DIFFUSION WEIGHTED IMAGING AS A PREDICTOR OF VISUAL OUTCOME IN ACUTE OPTIC NEURITIS

Dissertation submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the requirements for the degree of MS Ophthalmology

BRANCH - III

OPHTHALMOLOGY

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CERTIFICATE

This is to certify that this dissertation entitled **"DIFFUSION WEIGHTED IMAGING AS A PREDICTOR OF VISUAL OUTCOME IN ACUTE OPTIC NEURITIS**" is a bonafide work done by **Dr.N.M. Tharani** under the guidance and supervision of Dr. Mahesh Kumar, in the Neuro-ophthalmology Department of Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai during the period of her post graduate training in Ophthalmology for June 2015-May 2018.

Guide
Dr.Mahesh Kumar, DO., DNB.,
Professor and Head of Department
Neuro-ophthalmology
Aravind Eye Hospital,
Madurai.

Principal,
Dr.R.Rathinam,DO,DNB,Ph.D.,
Aravind Eye Hospital,
PG Institute of Ophthalmology,
Madurai.

Dr.N.Venkatesh Prajna DO, DNB, FRCOphth.,
Director,
Aravind Eye Hospital,
PG Institute of Ophthalmology,
Madurai.

DECLARATION FORM

I, Dr.N.M. Tharani, hereby declare that this dissertation entitled, **"DIFFUSION WEIGHTED IMAGING AS A PREDICTOR OF VISUAL OUTCOME IN ACUTE OPTIC NEURITIS"** is being submitted in partial fulfilment for the award **of M.S. in Ophthalmology Degree by the Tamil Nadu Dr. MGR Medical University** in the examination to be held in May 2018. I declare that this dissertation is my original work and has not formed the basis for the award of any degree or diploma awarded to me previously.

Dr.N.M.Tharani,

Aravind eye hospital,

PG Institute of Ophthalmology,

Madurai, Tamilnadu.

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I acknowledge with sincere gratitude all the people without whom this thesis would not have been a success.

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Most importantly I am grateful to all my patients who willingly participated in this study, the result of which I hope will be of some benefit to humanity.

Date -

Place – Madurai Dr.N.M. Tharani

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PART-1I

PART-1

INTRODUCTION

Optic neuritis is an inflammation of optic nerve. Based on clinical examination it is classified into retrobulbar neuritis, papillitis or neuroretinitis. Etiology is multifactorial. The usual triad of symptoms consist of ipsilateral eye pain, vision loss and dyschromatopsia. Clinical signs include reduced visual acuity, dyschromatopsia, altered contrast sensitivity, afferent pupillary defect, visual field defects, optic disc and retinal changes .25% - 30% is usually found associated with Multiple sclerosis. MRI remains the imaging modality of choice in diagnosing and in assessing the visual outcome in optic neuritis. More data is provided by Diffusion-weighted and diffusion-tensor imaging on treatment and/or on prognosis. The loss of anisotropy manifested by an increase in the apparent diffusion coefficient or associated with demyelination and/or axonal damage may be more sensitive and/or yield more prognostic information than anatomic imaging findings. The shortcoming of diffusion -weighted and diffusion-tensor imaging of the optic nerves are that it is too time consuming. The main stay of treatment in optic neuritis based on ONTT (Optic Neuritis Treatment Trial) is corticosteroids both intravenous and oral at present, although newer treatment modalities are underway.

REVIEW OF LITERATURE

***Nettleship E*.** On cases of retro-ocular neuritis. Trans Ophthal Soc UK 1884;4: 186-226. 3.

By the 1880's, in the pre –ophthalmoscopic era, von Graefe and Nettleship, had given description of many of the classical features of idiopathic optic neuritis.

Nettleship described optic neuritis to be characterized by decreased sight usually limited to one eye, may present along with neuralgic pain around the temple and orbit and pain in eye movements; though eventual recovery usually occurs, permanent damage or even total blindness can occur; at times there is no ophthalmoscopic change, but usually the disc n becomes atrophic over a few weeks, and now and then there are few retinal changes.

Gunn RM. Discussion on retro-ocular neuritis. Trans Ophthal Soc UK 1897;17: 107-217.

Retroocular neuritis was divided into three groups based on etiology:

Infection of the orbit, paranasal sinuses or meninges 2) systemic infectious diseases (syphilis, tuberculosis), and 3) disseminated sclerosis. He described the relatively ill sustained pupillary constriction to direct light in the affected.

It was suggested from their study, to look at the pupil reaction to light. Care should be taken while checking the reaction as it is only in marked degrees of amblyopia, the pupil does not act moderately well. In such cases also, where the pupillary contraction in the amblyopic eye seems normal, the pupil will fail to maintain the contraction when exposed to light continuously.

For this contribution he received the credit for "Marcus Gunn pupil". ***Adie WJ.*** Acute retrobulbar neuritis in disseminated sclerosis. Trans Ophthal Soc UK 1930; 50:262-267. 53.

Adie meant that in multiple sclerosis optic neuritis can be the only clinical manifestation. They also noted down that there was a relationship between acute retrobulbar neuritis and disseminated sclerosis.

Roy W. Beck[33], Robin L. Gal, **Treatment of Acute Optic Neuritis.** ***A Summary of Findings from the Optic Neuritis Treatment Trial.*** ARCH **OPHTHALMOL/VOL 126 (NO. 7), JULY 2008**

The conclusions of ONTT showed that without MRI lesions the risk of developing Multiple sclerosis is 16% at 5 years,22% at 10 years and 25% at 15 years. This shows that there is only 3% increase after 10 years.

While the risk of developing Multiple sclerosis with MRI lesions is 37% at 5 years when MRI showed 1-2 lesions; 51% with ≥ 3 lesions at 5 years; 56% with ≥ 1 lesion at 10 years and 75% with ≥ 1 lesion at 15 years.

***Simon J Hickman*[22] et al, "Optic nerve diffusion measurement from diffusion weighted imaging in optic neuritis" AJNR Am J Neuroradiol 26;951-956, April2005.

From their study they came to a conclusion that ADC gives a supportive measurement of axonal disruption in chronic post inflammatory optic nerve pathology.

Zareen Fathima*[6] *et al "Diffusion weighted imaging in optic neuritis". Canadian Association of Radiologists Journal 64 (2013) 51-55.

They found from their study that there was marked differences in the optic nerve diameters, increased intensity on DWI, apparent diffusion coefficient of optic nerves in acute and chronic optic neuritis and in control groups.

Rohit Saxena *et al* in his study titled "Clinical profile and short-term outcomes of optic neuritis patients in India."

Concluded in his study that the clinical profile of optic neuritis was not the same in Indian and Western population. He also concluded that the even though the recurrence rates were lower in Indian population the outcomes were poorer.

ANATOMY OF THE OPTIC NERVE

The second cranial nerve is called the optic nerve. It extends from the lamina cribrosa up to the optic chiasma and measures about 47-50mm in length. The nerve is covered by meningeal sheaths –the dura, the arachnoid and the pia, of which the sub-arachnoid space is continuous with that of the brain. At the optic disc the fibers of the nerve fiber layer of the retina pass the optic nerve. The fibres are very thin about 2- 10 um in diameter.

Four parts of the optic nerve are:

1. Optic nerve head and intraocular part (1mm)
2. Intra-orbital part (25mm)
3. Intra-canalicular part (4-10mm)
4. Intracranial part (10mm)

The Optic Nerve Head

1. The surface nerve fiber layer
2. The prelaminar region
3. The lamina cribrosa region

Optic disc, (synonym “papilla”, optic nerve head,) is the anterior-most part of the optic nerve. The optic nerve head measures about 1 mm long and about 1.5 mm in diameter, the vertical diameter being slightly

greater than the horizontal. The configuration of the optic disc and of the physiological cup depends upon the size, shape and direction of the optic canal, and the diameter of Bruch's membrane opening and scleral canal. Histologically

The Optic Nerve Head has 4 layers

1. The surface nerve fiber layer
2. The prelaminar region
3. The lamina cribrosa region
4. Retrolaminar region

1. The Surface Nerve Fiber Layer

This is the most anterior layer, where nerve fibers from all over the retina converge and run into the optic nerve. The inner limiting membrane of Elschnig (composed of astrocytes) separates it from the vitreous. There are a large number of blood vessels in this layer.

(***2) Prelaminar region,***

Enormous number of glial cells are in this layer and they are loosely arranged. This arrangement may have a role to play in the pathologic swelling of optic disc. Central depression corresponds to the physiological cup. It is separated by many layers of astrocytes from the deeper layers of the retina called –Intermediate tissue of Kuhnt and from adjacent choroid where it is called Border tissue of Jacoby. The axons are 150 Å separated

from each other The nerve fibers from retina bend 90 degrees in the surface layer of the optic nerve head to run back in the optic nerve.

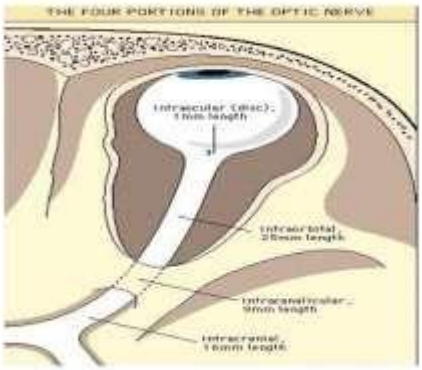
(3) Lamina cribrosa

Posteriorly it is convex and anteriorly concave. Here connective tissue fibers are tightly packed and has many openings for the transmission of the optic nerve fiber bundles. Large amount of elastic tissue is present in the lamina cribrosa. Superior and inferior parts contain larger pores and thinner connective tissue septa than the nasal and temporal parts. It consists of elastin fiber and collagen III and IV and laminin. Ageing increases density of collagen types I, III, IV and elastin and increase in density of collagen type IV. It is pierced through its entire thickness centrally by the central retinal vessels.

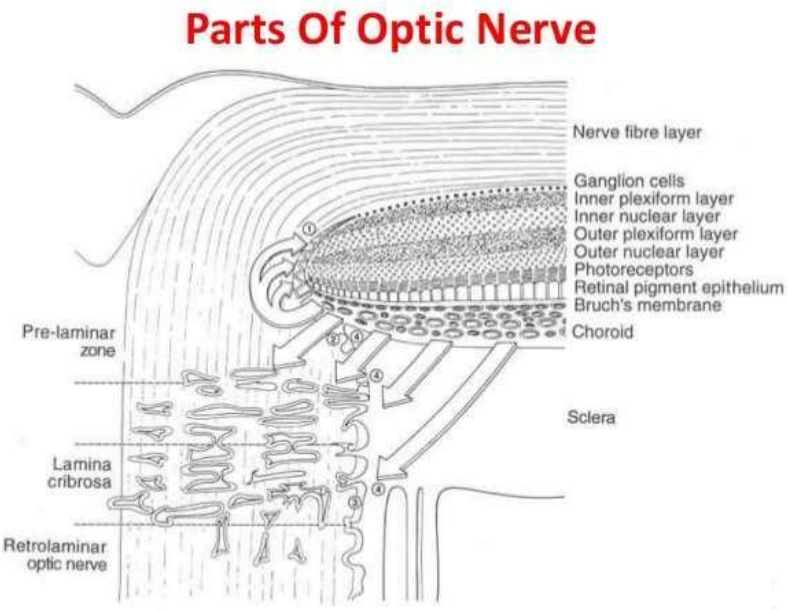
4.Retrolaminar region

In this region astrocytes decrease and myelin acquisition increases which leads to increase in diameter of optic nerve.

Picture 1



Picture 2



PARTS OF THE OPTIC NERVE (Ref Picture 1 and 2)

INFRAORBITAL PART

Extending from the eyeball to optic canal this part is sinuous and plays a role in eye movements. The nerve fibres become myelinated here and thence after. The central retinal vessels lie in the centre of anterior intra-orbital part. In the beginning of this part optic nerve lies infero - lateral-medial to ophthalmic artery. It lies inferior and lateral to ophthalmic artery at optic foramen. In the posterior orbit laterally, it is related to -inferior division of third nerve, sixth nerve nasociliary artery and ciliary ganglion. Optic nerve is surrounded by annulus of Zinn at orbital apex.

INTRA-CANALICULAR PART

This constitutes the part within the bony optic canal. It is surrounded by the meningeal sheath where numerous thick fibrous bands connect the dura to the pia. The subarachnoid space is almost a capillary size here. This kind of anatomy, makes the sheath in the optic canal play a crucial role in conveying the cerebrospinal fluid pressure of the cranial cavity into the sheath of the optic nerve.

INTRACRANIAL PART

Relation of the optic nerve in this region are:

In the beginning to the diaphragm sellae below and then to cavernous sinus below; infero-laterally to ophthalmic artery and laterally to the internal carotid artery.

It is covered by the pia mater but not by meningeal sheath.

One million in number optic nerve fibres are of 5 types

(1) Visual afferent (carrying visual information and goes to the lateral geniculate body),

(2) Pupillary afferent (pupillary reflex function and goes to the tectum),

(3) Efferent to the retina,

(4) Photostatic (running to the superior colliculus) and

(5) Autonomic fibers

The diameter of nerve fibers varies between 0.7 and 10 µm, mostly 1 µm. The smaller axons come from the central retina and the larger axons from the peripheral retina.

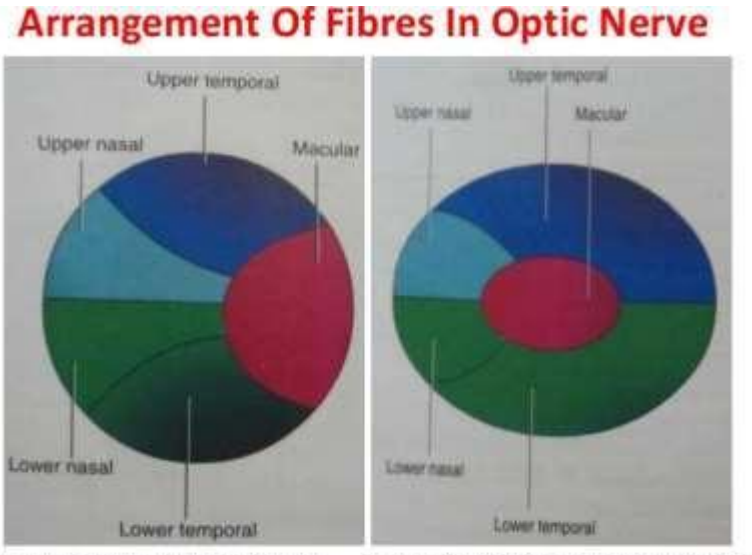
IN THE OPTIC NERVE HEAD (Refer Picture 3)

- On the same side temporal macular fibres remain
- Nasal fibres cross
- Macular fibres separate upper temporal fibres from those below

IN THE DISTAL REGION

- the temporal half of optic nerve lie the upper and lower temporal fibres separated by the papillo-macular bundle
- On the nasal half of optic nerve lie the upper and lower nasal fibres

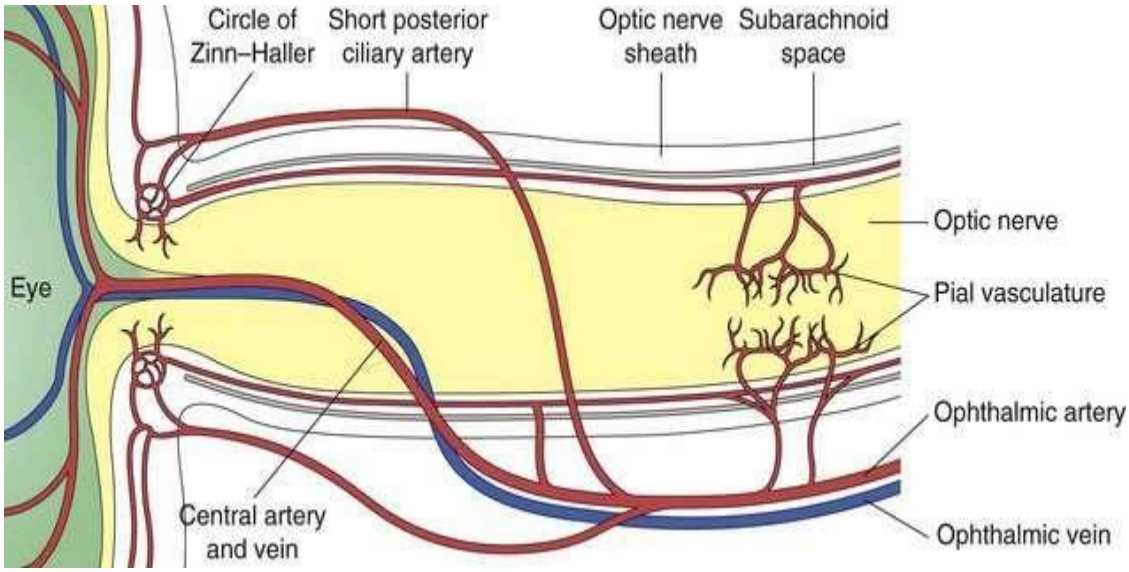
Picture 3



Arrangement of fibres in ON head & distal region

Arrangement of fibres in proximal region of ON

Picture4



IN THE REGION NEAR CHIASMA

Macular fibres are centrally placed

NERVE FIBRE LAYER THICKNESS AT DISC

It is thickest in the upper nasal and lower nasal quadrant **and** thinnest at the most lateral quadrant.

