



A Clinical Study to See the Relationship between CNS Tuberculosis and Various Demographic Factors in a Population Attending a Tertiary Hospital in Northern India (Original Study)

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Abstract

Introduction: *Tuberculosis is a granulomatous disease caused by Mycobacterium tuberculosis AIM: Tuberculosis is very common in our part of world. Though a lot of study has been done on this topic but regarding CNS tuberculosis we have only few prospective studies available. There is a desperate need for such a study in our part of country.*

Materials and Methods: *The study was conducted in Department of Pathology, in a tertiary care Institute in Northern India. The study was retrospective for a period of 8 years (May 2001 to May 2009) and prospective for a period of 2 years (May 2009 to May 2011).*

In retrospective the slides of all the CNS tuberculosis cases diagnosed were searched from the records section of the department. In prospective study all cases of histologically proven cases of CNS tuberculosis were included in the study. Age was no bar for inclusion in the study. Patients with features of meningitis were excluded from the study. The clinical details of these patients were noted especially patient particulars, history (present, past &

relevant), clinical features & investigations done. Blood and CSF PCR was done for detecting mycobacterium tuberculosis. In cases where there was abscess formation, abscess fluid was sent for PCR. Patients suffering from tubercular meningitis were excluded from this study.

Observations: In the present series which included a retrospective study of 8 years and a prospective study of 2 years, a total no of 90 cases of CNS tuberculosis were analysed. The age range for CNS tuberculosis was 13-73 years with a mean age of 37.98 years. Age range for brain tuberculosis was 15-65 years with a mean age of 40.63 years. Out of total 90 patients 58(64.4%) were males and 32(35.5%) were females with a male to female ratio of (1.8:1). In brain tuberculosis 21(65.6%) were males and 11(34.3%) were females with a ratio of (1.91:1). The predominant age group was 21-40 years with 40(44.4%) patients falling in this age group. Twelve (13.3%) of the patients were below the age of 20 years and 06(6.66%) patients were above 60 years

Summary: It has been observed that prevalence of tuberculosis of CNS is high in this part of country. The age range of our patients was 13-73 years with a mean age of 37.98 years. Male to female ratio was found to be 2:1. Past history of tuberculosis was the major risk factor for development of CNS Tuberculosis. So the emphasis is proper management of every tuberculous patient so that future risk of CNS involvement is minimized.

Key Words: Tuberculosis, CNS, Granulomatous Disease

INTRODUCTION

Tuberculosis is a granulomatous disease caused by Mycobacterium tuberculosis a slow growing, gram-positive rod, which is resistant to acid decoloration when stained with aniline dyes. Its lipid wall contributes to the acid-fast quality, whereas its tuberculoproteins are associated with tissue hypersensitivity in the characteristic granulomatous reaction¹. Tuberculosis is endemic in developing countries, but even in the developed countries after an initial decline up to 1980s, the incidence of tuberculosis is on the rise. The acquired immunodeficiency syndrome epidemic, emergence of multidrug-resistant strains, and immigration of people from endemic areas are some of the factors contributing to this increase². According to the World Health Organization, there are approximately 9.2 million new cases of tuberculosis and 1.7 million deaths secondary to

tuberculosis every year.³ According to the data of Revised National TB Control Programme (RNTCP) in India, out of the total new TB cases in first two quarters of 2008, 18% were of extra-pulmonary TB. Since 2004, cases of extra-pulmonary TB have increased by 3% in 2008, as per RNTCP data. Out of these extra-pulmonary TB, 30% were of pleural effusion, 10% abdominal TB, 8% bone TB, 47% lymph node TB, 2% TB meningitis and 3% TB elsewhere in body except lungs. More than 11,000 people had died due to extra-pulmonary TB (2005-07) in India alone.

CNS tuberculosis is an uncommon manifestation & accounts for approximately 10-15% of all cases of tuberculosis, carries a high mortality and a distressing level of neurological morbidity, and disproportionately afflicts children and human immunodeficiency virus (HIV)-infected individuals⁴.

