ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

Original Research Article

The Ocular Manifestations of Systemic Tuberculosis –A Hospital Based Observational Study

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Received: 13-05-2024 / Revised: 23-05-2024 / Accepted: 30-06-2024

ABSTRACT

Aim
To determine the prevalence and factors associated with ocular manifestations of tuberculosis in a population of persons with tuberculosis in central Kerala

Methods
A cross sectional study of persons with tuberculosis referred to the ophthalmology department by the RNTCP program with a confirmed diagnosis of tuberculosis. All patients underwent a detailed ophthalmology assessment including visual acuity, colour vision, and anterior and posterior segment assessments. A Fishers exact test was used to explore for associations with ocular tuberculosis in a bivariate analysis.

Results
The study included 143 patients and eleven patients (7.69%, 95% CI: 4.35, 13.25) had ocular manifestations of tuberculosis. One hundred and six patients (74.13%) were diagnosed as pulmonary tuberculosis and 21 (14.69%) had extrapulmonary tuberculosis. Posterior uveitis was seen in 5 (3.50%) patients and optic nerve involvement in 3 (2.10%) patients. The distribution of ocular TB was not associated with age, gender, site of TB, and other diagnostic test results in the study population.

Conclusion
The results of our study suggest that a targeted screening for ocular TB only in a subgroup of persons with tuberculosis may not be a feasible strategy. The presumptive diagnosis, difficulty in confirmation of the diagnosis and the possibility of vision loss due to posterior uveitis that

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

involves the macula or optic nerve involvement makes it imperative that every person with tuberculosis is screened for ocular manifestations.

Key Words: Tuberculosis, Ocular tuberculosis, Posterior Uveitis, Optic Neuritis.

INTRODUCTION

The World Health Organization estimates that approximately 2 billion people worldwide have tuberculosis (TB) that includes 10% with symptoms and 90% with latent infection.[1] The incidence of tuberculosis is increasing worldwide due to multidrug-resistant TB, human immunodeficiency virus (HIV), and global migration.[2-4] Approximately 40% of the Indian population is affected with Mycobacterium tuberculosis with most of the infection latent in nature. The incidence of TB in Kerala is 67/100000, which is only half the national rate of 138/100000 as per RNTCP. Ocular TB is defined as a mycobacterium tuberculosis infection in the eye, around the eye, or on its surface that is usually not associated with clinical evidence of pulmonary TB, as up to 60% of extrapulmonary TB patients may not have pulmonary TB.[5,6] Ocular TB can be primary when the eye is the primary port of entry of the mycobacterium into the body, or secondary when ocular manifestations are a result of seeding by hematogenous spread from a distant site. Inflammation of the uveal tract is the most common eye manifestation of the disease due to its high blood supply and oxygen tension.[7,8] The prevalence of tuberculosis as a cause of uveitis ranges from 0.5% in the USA to 6.9% in Japan, 9.86% in north India, 10.5% in Saudi Arabia, and 11.4% in Iraq.[9-13] We designed a cross sectional study to determine the prevalence of ocular morbidity in systemic tuberculosis, and factors associated with ocular manifestations in a population of persons with tuberculosis attending the ophthalmology unit of a tertiary care teaching hospital in central Kerala.

MATERIALS & METHODS

The study protocol that utilized a cross sectional study design was approved by the institutional ethics committee. Informed consent was obtained from all participants before enrolment in the study. The study included consecutive patients with tuberculosis who were referred to the ophthalmology department of the study institute as part of the RNTCP protocol from February 2019 to February 2020. The study excluded patients with exclusive ocular tuberculosis and those already diagnosed with mimicking conditions like Sarcoidosis and Brucellosis. The sample size for the study was estimated based on an anticipated prevalence of 15% and a d of 5 and using the formula $N= 4PQ/d^2$.

A detailed history including age, sex, drug history, co morbid conditions, medical history, date of diagnosis, date of initiation of antitubercular therapy was collected from the case records of each participant. Each participant underwent a detailed ophthalmic examination that included best corrected visual acuity, near vision, colour vision, anterior segment assessments using slit lamp biomicroscopy and posterior segments assessments with direct and indirect ophthalmoscopy. A fundus fluorescein angiography was done if the posterior segment assessment indicated retinal or choroidal involvement. Details of additional investigations including Sputum AFB, Mantoux test, chest x-ray PA views, ESR, serum calcium/ACE levels, routine blood test, random blood sugar and HIV/ELISA tests were documented.

Statistical Analysis

The data collected was entered into an anonymized MS Excel spreadsheet and subsequently exported to the statistical software SPSS v 20.0 for further analysis. The distribution of ocular manifestations of TB were expressed as a proportion. Bivariate analysis was performed using a Fishers Exact test to explore for associations of various factors with ocular TB. A p value <0.05 was considered as statistically significant.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

RESULTS

The study included 143 patients who were examined at the ophthalmology department of the study institute after referral from the RNTCP program. Eleven of the 143 patients (7.69%, 95% CI: 4.35, 13.25) had ocular manifestations of tuberculosis. Most of the study participants were aged >50 years (n=67, 46.83%) and 91 (63.64%) were males. The baseline characteristics of the study population are presented in Table-1. One hundred and six patients (74.13%) were diagnosed as pulmonary tuberculosis and 21 (14.69%) as extrapulmonary tuberculosis. Disseminated TB was found in 4 patients, CNS involvement in 2 and TB in other locations in 8 patients. Two patients were considered as a relapse/failed primary therapy. One hundred and thirty-two (92.31%) patients did not have any ocular manifestations of TB. Posterior uveitis was seen in 5 (3.50%) patients and included fresh choroiditis patches in 2 patients, old choroiditis patches in 2 patients and early vasculitis in 1 patient. Optic nerve involvement was seen in 3 (2.10%) patients and included disc pallor after antitubercular therapy in 2 patients. The cornea, anterior segment, and conjunctiva was involved in 1 patient each. The distribution of ocular TB was not associated age, gender, site of TB, and other diagnostic test results in the study population (see Table-2).

