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Original Research Article

A Study on Clinical Profile of Intraocular Tuberculosis in a Tertiary Institute in Central Region of India

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Abstract

Objectives: (1). To study ocular manifestations in undetected cases of intraocular Tuberculosis. (2). To study the socio demographic status of patients with intraocular Tuberculosis. (3). To aware the patients and their family about National Tuberculosis elimination Programme (NTEP).

Methodology: This prospective observational study was done in the Department of Ophthalmology at Gandhi Medical College, Bhopal. The material for the present study has been drawn from patients attending the Department of Ophthalmology at Hamidia Hospital of Gandhi Medical College, Bhopal in Eye OPD and referred patients from other departments during the period from August 2022 to February 2024 was included in the study.

Results: Majority (38.7%) of the study participants belonged to the age group 20-29 years. The mean age of the study participants was 37.03 ± 16.1 years. In majority of the participants single eye was affected (75.8%), although amongst these participants the both the eyes were affected almost equally with incidence being slightly higher in the right eye (38.7%) than the left eye (37.1%). In 24% of the cases involvement bilateral eyes was observed.

Conclusion: A significant correlation was found between a history of contact with TB patients and the occurrence of intraocular TB. Additionally, the study highlights the association between smoking and TB, with a notable percentage of participants being current or former smokers. Anemia was prevalent among the participants, suggesting it as a significant risk factor for TB. The presence of HIV in a subset of patients further underscores the need to consider co-infections in TB risk assessments.

Keywords: Intra Ocular Tuberculosis, Pulmonary Tuberculosis, NTEP, Clinical Profile.

Introduction

Tuberculosis is a chronic infectious disease caused by the bacterium Mycobacterium tuberculosis. It presents a global health challenge and stands among the top ten causes of death worldwide. Mycobacterium tuberculosis (MTB) infection, putting them at risk of developing the disease. TB is primarily transmitted through the air and can affect various organs in the body. Around 80% of cases involve the lungs (pulmonary TB), while the remaining 20% affect other organs, known as extra-pulmonary TB. These extra-pulmonary sites include the central nervous system, cardiovascular system, peritoneum, lymph nodes, skin, bones, joints, gastrointestinal tract, and even the eyes, as ocular tuberculosis (OTB). [1] Tuberculosis primarily affects populations in developing and low-resource countries due to poor living conditions and hygiene standards. Risk factors such as poor socioeconomic status, immunosuppression, and global migration contribute to the disease's prevalence. In recent years, multidrug-resistant TB and its association with HIV have led to a rise in TB cases worldwide. [2] The WHO report highlights that the incidence of TB for 2021 stood at 210 cases per 100,000 populations globally. Encouragingly, India saw an 18% reduction in TB

incidence. [1] Whereas, India TB Report of the year 2023, incidence of TB for the year 2021 was 197 per 100,000 population and 196 per 100,000 population for the year 2022. [3] The WHO's strategic plan for Madhya Pradesh indicates that case notification rates in the public sector increased from 131 per 100,000 population in 2015 to 149 per 100,000 population in 2018. At the district level within the public sector, case notification rates ranged from 88 to 258 per 100,000 population in 2018. [4]

Notably, a study demonstrated that among the Saharia tribal population in Madhya Pradesh, the incidence of bacteriologically positive pulmonary tuberculosis (PTB) was 1504 per 100,000 over a one-year period. [5] Considering the high burden of TB in India and the country's commitment to the National Tuberculosis Elimination Program (NTEP), this thesis aims to raise awareness about ocular tuberculosis. The goals include studying ocular manifestations in cases of intraocular TB, analyzing the socio-demographic status of patients with intraocular TB, as well as promoting awareness of the NTEP among patients and their families. This study is imperative because ocular tuberculosis often goes unnoticed and undertreated, overshadowed by the focus on pulmonary tb. This scholarly endeavour is an academic pursuit; which carries the torch of a much-neglected facet of tuberculosis – ocular tuberculosis.

