Original Article

Ocular manifestations in tuberculosis cases with HIV in Nepal

Subash Bhatta[1], D.N Shah[2], Meenu Choudhary[3], Ajit Thakur[4], Nayana Pant[1]

[1]Geta Eye Hospital
[2]NAMS, Bir Hospital
[3]Institute of Medicine, Kathmandu
[4]Dhristi Eye Hospital, Jhapa

Abstract

Introduction: TB has seen resurgence associated with HIV.Tuberculosis can affect any ocular tissue. The association of HIV with TB is supposed to increase the incidence and plethora of ocular manifestations in tuberculosis.

Objectives: To study the various ocular manifestations seen in tuberculosis patients with associated HIV infection.

Material and Methods: This hospital based, cross sectional descriptive study was conducted in Tribhuvan University, Teaching Hospital, Maharajgunj, Nepal and Geta Eye Hospital, Kailali from 2010 to 2015. Diagnosed cases of pulmonary and extrapulmonary tuberculosis with HIV coinfection were evaluated for ocular manifestations after excluding other opportunistic infections.

Results: Of 70 cases eligible for the study, extrapulmonary tuberculosis was seen in 60% of the cases. 5 patients (7.1 %) had ocular manifestations. CD4 counts were <50/ mm^3 in 3 cases. Ocular involvement was seen in the form of choroidal granulomas, papillitis, cranial nerve palsy, retinal vasculitis and central serous chorioretinopathy.

Conclusion: This study demonstrated that ocular involvement is a frequent finding in cases with tuberculosis and HIV. Ocular findings are more common in cases with lesser CD4 counts. As ocular tuberculosis can be visually devastating, we recommend regular ocular evaluation of all patients with HIV and systemic tuberculosis.

Key words: Tuberculosis, HIV, Choroidal tuberculoma, Retinal vasculitis, Sixth Nerve Palsy

Introduction

Human immunodeficiency virus (HIV) has contributed to the increase in the incidence of tuberculosis worldwide. It is a well-established fact that HIV increases the risk of development of active tuberculosis in patients infected with *Mycobacterium tuberculosis*(Styblo,1991). TB is a leading cause of morbidity and mortality among people living with HIV and as such TB remains a serious health risk for people living with HIV. WHO(2015) reported that out of estimated 8.7 million new cases of TB globally, 13% are co-infected with HIV. HIV co-infected cases account for 430, 000 deaths out of 1.4 million deaths a year due to tuberculosis. Globally, there are an estimated 9.6 million new cases and 1.5 million deaths from TB.

Financial Interest: Nil
Conflict of Interest: Nil
Received: 05.11.2018 Accepted: 07.06.2019

Corresponding author
Dr. Subash Bhatta
Consultant Ophthalmologist,
Geta Eye Hospital, Kailali
Email: subashbhatta@gmail.com,
Ph No.: 00977-9841930145, fax no. 091-575112

About 58% of cases are in the South-East Asia and Western Pacific regions. In Nepal alone there are 44,000 new cases and 60,000 people living with TB, with 4,900 death a year. TB now ranks alongside HIV as a leading cause of death worldwide. HIV's death toll in 2014 was estimated at 1.2 million, which included the 0.4 million TB deaths among HIV positive people.

With a rising incidence of HIV and its noted association with tuberculosis, its implications for ocular tuberculosis are less clear. There are varying reports on prevalence of ocular tuberculosis in patients with HIV. Riffenburg(1993) reported that intraocular tuberculosis was found in only 2 eyes among autopsy eyes from 235 patients with AIDS. In Spain in 1997, 100 persons with TB were chosen at random and examinations revealed 18% had ophthalmic manifestations, and 11 of the 18 were HIV positive (Bouza et al, 1997). In Malawi, Africa, 2.8% of TB patients, 94% of whom were coinfected with HIV, had choroidal granulomas suggestive of ocular TB (Beareet al, 2002). Babu et al (2006) found the incidence of ocular TB in HIV patients to be 1.95%. A study from the same population reported that 1.39% of patients with active PTB and EPTB had ocular TB, suggesting that the HIV co-infection does not dramatically increase the rate of ocular TB (Biswas et al, 1996).

