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Clinical, Structural, and Genetic Features of Leber Hereditary Optic Neuropathy in Colombia: A Multicenter Retrospective Cohort Study

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ABSTRACT

This study characterizes the clinical, structural, and genetic profile of Colombian patients with Leber's Hereditary Optic Neuropathy (LHON) through a multicenter retrospective cohort with longitudinal follow-up. Medical records from five neuro-ophthalmology centers (2019–2024) were reviewed. Inclusion criteria were genetically confirmed LHON, age ≥ 10 years, and complete ophthalmologic evaluation (best corrected visual acuity (BCVA), visual fields, and optical coherence tomography (OCT)). Twenty-one patients (42 eyes) were included. Median follow-up was 14.2 months (IQR 11.0–17.8). The predominant mutations were m.11778G>A (61.9%), m.14484T>C (28.6%) and m.3460G>A (9.5%). Median age at diagnosis was 37 years. BCVA showed no significant change during follow-up ($p = .62$). However, OCT revealed significant thinning in both retinal nerve fiber layer (median decrease: 11.0 µm, $p = .0005$) and ganglion cell complex (median decrease: 2.6 µm, $p = .0040$). Post-hoc power was high for RNFL (0.957) and moderate for GCC (0.534), but insufficient for visual acuity (0.095). This is the largest LHON cohort reported in Colombia to date. Despite stable visual acuity, progressive retinal thinning was observed. These findings highlight the importance of structural imaging for disease monitoring and the need to optimize diagnostic timelines through referral pathways, genetic testing access, and national registries.

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Introduction

Leber hereditary optic neuropathy (LHON) is a maternally inherited mitochondrial disease that leads to bilateral, painless, central vision loss. It primarily affects young adult males and results from pathogenic point mutations in mitochondrial DNA (mtDNA) that impair Complex I function in the respiratory chain.[1] The three most prevalent mutations, m.11778G>A in MT-ND4, m.3460G>A in MT-ND1, and m.14484T>C in MT-ND6, account for over 90% of genetically confirmed cases worldwide.[2,3] Among these, the m.11778G>A mutation is most frequently encountered and is consistently associated with more severe visual outcomes and lower rates of spontaneous recovery.[4]

Despite the relatively high carrier frequency of LHON-associated variants, estimated at approximately 1 in 1000 individuals, clinical penetrance remains low and sex-dependent. Current data suggest that the lifetime risk of vision loss in male carriers is approximately 17.5%, compared to 5.4% in females, underscoring the importance of sex-specific expression in the disease's natural history.[5] While regional studies from Chile, Brazil, and Cuba have provided initial genotype data,[6–8] Colombia lacks systematic cohort-level reports.

In Colombia, LHON is designated as an orphan disease, with an estimated prevalence of 0.18 per 5,000 inhabitants, according to national surveillance data.[9] However, the absence of population-based registries and standardized diagnostic pathways hinders early recognition and comprehensive characterization of affected individuals. International consensus guidelines emphasize the importance of

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early recognition and standardized diagnostic approaches[10] but these protocols have not been adapted to resource-limited settings. There is a critical gap in understanding the regional mutation spectrum, clinical presentation, and trajectory of LHON, which limits the development of diagnostic algorithms and genetic counseling strategies suited to local needs. Additionally, there are currently no evidence-based clinical diagnostic criteria tailored to the Colombian healthcare context.

This study aims to characterize the clinical, demographic, and genetic features of patients with genetically confirmed LHON in a multicenter Colombian cohort. Based on prior international evidence, we hypothesized that the MT-ND4 mutation would be the predominant genotype and that affected individuals would display clinical patterns consistent with previously described LHON populations. We also describe clinical features that may help ophthalmologists and neurologists recognize suspected LHON and refer patients for genetic confirmation in settings where molecular testing may be delayed or unavailable.

Materials and methods

This was a retrospective, multicenter cohort study conducted at five neuro-ophthalmology referral centers serving the Colombian Caribbean region. The study period spanned from January 2019 through December 2024. Neuro-ophthalmology consultation in this region is available mainly in Barranquilla, Cartagena, Valledupar, and Santa Marta; patients from peripheral departments often require referral to these cities for subspecialty assessment. Participating centers had access to the main diagnostic and supportive resources required for LHON evaluation and follow-up, including optic nerve and macular optical coherence tomography (OCT), automated visual field testing, visual evoked potentials, electrophysiology, and low-vision rehabilitation services. A retrospective design was chosen to enable the evaluation of real-world clinical, structural, and genetic data in patients with confirmed Leber hereditary optic neuropathy (LHON), a rare mitochondrial disorder for which prospective registries are not yet established in the country.