Material and Methods

This was a prospective observational clinical study conducted in the Department of Ophthalmology at Gandhi Medical College, Bhopal. The material for the present study has been drawn from patients attending the Department of Ophthalmology at Hamidia Hospital of Gandhi Medical College, Bhopal in Eye OPD and referred patients from other departments during the period from August 2022 to February 2024 was included in the study.

The approval for the study protocol was taken from the Scientific Review committee and the Ethical Review Committee. The study was started after the clearance was received from both the committees to which Hamidia hospital is affiliated. All the patients of presumptive ocular tuberculosis visiting the hospital during the study period (August 2022 to February 2024) and meeting the inclusion criteria were included in this study. Written informed consent was taken from the participants after explaining them about the study in details in their own local language. Patients were diagnosed clinically with intraocular tuberculosis and investigations were conducted, including molecular Rapid Test - CBNAAT and PCR. If these tests were found positive, they were sent to the DOTS Centre TB hospital lalghati for taking ATT. Data regarding socio-demographic profile, previous history of tuberculosis, clinical findings, any previous treatment, extra pulmonary manifestations, and blood investigations were collected, and all data were entered into a pre-tested semi-structured proforma. Patients were followed up for up to 1 month or until the confirmation of diagnosis.

Inclusion Criteria:

- All patient who attending OPD, IPD and emergency department of ophthalmology with suspicious clinical findings of intraocular TB
- All referred cases from other department like TB Chest, Medicine, Pediatric and other with suspicion of intraocular TB

Exclusion Criteria:

- Those who are not willing to participate in the study.
- Patients who have any other intra-ophthalmic disease with signs and symptoms overlapping those of tuberculosis.

Proper history and examination done for both eyes. Descriptive analysis was done in the form of mean and standard deviations or proportions wherever appropriate. Statistical difference between means were calculated using the independent t test. Chi-square test was used to analyze the difference between proportions. P value of less than 0.05 was considered statistically significant.

Observation and results

Table 1: Age-wise distribution of cases with ocular tuberculosis (n = 62)

Age Groups (Yrs)	Frequency	Percentage	
<10	0	0	p <0.05
10 – 19	1	1.6	
20 – 29	24	38.7	
30 – 39	14	22.6	
40 – 49	10	16.1	
50 – 59	6	9.7	
60 – 69	5	8.1	
>70	2	3.2	
Total	62	100.0	

The above table shows distribution of the ocular TB patients according to their age. Majority (38.7%) of the study participants belonged to the age group 20-29 years. The mean age of the study participants was 37.03 ± 16.1 years.

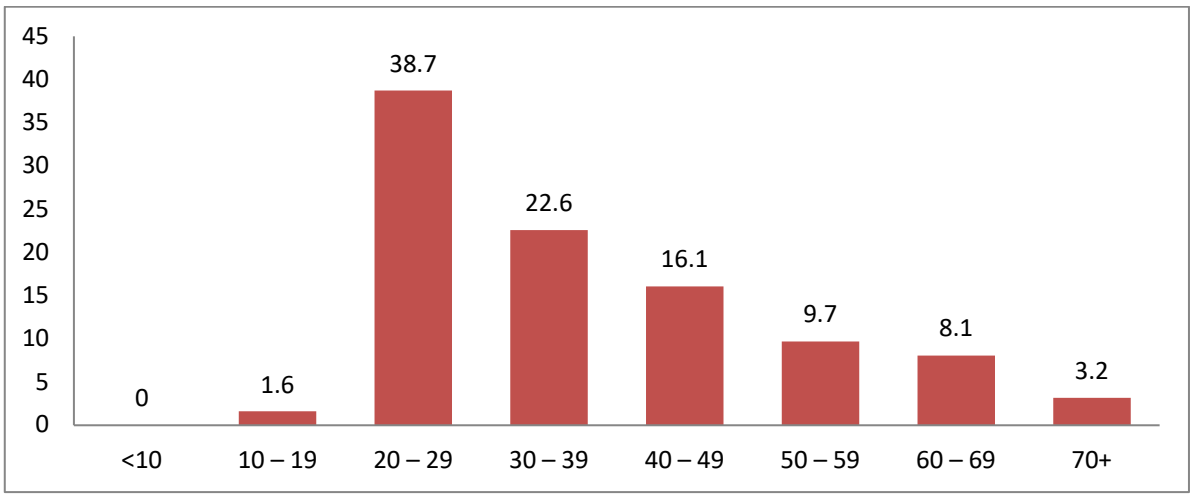

Figure 1: Column graph showing Age-wise distribution of cases with ocular tuberculosis

