Etiological Profile of Optic Neuropathy in Tertiary Hospital in Eastern India- A Cross Sectional Observational Study

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Abstract- Background- Optic neuropathy refers to damage to the optic nerve due to any cause (inflammatory or non-inflammatory). Optic neuropathy can be clinically diagnosed by diminution of vision, dyschromatopsia, and uniocular visual field defect (in unilateral optic neuropathy) with or without afferent pupillary defect and change in optic disc appearance. There is no uniform availability of reliable data on optic neuropathy. Most of the studies concentrate on individual etiologies of optic neuropathy. Hence, in the present study, the clinical, biochemical, electrophysiological and imaging profile of optic neuropathy was studied along with age and sex distribution.

Methods- The present study was 1 year 5 months cross sectional observational study done at Neurology department, Bangur Institute of Neurosciences (B.I.N), Kolkata. The study was approved by institutional ethical committee of I.P.G.M.E&R. Kolkata. Informed consent was obtained from the participant. This study recruited consecutive patient admitted in neurology indoor who fulfilled the inclusion criteria of the study. A pre-designed proforma was used to collect the relevant clinical details, electro diagnostic findings, laboratory and imaging features. 89 patients having both diminution of vision and abnormal VEP were seen during the course of study.

Results- Most of the patients was in between 21-50 years. Most of patients had sub-acute onset. Out of 80 patients, 63.75% had bilateral involvement. Eye pain or pain on eye movement was uncommon. Headache as associated feature was seen in 32.5% patients. The four most common etiologies of optic neuropathy were idiopathic optic neuritis (35%), tuberculosis related optic neuropathy (18.75%), multiple sclerosis (10%) and anterior ischemic optic neuropathy (7.5%).

Conclusion- In conclusion the present study confirms the high frequency of optic neuropathy with a relative frequency of 12 % among indoor patients of neurology department in a tertiary care hospital in Kolkata. A significant correlation between these investigations and etiologies of optic neuropathy was observed.

Key words- MacDonald criteria; multiple sclerosis; optic neuritis, optic neuropathy, tuberculosis; visual evoked potential; visual field

Introduction-

The domain of vision is our most important way of getting information about world. Optic neuropathy refers to damage to optic nerve and presents as diminution of vision. It can occur due to any cause and is a frequently encountered entity in day to day neurology practice. No symptom may be as disturbing to a patient as acute visual loss. The optic nerve, which is a CNS structure, contains over a million fibers and constitute the axonic projections of the retinal ganglion cells carrying visual information from retina to lateral geniculate bodies.[1] The peripheral nerves are myelinated by Schwann cells whereas optic nerve is myelinated by the oligodendrocytes (like CNS white matter)[2]. So, rather than being a peripheral nerve, the optic nerve can be thought of as an extension of brain's white matter. It is not surprising therefore, that diseases that affect white matter of the brain would also affect

the optic nerve. Attesting to its importance is the magnitude of its representation in the central nervous system (CNS).

The etiologies of optic neuropathy are numerous and depend on many variable including age, sex, geographical location and drug exposure, etc. Primary or idiopathic optic neuritis, multiple sclerosis, optic neuropathy related to other autoimmune disease, infections, toxin and drugs, ischemic optic neuropathy, and optic neuropathy secondary to prolonged intracranial pressure are few neurological conditions those are encountered frequently in neurology ward. Clinical features, imaging (especially MRI Brain), visual evoked potential (VEP) and relevant tests help in diagnosis of many of these. VEP is a sensitive test to assess optic nerve function but ocular diseases and bilateral posterior pathway lesions can give false positive results. Ocular examinations and imaging are very useful in excluding these possibilities. In addition imaging may give important clues about the diagnosis. CSF studies are especially helpful in cases of infective and autoimmune etiologies. In substantial number of patients of optic neuropathy however, the etiology is elusive. This study is an attempt to know optic neuropathy and its etiologies by analysing the history, clinical, laboratory, electrophysiological and radiological profile. This will help in early recognition of the disease and knowing the common causes of optic neuropathy prevalent in our community.

