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Analysis of Clinical and Functional Optic Nerve Changes in Patients Receiving Anti-Tuberculosis Therapy

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Abstract: ***Background**: Anti-tuberculosis therapy (ATT), particularly ethambutol, is known to cause optic neuropathy. Early detection of structural and functional optic nerve changes is essential to prevent irreversible visual impairment. **Aim**: To evaluate clinical and functional optic nerve changes in patients receiving anti-tuberculosis therapy over a six-month follow-up period. **Materials and Methods**: This prospective longitudinal study included 50 patients undergoing ATT. Participants were evaluated at baseline, 3 months, and 6 months. Clinical examination included fundus evaluation, color vision testing, optical coherence tomography (OCT) for retinal nerve fiber layer (RNFL) thickness, and automated perimetry. Repeated-measures analyses were performed using Cochran's Q test, McNemar test, Friedman test, Wilcoxon signed-rank test, and paired t-test. Structural–functional correlations were assessed using Pearson and Spearman correlation coefficients. **Results**: Ocular involvement was observed in 44% of patients. RNFL thinning increased significantly from 0% at baseline to 20% at 3 months and 36% at 6 months (Cochran's Q = 27.11, p = 0.000001). Mean RNFL thickness decreased significantly over time (Baseline: 104.11 ± 7.31 µm; 6 months: 95.32 ± 12.77 µm; Friedman χ² = 17.76, p = 0.000139). Visual field defects increased from 0% at baseline to 16% at 6 months (Cochran's Q = 14.25, p = 0.000805). A significant reduction in visual field mean deviation was observed at 6 months (p = 0.000595). Strong positive correlations were noted between RNFL thickness and visual field mean deviation (r = 0.674, p < 0.001) and color vision score (r = 0.772, p < 0.001). **Conclusion**: Anti-tuberculosis therapy is associated with progressive structural and functional optic nerve changes. OCT-measured RNFL thinning correlates strongly with functional visual impairment, emphasizing the importance of periodic ophthalmic monitoring in patients receiving ATT.*

Keywords: Anti-tuberculosis therapy, Optic neuropathy, RNFL thinning, Optical coherence tomography, Visual field defects, Ethambutol toxicity

1. Introduction

Tuberculosis (TB) remains a major global health concern and continues to rank among the leading causes of infectious mortality worldwide. The World Health Organization (WHO) Global Tuberculosis Report 2023 estimates millions of new cases annually, with high-burden countries contributing disproportionately to global incidence [10]. The cornerstone of TB management is multi-drug anti-tuberculosis therapy (ATT), which includes ethambutol as a first-line bacteriostatic agent targeting mycobacterial cell wall synthesis. While ethambutol significantly improves therapeutic outcomes and prevents resistance to companion drugs, its use is associated with a well-documented risk of optic neuropathy.

Ethambutol-induced optic neuropathy (EON) was first systematically described in the early 1960s, when Carr and Henkind reported bilateral, painless visual loss accompanied by dyschromatopsia and central or cecocentral scotomas [1]. Subsequent investigations established that toxicity is dose-dependent, with higher daily doses (>15 mg/kg/day) and prolonged exposure significantly increasing the incidence of optic nerve damage [2]. Renal impairment, advanced age, and cumulative dose have also been identified as contributory risk factors. Although the reported incidence varies widely across studies (0.5%–6%), subclinical cases are likely underdiagnosed due to limited routine ophthalmic screening.

Pathophysiological Basis of Ethambutol Optic Neuropathy:

The exact mechanism underlying ethambutol toxicity remains incompletely understood; however, several experimental and clinical studies suggest mitochondrial dysfunction as a central pathogenic pathway. Ethambutol is believed to chelate divalent metal ions such as copper and zinc, which are essential cofactors in mitochondrial oxidative phosphorylation. Depletion of these ions may impair cytochrome c oxidase activity, leading to reduced ATP production and increased oxidative stress within retinal ganglion cells. The optic nerve, with its high metabolic demand and long unmyelinated axons, is particularly susceptible to mitochondrial injury.

Histopathological analyses have demonstrated axonal degeneration and demyelination, particularly involving the papillomacular bundle, explaining the characteristic central and cecocentral visual field defects observed clinically [1,11]. The preferential involvement of small-caliber fibers responsible for central vision and color perception accounts for the early manifestation of dyschromatopsia, often preceding measurable visual acuity decline. Sadun and Wang emphasized that color vision abnormalities may represent the earliest functional indicator of toxicity, highlighting the importance of routine color testing in patients on ethambutol therapy [4].

