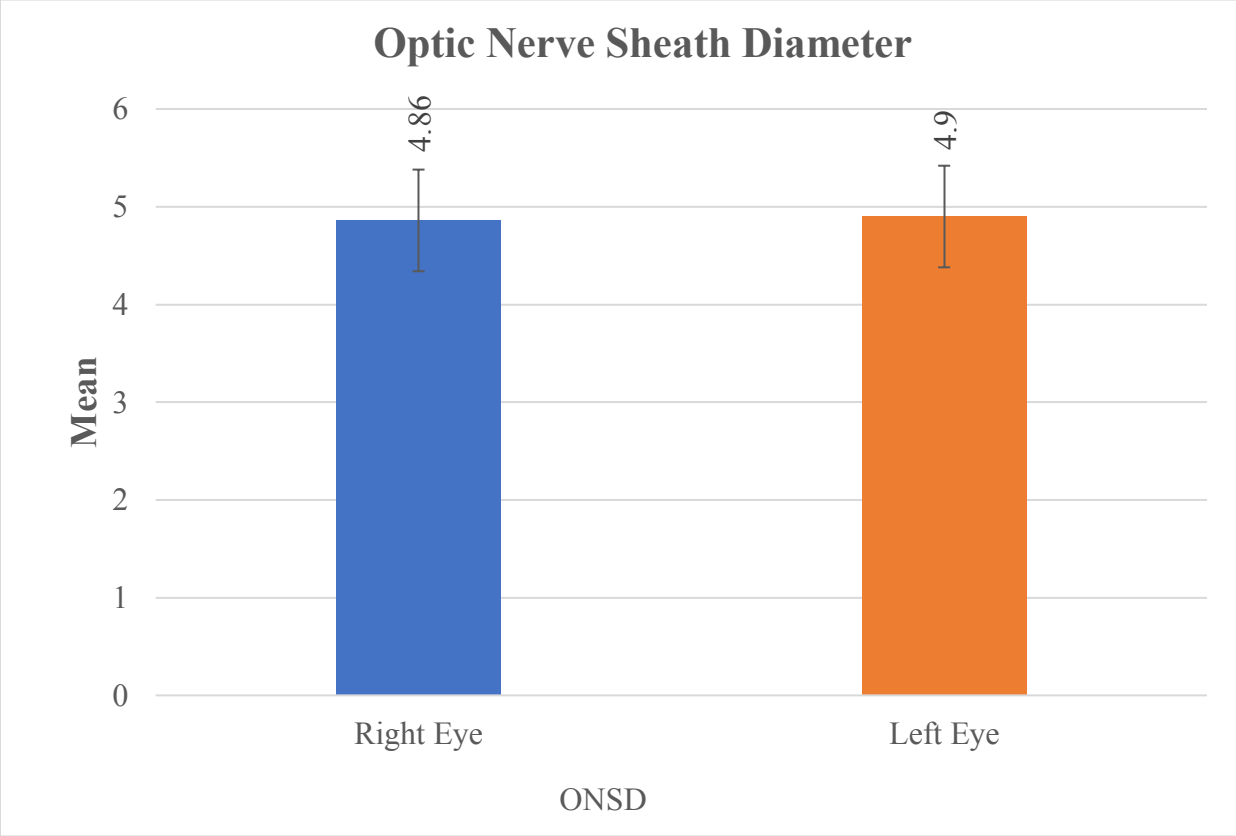


Graph 3: Bar diagram showing Frisen's Severity Grade distribution of subjects

Table 7: ONSD distribution of subjects

ONSD	Mean	SD	Median
Right Eye	4.86	0.52	5
Left Eye	4.90	0.52	5

Mean ONSD of Right Eye was 4.86 ± 0.52 and on left eye was 4.90 ± 0.52 mm.

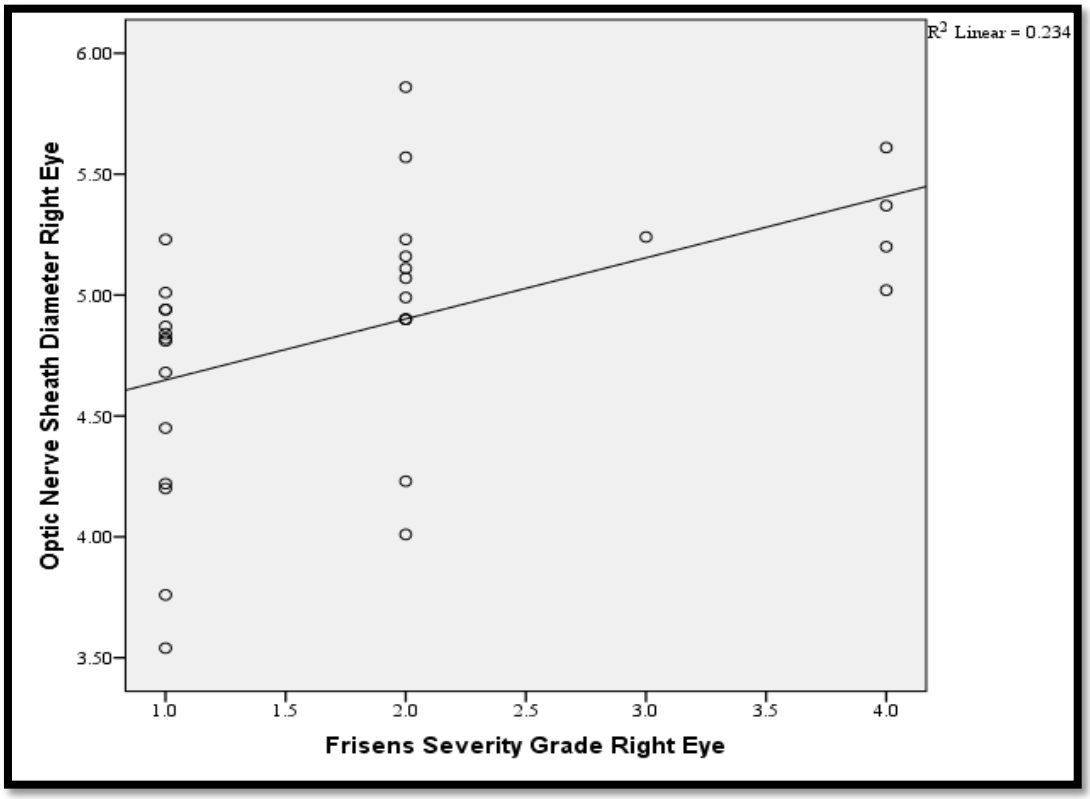


Graph 4: Bar diagram showing ONSD distribution of subjects

Table 8: Correlation between ONSD and Frisens Severity Grade right eye

			Frisens Severity Grade Right Eye	ONSD of the Right Eye
Spearman's rho	Frisens Severity Grade Right Eye	Correlation Coefficient	1.000	0.622**
		Sig. (2-tailed)		<0.001*
		N	31	31

In the study on right side a significant positive correlation existed between Frisens Severity Grade and ONSD i.e. as the Frisens **Severity Grade increased there was increase in ONSD and vice versa.**