There is no literature from Nepal about ocular involvement in the cases of TB with HIV. In this study we aim to evaluate the ocular involvement in those cases diagnosed with both TB and HIV co infection in a Nepalese population presenting to hospitals in central and far western Nepal.

Methodology

A Hospital based, cross sectional descriptive study was conducted in BP Koirala Lions Center for Ophthalmic Studies (BPKLCOS), Tribhuvan University Teaching Hospital, Kathmandu, and Geta Eye Hospital, Kailali, Nepal after approval from institutional review board of Institute of Medicine.The study was explained to all eligible people in their own language, and consent obtained if they agreed.

The patients referred to us with established diagnosis of TB and HIV were evaluated for ocular manifestations. Detail ocular evaluation of the cases was conducted by an ophthalmologist. Visual acuity was assessed by Snellen Vision Chart with multiple optotypes. Periorbital area and anterior segment were first examined with diffuse torchlight. Haag Streit 900 slit lamp was used in appropriate magnification and illumination for further evaluation of anterior and posterior segment. Posterior vitreous and fundus were evaluated under dilatation by biomicroscope using 90 diopters Volk aspheric lenses and indirect ophthalmoscope using 20 diopters Volk aspheric lens. Necessary ocular investigations (Fundus fluorescein angiography and optical coherence tomography) were done in selected cases.

Those cases of TB and HIV with evidence of any other opportunistic infections in the eye were excluded from the study. Total of 70 cases were included in the study. Aim of the study was to find out the frequency and types of ocular involvement in cases co infected with tuberculosis and HIV. Data analysis was done using SPSS statistics 20.0 software.

Results

70 cases of TB with HIV were enrolled in the study after exclusion of cases that didn't meet the inclusion criteria.

The mean age of the patients was 34.1 years with more than half of the cases (54 %) included in the study within the age group of 31-40. There were 48 males (69%) and 22 females (31%).

Types of tuberculosis observed in cases with

TB and HIV

Extrapulmonary tuberculosis was more common among all age groups except for 11-20 age group (2 cases each) and > 50 age group where there were two male cases with pulmonary TB.

Extrapulmonary TB (60%) was more common than pulmonary TB (40%) in patients with TB and HIV. Among cases with extrapulmonary TB, lymph node TB was the most common type comprising 71% of cases of extrapulmonary tuberculosis.

CD4 count in cases with TB and HIV

43% of HIV cases having TB had a CD4 count within the range of 50-199. 20% cases had CD4 count below 50.

7.1 % (5 cases) of the study population had ocular manifestations with choroidal granuloma seen in three eyes of two patients, as the most common finding. Four (80%) of the involved cases were males.

Cranial nerve palsy in form of lateral rectus palsy and papillitis were present in both eyes of a single patient.

Visual status of cases with ocular manifestations

Out of 7 eyes of affected 5 patients, 2 eyes of the same patient with papillitis were legally blind. One patient with choroidal granuloma had active lesion in macular area with vision of 5/60. Two eyes with retinal vasculitis involving peripheral retina had a vision of 6/6 while the other patient with unilateral CSR had a vision of 6/24.

Table 1: Age and sex wise distribution of TB cases with HIV

	Age group	**0-10**	**11-20**	**21-30**	**31-40**	**41-50**	**>50**	**Total**
Pulmonary	M		0	4	10	4	2	20
	F		2	2	4			8
Extra Pulmonary	M		2	4	16	6		28
	F		0	4	8	2		14
Total			**4**	**14**	**38**	**12**	**2**	**70**

Table 2: Distribution of TB cases according to site of involvement

Systemic TB	**No. of cases**	**Percentage**	**No. of cases with ocular findings**
Pulmonary TB	28	40%	2
Extrapulmonary TB	42	60%	3
	Lymph node TB: 30		
	TB meningitis: 6		
	Pott's spine: 4		
	Abdominal TB:2		
Total	70		5

Table 3: CD4 count in TB cases with HIV co-infection

CD4 count(cells/mm^3)	**No. of patients**	**Percentage (%)**	**No. of patients with ocular findings**
200-500	26	37	1
50-199	30	43	1
<50	14	20	3