Methodology-

The present study is a cross sectional observational study done at Neurology department, Bangur Institute of Neurosciences (B.I.N), Kolkata. The study was approved by institutional ethical committee of I.P.G.M.E&R. Kolkata. Indoor patients of department of Neurology, Bangur Institute of Neurosciences Kolkata from February 2010 to July 2011. Informed consent was obtained from the participant. A pre-designed proforma was used to collect the relevant clinical details, electro diagnostic findings, laboratory and imaging features.

Patients presenting with diminution of vision of one or both eyes and an abnormal Visual Evoke Potential by chessboard pattern reversal method included in the study and patients having visual symptoms due to ocular causes such as glaucoma, uveitis, and retinal detachment, in whom proper visual assessment is not possible, children below 5 yrs, demented patients, and non-co-operative patients, imaging findings suggesting other diagnosis such as bilateral parieto-occipital lesions (tumor, infarct, demyelination) causing visual impairment, unwillingness to participate in this study were exclusion criteria of the study.

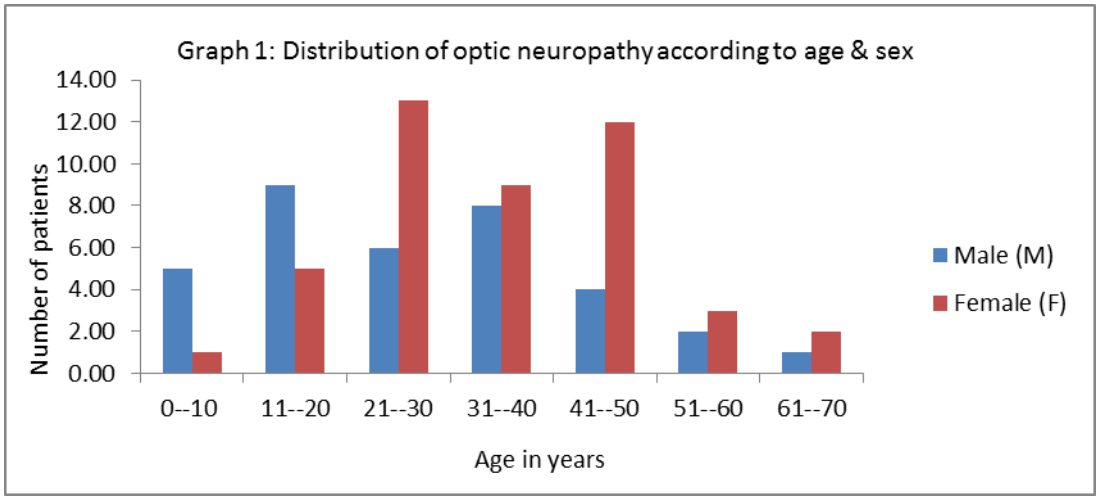
89 patients having both diminution of vision and abnormal VEP were seen during the course of study. Out of these, 80 were finally included in the study. 9 patients were excluded

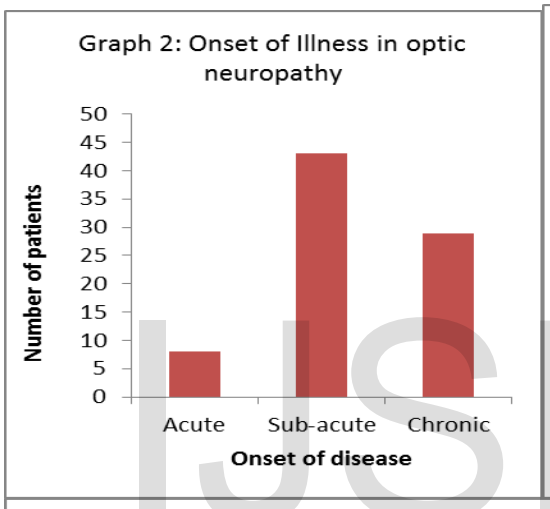
as 4 had cataract while another 3 had diminution of vision due to posterior visual pathway dysfunctions. One patient each had glaucoma and orbital cellulitis with possible endophthalmitis and consequently not included in the study. Assessment of visual evoked potential (VEP) by chessboard pattern reversal method was done in these patients. Visual field was assessed by confrontation method and perimetry was done only when required.