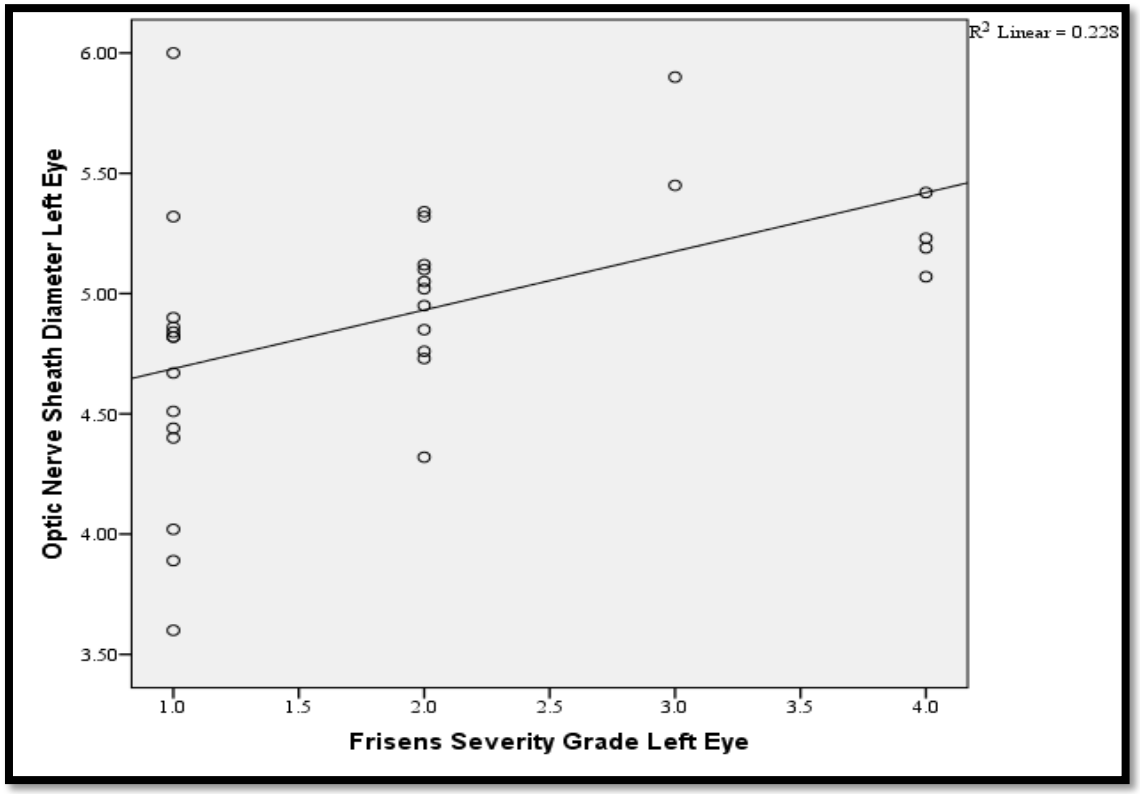


Graph 5: Scatter plot showing Positive Correlation between ONSD and Frisens Severity Grade right eye

Table 9: Correlation between ONSD and Frisens Severity Grade Left eye

			Frisens Severity Grade Left Eye	ONSD of the Left Eye
Spearman's rho	Frisens Severity Grade Left Eye	Correlation Coefficient	1.000	0.576**
		Sig. (2-tailed)		0.001*
		N	31	31

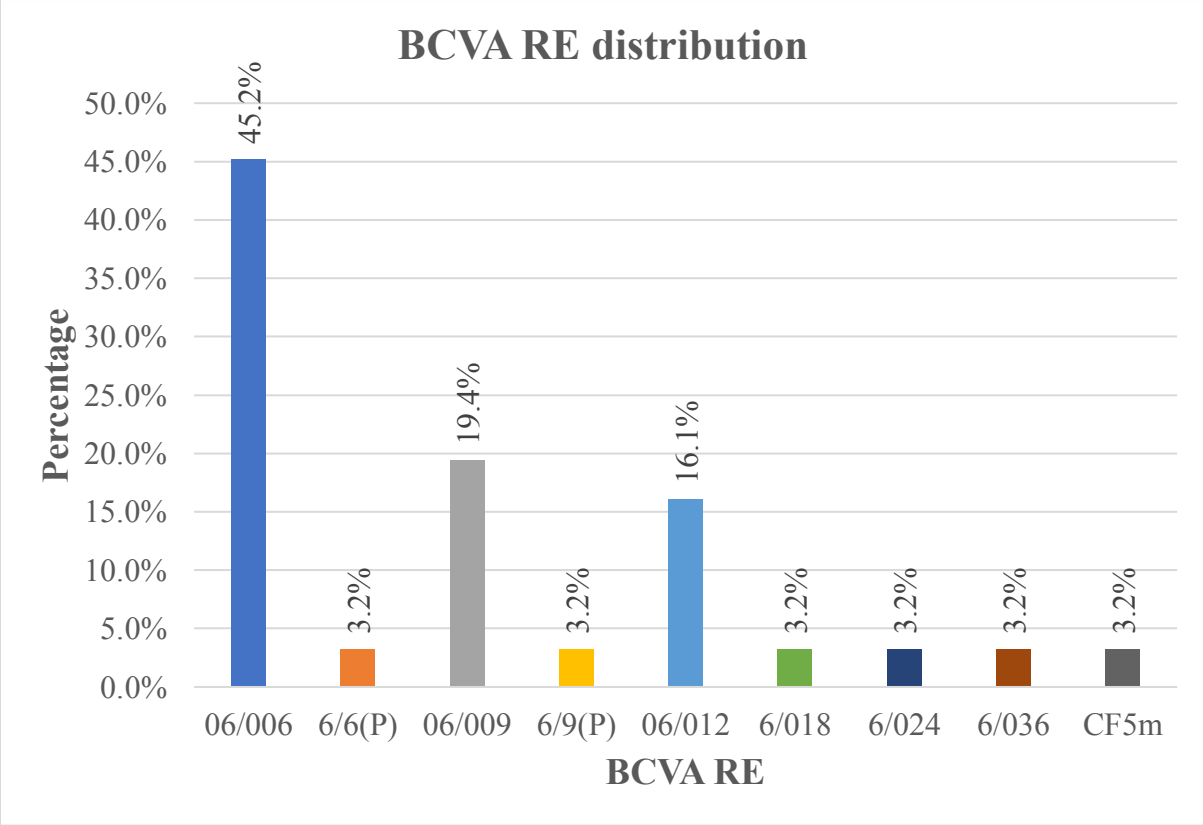
In the study on Left side a significant positive correlation existed between Frisens Severity Grade and ONSD i.e. as the Frisens Severity Grade increased there was increase in ONSD and vice versa.



