



A STUDY OF CHILDREN ADMITTED WITH TUBERCULOUS MENINGITIS IN A TERTIARY HOSPITAL IN CENTRAL INDIA

Dr. Manoj Bhatnagar Associate Professor in the department of Paediatrics, GMC, Chandrapur.

Dr. Samata Warudkar* Medical officer, IGGMC, Nagpur *Corresponding Author

ABSTRACT

OBJECTIVE: To study the clinical presentations and outcomes of the children admitted with tuberculous meningitis.

METHODS: This was a prospective, descriptive study conducted in the department of paediatrics in a tertiary hospital in central India from January to December 2017.

RESULTS: Of the 40 participants, 25(62.5%) were males and 15(37.5%) were females. The mean age of the patients was 4.24 ± 3.32 years. Besides, 26(65%) patients were less than 5 years of age. All the patients (100%) were categorised as stage 3 tuberculous meningitis. The history of prolonged duration of fever 39(97.55%) and altered level of sensorium 40(100%) were the most common clinical presentations.

CONCLUSION: The children were the most vulnerable group for the worst form of tuberculous meningitis and had a grave outcome.

KEYWORDS : Tuberculous meningitis

INTRODUCTION:

It is estimated that one-third population on this planet is infected with M. Tuberculosis, but only about 5-10% of these infected persons develop active TB in their lifetime.¹ Tuberculosis is one of the common and serious diseases of children. Globally in 2014, one million children were infected with TB and 0.14 million children died because of TB.² It is reported that up to 25% of cases occur in the child age group. Pakistan is one of the high-risk countries for tuberculosis. Tuberculosis is a preventable disease. Bacillus Calmette-Guérin (BCG) vaccine, a live attenuated vaccine is used for the prevention of tuberculosis. It reduces severe, non-pulmonary forms such as childhood meningitis by 70%. Immunity induced by it lasts from 3-12 years and 5-8 years on an average.³ Tuberculous meningitis (TBM) is the most common manifestation of central nervous system (CNS) tuberculosis in the child age group. It is 100% fatal if left untreated and delays in treatment lead to permanent brain damage.⁵ Tuberculous meningitis is difficult to diagnose because of early non-specific clinical features and lack of readily available sensitive test. The definitive diagnosis of Tuberculous meningitis depends on the recovery of Mycobacterium tuberculosis organism from the cerebrospinal fluid (CSF) sample but that needs a large CSF sample almost of 10-20 ml, takes long time of 6-8 weeks for results but the sensitivity of CSF culture is very low (12.5%).⁶ There is no clear-cut time period in which one stage of TBM shifts to the next stage. The patients who survived suffer severe neurological disability, including motor deficits, cognition decline, seizures, hydrocephalus and cranial nerve palsies.^{7,8}

The current study was planned to identify the clinical presentations and outcomes of TBM.

METHODOLOGY:

This was a prospective, descriptive study conducted in the department of paediatrics in a tertiary hospital in central India from January to December 2017. Written informed consent was obtained from the patients' parents. Children aged 1 month to 12 years were enrolled by using the purposive consecutive sampling technique. The sample size was calculated according to the study type.⁹ All the data was analysed using SPSS 19.

RESULTS:

Of the 40 participants, 25(62.5%) were males and 15(37.5%) were females. The mean age of the patients was 4.24 ± 3.32 years. Moreover, 26(65%) participants were less than 5 years of age. The mean duration of admission to the beginning of anti-tuberculosis treatment was 2.76 ± 2.57 days (range: 1-12 days). The mean duration of hospital stay was 12.95 ± 7.11 days (Table 1).

History of prolonged fever and altered level of consciousness were the most common clinical presentations, occurring in 39(97.55%) and 40(100%) patients, respectively (Table 2).

Funduscopy examination revealed optic disc atrophy in 19(47.5%) patients. The mean CSF white blood cell count was 98.03 ± 160.16 per cm, mean protein level was 131.5 ± 104.04 mg/dl and mean sugar level was 42.53 ± 30.17 mg/dl (Table 3).

