



“ A STUDY ON OCULAR MANIFESTATIONS OF TUBERCULOSIS AND PROGNOSTIC VALUE OF ANTI-TUBERCULAR TREATMENT”

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ABSTRACT **MATERIAL AND METHODS** :- A Interventional Prospective study was conducted at Upgraded Department of Ophthalmology, Pt. J.N.M. Medical Collage and Dr. B .R. A. M. Hospital,Raipur from January 2016 – June 2017. Patients having diagnosed or suspected case of ocular tuberculosis or systemic tuberculosis with ocular complaints attending OPD or admitted in ward of department of Ophthalmology, Dr.B.R.A.M.Hospital, Raipur Chhattisgarh (C.G.) were recruited. History , clinical & ophthalmological examination e.g.-Visual acuity determination, torch light examination, Slit lamp examination, Fundus examination done. Investigations-Hematological, Biochemical, Chest X-Ray(PA-view), B-Scan, Mantoux test, Sputum for AFB, HIV, HbS-Ag test, some special test like TB-Gold, CB-NAAT test done.

RESULTS & DISCUSSION :- 40 patients were recruited having systemic tuberculosis with ocular manifestation or diagnosed or suspected case of ocular tuberculosis with male:female ratio-1.6:1(25:15). Tuberculosis can affect any part of eye.We have got different ocular manifestations of tuberculosis- e.g.-Anterior staphylooma with granuloma, Ptosis, Scleritis, Conjunctival dryness, Conjunctivitis, Corneal ulcer, Complicated cataract, Uveitis(anterior, posterior & pan-uveitis), Retinal detachment, Optic atrophy & pale disc. Significant number of patients were mantoux test positive (39 out of 40). AFB sputum was negative in all patients. Chest X-ray suggestive of tubercular changes found in very few patients. Significant number of patients shows visual or structural improvement after starting of anti-tubercular treatment. Few patients also receive systemic steroid to decrease intraocular inflammation.

CONCLUSION :- Significant proportion of patients show ocular manifestation of tuberculosis . Most common ocular manifestation is uveitis. Significant number of patients showed improvement after starting of anti-tubercular treatment.

KEYWORDS : Ocular manifestation, tuberculosis, anti-tubercular treatment

INTRODUCTION :-

Tuberculosis (TB) is a chronic infection caused by Mycobacterium tuberculosis and it is a leading cause of death worldwide.^{3,16} The World health organization (WHO) has declared tuberculosis to be a global emergency as it remains the most common cause of morbidity and mortality worldwide¹⁴. Tuberculosis (TB) is an ancient disease that has been detected in 3000 year old Egyptian mummies.^{8,9,21} The majority of TB manifestation are pulmonary with extra pulmonary to comprising only about 15% of reported cases.

Maitre-Jan is credited with the earliest written description of ocular tuberculosis in 1711, when he described a case of an iris lesion, which eventually caused perforation. In 1830, Guenea de Mussy was the first to recognize choroidal tubercles.

Tuberculosis can affect practically any structure of the eye and its adnexae^{16,18}. Hematogenous dissemination²¹ may result in involvement of the uvea due to its great vascularity¹⁶. TB can cause a wide variety of ophthalmic finding, ranging from the ocular surface through the optic nerve and to the central nervous system²⁴. TB may manifest in the eye in disseminated primary infection, reactivated latent infecting or occasionally in the form of immune mediated disease with usually no viable⁸. TB may manifesting¹⁴ as eyelid abscesses, orbital cellulites, dacryocystitis, lacrimal gland infiltration, corneal ulcer, chronic conjunctivitis¹, scleritis⁴⁰, phlyctenules, iris infiltrations, optic neuritis, neuroretinitis, uveitis, choroidal tubercles, chorioretinitis, and intraocular masses simulating tumors. Immune mediated manifestation include scleritis, keratitis, anterior uveitis, intermediate uveitis (Including pars plainitis), posterior uveitis⁷, panuveitis and retinal vasculitides.