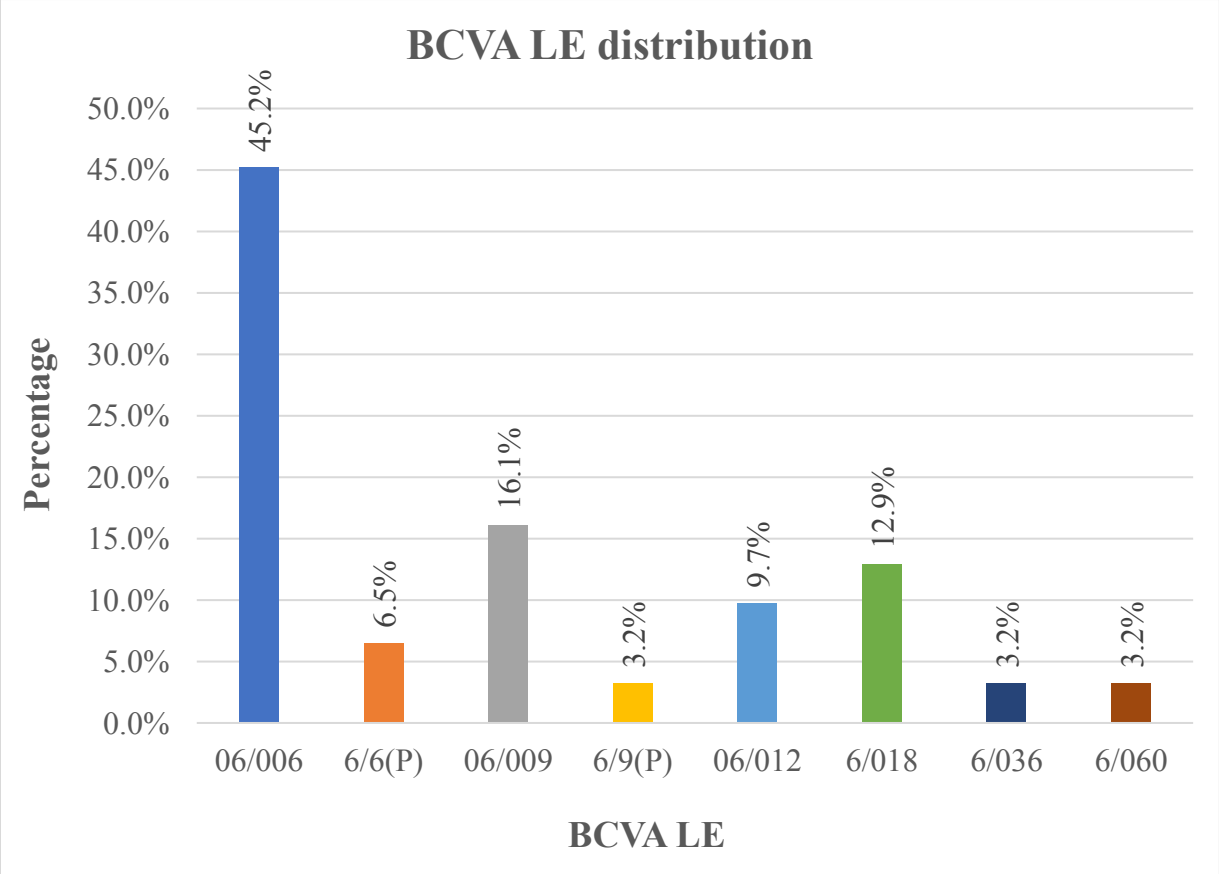
Graph 6: Scatter plot showing Positive Correlation between ONSD and Frisens Severity Grade left eye

Table 10: BCVA distribution on Right and Left eye

		Count	%
BCVA RE	6/6	14	45.2%
	6/6(P)	1	3.2%
	6/9	6	19.4%
	6/9(P)	1	3.2%
	6/12	5	16.1%
	6/18	1	3.2%
	6/24	1	3.2%
	6/36	1	3.2%
	CF5m	1	3.2%
BCVA LE	6/6	14	45.2%
	6/6(P)	2	6.5%
	6/9	5	16.1%
	6/9(P)	1	3.2%
	6/12	3	9.7%
	6/18	4	12.9%
	6/36	1	3.2%
	6/60	1	3.2%



Graph 7: Bar diagram showing BCVA RE distribution

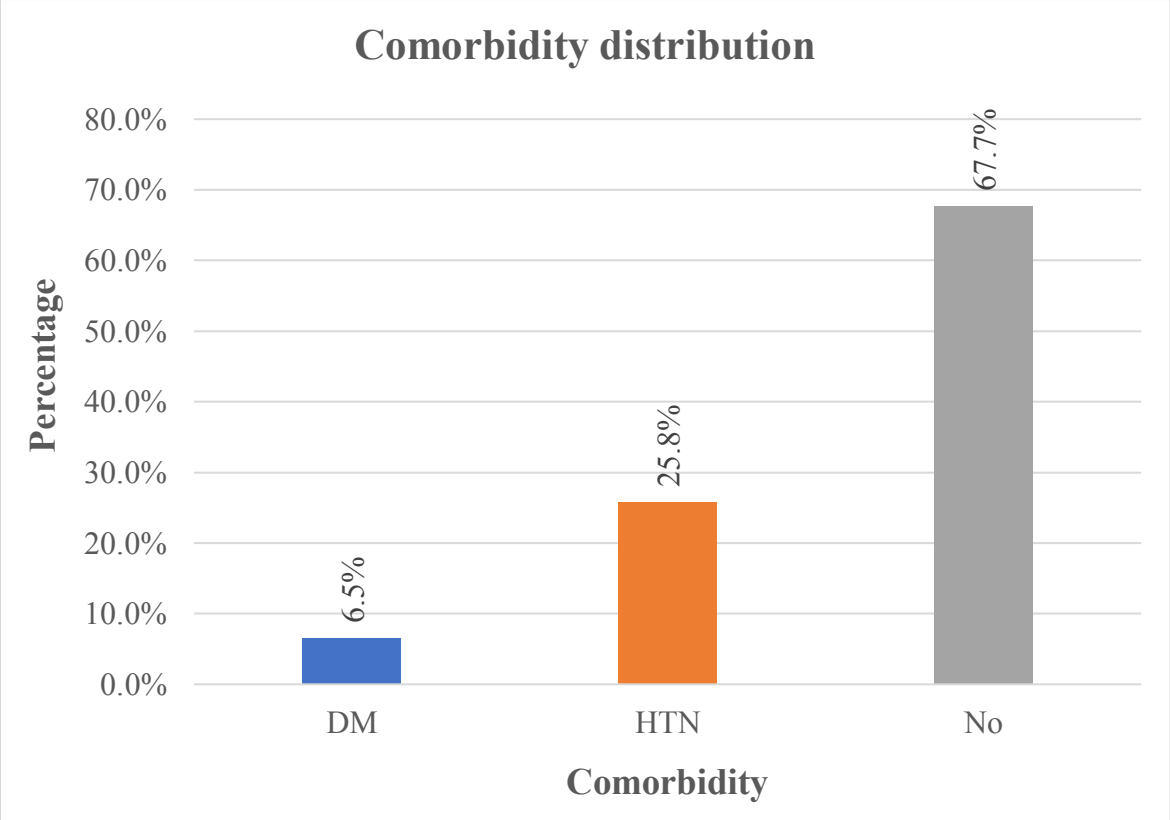


Graph 8: Bar diagram showing BCVA LE distribution

Table 11: Comorbidity distribution among subjects

		Count	%
Comorbidity	Diabetes Mellitus (DM)	2	6.5%
	Hypertension (HTN)	8	25.8%
	No	21	67.7%

In the study 25.8% had HTN and 6.5% had DM as Comorbidity.