DISCUSSION:

Tuberculosis is common in our area and our patient's profile in which clinical features, CSF and radiological findings were very much consistent with the diagnosis of tuberculous meningitis. The diagnosis of definite TBM was based on acid-fast bacilli (AFB) staining or mycobacterial culture, but that needs a long time to wait for the results. These tests are not widely available everywhere and the sensitivity of these tests are low. A scoring system was adopted internationally as well as by the WHO to diagnose tuberculosis in childhood. This scoring system is based on the following characteristics: (1) clinical history and examination (2) CSF results and (3) neuroimaging findings that are in favour of TBM. In our study, the focus was on the probable diagnosis that was based on the PPA scoring chart for the diagnosis of TBM.^{10,11} In this study, we found that the majority of the enrolled patients were males (62.5%) most participants were less than 5 years of age (65%). This shows that this age group is more susceptible to this deadly infectious disease. BCG scar was present in 23(57.5%) patients. The preponderance of children less than 5 years of age with severe form of TBM in our study is consistent with other international studies.¹²⁻¹⁴ All of our patients fell into the category of stage 3 TBM, which means that our children suffered with very severe form of TBM. In a study conducted by Günes et al., 32.4% patients had TBM stage 3, but in a study by Van Well GT et al., 97% patients had stage 3 TBM.^{15,16} The common presentations in the TBM stage 3 patients were: fever of prolonged duration, headache, vomiting, seizures and altered conscious level. A study conducted by Shrestha S. et al. had similar results regarding clinical presentations.¹⁷

The mean time interval from the onset of symptoms to the hospital admission was 28.17 ± 38.85 days. In contrast to a study by Shaikh MA, in which the mean time interval from onset of illness to admission in the hospital was 21.75 ± 9.75 days.¹⁸ The duration of symptoms in our patients was much longer. In our patients, the funduscopy examination findings were of optic disc atrophy in 47.5% patients and papilledema in 20% patients, but in a study conducted by Sher K. et al., papilledema was the most common (46.4%) funduscopy findings in TBM stage 3 patients.

CT brain imaging was abnormal in all of our patients. The most common finding was hydrocephalus (80%), which was similar to the results mentioned in the Tinsa et al. study.¹⁹ In our study, mortality was 5%, and 95% patients survived with severe neurological disabilities. This number is very much higher than documented in the international studies. It means that we are at the worse end of tuberculous meningitis. In the Nicolette NB et al. study, the outcome at discharge was: 8% patients died, 43% improved without neurological disability and 49% improved with neurological disability.²⁰ The neurological sequelae were in the form of low GCS, motor handicapped, speech and vision problems, epilepsy and hydrocephalus. These outcomes regarding neurological sequelae are in accordance with the Saitoh A. et al. study.²¹ We recommend a larger prospective study to further understand the outcome of children with TBM.

CONCLUSION:

The children were the most vulnerable group for the worst form of tuberculous meningitis and had a grave outcome. There was 100% morbidity with multiple and severe neurological sequelae. Tuberculous meningitis is disastrous for patients as well as their families, and puts much burden on the health care system which is already under stress.

1. Demographic data of TBM patients.

Age (years) Mean:	4.24 ± 3.32		Male female ratio: 1.6: 1
Range :	8 months to 12 years		
Age groups:	< 5 years- 26 (65%) 6-10 years – 11 (27.5%) 11-15 years – 03 (7.5%)		
Gender	Male no. (%)	Female no. (%)	
h/o TB contact	Positive no. (%) 19 (47.5%)	Negative no. (%) 21 (52.5%)	
BCG scar	Present 23 (57.5%)	Absent 17 (42.5%)	
3rd degree malnutrition	Present 13 (32.5%)	Absent 27 (67.5%)	
Stages of TBM	STAGE 3 IN 40 (100%) PATIENTS		
Duration of stay (days)	12.95 ± 7.11 days	Range : 1-33 days	

2. Table showing frequencies and percentages of clinical presentation

Clinical presentations	No. (%)	Duration of symptoms (days) Mean ± SD
Fever	39 (97.55)	71.93 ± 74.98
Headache	12 (30)	22.13 ± 44.56
Vomiting	19 (47.5)	19.45 ± 33.49
Seizures	29 (72.5)	12.25 ± 17.51
Altered conscious level	40 (100)	15.08 ± 23.70

3. CSF and CT brain findings

CSF	MEAN ± SD		
CSF WBC (/CM)	98.03 ± 160.16		
NEUTROPHILS (%)	18.52 ± 31.71		
LYMPHOCYTES (%)	78.97 ± 34.07		
PROTEIN (MG/DL)	131.5 ± 104.04		
SUGAR (MG/DL)	42.53 ± 30.17		
CT BRAIN (PLAIN AND IV CONTRAST)	FINDINGS	No.	Percentage
	Hydrocephalus	32	80%
	Basilar cistern enhancement	6	15%
	Tuberculomas	8	20%

REFERENCES

- Rangaka MX, Wilkinson KA, Glynn JR, Ling D, Menzies D, Mwansa-Kambafwile J, et al. Predictive value of interferon-γ release assays for incident active tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis.* 2012; 12:45-55.
- Lonnroth K, Castro KG, Chakaya JM, Chauhan LS, Floyd K, Glaziou P, et al. Tuberculosis