BLOOD SUPPLY OF THE OPTIC NERVE (Refer Picture 4)

1. OPTIC NERVE HEAD:

SURFACE NERVE FIBRE LAYER

- Mainly supplied by peripapillary and epipapillary arterioles of Central retinal artery.
- It forms a rich anastomosis with the prelaminar region and occasional anastomosis with chorio-capillaries.

- Cilioretinal arteries when present give precapillary branches to this layer.

PRELAMINAR REGION

- Mainly supplied by scleral short posterior ciliary artery branches
- In 10% of cases by recurrent choroidal arteries
- Infrequently by cilioretinal arteries
- and laminar vessels

LAMINAR REGION

- Mainly supplied by scleral branch of short posterior ciliary artery
- and paraoptic branches of short posterior ciliary artery

  forming circle of Zinn-Haller

RETROLAMINAR REGION

- Mainly supplied by arteries and arterioles of pial sheath of Leptomeninges
- Scleral short posterior arteries
- Direct choroidal arteries
- Intraneural branch of central retinal artery

INFRA ORBITAL REGION

1.PERIAXIAL

- Long posterior ciliary artery
- Short posterior ciliary artery
- Ophthalmic artery
- Central retinal artery of retina
- Lacrimal artery
- Circle of Zinn

2.AXIAL

- Central artery of optic nerve
- Intraneural branches of central retinal artery
- Central collateral arteries

INTRACANALICULAR

- Mainly supplied by the periaxial system of vessels
- Ophthalmic artery supplies pial plexus which in turn supplies this part.

INTRACRANIAL PART

- The periaxial system of vessels
- Pial plexus supplied by

1. Internal carotid artery branches directly or through recurrent branch of anterior superior hypophyseal artery
2. Anterior cerebral artery branches
3. Ophthalmic artery- small recurrent branches
4. Twigs from anterior communicating artery

VENOUS DRAINAGE

- Mainly by the Central retinal vein
- To a lesser extent by Pial venous system

  Both of these drain into
- Ophthalmic vein
- Cavernous sinus Pial veins
- In the orbit and optic canal-Ophthalmic vein
- Intracranial pial veins-adjacent venous sinuses

DEMOGRAPHY

Demographic data in Asian population varies from that of Western literature. From the studies conducted in this region it was found that Retrobulbar neuritis is less common than papillitis. Most of the cases presented bilaterally, the incidence of Multiple Sclerosis was low and prognosis was moderate. Female preponderance is seen in this region.

CLASSIFICATION

OPHTHALMOSCOPICALLY

- Retrobulbar neuritis – (no optic disc swelling)
- Papillitis – hyperemia and edema of optic disc
- Perineuritis - optic nerve sheath inflammation
- Neuroretinitis - papillitis and macular star (inflammation of retinal nerve fibre layer)

B) ETIOLOGICALLY

1. Primary demyelinating optic neuritis

a) Isolated optic neuritis

b) Multiple sclerosis

c) Devic disease

d) Schilder disease

2. Infectious and para-infectious

- -Viral (adenovirus, coxsackievirus, measles, mumps, rubella, varicella zoster)
- -Bacterial (syphilis, tuberculosis, Lyme disease, cat scratch disease,
- β-Hemolytic streptococcal infection, Brucellosis, typhoid fever, meningococcal infection, Whipple's disease)

3. Others

- -Post vaccination
- -Inflammation (sarcoidosis, vasculitidis e.g. polyarteritis nodosa, SLE)
- -Miscellaneous (bird shot retinochoroidopathy, intraocular nematode
- infection, toxoplasmosis, toxocariosis, Gullain Barre syndrome).
- -Drugs and toxins

PATHOPHYSIOLOGY

There are similar pathophysiological mechanisms between optic neuritis and multiple sclerosis. Both are due to autoimmune mechanisms where environment factor e.g.: virus acts as a trigger in susceptible people.

When CD4+ T-helper cells are activated in the periphery by an environmental factor they cross the blood-brain or blood-optic nerve barrier. After encountering the neural auto-antigens in the CNS they proliferate, activate and recruit other inflammatory cells, and local immune and parenchymal cells such as microglia and astrocytes are stimulated to produce pro-inflammatory cytokines. CD8+ cells, B cells, antibody, and complement are also involved in producing neural damage.

These bring about the pathological features of the optic nerve: inflammation, demyelination, axonal loss, and gliosis. Neural recovery is seen as a combination of resolution of inflammation, re-myelination, and neural plasticity. MRI helps to quantify the loss of axons and neurons. Mitochondrial dysfunction leading to free radical damage and glutamate excitotoxicity plays an important role in the axonal and myelin damage.

MULTIPLE SCLEROSIS

It is a neurodegenerative disorder. It is acquired, autoimmune and T cell mediated. It is a chronic disease and affects the brain, spinal cord

and optic nerve. The disease causes inflammation and demyelination of myelin surrounding the nerves. Optic neuritis is the initial presentation of Multiple sclerosis (MS) in 15%-20% of people. In 10 years the chances of a person with optic neuritis developing MS is 56% if associated with brain abnormalities in MRI. All the above incidence reports are from western literature. In Asian countries and India, the incidence is low.

Clinical features suggestive of MS are:

1. Age of onset between 15 years to 50 years.
2. Lesions in multiple areas of brain and spinal cord.
3. Optic neuritis
4. Internuclear ophthalmoplegia
5. Lhermitte's sign
6. Fatigue
7. Uhthoff's phenomenon

CLINICAL ASSESSMENT

Optic neuritis is defined a demyelinating inflammation of the optic nerve. As time progresses there is a gradual recovery of visual acuity in optic neuritis, though permanent color vision deficits and reduced contrast and brightness sensitivity is common.

History

The patient may reveal a history of:

- Preceding viral illness
- Mostly occurs in age group 20 to 50 years
- Female preponderance is seen
- Rapidly progressing visual impairment in one eye or, rarely may present bilaterally.
- Dyschromatopsia: more common than reduced vision.
- Retro-orbital or ocular pain: associated with the vision
- impairment and increased on eye movement; the pain may occur prior to vision loss
- Uhthoff phenomenon- heat or exercise exacerbates vision loss
- Pulfrich phenomenon-appearance of curved trajectory of disc objects moving in a straight line.
- Phosphenes- bright fleeting flashes of light

Physical examination

Signs of optic neuritis are:

- Reduced pupillary light reaction in the affected eye: A relative afferent pupillary defect (RAPD) or Marcus Gunn pupil is usually seen. In case of bilateral optic neuritis, RAPD may not be apparent
- Vision may vary from slightly decreased visual acuity to total loss of vision.
- Impaired contrast sensitivity and color vision
- Altitudinal field defects
- Arcuate defects
- Nasal steps
- Central scotoma
- Centrocecal scotoma
- Papillitis

VISION LOSS

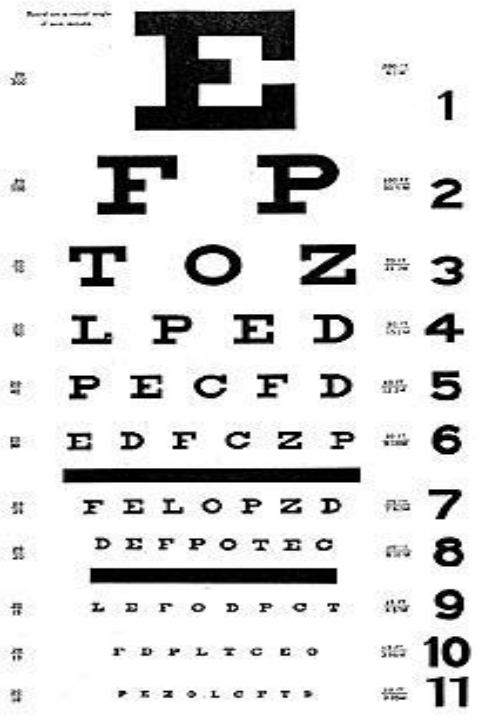
Defective or reduced visual acuity is the hallmark of most cases of acute optic neuritis. Sudden in onset: the time period may vary from few hours to days. Some may present with profound loss of vision resulting in no perception of light, others may present with just a meagre reduction

like not able to read all letters in the last line of Snellen chart., or just a reduction in central fields with normal visual acuity. (Refer Picture 5)

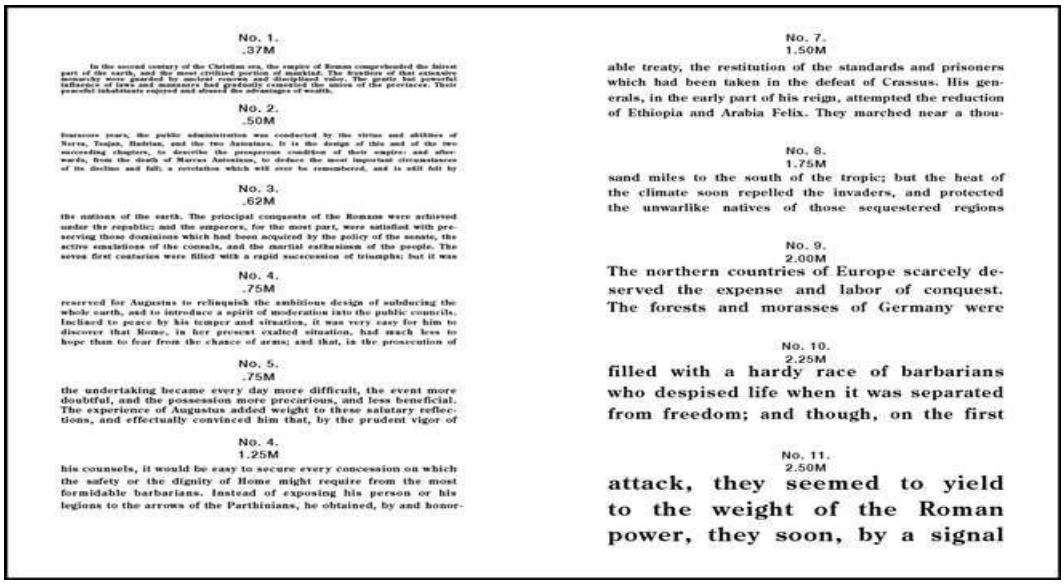
Visual acuity is measured using Snellen chart. It was named after Dutch Ophthalmologist Herman Snellen in 1862.Visual acuity is a measure of form sense. He described visual acuity as the ability of the eye to resolve detail and this is shown as the reciprocal of minimum angular separation which can be resolved as separate and this forms an angle of one minute in the human eye.

It contains block letters printed in eleven lines but commonly Snellen with the first 8 lines from top is used. In the first line there is only one large letter. In the rows which follow the number of letters increase but decrease in size. The symbols are called optotypes. An angle of 5 minutes is subtended by each individual letter and an angle of 1 minute is subtended by each component of letter. Visual acuity is measured by numerical convention method. The numerator is the distance between patient and chart. The denominator is the distance where the smallest optotype identified subtends an angle of 1 minute of arc. The top line should be read clearly at a distance of 60m, following lines are read at 36m, 24m,18m,12m,9m,6m,5m respectively.

Picture 5: Snellen chart



Picture 6: Near vision chart



Testing procedure:

Minimum of 20foot candles should be used to illuminate the chart. The patient is seated at 6m. If the patient is seated at 3m then a half - sized chart in which the letters subtend the same angle is used. An alternative is to use a reversed chart which is projected and viewed through a mirror is used.

The trial frame is worn by the patient and the interpupillary distance is adjusted. Each eye is tested separately with the occluder in the trial frame of other eye. The patient is asked to read from the topmost letter in the Snellen's chart. From the smallest line the patient is able to read, his vision is recorded as 6/6,6/9,6/12, 6/18,6/24,6/36 and 6/60. If the patient is not able to read the first line of the chart the patient is asked to move step by step forwards towards chart and vision recorded at 5m as 5/60, 4m as 4/60, 3m as 3/60, 2m as 2/60 and 1m as 1/60.

If even at one metre distance the patient is unable to read the top line then vision is assessed by asking patient to count fingers of the examiner is and recorded as CF3FT, CF2FT, CF1FT, CF close to face. If patient is unable to count fingers close to face then patient is asked whether he is able to perceive hand movements when the examiner moves his hand in front of the patients face. Vision is recorded as HM+.

If hand movements are also not appreciated then whether the patient perceives light or not is noted as PL+ OR PL-. If PL+ then light is thrown in all directions and projection of rays appreciated by the patient is noted as present or absent. The other eye is tested in a similar way.

In illiterate patients

Landolt's ring or E chart is used.

NEAR VISION (Picture 6).

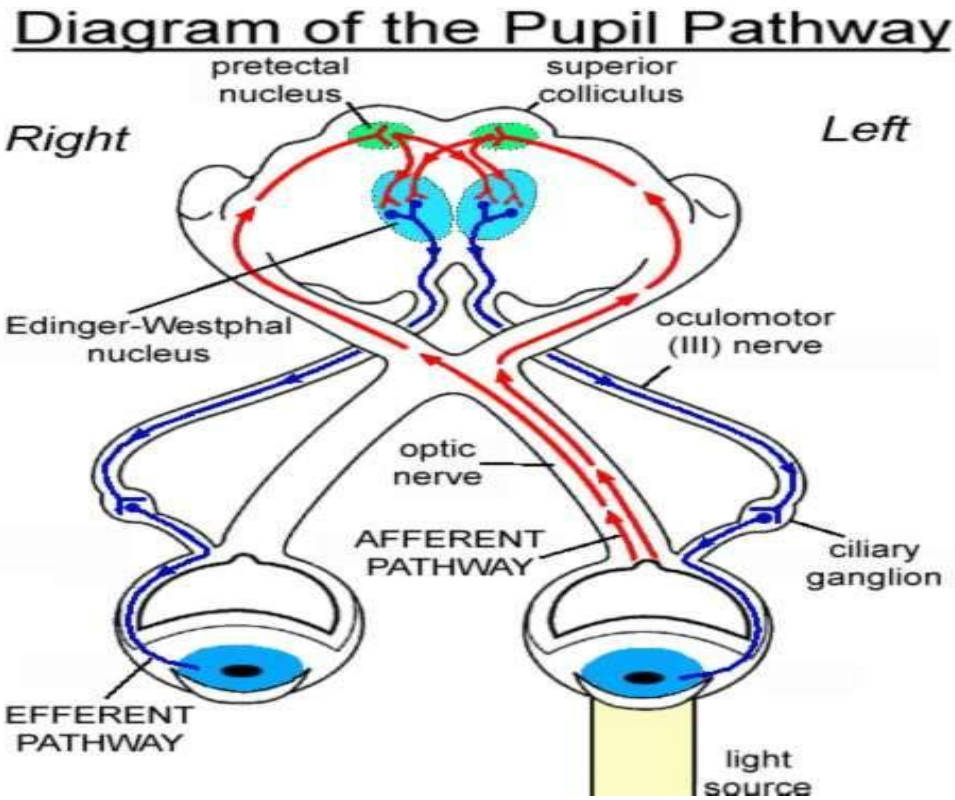
Tested with Snellen near vision chart, Jaeger chart or Roman test type charts. The patient is made to sit with his back facing light. Distance correction lens is worn and the eye is tested with occluder in the trial frame of the other eye. Patient holds the near vision chart at a distance of 25 to 33cms. Near vision recorded according to the size of letter read. The other eye is tested in a similar way.

PUPILLARY PATHWAY (Refer Picture 7)

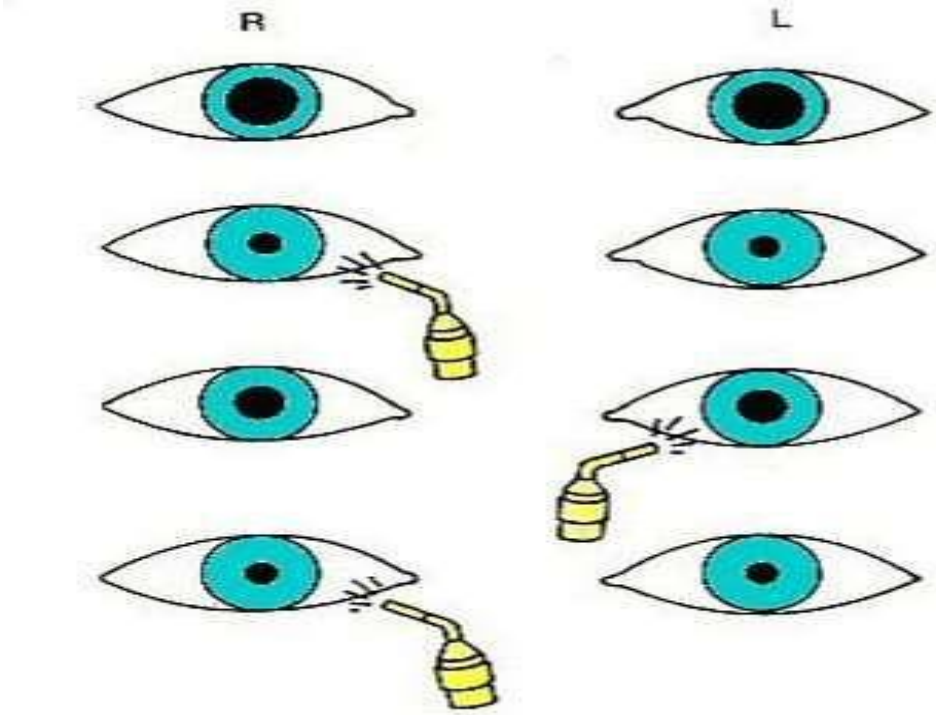
The pupillary pathway consists of two components:

1. Afferent pathway
2. Efferent pathway which in turn has two components: sympathetic and parasympathetic

Picture 7



Picture 8



Afferent pathway

The afferent pathway carries sensory stimuli from the retina via the optic nerve to the pretectal nucleus in the midbrain at level of superior colliculus.