Table 2: Gender-wise distribution of cases with ocular tuberculosis (n = 62)

Gender	Frequency	Percentage	
Male	40	64.5	p <0.05
Female	22	35.5	
Total	62	100.0	

The above table shows the gender wise distribution of study participants, majority of the study participants were observed to be males (64.5 %).

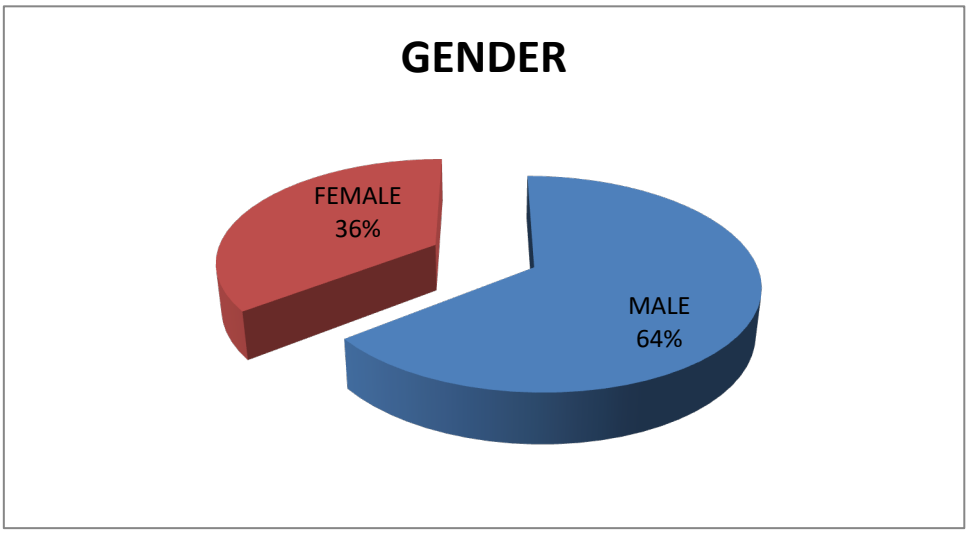

Figure 2: Pie chart Gender-wise distribution of cases with ocular tuberculosis

Table 3: Laterality in cases with ocular tuberculosis (n = 62)

Laterality	Frequency	Percentage	
Unilateral Left	23	37.1	p <0.05
Unilateral Right	24	38.7	
Bilateral	15	24.2	
Total	62	100.0	

In majority of the participants single eye was affected (75.8%), although amongst these participants the both the eyes were affected almost equally with incidence being slightly higher in the right eye (38.7%) than the left eye (37.1%). In 24% of the cases involvement bilateral eyes was observed.