Due to the retrospective nature of the study and the ultra-low prevalence of LHON in the Colombian population, no formal sample size calculation was performed. Instead, we included all genetically confirmed cases identified across the study sites during the five-year period. This comprehensive inclusion strategy aimed to maximize cohort representativeness and descriptive power.

Patient identification and inclusion criteria

Patients were identified through a systematic search of both paper-based and electronic medical records using ICD-10 codes associated with optic neuropathies. These included H47.2 (optic atrophy), H48.8 (other disorders of the optic nerve and visual pathways), H46.X (optic neuritis), and H47.0 (unspecified optic nerve disorder). From this initial pool, cases were included if they met the following criteria: confirmed diagnosis of LHON by mtDNA testing (via targeted mutation analysis or full mitochondrial sequencing), age ≥ 10 years at diagnosis, and availability of comprehensive ophthalmologic evaluation including best corrected visual acuity (BCVA), visual field testing, and optic nerve optical coherence tomography (OCT). Genetic testing was processed through a centralized reference laboratory in Bogotá (Gencell Pharma / Genética Avanzada), using targeted mutation analysis or mitochondrial sequencing according to the test requested in routine care. In clinically suspected cases screened during record review, laboratory reports included assessment of primary and secondary/less common LHON-associated mitochondrial DNA variants; cases without pathogenic variants were excluded from the final cohort. The median longitudinal follow-up was 14.2 months (IQR 11.0–17.8), allowing the identification of progressive anatomical changes despite functional stability.

Exclusion criteria

Exclusion criteria were incomplete or inconclusive genetic results, absence of key visual or structural data, or documentation of a known alternative etiology for optic neuropathy (e.g., ischemic, inflammatory, toxic, or compressive causes).

Data collection procedures

Data were extracted using a standardized protocol to ensure consistency and reduce information bias. Sociodemographic variables included sex, age at diagnosis, municipality of residence, and socioeconomic classification based on Colombia's six-level stratification system.[11] In this system, socioeconomic stratum is assigned to residential properties; stratum 1 represents the lowest socioeconomic category and is commonly used in Colombian health research as a proxy for socioeconomic vulnerability rather than as a direct measure of individual income. Clinical history was assessed for relevant comorbidities and family history of LHON or unexplained vision loss, particularly among maternal relatives. Ophthalmologic parameters included BCVA (converted to LogMAR units), type of visual field defect, and funduscopic findings at baseline. Structural retinal data, specifically, RNFL and GCC thickness, were recorded from OCT reports when available. Standard automated perimetry was performed using the Humphrey Visual Field Analyzer 30–2 program. Visual field defect categories, including "absolute scotoma," were recorded as documented in the clinical perimetry report. Alcohol consumption history was systematically assessed from the medical record at the time of neuro-ophthalmology evaluation and recorded based on clinician documentation. Biochemical parameters such as serum vitamin B12 and folate were also documented. Management data included idebenone use, treatment-initiation dates when documented, and referral to low vision services. In cases of bilateral involvement, each eye was analyzed separately for structural and functional findings, though demographic and systemic data were linked to the individual as the unit of analysis.

Outcome measures

The primary outcome of interest was the clinical characterization of patients with genetically confirmed LHON, including visual acuity, visual field changes, optic nerve morphology, and OCT parameters at baseline and follow-up. Secondary outcomes included the relative frequency of specific mtDNA mutations and descriptive data on management strategies, such as idebenone use and low vision rehabilitation.

Bias control and missing data

Selection bias was minimized by systematically screening all potentially relevant ICD-10 entries, regardless of final diagnosis. Information bias was mitigated by applying uniform data collection criteria and excluding incomplete records. Missing data were present for ancillary laboratory variables (vitamin B12, folate, and vitamin B6), which were available for 18 of 21 participants. Analyses were performed using available data without imputation, and paired longitudinal tests used complete baseline – follow-up observations for each outcome.

Statistical analysis

Statistical analyses were conducted using R software version 4.5.2 (R Foundation for Statistical Computing, Vienna, Austria).[12] Categorical variables were summarized as absolute counts and percentages. Continuous variables were assessed for normality using the Shapiro-Wilk test and reported as medians with interquartile ranges (IQR) due to non-parametric distribution.

Paired comparisons between baseline and follow-up values were performed using the Wilcoxon signed-rank test. A two-tailed p-value $< .05$ was considered statistically significant. A post-hoc power analysis was conducted to assess sensitivity for detecting changes in key outcomes. All analyses were exploratory and intended to inform future prospective studies.