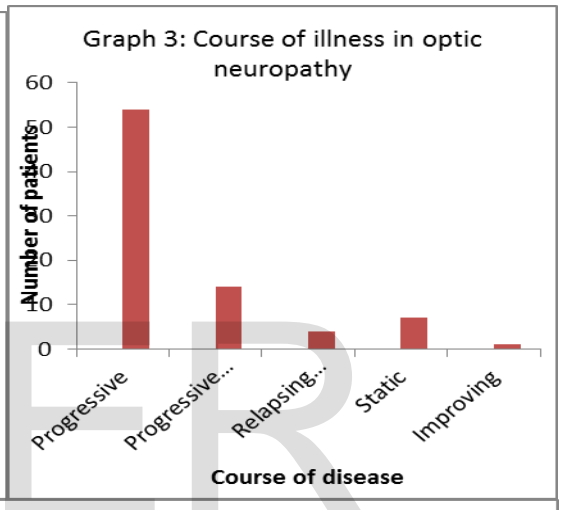
Demographic and clinical characteristics, VEP finding, laboratory and radiological features were noted in proforma. Tuberculosis related optic neuropathy, multiple sclerosis, Ischemic optic neuropathy and Idiopathic intracranial hypertension was diagnosed by presence of more than one of following- CSF finding, Montoux test > 20mm, chest X ray suggestive of tuberculosis, Positive CSF PCR for tuberculosis, CSF ADA >10 U/l, demonstration of AFB in CSF smear by microscopy or culture, MRI/ CT scan Brain showing one or more granulomatous lesion consistent with tuberculoma, revised Mc Donald criteria and of neuromyelitis optica was based on diagnostic criteria by Wingerchuk et al in 2006, International Headache Society's (IHS) criteria. Selected patients were thoroughly evaluated clinically. Relevant laboratory, electrophysiological and radiological investigations were done after taking informed consent. Data was collected in proforma. SPSS software was used for analysis and chi square test was used for significance. P value less than 0.05 was considered significant.

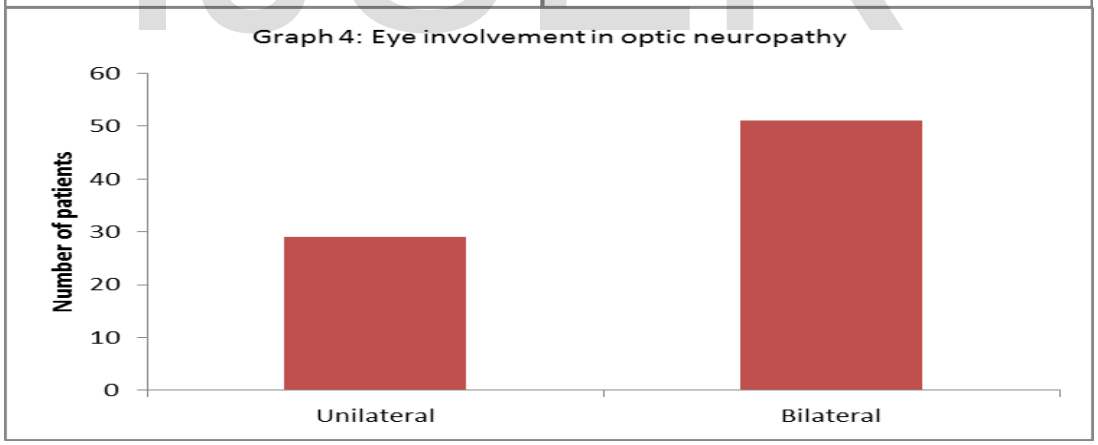
Results-

In the present study, clinico-electrophysiological and radiological evaluation of the patients who presented with optic neuropathy was done to know the possible etiologies of this disease. Further, the distribution of clinical, electrophysiological (visual evoke potential) and radiological findings were studied in different etiologies of optic neuropathy. A total of twelve parameters which include age, sex, onset of illness, course of illness (at presentation and hospital stay), eye involvement, eye pain or pain on movement of eye, addiction history, family history, fundoscopic findings, VEP, brain imaging and cerebrospinal fluid (CSF) findings were analysed for optic neuropathy.