Characteristics	Number of patients (percentage)
Age < 20 years	8 (5.59%)
Age 20-40 years	39 (27.27%)
Age 40-50 years	27 (19.15%)
Age >50 years	67 (46.83%)
Males	91 (63.64%)
Sputum Positive	46 (32.17%)
CBNAAT Positive	54 (37.76%)
ESR >50	68 (47.55%)
HIV Positive	1 (0.70%)
Random Blood Sugar >160	31 (21.68%)
Colour Vision Normal	117 (81.82%)
Visual Acuity better than 6/18	105 (73.43%)
Visual Acuity worse than 6/60	11 (7.69%)

Table-1: Baseline characteristics of the study population

Factor	P- Value (Fishers Exact Test)
Age	0.94
Sex	0.26
Sputum Positivity	0.70
CBNAAT Positivity	0.08
ESR	0.84
Random Blood Sugar	0.50
Location of TB	0.41

Table-2: Clinical and demographic associations with ocular Tuberculosis in the study population

DISCUSSION

The prevalence of ocular manifestations in this study (7.69%) is consistent with a previous study from North India that reported a prevalence of 9.86%.[11] The prevalence of posterior uveitis (45.45%) in the study population is also consistent with a previous study from India that reported a prevalence of 42% for posterior uveitis.[14] The diagnosis of ocular TB is often

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

problematic due to a wide spectrum of presentations and the difficulty to have a definitive histopathological diagnosis and hence the diagnosis of ocular TB is presumptive in most cases.[8.15] Tuberculous uveitis mimics various other causes of uveitis and can be considered in the differential diagnosis of any type of intraocular inflammation especially in areas where TB is endemic. The management of tuberculous uveitis is affected by the uncertainty whether the ocular manifestations result from a direct mycobacterium infection or hypersensitivity reaction. The presence of choroidal nodules may suggest direct hematogenous infection, but immune hypersensitivity is a more likely cause for vasculitis and choroiditis.[16,17]

We did not find an association of pulmonary TB with ocular manifestations of tuberculosis in this study. These results are consistent with previous studies that have reported that most patients with ocular involvement have no history of pulmonary or other systemic forms.[18] Ocular TB can be present even in the absence of clinically evident pulmonary TB as nearly 60% of patients with extrapulmonary TB have no evidence of pulmonary TB and chest X-rays are normal in cases of latent TB.[19,20]

The lack of associations and the presumptive diagnosis are important considerations in the management of uveitis that may presumably be due to TB. Several studies have reported a favourable response when systemic corticosteroids are administered simultaneous with antitubercular therapy.[14,21,22] Use of ATT in these patients may help by killing the intraocular microorganisms and eliminating the antigen load, the recurrences, and the resultant hypersensitivity inflammation.[15] In eyes with presumed TB uveitis, it might be better to add systemic steroids only when lesions are involving or threatening the macula or to reduce macular scarring.[15] The difficulty in establishing a diagnosis and the lack of associations with ocular manifestations of TB can lead to diagnostic and clinical management challenges. The lack of association in our study can be a true lack of association or possibly can be due to the small number of patients with ocular TB in our study. Our study coincided with the implementation of lockdown for the COVID-19 pandemic and hence had to be stopped.

Newer diagnostic modalities may help reduce the clinical management difficulties. Interferon gamma release assay (IGRA) is based on gamma interferon production by T cells sensitized to specific antigens that are specific to mycobacteria TB and are not influenced by BCG and most nontuberculous bacteria. The IGRA test is more sensitive and specific compared to the tuberculin skin test to detect active pulmonary infections but are less sensitive to detect latent infections.[15] The accuracy of diagnosing TB uveitis increases when IGRA and Tuberculin skin testing are used in combination with suggestive clinical signs.[23] Polymerase chain reaction (PCR) tests are increasingly used based on skin, conjunctiva, aqueous, vitreous, choroidal tissue, epiretinal membrane. A case control study in tuberculous uveitis showed 77.2% sensitivity and 92.1% specificity for PCR[24] but several studies have reported a low sensitivity as many ocular manifestations may represent a delayed hypersensitivity reaction making the analysis of a fluid sample from the eye less sensitive.[8,25]

The results of our study suggest that a targeted screening for ocular TB only in a subgroup of persons with tuberculosis may not be a feasible strategy. The presumptive diagnosis, difficulty in confirmation of the diagnosis and the possibility of vision loss due to posterior uveitis that involves the macula or optic nerve involvement makes it imperative that every person with tuberculosis is screened for ocular manifestations. The screening becomes important when medications like Ethambutol are considered for the management. Further studies on a larger population of patients with ocular TB will help to understand possible associations with the onset and progress of ocular TB.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 07, 2024

CONCLUSION

Our study suggests that targeted screening for ocular TB in select TB patients may not be effective due to diagnostic challenges and potential vision loss. Therefore, all TB patients should be screened for ocular manifestations at the initial time of diagnosis of the disease itself.

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