Ethical considerations

This study was classified as minimal-risk according to Colombian Ministry of Health Resolution 8430 of 1993. Ethical approval was obtained from the Bioethics Committee of Universidad del Sinú, Cartagena Campus (approval code OFT2023II3E). All data were anonymized prior to analysis. Given the

retrospective nature of the study, individual informed consent was waived in accordance with national ethical guidelines.

Results

Patient identification and genetic confirmation

Between 2019 and 2024, a total of 1,100 medical records were reviewed from neuro-ophthalmology services in five departments of the Colombian Caribbean region. Thirty-seven patients were initially identified with suspected Leber Hereditary Optic Neuropathy (LHON) based on clinical presentation and diagnostic coding. Among them, 21 individuals (56.8%) had genetic confirmation of pathogenic mitochondrial DNA (mtDNA) variants, constituting the final study cohort. A total of 42 eyes were analyzed. All included patients had complete demographic and core ophthalmologic data, and none were lost to follow-up after genetic confirmation (Figure 1). Among the 16 clinically suspected cases excluded from the final cohort, genetic testing assessed both primary and secondary/less common LHON-associated mitochondrial DNA variants, and all were negative.

Demographic and geographic characteristics

The median age at diagnosis was 37 years (interquartile range [IQR] 27–42). Male patients represented the majority ($n = 17$, 81.0%), with a median age of 34 years (IQR 22–42), while female patients ($n = 4$, 19.0%) were diagnosed at a median age of 39 years (IQR 34–58). Most participants belonged