FUNDOSCOPIC FINDINGS AND VEP FINDINGS IN OPTIC NEUROPATHY

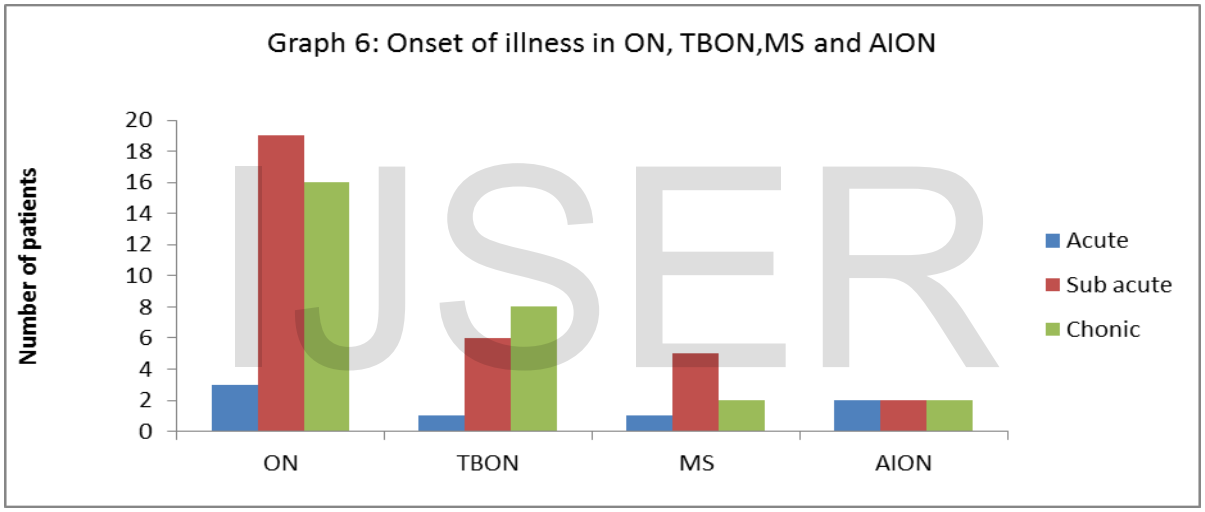
Majority (53.75%) of patients had pale optic disc. Blurring of disc of margin was seen in 27.5% of patients. Normal appearing fundus and haemorrhage were seen in 8.75% and 6.25% cases. Prolonged P 100 latency was noted in 57.5% of cases. Reduced P 100 amplitude was seen in 22.5% of cases. No definite waves were formed in 20% of cases.