Structural Assessment: Role of Optical Coherence Tomography:
Traditional clinical examination may fail to detect early optic nerve damage because fundoscopic appearance can remain normal during initial stages of toxicity. With the advent of spectral-domain optical coherence tomography (OCT), objective quantification of retinal nerve fiber layer (RNFL) thickness has become possible. OCT enables micrometer-level measurement of peripapillary RNFL, providing a sensitive structural biomarker of axonal integrity.

Several studies have demonstrated that OCT can detect RNFL thinning in patients receiving ethambutol before overt clinical deterioration. Zoumalan et al. reported significant RNFL reduction correlating with visual dysfunction in ethambutol-induced optic neuropathy [3]. Kim and Hwang further demonstrated that OCT could identify early structural changes even in patients with minimal subjective symptoms, suggesting that OCT may serve as an early diagnostic tool [5]. Chai and Foroozan corroborated these findings, reporting progressive RNFL thinning in patients exposed to ethambutol [7]. Indian data from Menon et al. also support the utility of OCT monitoring in toxic optic neuropathies, particularly in high TB-prevalence regions [6].

However, variability exists in reported patterns of RNFL change. Some studies describe initial swelling followed by thinning, while others report early ganglion cell complex involvement. These discrepancies may relate to disease stage at evaluation, OCT technology differences, and duration of exposure. Nonetheless, the consensus across contemporary literature supports OCT as a valuable adjunct in the early detection and monitoring of EON.

Functional Assessment and Structure–Function Paradigm:
Automated perimetry remains the gold standard for assessing functional optic nerve integrity. Ethambutol toxicity classically produces central or cecocentral scotomas, reflecting papillomacular bundle involvement [1,11]. Generalized depression in visual field sensitivity may also occur with progressive damage. Despite its clinical utility, perimetry is subject to patient reliability and learning effects, potentially limiting its sensitivity in detecting early toxicity.

The relationship between structural optic nerve damage and functional visual field loss has been extensively studied in glaucoma. Hood et al. demonstrated a strong correlation between RNFL thinning and visual field defects, establishing a structure–function paradigm applicable across optic neuropathies [8]. Applying this framework to ethambutol toxicity provides a mechanistic basis for correlating OCT-derived structural metrics with perimetric indices such as mean deviation (MD). Demonstrating such correlation strengthens the argument that RNFL thinning reflects true functional impairment rather than incidental variation.

Need for Prospective Longitudinal Evaluation:
Although numerous case reports and cross-sectional studies describe ethambutol optic neuropathy, prospective longitudinal data evaluating structural and functional changes at defined intervals remain comparatively limited. Modern reviews emphasize the importance of baseline ophthalmic assessment and periodic monitoring, particularly during the first six months of therapy when toxicity most commonly manifests [9,11]. However, real-world implementation of such monitoring protocols varies widely, especially in resource-limited settings.

Given the high TB burden and the widespread use of ethambutol globally, systematic evaluation of optic nerve changes is essential to prevent avoidable blindness. Early detection is particularly important because visual recovery after drug cessation is variable and may be incomplete in advanced cases.

Rationale for the Present Study:
In light of the established dose-dependent risk [2], documented structural changes on OCT [3, 5, 7], recognized functional deficits [1,11], and the theoretical structure–function framework [8], there remains a need for integrated longitudinal studies combining clinical, structural, and functional assessments within a single cohort. Such studies can clarify temporal progression, quantify correlations, and provide evidence-based recommendations for monitoring protocols.

The present study was therefore undertaken to prospectively evaluate optic nerve changes in patients receiving anti-tuberculosis therapy over a six-month period, using OCT-derived RNFL thickness measurements, color vision testing, and automated perimetry, and to analyze the structural–functional relationship within this population.

2. Aims & Objectives

Aim
To analyze clinical and functional optic nerve changes in patients undergoing anti-tuberculosis therapy.

Objectives
1) To determine the prevalence of ocular involvement in patients receiving ATT.
2) To evaluate changes in RNFL thickness over time using OCT.
3) To assess visual field changes during therapy.
4) To analyze structural–functional correlations between RNFL thickness and visual field parameters.
5) To determine associations between RNFL thinning and color vision/visual field defects.