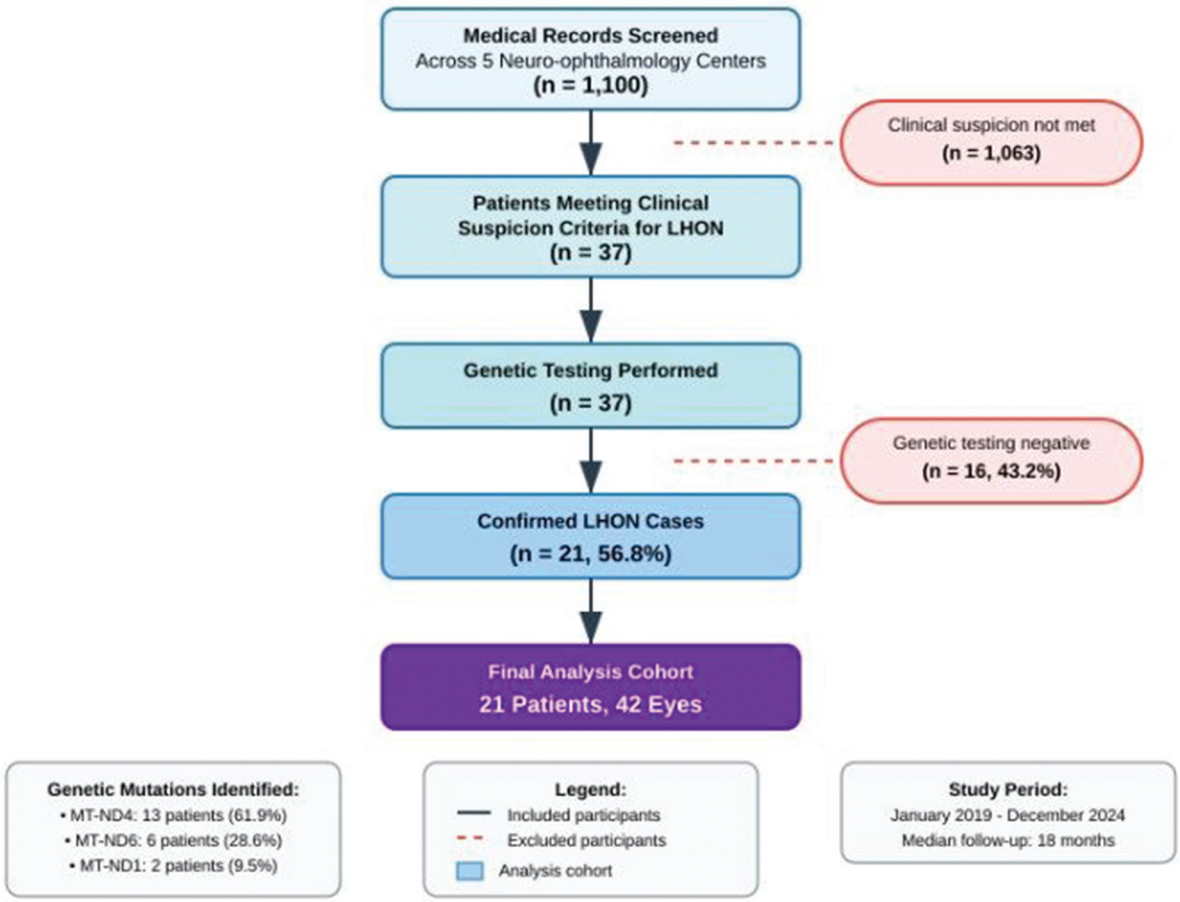


Figure 1. Patient flow diagram – screening, inclusion, and genetic confirmation. Medical records from five neuro-ophthalmology centers were screened ($n = 1,100$). Patients meeting clinical suspicion criteria for Leber hereditary optic neuropathy (LHON) underwent genetic testing ($n = 37$); 21 patients had genetically confirmed LHON and were included in the final analysis (42 eyes). Sixteen clinically suspected cases were excluded due to negative genetic testing for LHON-associated mitochondrial DNA variants (primary and secondary/less common variants).

to socioeconomic strata 1 (71.4%), with the remaining 28.6% classified as stratum 2. The primary municipalities of origin were Cartagena (52.4%) and Barranquilla (23.8%), with smaller numbers from Sucre, Magdalena, Cesar, and La Guajira.

Clinical features and comorbidities

Initial diagnoses included "optic nerve disorder" in 66.7% of patients and "optic neuritis" in 23.8% (bilateral in four cases, unilateral in one). A family history suggestive of LHON was reported in seven patients (33.3%), primarily involving siblings, nephews, uncles, or fathers. Alcohol consumption history was assessed in all patients; no participant had documentation compatible with problematic alcohol use, although occasional alcohol consumption was reported in some cases. Two patients had concurrent neurologic diagnoses (Parkinson's disease and a demyelinating disorder consistent with multiple sclerosis) and underwent additional evaluation (brain magnetic resonance imaging and cerebrospinal fluid analysis) to assess alternative etiologies and LHON-plus phenotypes; one case was considered consistent with an LHON-plus phenotype (Table 1).

Genetic analysis

All 21 patients had a single confirmed pathogenic mtDNA variant. The most frequent mutation was m.11778G>A in the MT-ND4 gene, observed in 13 patients (61.9%, 95% CI: 40.9–79.2%). The second most common was m.14484T>C in MT-ND6 (6 patients, 28.6%, 95% CI: 13.8–50.0%), followed by m.3460G>A in MT-ND1 (2 patients, 9.5%, 95% CI: 2.7–28.9%). No dual or multiple mutations were detected.

All patients with the m.11778G>A mutation were male, with a median age at diagnosis of 39 years (IQR 27–43). This subgroup exhibited the highest mutation-specific prevalence in the cohort (Figure 2).

Ophthalmological evaluation

Visual function

Baseline best-corrected visual acuity (BCVA) showed a median LogMAR of 1.0 (IQR 0.8–1.2), equivalent to 20/200 Snellen. At follow-up, visual acuity remained stable (LogMAR 1.0; IQR 0.7–1.3; $p = .62$). The effect size for this change was small ($r = 0.326$), and post-hoc power was insufficient (power = 0.095).

Visual field defects

Visual field testing identified central scotomas in 38.1% of eyes, absolute scotomas in 31.0%, and paracentral defects in 19.0%. In this study, "absolute scotoma" refers to a dense visual field defect documented in the clinical Humphrey 30–2 report as not perceived at the maximum stimulus intensity in the affected test locations. Centrocecal and nasal losses were each noted in 11.9% of cases. No statistically significant longitudinal changes were observed in the distribution of these defects (McNemar $p > .5$ for all categories).

Fundus examination

At baseline, 47.6% of eyes exhibited temporal optic disc pallor, while 45.2% showed generalized pallor. Optic disc edema (11.9%) and

Table 1. Baseline characteristics of Colombian patients with genetically confirmed LHON ($n = 21$).

Characteristic	Value	95% CI
Age at diagnosis, y	37 (27–42)*	29.6–42.7
Male sex	17 (81.0%)	60.0–92.3
m.11778G>A (MT-ND4)	13 (61.9%)	40.9–79.2
m.14484T>C (MT-ND6)	6 (28.6%)	13.8–50.0
m.3460G>A (MT-ND1)	2 (9.5%)	2.7–28.9
Family history of LHON	7 (33.3%)	17.2–54.6%
Low-vision services at baseline	0 (0%)	0–15.5

*Median (IQR); otherwise n (%). 95% confidence intervals calculated using Wilson's method.