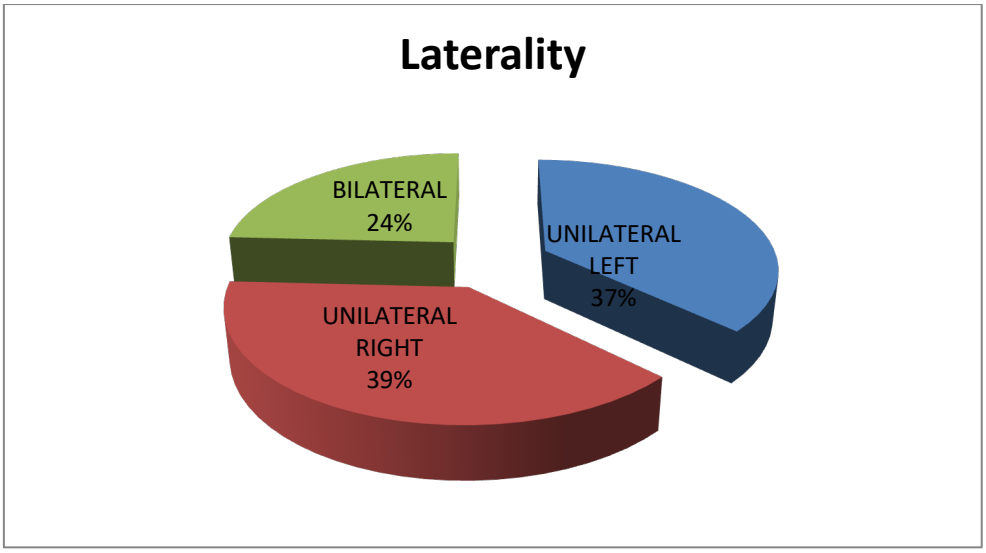

Figure 3: Pie chart

Table 4: status of colour vision (on Ishihara chart) in cases with Ocular TB (n=62)

Color Vision	Frequency	Percentage	
Defective Vision	4	6.5	p <0.05
Normal Vision	58	93.5	
Total	62	100.0	

Majority (93.5%) of the ocular Tuberculosis patients retained normal colour vision when examined with Ishihara charts.

Table 5: correlation of Socioeconomic Status with ocular tuberculosis (n = 62)

Socioeconomic Status	Frequency	Percentage	
Lower Class	55	88.7	p <0.05
Middle Class	7	11.3	
Upper Class	0	0.0	
Total	62	100.0	

The above table shows the Socio-economic status of Ocular TB patients as per the Modified Kuppuswami Classification, majority of the study participants were of lower class (88.7%).

Table 6: correlation of various risk factors with TB Patient with ocular tuberculosis (n=62)

Risk Factors Of Ocular Tuberculosis			
	Frequency	**Percentage**	**P Value**
Contact History Of TB			
No	16	25.8	P <0.05
Yes	46	74.2	
Total	62	100.0	
History Of Smoking			
No	27	43.5	P <0.05
Yes	35	56.5	
Total	62	100.0	
Anemic Status			
Severe Anemia(<8)	10	16.1	p <0.05
Moderate Anemia (8-10.9)	19	30.6	
Mild Anemia (11-12.9)	13	21.0	
Normal (≥13)	20	32.3	
Total	62	100.0	
HIV Status			
HIV Positive	4	6.5	p <0.05
Non-Reactive	58	93.5	
Total	62	100.0	

A significant portion (74.2%) of the participants reported having a history of contact with a known case of tuberculosis. The high prevalence of this factor in our study suggests a strong significant correlation between contact history and the occurrence of TB. 56.5% of the study participants were smokers or had a history of smoking. Smoking weakens the immune system and damages the lungs, making individuals more susceptible to respiratory infections. The elevated prevalence of smoking among the participants indicates a strong association between smoking and TB infection. The majority of the study participants (67.7%) were found to be anemic, with a mean hemoglobin value of 10.86 ± 3.1 mg/dl, ranging from 3.1 mg/dl to 16.3 mg/dl. Malnutrition and deficiencies like anemia impairs the body's ability to fight infections, thus increasing the risk of developing TB. The high prevalence of anemia highlights its role as a significant risk factor for TB. 6.5% of the patients were also found to be HIV positive. HIV severely weakens the immune system, making individuals more vulnerable to infections like TB. The presence of HIV in a portion of the study population underscores the importance of considering HIV status in TB risk assessments.