Because of lack of uniformity in the diagnostic criteria for intraocular tuberculosis and the difficulty of confirming the diagnosis by laboratory method there are no reliable data to indicate its true prevalence¹⁴. Positive or presumptive diagnosis² can be made on the basis of clinical picture⁶, exclusion of other possible etiological factor, demonstration of systemic source, positive tuberculin skin test²² and therapeutic diagnostic test . Tuberculosis foci else where in the body

may be either the cause or the result of a tubercular lesion in the eye. The diagnosis^{17,20} of ocular tuberculosis is usually presumptive and depends upon indirect evidence. However establishing the diagnosis of intraocular TB is of utmost importance , as specific therapy needs to be instituted.

Treatment of ocular tuberculosis is the same as for pulmonary tuberculosis. The treatment required anti-tuberculosis therapy with use of concomitant corticosteroid and carries good prognosis provided the treatment is started in the early stage. The CDC recommends the use of all four drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) for an initial 2-Month period followed by a choice of different options over next 4 to 7 months for treatment of Tuberculosis . Early diagnosis and treatment intervention is critical to prevent irreversible complications.⁶

With the above background the present study will be conducted to assess the various ocular manifestations of tuberculosis and prognostic value of starting of ATT on visual and structural outcome.

PATHOGENESIS²⁴- M. tuberculosis an obligate aerobe affects organs in the body with high oxygen tension such as lungs, kidneys, bone, meninges and choroid in the eye^{7,14,27}. The uveal tract in the eye has a high blood supply making it the commonest ocular site for TB²⁷. Ocular TB may not always have clinical evidence of systemic tuberculosis.²⁸ TB may manifest in the eye in disseminated primary infection, reactivated latent infection or occasionally in the form of immune mediated disease.

AIM & OBJECTIVES - “ To find out the various ocular manifestations of tuberculosis and determine the correlation between ocular improvement with duration of anti-tuberculosis treatment.”

MATERIAL AND METHODS :- A Interventional Prospective study was conducted at Upgraded Department of Ophthalmology, Pt. J.N.M. Medical Collage and Dr. B .R. A. M. Hospital,Raipur, Chhattisgarh from January 2016 – June 2017. Patients having diagnosed or suspected case of ocular tuberculosis or systemic tuberculosis with

ocular complaints attending to OPD or admitted in ward of department of Ophthalmology, Dr.B.R.A.M.Hospital, Raipur Chhattisgarh (C.G.) were recruited. History, clinical & ophthalmological examination e.g.- Visual acuity determination, torch light examination, Slit lamp examination, Fundus examination done. Investigations-Hematological, Biochemical, Chest X-Ray(PA-view), B-Scan, Mantoux test, Sputum for AFB, HIV, HbS-Ag test, some special test like TB-Gold, CB-NAAT test done. On basis of clinical picture, systemic evaluation, investigation and exclusion of other etiological factor we were started anti-tubercular treatment, steroid (systemic or local when required) and subsequent follow up done to see the response of treatment. We were excluded those patients who were defaulter or lost their follow up.

OBSERVATION-

Table : H/o contact with tuberculosis patients in study subjects

H/O contact with TB pt	Frequency	Percent
No	34	85.0
Yes	6	15.0
Total	40	100.0

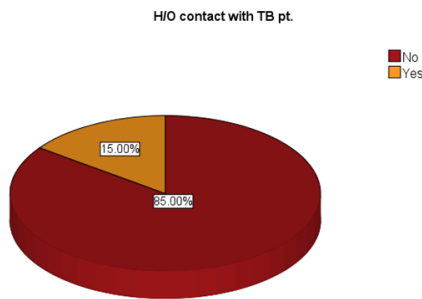


Table : Diagnosis in study subjects

Diagnosis	number of subjects	Percentage
Uveitis	19	47.5
Corneal ulcer	7	17.5
Optic atrophy	2	5
Cataract	2	5
Sciritis	2	5
Ptosis	2	5
Allergic conjunctivitis	1	2.5
Anterios staphyloma	1	2.5
Glaucoma	1	2.5
Lateral rectus palsy	1	2.5
Conjunctival Tuberculoma	1	2.5
NAD	1	2.5