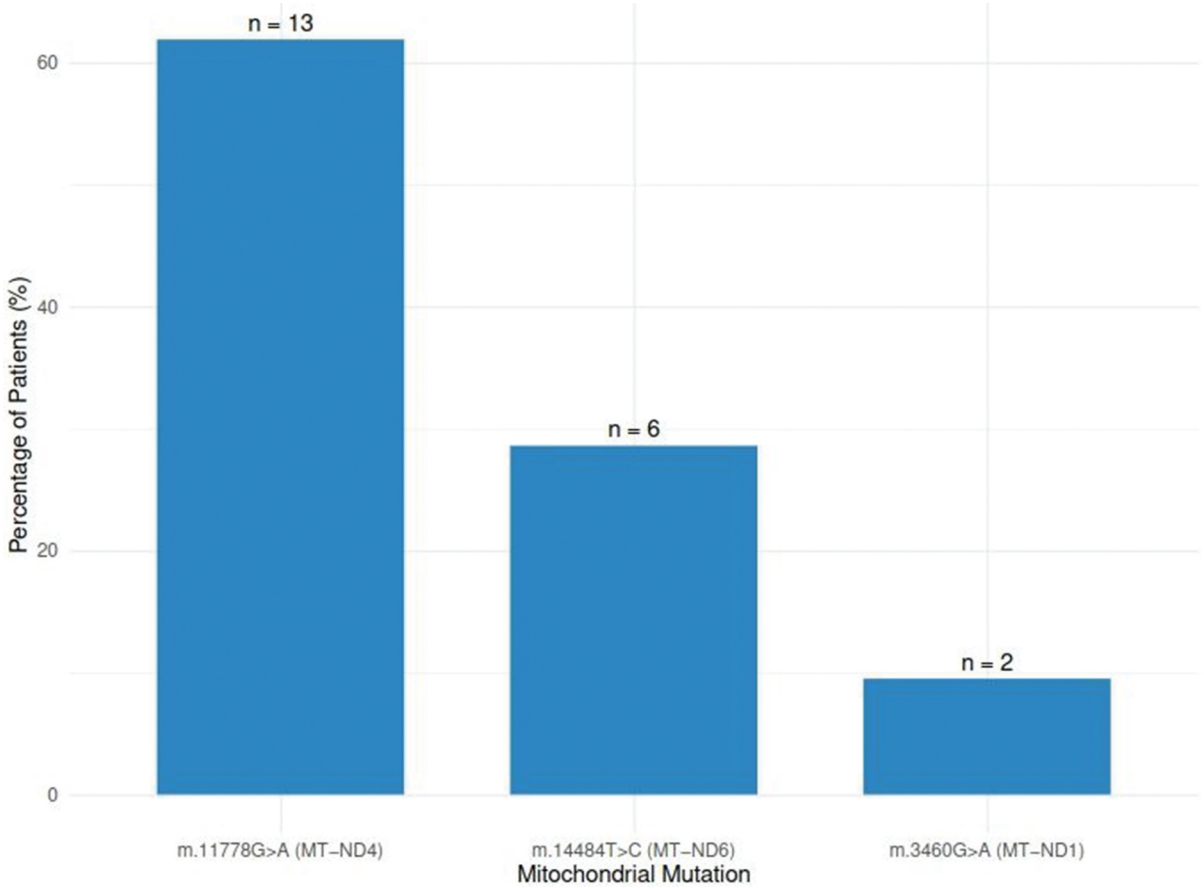


Figure 2. Distribution of pathogenic mtDNA mutations among Colombian LHON patients.

telangiectasias (7.1%) were uncommon and co-occurred in some patients.

Optical coherence tomography

Initial retinal nerve fiber layer (RNFL) thickness had a median of 73.5 µm (IQR 61.2–106.2), and ganglion cell complex (GCC) thickness was 60.5 µm (IQR 52.2–67.0). Follow-up revealed a statistically significant reduction in both parameters: 1) RNFL decreased by a median of 11.0 µm ($p = .0005$; $r = 0.721$). 2) GCC decreased by a median of 2.6 µm ($p = .0040$; $r = 0.582$). These changes suggest progressive structural retinal degeneration despite stable visual acuity (Table 2).

Post-hoc power analysis

A post-hoc power analysis was conducted to assess the adequacy of the sample size to detect significant longitudinal changes. The power to detect change in RNFL thickness was high (power = 0.957), reflecting a large effect size (Cohen's d = 0.581). For GCC, the statistical power was moderate (power = 0.534). Visual acuity changes were underpowered for detection (power = 0.095).

Treatment and supportive care

Fourteen patients (66.7%) received idebenone therapy at some point during the study. The majority (71.4%) were enrolled in low-vision rehabilitation

Table 2. Longitudinal changes in visual and structural parameters (per eye).