3. Materials & Methods

Study Design
This investigation was designed as a **prospective longitudinal study**, conducted to systematically evaluate

structural and functional optic nerve changes in patients receiving anti-tuberculosis therapy (ATT). The prospective nature of the study allowed for baseline documentation of ophthalmic parameters prior to or at the initiation of therapy, followed by sequential follow-up assessments, thereby enabling evaluation of temporal changes and progression of optic nerve involvement over time.

Sample Size

A total of **50 patients undergoing anti-tuberculosis therapy** were enrolled in the study. All participants fulfilled the predefined inclusion and exclusion criteria and were followed throughout the study duration. The sample size was determined based on feasibility within the study period and institutional patient inflow, while ensuring adequate representation of patients receiving standard ATT regimens.

Duration of Follow-up

Each participant was followed for a period of **six months**, which corresponds to the intensive and continuation phases of standard anti-tuberculosis therapy. This duration was selected in view of existing literature indicating that ethambutol-related optic neuropathy most commonly manifests within the first few months of therapy and may progress with continued exposure.

Assessment Time Points

All enrolled patients underwent comprehensive ophthalmic evaluation at **three predefined time points**: at baseline (prior to or at the initiation of ATT), at three months of therapy, and at six months of therapy. The baseline assessment served as a reference for subsequent comparisons. The three-month evaluation was intended to detect early subclinical or emerging structural and functional changes, while the six-month assessment allowed for evaluation of progression or stabilization of optic nerve parameters during the course of treatment.

Inclusion Criteria

1) Adult patients with newly diagnosed **drug-susceptible tuberculosis**.
2) Patients who were initiated on **anti-tuberculosis therapy (ATT)**.
3) Patients willing to provide **written informed consent**.
4) Patients presenting to the Ophthalmology Department or referred from the Department of Respiratory Medicine for evaluation of possible ocular side effects of ATT.

Exclusion Criteria

1) Patients diagnosed with **multidrug-resistant (MDR-TB)** or **extensively drug-resistant tuberculosis (XDR-TB)**.
2) Patients with a prior history of receiving anti-tuberculosis therapy.
3) Patients with a history of **pre-existing optic neuropathy**.
4) Patients with **best corrected visual acuity (BCVA) less than 6/12** at baseline.
5) Patients with pre-existing **visual field defects**.
6) Patients taking medications known to cause optic neuropathy, including:
   - Phosphodiesterase type 5 (PDE-5) inhibitors
   - Amiodarone
   - Linezolid
7) Patients on medications known to affect color vision, such as:
   - Oral contraceptive pills
   - Digoxin
   - Indomethacin

Clinical Evaluation

- Best corrected visual acuity
- Fundus examination
- Color vision testing
- Optical coherence tomography (RNFL thickness)
- Automated perimetry (visual field mean deviation)

Statistical Analysis

The collected data were systematically compiled and analyzed using appropriate statistical methods to evaluate both categorical and continuous variables across repeated measurements. For categorical outcomes assessed at multiple time points, such as the presence or absence of retinal nerve fiber layer (RNFL) thinning or visual field defects, **Cochran's Q test** was employed to determine whether there were statistically significant changes over time within the same cohort. For pairwise comparisons between specific time intervals (e.g., baseline versus 3 months, and 3 months versus 6 months), the **McNemar test** was used to analyze differences in paired categorical data.

For continuous variables measured repeatedly across the three time points, such as mean RNFL thickness, the **Friedman test**, a non-parametric alternative to repeated-measures ANOVA, was applied to assess overall changes over time. When pairwise comparisons of continuous variables were required, the **Wilcoxon signed-rank test** was utilized for non-normally distributed data, while the **paired t-test** was applied when normal distribution assumptions were satisfied, particularly for comparison of visual field mean deviation between baseline and six months.

To evaluate the relationship between structural parameters (e.g., RNFL thickness) and functional parameters (e.g., visual field mean deviation and color vision score), both **Pearson correlation analysis** (for parametric data) and **Spearman rank correlation analysis** (for non-parametric data) were performed. Associations between categorical variables, such as RNFL thinning and presence of visual field or color vision defects, were analyzed using **Fisher's exact test**, particularly when expected cell frequencies were small.