Efferent pathway

From the pretectal nucleus crossed and uncrossed fibres project to ipsilateral and contralateral Edinger-Westpal nucleus in the midbrain. From here parasympathetic fibres project along with oculomotor (III cranial nerve) to synapse with postganglionic parasympathetic neurons of ciliary ganglion innervating ciliary sphincter. Due to decussation twice, one in optic chiasm and the other between pretectal nuclei and Edinger-Westpal nucleus, direct pupillary response in one eye equals consensual response in the other eye.

Relative afferent pupillary defect (Refer Picture 8)

It is a condition in which the affected pupil responds differently to light stimuli due to lesions in the retina, optic nerve, optic chiasm or optic tract. It is a sensitive measure of testing the anterior visual pathway function. It is tested by the swinging flashlight test. (Refer picture 1)

1. The first row indicates dilated pupils in dark room
2. The second row indicates when light is shown in the right eye pupil of both eyes

3. constrict. This indicates right eye afferent limb and both eyes efferent limbs are intact.
4. The third row shows that when light is swung to the left eye, the left eye instead of constricting dilates paradoxically. This indicates that the afferent limb of the left eye is at fault. This is relative afferent pupillary defect.
5. The fourth row shows that when light is swung again to right eye both eyes constrict.

CONTRAST SENSITIVITY

It is the ability to recognize mild changes in brightness between areas that are not separated by clear borders. It is important to identify the definite outlines of comparatively smaller objects.

Pelli Robson chart

Same sized letters with decreasing contrast is used. Every row has six letters with two triplets of different contrast. Chart illumination is 85cd/mm2.It is read at a distance of one meter. The patient is given a score according to the faintest triplet he or she is able to read. The scoring pad gives the log CS value for that triplet.

Bailey Lovie chart

Contrast sensitivity is tested in presence of glare.

Same number of symbols and spacing between rows and letters is kept constant. It is a chart based on log of minimal angle of resolution or log MAR.

CAMBRDGE LOW CONTRAST GRATING

It is tested at a distance of 6m and is a rapid, simple screening test. 12 pairs of varying contrast plates are used in the test. One is for demonstration. Patient is tested from plate one, one by one till patient is not responding. Next a new test is started from 4 plates prior to the plate which the patient failed to respond. Such series of test are done four times. Score is calculated from the number of plates read and added. The total is converted into contrast sensitivity from a table.

ARDEN SINE WAVE GRATINGS

Vertically oriented gratings of varying contrast contained in a booklet is used for the test. The lowest contrast grating is at the top and contrast increases towards the bottom.

VISTECH CONTRAST SENSITIVITY CHART

The sine wave gratings in this chart are arranged as circular photographic plates against gray background. All charts used in this test consist of 5 rows and 9 columns of these plates. The contrast in each row decreases from left to right. The gratings are oriented vertically 90 degrees and 15 degrees clockwise and anticlockwise.

Of the two Vistech charts available, Vistech -6500 is used for testing distance and Vistech-6000 is used for testing near. Useful for documenting performance of low vision patients.

Other charts which are available are:

Functional acuity contrast testing, Regan charts

COLOUR VISION

Colour vision which is basically a function of cone, is the ability of the eye to recognize a distinction between colors excited by light of different wavelength. Well appreciated in well-lit conditions.

Well known theories of colour vision are:

Trichromatic theory:

Young and Helmholtz postulated that every cone has a different photopigment and each one is very sensitive to any one of 3 primary colour.

Opponent theory:

3 opposing colour pairs are formed by connections between cone photoreceptors. When one pair is activated it inhibits others. No 2 pairs have same location in the cones.

When photoreceptors or optic nerve fibres are affected to varied etiology colour vision is also affected.

Kollner's rule:

Tritan defect occurs when there is damage to the retina and red green defect occurs when there is damage to the optic nerve.

COLOR VISION TESTS:

Isihara chart

This chart is mainly used to detect red green color deficiency. It contains a series of plates with colored dots forming a number or pattern against similar sized colored dots in the background. Persons with normal color vision will be able to identify the numbers. Persons with color deficiencies either don't identify the numbers or read it differently.

Holmgren wool test

Patient is given a coloured wool and asked to pick up a similar coloured wool from a set of coloured.

Eldridge green lantern

This instrument has a light source at the centre and a window through which different colors can be appreciated by rotating the color disc. The color filters can be used to simulate fog and mist. This test is specially used to testing transport workers i.e. their ability to identify colors in varied atmospheric conditions.

RED DESATURATION

Procedure

The patient wears his best corrected near vision for this test. Each eye is tested separately with bright red coloured objects. The patient is told to compare the amount of redness perceived by him. The amount of saturation is given percentage according to the redness perceived by the patient.

BRIGHTNESS COMPARISON

This was done using indirect ophthalmoscope at 6V. At a distance of 30 cm the patient is asked to fixate at a bright source of light. The light source is then shown on the other eye for an equal length of time. Patient is asked to assess whether the brightness was equal in both eyes, or one was brighter than the other. Roughly expressed as percentage.[45,37]

VISUAL FIELDS

Optic nerve can get damaged anywhere in the visual pathway, giving rise to diverse visual field defects.

Four common methods are used for visual field testing:

1. Confrontation method
2. Amsler grid
3. Bjerrum’s screen
4. Goldmann perimetry

Confrontation methods

In this the peripheral field of the patient is compared to that of the examiner.

Technique:

The patient should be seated at a distance of 60 cm from the examiner. Chair height is adjusted so that both the patients and the examiner's eyes are at the same level. If the patient covers right eye, the examiner covers his left eye and vice versa. If the patient is not able to see the examiners face while fixating it indicates the patient has a large scotoma.

The test can be done with target objects, or by simply asking to count fingers in each of the quadrants. A reliable comparison between the two hemifields and detection of altitudinal field defects can be done by this method.

Amsler grid

This test is used to test visual field about 10 degrees surrounding fixation. Patient is corrected for near vision first. Non-testing eye is occluded and patient is asked to fixate at the black dot at the centre of the Amsler grid. Patient has to identify if there is any distortion of lines or any scotoma.

Bjerrum or Tangent screen

Central 30 degrees of the visual field can be evaluated by this method.

Technique:

Each eye is tested separately with the other eye patched. The patient is seated at 1 metre away from a black screen and asked to fix his eye at a central spot. The target is a white flat disc, 1mm in size on a black wand. The other side of the disc is black in colour, so that the examiner can flip over the wand during testing. The target is moved from a non-seeing area to the seeing area and the patients visual field defect and blind spot defects are identified.

Goldmann perimetry

Targets are presented on a bowl set at a distance of 33cm from the patient's cornea. Central and peripheral visual fields can be evaluated. The test light of varying sizes and intensity is presented on the bowl. When the test light is presented in the same location it is called static perimetry. When it is moved from the outer edge of the visual field radially towards the centre it can be used as a kinetic perimeter.

Additional test which could be done are:

1. Stereo acuity
2. Visual evoked potential

3. Pattern encephalogram

4. Infrared reflection to detect pupillary light reflex latency

5. Authorn Flicker test

ATYPICAL OPTIC NEURITIS

In contrast to typical presentation of optic neuritis mentioned above atypical optic neuritis has

- A progressive course
- Affected group are usually less than 12 years and more than 50 Years
- Vision loss is bilateral
- Vision does not improve spontaneously
- Vision continues to deteriorate even after corticosteroids
- Initially painless, later accompanied by pain
- Optic disc swelling may be severe
- Hemorrhage in optic disc
- Varying signs and symptoms depending on etiology.

Diagnosis

When a patient presents with typical features of optic neuritis diagnosis is based on clinical features alone. But when a patient presents with atypical features of optic neuritis, recurrent optic neuritis, acute optic

neuritis in children or presence of systemic inflammatory disease investigations are needed to rule out progressive optic neuropathy.

- CBC
- Serum electrolytes, blood sugar-random
- Chest X-ray
- Erythrocyte sedimentation rate
- Mantoux
- Thyroid function tests
- Antinuclear antibodies
- Angiotensin-converting enzyme
- Rapid plasma reagin
- Mitochondrial deoxyribonucleic acid (DNA) mutation studies
- FTA-ABS
- VDRL
- Serology for culture of bartonella
- CSF tap
- PCR for viral infections
- MRI

Ophthalmic investigations include

- Visual acuity assessment
- Colour vision assessment
- Contrast sensitivity
- Visual evoked response
- Colour fundus photography and fluorescein angiography
- USG orbit
- Optical coherence tomography/SD-OCT
- The last four are not routinely used to investigate typical optic neuritis although they might be used for atypical forms. Of all the investigations MRI has been found to well predict the development of multiple sclerosis in a patient with optic neuritis and serve as a guideline for starting therapy with interferon alpha-1a.

NEUROIMAGING IN OPTIC NEURITIS

INTRODUCTION

MRI- magnetic resonance imaging -was discovered by Paul C Lauterbur and Peter Mansfield. MRI a spectroscopic imaging technique. Its components are magnetism, radio waves and computer processing and thereby creates fine images of almost every part of body. The first MRI was done on a human being in 1977.

MRI MAGNET

Magnetic field is measured in units of Tesla. 1 Tesla=1NEWTON/AMPERE METER.

Current day magnets use 0.5 tesla to 3.0 tesla range (5000-30000 Gauss). In research higher values are used.

All the atom components i.e. protons, neutrons and electrons have spin. Every spin will have a small magnetic field. It is described in terms of + or – sign and in multiples of ½.

Hydrogen constitutes 9.5% out of the 26 elements that form the human body.

Principle of MRI:

Certain atoms nuclei are aligned or polarized when placed in a strong magnetic field. This is done through absorption and emission of energy within the radiofrequency range of electromagnetic spectrum.

In ionic state hydrogen is a proton with positive charge and magnetic spin. Hydrogen ion gives the most intense and the best signal compared to other nuclei. These protons move randomly without the influence of external magnetic field.

A coil applies the radiofrequency pulses to the specific part of the body scanned. The hydrogen protons line up either in direction of feet or head.

When the protons are aligned they not only rotate around themselves but also on their axis of rotation forming a cone called precession. The number of precessions of proton per second is expressed in hertz. It is directly proportional to the external magnetic field. Radiofrequency pulses (high wavelength low energy electromagnetic waves) push the aligned protons to a to higher energy level and make them to spin in a different direction known as resonance (whose frequency is called Larmor frequency).

Larmor's equation is $W_o = yB_o$

[W_o = precession frequency in Hz,

Bo =strength of external magnetic field in tesla

Y=Gyromagnetic ratio specific to a particular nucleus]

Wo for hydrogen proton for 1 Tesla is 42 MHz and 1.5 Tesla is 64MHz.

LONGITUDINAL MAGNETISATION

When the protons are aligned under external magnetic field they align parallel and antiparallel to it. The forces cancel each other. However, protons which are aligned parallel are more than those which are aligned antiparallel and these proton forces are not cancelled. These forces add up to form magnetic vector called longitudinal magnetization. It cannot be directly measured, hence for measurement it has to be transverse.

TRANSVERSE MAGNETISATION

When a radiofrequency pulse is sent some of the precessing protons start precessing antiparallel at higher energy level causing magnitude of longitudinal magnetization to reduce. These proton forces add up to form new magnetic vector called transverse magnetization.

When the precession frequency is same as the radiofrequency pulse frequency exchange of energy occurs between the two. This is called resonance or R in MRI.

Main magnetic field is altered by rapidly turning the gradient magnets along X, Y AND Z axis on and off. The three gradients are:

1. Slice selection gradient-Z axis
2. Phase encoding gradient-Y axis
3. Frequency encoding gradient-X axis

When radiofrequency pulse is turned off the hydrogen protons return to their natural alignment. On doing so they release the excess stored energy. The energy is either released as heat or absorbed by other protons or released as radio waves. The magnitude of longitudinal magnetization (T1) increases.

Longitudinal relaxation rate is 1/T1.Stronger the magnetic field longer the

T1. Depending on tissue composition, structure and surroundings T1 differs (water has a long T1 and fat has a short T1.

The protons which were precessing in phase with the radiofrequency pulse (RF) lose phase once the RF pulse is switched off. This results in decrease in magnitude of transverse magnetization and is termed as transverse relaxation. Inhomogeneity of external magnetic field local magnetic move slowly. So, they have a short T2 e.g. fat.

SPIN – ECHO SEQUENCE

90-degree pulse

↓

180-degree pulse

↓

Echo

TR AND TE

The time interval between the beginning of one RF pulse to the next is called TIME TO REPEAT or TR.

The time interval between the beginning of one RF pulse to the signal or echo reception is called TIME TO ECHO or TE.

Short TR is <500ms.

Long TR is >1500ms

Short TE is 15-20ms

Long TE IS 70-75ms.

T1 WEIGTHED IMAGE

Short TR

↓

Early or maximum regain of LM

↓

Stronger the TM

↓

Brighter the signal

T2 WEIGTHED IMAGE

Short TE

Stronger the TM

PD-PROTON DENSITY IMAGE

Density of protons in a tissue determine the amount contrast in the image. Long TR reduces T1 effect and short TE reduces T2 effect. By doing so we get PD weighted image.

The radiofrequency antenna coil picks up the moving proton vector signal and sends it to the computer which makes use of mathematical data and converts through a Fourier equation into an image.

NEUROIMAGING TOOLS

- T1WI
- T2WI
- DIFFUSION TENSOR IMAGING
- MRV
- MRA
- GADOLINIUM
- DWI
- ADC
- DIFFUSION TENSOR IMAGING

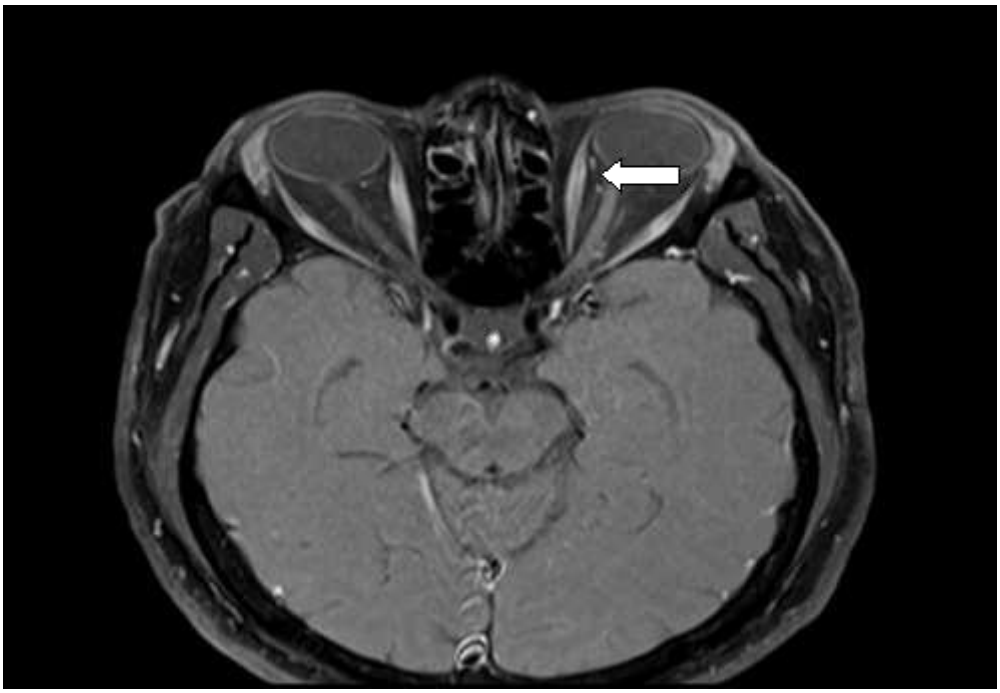
- f MRI
- PERFUSION MAPPING
- CSF FLOW MAPPING
- MR SPECTROSCOPY

Optic nerve evaluation is done using a thin coronal and axial T1 – used for evaluation of anatomy-Fat is bright and CSF is dark short tau inversion recovery (STIR) suppresses the fat signal allowing better detection of optic nerve lesions T2 -evaluate edema resulting from pathologic process Preferred section thickness is 3-4 mm with an interslice gap of 0-1mm.