Table 4: Ocular manifestations among cases with TB and HIV

Manifestations	No. of patients	No. of eyes	Percentage (%) of involved eyes
Choroidal granulomas	2	3	42.8
Papillitis and CN Palsy	1	2	28.6
Retinal vasculitis	1	1	14.3
CSCR	1	1	14.3
Total	**5**	**7**	**100**

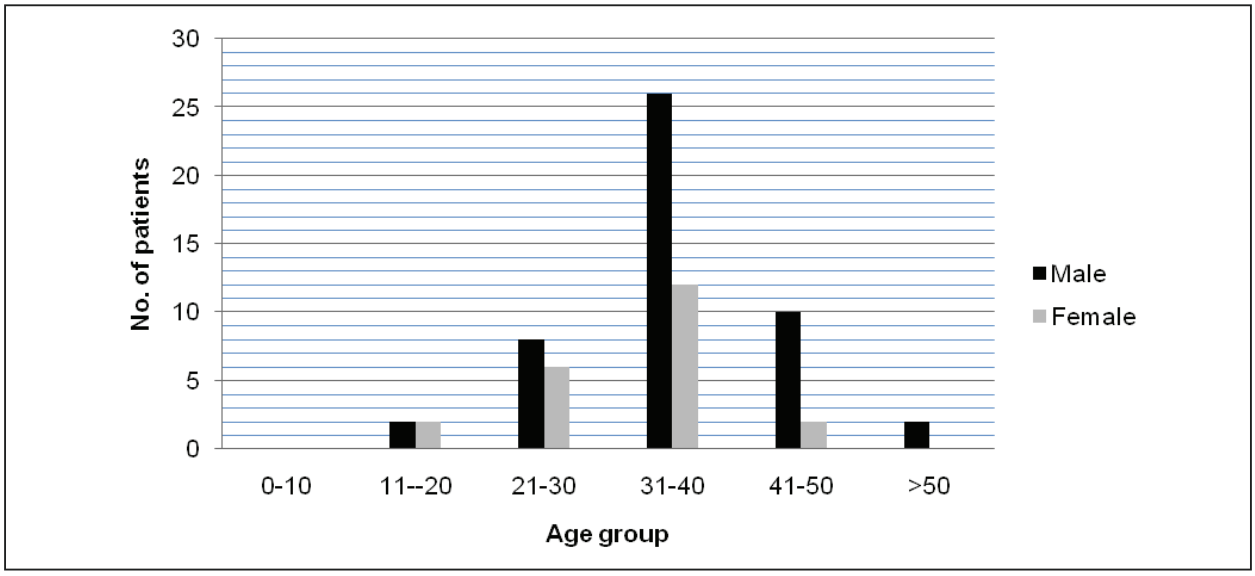

Fig 1: Age group specific sex wise distribution of TB cases with HIV

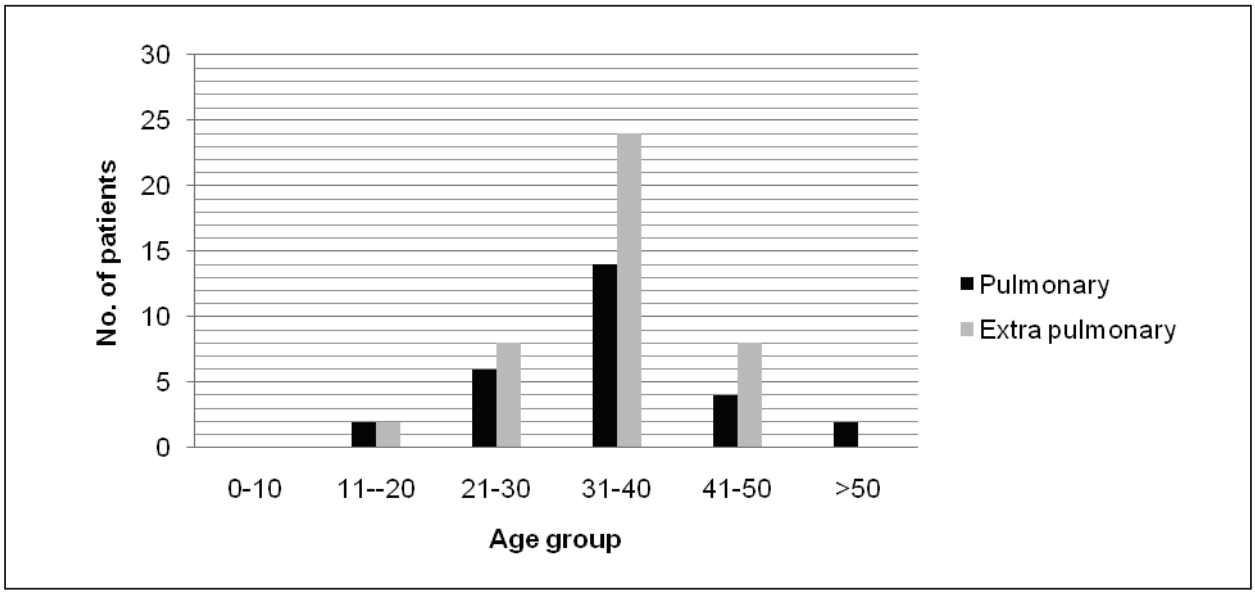

Fig 2: Age wise distribution of pulmonary and extra pulmonaryTB cases with HIV

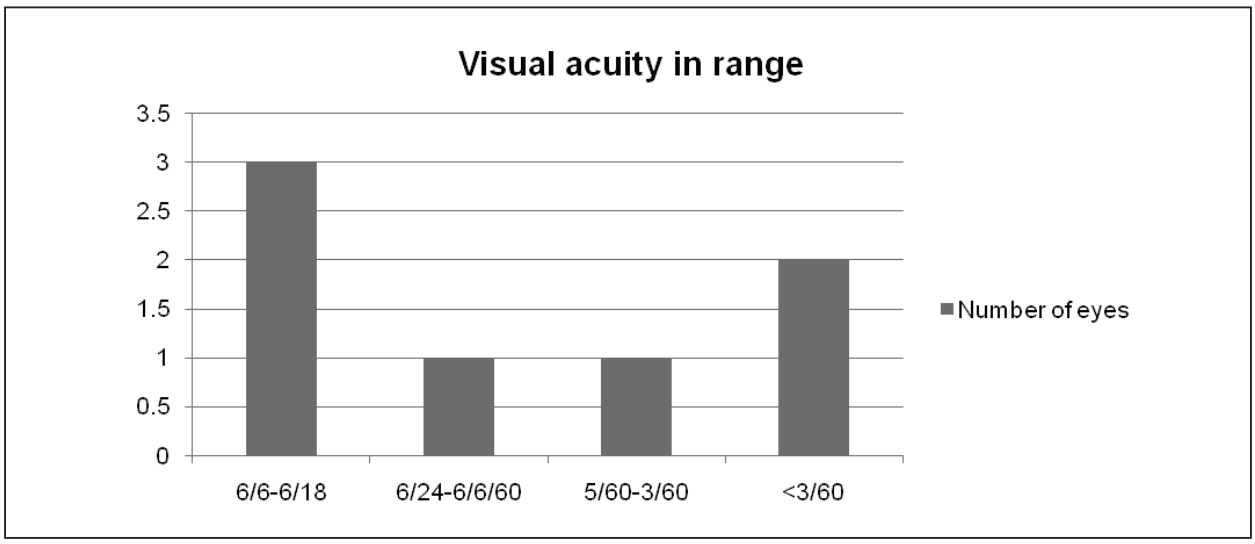

Fig 3: Visual acuity in affected eyes of patients with TB and HIV.

Discussion

Productive age group was involved with mean age of the patients being 34.1 years. More than half of the cases (54 %) included in the study were within the age group of 31-40. 69% (n= 48) cases were males.

In our study, 5 out of 70 cases had ocular manifestations with a frequency of 7.1% of ocular manifestations in patients with TB and HIV. In a study from Spain, out of 100 patients with culture positive tuberculosis, ocular lesion was present in 18 patients (18%) of which 11 patients alsohad HIV infection (Bouza et al, 1997).

However a large study in Chennai, India from 1993 to 2005 found the incidence of ocular TB in HIV patients to be 1.95% (Babu et al, 2006). Riffenberg et al (1993) reported autopsy findings of eyes from 235 patients with AIDS in which intraocular tuberculosis was found only in 2 eyes. The lower incidence reported in these studies as compared to our study might be due to difference in criteria of case selection. These studies reported ocular tuberculosis in diagnosed cases of HIV, irrespective of presence or absence of known tuberculosis infection whereas all the cases included in our study were diagnosed cases of TB with HIV coinfection.

