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Original Research Article

Outcome of children with tuberculous meningitis: a prospective study from a tertiary care centre in Southern India

Jesinth Mohan[1], Rakesh P. S.[2]*, Prabhakar D. Moses[1], Sneha Varkki[1]

[1]Department of Child Health, [2]Department of Community Health, Christian Medical College, Vellore, India

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***Correspondence:**
Dr. Rakesh P. S.,
E-mail: rakeshrenjini@gmail.com

ABSTRACT

Background: TB Meningitis is one of the most serious forms of Tuberculosis. Objective of the current study was to assess the clinical outcome of children presented with TB Meningitis in a tertiary care centre in southern India by following them up and assess their present state in terms of neurological deficits, hearing and visual deficits, learning difficulties and day to day performances.
Methods: Children between 0 - 15 years diagnosed to have TB meningitis in a 2700 bedded hospital in Tamilnadu, India, during the time period 1999-2003 were identified through medical records. These children were called back after 2 to 7 years and health status in terms of neurological deficits, learning deficits, persisting seizures and day to day performance, hearing, ophthalmologic assessment and Intelligence quotient assessment were assessed.
Results: Nearly one third of the children with TB meningitis showed complete recovery. One third died and another one third had some disability. Major problem (46%) encountered in TB meningitis survivors was behavioural problems; the commonest being hyperactivity. Ten out of 27 children had poor scholastic performances, six had neurological deficits and four had seizure disorders. Of 17 children assessed, two had hearing impairment and five had visual impairment. All children with hydrocephalus and were shunted within five days had fully recovered. Of the children shunted later, 9 children (60%) had some sequelae.
Conclusions: Childhood TB meningitis has very poor outcomes. Poor prognosis and difficult early diagnosis emphasise the importance of preventive therapy for child contacts of patients with tuberculosis.

Keywords: Behavioural abnormalities, Childhood TB, Hydrocephalus, Tuberculosis, TB Meningitis

INTRODUCTION

India has one of the highest burdens of tuberculosis (TB) globally, accounting for around 20% of all new TB cases annually.[1] Children form a major percentage of this burden but it has been difficult to estimate the exact burden due to difficulties in definitive diagnosis, increased prevalence of extra pulmonary disease and lack of standard case definition. It is estimated that childhood TB constitutes 10–20% of all TB in high-burden countries accounting for 8–20% of TB-related deaths.[2,3]

Neuro-tuberculosis is the most serious complication of tuberculosis in children. Among the various forms of neuro-tuberculosis, TB meningitis remains the most severe and commonest in developing countries, others being tuberculomas, tuberculous encephalopathy and tuberculous vasculopathy.

Approximately 10% of cases of tuberculosis in children have central nervous system involvement.[4,5] The estimated mortality due to TB meningitis in India is 1.5 per 100,000 population.

Despite great advances in immunology, microbiology, and drug development, the morbidity and mortality still remains high in children with TB meningitis and it continues to remain among the great public health challenges. Overall mortality associated with TB meningitis is reportedly around 22 -39 %.[4,6] There have been few studies looking at the clinico-patho-radiological spectrum of TB meningitis in children from India.[7,8] In these backgrounds a study was conducted to look at the clinical outcome of children presented with TB Meningitis in a tertiary care centre in southern India by following them up and assess their present state in terms of neurological deficits, hearing and visual deficits, learning difficulties and day to day performances.

METHODS

The study was done in a 2700 bedded tertiary care academic centre in Tamilnadu, southern India which offers a huge range of different medical specialities, with advanced diagnostic and therapeutic services, Cohort of children 0 – 15 years diagnosed to have TB meningitis in the Child Health Department of CMC Hospital Vellore during the period 1999-2003 were followed up and looked at their current status.

The essential criteria for diagnosis of TB Meningitis followed was CSF pleocytosi with >50% lymphocytes and protein >60 whereas supportive criteria included fever for more than 2 weeks, history of contact with tuberculosis, generalized lymphadenopathy, positive mantoux >10cm, positive chest x-ray findings, CT showing hydrocephalus or basal exudates, gastric juice AFB positive or isolation of AFB from other sites and proven tuberculous lymphadenitis. Definitive diagnosis of TB Meningitis was made only for culture positive cases. Probable TB Menigitis required essential criteria and two supportive criteria where as possible diagnosis of TB Meningitis was made if essential criteria and only one supportive criterion was satisfied.