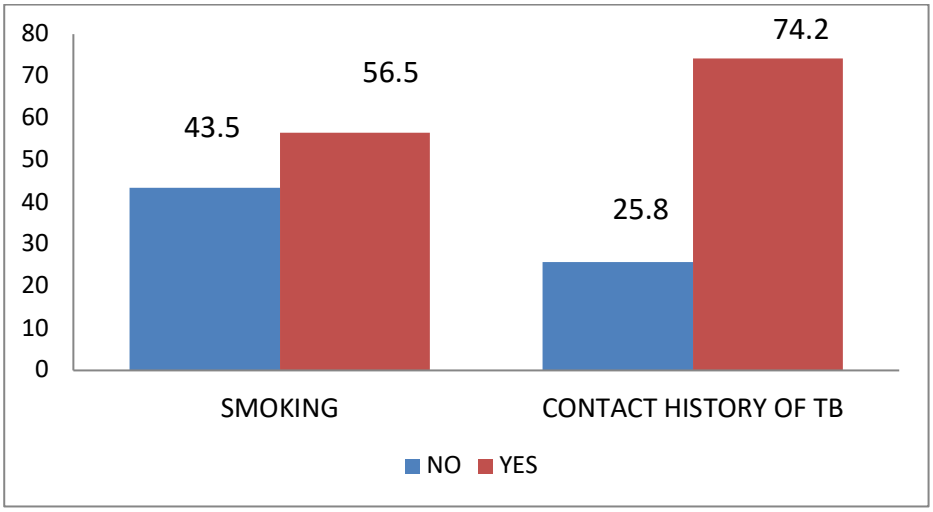

Figure 6: Figure showing the presence of risk factors like history of smoking and contact with TB patient

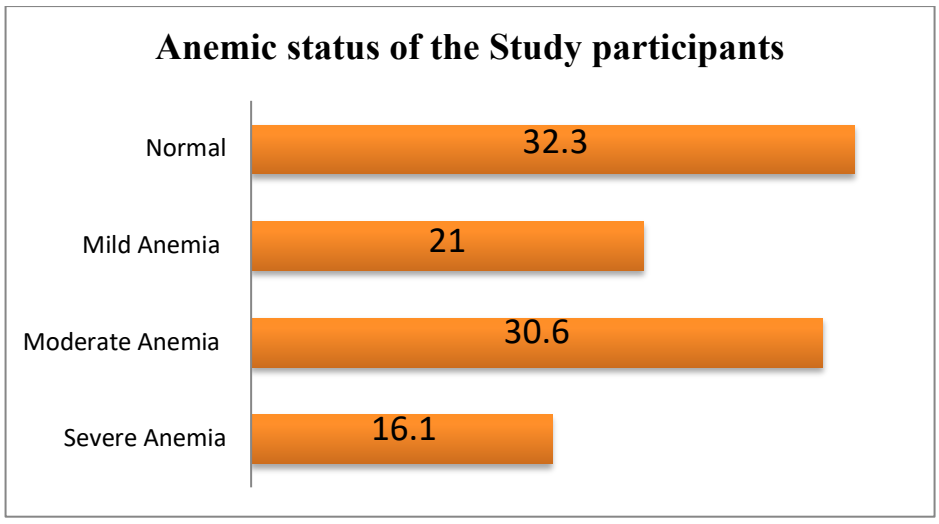

Figure 7: Bar Graph showing the anemic status of the Study participants

Table 7: involvement of other organs in Ocular TB (n=62)

Organs Affected	Frequency	Percentage	
Pulmonary	11	17.7	p <0.05
Abdomen	2	3.2	
CNS	4	6.5	
Skeletal	0	0.0	
None	45	72.6	
Total	62	100.0	

Majority (72.6%) of the study participants did not show multi systemic involvement and only had symptoms of ocular tuberculosis. Amongst the participants with multi system involvement incidence of pulmonary tuberculosis was the highest 17.7%

Table 8: Sensitivity and specificity of different Diagnostic investigational test in cases with ocular TB

Investigations		**Positive**		**Negative**		**p value <0.05**
		Frequency	**Percentage**	**Frequency**	**Percentage**	
Immunological Test	Mantoux	43	69.3	19	30.1	
Microscopic Test	Sputum AFB	15	24.2	47	75.8	
Molecular Test	IGRA	48	77.4	14	22.6	
	CBNAAT	14	22.6	48	77.4	

TEST	Sensitivity	Specificity	PPV	NPV
Mantox	0.694	1	1	0.99
IGRA	0.774	1	1	0.99
CBNAAT	0.226	1	1	0.99
Sputum AFB	0.242	1	1	0.99

All the participants in our study underwent Mantoux test, Sputum AFB examination, IGRA test as well as CBNAAT test to aid the diagnosis of Tuberculosis. 69.3% participants showed a positive Mantoux test indicating that all had a history of exposure to TB Bacilli. IGRA was found reactive in 77.4% of the study participants.
Whereas Sputum AFB and CBNAAT were found positive only in 24.2% and 22.6% cases respectively.