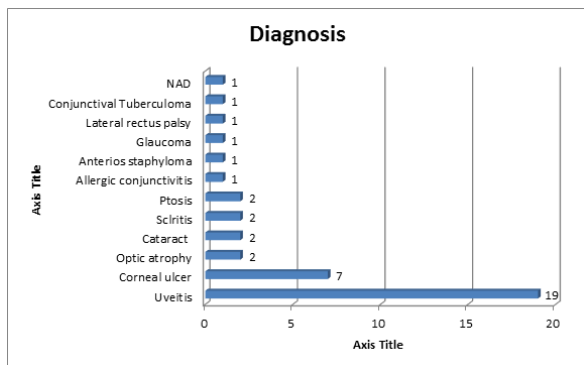


Table : Type of Uveitis in study subjects

Diagnosis	number of subjects	Percentage
Anterior uveitis	7	17.5
Posterior uveitis	6	15
Intermediate uveitis	1	2.5
Panuveitis	5	12.5

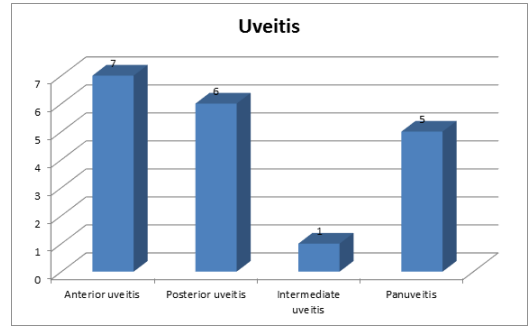


Table : Moutox test findings in study subjects

Moutox test	Frequency	Percent
Negative	1	2.5
Positive	39	97.5
Total	40	100.0

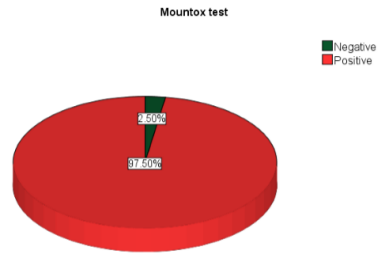


Table : Systemic treatment in study subjects (Anti-tubercular treatment)-

Systemic treatment	Frequency	Percent
ATT cat-1	31	77.5
ATT cat-2	9	22.5
Total	40	100.0

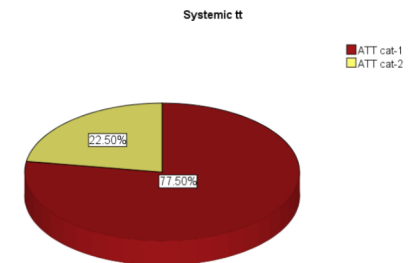


Table : Other Systemic treatment in study subjects

Other Systemic treatment	number of subjects	Percentage
Steroids	19	47.5
Antibiotics	10	25

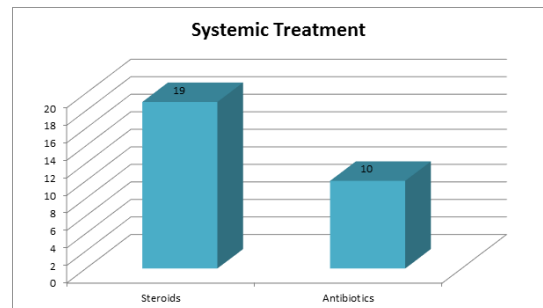


Table : Local treatment in study subjects

Local	number of subjects	Percentage
Steroids	20	50
Antibiotics	10	25
Cycloplegics	22	55