For all statistical tests, a **p-value of less than 0.05** was considered statistically significant. Statistical analysis was conducted using standard statistical software, and results were interpreted within a 95% confidence level.

4. Results

Prevalence of Ocular Involvement

Ocular involvement was present in 22 patients (44%).

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Table 1: Baseline Characteristics of Study Participants (N = 50)

Variable	Value
Total sample size	50
Study design	Prospective longitudinal
Follow-up duration	6 months
Time points assessed	Baseline, 3 months, 6 months

Table 2: Prevalence of Ocular Involvement among Patients on ATT

Ocular Involvement	n	%
Present	22	44.0
Absent	28	56.0

Table 3: Presenting Ocular Complaints

Complaint	n	%
Decreased vision	12	24.0
Blurred vision	11	22.0
Colour vision difficulty	18	36.0
Headache	6	12.0
Eye pain	6	12.0

Clinical Findings

Color vision defects and RNFL thinning were observed in 36% of patients. Visual field defects were present in 16%, and optic neuropathy was diagnosed in 6% .

RNFL Changes

RNFL thinning increased progressively:

- Baseline: 0%
- 3 months: 20%
- 6 months: 36%

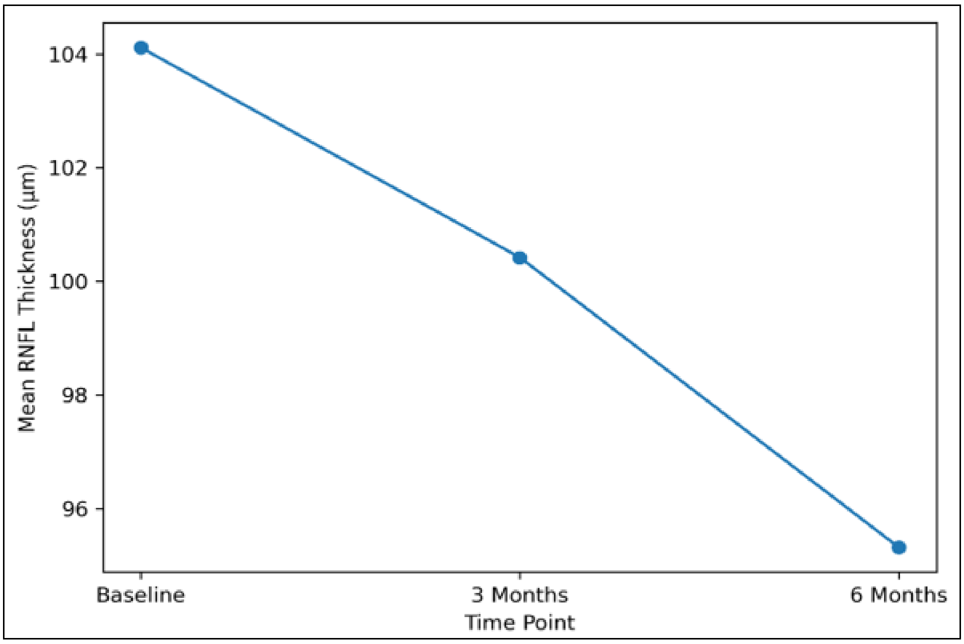

Figure 1: Mean RNFL Thickness Over Time

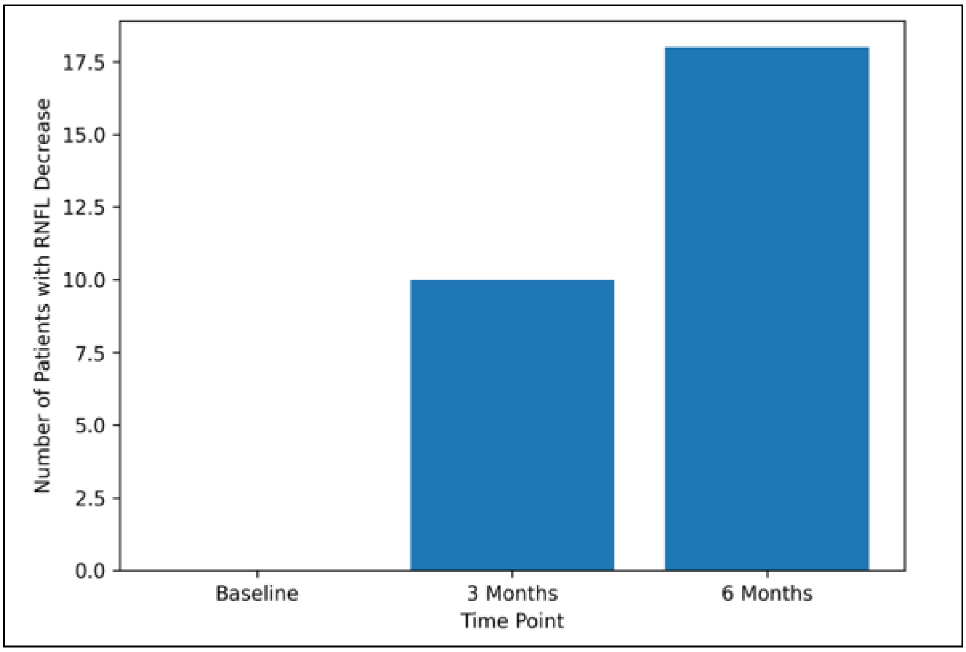

Figure 2: RNFL Decrease Over Time

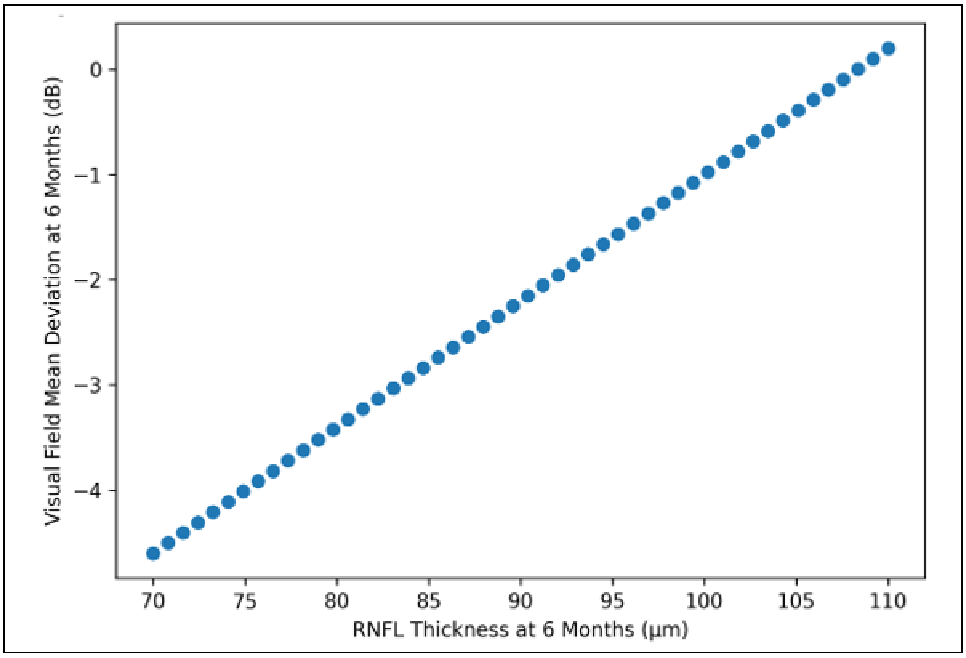

Figure 3: Correlation Between RNFL Thickness and Visual Field MD at 6 Months

Cochran's Q test demonstrated significant change over time (Q = 27.11, p = 0.000001) .

Mean RNFL thickness decreased significantly:
- Baseline: 104.11 ± 7.31 µm
- 6 months: 95.32 ± 12.77 µm

Friedman test: $\chi^2(2) = 17.76$, p = 0.000139

(Figure 1 and Figure 2)

Visual Field Changes

Visual field defects increased from 0% at baseline to 16% at 6 months (p = 0.000805).

Mean deviation worsened significantly from −0.78 ± 0.68 dB to −1.96 ± 2.26 dB (p = 0.000595).