Parameter	n	Baseline	Follow-up	Change (95% CI)	p-value
Visual acuity (LogMAR)	21	1.0 (0.8–1.2)	1.0 (0.7–1.3)	−0.04 (−0.19 to 0.10)	.62
RNFL (µm)	42	73.5 (61.2–106.2)	65.0 (58.2–78.8)	−11.0 (−17.0 to −5.1)	$p < .001$
GCC (µm)	42	60.5 (52.2–67.0)	56.0 (51.0–60.8)	−2.6 (−5.1 to −0.1)	$p < .001$

p-values from Wilcoxon signed-rank test. *$p < .01$.

services. The time from symptom onset or genetic confirmation to idebenone initiation was not consistently documented in the medical records and therefore could not be analyzed. Serum levels of vitamin B12, folic acid, and vitamin B6 were available for 18 participants (85.7%) and remained within normal ranges for all.

Discussion

To our knowledge, this study presents the largest known cohort of genetically confirmed Leber hereditary optic neuropathy (LHON) in Colombia. The predominant molecular finding was the m.11778G>A mutation in the MT-ND4 gene, aligning with global data reporting this variant in approximately 60–70% of cases.[13] Our cohort demographics align with international registries in Europe and North America, where similar age and sex distributions have been documented.[14,15]

Regional data from Latin America remain limited, but available cohorts from Chile, Cuba, Brazil, and Argentina support a similar male predominance and a mutation spectrum in which m.11778G>A is frequently reported.[6–8,16] Differences in referral pathways and access to genetic testing can influence case ascertainment and the apparent timing of diagnosis across countries. In this context, our findings place the Colombian cohort within regional patterns while reinforcing the need for standardized diagnostic pathways and multicenter registries to improve comparability across Latin America.

Structurally, the longitudinal analysis revealed a statistically significant reduction in both retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thickness during follow-up. These findings suggest that LHON progression is detectable through optical coherence tomography (OCT), even in the absence of changes in visual acuity. The lack of significant BCVA variation is compatible with previous reports showing that most patients with m.11778G>A do not experience spontaneous visual recovery.[17–19] Post-hoc power analysis confirmed that the sample was sufficient to detect changes in RNFL but underpowered for GCC and visual acuity, underscoring the value of structural biomarkers over functional ones in short-term follow-up.

Visual field analysis showed persistent central and centrocecal scotomas, with no meaningful variation between initial and follow-up assessments. The fundoscopic findings of optic disc pallor, either temporal or generalized, were present in most cases and are in line with the classic neuro-ophthalmic presentation of LHON.[20,21] These structural changes further validate the pathogenic role of mitochondrial dysfunction in retinal ganglion cell apoptosis and axonal loss.[22,23]

Our data do not support clinical improvement over time, but they do demonstrate measurable anatomic progression in retinal degeneration. This highlights the utility of OCT in both diagnosis and follow-up, particularly in regions where access to molecular testing may be delayed. However, the diagnostic process remains protracted. The median interval between symptom onset and definitive diagnosis was approximately one year, suggesting that LHON continues to be misrecognized or underdetected at first contact, even in tertiary care settings.

The regional care context is relevant to this diagnostic delay. In the Colombian Caribbean, neuro-ophthalmology care is concentrated in selected referral cities rather than uniformly distributed across all departments. Local specialist experience indicates that other frequent causes of optic atrophy evaluated in this setting include neuromyelitis optica spectrum disorder/Devic disease, inflammatory optic neuritis, tumor-related or compressive optic neuropathies, and toxic-metabolic optic neuropathies. These conditions are part of the clinical differential diagnosis at presentation, but the present cohort cannot estimate their relative frequency because the analytic dataset was restricted to genetically confirmed LHON cases.

Several limitations must be acknowledged. First, the retrospective design limits the uniformity of follow-up intervals and introduces potential information bias, particularly in subjective outcomes such as symptom duration. Second, although the study includes the largest confirmed LHON cohort in Colombia, the sample remains limited for mutation-specific or sex-stratified analyses. Third, the study was not designed to estimate the relative

frequency of LHON compared with other causes of optic atrophy in the Colombian Caribbean. The screening pool of 1,100 records was used to identify suspected LHON cases for genetic confirmation, but it was not systematically classified by final optic atrophy etiology. Fourth, quadrant-level RNFL measurements were not consistently available in the study database or OCT exports, and RNFL was recorded as a global average only, precluding sectoral RNFL analyses. Structural measurements were obtained across different OCT platforms, which can introduce inter-device variability despite routine clinical quality control at each center. Fifth, idebenone access in Colombia was limited because the drug was not routinely available through ordinary commercial channels. During the study period, it could be obtained only case by case through the Colombian Medicamento Vital No Disponible pathway, a regulatory mechanism that allows exceptional patient-specific access to medicines without routine local market availability when clinically justified.[24,25] Because treatment-initiation timing was not consistently documented, this cohort cannot support treatment-effect analyses. Finally, the power to detect changes in visual acuity was insufficient, suggesting that larger samples or longer follow-up periods may be necessary to assess potential functional outcomes.