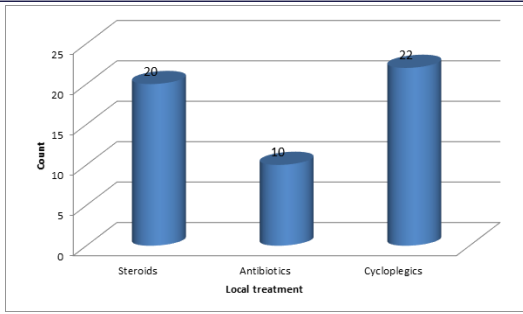


Table : Condition on follow up after treatment-

Condition/Response	Follow ups		
	First follow up	Second follow up	Third follow up
Improved	30 (75%)	35 (87.5%)	35 (87.5%)
Not improved or deteriorate	4 (10%)	2 (5%)	2 (5%)
Same	6 (15%)	3 (7.5%)	3 (7.5%)
Total	40 (100%)	40 (100%)	40 (100%)

RESULT- The present study comprised of 40 cases presented with ocular tuberculosis in our institute between January 2016 to June 2017 as per the inclusion and exclusion criteria. Out of 40 cases, majority of cases were middle age group between 21 to 30 years. (13 cases-32.5%). 25 cases were male (62.5%) and 15 female (37.5%). Maximum number of cases were young adult male. Male to female ratio was 1.6:1.

Diminution of vision was most common presenting complaints (75%) followed by pain and photophobia (37.5%). Unilateral involvement (57.5%) either right or left eye is more common than bilateral involvement. History of contact with tuberculosis patients were found in 6 cases (15%). Maximum number of patients presented with vision counting finger close to face(22.5%). IOP was within normal range in most of the cases (95%) except 2 cases had low IOP. Most of patients had no external abnormality found. Most common anterior segment finding in slit lamp examination was conjunctival congestion (80%) followed by cells and flare (17.5%), hypopyon (17.5%) and keratic precipitates (15%). Most common abnormal posterior segment finding is vitritis (15%). Maximum number of cases were of chronic uveitis (47.5%). Out of total uveitis patients maximum case were of anterior uveitis followed by posterior uveitis, pan uveitis and intermediate uveitis.

97.5% cases were Mantoux test positive. Only 22.5% cases had abnormal chest X-ray finding suggestive of tuberculosis. None of cases were AFB sputum positive for pathogenic organism. CBNAAT/ TB-GOLD test was performed in 6 patients, out of which 4 cases were positive. In serological investigation only raised ESR (17.5%) was supportive.

Out of 40 cases, 31 cases (77.5%) were treated with category 1 ATT and 9 (22.5%) category 2 ATT. 19 (47.5%) cases also received systemic steroid to reduce inflammation and they respond very well. 10 cases (25%) also received systemic antibiotic to reduce infection. 50% cases were also treated by topical steroid to reduce inflammation. 25 % cases also receive topical antibiotic and 55% cases cycloplegics. No definit surgical treatment required for ocular tuberculosis. Good visual and structural outcome was seen in patients treated with anti-tuberculosis treatment. There was no adverse reaction or recurrence seen in our study subjects. All follow up findings were in coherence.

DISCUSSION :

In our study most of patients (13 patients -32.5%) are middle age group (between 21-30 yrs) . Males (25 patients-62.5%) are more prone than female in our study . Cause of this distribution i.e. middle age males are more prone for tubercular infection due to their outdoor and high risk activity5.

In Survey of Ophthalmology (1993)by Holland and Helm, any age can be affected and there was no gender predilection.

In our study subjects most of the patients were present with the

complaints of diminution of vision (30 patients- 75%), pain and photophobia (15 patients- 37.5%). Other presenting complaints were watering of eye, redness, foreign body sensation, headache. Tuberculosis mainly cause uveitis, and above ocular complaints are found in uveitic patients.

17 patients (42.5%) were presented with both eye involved, 12 patients (30%) with right eye and 11 patients (27.5%) with left eye involvement. Cause of unilateral involvement in our study is early intervention by proper diagnosis and treatment with ATT, systemic steroid and local treatment. In case of bilateral involvement there were unequal involvement between both eyes.21

Out of 40 patients only 6 patients (15%) have history of contact with tuberculosis patient.3 History of contact was mainly found in systemic tuberculosis patients presenting with ocular complaints and they were respond very well to systemic (ATT and steroid) as well as local treatment. There is no difference in presentation between exposure and non-exposure.