Children between 0 - 15 years diagnosed to have TB meningitis based on the above criteria during the time period 1999-2003 were identified through medical records. Medical records were reviewed and the age and stage at presentation to hospital, time period before starting treatment, vaccination status, serum sodium level, treatment given and the condition at discharge were recorded using a standard Proforma. Staging was done by British Medical Research Council's staging of TB meningitis.[9] These children were called back after 2 to 7 years and current health status were recorded in terms of neurological deficits, learning deficits, persisting seizures and day to day performance in all patients. Hearing and ophthalmologic assessment were done in patients who were not assessed till then. Intelligence Quotient (IQ) assessment was also done for children.

Present outcome was graded as per the following criteria.

- **Complete recovery**: No residual neurological deficits, at normal school and unaided day to day activities
- **Some disability**: Mild neurological deficits, at special school or below average in school, needing aids for few day to day activities
- **Severe disability**: Bed ridden, not going to school and requires assistance in all activities of daily living
- **Death**

Data was entered in Microsoft Excel and analysed. Descriptive statistics was done using frequencies and percentages.

RESULTS

A total of 65 children were eligible to be included in the study. 13 of the 65 (20%) children had definite TB meningitis, 43 (66.2%) had probable TB meningitis and 9 (13.8%) had possible TB meningitis. At diagnosis 53 (81.5%) children had stage III tuberculosis meningitis and 12 (18.5%) had stage II. There were no children with stage I.

Table 1: Characteristics of the study participants at the time of diagnosis.

Characteristics	Number (N=65)	Frequency
Age		
6-12 months	09	14
13-60 months	33	51
>60 months	23	35
Gender		
Male	41	63
Female	24	37
Nutrition		
Normal	18	28
Grade I PEM	22	35
Grade II PEM	13	20
Grade III PEM	09	14
Grade IV PEM	02	03

In the study, 33 out of 65 (50.8%) children were between 1 – 5 years. Nine (13.8%) children were between 6 – 12 months and 23 (35.4%) were over 5 years. The mean age was 58 months and standard deviation was 39.45. The youngest child was 6 months old and oldest was 14 years. 41 out of 65 (63.1%) were males.

All children were started on 4 drug therapy with anti tuberculosis drugs. Most of them had received 2HRZE and 10HRE. Few had received regimes with streptomycin and few treated for 18 months. All children were simultaneously started on steroids. Anticonvulsants were used as required. Of the 61 children who had Computerized Tomography done during the course of hospitalization, 50 children had hydrocephalus (82%). Of the 50 children who showed hydrocephalus on CT Brain, external ventricular drain was inserted in 27 children. 16

of these children underwent subsequent Ventriculo-peritoneal shunting. Other 11 were not shunted as they showed no improvement with extra ventricular drain. 11 children were directly taken up for Ventriculo- peritoneal shunting. 12 children were not intervened at all. From the day of hospitalization, only three children were shunted within the first five days, most of them 17 (63%) were shunted between 6 to 14 days after hospitalisation.

Table 2: Outcome of children with TB Meningitis (N=41).

Outcome	Number	Percentage
Dead	14	34
Severe disability	1	2.4
Some disability	14	34
Complete recovery	12	29.3

Four of them died during the course of hospitalization and eight were discharged at request from the hospital at terminal stages of their disease. The rest 51 children were invited to review in the child health OPD to assess their present neurological status, day to day activities, hearing, vision and intelligence. In spite of repeated reminders 24 did not respond. Few addresses could not be traced. Parents of two children responded that their children died. Parents of two other children who could not bring their children for follow up for various reasons replied back writing about their children's present condition. Hence the current clinical status was assessed for 27 children.

Of the children followed up, defining by our outcome criteria, 12 showed complete recovery from illness, 14 showed some disability, one showed severe disability. The discharges at requests were considered as deaths as they were all discharged at the terminal stages of their illnesses. Including that a total of 14 children out of 65 died.