Table 9: Occurrence of clinical ocular manifestations in Ocular TB (n=62)

Diagnosis	**Frequency**	**Percentage**
Sclero-uveitis	2	3.2
Chronic Anterior Uveitis	7	11.3
Intermediate Uveitis	10	16.1
Panuveitis	7	11.3
Multifocal Choroidits	8	12.9
Serpiginous like Choroditis	4	6.5
Eale's Disease	4	6.5
Retinal Detachment	1	1.6
Vitreous Hemorrhage	1	1.6
Papiloedema	2	3.2
Retro Bulbar Neuritis	1	1.6
Chronic Anterior Uveitis	4	6.5
Choroid Tuberculoma	15	24.2
Total	62	100.0

The above table shows the distribution of various ocular manifestations among the participants. Choroid tuberculoma was the most common, observed in 24.2% of cases.

Other significant conditions included intermediate uveitis (16.1%), chronic anterior uveitis (11.3%), multifocal choroiditis (12.9%), and panuveitis (11.3%). Additional manifestations noted were chronic anterior uveitis, Eale's disease, serpiginous-like choroiditis, papilledema, sclero-uveitis, vitreous hemorrhage, retinal detachment, and retrobulbar neuritis. During our study period from August 2022 to February 2024, a total of 33,506 patients visited the Ophthalmology Outpatient Department at Hamidia Hospital, Bhopal.

Among these, 62 were diagnosed with ocular tuberculosis, resulting in an occurance rate of 0.18% of ocular tuberculosis amongst all the ocular pathologies.

Discussion:

This study titled "A Study on Clinical Profile of Intraocular Tuberculosis in a Tertiary Institute in Central India," was conducted in the Ophthalmology Department at Gandhi Medical College, Bhopal. A total of 62 patients, attending the Eye OPD and referred from other departments at Hamidia Hospital, were included between August 2022 and February 2024. Tuberculosis is a disease that affects all age groups. In our study, we observed that over half of the participants (61.3%) were between the ages of 20 and 39. Specifically, 38.7% were in the 20-29 age group, followed closely by 22.6% in the 30-39 age group. The mean age of ocular tuberculosis patients in our study was 37.03 ± 16.1 years. Similar age distributions have