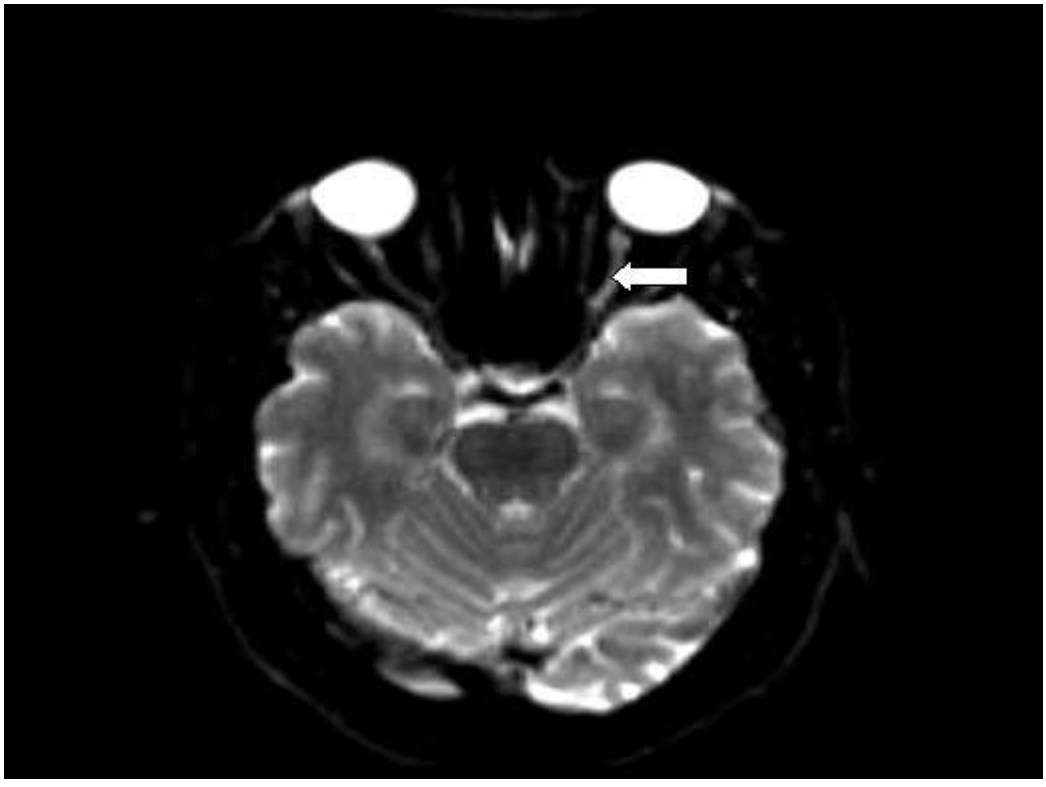
MRI was commonly advised in case of optic neuritis to evaluate the location, structural changes, breakdown of blood brain barrier and to identify the demyelinating foci in the brain.

Nowadays Diffusion-weighted imaging (DWI), fluid attenuated inversion recovery (FLAIR), and susceptibility-weighted imaging (SWI) for the entire brain are used routinely.

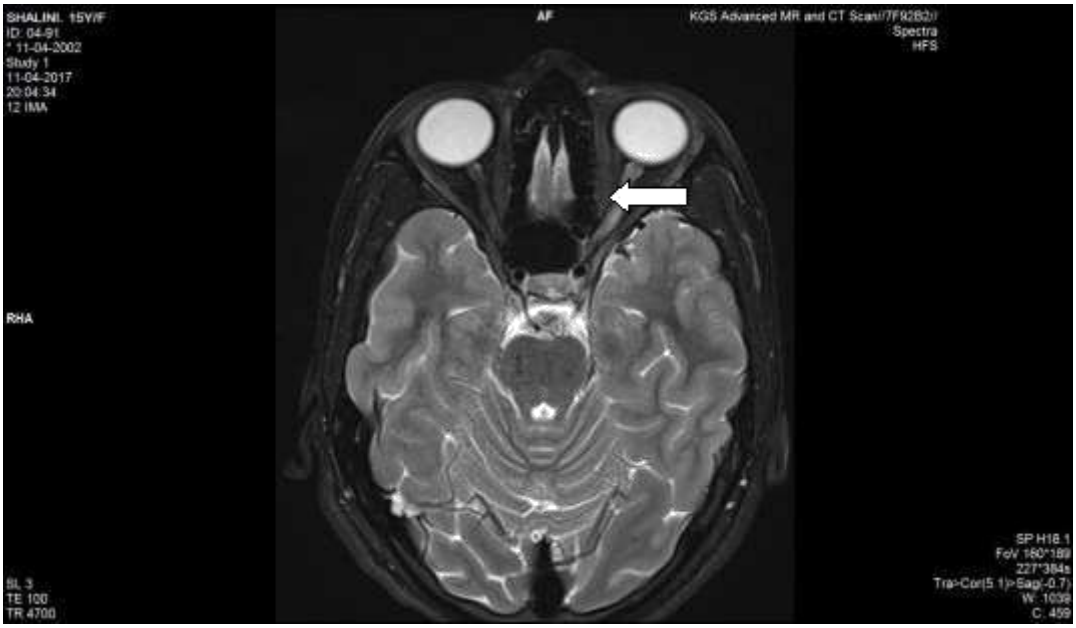
FLAIR- Shows periventricular hyperintense lesions, such as multiple sclerosis (MS) plaques by adjusting the long TI (inversion time) to a zero-crossing point for water and thereby suppressing the CSF signal.



LE contrast enhancement



LE dwi restriction



LE optic nerve thickening in T2W axial image

DIFFUSION WEIGHTED IMAGING

It is an example of endogenous contrast. Signal changes are brought by changes in proton motion. It images the Brownian movement of water molecules diffusing through the extracellular space. This is done by adding a pair of motion probing gradients applied before and after the 180degree spin echo refocusing pulse along same directional axis of a T2 weighted sequence. Signal is retained by water molecules which are stationary as they are not affected by the paired gradients. The application of two diffusion sensitising gradients result in incomplete rephasing of spins and thus loss of signal of nonstationary water molecules. Regions with rapid diffusion i.e. high mobility appear dark. Areas where water molecules motion is restricted e.g. in areas of cytotoxic edema appear bright due to less signal loss. This is contrast to conventional T2 weighted images which show change in signal due to vasogenic edema. Nerves exhibit restricted diffusion because of their anatomical components like axons and myelin sheath. When there are alterations in anatomical barriers due to some pathology there are changes in diffusion pattern.

Contrast images are obtained post- gadolinium injection. Relaxation times are different for different tissues. These differences are used to generate contrast in the image.

A high field 1.5 T echo planar system is needed to get diffusion weighted images. “b-value” is the degree of diffusion weighted imaging weighting. b α q2Δ where q denotes the gradient strength, is the time difference between two gradients.

The aim of our study was to determine the imaging characteristics of acute optic neuritis which can assist in the prediction of visual prognosis of the same.

APPARENT DIFFUSION COEFFICIENT

Images in DWI are essentially T2 weighted. Therefore, lesions which show long T2 relaxation will be bright even when they don’t restrict diffusion. Lesions which show fast diffusion would not have lost much signal will appear bright. In order to eliminate T2 effects and avoid spurious bright spots, Diffusion coefficient is calculated using many DWI series with many distinct b values.

Another name for ADC is diffusion map. It is calculated from two or more images with different duration gradient and amplitude. It determines the amount of signal intensity loss in each voxel. It is helpful to estimate the age of DWI lesions. Lower ADC are seen with hyper acute ischemic lesions whereas in subacute lesions and chronic lesions normalised ADC values are seen. They rapidly decrease after acute ischemia and rise over 7-10 days (pseudo-normalisation). Non-ischemic

causes for reduced ADC are Multiple Sclerosis, Lymphoma, abscess, etc…ADC is calculated by the following equation.

ADC = LN (signal intensity at b value of 1000

/signal intensity at b value of 0/1000

Where LN denotes negative logarithm.

OPTIC NEURITIS TREATMENT TRIAL

This multicentric randomised clinical trial was done during the period 1988-2006 in the white population.457 patients with unilateral optic neuritis between 18-46 years of age were enrolled. The patients enrolled had no other systemic cause other than Multiple sclerosis.

This study aimed at 3 things mainly:

- To know the natural course of visual acuity in patients with optic neuritis.
- Benefits and side effects of corticosteroids in optic neuritis.
- Risk factors of developing Multiple sclerosis in patients with optic neuritis. Questions asked were:
- Whether oral prednisolone alone or intravenous prednisolone followed by oral prednisolone brought improvement in vision in optic neuritis.
- Does the above treatment regime bring about speedy recovery of vision?

- Are the benefits of treatment more than the complications involved?

PHASES

It involved two phases:

1. Treatment phase- ONTT (Optic neuritis treatment trial)
2. Follow up phase- LONS (Longitudinal optic neuritis study)

Eligibility criteria of the patients enrolled in this study were:

- Age – 18-46 years
- Vision problems of less than 8 days duration
- RAPD and visual field defects
- No history of previous episodes
- No previous corticosteroid treatment
- Only Multiple sclerosis as a systemic cause of optic neuritis.

The patients were randomised into 3 groups:

1. 1st group- received 250 mg methylprednisolone qid for 3 days followed by oral prednisolone 1mg/kg for 11 days then tapered.
2. 2nd group-received oral prednisolone 1mg/kg for 14 days then tapered.
3. 3rd group-received oral placebo for 14 days.

Patients were followed over the years till 2006.Baseline tests used for comparison of outcome were:

- Visual acuity
- Fields
- Colour vision
- Contrast
- Neurological evaluation
- Life questionnaire affecting vision quality
- MRI changes

Results obtained in ONTT were:

VISUAL ACUITY:

- In 3 weeks duration 79% started recovering and in 5 weeks duration 96%
- At 1 year :93% had VA >20/40 and 20/20 vision was achieved by 69%
- At 15 years :92% had VA >20/40 and 20/20 vision was achieved by 72%
- 85% patients with VA of 20/200 at presentation had VA of 20/40 eventually.

Initial visual acuity was the best predictor of the final visual outcome.

ROLE OF STEROID

- Oral steroid had no role and it was associated with recurrent optic neuritis
- IV Methylprednisolone (IVMP) can shorten the period of recovery
- Steroids don't affect the final visual outcome.

The use of IVMP in classical demyelinating optic neuritis are:

- One eyed patients
- Bilateral severe visual loss and
- For occupational necessity

RISK OF MS

In western population the overall risk

- at 10 years is 38%
- at 15 years is 50%

Gender

75% Females eventually develop MS compared to 35% males. Over 2 years of follow up IVMP seems to have had a protective role from developing. But after 3 years this finding was not significant.

RISK OF MS BASED ON MRI FINDINGS

- 1-2 lesions – at 5 years the risk was 37%
- $\geq$ 3 lesions – at 5 years the risk was 51%

- ≥ 1 lesion – at 10 years the risk was 56%
- ≥1 lesion – at 15 years the risk was 75%

FACTORS PLAYING PROTECTIVE ROLE AGAINST DEVELOPING MS ARE:

- Males
- Severe visual loss at presentation – no perception of light
- Absence of pain
- Presence of retinal exudates
- Disc edema – severe

POSSIBILITY OF DEVELOPING MS BASED ON MRI FINDINGS

- If there are no baseline MRI lesions risk is 22%
- If there are ≥1 baseline MRI lesions risk is 56%
- If there are more baseline MRI lesions risk increases

CONCLUSIONS DERIVED FROM ONTT

1. Oral prednisolone should not be used in treatment of acute optic neuritis as it did not improve outcome and increased the risk of recurrences.
2. All patients with acute optic neuritis should have MRI brain done. If lesions found to give supportive evidence of MS IVMP should be initiated immediately irrespective of clinical presentation. This is followed by oral prednisolone 1mg/kg/BW for 11 days.

3. When a patient presents with typical features of optic neuritis investigations like chest x- ray, lumbar puncture and blood tests are not indicated.
4. MRI – T2weighted1.5 TESLA, plays an important prognostic role in predicting development of MS in future.

LIMITATIONS

1. ONTT failed to explain why increased ON recurrences rates was not associated with increased chances of developing MS.
2. Further studies needed to show oral corticosteroids were associated with increased recurrences rates.
3. In patients with severe vision loss there is slight benefit of giving IVMP. This was not explained in the study.
4. Only steroids were used for treatment. No other treatment used.

LONGITUDINAL OPTIC NEURITIS STUDY

It was a 15 centre study. It was designed to assess the benefits and side effects of corticosteroid treatment in patients with ON; to know the natural course of vision in ON; and to provide insight about the risk factors in ON that lead to the development of MS.

CHAMPS STUDY

It was designed to study the effect of interferon B1a treatment in patients with ON.30μg INF β1a should be given within 27 days of acute

optic neuritis. Over a 3 year follow up it was found that the development of new lesion of MS and the occurrence of recurrences in the treated group was significantly lower.

CHAMPIONS STUDY

(Controlled High Risk Avonex Multiple Sclerosis Prevention Surveillance)

Early versus delayed treatment in CHAMPS study were analyzed over a 10year period. It showed the end result to be: recurrence rate was doubled in the delayed group.

RP CENTRE STUDY

(Rajendra Prasad centre study) This study was conducted in the year 2010.The inferences were:

Intravenous pulse dexamethasone was easy to administer, cost effective and equally efficacious as mega-dose intravenous methylprednisolone therapy in acute optic neuritis.

The PRISMS

(Prevention of Relapses and Disability by Interferon -1aβ Subcutaneously in Multiple Sclerosis)

The efficacy of interferon (IFN)- 1a given subcutaneously in dosages of 22 µg and 44 µg were assessed. It was inferred that relapses were less in both groups vs placebo group.

BENEFIT study-

{Betaferon in Newly Emerging Multiple Sclerosis for Initial Treatment (BENEFIT) study} It was a 2 year study.

Inference: Interferon- 1b (Betaseronβ) given in a Standard dose reduces the risk of MS by 50% in patients with minimum two MRI lesions.

Natalizumab (Antegren)

This new drug gets attached to alpha 4 integrin, a protein on WBC, thereby hindering immune cells causing significant damage to brain and spinal cord from crossing the blood brain barrier.

RECENT ADVANCES

Studies on aquaporin 4 autoantibodies and serological markers like GFAP and N-acetyl aspartate are going on and hold promise in the future treatment of acute optic neuritis.

PART-1I

PART II

AIM AND OBJECTIVES

Aim

To determine that Diffusion weighted imaging can be used as a predictor of visual outcome in patients with Acute optic neuritis at a tertiary eye care Centre in Southern India.

Objectives

- To detect acute optic neuritis by MRI.
- To determine that DWI can be used as a predictor of visual outcome in acute optic neuritis.
- To determine the specificity of Diffusion restriction, contrast enhancement and ADC in detecting acute optic neuritis.

MATERIALS AND METHODS

- Approval from Institutional Review Board was obtained. IRB Code No. IRB201500225 dated 12-12-2015 (Enclosed).
- Design: Prospective, observational study.
- Study population: all clinically proven cases of acute optic neuritis attending the neuro ophthalmology department in AEH, Madurai during the study period and those who are willing to take part in this study will be included.

START AND FINISH DATE

- Study period:15 months
- Case recruitment: 1 year from 1/12/2015 to 30/11/2016
- Follow up: 3 months

Data source: Hospital records (Aravind eye Hospital) Sample size: 28 patients / 31 eyes.

Informed consent was obtained from all patients participating in the study.

INCLUSION CRITERIA

- AGE 18-65 Years
- Loss of visual acuity or visual field, with or without pain less than 1month duration
- Relative afferent pupillary defect
- Fundus findings consistent with optic neuritis (Disc may be edematous or normal)

Field defects consistent with optic neuritis-centrocaecal scotoma-central scotoma, altitudinal defect, hemi-anopic defect or generalized constriction of the visual field.

EXCLUSION CRITERIA

- Age < 18 years
- Visual loss due to toxic, nutritional, metabolic, vascular, hereditary, glaucomatous, traumatic, compressive neuropathies.
- Prior occurences of optic neuritis in the affected or fellow eye will be excluded from the study.

A collection of 31 eyes of 28 patients who were diagnosed as acute optic neuritis in our Neuroophthalmology clinic in Aravind eye Hospital, were included in our study.

From history, duration of symptoms (only patients who had symptoms less than a month duration with no previous episodes were

included in the study) and clinical assessment which included defective vision, pain on eye movements, headache, dyschromatopsia, relative afferent pupillary defect, disc changes, a diagnosis of acute optic neuritis can be made. All of them were subjected to a series of ophthalmological, neurological examination and to neuroimaging.

In the proforma data of the patients name, age, gender, address were noted. A complete history of each symptom was noted down. Any history of previous episodes were also asked and they were excluded from the study.

All included in our study group underwent

1. Visual acuity testing using Snellen chart. If the patient was not able to read any letter in the snellen chart at 6m, then the chart was moved towards the patient and vision was tested at 5m, 4m, 3m, 2m, 1m respectively. If the patient was not able to read any letter at 1m then the ability to count fingers close to face, ability to identify hand movements, ability to perceive light was assessed.
2. Examination of eyelids, conjunctiva, anterior segment, pupillary reaction with torch light
3. If more than 40 years measurement of intraocular pressure by non-contact tonometry

4. Examination of fundus by direct ophthalmoscope and slit lamp biomicroscopy using +90 dioptre lens.
5. Ishihara's- 21plates were used to test colour vision. If one or more plates are not identified by the patient the test was considered abnormal.
6. Red desaturation : This was a subjective test . The patient was asked to tell the amount of red saturation of the red coloured objects in terms of percentage. If less than 100% it was noted down as reduced.
7. Brightness sensitivity - This was a subjective test . The patient was asked to tell the amount of brightness of the bright torch shown in the eyes in terms of percentage. If less than 100% it was noted down as reduced.
8. Bjerrum's screen for central fields testing. The central 30 degrees of the visual field was tested using the Bjerrum's screen. Any field defect was noted down accordingly.
9. If visual acuity was $\leq$ 3/60 by snellen chart perimetry, colour vision, brightness sensitivity and red desaturation was not done.
10. Neuroimaging especially DWI MRI depending on the affordability of patients.

11. The diffusion characteristics, contrast enhancement and ADC values were assessed. They were compared to the unaffected eye in case of unilateral cases and in eyes with bilateral involvement they were compared to the age matched controls. The regions of interest were adjusted and placed in the centre of optic nerve by increasing the size of the image. ADC values and optic nerve diameters were then calculated.

12. All patients in our study received 1gm of intravenous methyl prednisolone for 3 days followed by prednisolone 1mg/kg/ BW for 2-4 weeks.