Despite these constraints, this study provides the first detailed description of the clinical and structural trajectory of LHON in a Colombian population. It reinforces the predominance of the m.11778G>A variant and offers evidence of measurable disease progression through OCT-based metrics. These results should inform future research on diagnostic accuracy, early intervention strategies, and long-term outcomes.

The prolonged diagnostic interval observed in this cohort reflects the lack of structured care pathways for mitochondrial optic neuropathies in Colombia. Although this study did not evaluate diagnostic algorithms, the consistency of clinical findings, particularly bilateral, painless central vision loss in young males with OCT evidence of optic atrophy, supports earlier clinical suspicion and referral for genetic confirmation. Future research should prioritize prospective validation of diagnostic pathways in real-world settings. National registries and longitudinal follow-up cohorts will also be needed to characterize phenotypic variability, diagnostic timing, treatment access, and long-term outcomes in Latin American LHON populations.

Conclusion

This study confirms that Colombian patients with LHON share core clinical and molecular features with global populations, notably the predominance of the m.11778G>A mutation and limited visual recovery during follow-up. The consistent presentation of bilateral, painless central vision loss and progressive retinal thinning underscores the need for earlier recognition and referral for genetic confirmation. These findings should be interpreted within the regional care context, where neuro-ophthalmology services are concentrated in selected referral cities and access to idebenone depends on patient-specific regulatory pathways. Future efforts should focus on validating diagnostic algorithms, strengthening referral networks for genetic testing and follow-up, and integrating LHON into rare disease care strategies in Colombia.

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All authors reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Author contributions

CRediT: **Jhon Jairo Cuevas Villamizar:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing; **Mónica Paola Contreras Amorocho:** Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing; **María Del Socorro Cabarcas Solano:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing; **Heidy Patricia Visbal Alemán:** Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – original draft; **Enrique Carlos Ramos Clason:** Data curation, Formal analysis, Methodology, Software, Validation, Visualization, Writing – original draft.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The dataset analyzed in this study is not publicly available due to institutional and legal restrictions but may be made available upon reasonable request to the corresponding author.