been reported in other studies. For instance, S. Basu et al. found a median age of 33.5 years, with ages ranging from 12 to 60 years [6]. Rosen et al. documented a mean age of 35.5 years, ranging from 19 to 56 years in his case report on ocular tuberculosis patients. [7] Khochtali et al. in North Africa reported a mean age of 42.7 years [8], and Hamade and Tabbara in Riyadh, Saudi Arabia, also observed an average age of 45 years, ranging between 12 to 76 years [9]. Although the average age of participants in other studies tends to be higher than in our study, the age distribution ranges are similar. This consistency suggests that the prevalence of ocular tuberculosis across various age groups remains comparable in both developed and developing countries. Our study observed that 64.5% of the participants were male. Similarly, S. Basu et al. in Eastern India reported that 60.4% of TB patients were male. [6] Shirley et al. also found that 28 out of 48 individuals enrolled over a one-year period were male.[10] Similarly, a study by Lara and Ocampo et al. in the Philippines in 2013 also reported that 62% of the 103 patients recruited were males [11]. Tuberculosis (TB) affects all genders and age groups, but its incidence is slightly higher in males. This trend is often attributed to men working outside the home more frequently, increasing their risk of exposure to infectious diseases like TB. According to the Modified Kuppuswami Classification, the majority of ocular TB patients in our study belonged to the lower socioeconomic class (88.7%). Similar observations were made by Visvanathan et al in their study on 676 patients in India between 2020 and 2021. They found that most ocular TB patients were from lower socioeconomic backgrounds and rural areas, primarily due to poor living conditions and low literacy rates.[12] Ivanovs et al in their research on 304 patients in Latvia also highlighted socioeconomic challenges, revealing that the per capita family income of these study participants was below the national average (USD 0–200). Additionally, 41.2% of TB patients were unemployed, had lower educational levels than the general population, and lived in substandard housing conditions. [13] Similarly, Subramaniam et al. also found that most patients in their study came from middle-class families. [14] Lower socioeconomic status are more vulnerable to TB due to factors such as poor living conditions, overcrowding, limited access to healthcare services, and malnutrition. These factors not only increase the risk of contracting TB but also contribute to delays in diagnosis and treatment, leading to higher transmission rates and poorer treatment outcomes. Therefore, addressing the socioeconomic determinants of health is crucial in the fight against tuberculosis, as it can lead to timely diagnosis, successful treatment and more effective prevention, of the disease. Our study revealed that a significant portion (74.2%) of the participants had a history of contact with a known case of tuberculosis, suggesting a strong correlation between contact history and the occurrence of TB. This finding is consistent with previous researches, a study by Shirley et al. reported that 50% of their study participants had known exposure to individuals with TB, and 12.5% had a history of TB. [10] Additionally, we observed that 56.5% of the participants were smokers or had a history of smoking. The elevated prevalence of smoking among our participants aligns with findings from Lönnroth et al., who identified active smoking as a significant risk factor for TB (RR: 2.6) [15]. Our study also found that 67.7% of the participants were anaemic, with a mean haemoglobin value of 10.86±3.1 mg/dl, ranging from 3.1 mg/dl to 16.3 mg/dl. Severe anaemia was present in 16.1% of the participants, moderate anaemia in 30.6%, and mild anaemia in 21.0%. Narasimhan et al., who highlighted malnutrition as a critical determinant of TB risk at both individual and population levels. [16] Furthermore, 6.5% of the patients in our study were found to be HIV positive. Our findings are also in line with other studies that have identified multiple risk factors associated with TB. For instance, Shahidatul-Adha et al. observed that 38.2% of their patients had prior contact with pulmonary tuberculosis, with 26.5% having underlying diabetes mellitus and one patient with HIV infection. [17] These overlapping risk factors show the complex interplay of socioeconomic, behavioral, and biological factors in the development and transmission of Tuberculosis. Our study provides a comprehensive analysis of the clinical profile and risk factors associated with intraocular tuberculosis. Our findings stress the necessity for comprehensive public health strategies targeting the identified risk factors. Smoking cessation programs, nutritional interventions, and integrated healthcare for co-infections like HIV should be integral components of TB control efforts. Moreover, raising awareness about TB transmission, particularly the risk of ocular TB, is crucial for early diagnosis and effective management.

In our study, all 62 participants underwent the Mantoux test, Sputum AFB examination, IGRA test, and CBNAAT test to diagnose tuberculosis. Notably, 69.3 % showed a positive Mantoux test, indicating prior exposure to TB bacilli. The IGRA test was reactive in 77.4% of participants, while Sputum AFB and CBNAAT tests were positive in only 24.2% and 22.6% of cases, respectively. Diagnosing ocular tuberculosis (TB) is particularly challenging due to its diverse clinical presentations. In many cases, the diagnosis remains presumptive. For instance, Visvanathan et al. found that the Mantoux test was positive in 67% of cases, chest X-ray/CT chest in 20%, and QuantiFERON gold

test in 30%. For 13% of the patients, a presumptive diagnosis of ocular TB was made. [12] In another study, Gupta et al. found that 15 out of 32 presumed ocular TB cases tested positive on PCR. [18] Only 21% of the studies conducted local examinations, such as culture and PCR analysis, to support their diagnosis. Six studies used the response to anti-tubercular therapy as a diagnostic criterion, while nine studies utilized both Tuberculin Skin Test (TST) or QuantiFERON-TB Gold and chest X-rays. [19]