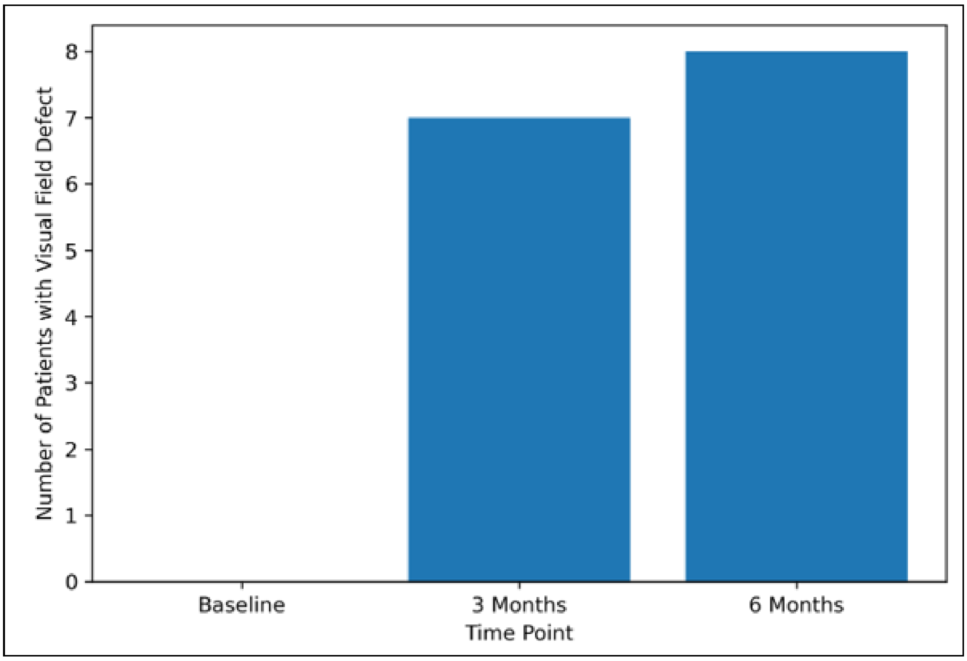

Figure 4: Visual Field Defects

Table 4: Visual Field Defects Over Time

Time Point	Cecocentral Scotoma n (%)	Peripheral Constriction n (%)	Bitemporal Hemianopia n (%)	Any Defect n (%)
Baseline	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3 Months	2 (4%)	5 (10%)	0 (0%)	7 (14%)
6 Months	2 (4%)	6 (12%)	0 (0%)	8 (16%)

Structural–Functional Correlation

At 6 months:
- RNFL thickness vs Visual field MD: Pearson r = 0.674 (p < 0.001)
- RNFL thickness vs Color score: Pearson r = 0.772 (p < 0.001)

Table 5: Distribution of Clinical Optic Nerve Findings (N = 50)

Finding	n	%
Normal fundus	28	56.0
Colour vision defect	18	36.0
RNFL thinning	18	36.0
Visual field defect	8	16.0
Optic neuropathy	3	6.0

Association Analysis

RNFL thinning showed:

- No significant association with visual field defect (OR = 2.00, p = 0.436)
- Strong association with color vision defect (OR significant)

Table 6: RNFL Thickness Status at Baseline, 3 Months and 6 Months

Duration of ATT	Normal n (%)	Decrease n (%)
Baseline	50 (100%)	0 (0%)
3 Months	40 (80%)	10 (20%)
6 Months	32 (64%)	18 (36%)

Table 6: Repeated-Measures Analysis for RNFL Decrease

Test	Statistic	df	p-value
Cochran's Q	27.11	2	0.000001
McNemar (Baseline vs 3m)	—	—	0.001953
McNemar (3m vs 6m)	—	—	0.007812
McNemar (Baseline vs 6m)	—	—	0.000008

Table 7: Mean RNFL Thickness (µm) Over Time

Time Point	Mean ± SD (µm)
Baseline	104.11 ± 7.31
3 Months	100.42 ± 8.60
6 Months	95.32 ± 12.77

Friedman Test: $\chi^2(2) = 17.76$, p = 0.000139

Post-hoc Wilcoxon (Holm corrected):

- Baseline vs 3m: p = 0.001432
- Baseline vs 6m: p = 0.000143
- 3m vs 6m: p = 0.000024

Table 8: Repeated-Measures Analysis for Visual Field Defects

Test	Statistic	df	p-value
Cochran's Q	14.25	2	0.000805
McNemar (Baseline vs 3m)	—	—	0.015625
McNemar (3m vs 6m)	—	—	1.000000
McNemar (Baseline vs 6m)	—	—	0.007812