Vision in study subjects - In our study subjects vision in 4 patients (10%) were No perception of light, 5 patients (12.5%)- only Perception of light, 7 patients (17.5%) -Hand movement, 9 patients (22.5%)- Counting finger close to face, 8 patients (20%)- between 6/60- 6/24, 7 patients (17.5%)- 6/18- 6/6. After anti-tuberculosis treatment visual improvement occurs. But patients with optic atrophy no visual recovery seen because of late presentation.

Abnormal external findings in our study subjects are- lid edema (4 patients-10%), meibomitis (3 patients-7.5%), blepharitis(1 patient-2.5%) , esotropia(1 patient-2.5%), exotropia(1 patient-2.5%),cicatricial ectropion(1 patient-2.5%), trichiasis(1 patient-2.5%), proptosis(1 patient-2.5%), ptosis(2 patients-5%), horizontal nystagmus(1 patient-2.5%). Anterior segment findings (Slit lamp examination)12,19 in our study subjects include- conjunctival congestion, conjunctival cystic lesion, scleritis40, sclera thinning, epithelial defect, corneal ulcer, corneal infiltration, corneal edema, corneal opacity, endothelial plaque, anterior staphyloma, keratic precipitates, hypopyon, cells, flare, complicated cataract, peripheral posterior synechiae12, Festooned pupil and iris pigment over lens. In our study subjects abnormal fundus findings7,19 include- disc edema, cupping, pale disc, macular edema, macular scar, occluded blood vessel, perivascular sheathing, choriaretinal atrophy, chorioiditis12, traction band, retinal detachment, PVR changes, and vitritis. Abnormal B-scan findings were choroidal and retinal detachment, floating membrane, vitreous degeneration, traction band, retinal thickening, vitritis . This is useful where posterior segment is not visible.

In this study uveitis is the most important clinical and diagnostic sign for ocular tuberculosis as it was present in 19 patients (47.5%) of cases.21 Other diagnosis3 include corneal ulcer in 7 patients (17.5%), optic atrophy in 2 patients (5%), cataract in 2 patients (5%), scleritis in 2 patients (5%), ptosis in 2 patients (5%), allergic conjunctivitis in 1 patient (2.5%), anterior staphyloma in 1 patient (2.5%), glaucoma in 1 patient (2.5%), lateral rectus palsy in 1 patient (2.5%), conjunctival tuberculoma in 1 patient (2.5%), and 1 patient has no abnormality suggestive of ocular tuberculosis. These diagnosis are similar in previous studies.2,3,6,9,10,11,12. In our study subjects out of 19 uveitis patients- 7 (17.5%) were case of anterior uveitis, 6 (15%) were posterior uveitis, 5 (12.5%) were panuveitis and only 1 (2.5%) patient was of intermediate uveitis15.

According to Hussain et al16 posterior uveitis is more common followed by anterior uveitis followed by intermediate uveitis. According to Sharma A et al posterior uveitis is most common followed by anterior uveitis, panuveitis and intermediate uveitis. Cause of posterior segment involvement is either hematogenous dissemination or hypersensitivity reaction11. In our study anterior uveitis is more common than posterior uveitis, this is opposite to several previous studies because of short duration of our study period and patients presented earlier at our department. So that early intervention (systemic ATT and steroid as well as local steroid) taken in our study subjects and posterior segment involvement is less likely.

All cases with tubercular uveitis and positive mantoux test22

responded well to anti-tuberculosis therapy (ATT) in our study. In the current study, out of 40 patients, 39 patients with presumed ocular tuberculosis (97.5%) were Mantoux test positive, while it was negative in 1 patient (2.5%) patient. False positive Moutoux test can occur as the test uses a mixture of antigens from mycobacterium and some patients have already received bacille Calmette-Guerin (BCG), but strongly positive test is unlikely to be due to prior BCG vaccination.