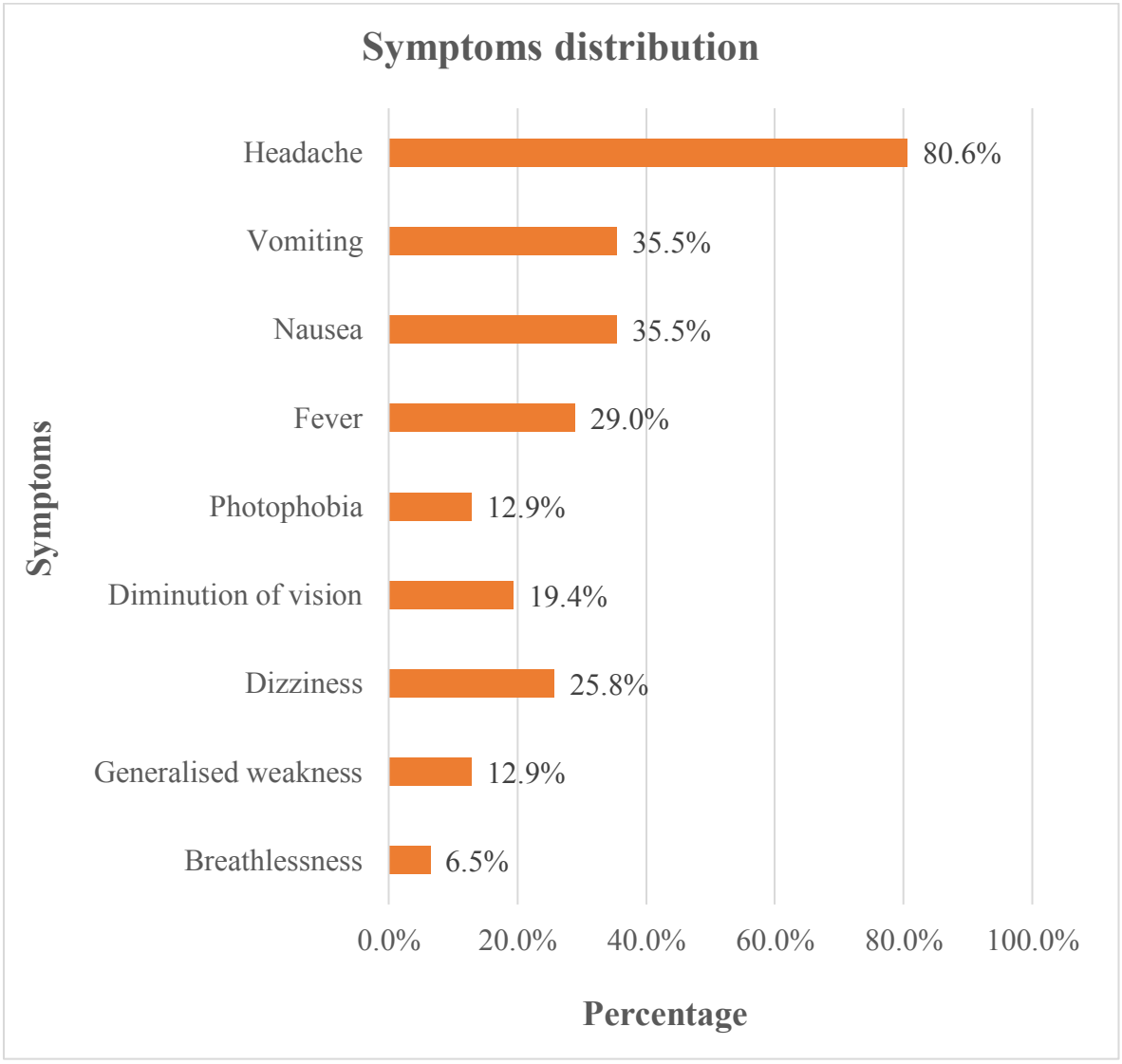
Graph 9: Bar diagram showing Comorbidity distribution among subjects Table 9:

Symptoms distribution among subjects

Table 12 : Symptoms amongst patients

	No		Yes	
	Count	Row N %	Count	Row N %
Headache	6	19.4%	25	80.6%
Vomiting	20	64.5%	11	35.5%
Nausea	20	64.5%	11	35.5%
Fever	22	71.0%	9	29.0%
Photophobia	27	87.1%	4	12.9%
Diminution of vision	25	80.6%	6	19.4%
Dizziness	23	74.2%	8	25.8%
Generalised weakness	27	87.1%	4	12.9%
Breathlessness	29	93.5%	2	6.5%

In the study 80.6% had headache, 35.5% had Vomiting and Nausea respectively, 29% had Fever, 12.9% had H/0 Road traffic accident (RTA), 19.4% had Diminution of vision, 25.8% had Dizziness, 12.9% had Generalised weakness and 6.5% had Breathlessness.