Improvement in patient's Visual acuity, Colour vision and Central fields of the affected eyes were assessed at 15 days, 1month and 3 months. Data for comparison was taken at baseline and at 3 months. The incidence of acute optic neuritis was calculated using hospital statistics from the total number of neuro-ophthalmology cases during the study period.

STATISTICAL METHODS

The information collected regarding all the selected cases was recorded in a Master Chart. The statistical analysis was done with STATA 11.1 (College Station TX USA). Using this software range, frequencies, percentages, means, standard deviations, paired t test and 'p' values were calculated. Paired t test, wilcoxon signed rank test were used to test the significance of difference between quantitative variables and [C]Cochran Q test for qualitative variables. A 'p' value less than 0.05 denotes significant relationship. The ADC and optic nerve diameter correlation to visual acuity was done by Pearson chi square test using SPSS software 17. A 'p' value less than 0.05 denotes significant relationship.

RESULTS

Study included 31 eyes of 28 patients with acute optic neuritis..

TABLE 1. INCIDENCE

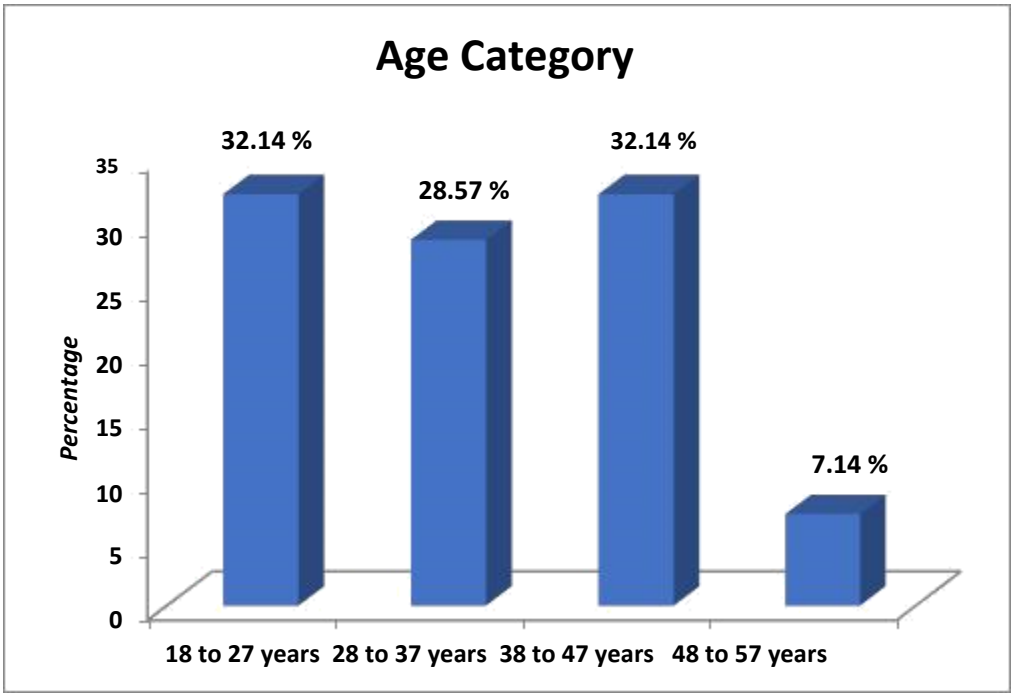
Cases	n	Incidence
Total number of Neuro-ophthalmology cases during the study period	9945	40.8 per thousand
Total number of cases with optic neuritis	406	
Total number of cases with acute optic neuritis	28	2.8 per 1000

TABLE 2: AGE

The mean age was 34 years ± 10.27(SD) and the range is to 19-55 years.

TABLE 2:AGE

AGE	**n (%)**
18 to 27 years	9 (32.14)
28 to 37 years	8 (28.57)
38 to 47 years	9 (32.14)
48 to 57 years	2 (7.14)
Total	28 (100)



In a study by Dr. Rohit saxena[6] et al in INDIA it was found that the mean age of presentation of optic neuritis was 23.5 ±10.9 (SD). In our study the mean age of presentation was 34 ±10.27(SD). Thus in our study the mean age of presentation was slightly higher.

Duration of Onset of Symptoms:

TABLE 3: Duration of symptoms

Duration of Onset of Symptoms	n	Mean (SD)	Median	Min - Max
	28	9.11 (6.95)	7	1 - 30

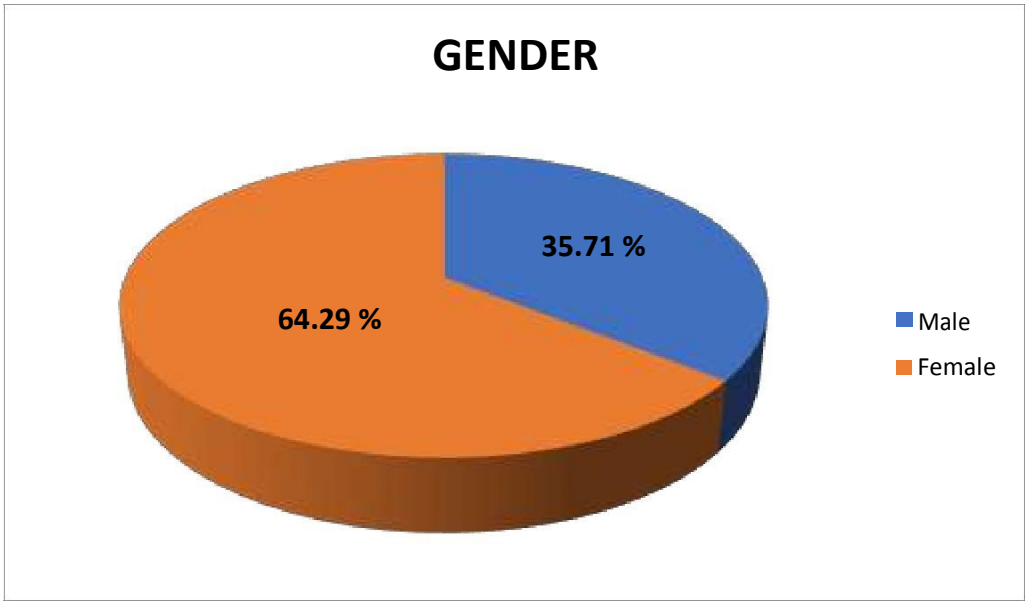
The mean duration of onset of Symptoms was 9.11 days ± 6.95 (SD).

TABLE 4: GENDER DISTRIBUTION

Of the total 28 patients 10 were males (35.7%) and 18 were females (64.3%).

Gender	n (%)
Male	10 (35.71)
Female	18 (64.29)
Total	28 (100)

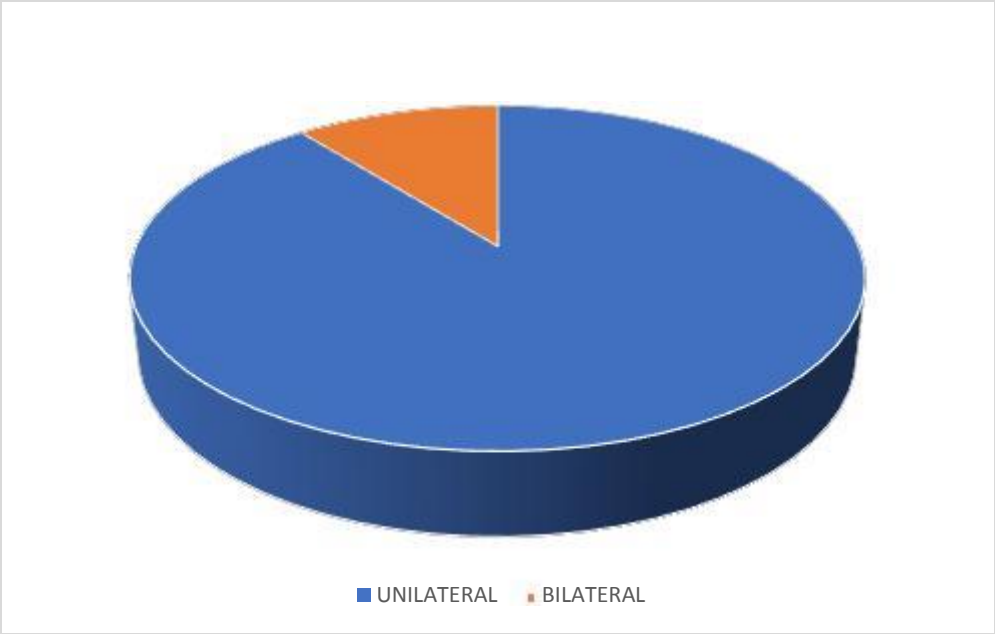
Males-35.71%;Females-64.2



In a study by Dr. Rohit saxena[6] et al in India, 70% of the patients were females. In our study 64.3% of the patients were females. Thus like other studies our study also showed female preponderence.

TABLE 5: LATERALITY

Of the 28 patients , 25 (89.3%) showed involvement of one eye while 3 (10.7%) showed bilateral involvement.



Of the 25 patients who showed unilateral involvement right eye was involved in 10 cases (40%) and left eye was involved in 15 cases (60%).

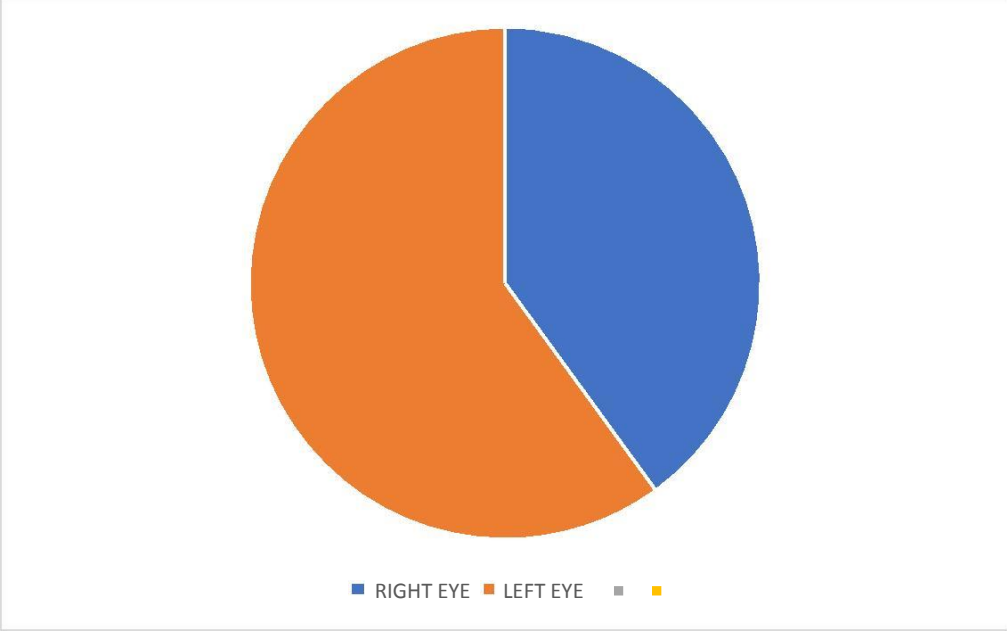
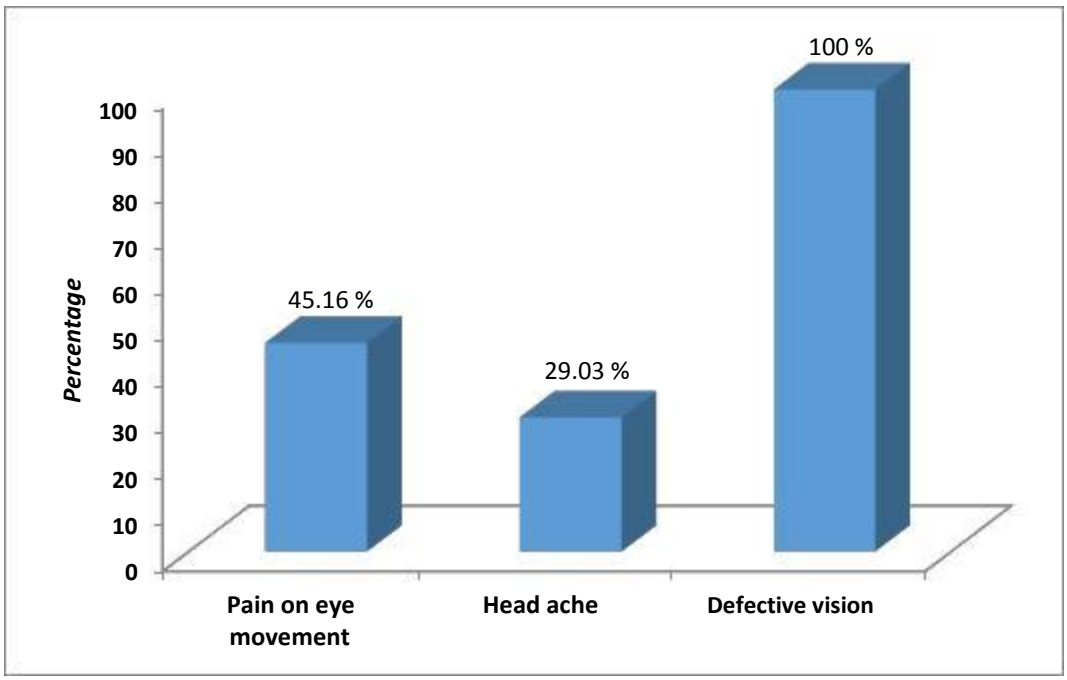


TABLE 6 : COMPLAINTS

Defective vision was the main complaint in 31 eyes (100%). Pain on eye movements was present in 14 eyes (45.2%). Headache was present in 9 out of 28 patients (28.6%).

Variables

Variables	Present n (%)	Not present n (%)	Total n (%)
Pain on Eye movement	14 (45.16)	17 (54.84)	31 (100)
Head ache	9 (29.03)	22 (70.97)	31 (100)
Defective vision	31 (100)	-	31 (100)



The most complaint was defective vision in our study.

TABLE 7: VISUAL ACUITY

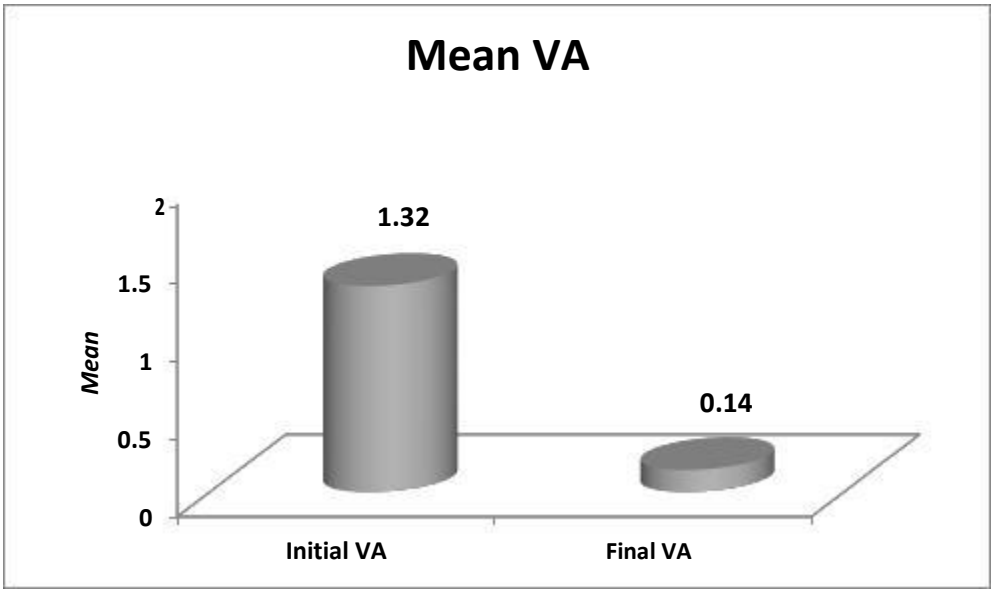
Visual acuity

VA	n	Mean (SD)	Min – Max	P value [s]
Initial VA	31	1.32 (0.86)	0.18 – 3.20	< 0.001
VA at 3 months	31	0.14 (0.24)	0.00 – 1.18	

[s] *Signed rank test*

Logmar vision

There was statistitically significant improvement in visual acuity at 3 months from the baseline.Median LogMAR at baseline was 1.32 ± 0.86 which improved to after 3 months to 0.14 ± 0.24.



By Snellen equivalent

5 (16.1%) eyes had visual acuity between 6/6-6/18 ,

11 (35.5%) eyes had visual acuity between 6/24-6/60 and

15 (48.4%) eyes had visual acuity < 6/60.

PUPIL

Normal pupillary reaction at baseline was found in 3 eyes. RAPD was found in 28 eyes.

