Visual Outcome and Prognostic Factors of Optic Neuritis: A Perspective from the East

Digvijay Singh1, Rohit Saxena2
1Division of Ophthalmology, Medanta-The Medicity, Gurgaon, India
2Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Abstract
Optic neuritis is an inflammatory disorder of the optic nerve often resulting in a demyelination process. In the west and in Caucasian populations, the optic neuritis treatment trial demonstrated good recovery and excellent visual outcomes with a significant risk of conversion into multiple sclerosis. However recent reports from the Asian and African continents have noted a significantly different clinical profile and outcomes are reported to be worse than the West. Prognostic factors for visual recovery in optic neuritis have been found to include visual acuity at presentation, clinical signs in the form of retrobulbar pain and disc edema, race and ethnicity, age and retinal thinning on OCT. The risk of conversion to multiple sclerosis is low and values ranging from 0-5% have been reported in various studies. This review collates information about optic neuritis from the Eastern part of the world with regard to clinical profile, visual outcome, prognostic factors and risk of conversion to multiple sclerosis.

Keywords: optic neuritis, outcome, prognostic factors, vision, multiple sclerosis

Introduction
Optic neuritis (ON) refers to inflammation of the optic nerve.1,2 Optic nerve forms a channel to carry visual information to the primary visual nuclei, most of which is relayed to the occipital cortex of the brain where it is processed into vision. Inflammation of the optic nerve causes loss of vision usually due to the swelling and destruction of the myelin sheath covering the optic nerve. Direct axonal damage may also play a role in nerve loss in many cases. The most common aetiology is multiple sclerosis (MS). Up to 50% of patients with multiple sclerosis will develop an episode of optic neuritis, and in about 20% of the cases, optic neuritis is the presenting sign of multiple sclerosis.1,2 Symptoms of optic neuritis include sudden loss of vision with an afferent pupillary defect in the involved eye, pain on movement of affected eye, and impairment of visual functions such as color vision, contrast sensitivity and visual fields. Typically, there is spontaneous recovery of vision and this has been shown to get accelerated by steroids.

Classification
Broadly, optic neuritis can be classified into the following categories depending upon aetiology and course:
1. Idiopathic/Clinically isolated: When ON is diagnosed in the absence of MS or other systemic disease.
2. ON associated with MS: When ON is associated with MS.
3. Infective or ON secondary to an autoimmune disorder: When ON is found to be secondary to an infective process, e.g. syphilis, or associated with an autoimmune condition, such as Sjogren’s syndrome or Systemic Lupus Erythematosus.
4. Autoimmune ON: If ON is corticosteroid dependent with positive autoimmune markers, but does not fit the diagnostic criteria for a specific autoimmune disorder.
5. Recurrent idiopathic ON: In cases where ON is recurrent in accordance with the McDonald criteria but not associated with MS or any other systemic disease.
6. Neuroretinitis: When ON is associated with retinal oedema and macular star formation, usually secondary to an infective aetiology.

Clinical Profile and Visual Outcome
In Caucasians, the commonest cause for optic neuritis is multiple sclerosis and it is associated with a favourable visual outcome as demonstrated in the optic neuritis treatment trial.3-5 Optic neuritis is known to have a spontaneous recovery and therapy with intravenous steroids only hastens it with no bearing on the final visual outcome. This was demonstrated in the Caucasian race by the optic neuritis treatment trial and is believed to apply to all populations. However, recently, literature and experience has shown that race and ethnicity has a bearing on the demography, clinical profile and outcomes of optic neuritis.6 The outcome of optic neuritis in the Asian countries has been shown to be poorer than the west.7,8-17 There are a few studies from developing countries in Asia and Africa which have shown similar visual outcomes as the Optic Neuritis Treatment Trial and conflict with the other studies from similar geographic locations.8,18 A study on optic neuritis from India has shown a clinical profile and outcome similar to majority of studies from the Asian continent and significantly different from the West.19 The difference in outcome of optic neuritis between the west and the east has been attributed to the higher incidence of atypical optic neuritis and possibly a racial difference in the course of the disease. Saxena et al examined the clinical profile and short-term visual outcome of all forms of optic neuritis in 99 eyes of 83 Indian patients.19 The patients were
The study found that visual outcome was worse in patients with multiple sclerosis than among those without multiple sclerosis. The study concluded that long-term visual outcome is favourable for majority of the patients who experience optic neuritis even when multiple sclerosis is present. Chuenkongkaew W et al retrospectively evaluated 81 patients in Thailand and observed the visual outcome after steroid therapy for optic neuritis. While majority of their patients were clinically isolated optic neuritis (78%), the others were having a demyelinating disease. Those with isolated optic neuritis achieved a visual acuity of 6/12 or better in 60% of the cases as against 25% in the demyelinating disease group.