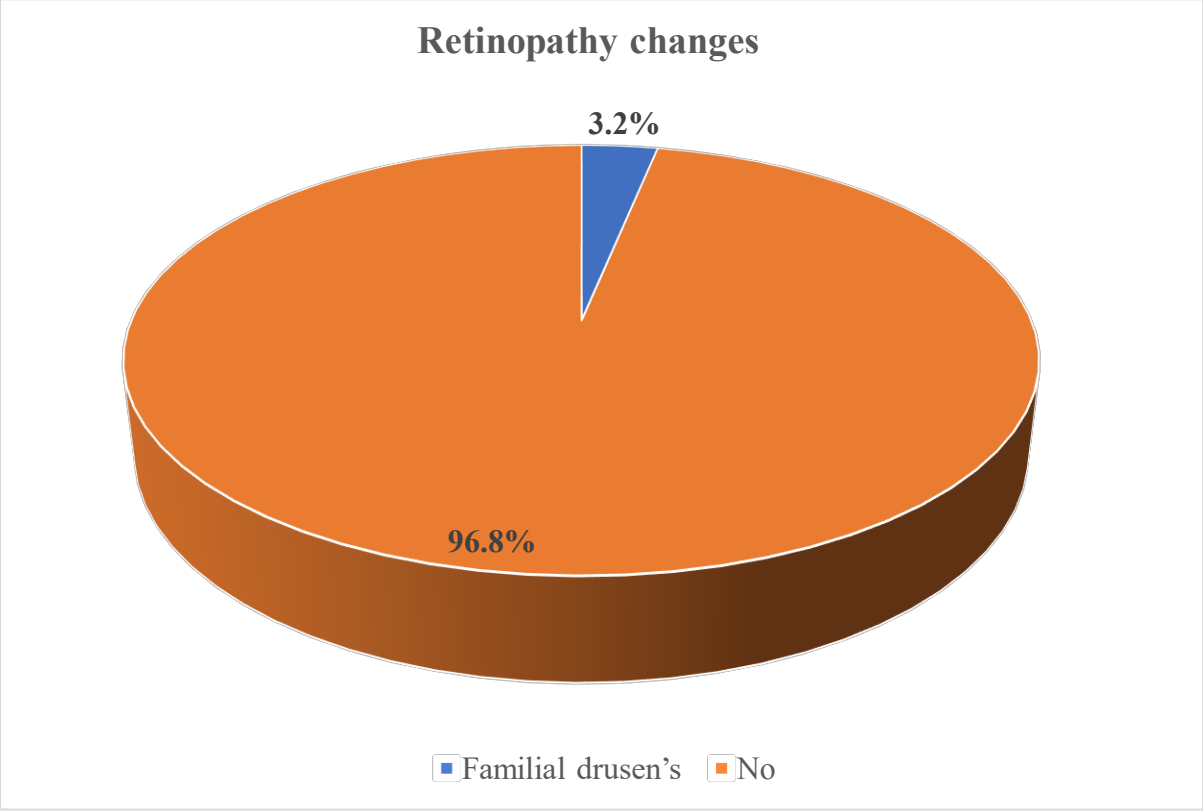


Graph 10: Bar diagram showing Symptoms distribution among subjects

Table 13: Retinopathy changes or any other fundus changes distribution among subjects

		Count	%
Retinopathy changes or any other fundus changes	Familial drusen's	1	3.2%
	No	30	96.8%

In the study 3.2% had Retinopathy changes or any other fundus changes.

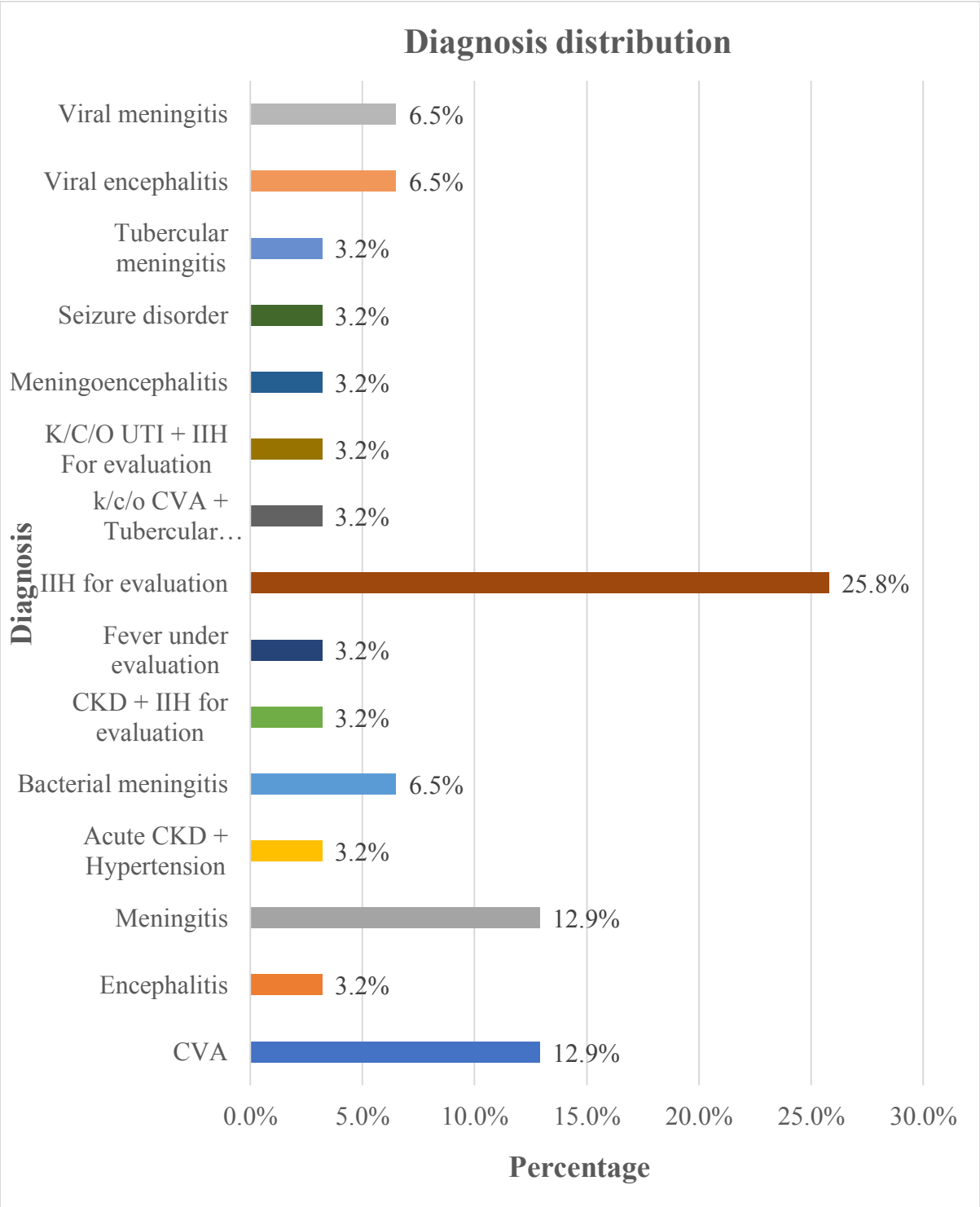


Graph 11: Pie diagram showing Retinopathy changes or any other fundus changes distribution among subjects

Table 14: Diagnosis distribution among subjects

		Count	%
Diagnosis	Cerebrovascualar accident (CVA)	4	12.9
	Encephalitis	1	3.2%
	Meningitis	4	12.9%
	Acute on (Chronic kidney disease) CKD + Hypertension	1	3.2%
	Bacterial meningitis	2	6.5%
	CKD + IIH for further evaluation	1	3.2%
	Fever under evaluation	1	3.2%
	IIH for further evaluation	8	25.8%
	k/c/o CVA + Tubercular meningitis	1	3.2%
	K/C/O Urinary tract infection (UTI) + Headache under evaluation	1	3.2%
	Meningoencephalitis	1	3.2%
	Seizure disorder	1	3.2%
	Tubercular meningitis	1	3.2%
	Viral encephalitis	2	6.5%
	Viral meningitis	2	6.5%

In the study most, common diagnosis was IIH for further evaluation (25.8%), followed by Meningitis in 12.9% and others as shown in above table.