Infection of the CNS is one of the most devastating clinical manifestations of tuberculosis. In a large-scale epidemiological study of extrapulmonary tuberculosis in the United States, CNS involvement was noted in 5 to 10% of extrapulmonary tuberculosis cases⁵. In the largest prospective epidemiological study on CNS tuberculosis, the chance of developing CNS tuberculosis was 1.0% among 82,764 tuberculosis cases from 1970 to 2001 in a Canadian cohort⁶. Four major patterns of CNS tuberculosis are seen which include²:

1. Tubercular meningitis (TBM)
2. Tuberculomas in brain
3. Tubercular brain abscess (TBA)
4. Tuberculous encephalopathy
5. Spinal tuberculosis and tuberculomas.

TBM is the most common form of CNS tuberculosis. Rich and McCordock⁷ demonstrated on autopsy that the majority of patients with TBM displayed a caseating focus in the brain parenchyma or meninges.

Tuberculomas are mass lesions and are rare in the developed countries but tuberculomas remain a common problem in tropical countries, where tuberculosis is rampant and represents the most frequent form of intracranial mass lesion^{8,9}. Tuberculomas may be single, but are more often multiple. Before the advent of chemotherapy for tuberculosis, tuberculomas accounted for 30% to 34% of all intracranial space-occupying lesions^{10,11}. These occur usually above the tentorium in adults and below it in children. The common sites of location are: the paracentral lobule, cerebellum, and the pontine

tegmentum^{10,11,12}. Other less common sites are cavernous sinus, hypothalamus, sella, Meckel cave, cerebellopontine angle, and intraventricular area¹². Tuberculomas have to be differentiated from space-occupying lesions such as pyogenic abscess, toxoplasmosis, sarcoidosis, syphilitic gummas, and primary or metastatic malignant diseases. MRI may be a helpful tool in determining the correct diagnosis¹³.

There are 3 patterns of enhancement in intracranial tuberculomas that is solid-enhancing lesions, ring-enhancing lesions, and mixed-enhancing lesions¹⁴

TBA are extremely rare. In a review by whitner¹⁵ only 57 published cases were seen. The criteria for diagnosis of tubercular abscesses are Pus within the brain, bacteriologic proof (presence of acid-fast bacilli/culture/ PCR) & histologic confirmation of abscess.

Computed tomographic scan shows hypodense lesions surrounded by enhanced ring. There may be associated edema. At times, it is difficult to differentiate tubercular abscess from the pyogenic abscess on the basis of clinical and radiologic findings. AFB should be demonstrated on Zeil-Nielsen stain for confirmation¹⁶.

Several risk factors for CNS tuberculosis have been identified. Both children and HIV-coinfected patients^{17,18} are at high risk for developing CNS tuberculosis. Other risk factors include malnutrition and recent measles in children¹⁹ and alcoholism, malignancies, and the use of immunosuppressive agents in adults^{20,21,22}. Studies conducted in developed countries have also identified that foreign-born individuals

Tuberculosis remains a worldwide burden, with a large majority of new active tuberculosis cases occurring in underdeveloped and developing countries²³. In 80% of new tuberculosis cases, demographic factors such as poverty, crowding, malnutrition, and a compromised immune system play a major role in the worldwide epidemic, while the remaining 20% of tuberculosis cases are associated with HIV in sub-Saharan Africa^{23,24} (individuals born outside of developed countries) are overrepresented among CNS tuberculosis cases²³

Tuberculosis is very common in our part of world Though a lot of study has been done on this topic but regarding CNS tuberculosis we have only few prospective studies available. There is a desperate need for such a study in our part of country. This present study is planned with such a perspective in mind especially to see its demographic profile

MATERIALS AND METHODS

The study was conducted in Department of Pathology, in a tertiary care Institute in Northern India. The study was retrospective for a period of 8 years(May 2001 to May 2009) and prospective for a period of 2 years (May 2009 to May 2011). In retrospective the slides of all the CNS tuberculosis cases diagnosed in department of pathology were searched from the records section

of the department .There slides were taken out and reviewed. The clinical details of these respective cases were taken from the records section of the Institute by looking into the files of these patients. In prospective study all cases of histologically proven cases of CNS tuberculosis were included in the study. Age was no bar for inclusion in the study. Patients with features of meningitis were excluded from the study.

The clinical details of these patients were noted especially patient particulars, history (present,past & relevant),clinical features& investigations done. Blood and CSF PCR was done for detecting mycobacterium tuberculosis.