Table: 8

Pupil	**n (%)**
Normal	3 (9.68)
RAPD	28 (90.32)
Total	31 (100)

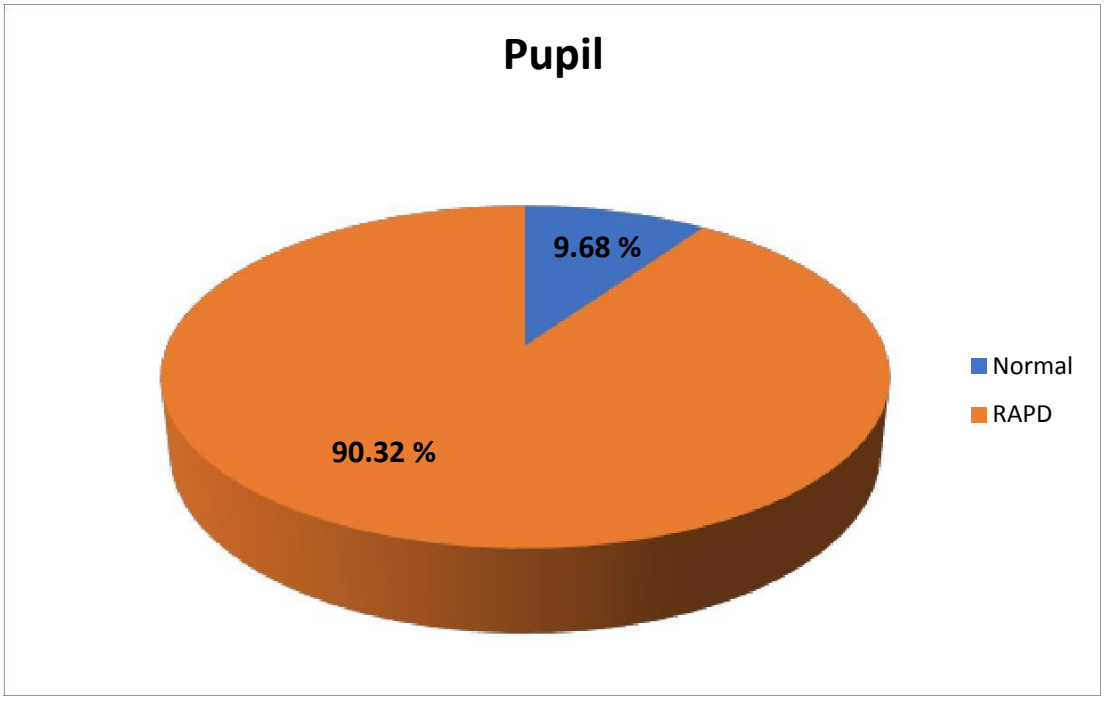
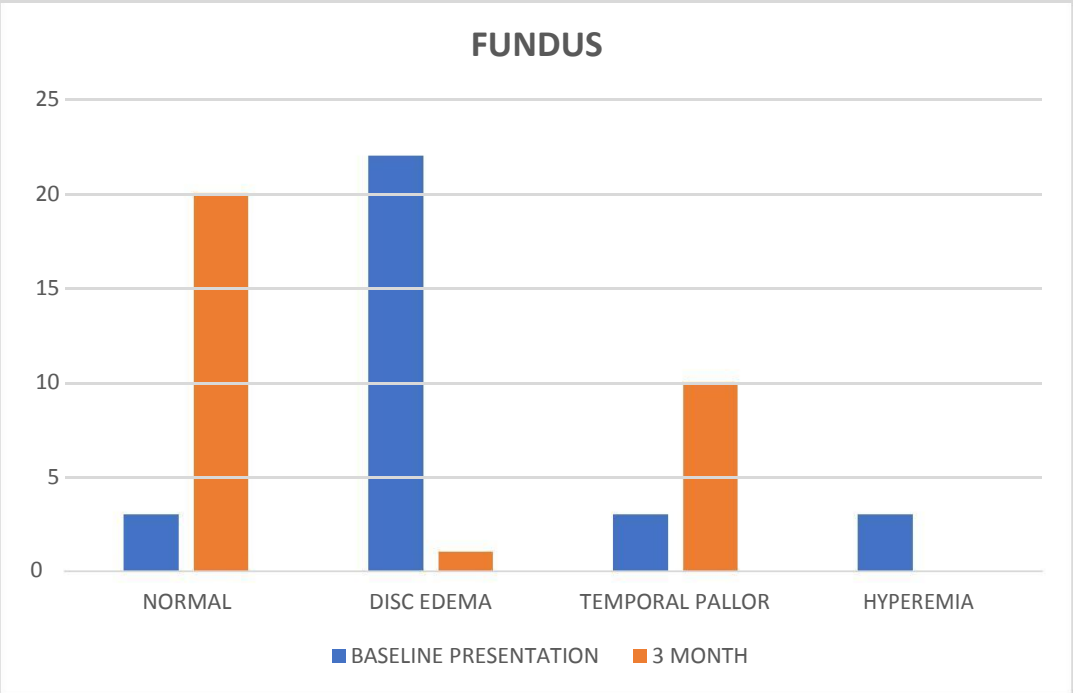


TABLE 9 : FUNDUS

FUNDUS	BASELINE PRESENTATION	3 MONTH	P value
NORMAL	3	20	<0.001
DISC EDEMA	22	1	
TEMPORAL PALLOR	3	10	
HYPEREMIA	3	0	
TOTAL	31	31	

[c]Cochran Q test



At baseline presentation optic disc was normal in 3 eyes (9.7 %), 22 eyes (70.9%) showed disc edema, 3 eyes showed temporal pallor (9.7%),

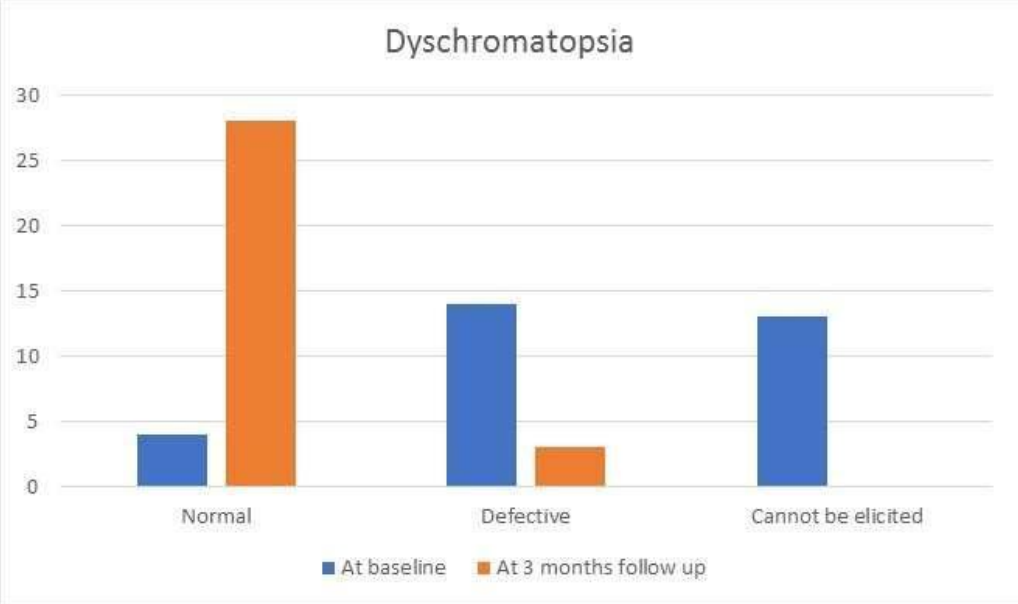
hyperemic disc was found in 3 eyes (9.7%). At 3 month follow up optic disc was normal in 20 eyes and 10 eyes showed temporal pallor .

At baseline, 31 eyes were assessed and 3 eyes were normal and others were abnormal. At 3 month follow up of 31 eyes, (none were lost to follow up), 20 eyes were normal and others were abnormal. Out of 28 eyes, 60.7% were normal at final visit which had an abnormal fundus at the first visit.

TABLE 10: DYSCHROMATOPSIA

Colour vision	**At Baseline n (%)**	**At 3rd month n (%)**	**P-value**
Normal	4 (12.90)	27(87.09)	<0.001
Defective	14 (45.16)	4(12.9)	
Not done (low vision)	13 (41.94)	-	
Total	31 (100)	31 (100)	

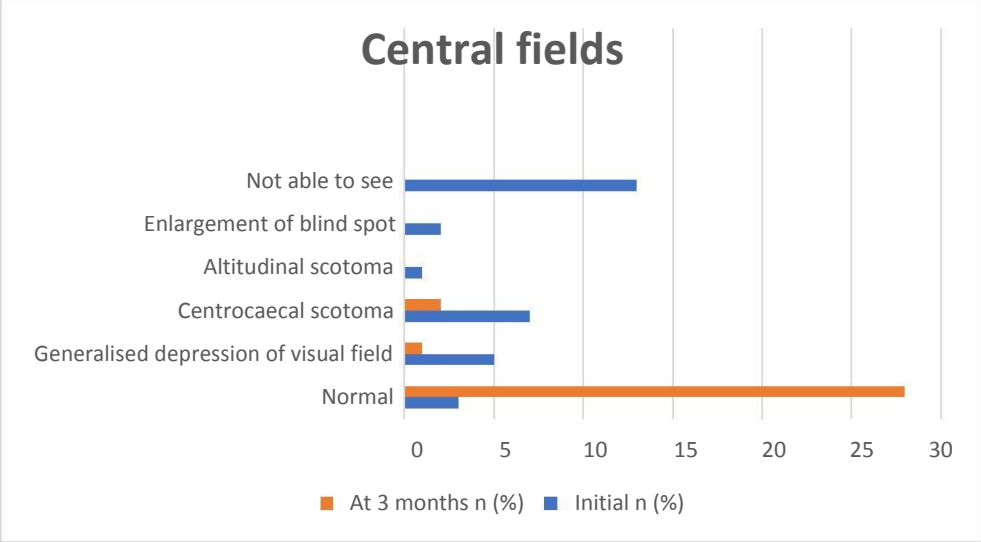
C Cochran Q test



At baseline 12.9 % (4 eyes) were normal, 45.2 % (14 eyes) were abnormal and in 13 eyes cc due to low vision colour vision could not be checked. At follow up of 1 month of 31eyes 90.3 % (28) were normal , 9.7 % (3) were abnormal. . 24 eyes (88.9%) out of 27 eyes were normal at final visit who had an abnormal at the first visit. Colour vision at 3 month follow up statistically showed significant improvement. (P value= <0.001 ,using Cochran Q test).

TABLE 11: CENTRAL FIELDS

At baseline 9.7 % (3) eyes were normal, 90.3% (28) eyes were abnormal. At follow up of 1 month of 31 eyes, 90.3% (28) were normal , 9.7 % (3) were abnormal. 89.3 % out of 25 eyes were normal at final visit which had an abnormal field at the first visit. Central fields at 3 month follow up statistically showed significant improvement. (P value <0.001, using Cochran Q test).



Central fields	Initial n (%)	At 3 months n (%)	P value
Normal	3	28	<0.001
Generalised depression of visual field	5	1	
Centrocecal scotoma	7	2	
Altitudinal scotoma	1	-	
Enlargement of blind spot	2	-	
Not able to see	13	-	
	31 (100)	31 (100)	

[c]Cochran Q test

TABLE 12: BRIGHTNESS SENSITIVITY

At baseline 9.7 % (3) were normal, 48.4 % (15) were abnormal and in 13(41.9%) eyes due to low vision the test could not be done. At follow up of 1 month of eyes 87.1 % (27) were normal , 12.9 % (4) were abnormal. 85.7 % out of 28 eyes were normal at final visit who had an abnormal sensitivity at the first visit. Brightness sensitivity at 3 month follow up statistically showed significant improvement. (P value = <0.001, using [c]Cochran Q test).

Brightness sensitivity	At baseline	At 3 months follow up	P value
Normal	3 (9.7%)	27(87.1%)	<0.001
Reduced	15(48.4%)	4(12.9%)	
Cannot do	13 41.9%)	0	
Total	31(100%)	31(100%)	

[c]Cochran Q test

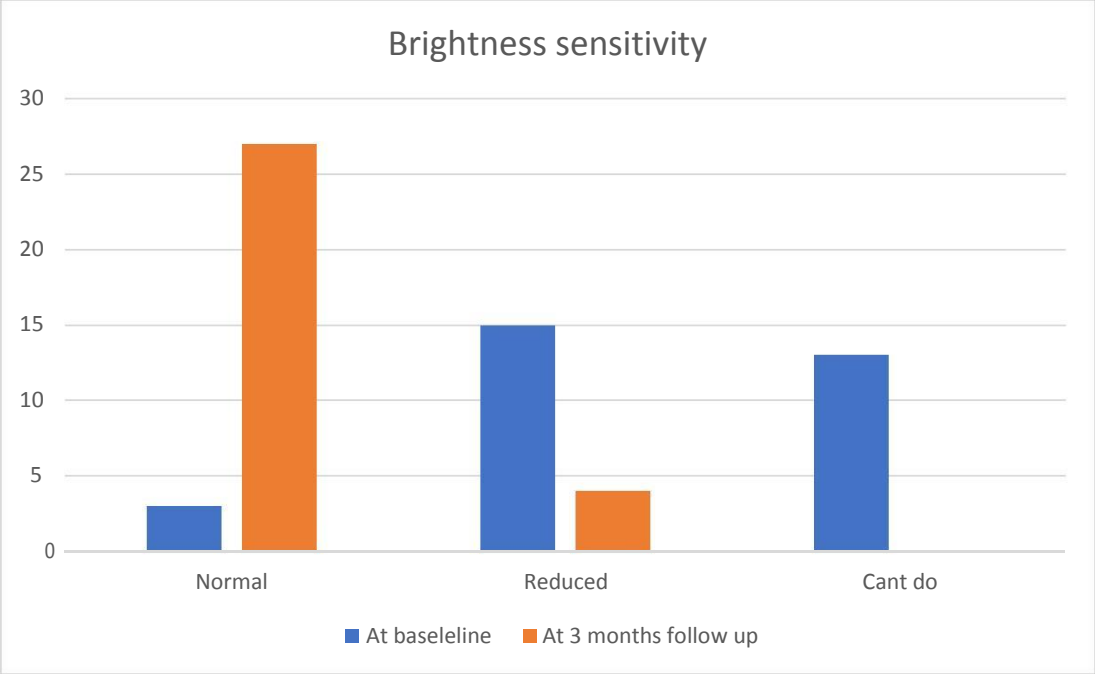


TABLE 13: RED DESATURATION

At baseline 9.7 % (3) were normal , 48.4 % (15) were abnormal and in 13(41.9%) eyes due to low vision the test could not be done. At follow up of 1 month of eyes 87.1 % (27) were normal , 12.9 % (4) were abnormal. 85.7 % out of 28 eyes were normal at final visit who had an abnormal red desaturation at the first visit. Red desaturation at 3 month follow up statistically showed significant improvement. (P value <0.001, using Cochran Q test).

Red colour desaturation	At baseline in the affected nerve	At 3 months follow up	P value
Normal	3 (9.7%)	27(87.1%)	<0.001
Reduced	15 (48.4%)	4(12.9%)	
Can't do	13 (41.9%)	0	
Total	31(100%)	31(100%)	

Cochran Q test

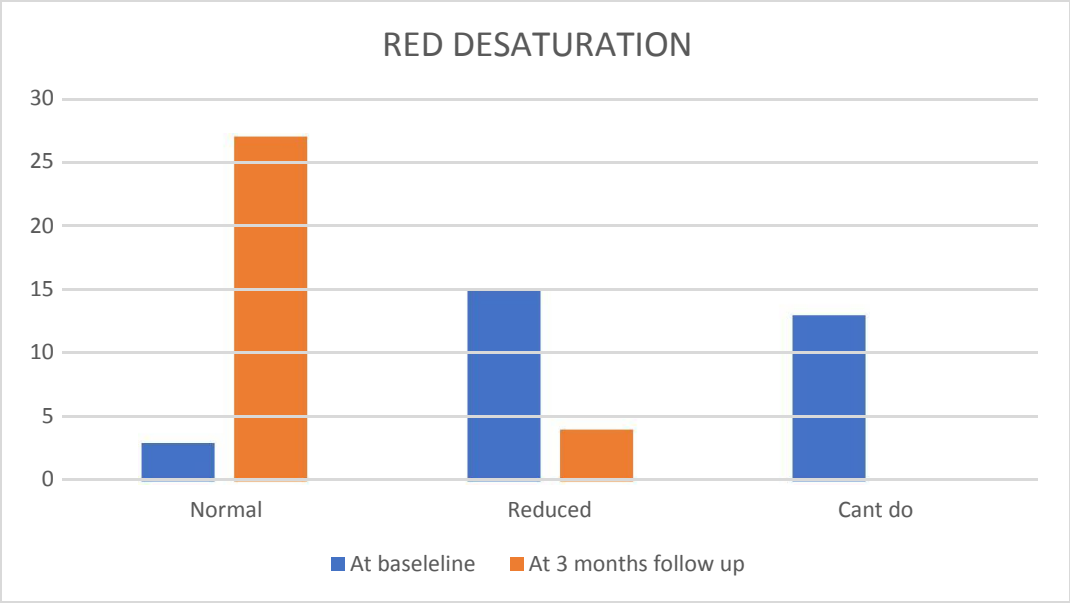


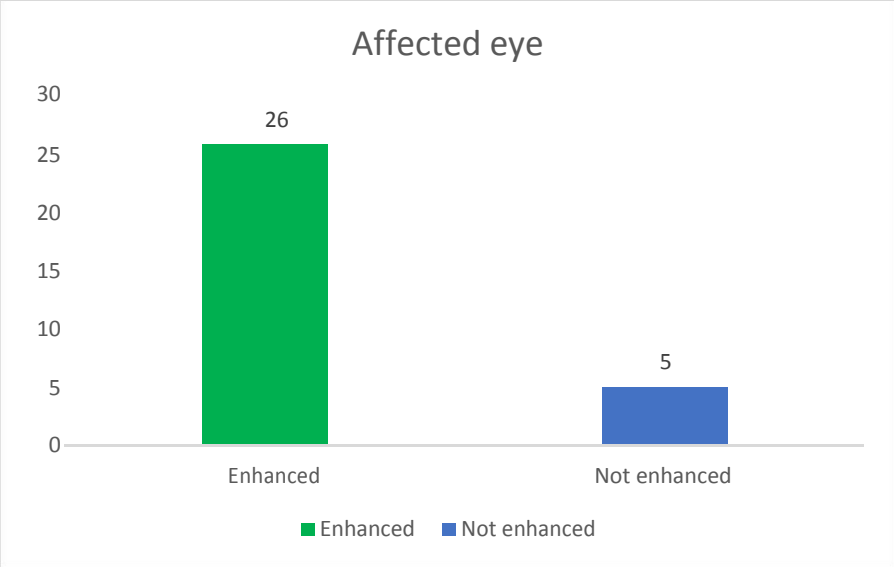
TABLE 14 : DIFFUSION RESTRICTION

In our study 26 (83.9%) eyes with acute optic neuritis showed diffusion restriction in DWI.