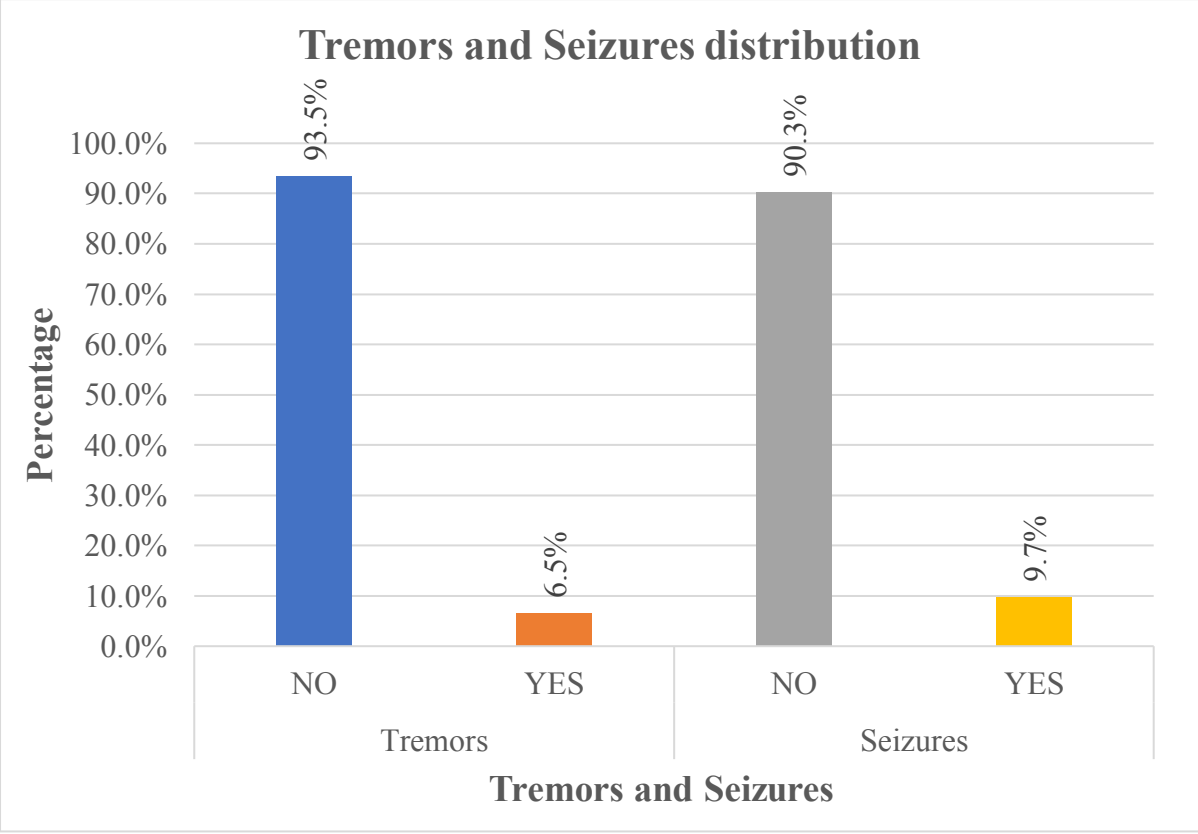


Graph 12: Bar diagram showing Diagnosis distribution among subjects

Table 15: Tremors and Seizures distribution among subjects

		Count	%
Tremors	No	29	93.5%
	Yes	2	6.5%
Seizures	No	28	90.3%
	Yes	3	9.7%

In the study 6.5% had Tremors and 9.7% had Seizures.



Graph 13: Bar diagram showing Tremors and Seizures distribution among subjects

DISCUSSION

Most of the time, elevated ICP is linked to worse neurological outcomes and more morbidity and mortality. Stroke, liver failure, meningeal inflammation , meningoencephalitis, metabolic encephalopathy,and post resuscitation syndrome are all possible causes. [144-149] In such circumstances, it is necessary to treat early and promptly by detecting raised ICP. However, it might also come with difficulties. [147,150] The gold standard is invasive ICP monitoring. It is related with intricacies like infection, bleeding and being costly. There are risks associated with transporting these critically ill patients to radiology for routine CT and MRI comparisons.[151] Bedside modality ocular USG for ONSD measurement can be useful for detection of elevated ICP. There are advantages of it being a non invasive, easier to do at the bedside, portable and is less time consuming. It can be repeated for evaluating again since there is no radiation risk. The relatively inelastic dura, cranium, and vertebral canal all combine to form a rigid chamber. As a result, the ICP will typically rise as the amount of brain volume, blood or CSF in the body increases. "Monro - Kelly doctrine relationship states that small increases in brain volume do not lead to immediate increase in ICP due to the ability of the CSF to be displaced into the spinal canal, as well as the slight ability to stretch the falx cerebri between the hemispheres and the tentorium between the hemispheres and the cerebellum." After ICP gets to 20-25mmHg, intracranial compliance failure can result in significant ICP elevations from even a modest increase in brain volume.[152] ICP only slightly rises during stage 1. When the change in volume is greater than 100-200 milliliters in stage 2, the ICP dramatically rises. Stage 3 is characteristic of persistently elevated ICP, which changes dramatically with small volume changes. As the ICP nears the mean arterial pressure getting blood into intracranial space becomes more difficult. This reduces cerebral perfusion widely, which eventually results in brain ischemia and infarction of the brain. By and large if there is an ascent in ICP, common clinical features include headache, altered sensorium, vomiting and loss of consciousness. Coughing, bending, sneezing can aggravate the headache

progressively worsening over time.[153,154] The ONS is continuous with dura mater anatomically and has a arachnoid space which is trabeculated through which CSF percolates slowly.[114]

On ultrasound, ON appears homogeneous, with low internal reflectivity compared to the high reflectivity of the nerve sheath. Ossoinig used this when he performed the 1st ultrasound measurement of ON using an Ascan technique and later described standardised A scanning.[114]

Several studies have been conducted to investigate relationship between ONSD as measured by Ascan and ICP. Cennamo et al[155] and Gangemi et al[116] found a +ve linear relationship between the 2 variables in neurosurgical patients, as well as an immediate change in ONSD with a change of ICP.

USG based ONSD measurement is based on fact that SAS around ON is in continuity with intracranial SAS. Hence, any increase in ICP will be transmitted to ON SAS. This will lead to inflation of retrobulbar portion of ONS which can be measured using B-scan.[156]

The ultrasound contrast is highest 3mm behind globe making results more reproducible and hence this position was chosen. Hansen et al. presented data for the ONSD measurement using a transorbital Bscan approach.[157] This method allowed them to select a distance behind globe to consistently measure nerve, which is difficult with Ascan. In cadaver studies, Helmke and Hansen[158, 65] confirmed Liu and Kahn's[77] findings that the ONSD increased by up to 60% at 3mm behind globe compared to only 35% at 10mm. They demonstrated that optimal experimental scanning position was axial, which had lowest interobserver variability. Based on the literature, we used a similar approach for all of the patients in our current study, measuring the ONSD 3mm behind globe with a B scan.