In our study, 43% of HIV cases having TB had a CD4 count within the range of 50-199. Twenty Percent cases had CD4 count below 50. Ocular findings were more common in cases with lesser CD4 counts with 3 out of 5 affected cases (60%) having CD4 count less than 50cells/mm^3. Pearson correlation coefficient for CD4 count and ocular involvement was 0.215 which was statistically not significant with p value of 0.074. Lee et al (2000) also found that most cases of TB with HIV were in the advanced stages of HIV infection, 93% having CD4 cell count less than 200/mm^3. Jones et al(1993) observed that the risk of extrapulmonary tuberculosis and mycobacteremia increases with advancing immunosuppression.

Extrapulmonary TB (60%) was more common than pulmonary TB (40%) in patients with TB and HIV. Among cases with extrapulmonary TB, lymph node TB was the most common type comprising 71% cases of extrapulmonary tuberculosis. Similar observation has been made in many other studies which report that extrapulmonary involvement can be seen in more than 50 percent of patients with

concurrent AIDS and tuberculosis (Reder et al, 1990; Chaisson et al, 1987; Shafer et al, 1991). Chances of ocular involvement in pulmonary and extrapulmonary TB were same as the odds ratio was 1.

Three eyes of two cases, both male, had choroidal granulomas, which was the most common ocular manifestation (42.8% of involved eyes) in cases with HIV and TB in our study. One case with pulmonary TB with CD4 count of 170/ mm^3 had unilateral involvement with single lesion involving macula causing significant loss of vision. Another case withTB meningitis had bilateral involvement with multiple peripheral granulomas. He had CD4 count of 40/mm^3. Choroidal granulomas were also found to be the most common form of ocular tuberculosis in other studies.(Biswas et al, 1996; Sahu et al,1998) In Malawi, Africa, 2.8% incidence of choroidal granuloma was reported among 109 patients with fever and tuberculosis[17].

In our study, one recently diagnosed female patient with lymph node tuberculosis and HIV had papillitis in both eyes with a vision of 2/60 in the right eye and 1/60 in the left eye. His CD4 count was 9 per mm^3. Literatures have reported that optic nerve involvement may lead to optic neuritis or optic atrophy (Woods, 1972; Lamba et al, 1986). Tuberculous optic neuropathy and neuroretinitis could result from contiguous spread from the choroid or from disseminated hematogenous spread of the tuberculous organisms from the pulmonary or other primary infectious focus and should be considered as a differential diagnosis while evaluating patient of neuroretinitis (Ray et al 2001; Reed et al, 1998). Same case had bilateral lateral rectus palsy. CT scan showed multiple lacunar infarcts in brain, with no evidence of raised intracranial pressure. There have been reports of cranial nerve palsies from direct involvement of cranial nerves in cases with tuberculosis and HIV(Moon et al, 2008; Kama et al, 2001). Tuberculosis can also cause meningitis, and increased intracranial pressure can result in palsy of the sixth cranial nerve (Lamba et al, 1986). Sahu et al(1998) described 1 case of cranial nerve palsy out of 55 cases of ocular tuberculosis.

Another case, a 28 year male with miliary TB had retinal vasculitis in right eye and had CD4 count of 17/mm^3. Posterior pole was not affected and his vision was 6/6 in both eyes. Bouza et al (1997) described a case of retinal vasculitis in a patient with tuberculosis and HIV. A number of studies in recent years have reported vasculitis due to tuberculosis (Reny et al, 1996; Romero et al, 2004; Rosen et al, 2004). The diagnosis of tubercular vasculitis is often presumptive as there may be no confirmatory evidence of tuberculosis in these patients. The characteristic features include vitreous infiltrates (vitritis), retinal hemorrhages, neovascularization, and neuroretinitis.

Central serous chorioretinopathy (CSCR) was noted in one male patient with Pott's spine and HIV, his CD4 count being 268/mm^3. There has not been much literature to prove the association of CSCR with HIV or TB, however some case studies have found CSCR in patients with history of tuberculosis and with HIV (Chang et al, 1973; Spalding, 1999).

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