Diffusion restriction in DWI MRI	Affected eye
Restricted	26
not restircted	5

TABLE 15: CONTRAST ENHANCEMENT

Contrast enhancement in DWI MRI	Affected eye
Enhanced	26
Not enhanced	5



In our study 26 eyes with acute optic neuritis showed contrast enhancement in DWI.

TABLE 16 : APPARENT DIFFUSION COEFFICIENT

Comparison between ADC of optic nerve in affected eye and non-affected eye:

Apparent Diffusion Coefficient	**n**	**Mean (SD) × 10^{-6} mm^2/sec**	**Median**	**Min – Max**	**P value***
ADC in affected eye	31	1009.76 (299.90)	893	690 – 1700	0.002
ADC in non-affected eye	25	1206.51 (425.64)	1126	119 – 2197	

*Paired t test

The above P value is 0.002 (< 0.05) shows that there is a significant statistical difference between ADC of the affected and non-affected eye.

Crosstab

LATERALITY				ADC INCREASED	ADC DECREASED	Total
RIGHT EYE	BCVA at baseline	NO PL	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	7.7%	7.7%
		HM	Count	0	2	2
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	15.4%	15.4%
		1/60	Count	0	2	2
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	15.4%	15.4%
		2/60	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	7.7%	7.7%
		3/60	Count	1	0	1
			% within BCVA at baseline	100.0%	.0%	100.0%
			% of Total	7.7%	.0%	7.7%
		5/60	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	7.7%	7.7%
		6/36	Count	0	3	3
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	23.1%	23.1%
		6/24	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	7.7%	7.7%
		6/18	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	7.7%	7.7%
	Total		Count	1	12	13
			% within BCVA at baseline	7.7%	92.3%	100.0%
			% of Total	7.7%	92.3%	100.0%
LEFT EYE	BCVA at baseline	PL	Count	1	1	2
			% within BCVA at baseline	50.0%	50.0%	100.0%
			% of Total	5.6%	5.6%	11.1%
		HM	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	5.6%	5.6%
		1/60	Count	1	1	2
			% within BCVA at baseline	50.0%	50.0%	100.0%
			% of Total	5.6%	5.6%	11.1%
		2/60	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	5.6%	5.6%
		5/60	Count	0	1	1
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	5.6%	5.6%
		6/60	Count	0	3	3
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	16.7%	16.7%
		6/36	Count	0	5	5
			% within BCVA at baseline	.0%	100.0%	100.0%
			% of Total	.0%	27.8%	27.8%
		6/18	Count	1	0	1
			% within BCVA at baseline	100.0%	.0%	100.0%
			% of Total	5.6%	.0%	5.6%
		6/12	Count	1	1	2
			% within BCVA at baseline	50.0%	50.0%	100.0%
			% of Total	5.6%	5.6%	11.1%
	Total		Count	4	14	18
			% within BCVA at baseline	22.2%	77.8%	100.0%
			% of Total	22.2%	77.8%	100.0%

Chi-Square Tests

LATERALITY		Value	df	Asymp. Sig. (2-s ided)
RIGHT EYE	Pears on Chi-Square	13.000[a]	8	.112
	Likelihood Ratio	7.051	8	.531
	Linear-by-Linear Ass ociation	.039	1	.843
	N of Valid Cas es	13		
LEFT EYE	Pears on Chi-Square	9.321[b]	8	.316
	Likelihood Ratio	10.752	8	.216
	Linear-by-Linear Ass ociation	.015	1	.904
	N of Valid Cas es	18		

a. 18 cells (100.0%) have expected count les s than 5. The minimum expected count is .08.

b. 18 cells (100.0%) have expected count les s than 5. The minimum expected count is .22.

Crosstab

			ADC		
			INCREASED	*DECREASED*	*Total*
BCVA AT 3 MONTHS	*4/60*	*Count*	*1*	*0*	*1*
		% within BCVA AT 3 MONTHS	*100.0%*	*.0%*	*100.0%*
		% of Total	*3.2%*	*.0%*	*3.2%*
	6/12	*Count*	*2*	*2*	*4*
		% within BCVA AT 3 MONTHS	*50.0%*	*50.0%*	*100.0%*
		% of Total	*6.5%*	*6.5%*	*12.9%*
	6/9	*Count*	*2*	*7*	*9*
		% within BCVA AT 3 MONTHS	*22.2%*	*77.8%*	*100.0%*
		% of Total	*6.5%*	*22.6%*	*29.0%*
	6/6	*Count*	*0*	*17*	*17*
		% within BCVA AT 3 MONTHS	*.0%*	*100.0%*	*100.0%*
		% of Total	*.0%*	*54.8%*	*54.8%*
Total		*Count*	*5*	*26*	*31*
		% within BCVA AT 3 MONTHS	*16.1%*	*83.9%*	*100.0%*
		% of Total	*16.1%*	*83.9%*	*100.0%*

ADC was decreased in 26 eyes and was associated with better visual outcome at 3 months compared to 5 eyes with increased ADC at baseline.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-s ided)
Pears on Chi-Square	12.109[a]	3	.007
Likelihood Ratio	12.312	3	.006
Linear-by-Linear Ass ociation	10.325	1	.001
N of Valid Cas es	31		

a. 6 cells (75.0%) have expected count less than 5. The minimum expected count is .16.

Analysis by Pearson chisquare test shows that decrease in apparent diffusion coefficient in DWI was associated with good visual outcome and was statistically significant.

TABLE 17 : MEAN DIAMETER OF THE OPTIC NERVE

Mean Diameter of Optic nerve	**n**	**Mean (SD)**	**Median**	**Min – Max**	**P value***
MRI affected eye	31	4.42 (0.99)	4.5	2 – 6.2	<0.002
MRI non-affected eye	25	3.60 (1.03)	3.9	1.89 – 5.9	

*Paired t test

The p-value (0.002 < 0.05) shows that there is a significant difference between optic nerve diameter of the affected and unaffected

nerve. The optic nerves of 27 eyes showed increased diameter compared to controls. 4 eyes showed decrease in optic nerve diameter. Analysis by Pearson chisquare test shows that increase in optic nerve diameter is associated with better visual outcome and is statistically significant.

Crosstab

			ON DIA		
			INCREASED	DECREASED	Total
BCVA at bas eline	NO PL	Count	1	0	1
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	3.2%	.0%	3.2%
	PL	Count	1	1	2
		% within BCVA at bas eline	50.0%	50.0%	100.0%
		% of Total	3.2%	3.2%	6.5%
	HM	Count	3	0	3
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	9.7%	.0%	9.7%
	1/60	Count	3	1	4
		% within BCVA at bas eline	75.0%	25.0%	100.0%
		% of Total	9.7%	3.2%	12.9%
	2/60	Count	2	0	2
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	6.5%	.0%	6.5%
	3/60	Count	1	0	1
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	3.2%	.0%	3.2%
	5/60	Count	2	0	2
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	6.5%	.0%	6.5%
	6/60	Count	3	0	3
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	9.7%	.0%	9.7%
	6/36	Count	8	0	8
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	25.8%	.0%	25.8%
	6/24	Count	0	1	1
		% within BCVA at bas eline	.0%	100.0%	100.0%
		% of Total	.0%	3.2%	3.2%
	6/18	Count	1	1	2
		% within BCVA at bas eline	50.0%	50.0%	100.0%
		% of Total	3.2%	3.2%	6.5%
	6/12	Count	2	0	2
		% within BCVA at bas eline	100.0%	.0%	100.0%
		% of Total	6.5%	.0%	6.5%
Total		Count	27	4	31
		% within BCVA at bas eline	87.1%	12.9%	100.0%
		% of Total	87.1%	12.9%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-s ided)
Pears on Chi-Square	15.428[a]	11	.164
Likelihood Ratio	13.798	11	.244
Linear-by-Linear Ass ociation	.010	1	.921
N of Valid Cas es	31		

a. 23 cells (95.8%) have expected count les s than 5. The minimum expected count is .13.

Patients in our study were treated with iv methylprenisolone and oral corticosteroids as suggested in ONTT .

Crosstab

			ON DIA		
			INCREASED	DECREASED	Total
BCVA AT 3 MONTHS	4/60	Count	0	1	1
		% within BCVA AT 3 MONTHS	.0%	100.0%	100.0%
		% of Total	.0%	3.2%	3.2%
	6/12	Count	2	2	4
		% within BCVA AT 3 MONTHS	50.0%	50.0%	100.0%
		% of Total	6.5%	6.5%	12.9%
	6/9	Count	8	1	9
		% within BCVA AT 3 MONTHS	88.9%	11.1%	100.0%
		% of Total	25.8%	3.2%	29.0%
	6/6	Count	17	0	17
		% within BCVA AT 3 MONTHS	100.0%	.0%	100.0%
		% of Total	54.8%	.0%	54.8%
Total		Count	27	4	31
		% within BCVA AT 3 MONTHS	87.1%	12.9%	100.0%
		% of Total	87.1%	12.9%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-s ided)
Pears on Chi-Square	14.192[a]	3	.003
Likelihood Ratio	12.018	3	.007
Linear-by-Linear Ass ociation	11.951	1	.001
N of Valid Cas es	31		

a. 6 cells (75.0%) have expected count less than 5. The minimum expected count is .13.

DISCUSSION

Jain et al had made a report that in India the clinical profile of patients with Optic neuritis was not similar to that of Western population.

Our prospective study included 28 patients. Mean age was 34 years. In our study out of 28 patients, 18 were females (64 %) and 10 were males (36 %). Our study was similar to *ONTT* where 77% of those affected were females. This female preponderence was also found in a similar study by *Lim*[12] *et al.*

The most common complaints in our study were defective vision (100%), pain on eye movement (45.16%) and headache (29 %). Our study was similar to a study by *Ismail Shatriah et al* . In their study defective vision was found in 77.3% and pain on eye movemnt is seen in 31.7%.

The average time duration of presentation was 9.11 days ± 6.95 (SD).

In our study, median LogMAR at baseline was 1.32 ± 0.86 which improved to after 3 months to 0.14 ± 0.24.

By snellen chart , 15 (48.4%) eyes had visual acuity < 6/60.

Rohit Saxena[6] *et al* showed in his study a similar improvement in visual acuity from baseline logMAR of 1.6 ± 0.8 to 0.2 ± 0.6 after treatment .

In our study pupillary reaction was normal in 3 eyes, RAPD was found in 28 eyes.

Fundus examination showed disc edema or papillitis (70.9%) eyes, hyperemia (9.7 %) eyes, temporal pallor (9.7 %) eyes and normal fundus in (9.7%) eyes. Our study was similar to the study by *Rohit Saxena*[6] *et al* where papillitis was the most common fundus finding in optic neuritis. In his study papillitis was found in 53.5% of patients, whereas in our study papillitis was found in 70.9% eyes.

In our study colour vision was normal at baseline in 4 (12.9 %) eyes, defective in 14 (45.2 %) eyes and could not be done in 13 eyes (41.9 %) eyes because of low vision. At three months follow up colour vision was normal in 28 eyes (90.3%). This was statistically significant with a probability value <0.001%.

Central fields were normal in 3 (9.7%) eyes, defective in 28 (90.3 %) eyes. In 13 eyes central fields could not be done as visual acuity was very low. Central fields showed centrocecal scotoma in 18 eyes (38.9%).

The sequence of events which occur at histopathological level in untreated acute optic neuritis are inflammation, demyelination , followed by gliosis and optic atrophy.The chances of recovery depends on the

extent and severity of the insult. DWI aids in evaluating the extent of damage and thereby the visual outcome also.

Zareen Fathima et al in a study on DWI in optic neuritis concluded that ADC values were significantly decreased in patients with acute optic neuritis. In our study there was a remarkable difference between the optic nerve diameters measured by imaging of the affected and unaffected eye

. The diameter was increased in most of the affected optic nerves. On DWI all the 31 affected eyes showed hyperintensity in the intraorbital, and intracanalicular porrtions of the optic nerve. The mean ADC values of the affected eyes at baseline was 1009.76 ± 299.90 (SD) × 10^{-6} mm^2/sec, compared to the mean ADC values of the unaffected eyes,

1206.51 ± 425.64× 10^{-6} mm^2/sec. There was statistically significant difference between the ADC values in eyes with acute optic neuritis and their controls (unaffected eyes) with p value of 0.002 respectively. ADC values were decreased in 26 eyes, and increased in 5 eyes.The visual acuity of the 26 eyes with decreased ADC 17 had visual acuity of 6/6(65.4%),7 had 6/9 (27%) at 3 months, except two who had visual acuity of 6/12 (7.6%). Out of the 5 eyes which showed increased ADC 2 had visual acuity of 6/9(40%), 2 had visual acuity of 6/12 (40%) and one had visual acuity of 4/60 (20%). Optic nerve diameter was increased in 27 eyes in our study. 4 eyes which showed reduced diameter compared to the

control eyes. Two eyes had 6/12 vision, 1 eye had 6/9 vision and 1 eye had 4/60 vision. The eye with 4/60 vision had reduced optic nerve diameter, enhanced contrast enhancement and increased ADC. The eye with 6/12 vision at 3 months follow up had reduced ADC and reduced optic nerve diameter at baseline presentation. Though specificity was not 100%, DWI was found to have high specifity in identifying acute optic neuritis in our study similar to previous studies done by *Hickman*[22] *SJ et al, Barker GJ et al Kupersmith*[7] *et al* .

LIMITATION

The sample size was small in our study.

This study was done in our institution only. If many centres are included in the study, the number of patients will be more, which will increase the yield and results will be more accurate for our population.

Only patients who were able to do MRI were included in our study. Thus 15 patients who had acute optic neuritis and were not able to afford were not included in our study.

Post treatment MRI could not be done due to financial constraints of the patients.

CONCLUSION

- In our study many were female (64 %).
- The mean age group was 34 years.
- The most common presenting complaint was defective vision.
- 15 (48.4%) eyes had visual acuity < 6/60.
- RAPD was found in 28 eyes.
- Colour vision was impaired in 3 (9.7%) of patients, central fields were abnormal in 3(9.7 %) of patients at 3 months follow up.
- In DWI, Diffusion was restricted in 26 eyes (83.9 %) with acute optic neuritis;
- ADC was statistically significantly reduced, Optic nerve diameter was increased and contrast was enhanced in patients with acute optic neuritis in 26 eyes which was statistically significantly associated with good visual outcome on follow up.
- Diffusion weighted imaging adds value in assessing the level of damage and in predicting the visual outcome in acute optic neuritis.