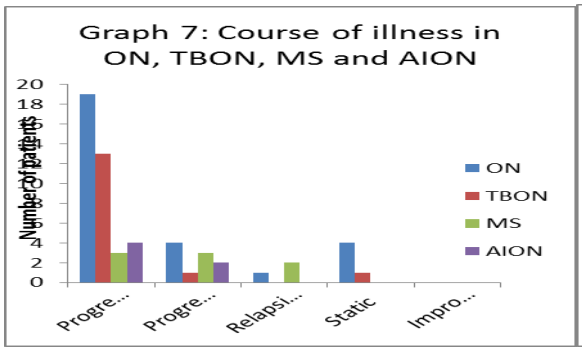
BRAIN IMAGING (MRI/CT) AND CSF FINDINGS IN OPTIC NEUROPATHY

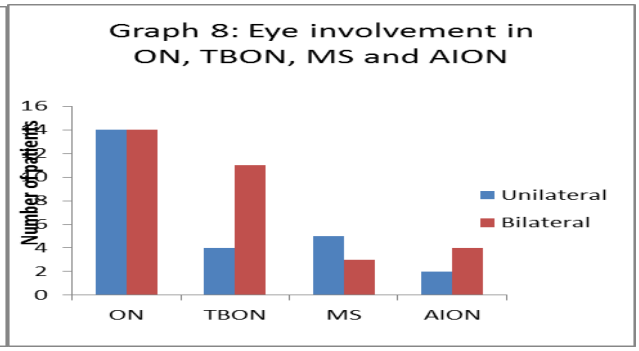
Out of 80 patients 77 underwent MRI brain while 3 had only CT scan brain. Total 50% patients had normal brain imaging including 3 normal CT scan brain. MRI Brain of 26.25% of patients had long TR interval hyper intensities in white matter suggesting demyelination. Presence of granuloma was the second most common (6.25%) brain imaging finding. Out of 80 patients, 45% had normal CSF study. The most common (28.75%) abnormal finding was increase in CSF protein with normal CSF cells and CSF sugar. Only pleocytosis was seen in 3.75% cases.

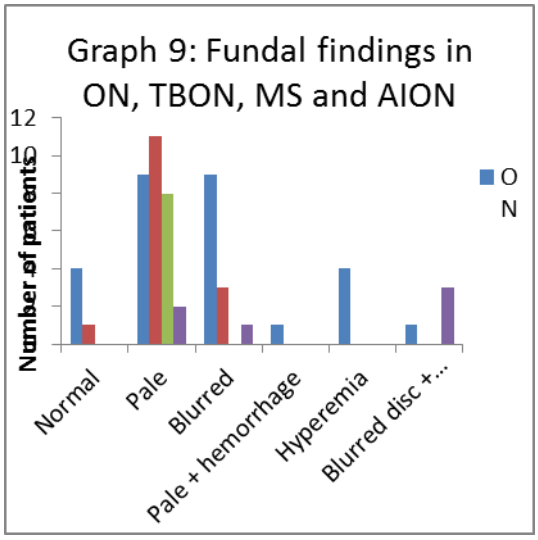
ETIOLOGIES OF OPTIC NEUROPATHY

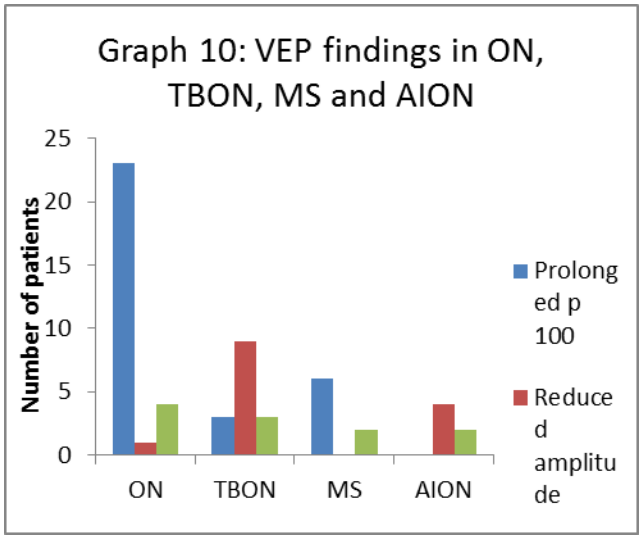
Of the total cases of optic neuropathy the most common etiologies were idiopathic optic neuritis (35%), tuberculosis related optic neuropathy (18.75%), multiple sclerosis (10%) and anterior ischemic optic neuropathy (7.5%). The less common etiologies include degenerative optic neuropathy (3.75%), NMO (1.25%), toxic optic neuropathy (1.25%).

