# Clinical Profile of Patients with Leber Hereditary Optic Neuropathy—An Ambispective Study in Cohort from Northern Part of India

Dear Editor in Chief

We thank the authors for their keen interest in our article.

Ample data on Leber hereditary optic neuropathy (LHON) has been described from the west. However, systematic literature on LHON from the Indian subcontinent is still limited. Most of the available studies focus on epidemiological or genetic data. More so, the data available from the Indian subcontinent show a different genetic profile in patients with LHON. Our cohort represents the clinical profile and the frequency of mutations linked with LHON in the North Indian population.

In this ambispective study, most of the data were obtained retrospectively from the case record files, and the study was not designed as an epidemiological study.[1] The scope of determining the genetic status of first-degree relatives of LHON patients was discussed but was dropped due to the inability of tracing retrospective patients and the cost implications of such an exercise. The genetic data of the family members especially mothers were hence not available due to financial, technical, and especially social constraints. Knowing whether the mutations are inherited or sporadic in a given patient may help in further elucidating the natural history of LHON.[2] Though an affected individual or family may carry an LHON mutation also in the heteroplasmic constellation, it is intriguing to note that LHON variants mostly occur in the homoplasmic state. All but one mutation-positive patient in our cohort carried a homoplasmic variation.

LHON-Plus is a well-described entity wherein up to 59% of patients with LHON have been noted to develop additional neurological symptoms.[3,4] These patients are known to begin with optic nerve involvement and later can develop progressive neurological syndromes over time with postural and action tremors being the most common one.[3] A subset of these patients may even develop a multiple-sclerosis-like illness known as "Harding's disease," whose exact pathophysiology is not clear. Our cohort, however, included patients with only ocular manifestations. A detailed clinical examination and neuroimaging were done in all the participants and none of the patients included in our cohort had any extraocular manifestation. Since these patients were recruited from the neuro-ophthalmology and ophthalmology clinics where they presented with vision loss, there might have been a screening bias in patients who would present without any visual complaints.

Given the nature of the study and ambispective collection of data, there was variation in treatment received amongst the patients.[1] The most commonly used agents were idebenone, coenzyme Q-10, multivitamins (folic acid, vitamin B12, thiamine, and riboflavin), l-carnitine, l-arginine, and creatine. The duration of treatment was also highly varied and many patients lost to follow-up. None of the patients in our cohort received gene therapy as gene therapy is not available or cleared by the existent authorities for drug control at the time of study.

Any comment about treatment response and visual recovery would be inadequate at best in a retrospectively collected data. The patients included prospectively are being systematically followed up for their treatment response and visual outcome.

While improvement has been noted in patients on treatment, a systematic randomized design can shed light on the patients improving "spontaneously."

Though a comprehensive genetic analysis of patients and their families can definitely provide further insights into the disease pathophysiology, these are often financially and technically challenging. Studying varied population cohorts can help assess the impact of environmental factors and genotype–phenotype variations.[5,6] A systematic randomized cohort can provide answers to many missing links especially with response to therapy.

Despite a rise in recent interest and world literature on LHON, there is nonavailability of standardized treatment, diagnostic, and management guidelines. Additional data from across various ethnicities may provide further insight about the natural history, clinical, and genetic profile of the disease.

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## Conflicts of interest

There are no conflicts of interest.

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