In cases where there was abscess formation, abscess fluid was sent for PCR

Note: Patients suffering from tubercular meningitis were excluded from this study.

OBSERVATIONS:

In the present series which included a retrospective study of 8 years and a prospective study of 2 years,a total no of 90 cases of CNS tuberculosis were analysed.

Demographic Characteristics:

The age range for CNS tuberculosis was 13-73 years with a mean age of 37.98 years. Age range for brain tuberculosis was 15-65 years with a mean age of 40.63 years.

Site	No of pts	Mean age	Std. Deviation	Std. Error Mean
Brain	32	40.63	14.500	2.563

Out of total 90 patients 58(64.4%) were males and 32(35.5%) were females with a male to female ratio of (1.8:1).In brain tuberculosis 21(65.6%)

were males and11(34.3%) were females with a ratio of(1.91:1).

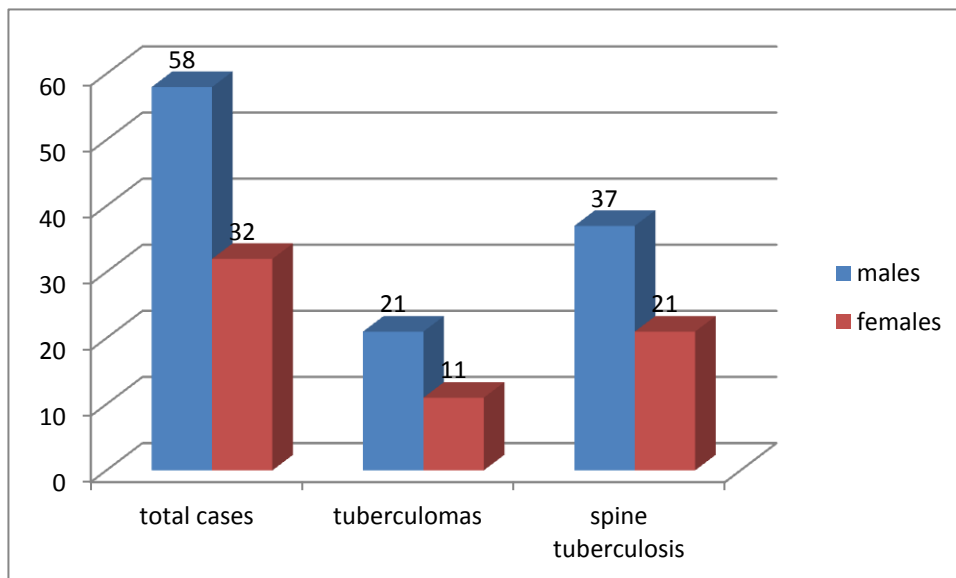
Table 1: Gender Distribution of CNS tuberculosis

CNS Tuberculosis			M/F ratio
Gender	No of patients	%age	
Males	58	64.4	1.8
Females	32	35.5	
Total	90	100	

Table2: Gender distribution of Brain Tuberculosis

Brain tuberculosis			
Gender	No of patients	%age	M/F
Males	21	65.6	1.9
Females	11	34.3	
Total	32	100	

Fig 1: Gender distribution of CNS Tuberculosis



The predominant age group was 21-40 years with 40(44.4%) patients falling in this age group. Twelve (13.3%) of the patients were below the

age of 20 years and 06(6.66%) patients were above 60 years..Age distribution of patients is shown in tabulated form:

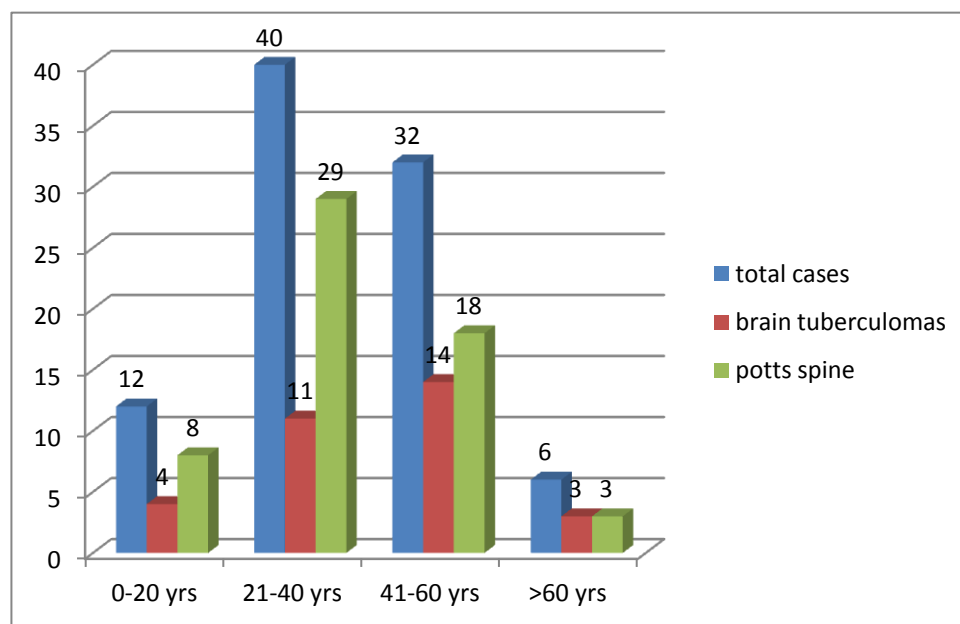
Table 4: Age Distribution of CNS Tuberculosis

CNS Tuberculosis		
Age Range(years)	No of patients	%age
0-20	12	13.33
21-40	40	44.44
41-60	32	35.55
Above 60	06	6.66
Total	90	100

Table 5: Age Distribution of Brain Tuberculosis

Brain tuberculosis		
Age Range(years)	No of patients	%age
0-20	4	12.5
21-40	11	34.37
41-60	14	43.75
Above 60	3	9.37
Total	32	100

Figure 2: Age distribution of CNS Tuberculosis



DISCUSSION

CNS tuberculosis is very common in developing countries with a high morbidity and mortality²³. Tuberculosis is endemic in developing countries, but even in the developed countries after an initial decline up to 1980s, the incidence of tuberculosis is on the rise. The acquired immunodeficiency syndrome epidemic, emergence of multidrug-resistant strains, and immigration of people from endemic areas are some of the factors contributing to this increase².

The diagnosis of CNS tuberculosis is based on clinical and laboratory findings. CT & MRI are very sensitive in preoperative diagnosis of tuberculosis¹¹ and have abated the need for routine histopathological diagnosis of tuberculosis.

In our study histopathologically proven cases of CNS tuberculosis were included and a comparative evaluation of clinical, lab & radiological features was done. Our study included only parenchymal brain lesions (tuberculomas and tubercular brain abscess). Observations achieved will be discussed under following headings.

Age:

In our study age range was 15-65 for brain tuberculomas with a mean age of 40.63. About 15 (46.85%) patients were below the age of 40 years. 41-60 age group was predominant age group with 14 patients (43.75%) falling in this group.

In study done by Cicek Bayinder et al²⁵ the age range was 3-67 years with a mean age of 31.8 years. In a study done by EL Sayed MM et al²⁶ age range was 22-50 years. The predominant population involved in our study were patients

less than 40 years (57.7%). In study done by Ramdurg SR et al²⁷ age range was 18-45 years. Our result was similar to the study done by L.F Owalabi et al²⁸ in which age range was 15-70 years. Mean age in study done by Lakatos B Prinz et al²⁹ was 54.5 years higher than our study. In our study only 8 (8.88%) patients were below the age of 15 years. Children are at high risk for developing CNS tuberculosis^{21,22}. N Vithalani³⁰ analysed 292 cases of autopsy proved tuberculosis and found 200 patients were children below 15 years. This is a sharp contrast to our study. The reason is selection bias of cases. Most of the pediatric cases of CNS tuberculosis are treated in pediatric hospitals and only few cases are referred to our centre.

Gender:

In our study on brain tuberculomas males predominated and constituted 65.6% of the cases. Similarly in study done by Cicek Bayinder et al²⁵ 57% of patients were males. In study done by EL Sayed MM males almost excluded females constituting about 95% of cases which was not seen in our study.