Table 10: Visual Field Mean Deviation (dB) – Baseline vs 6 Months

Time Point	Mean ± SD (dB)
Baseline	−0.78 ± 0.68
6 Months	−1.96 ± 2.26

Test	Statistic	p-value
Paired t-test	t (49) = −3.67	0.000595
Wilcoxon signed-rank	—	0.00103

Table 11: Structural–Functional Correlation at 6 Months

Variables Compared	Correlation	p-value
RNFL (6m) vs VF MD (6m) – Pearson	r = 0.674	8.19×10^{-8}
RNFL (6m) vs VF MD (6m) – Spearman	ρ = 0.658	2.07×10^{-7}
RNFL (6m) vs Color Score (6m) – Pearson	r = 0.772	5.11×10^{-11}
RNFL (6m) vs Color Score (6m) – Spearman	ρ = 0.842	1.82×10^{-14}

Table 12: Association Between RNFL Decrease and Visual Field Defect at 6 Months

	VF Defect Present	VF Defect Absent	Total
RNFL Decrease	5	13	18
RNFL Normal	3	29	32

Fisher's Exact Test: OR = 2.00, p = 0.436

Table 13: Association Between RNFL Decrease and Color Vision Defect at 6 Months

	Color Defect Present	Color Defect Absent	Total
RNFL Decrease	15	3	18
RNFL Normal	3	29	32

5. Discussion

Ethambutol-induced optic neuropathy (EON) has long been recognized as a dose-related adverse effect of anti-tuberculosis therapy. Carr and Henkind first described the characteristic ocular manifestations including bilateral visual loss, dyschromatopsia, and central scotomas [1]. Leibold further established the dose-dependent nature of ethambutol toxicity, emphasizing that higher cumulative doses significantly increase the risk of optic neuropathy [2]. Our findings of progressive structural and functional deterioration over six months are consistent with these early clinical observations.

The prevalence of ocular involvement (44%) in our cohort highlights the clinical relevance of monitoring during ATT. Similar observations have been emphasized in modern reviews, which stress that optic neuropathy may develop insidiously and require proactive screening [11]. The WHO Global Tuberculosis Report underscores the widespread use of ethambutol globally, reinforcing the public health importance of early detection strategies [10].

In our study, RNFL thinning increased significantly over time, with mean RNFL thickness declining from 104.11 µm at baseline to 95.32 µm at six months. Zoumalan et al. demonstrated that OCT could detect RNFL thinning in ethambutol-induced optic neuropathy and that structural changes correlate with visual dysfunction [3]. Similarly, Kim and Hwang reported that OCT can identify early RNFL changes even before marked visual acuity decline becomes evident [5]. Chai and Foroozan further confirmed progressive RNFL thinning in patients exposed to ethambutol, supporting the longitudinal structural deterioration observed in our cohort [7].

Indian data from Menon et al. also support the use of OCT in toxic optic neuropathy, particularly in populations with high

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tuberculosis burden [6]. Our findings align with these reports, strengthening the argument that OCT should be incorporated into routine monitoring protocols for patients receiving ATT.

Visual field analysis in our study revealed a progressive increase in defects, predominantly peripheral constriction and cecocentral scotomas. This pattern mirrors the classical presentation described in early literature [1] and is further supported by contemporary reviews emphasizing that central and cecocentral defects are hallmark features of ethambutol toxicity [11]. The significant worsening in mean deviation at six months confirms measurable functional decline.

A particularly important finding in our study is the strong structural–functional correlation between RNFL thickness and visual field mean deviation (r = 0.674) as well as color vision score (r = 0.772). Hood et al., although studying glaucoma, provided strong methodological evidence that structural loss in the RNFL correlates closely with functional visual field impairment [8]. Our findings extend this structural–functional paradigm to ethambutol-induced optic neuropathy, reinforcing the biological plausibility of OCT as a surrogate marker for functional damage.

Sadun and Wang emphasized that early color vision loss may precede significant visual acuity deterioration and advocated routine monitoring to prevent avoidable blindness [4]. In our cohort, the strong association between RNFL thinning and color vision defect further supports dyschromatopsia as an early and sensitive clinical marker.

Sivakumaran et al. recommended routine ophthalmic monitoring for patients on ethambutol therapy, especially during the first few months of treatment [9]. Our results strongly validate this recommendation, as significant structural and functional changes were evident by three months and progressed by six months.

