Original Research Article

Epidemiological pattern of neurotuberculosis in children

Ramdas Dahiphale

Assistant Professor, Department of Pediatrics, Bharati Medical College and Hospital, Dhankawadi, Pune, Maharashtra, INDIA.
Email: dr_ramdas@yahoo.com

Abstract

Background: Tuberculosis is a disease of the family and community. Neurotuberculosis is the most severe and life threatening form of disease in children. The incidence of neurotuberculosis is closely related to the prevalence of tuberculosis infection in general. **Aim:** To determine the epidemiological pattern of neurotuberculosis in children. **Material and Methods:** Children with neurotuberculosis aged less than 12 years admitted to our hospital were enrolled. Data was collected about age, sex, clinical features, history of contact with tuberculosis case, past history of Koch's, BCG vaccination along with BCG scar mark. **Results:** Out of 70 patients 33 were male and 37 were female with male:female ratio of 1:1.1. The incidence of neurotuberculosis in children is more in age group of 1 to 5 years (47.1%) with 71.4% cases less than 5 years. Most of the patients presenting with neurotuberculosis, were from lower socioeconomic status and 75.7% cases had malnutrition. 78.6% patients had received BCG vaccination at birth and on examination BCG scar was present in 61.4% patients. **Conclusion:** Younger age group is more susceptible for the development of neurotuberculosis. Malnutrition is more at risk for developing neurotuberculosis but not associated with increased mortality.

Key Word: neurotuberculosis.

*Address for Correspondence:
Dr Ramdas Dahiphale, Assistant Professor, Pediatric Department, Bharati Medical College and Hospital, Dhankawadi, Pune – 43, INDIA.
Email: dr_ramdas@yahoo.com

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INTRODUCTION

Tuberculosis (TB) is a serious health problem is poor countries and a leading cause of death. Tuberculosis is less a disease of the individual and more strikingly a disease of the family and of the community. This is even more the case with tuberculosis in children. Approximately 10% cases of tuberculosis have central nervous system (CNS) involvement. TB of CNS is the most severe and life threatening form of disease in children. The incidence of CNS TB is closely related to the prevalence of tuberculosis infection in general. Children are rarely smear positive, approximately 95% of children of less than 12 years old with TB are smear negative. Hence, are much less likely to be a source of infection for others.[1] Children are more likely to develop disease after infection and are significantly more likely to develop extrapulmonary and severe disseminated disease than adults. Tuberculous infection of CNS usually presents over weeks or months and because of insidious onset of symptoms, diagnosis may be delayed. At the disease progresses, symptoms attributable to CNS appear, depending on the area of brain involved and the type of lesion. The present study was conducted to determine the epidemiological pattern of neurotuberculosis in children.

MATERIAL AND METHODS

Study design

Combined retrospective and prospective observational study.

Patient enrollment[2-5]

Children with neurotuberculosis aged less than 12 years admitted to our hospital were enrolled. The study was conducted over a period of 30 months. All patients had an informed consent form signed by their parents. Patients incompletely investigated, with diagnostic doubts, with incomplete records or presence of other obvious factors for

the patient's neurological conditions such as history of birth asphyxia in a case of cerebral palsy or head injury or congenital malformations of the brain, were excluded from study. Data was collected about age, sex, clinical features, history of contact with tuberculosis case, past history of Koch's, BCG vaccination along with BCG scar mark.
Cases were diagnosed on the basis of -

- Clinical features - altered sensorium, ranging from irritability and lethargy through the four stages of coma, fever, persistent vomiting, and signs of meningitis, convulsions, neurological deficit, cranial nerve palsies, paralysis, and decerebrate rigidity.
- Details physical and neurologic examination at the time of admission
- Mantoux test
- X-ray picture suggestive of tuberculosis
- Cerebrospinal fluid (CSF) showing pleocytosis and protein level more than 40mg%
- CT scan or ultrasound skull showing ventricular enlargement and/or basal exudates or tuberculomas
- Isolation of acid fast bacilli by Ziehl-Neelson staining and culture of gastric aspirate and CSF

Classification

TBM cases were classified into three stages according to the British Medical Council classification modified by Gordon and Parsons.[5]
Stage I: Fully consciousness, No definite neurological symptoms at admission or in the history before admission.
State II: Signs of clouding, consciousness with neurological deficits without coma
Stage III: Coma, stupor, multiple cranial nerve palsies with neurological deficits

Nutritional status

Malnutrition was classified according to the Indian Academy of Paediatric Classification[21] as follow: Normal- >80%, I- 71-80%, II- 61-70%, III - 51-60%, IV - <50% expected weight.