Of the 27 children reviewed 25 were able to manage their day to day activities unaided, one needed minimal supports and one was totally dependent. Of them, 46 % had some behavioural problems. The most commonly observed behavioural abnormality was hyperactivity. Intelligence quotient assessment was done on 12 children. 3 children had normal intelligence, 3 had borderline intelligence, 5 had mild mental retardation and 1 child had moderate mental retardation. Two of the children had hearing impairment. One child had severe sensori-neural hearing loss. The other child had conductive deafness.

Five children had visual impairment. Two children had opto-chiasmatic arachnoiditis and loss of vision. One child was treated for tuberculous choroiditis. One of them had signs of early optic atrophy and another had refractory error and benign flecked retinal syndrome. One of children had presented a year after diagnosis of tuberculous meningitis with bitemporal hemianopia, right hemiparesis and right facial palsy. The child was diagnosed to have a TB brain abscess that was drained. However he later developed hypopituitarism and is on hormonal supplements now. One child had presented with signs of precocious puberty at 3 years of age- two year after completing anti tuberculous treatment.

Only 12 children consented to undergo an intelligence assessment. Of them, 25% had normal intelligence. Another 25% had borderline intelligence, 42% had mild mental retardation and 8% had moderate mental retardation.

All children with hydrocephalus and were shunted within five days had fully recovered. Of the children shunted later, 9 children (60%) had some sequelae.

Table 3: Sequelae of children with TB meningitis.

Characteristics	Number of children assessed for the condition	Number of children with the condition	Percentage
Neurology deficit	27	6	22
Seizure disorder	27	4	15
Behavioral problems	27	13	46
Poor School performance	27	10	45.5
Dependent for daily activities	27	2	7.4
Visual impairment	17	5	29
Hearing impairment	17	2	12
Intelligence Quotient	12		
Normal		3	25
Borderline intelligence		3	25
Mild mental retardation		5	42
Moderate mental retardation		1	8

DISCUSSION

Tuberculous meningitis disproportionately affects young children. Of all the manifestations of Tuberculosis, meningitis is undoubtedly the most serious. Notwithstanding the availability of potent and specific drugs, fatality rate of TB meningitis still remains considerably high as compared to that of all other manifestations. Even when it is not fatal, the sequela are many times distressing. We aimed to characterise treatment outcomes for this deadliest and most debilitating form of tuberculosis.

In the current study, nearly one third of the children with TB meningitis showed complete recovery. One third died and another one third had some disability. A systematic review of 19 studies with 1636 TB meningitis affected children estimated the risk of death as 19·3% (95% CI 14·0–26·1) and probability of survival without neurological sequelae as 36·7% (27·9–46·4). Among survivors, risk of neurological sequelae in the same review was 53·9% (95% CI 42·6–64·9).[10]

A study from Lokmanya Tilak Medical college, Mumbai between 2000 and 2003 showed that 23% of children with TB meningitis died, 25% recovered completely and 57% survived with disability while a study done at JIPMER reported a mortality of only 10%.[7,8] Our study showed a higher mortality probably because of the fact that most of our patients were already in stage III at presentation. It could also be due to the fact that we could not follow up a significant proportion of children. Our figures might have been different if we could have followed up more children. We had only 2.4% with severe disability as compared to 28% in the JIPMER study[8]. It is also possible that only the children who were better had come for review.

In the current study, major problem encountered in TB meningitis survivors was behavioural problems. Of the children followed up, 46 % of our children had various forms of behavioural problems; the commonest being hyperactivity. Of them, 45% had poor scholastic performance. Similar observations were made by in a follow up study done between 1985 to1995 in Capetown.[5]

The study is based on children presented to a single centre. Being a referral tertiary care centre, most of the children were in advanced stages of presentation. Hence the picture may not be representative. Also we could not follow up a good number of children. Despite these limitations, this study finding adds evidences to the epidemiology of TB meningitis.

CONCLUSION

To summarise, childhood TB meningitis has very poor outcomes. The only way to reduce mortality and morbidity is by early diagnosis and timely recognition of complications and institution of the appropriate treatment strategies. However, still the most challenging aspect is early diagnosis with certainty, and the diagnosis is hampered by slow and insensitive diagnostic methods. Poor prognosis and difficult early diagnosis emphasise the importance of preventive therapy for child contacts of patients with tuberculosis.

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