In a retrospective review of 27 cases of optic neuritis in Chinese patients, Bee YS et al found a higher incidence of papillitis than the optic neuritis treatment trial along with a higher incidence of bilaterality. The study found that visual acuity improved slowly after 2 weeks of treatment and final outcome resulted in residual abnormality in the visual functions and electrophysiology. The visual outcome for unilateral optic neuritis was found to be better than bilateral optic neuritis. Pokroy R et al evaluated 10 South African black patients with idiopathic isolated optic neuritis and followed them for at least 3 months after the attack. They found that the presenting visual acuity was less than 6/60 in 17 of 18 eyes, with severe dyschromatopsia in all eyes. After therapy, 6 eyes recovered vision of 6/12 or better, with only 3 eyes recovering colour vision of 10/13 or better on Ishihara plate testing.

A multicentric study was conducted by Wakakura et al to establish the baseline characteristics of optic neuritis in Japanese patients. In the study, it was observed that the clinical profile of optic neuritis was significantly different from the western population (compared to a US study) with a lower risk of multiple sclerosis. However the study demonstrated similar visual function changes and outcomes as the western population. This is unlike most other Asian studies where the visual outcomes are seen to be worse than the west. Wang JC et al studied 39 eyes of 31 patients with optic neuritis in Singapore to look for visual outcome. The cases were followed up for 6 months and within the follow-up period, 83.9% with idiopathic optic neuritis attained a visual acuity of 6/12 or better with 38.7% recovering to 6/6 or better. This study demonstrated that typical optic neuritis has a good outcome even in the Asian population and was one of the early studies in the Asian population.

A study from Singapore with 60 patients concluded that the clinical profile of optic neuritis in Singapore was significantly different from the West and similar to other Asian countries. On the visual outcome front, the study contradicted a previous study from Singapore and found the visual outcome to be worse, in the whole heterogeneous group of optic neuritis, than the West. In the unilateral group, 75.9% achieved 6/12 or better visual acuity and the visual outcome was worse in patients with more severe loss at the outset. Thus for patients with initial visual acuity of counting fingers or worse only 38.8% recovered to 6/12 or better at six months. Recovery of colour vision paralleled that of visual acuity with 69.0% of patients being able to identify 13–15 of 15 Ishihara plates at six months. In the bilateral
group, all patients achieved 6/12 or better visual acuity and identified 13–15 of 15 Ishihara plates at six months even in the eye with more severe initial involvement. The Optic Neuritis Treatment Trial was a landmark study in optic neuritis and enrolled all patients with optic neuritis and defined the criteria for typical optic neuritis. At enrolment, about 10% of cases had a visual acuity of 20/20 or better with majority having visual acuity in the range of 20/200. The patients improved significantly over time with or without the use of steroids and over 94% achieved a visual acuity of 20/40 or better in the involved eye. The study showed the remarkable recovery seen in typical optic neuritis. However, the studies from Asia seemed to show a different outcome with however visual recovery.

**Prognostic Factors**

Few studies have evaluated the prognostic factors for visual outcome in cases of optic neuritis and they present varied results.