In a study by Raghunandan and colleagues done in India, they compared ONSD of normal patients to the subjects having clinical diagnosis of PE. ONSD of 3.12 ± 0.22mm was noted in normal individuals and subjects having clinical diagnosis of PE had an ONSD of 4.89 ± 0.65mm. [156] The ONSDs were on a higher side in subjects having clinical diagnosis of papilledema in comparison to normal individuals. Similarly, in a study by Bauerle et al done in Germany compared to controls ONSD was significantly on higher side among patients with IIH bilaterally which was 6.4 ± 0.6 mm versus 5.4 ± 0.5 mm.[133] In contrast to the mentioned studies where a comparison was done amongst cases and controls in terms of ONSD measurement, our study didn't have controls. The present cross sectional study included patients with established PE of whom ONSD measurement by B scan was done. In a study by Geeraerts and co done in France, mean ONSD in patients with high ICP was found to be 6.2 ± 0.4mm and 6.3 ± 0.6mm for right and left eyes respectively. Controls had mean ONSD of 4.9±0.3mm and 4.8 ± 0.5mm. Also, the values of mean ONSD of both eyes was also similar without much difference between the two eyes.[159] In our study the mean ONSD was calculated separately for right eye and left eye. For the right eyes, the mean ONSD obtained was 4.86 ± 0.52mm and for left eyes the ONSD was 4.90 ± 0.52mm. The mean values in both eyes were found to be similar. Our study has similar results of mean ONSD to the one found in patients of PE in study by Raghunandan et al. [156]

Similarly other studies which were done such as Goeres et al study showed mean ONSD to be 3.68mm, Shirodkar et al showing 5.43 ± 0.53 mm and Wang et al study resulting in 4.18 ± 0.61mm in patients with raised ICP. [134, 157, 160]

The symptom with which patients with established papilledema presented the most was headache which was in 80.6% patients. Nausea (35.5%) and vomiting (35.5%) were also

noted in our study followed by fever (29%). Dizziness (25.8%) and generalised weakness (12.9%) were also complained by our patients.

Around 12.9% of patients had a history of RTA but we had excluded patients with any intracranial or intraocular surgeries done. A few patients presented with breathlessness (6.5%).

Mohson et al study evaluated ONSD by ultrasonography in patients with clinically detected papilledema, the patients had complaints on visual impairment and headache. [161] In a study by Momtaz et al raised ICP causes in their study were tumours within cranium, intracranial hemorrhage, head trauma, uremic encephalopathy, hypernatremia, diabetic ketoacidosis, hepatic encephalopathy, Carbon dioxide (CO_2) narcosis, brain abscess, ischemic stroke followed by post-arrest in a patient. [162] In our study we found maximum patients (25.8%) had suspected idiopathic intracranial hypertension for further evaluation followed by patients who were diagnosed with meningitis but the cause was unknown and in few patients further evaluation wasn't completed . Patients with cerebrovascular accident accounted for 9.7% of all the patients. Around 6.5% of the patients were diagnosed with bacterial meningitis, viral encephalitis and viral meningitis each. Cases of encephalitis with unknown cause (3.2%) were also included in our study. Chronic kidney disease patients had also presented with complaints of headache and were noted to have established PE (3.2%) and were hence also included in our study. One patient presented with fever which was considered for further evaluation. Similarly, our study also had patients with known seizure disorder, urinary tract infection and meningoencephalitis. 12.9% of the patients also had a history of road traffic accident causing head injury. None of the patients in our study had any intracranial mass or

bleed. This was contradictory to the above study mentioned by Momtaz et al who had considered patients with intracranial tumours and bleed.

IIH (pseudotumor cerebri syndrome) is one form of IH, whereas structurally recognised causes are the other. An ICP without neuroradiological abnormalities characterises and defines IIH, a condition with unclear cause. Headache, pulsatile tinnitus, TVOs, blurred vision, diplopia, and PE are common indicators of IIH.[163] Our study consisted of maximum patients with IIH which was considered for further evaluation. These patients had presented with symptoms of diminution of vision and headache. All the investigations which patients had underwent before presenting to our department had no significant abnormality. On fundus examination, all these patients had bilateral established papilledema. Similarly, the majority of patients in study by Lochner and co had IIH.[164] In our study, maximum patients belonged to age group less than 30 years (25.8%).

Raghunandan and colleagues had patients of mean age 35.66 their study while Lochner and co in their study had patients of 36 ± 10.8 years.[156, 164] Females were seen more (54.8%) than males (45.2%) in current study and had similarity to study by Raghunandan and co, Patterson and colleagues, Carter and co[156, 165, 92] thereby showing a similar demographic profile between our study and the above mentioned studies.

Our study results showed that patients with Frisen's severity grade 1 (45.2% in both eyes) and grade 2 (38.7% and 35.5% in OD and OS respectively) were more than the other grades which is comparable Raghunandan and colleagues study. Raghunandan and co in their study had considered all the stages of papilledema and their results showed that as the stages of papilledema progressed, Frisens severity grading of the patients also progressed and a correlation between the two was obtained.[156] In our study, we had only considered established

papilledema stage to see the variation of Frisen's severity grading in that stage itself and had correlated ONSD with Frisen's severity grading.

67.7% of the total patients in our study had no comorbidities. Around 25.8% of the patients were hypertensive and 2 patients (6.5%) were diabetics. Also, 9.7% of the patients had history of seizure episodes.

Studies have linked ONSDs to the opening pressures of cerebrospinal fluid (CSF) by lumbar punctures.[24-26] The research by Wang et al. shows that the ONSD drops right away after a drop pressure of CSF, proving that ONSD responds to ICP in real time.[25] They had considered lumbar puncture to confirm rasied ICP and on basis of ICP they had divided the study participants. In our study, we only performed fundus examination to look for papilledema and hence suspected raised ICP in these patients.

As a result, measuring ONSD in patients having elevated ICP can also be used to track therapy response, especially in patients with illnesses that have persistently elevated ICPs, such as IIH and CVT, as well as in children.[17,119,157]

Also, in a study by Shirodkar and colleagues in which they measured ONSD(marker for ICP evaluation and prognostication) had taken Glasgow coma scale into consideration which wasn't included in our study. They had done CSF analysis with following up patients included in their study.[134] They and Raghunandan et al had included management of these patients as well in their study.[134,156]

CONCLUSION

When assessing patients with elevated ICT, a thorough ophthalmoscopic examination and clinical history are crucial. This study reveals that elevated ICP in patients with suspected IH may be detected by sonographic assessments of ONSD values. There was correlation seen in our study between the ONSD measured by B scan and Frisen's severity grading suggesting that higher the Frisen's grading, more the ONSD. The strength of our study was that it was only done in one stage of PE which is established papilledema showing variation of Frisen's grading in the same stage itself. Our study's shortcomings include smaller sample size, not taking into account GCS and not including patient follow-up in the study. When compared to other imaging techniques like CT scan and MRI, the B scan is far less expensive. It is non-invasive, quick, and can also be used as a bedside modality to monitor ICP by measuring the ONSD, which is why it plays a critical role in early detection of ICP rise as well as timely monitoring and management of the patient, particularly in emergency rooms and ICUs.