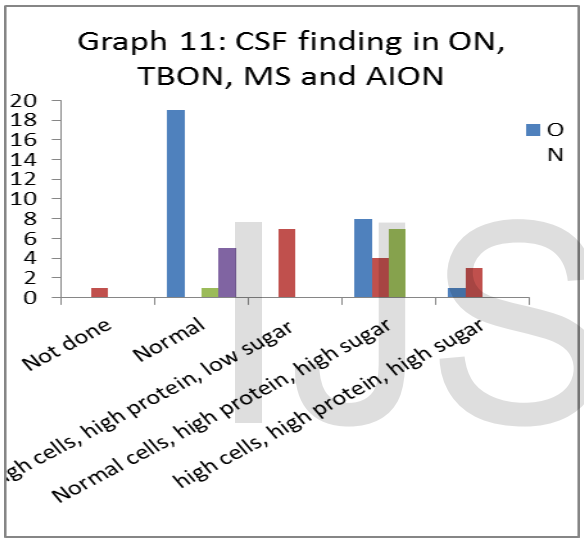


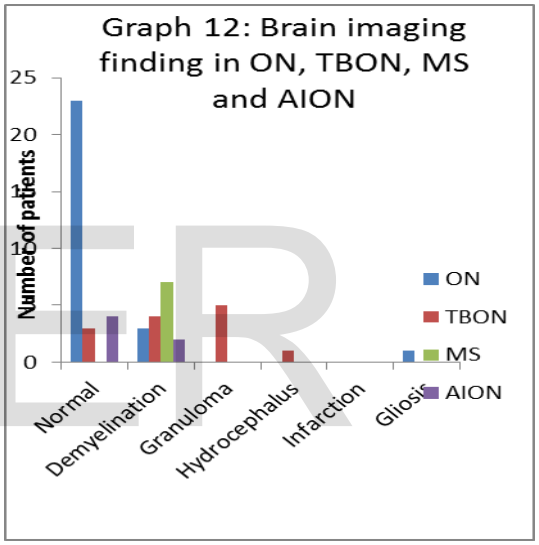












MULTIPLE SCLEROSIS

There were 8 (10%) cases of multiple sclerosis in the study. Age group of 31-40 years constituted 50% of cases. There was female preponderance (M:F::1:1.67). Onset was sub-acute in most (62.5%) cases. Unilateral involvement was present in 62.50%. Eye pain was found in only one patient. Paleness of optic disc was found in all(100%). VEP showed prolonged P100 latencies in 75% cases.CSF showed increased protein with normal cells and sugar in 87.55% cases. Weakness of limbs with spasticity was the most common (75%) associated findings. Only 1 patient had epilepsy as co morbid condition.

ANTERIOR ISCHEMIC OPTIC NEUROPATHY (AION)

Of all cases of optic neuropathy anterior ischemic optic neuropathy (AION) was seen in 6 patients. All (100%) patients were in age group 31-50 years. There was female preponderance (83.33%) with male to female ratio 1:5. Acute, subacute and chronic onset

was seen in 2 each cases of AION. Course was progressive in majority (66.67%) of patients. Bilateral involvement was present in 66.67%. Eye pain was found in only one patient.

OPTIC NEURITIS SECONDARY TO SYSTEMIC VASCULITIS (SON)

Optic neuritis secondary to systemic vasculitis was diagnosed in 5 patients. Most cases were in age group of 21-30 years. The male to female ratio of 1: 1.5 was noted. Most (60%) patients had chronic onset. Bilateral eye involvement, pale fundus, prolonged P100 latencies on VEP, normal CSF and stroke on MRI was seen in most of cases (80%). None of the patient had eye pain. Isolated involvement of optic nerve was seen in 40% of cases. Co morbid illnesses such as hypertension, nephropathy, seizure and stroke were present in 60% of cases.

Idiopathic intracranial hypertension (iih)

Among IIH patient majority of the patients were in 21-30 years age group and were females. Most of patients had sub-acute to chronic onset and progressive course. Bilateral eye involvement, blurred disc margin on fundoscopy, normal CSF and normal MRI findings were present in all (100%) cases. There was no eye pain. VEP showed prolonged P 100 latency in majority. Headache was most common associated feature and there were no co-morbidity.

Degenerative and hereditary optic neuropathy

First decade was the most common age group noted with a M:F ratio of 2:1. Most of patients had chronic onset and progressive course. Family history was positive in 2 out of 3 patients.