6. Clinical Implications

Taken together, the findings from our study and existing literature suggest:

- Ethambutol toxicity is progressive and dose-related [2].
- Structural changes may precede overt functional loss [5].
- OCT is a sensitive tool for early detection [3,5,7].
- Color vision testing is a simple yet valuable screening method [4].
- Routine ophthalmic monitoring is essential in ATT patients [9,11].

7. Limitations

Although our study demonstrates clear progression of optic nerve changes, larger multicentric studies incorporating dose stratification and longer follow-up would further clarify risk factors and reversibility patterns described in previous literature [2,11].

8. Conclusion

The present prospective longitudinal study demonstrates that anti-tuberculosis therapy, particularly regimens containing ethambutol, is associated with **progressive structural and functional optic nerve changes over a six-month period**. A significant reduction in retinal nerve fiber layer (RNFL) thickness was observed with increasing duration of therapy, indicating ongoing axonal involvement. Concurrently, measurable deterioration in visual field parameters and color vision scores highlights the functional consequences of this structural damage.

Importantly, the study establishes a strong and statistically significant structural–functional relationship, as evidenced by the positive correlations between RNFL thickness and visual field mean deviation, as well as between RNFL thickness and color vision performance. These findings reinforce the concept that OCT-derived structural measurements reliably reflect functional visual impairment in patients receiving ATT. The demonstration of this correlation strengthens the clinical utility of OCT as an objective and sensitive tool for early detection of ethambutol-induced optic neuropathy.

The emergence of RNFL thinning and functional deficits as early as three months into therapy underscores the need for vigilant monitoring during the initial and continuation phases of treatment. Given the potentially irreversible nature of ethambutol-related optic nerve damage, early identification of subclinical changes is critical to prevent permanent visual loss.

Therefore, routine ophthalmic evaluation should be integrated into standard treatment protocols for patients receiving anti-tuberculosis therapy. Baseline assessment followed by periodic monitoring- including optical coherence tomography, color vision testing, and automated perimetry—can facilitate timely detection of toxicity and enable prompt intervention, including dose modification or discontinuation of the offending agent when necessary.

In regions with a high burden of tuberculosis and widespread ethambutol use, implementation of structured ophthalmic surveillance programs may significantly reduce preventable visual morbidity. Further large-scale, multicentric studies with extended follow-up are warranted to refine screening intervals, identify high-risk populations, and develop standardized monitoring guidelines aimed at preserving visual function while maintaining effective tuberculosis control.

References

[1] Carr RE, Henkind P. Ocular manifestations of ethambutol toxicity. Arch Ophthalmol. 1962;67:566-571.
[2] Leibold JE. The ocular toxicity of ethambutol and its relation to dose. Ann N Y Acad Sci. 1966;135(2):904-909.
[3] Zoumalan CI, Danesh-Meyer HV, Savino PJ, Sergott RC. Optical coherence tomography in ethambutol-induced optic neuropathy. Clin Exp Ophthalmol. 2005;33(4):389-392.
[4] Sadun AA, Wang MY. Ethambutol optic neuropathy: how we can prevent 100,000 new cases of blindness each year. Curr Opin Ophthalmol. 2008;19(6):464-467.

[5] Kim U, Hwang JM. Early detection of ethambutol optic neuropathy using optical coherence tomography. Ophthalmology. 2009;116(3):591-596.
[6] Menon V, Jain D, Saxena R. Optical coherence tomography in toxic optic neuropathy. Indian J Ophthalmol. 2013;61(11):611-614.
[7] Chai SJ, Foroozan R. Decreased retinal nerve fiber layer thickness detected by optical coherence tomography in patients with ethambutol-induced optic neuropathy. J Neuroophthalmol. 2013;33(4):365-369.
[8] Hood DC, Anderson SC, Wall M, et al. Structure versus function in glaucoma: application to RNFL and visual field defects. Arch Ophthalmol. 2007;125(3):337-346.
[9] Sivakumaran P, Harrison AC, Marschner J, Martin P. Ocular toxicity from ethambutol: review and recommendations. Med J Aust. 1998;169(11-12):598-600.
[10] World Health Organization. Global tuberculosis report 2023. Geneva: World Health Organization; 2023.
[11] Chen HY, Lai CC, Chen TL, et al. Ethambutol-induced optic neuropathy: a review of clinical characteristics and management. Curr Opin Ophthalmol. 2015;26(6):450-457.