Socioeconomic status

Patients' defined according to modified Kuppuswami's scale[6]

Management of cases

All children received standard antituberculous therapy (ATT) as recommended by the Indian Academy of Pediatrics: Isoniazid (5mg/kg/d), Rifampicin (10mg/kg/d), Pyrazinamide (25mg/kg/d) and Ethambutol (20mg/kg/d) for two months followed by Isoniazid, Rifampicin, and Ethambutol for 10 months. Intravenous Dexamethasone (0.6-1.2mg/kg/d) in three divided doses for first 7 days followed by oral Prednisolone (2mg/kg/d) was given for 1 month and then gradually tapered. In cases of drug induced hepatitis we had stopped 4 drug anti Koch's treatment for 7 days and patients started on Streptomycin, Ciprofloxacin and Ethambutol till liver functions returned to normal. Once liver functions were normal we introduced Isoniazid in first week followed by Rifampicin in second, initially in half dose and later on in full doses. In cases having seizures, Phenytoin was used along with Phenobarbitone, Diazepam as and when needed. In cases of raised intracranial tension Mannitol, Acetazolamide, or Glycerol were used. Nutrition and fluid requirement were taken care by intravenous maintenance fluid and nasogastric feeding. All the children who had neurological deterioration during the course of the hospital stay were subjected to repeat CT brain. Children with moderate to severe hydrocephalus and neurologic deterioration were subjected to ventriculo-peritoneal (VP) shunt. When the CSF protein was more than 1gm/L or where VP shunt surgery was not possible the child received initial external ventricular draining by ventricular tapping and later it was converted to VP shunt with the decline in CSF protein. Liver function tests were done initially at weekly interval to monitor ATT related hepatotoxicity. After management of acute stage, the cases were discharged and were followed up in the outpatient department (OPD) of the hospital.

Outcome assessment

Survival and death was the outcome measure. Survival was further categorized into-

1. Discharge with complete recovery without neurologic deficit,
2. Discharge with disability (neurologic deficit)

A univariate analysis was initially performed by the Chi-square test to assess the relationship between different variables and the three outcomes viz. complete recovery, survival with disability, and death.

RESULTS

The total number of patients included in study was 70. Maximum distribution of neurotuberculosis was in the age group of 1 to 5 years (71.1%). Second commonest group affected was between 5 to 12 years (28.6%) the mean age group of patients in our study was 3.9 years. In our series there was no significant difference in sex distribution. Male: Female ratio was 1:1.1. Out of 70 patients 48 (68.6%) patients were from lower socioeconomic status. 17 (24.3%) and 5 (7.1%) patients were from lower middle class and upper middle class respectively.

Table 1: Demographic characteristics

Characteristics	No. of cases	Percentage
Age groups		
< 1 year	17	24.3
1-5 years	33	47.1
5-12 years	20	28.6
Sex		
Male	33	47.1
Female	37	52.9
Socioeconomic status		
Lower class	48	68.6
Lower middle class	17	24.3
Upper class	05	7.1

Out of 70 patients in our study 8 patients (11.4%) had past history of tuberculosis and 12 patients (17.1%) had Koch's contact. 55 patients (78.6%) had received BCG vaccine and 43 patients (61.4%) had BCG scar.

Table 2: source of infection and immunization (N=70)

Symptoms	Present	
	No. of cases	Percent
Past h/o TB	08	11.4
Koch's contact	12	17.1
BCG scar	43	61.4
BCG vaccine	55	78.6

In our study we found very high incidence of malnutrition (75.7%). Grade II PEM was found is 20 patients (28.5%) followed by grade I PEM (22.8%), grade III PEM (18.5%) and grade IV PEM (5.7%).

Table 3: Nutritional status (N=70)

PEM grading	No. of cases	Percent
Grade I	16	22.8
Grade II	20	28.5
Grade III	13	18.5
Grade IV	4	5.7
Total	**53**	**75.7**

The most common symptom was fever (81.4%) followed by convulsion (70%), vomiting (54.3%), weakness (51.4%), altered sensorium (50%), headache (34.3%) and cough (21.4%). Abnormal movement was the least common symptom among the patients (11.4%). The most common sign was increase intracranial tension (74.3%). The commonest presentation was that of increase intracranial tension and convulsion.