- control and elimination 2010-50: cure, care, and social development. *Lancet Infect Dis.* 2010; 375:1814-29.
- Syed SS, Basit AK, Mohammad S, Ghumman MZ, Sattar A, Islam A. Screening of childhood tuberculosis with Pakistan pediatric association scoring chart system. *Pak Ped J.* 2012; 36:220-4.
- Rodrigues LC, Diwan VK, Wheeler JG. Protective effect of BCG against tuberculous meningitis and military tuberculosis: a meta-analysis. *Int J Epidemiol.* 1993; 22:1154-8.
- Chatterjee S. Brain tuberculomas, tubercular meningitis, and post-tubercular hydrocephalus in children. *J Pediatr Neurosci.* 2011; 6:S96-S100.
- Wang T, Feng GD, Pang Y, Yang YN, Dai W, Zhang L, et al. Sub-optimal Specificity of Modified Ziehl-Neelsen Staining for Quick Identification of Tuberculous Meningitis. *Front Microbiol.* 2016; 7:2096.
- Chiang SS, Khan FA, Milstein MB, Tolman AW, Benedetti A, Starke JR, et al. Treatment outcomes of childhood tuberculous meningitis: a systematic review and meta-analysis. *Lancet Infect Dis.* 2014; 14:947-57.
- Van Well GT, Paes BF, Terwee CB, Springer P, Roord JJ, Donald PR, et al. Twenty years of pediatric tuberculous meningitis: a retrospective cohort study in the western cape of South Africa. *Pediatrics.* 2009; 123:e1-8.
- Charan J, Biswas T. How to Calculate Sample Size for Different Study Designs in Medical Research? *Indian J Psychol Med.* 2013; 35:121-6.
- Cartaxo C, Rodrigues L, Braga C, Ximenes R. Measuring the accuracy of a point system to diagnose tuberculosis in children with a negative smear or with no smear or culture. *J Epidemiol Glob Health.* 2014; 4:29-34.
- Karande S, Gupta V, Kulkarni M, Joshi A. Prognostic clinical variables in childhood tuberculous meningitis: an experience from Mumbai, India. *Neuro India.* 2005; 53:191.
- Moyo S, Verter S, Mahomed H, Hawkrigde A, Kibel M, Hatherill M, et al. Age-related tuberculosis incidence and severity in children under 5 years of age in Cape Town, South Africa. *Int J Tuberc Lung Dis.* 2010; 14:149-54.
- Van Well GT, Paes BF, Terwee CB, Springer P, Roord JJ, Donald PR, et al. Twenty years of pediatric tuberculous meningitis: a retrospective cohort study in the western cape of South Africa. *Pediatrics.* 2009; 123:e1-8.
- Wang PD. Epidemiological trends of childhood tuberculosis in Taiwan, 1998-2005. *Int J Tuberc Lung Dis.* 2008; 12:250-4.
- Güneş A, Ulucu Ü, Aktar F, Konca Ç, Şen V, Ece A, et al. Clinical, radiological and laboratory findings in 185 children with tuberculous meningitis at a single center and relationship with the stage of the disease. *Ital J Pediatr.* 2015; 41:75.
- Van Well GT, Paes BF, Terwee CB, Springer P, Roord JJ, Donald PR, et al. Twenty years of pediatric tuberculous meningitis: a retrospective cohort study in the western cape of South Africa. *Pediatrics.* 2009; 123:e1-8.
- Shrestha S, Bichha RP, Sharma A, Upadhyay S, Rijal P. Clinical profile of tuberculosis in children. *Nepal Med Coll J.* 2011; 13:119-22.
- Shaikh MA, Shah M, Channa F. Criteria indicating morbidity in tuberculous meningitis. *J Pak Med Assoc.* 2012; 62:1137-9.
- Tinsa F, Essaddam L, Fitouri Z, Boussetta K, Becher SB, Bousnina S. Central system nervous tuberculosis in infants. *J Child Neurol.* 2010; 25:102-6.
- Nicolette NB, Wilmschurst J, Muloiwa R, James N. Presentation and outcome of tuberculous meningitis among children: experiences from a tertiary children's hospital. *Afr Health Sci.* 2014; 14:143-9.
- Saitoh A, Pong A, Waeckerle NJ, Leake JA, Nespeca MP, Bradley JS. Prediction of neurologic sequelae in childhood tuberculous meningitis: a review of 20 cases and proposal of a novel scoring system. *Pediatr Infect Dis J.* 2005; 24:207-12.