Discussion-

Optic neuropathy is a clinical diagnosis characterised by diminution of vision, dyschromatopsia, and uniocular visual field defect (in unilateral optic neuropathy) with or without afferent pupillary defect and change in optic disc appearance. Till early 19th century, a little was known about optic neuropathy. With the advent of newer diagnostic techniques analysis of visual evoked potential (VEP) and magnetic resonance imaging (MRI), a surge is seen in literature on optic neuritis and its relation to multiple sclerosis in last two decades. Simultaneously, many studies have been also done on other etiologies of optic neuropathy and their management.[2] Optic neuropathy may occur in isolation or as sequel to many disease processes and frequently presents as a diagnostic dilemma to both neurologists and ophthalmologists. There is no uniform availability of reliable data on optic neuropathy. Most of the studies concentrate on individual etiologies of optic neuropathy. The prevalence of optic neuropathy is unknown but it is frequently encountered entity in neurology ward. In the present study conducted at a tertiary care hospital of Eastern India, approximately 12% of

neurology indoor patients had optic neuropathy. A population based study will be required to know the accurate prevalence of optic neuropathy in this part of world.

The etiologies of optic neuropathies can be classified on the basis of pathological process into optic neuritis (idiopathic optic neuritis and optic neuritis related to multiple sclerosis), optic neuritis secondary to systemic vasculitis and other autoimmune disease, infective optic neuropathy, ischemic optic neuropathy, hereditary and degenerative optic neuropathy, toxic and nutritional optic neuropathy, optic neuropathy secondary to prolonged raised intracrainial pressure, and others (infiltrative such as lymphoma, leukemia, space occupying lesion such as sellar or perisellar space occupying lesions and trauma). The present study was done in neurology department, hence, concentrated on medical causes of optic neuropathy. Optic neuropathy secondary to trauma and tumor were thus not represented.

In this study, the most common etiologies of optic neuropathy were idiopathic optic neuritis (35%), tuberculosis related optic neuropathy (18.75%), multiple sclerosis (10%) and anterior ischemic optic neuropathy (7.5%). The difference in frequency of etiologies of optic neuropathy is due to fact that present study is conducted in neurology department whereas the previous study was conducted in neuro-ophthalmology clinic. However, the finding of most common etiology that is idiopathic optic neuritis was in accordance with the study in India.[3]

The incidence of AION is about 2-3 per 100,000 persons over the age of 50 years and 0.54 per 100,000 for all ages. It is more common among Caucasians, and this may be result from genetic differences including the cup to disc ratio. In the present study 7.5% patient had anterior ischemic optic neuropathy. Less frequency of AION patients in present study can be explained by the fact that study was conducted in admitted patients and most of AION patients do not require admission and hence excluded from the study.

Menon et al. concluded that most (45%) of optic neuropathy patients had presentation at age group 20-40 and there was no significant sex predilection.[4, 5] In the present study most (65%) of patients belong to age group 20-50years. In the present study male to female ratio was 1:1.4. Most patients were 21-30 years age group for idiopathic optic neuritis (28.57%) while an age group of 31-40 years was seen in tuberculosis related optic neuropathy (26.67%), multiple sclerosis (50%), and anterior ischemic optic neuropathy (50%).

Behbehani R reviewed optic neuropathy and stated that most of cases of optic neuritis, ischemic optic neuropathy and inflammatory optic neuropathy have rapid onset and a gradual onset over months is typical of compressive toxic/nutritional and degenerative optic neuropathy. In present study about 78% of idiopathic optic neuritis patients, 75% of multiple sclerosis related optic neuritis patients and 67% of anterior ischemic optic neuropathy

patients had either acute or sub-acute onset. Presentation over months (chronic onset) was mostly seen in tubercular and degenerative pathology. In the present study most (67.5%) of patients had progressive course. The likely explanation is that in present study course of illness was based on history and observation during stay in hospital.[4]

Idiopathic optic neuritis and optic neuritis related to multiple sclerosis have mostly unilateral presentation as stated by Sham et al . However, Asian and Indian studies done by Lin et al (34.4%), Jain et al (62%), Saxena et al (32.5%) showed higher percentage of bilateral involvement. In the present study, 50% of idiopathic optic neuritis had bilateral involvement similar to high percentage of bilateral involvement in Indian study which is in accordance with geographical and ethnic variation. In the present study 62.5% of multiple sclerosis patients had unilateral disease similar to Sham et al (115). Bilateral involvement was seen in 77.3% patients of tuberculosis related optic neuropathy and 66.7% of anterior ischemic optic neuropathy patients. The bilateral involvement in the cases of tuberculosis related optic neuropathy can be attributed to systemic nature of disease and due to opto chiasmatic involvement. The presence of vascular risk factors in anterior ischemic optic neuropathy patients lead to bilateral involvement of eye.[6-9]