Table 4: Clinical presentation (N=70)

Symptoms	Present	
	No. of cases	Percentage
Fever	57	81.4
Cough	15	21.4
Altered sensorium	35	50
Convulsion	49	70
Weakness	36	51.4
Vomiting	38	54.3
Headache	24	34.3
s/o increased ICT /meningitis	52	74.3
Abnormal movements	8	11.4

In our study we found that hydrocephalus was present on cranial CT scan in 40 patients (57%), meningitis with basilar exudates in 39 patients (55.7%), tuberculomas in 22 patients (31.4%), infarct / ischemia in 14 patients (20%), pott's spine in 3 patients (4.2%), and calcification in 2 patients (2.8%). Six patients (8.5%) had normal cranial CT scan. Incidentally we found six conditions one patient each of nephritic syndrome pyelonephritis, WPW syndrome, Dandy Walker malformation, lichen planus and venticular septal defect. In our study, we found overall mortality of TBM is 20%. Advanced stage of the disease has been associated with poor outcome. Stage I TBM has a good prognosis with almost complete gross recovery in the majority. Stage II TBM 45.5% patients completely recovered, 33.3% improved with some morbidity and 18.2% patients expired. Stage III TBM had high mortality (30.7%) and morbidity (57.7%), only 3 patients (11.5%) recovered completely in stage III TBM.

DISCUSSION

Of all the manifestations of tuberculosis, meningitis is undoubtedly the most serious. Notwithstanding the availability of potent and specific drugs, fatality rate of tuberculous meningitis still remains considerably high as compared to that of all other manifestation. Even when it is not fatal, the sequele are sometimes so distressing and disabling that the utility of life itself becomes questionable. On analyzing the age group distribution of our study, we found that the study population was widely distributed in all age groups. Maximum patients were below 5 years of age (71.4%) with a mean age group of 3.9 years. Females outnumbered males with male: Female ratio being 1: 1.1. AIIMS study (2000-2004)[7] includes 23 children in their study and they found mean age group of 4 years and male: female ratio being 2.2: 1. It includes 136 children with mean age group of 3.9 years and male preponderance. Philippine Children Medical Center (PCMC)[8] include 405 children in their study and they found neurotuberculosis is more common below 5 years of age (77%) with a mean age group of 3.81 yrs and male preponderance. Yaramis *et al.*[9] and Karande *et al.*[10] found similar results. Our observations correlate with the other studies in that the younger age group is more susceptible to neurotuberculosis. In our study, we found that, females outnumbered males in contracts to all other studies in which male preponderance. In our study, we found that malnutrition in these patients was rampant (75.7%). Grade II PEM in maximum patients (28.5%), followed by grade I PEM (22.8%), grade III PEM (18.5%) and grade IV PEM (5.7%). Satya Gupta *et al.*[11] found that patient with neurotuberculosis were more likely to be undernourished (34%). Karande *et al.*[10] found protein energy malnutrition in one third of patients of neurotuberculosis. Saroj Kumar *et al.*[12] in their study found 92% cases with PEM, grade I PEM (42%) grade II PEM (17%), grade III and IV PEM (42%). Being a public hospital draining the community, the level of socioeconomic status is poor (93%). This may account for high incidence of PEM seen in the study group thus our study correlate with other studies in that neurotuberculosis cases were more likely to be associated with malnutrition. However, it is difficult to say whether neurotuberculosis is because of under nutrition per se or due to associated social factors leading to inadequate treatment and delay in the treatment. In our study, we found that 8 cases (11.4%) had past history of Koch's. 12 cases (17.1%) had Koch's contact. 55 cases (78.6%) were BCG vaccinated and 43 cases (61.4%) had BCG scar. There was no correlation between stage of neurotuberculosis and past history of Koch's (P= 0.647), and Koch's contact (P=0.229), and BCG vaccine (P=0.69), and BCG scar (P=0.113). Other studies also found history of Koch's contact in PCMC study[8] (69%), Yaramis *et al.*[9] (66%), AIIMS[7] study (30.4%), Satya Gupta[11] (10-20%) and Etlik *et al.*[13] (12.5%). AIIMS[7] study found BCG scar in 50% cases and there was no difference between BCG scar and stage of TBM (p=0.65). In Saroj Kumar *et al.*[12] study, 5 cases (38.5%) developed TBM despite BCG vaccination at birth. In Sehoeman CJ *et al.*[14] study 35% patients developed TBM despite BCG vaccination at birth. Our observations correlate with the other studies in that the past history of Koch's, BCG scar and BCG vaccination were not correlated with stage of tuberculosis. In our study, 78.6% patients developed neurotuberculosis despite BCG vaccination at birth which raises doubts about its efficacy in preventing hematogenous infection. However, due to small sample size, definitive conclusion cannot be drawn about efficacy of BCG vaccine. In our study, we found fever as the most common presenting complaint in 57 patients (81.4%), followed by signs of increased ICT in 52 patients (74.3%), convulsions (70%), vomiting (54.3%), weakness (51.4%), cranial nerve palsy (51.4%), altered sensorium (50%), hepatomegaly (41.4%), headache (34.3%), cough (21.4%), and abnormal movements (11.4%). Various types of weakness (57.4%) like hemiplegia (21.4%), quadriplegia (20%) monoplegia (8.6%), and ataxia (1%) occur at the onset or during the course of the disease. Satya Gupta *et al.*[46] found fever (80-90%) as the most common presenting feature followed by signs of meningitis (80%), convulsion (50-60%), vomiting (40-45%), altered sensorium (20-45%), weakness (20%), cranial nerve palsy (10-30%). PCMC[8] study found similar result except signs of raised ICT in less frequency (11%). Etlik *et al.*[13] found signs of raised ICT as the most common presenting feature. Saroj Kumar *et al.*[12] found neurological deficit (62%) as the most common finding. Our study observation correlates with other studies. Maximum patients presented with fever, signs of raised ICT, convulsion, altered sensorium and vomiting. Most of the patients usually presented with symptoms similar to those of meningitis. We found headache was the least complained about because of the maximum number of patients being younger in age. In our study, CT scan / MRI of brain / Spine performed on all patients, 94% were abnormal with finding of hydrocephalus (57%), meningitis (55.7%), tuberculoma (31.4%), infracts (20%), Pott's spine (4.2%) and calcification (2.8%). Ozates *et al.*[15] found abnormal CT scan / MRI brain in 87% patients with hydrocephalus (80%), meningitis (15.4%), infracts (13.5%), and tuberculoma (4.2%). AIIMS study[7] found 100% abnormal CT scan/ MRI brain with features of hydrocephalus (65.2%), meningitis (47.8%), infarcts 34.8% and tuberculoma (30.4%). Intracranial calcification may occur in 20% to 48% patients with TBM.[7] Matloob Azam *et al.*[16] in their study found eight patients with caries spine, out of those 4 were thoracic and 2 were cervical and