Chest X-ray findings suggestive of tuberculosis like consolidation, hilar lymphadenopathy⁵, cavitation, fibrosis, calcification (Regillo et al 1991) found in only 9 patients (22.5%), rest 31 patients (77.5%) have normal chest X-ray finding. This is because ocular tuberculosis is a form of extra-pulmonary tuberculosis²⁸.

AFB sputum finding- No pathogenic organism found in any patient. Mucopurulent sputum found in 2 patients (5%), and non pathogenic organism found in 1 patient (2.5%). It may not provide positive results because of low yield of organism and ocular tuberculosis is a form of extrapulmonary tuberculosis.

CBNAAT/ TB-GOLD test^{34,35,36} Recent advances in diagnostic tools for ocular tuberculosis as detection of antibodies against purified cord factor and use of polymerase chain reaction can provide strong evidence of the infection (CBNAAT / TB-GOLD). In our study TB-GOLD test was done only in 6 patients out of which it is positive in 4 patients.

Only significant serological finding is raised ESR which is raised in only 7 patients (17.5%). Other laboratory investigations were not helpful. ³ Raised ESR is indicative of chronic inflammation.

Systemic and Local treatment given to our study subjects-

- In this study, out of 40 patients 31 patients (77.5%) received category-1 ATT and 9 patients (22.5%) received category-2 ATT.
- Out of 40 patients with presumed ocular tuberculosis 21 patients (52.5%) receive ATT drugs only. All patients treated with ATT drugs only had favorable response without concomitant use of systemic corticosteroids, and no recurrence was recorded.
- Systemic steroids were added to anti-TB therapy in 19 patients (47.5%) to decrease inflammatory reaction, retinal vasculitis, disc edema, macular edema and macular scarring. Oral prednisone can be used in treatment of ocular tuberculosis, in order to control coexisting inflammatory reaction, and reduce inflammation.
- It might be desirable diagnostically to delay steroid treatment in order to assess the response to ATT, this must be balanced with the risk of loss of sight. The use of steroids at the same time as ATT is recommended in other situations where inflammation and fibrosis caused by tuberculosis may lead to long-term complications, for example, tuberculous meningitis³³ or pericarditis³².
- Out of 40 patients, 10 patients also receive other systemic antibiotic to control infection.
- Some patients also receive local steroid (20 patients- 50%), topical antibiotics (10 patients- 25%) and cycloplegics (22 patients- 55%) to control local inflammation and infection, and they respond to these treatment. Local treatment reduce the disease severity and complication.

According to Vos AG et. Al. (2013) a history of TB contact, abnormalities on chest radiology, and extraocular manifestations of TB were associated with good response to ATT in the case of presumed tuberculous uveitis¹⁷.

No definite surgical treatment¹⁴ for ocular tuberculosis, but surgical treatment is required in some patients for complication of ocular tuberculosis.

Follow up findings showed significant visual and structural improvement in our study subjects After first follow up 30 patients (75%) showed improvement (either structural or visual or both), after second and third follow up 35 patients (87.5%) showed improvement. This indicate that duration of anti-tuberculosis treatment has a positive correlation. Some patients also require systemic as well as local steroid in tapering dose to control inflammation. These patients respond very well. Association of first follow up with second and third follow up finding was assessed and they indicate all follow up findings were in

coherence.

CONCLUSION- Tuberculosis is an infectious disease responsible for significant morbidity and mortality worldwide. Ocular tuberculosis may occur in the absence of pulmonary disease. Patients present with a spectrum of clinical signs. According to this study; chronic uveitis is the most common mode of presentation in patients with presumed ocular tuberculosis. All cases responded well to anti-tuberculosis therapy, systemic corticosteroids can be added to decrease inflammatory reaction, retinal vasculitis, macular edema and macular scarring. Drug regimens for ocular tuberculosis are similar to those for pulmonary or extra-pulmonary tuberculosis. Early diagnosis and treatment with ATT and local ocular treatment gives good result and patients will advise to complete course of ATT and local treatment to prevent recurrence and patient also need frequent long term follow up to see the response of ATT and local treatment.

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