Studies on fundal finding in optic neuropathy are less available. In the present study, 53.75% cases of pale disc, 26.25% cases of blurring of disc margin and 6.25% cases of haemorrhage were found. This study showed that different fundal findings are common in different etiologies of optic neuropathy with a p value of < 0.001. Blurred disc margin was found in 32.14% cases of optic neuritis, 20% cases of tuberculosis related optic neuropathy, and 33.33% cases of ischemic optic neuropathy. Pale optic disc was present in 73.33% of tuberculosis related optic neuropathy, 100% cases of multiple sclerosis, and 32.14% cases of idiopathic optic neuritis. Presence of hemorrhage on optic disc was found in 50% of cases of AION. In trials (ONTT) conducted on optic neuritis patients in USA, blurring of disc margin and disc hemorrhage were present in 35.3% and 5.6% of cases respectively. Asian studies by Lim et al (60%), Lin et al (53.2%) and Wakakura et al (50%) showed blurred disc margin as most common finding in optic neuritis patients. This was in accordance with the studies done by Jain et al (56%) and Saxena et al (62%) in India. In the present study, the most common fundal findings in optic neuritis are blurred disc margin (32.14%) and pale disc (32.14%).[3, 10, 7, 8, 11] In present study 50% of anterior ischemic optic neuropathy patients had disc hemorrhage.[2]

VEP can be abnormal in any optic neuropathy. It can be useful in patients with early or subclinical optic neuropathy which have no discernable optic change and normal pupillary

response. Kwak et al concluded prolongation of P100 latencies as most common finding among optic neuropathy patients. Out of 80 patients in the present study, prolonged P100 latency was noted in 57.5% of cases and thus being the most common finding. Only reduced P 100 wave amplitude and no wave formed were seen in 22.5% and in 20% of cases respectively on VEP testing.[4, 12]

The advent of MRI has highlighted the relationship between optic neuritis and multiple sclerosis. The real value of MRI in the typical demyelinating optic neuritis is not to image the optic nerve, but to image brain as a prognostic indicator for the further development of multiple sclerosis. Thus, MRI is recommended in all cases of optic neuritis.[2, 9] Out of 80 patients of optic neuropathy majority of patients (50%) had normal brain imaging. Brain imaging findings also showed significant distribution (p value < 0.002%). Normal imaging was seen in 82.1% of optic neuritis patients, 66.7% of anterior ischemic optic neuritis and 20% of tubercular optic neuropathy patients. Long TR hyper intensities suggesting demyelination was seen in 100% of multiple sclerosis patients, 26.7% of tubercular patients, and 10.7 % of idiopathic optic neuritis patients. Granuloma was the feature on brain imaging in 33.3% of tuberculosis related optic neuropathy patients which was the most common finding in these patients.

CSF study in multiple sclerosis showed elevation of CSF protein only in 40% of cases. Aaron et al concluded that there is a positive correlation in between CSF protein > 260 mg/dl and development of opto-chiasmatic tuberculosis.[1, 13] In the present study CSF was normal in 45% of cases. None of tuberculosis related optic neuropathy patient had normal CSF. Most common (28.75%) abnormal CSF finding was isolated elevation of CSF protein. CSF oligoclonal bands were not studied in present study. Most common (46.7%) abnormal finding in tuberculosis patients was combination of lymphocytic pleocytosis with high protein and low sugar. CSF study was helpful in differentiating various etiologies of optic neuropathy (p value<0.000).

Conclusion-

In conclusion the present study confirms the high frequency of optic neuropathy with a relative frequency of 12 % among indoor patients of neurology department in a tertiary care hospital in Kolkata. A significant correlation between these investigations and etiologies of optic neuropathy was observed.

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