SUMMARY

The B Scan is a rapid, minimally invasive instrument that aids in the evaluation of patients who have a clinical suspicion of papilledema, which calls for prompt assessment, therapy, and monitoring. True papilledema patients frequently present with little or few complaints. Pseudopapilledema patients could show up at the hospital with symptoms like headaches that are unrelated. In these patients, ancillary testing including brain MRI, MRI of the orbits, B scans for buried drusen or dilated retrobulbar ONSs, and LP for ICP measurement can support the clinical impression and look for structural intracranial lesions or signs of IH. It has also been reported that OCT, fluorescein angiography, and orbital CT scan can distinguish between these two disorders. Out of all these techniques and instruments, orbital ultrasonography, commonly referred to as a B scan, is a valuable one that is rapid, cheap, and offers no risk to patient safety. Timely diagnosis of raised ICT is important since most of the patients may have poor prognosis. Several previous studies have also shown correlation of ONSD measurement on B Scan with stages of papilledema and Frsien's severity grading and positive correlation has been obtained. Also, many previous studies have correlated ONSD with opening CSF pressures. Our study includes only patients with established papilledema stage in which ONSD measurements showed correlation with Frisen's grading.

Current observational study was carried out in Ophthalmology department, R.L.Jalappa. Hospital and Research Centre, attached to Sri Devaraj Urs Medical College , Tamaka, Kolar from December 2020 to June 2022.

In present study, females preponderance was observed than males and most of the patients were <30 years. Mean ONSD measured in patients with established papilledema in right eyes was 4.86±0.52 and in left eyes 4.90±0.52. According to spearman's rho there was a correlation between ONSD and Frisen's Severity Grade for right as well as left eyes and it

was statistically significant ($p < 0.001$). Also, most patients showed Frisen's severity grade 1 and 2 in our study.

Hence, it was noted that as the ONSD on B scan increased, higher Frsisen's severity grade was seen and hence the correlation was statistically significant ($p<0.001$).

Our study hence suggesting correlation emphasises on importance of B Scan modality for detection of rasied ICT. Though our study was mainly out patient based, this modality can be used in departments dealing with emergencies and intensive care where mobilising the patients is difficult and where patients need timely monitoring.

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ANNEXURE

ANNEXURE-I

"A CROSS-SECTIONAL STUDY ON MEASUREMENT OF OPTIC NERVE SHEATH DIAMETER BY B SCAN IN PATIENTS WITH ESTABLISHED PAPILLEDEMA AND ITS CORRELATION WITH FRISEN'S SEVERITY GRADING "

CASE PROFORMA

Group:	Case no:
Name:	Date:
Age:	IP no:
Sex:	Date of examination:
Occupation:	

Address:

Chief complaints:

History of Presenting illness:

Past history: DM/HTN/BA/Epilepsy

Family history:

Personal history:

Appetite – Sleep – Bowel –

Diet – Habits – Bladder –

GPE:

Pallor / Edema /Icterus / Cyanosis / Clubbing / Lymphadenopathy Vital signs:

a. Pulse – c) RR –

b. BP – d) Temp –

Systemic examination:

a. CVS – c. RS –

b. PA – d. CNS –

OCULAR EXAMINATION		
	RE	**LE**
1. Head posture 2. Ocular posture 3. Facial symmetry		
4. Ocular movements		
5. Visual Acuity Distant		
6. Anterior Segment		
7. Fundus (Slit Lamp +90D)		
8. Frisen's severity grading		
9. B Scan: • Optic nerve sheath diameter • Other findings		

ANNEXURE-II

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR

INFORMED CONSENT FORM

Group:

Case no:

IP no:

TITLE: "A CROSS-SECTIONAL STUDY ON MEASUREMENT OF OPTIC NERVE SHEATH DIAMETER BY B SCAN IN PATIENTS WITH ESTABLSIHED PAPILLEDEMA AND ITS CORRELATION WITH FRISEN'S SEVERITY GRADING"

I, the undersigned, agree to participate in this study and authorize the collection and disclosure of my personal information as outlined in this consent form.

I understand the purpose of this study, the risks and benefits of the technique and the confidential nature of the information that will be collected and disclosed during the study.

The information collected will be used only for research.

I have had the opportunity to ask questions regarding the various aspects of this study and my questions have been answered to my satisfaction.

I understand that I remain free to withdraw from this study at any time and this will not change my future care.

Participation in this research project does not involve any financial burden to me.

Name	Signature	Date	Time
Patient:			
Witness1:			
Witness 2:			
Primary Investigator/ Doctor:			

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR

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ANNEXURE-III

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR – 563101.

PATIENT INFORMATION SHEET

TITLE: **"A CROSS-SECTIONAL STUDY ON MEASUREMENT OPTIC NERVE SHEATH DIAMETER BY B SCAN IN PATIENTS WITH ESTABLISHED PAPILLEDEMA AND ITS CORRELATION WITH FRISEN'S SEVERITY GRADING"**

This information is to help you understand the purpose of the study "A CROSS-SECTIONAL STUDY ON MEASUREMENT OPTIC NERVE SHEATH DIAMETER BY B SCAN IN PATIENTS WITH ESTABLISHED PAPILLEDEMA AND ITS CORRELATION WITH FRISEN'S SEVERITY GRADING"

You are invited to take part voluntarily in this research study, it is important that you read and understand the purpose, procedure, benefits and discomforts of the study.

1. What is the purpose of this study?
   "A cross-sectional study on measurement optic nerve sheath diameter by B scan in patients with established papilledema and its correlation with Frisen's severity grading "

2. What are the various investigations being used? Are there any associated risks?
   Absolutely no risks are associated with the various investigations to be done which are assessing for distant vision using Snellens chart, Slit lamp examination using 90D lens, B scan.

3. What is the benefit for me as a participant?
   Correlating the B scan optic nerve sheath diameter measurement with Frisen severity grading in patients with established papilledema would be of importance in contributing towards studies that say assessment of optic nerve sheath diameter on B scan a feasible, non-invasive, quick method to detect papilledema.
   The identification of such benefits is that early diagnosis papilledema is possible thus reducing the burden of severe visual impairment. Such observation may also be of

importance in interpreting and/or planning treatment for protection of vision in patients having papilledema due to some or the other cause.

Participation in this research study may not change the final outcome of your eye condition. However, patients in the future may benefit as a result of knowledge gained from this study. You will not be charged extra for any of the procedures performed during the research study. Your taking part in this study is entirely voluntary.

You may refuse to take part in the study or you may stop your participation in the study at any time, without any penalty or loss of any benefits to which you were otherwise entitled before taking part in this study.

CONFIDENTIALITY

Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available. Your original records may be reviewed by your doctor or ethics review board. For further information, /clarification please contact Dr. MANJULA T.R., SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR – 563101

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DR. YUGANDHARA PATADE

JUNIOR RESIDENT

DEPARTMENT OF
OPHTHALMOLOGY, SDUMC,

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Contact: 7389813831.

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ANNEXURE-IV

Photograph 1: Slit lamp with 90D fundus examination.

Photograph 2 : B scan

KEY TO MASTER CHART

M : Male

F : Female

BCVA : Best corrected visual acuity

RE : Right eye

LE : Left eye

RTA : Road traffic accident

CKD : Chronic kidney disease

UTI : Urinary tract infection

AKI : Acute kidney injury

MODS : Multiple organ dysfunction syndrome

IIH : Idiopathic intracranial hypertension

CVA : Cerebrovascular accident