Our findings, along with those from other studies, highlight the complexities in diagnosing ocular TB. The diverse diagnostic approaches, including the Mantoux test, IGRA, Sputum AFB, CBNAAT, and various biopsy techniques, underscore the need for a multifaceted diagnostic strategy. The high prevalence of positive IGRA in our study aligns with Visvanathan et al. [12], reinforcing the test's utility in TB exposure assessment. However, the lower positivity rates for Sputum AFB and CBNAAT in our study compared to the Mantoux suggest variability in test sensitivity and the importance of using multiple diagnostic tools. Our study found that 75.8% of participants had unilateral ocular involvement, with the right eye being slightly more affected (38.7%) than the left eye (37.1%) whereas bilateral involvement was observed in 24% of cases.

Most patients (93.5%) retained normal colour vision, as assessed by Ishihara charts. 72.6% of participants exhibited only ocular tuberculosis symptoms without multisystem involvement. Among those with multisystem involvement, pulmonary tuberculosis was the most common (17.7%), followed by CNS involvement (6.5%) and abdominal TB (3.2%). The distribution of various ocular manifestations among the participants revealed that choroidal tuberculoma was the most prevalent, observed in 24.2% of cases. Other significant conditions included intermediate uveitis (16.1%), multifocal choroiditis (12.9%), and panuveitis (11.3%). Additional manifestations noted were chronic anterior uveitis (11.3%), Eale's disease (6.5%), serpiginous-like choroiditis (6.5%), papilledema (3.2%), sclero-uveitis (3.2%), vitreous hemorrhage (1.6%), retinal detachment (1.6%), and retrobulbar neuritis (1.6%). Our findings align with several other studies but also show some differences in the prevalence and types of ocular manifestations. Kalogeropolous et al. reported that among 6,191 uveitis cases, 2.4% were attributed to tuberculosis, with various types of uveitis including anterior, intermediate, posterior, and panuveitis. [20] Tsui and colleagues observed that retinal vasculitis was the predominant manifestation of ocular TB (42.1%), followed by scleritis, intermediate uveitis, and choroidal tuberculoma (15.8% each).

In comparison, our study found a higher prevalence of choroidal tuberculoma (24.2%).[21] Gupta et al. found that among 158 presumed intraocular tuberculosis patients, 42% had posterior uveitis, 36% had anterior uveitis, 11% had panuveitis, and 11% had intermediate uveitis.[18] Our study showed a higher prevalence of intermediate uveitis (16.1%) compared to Gupta et al. (11%).[18] Albert DM et al. reported diverse manifestations in ocular TB patients, including chronic uveitis (46 patients), iritis [28], sclerokeratitis [23], interstitial keratitis [14], scleritis [14], disseminated tuberculous retinitis [12], tuberculous periphlebitis (7), phylectenular conjunctivitis [6], tuberculous ulcers of the cornea [3], and tuberculosis of the optic nerve (1).[22] Our study had a lower prevalence of these conditions, with choroidal tuberculoma (24.2%) being the most common.[6] Our findings show a lower prevalence of posterior uveitis (11.3%) but a higher rate of intermediate uveitis (16.1%). [8] Our study highlights the importance of using a comprehensive diagnostic approach, incorporating clinical examination, imaging, and multiple laboratory tests to accurately diagnose ocular TB. The variability in test sensitivity and the diverse presentations of ocular TB necessitate a multifaceted diagnostic strategy to ensure accurate diagnosis and appropriate treatment.

Conclusion

This study emphasizes the complex interplay of various factors in the manifestation of intraocular tuberculosis. Addressing the identified risk factors and knowledge gaps through targeted interventions and policies can significantly reduce the burden of this disease. The insights from this study can aid in the improved identification and management of patients at risk for intraocular tuberculosis. Future research on ocular tuberculosis should focus on including larger, more diverse populations and examining the long-term impact of identified risk factors on TB progression and treatment outcomes.

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