ANNEXURES

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DIFFUSION WEIGHTED IMAGING AS A PREDICTOR OF VISUAL OUTCOME IN ACUTE OPTIC NEURITIS

Name _____ Date: _____

Age MR NO: _____

Gender M-Male, F-Female Study Sample NO:

Chief complaints

Duration of symptoms

Laterality	1.RE	
	2.LE	
Defective vision	RE	
	LE	
Pain on eye movements	RE	
	LE	
Headache	RE	
	LE	

OCULAR EXAMINATION

	RE	LE
BCVA		

NO PL-1, PL-2, HM-3, 1/60-4, 2/60-5, 3/60-6, 4/60-7, 5/60-8, 6/60-9, 6/36-10,6/24-11, 6/18-12, 6/12-13, 6/9-14, 6/6-15

PUPIL

REFLEX	RE	LE
DIRECT		
INDIRECT		

EOM 1. FULL
2.RESTRICTED

CLINICAL INVESTIGATION

	RE	LE
Colour vision		
Red color desaturation		
Brightness Sensitivity		

FUNDUS

	RE	LE
Normal		
Disc Edema		
Hyperemia		
Temporal pallor		
Primary optic atropy		

CENTRAL FIELDS	CODE	RE	LE
NORMAL	0		
GENERALISED DEPRESSION OF THE VISUAL FIELDS	1		
CENTROCECAL SCOTOMA	2		
ALTITUDINAL SCOTOMA	3		
HEMIANOPIA	4		
ENLARGEMENT OF BLIND SPOT	5		
NOT ABLE TO SEE	6		

NEUROLOGICAL EXAMINATION

Higher function

Cranial nerves

DWI	RE	LE
OPTIC NERVE DIAMETER		
DIFFUSION RESTRICTION		
CONTRAST ENHANCEMENT		
ADC		

TREATMENT

Medical 1.IV Steroids

2.Oral steroids

VISUAL ACUITY

VA	IMMEDIATE		3 MONTHS	
	RE	LE	RE	LE
DATE				
UCVA				
BCVA				

COLOUR VISION

	IMMEDIATE		3 MONTHS	
	RE	LE	RE	LE
DATE				
COLOUR VISION				

BRIGHTNESS SENSITIVITY

	IMMEDIATE		3 MONTHS	
	RE	LE	RE	LE
DATE				
BRIGHTNESS SENSITIVITY				

RED COLOUR DESATURATION

	IMMEDIATE		3 MONTHS	
	RE	LE	RE	LE
DATE				
RED COLOUR DESATURATION				

FUNDUS

FUNDUS	IMMEDIATE		3 MONTHS	
	RE	LE	RE	LE
DATE				
NORMAL				
DISC EDEMA				
HYPEREMIA				
TEMPORAL PALLOR				
PRIMARY OPTIC ATROPHY				

CENTRAL FIELDS

CENTRAL FIELDS	CODE	Baseline		At 3 months	
		RE	LE	RE	LE
NORMAL	0				
GENERALISED DEPRESSION OF THE VISUAL FIELDS	1				
CENTROCECAL SCOTOMA	2				
ALTITUDINAL SCOTOMA	3				
HEMIANOPIA	4				
ENLARGEMENT OF BLIND SPOT	5				
NOT ABLE TO SEE	6				

INFORMED CONSENT FORM

Study Title- Diffusion weighted imaging as a predictor of visual outcome in acute optic neuritis

Protocol Number:

Subject's Name: _____Subject's Initials: _____

Subject ID No: _____

Date of Birth / Age: _____

		Please put initial in the box (Subject)
(i)	I confirm that I have understood the information about the study, procedure and treatments for the above study and have had the opportunity to ask questions and I received satisfactory answers to all of my questions. I have been given a copy for the informed consent form to take home	[ ]
(ii)	I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason without my medical care of legal rights being affected.	[ ]
(iii)	I understand that the Investigator of the study has to access my health records for the research purpose. However, I understand that my identity will not be revealed or any information released to third parties or published	[ ]

(iv)	I agree not to restrict the use of any data or results that arise from this study, provided such a use is only for scientific purpose(s)	[ ]
(v)	I agree to take part in the above study	[ ]

Signature (or Thumb impression) of the Subject _____

Date:_____/_____/_____

Subject's Name _____

Signature of Investigator

_____ Date:_____

Investigator's Name _____

Signature of Witness _____ Date:_____

Name of witness _____

NAME	AGE	GENDER	MR NO	DURATION OFSYMPTOMSINDAYS	LATERALITY	BCVA	logMAR acuity	DEFECTIVE VISION	PAIN ON EYEMOVEMENT	HEADACHE	PUPIL	EOM	COLOUR VISION	RED COLOURDESATURATION	BRIGHTNESSSENSITIVITY	NEUROLOGICALEXAMINATION	DIFFUSIONRESTRICTION	CONTRASTENHANCEMENT	ON DIAMETER-RE	ON DIAMETER-LE	ADC-RE	ADC-LE	FUNDUS	CENTRAL FIELDS	BCVA AT 3 MONTHS	logMAR acuity AT 3MONTHS	FUNDUS AT 3MONTHS	CF AT 3 MONTHS	COLOUR VISION at 3MONTHS	BRIGHTNESSSENSITIVITYAT 3MONTHS	RED COLOURDESATURATION AT3MONTHS
SHOBHA M	33	2	P4336808	14	1	10	0.8	1	1	1	2	1	1	1	1	0	1	1	4.1	3	690	700	2	2	14	0.2	4	0	0	0	0
MASEEHA HASLIN	26	2	P4392810	7	2	12	0.3	1	0	0	1	1	0	1	1	0	2	22	5	3	119	744	2	5	7	1.2	4	1	1	1	1
SANGEETHA RAJAN	21	2	P4408209	7	1	10	0.8	1	0	1	1	1	1	1	1	0	1	1	3.3		893		2	5	15	0	1	0	0	0	0
		2	P4408209	7	2	8	1.1	1	0	1	1	1	1	1	1	0	1	1		4.4		793	2	1	15	0	1	0	0	0	0
MUTHU MEENA	26	2	P4406275	3	1	3	2	1	1	0	2	1	2	2	2	0	1	1	3.6	2.5	747	1096	2	6	15	0	1	0	0	0	0
VEERAMANI K	28	1	P4332498	21	2	4	1.8	1	0	0	2	1	2	2	2	0	2	2	4.3	4.1	732	871	1	6	14	0.2	4	0	0	0	0
VISHNU KR	19	1	P4350318	2	2	2	3	1	1	0	2	1	2	2	2	0	1	1	3.6	5.1	1238	933	1	6	14	0.2	4	0	0	0	0
UMA RANI	30	2	P4047366	4	2	2	3	1	0	0	2	1	2	2	2	0	2	2	4.2	2	1085	1700	2	6	13	0.3	4	0	0	0	0
LAKSHMANA N P	21	2	P4368711	7	2	3	2	1	0	0	2	1	2	2	2	0	1	1	2.7	6.2	1181	1071	2	6	15	0	1	0	0	0	0
NAGAMMAL	55	2	P4326734	7	2	9	1	1	0	0	2	1	1	1	1	0	1	1	5.9	6.2	1730	1655	2	1	15	0	1	0	0	0	0
YUVRAJ PADMARAJ PAWAR	37	1	P4402898	30	2	4	1.8	1	1	0	2	1	2	2	2	0	1	1	2.3	5	1108	800	3	6	13	0.6	4	2	1	1	1
MURUGESH P	40	2	P4403492	10	1	8	1.1	1	0	0	2	1	1	1	1	0	1	1	5	3.1	872	1115	2	1	15	0	1	0	0	0	0
DHINESH KUMAR	29	1	P4358266	2	1	11	0.5	1	0	1	2	1	1	1	1	0	1	1	3.8	4.2	1398	2017	2	0	13	0.3	1	0	0	0	0
ANGAMMAL	53	2	P4290050	15	2	10	0.8	1	1	1	2	1	1	1	1	0	1	1	2	2.71	1703	1343	2	2	14	0.2	1	0	1	1	1
KAHAMIR NIGAR	42	2	P4570075	8	1	1	3	1	1	0	2	1	2	2	2	0	1	1	4.5	2.1	839.6	1361	2	6	15	0	1	0	0	0	0
SHIJON K	25	1	P4358952	7	2	10	0.8	1	1	0	2	1	1	1	1	0	1	1	4.4	5.5	1224	967	2	3	15	0	1	0	0	0	0
SAROJA P	41	2	P4400391	3	2	9	1	1	0	1	2	1	1	1	1	0	1	1	3	5.7	1201	1063	3	1	15	0	1	0	0	0	0
PRIYANKA S	20	2	P4324903	1	1	4	1.8	1	1	0	2	1	2	2	2	0	1	1	5		868		2	6	14	0.2	4	0	0	0	0
			P4324903	1	2	10	0.8	1	1	0	2	1	1	1	1	0	1	1		4.5		707	4	2	14	0.2	4	0	0	0	0
KARPAM M	42	2	P4337568	8	2	5	1.5	1	0	0	2	1	2	2	2	0	1	1	2.8	3.5	1072	743	2	6	14	0.2	1	0	0	0	0
KALA K	45	2	P4313056	4	1	3	2	1	1	0	2	1	2	2	2	0	1	1	4	2	1481	1639	4	6	15	0	4	0	0	0	0
GOVINDHARAJAN P	37	1	P4395677	7	1	4	1.8	1	1	0	2	1	2	2	2	0	1	1	4.56	1.89	742	1265	4	6	15	0	4	0	0	0	0
GANDHIMATHI	30	1	P4301524	15	1	5	1.5	1	0	0	2	1	2	2	2	0	1	1	3.3	2.5	1139	1727	3	6	15	0	1	0	0	0	0
KARTHICK KUMAR	39	1	P4361O23	14	1	6	1.3	1	1	1	2	1	2	2	2	0	2	2	4.42		1126		2	6	13	0.3	2	2	1	1	1
			P4361O23	14	2	13	0.2	1	1		2	1	0	0	0	0	2	2		3.78		954	2	2	14	0.2	1	0	0	0	0
NAVAKODI	37	1	P4229981	25	2	13	0.2	1	0	0	2	1	0	0	0	0	1	1	4.2	4.7	2197	1698	1	0	15	0	1	0	0	0	0
FAREEDA BEGUM	44	2	P4291468	5	1	10	0.8	1	1	0	2	1	1	1	1	0	1	1	4.3	3.9	872	1539	2	2	15	0	1	0	0	0	0
BENASIR	24	2	P4392853	8	1	12	0.3	1	0	1	2	1	0	0	0	0	1	1	5	4	1021	1650	2	0	15	0	1	0	0	0	0
SHALINI	21	2	P4293476	6	2	10	0.8	1	0	0	2	1	1	1	1	0	1	1	4.2	5.1	1100	802	2	2	15	0	1	0	0	0	0
PANDEESWARI	47	2	P4378773	8	2	9	1	1	0	0	2	1	1	1	1	0	1	1	4.5	5.5	1250	1024	2	1	14	0.2	1	0	0	0	0
RAJA	42	1	P4329560	7	2	10	0.8	1	0	0	2	1	1	1	1	0	1	1	4	5.3	1012	746	2	2	15	0	1	0	0	0	0

CODING

AGE		
GENDER		
	MALE	1
	FEMALE	2
DURATION OF SYMPTOMS		
LATERALITY		
	RE	1
	LE	2
BCVA	logMAR	
	NO PL 3	1
	PL 3	2
	HM 2	3
	1/60 1.8	4
	2/60 1.5	5
	3/60 1.3	6
	4/60 1.2	7
	5/60 1.1	8
	6/60 1	9
	6/36 0.8	10
	6/24 0.6	11
	6/18 0.5	12
	6/12 0.3	13
	6/9 0.2	14
	6/6 0.0	15

SYMPTOMS:		
DEFECTIVE VISION		
	PRESENT	1
	NOT PRESENT	0
PAIN ON EYE MOVEMENT		
	PRESENT	1
	NOT PRESENT	0
HEADACHE		
	PRESENT	1
	NOT PRESENT	0
PUPIL: REACTION TO LIGHT		
	NORMAL	1
	RAPD	2
EXTRAOCULAR MOVEMENTS		
	FULL	1
	RESTRICTED	2
COLOUR VISION		
	NORMAL	0
	DEFECTIVE	1
	CANT DO	2
RED DESATURTION		
	NORMAL	0
	DEFECTIVE	1

	CANT DO	2
BRIGHTNESS SENSITIVITY		
	NORMAL	0
	REDUCED	1
	CANT DO	2
NEUROLOGICAL EXAMINATION		
	NORMAL	0
	CRANIAL NERVE INVOLVEMENT	1
DWI-DIFFUSION RESTRICTION		
	RESTRICTED	1
	NOT RESTRICTED	2
CONTRAST ENHANCEMENT		
	ENHANCED	1
	NOT ENHANCED	2
OPTIC NERVE DIAMETER		
APPARENT DIFFUSION COEFFICIENT		
	RE	
	LE	
FUNDUS		

	NORMAL	1
	DISC EDEMA	2
	HYPEREMIA	3
	TEMPORAL PALLOR	4
	PRIMARY OPTIC ATROPHY	5
CENTRAL FIELDS		
	NORMAL	0
	GENERALISED DEPRESSION OF THE VISUAL FIELDS	1
	CENTROCECAL SCOTOMA	2
	ALTITUDINAL SCOTOMA	3
	HEMIANOPIA	4
	ENLARGEMENT OF BLIND SPOT	5
	NOT ABLE TO SEE	6
OPTIC NERVE (ON) DIAMETER		
RE-RIGHT EYE		
LE-LEFT EYE		

ABBREVIATIONS

SLE-Systemic Lupus erythematosus

CNS- Central nervous system MRI-

Magentic Resonance Imaging MS-

Multiple Sclerosis

RAPD-Relative afferent pupillary

defect HM-Hand movements

PL-Perception of light CBC-

Complete blood count

FTA-ABS --Fluorescent treponemal antibody absorption test

CSF-Cerebrospinal fluid

PCR-Polymerase chain reaction

USG-Ultrasonogram

SD-OCT- Spectral domain optical coherence

tomography TR-TIME TO REPEAT

TE- TIME TO ECHO LM-

Longitudinal magnetization TM-

Transverse magnetization PD-

PROTON DENSITY IMAGE MRV-

Magnetic resonance venography

MRI-Magnetic resonance imaging

MRA- Magnetic resonance angiography

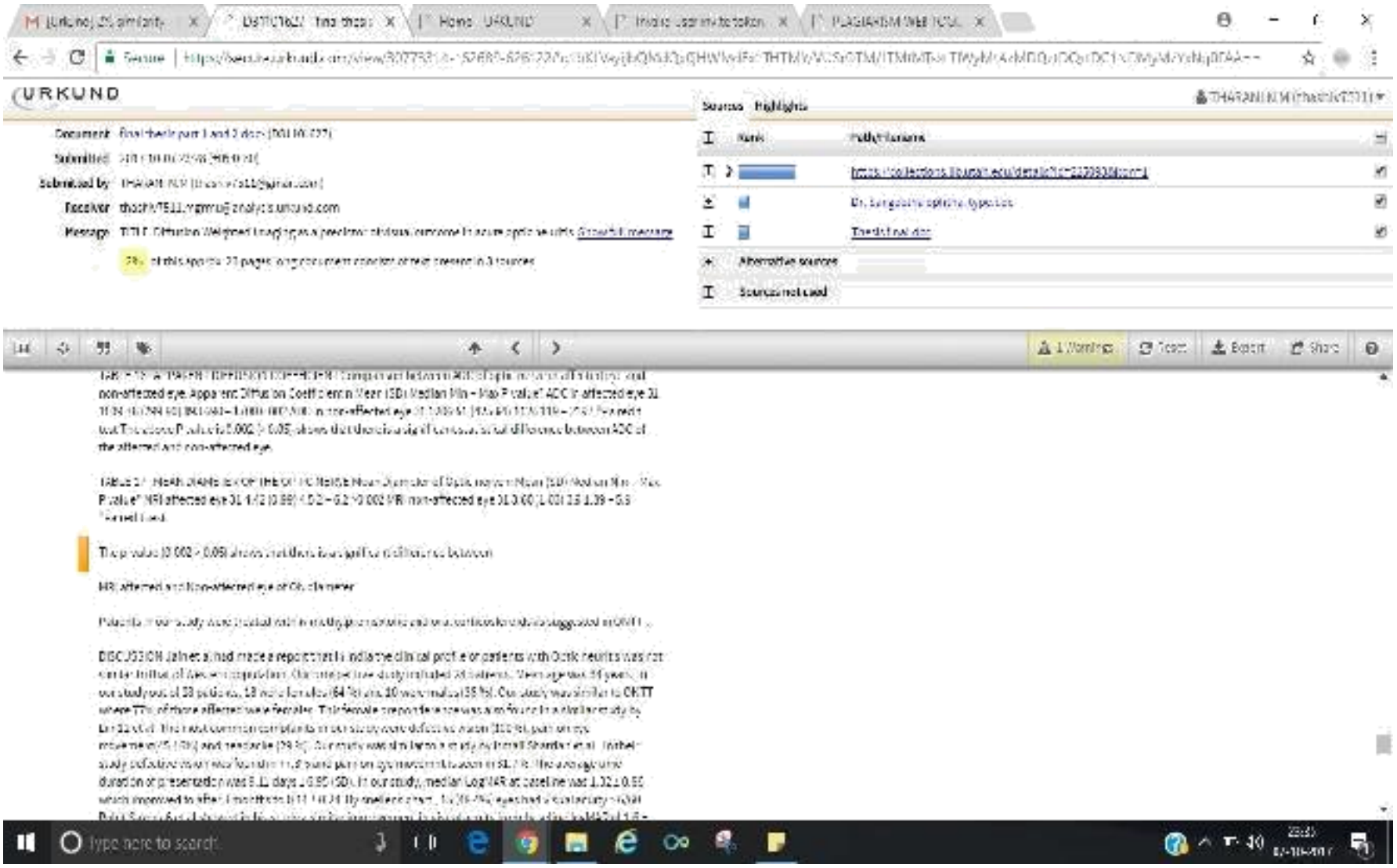
DWI- Diffusion weighted imaging

ADC- Apparent diffusion coefficient

IVMP-IV Methylprednisolone

WBC- White blood cells

GFAP- Glial fibrillary acidic protein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ARAVIND MEDICAL RESEARCH FOUNDATION
Institutional Ethics Committee
(REGISTRATION NO: ECR/182/Inst/TN/2013 DATED 20.04.2013)

12th December 2015

To
THARANI N M
MS Resident
Aravind Eye Hospital
Madurai

Dear Dr.Tharani,

Thesis Title: DIFFUSION WEIGHTED IMAGING AS A PREDICTOR OF VISUAL OUTCOME IN ACUTE OPTIC NEURITIS

IRB Code: IRB2015000225

Thank you for submitting your thesis and seeking the approval from the ethics committee. The documents provided by you for consideration which include the thesis protocol and informed consent forms were reviewed for the research methodology and scientific content. The Ethical committee did not find any correction and has recommended the thesis to go ahead in the present form.

Thanking you

Yours Sincerely,

Dr Lalitha Prajna
Member Secretary
Institutional Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
ARAVIND MEDICAL RESEARCH FOUNDATION
No.1, Anna Nagar, Madurai-625020

1, Anna Nagar, Madurai 625 020, Tamil Nadu, India. Phone: 0452-435 6550. Fax: 91-452-253 0984
E-mail: amrf@aravind.org; www.aravind.org