Risk factors:

In our study past history of tuberculosis (25.55%) was a major risk factor followed by family history (11.11%), extra-CNS tuberculosis in (7.77%) and diabetics in (6.66%) of cases. No significant risk factor was present in 48.88% of cases. Neeru Vithalani et al³⁰ found most of the CNS lesions in children were part of either disseminated disease or miliary tuberculosis (34%) while only 21.8% accounted for isolated CNS disease, whereas in adults isolated CNS

disease was present in 50% of cases. Matloob Azam³¹ from Pakistan found family history of tuberculosis in 41% of cases. Ramdurg SR et al²⁷ found previous history of tubercular meningitis in 20% and old pulmonary tuberculosis in (6.66%) of cases. Martinez³² found locus of extra-CNS tuberculosis in (62.5%) of cases with tuberculous pericardites in 12.5% of cases. In his study active pulmonary disease was found in 12.5% of cases. We did not find any case of HIV infection in our study which is in coherence with the study done by Cicek Bayinder²⁵. 25% of patients in study done by Martinez³² were HIV positive. L Cormican³³ found HIV positivity in 4.76% of cases. 20% of tuberculosis cases are associated with HIV positive infection in sub-Saharan Africa^{23,24}. Tuberculosis is endemic in our part of world² and thus past history and family history were important risk factors in our study as was in other studies done in this geographic domain. Besides this, unlike west, people in the subcontinent tend to remain in joint families with close person to person contact contributing to strong family history of tuberculosis in our cases.

Location:

In our study the majority of tuberculomas were supratentorial (93.75%) similar to results of Cicek Bayinder²⁵ in which (90.47%) of tuberculomas were supratentorial. About 81.25% cases were intra cerebral which was again in coherence with study done by Cicek Bayinder et al²⁵. In our study frontal and parietal were the predominant intracerebral sites (Both 22%) for tuberculomas. However in study of Cicek Bayinder²⁵ frontal lobe involvement was more common and constituted

about 42% of cases. In our study 50% of tuberculomas were located in the left lobe, 34% in right and 16% had bilateral involvement. Results were almost similar to the study done by EL Sayed MM et al²⁶ in which left hemisphere was involved in 55%, right 30% and bilateral in 15%. In our study multiple tuberculomas were present in 13% of cases. In study done by Teoh R³⁴ multiple lesions were present in 50% of cases. Multiple lesions were present in 66.66% cases in study done by Matloob Azam et al³¹. Unusual sites of involvement in our study were intraventricular (3%), suprasellar (6%), thalamic (3%) and cerebellar (6%). Akshan³⁵ in 1997 reported two cases of sellar tuberculoma with no evidence of extrasellar disease. Berthier et al³⁶ in 1987 reported 4 cases of intraventricular tuberculomas.

SUMMARY AND CONCLUSION

The study was conducted in Department of Pathology in a tertiary care institute. The study was retrospective for a period of 8 years (May 2001 to May 2009) and prospective for a period of 2 years (May 2009 to May 2011).

In retrospective cases, the slides of all the CNS tuberculosis cases diagnosed in department of pathology were taken out from the records section of the department & reviewed. The clinical details of these respective cases were taken from the records section of the Institute by screening the files of these patients.

In prospective study all cases of histologically proven cases of CNS tuberculosis were included in the study. Age was no bar for inclusion in the study. Patients with features of meningitis were

excluded from the study. The study was undertaken with an aim to know the demographics of the said population vis a CNS tuberculosis. The following conclusions drawn are summarized as:

1) It has been observed that prevalence of tuberculosis of CNS is high in this part of country. In the present study 90 cases were diagnosed on histopathological examination over a period of ten years, excluding meningitis, which is one of the largest case series published on the topic so far. However present study is still the tip of an iceberg as most of the cases remain undetected for not undergoing full diagnostic evaluation and most others are treated conservatively without a need for surgery or biopsy.

- 1) The age range of our patients was 13-73 years with a mean age of 37.98 years.
- 2) Male to female ratio was found to be 2:1.
- 3) Past history of tuberculosis was the major risk factor for development of CNS Tuberculosis. So the emphasis is proper management of every tuberculous patient so that future risk of CNS involvement is minimized.
- 4) Frontal and Parietal lobes were the most common sites involved in brain tuberculosis.

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