**Visual acuity**

Visual acuity at presentation has been a parameter which was evaluated in the optic neuritis treatment trial and it was found that a severe initial loss of visual acuity resulted in a worse outcome. Deschamps R et al also reported a similar finding in their study. However, a study from China has described a worse visual outcome in those patients who had a mild initial visual affliction. Kupersmith MJ et al used the Optic Neuritis Treatment Trial data to evaluate various cut-off points for baseline and 1-month vision levels that were predictive of abnormal 6-month vision. They found that the best cut-off points for baseline and 1 month were visual acuity ≤ 20/50, contrast sensitivity < 1.0 log units, and visual field mean deviation ≤ -15 dB. The study reported that the same levels of visual dysfunction at 1 month, but not at baseline, correlated with having a 6-month moderate-to-severe loss for each of these visual function parameters.

**Disc edema**

Disc swelling is another important parameter which has been evaluated as a prognostic marker for visual outcome. Du Y et al studied a series of bilateral optic neuritis cases and concluded that the presence of bilateral disc swelling predicted a negative visual outcome.

**Ethnicity/Race**

Moss et al performed a revaluation of the Optic Neuritis Treatment Trial using a longitudinal analysis method and found that while there is no relationship of age, sex, or treatment with visual outcomes, race/ethnicity was significantly related to contrast sensitivity and visual acuity during a 15-year period following acute optic neuritis. The black race/ethnicity was found to be associated with worse scores for visual functions unlike the original Optic Neuritis Treatment Trial publication which reported no significant difference in outcomes with respect to race/ethnicity.

**Early treatment**

Chuenkongkaew W et al retrospectively evaluated 81 patients in Thailand and observed the visual outcome after steroid therapy for optic neuritis. The outcome was found to be better for those who received the steroid therapy early (within 8 days of onset of neuritis). This study supports the need for early treatment and contradicts the results of the Optic nerve treatment trial.

**Laterality**

Du Y et al evaluated 41 Chinese and found that bilateral optic neuritis has worse outcome than unilateral optic neuritis.

**Location of Lesion**

Deschamps R et al retrospectively studied 50 patients of optic neuritis who had undergone a short tau inversion recovery (STIR) sequence of the MRI for optic nerve imaging and found that involvement of the intracanalicular part of optic nerve was associated with a worse visual outcome.

**Retro-orbital pain**

Absence of retro-orbital pain has been shown to result in a poorer visual outcome as compared to patients with retro-orbital pain.

**Age**

Older age of onset is associated with a worse visual acuity outcome though this has not been deemed to be of clinical significance.

**OCT Changes**

Wang et al reported from China that there was an association between visual outcome and RNFL thickness particularly in eyes which developed optic atrophy after an attack of optic neuritis. They found that there was lesser RNFL loss as compared to optic atrophy due to advanced open angle glaucoma but a correlation with visual outcome existed.

**Risk of Multiple Sclerosis**

The association of optic neuritis with multiple sclerosis in the eastern part of the world is not as strong as the west. Majority of the optic neuritis in this part of the world are clinically isolated syndromes with a low rate of conversion to multiple sclerosis. Wang et al noted a low risk of conversion to multiple sclerosis in their study. Pandit et al examined the records of 59 patients with optic neuritis from India and reported that over half of these converted to multiple sclerosis, and that among those having lesions on the brain MRI, all converted to multiple sclerosis. These values are nearly similar to those reported in the optic neuritis treatment trial and may possess the bias of being sourced from an entirely neurology setup whereas clinically isolated optic neuritis may often present to an ophthalmology setup as was demonstrated in another study from India which saw only 4 patients having multiple sclerosis among 83 optic neuritis cases. A study from Malaysia found the recurrence rate of optic neuritis to be 16% in their follow up and the rate of conversion to MS of about 3%. A study among native Africans of 18 patients with either unilateral or bilateral optic neuritis followed for at least 3 months reported that none of them converted to multiple sclerosis. It concluded a very low risk for MS among the black African race.
Conclusion
Optic neuritis in Asia and Africa has a varied clinical profile which is significantly different than that in the West. The visual outcome in the Asian race is poorer as compared to the Caucasians and does not follow the natural course of recovery demonstrated in the optic neuritis treatment trial. There are few factors which predict recovery in optic neuritis and these include vision at presentation, clinical signs and symptoms, race and administration of early treatment. Risk of progression to multiple sclerosis is lower in the eastern part of the world as compared to the west.

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