References

1. Newman NJ. Hereditary optic neuropathies: from the mitochondria to the optic nerve. *Am J Ophthalmol*. 2005;140(3):517–523. doi: 10.1016/j.ajo.2005.03.017.
2. Mackey DA, Oostra RJ, Rosenberg T, et al. Primary pathogenic mtDNA mutations in multigeneration pedigrees with Leber hereditary optic neuropathy. *Am J Hum Genet*. 1996;59:481–485.
3. Yu-Wai-Man P, Turnbull DM, Chinnery PF. Leber hereditary optic neuropathy. *J Med Genet*. 2002;39 (3):162–169. doi: 10.1136/jmg.39.3.162.
4. Mackey DA, Ong J-S, MacGregor S, et al. Is the disease risk and penetrance in Leber hereditary optic neuropathy actually low? *Am J Hum Genet*. 2023;110 (1):170–176. doi: 10.1016/j.ajhg.2022.11.014.
5. Lopez Sanchez MIG, Kearns LS, Staffieri SE, et al. Establishing risk of vision loss in Leber hereditary optic neuropathy. *Am J Hum Genet*. 2021;108 (11):2159–2170. doi: 10.1016/j.ajhg.2021.09.015.
6. Romero P, Fernández V, Slabaugh M, et al. Pan-American mDNA haplogroups in Chilean patients with Leber's hereditary optic neuropathy. *Mol Vis*. 2014;20:334–340.
7. Santiesteban-Freixas R, Rodríguez-Hernández M, Mendoza-Santiesteban CE, et al. Clinical manifestation and molecular identification of patients with Leber's hereditary optic neuropathy in a national reference center for neuro-ophthalmology in Cuba. *Rev Neurol*. 1999;29(5):408–415. doi: 10.33588/rn.2905.99208.
8. Miranda PMDAD, Matilde da Silva-Costa S, Balieiro JC, et al. Multiplex MALDI-TOF MS detection of mitochondrial variants in Brazilian patients with hereditary optic neuropathy. *Mol Vis*. 2016;22:1024–1035.
9. Instituto Nacional de Salud. Informe de eventos de enfermedades huérfanas-raras. Colombia - 2023. INS; 2023.
10. Carelli V, Carbonelli M, de Coo IF, et al. International consensus statement on the clinical and therapeutic management of Leber hereditary optic neuropathy. *J Neuro-Ophthalmol Off J N Am Neuro-Ophthalmol Soc*. 2017;37(4):371–381. doi: 10.1097/WNO.0000000000000570.
11. Departamento Administrativo Nacional de Estadística (DANE). Estratificación socioeconómica para servicios públicos domiciliarios [Internet]. Bogotá, Colombia: DANE. https://www.dane.gov.co/index.php/servicios-al-ciudadano/servicios-informacion/estratificacion-socioeconomica.
12. R Core Team. R: a language and environment for statistical computing. Version 4.5.2 (2025–10-31) – "[Not] part in a rumble" [Internet]. Vienna, Austria: R Foundation for statistical computing; 2025. https://www.R-project.org/.
13. Yu-Wai-Man P, Newman NJ, Carelli V, et al. Natural history of patients with Leber hereditary optic neuropathy-results from the REALITY study. *Eye Lond Engl*. 2022;36(4):818–826. doi: 10.1038/s41433-021-01535-9.
14. Stramkauskaitė A, Povilaityte I, Glebauskiene B, Liutkeviciene R. Clinical overview of Leber hereditary optic neuropathy. *Acta Medica Litu*. 2022;29(1):19. doi: 10.15388/amed.2022.29.1.19.
15. Poincenot L, Pearson AL, Karanjia R. Demographics of a large international population of patients affected by Leber's hereditary optic neuropathy. *Ophthalmology*. 2020;127(5):679–688. doi: 10.1016/j.ophtha.2019.11.014.
16. Buonfiglio PI, Menazzi S, Francipane L, et al. Mitochondrial DNA variants in a cohort from Argentina with suspected Leber's hereditary optic neuropathy (LHON). *PLOS ONE*. 2023;18(2):e0275703. doi: 10.1371/journal.pone.0275703.
17. Carelli V, Ross-Cisneros FN, Sadun AA. Mitochondrial dysfunction as a cause of optic neuropathies. *Prog Retin Eye Res*. 2004;23(1):53–89. doi: 10.1016/j.preteyeres.2003.10.003.
18. Shemesh A, Sood G, Blair K, Margolin E. Leber hereditary optic neuropathy (LHON). StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK482499/. 2025 [cited July 24, 2025]. Accessed July 24, 2025.
19. Nikoskelainen E, Hassinen IE, Paljärvi L, Lang H, Kalimo H. Leber's hereditary optic neuroretinopathy, a mitochondrial disease? *Lancet Lond Engl*. 1984;2 (8417–8418):1474. doi: 10.1016/s0140-6736(84)91669-6.
20. Barboni P, Carbonelli M, Savini G, et al. Natural history of Leber's hereditary optic neuropathy: longitudinal analysis of the retinal nerve fiber layer by optical

coherence tomography. *Ophthalmology*. 2010;117 (3):623–627. doi: 10.1016/j.ophtha.2009.07.026.

21. La Morgia C, Cascavilla ML, De Negri AM, et al. Recognizing Leber's hereditary optic neuropathy to avoid delayed diagnosis and misdiagnosis. *Front Neurol*. 2024;15:1466275. doi: 10.3389/fneur.2024.1466275.
22. Sadun AA, Win PH, Ross-Cisneros FN, Walker SO, Carelli V. Leber's hereditary optic neuropathy differentially affects smaller axons in the optic nerve. *Trans Am Ophthalmol Soc*. 2000;98:223–232. discussion 232-235.
23. Sadun AA, Carelli V. Mitochondrial function and dysfunction within the optic nerve. *Arch Ophthalmol Chic Ill 1960*. 2003;121(9):1342–1343. doi: 10.1001/archopht.121.9.1342-b.
24. Instituto Nacional de Vigilancia de Medicamentos y Alimentos (Invima). Medicamentos vitales no disponibles [Internet]. Bogotá, Colombia. https://www.invima.gov.co/productos-vigilados/medicamentos-y-productos-biologicos/medicamentos-vitales-no-disponibles.
25. Ministerio de Salud y Protección Social de Colombia. Decreto 481 de 2004: por el cual se dictan normas tendientes a incentivar la oferta de medicamentos vitales no disponibles en el país [Internet]. Bogotá, Colombia. https://www.invima.gov.co/biblioteca/decreto-481-2004-medicamentos-vitales-no-disponibles. 2004.