lumbar region respectively. Our study correlates with other studies. CT scan and MRI are useful for both, diagnosis of neurotuberculosis and monitoring management of increased intracranial pressure. We had three patients of pott's spine, all cervical region involvement. In present study, we found overall mortality 20% is TBM children. Stage I TBM had good prognosis with almost complete gross recovery in 72.7% cases, 27.2% cases improved with some morbidity like mental retardation, psychiatric disorders, seizures, blindness, deafness, ophthalmoplegia and hemiparesis. There was no mortality in stage I TBM. We found stage II TBM with 45.5% complete recovery, 36.4% improved with some morbidity and 18.2% mortality. Stage III TBM had high mortality rate 30.7%, 57.7% improved with some morbidity and only 11.5% were recovered fully. In present study, we found correlation between severity of neurotuberculosis and mortality (p=0.005). Our study observations are comparable with other study groups. Patients who presented later is disease process i.e. in stage III TBM had poor prognosis even after V-P Shunt surgery and had high chances of developing disability and mortality. Conservative management is helpful in patients who present early in the disease process. Zahra *et al.*[17] showed direct correlation between severity of neurotuberculosis on presentation and mortality (p=0.031).

CONCLUSION

Younger age group is more susceptible for the development of neurotuberculosis. There is no significant difference in males and females for developing neurotuberculosis. Malnutrition is more at risk for developing neurotuberculosis but not associated with increased mortality. Past history of Koch's or Koch's contact increases chances of developing neurotuberculosis but not corrected with stages of TBM. Patients developed neurotuberculosis despite BCG vaccination at birth, which raises doubts about its efficacy.

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