Original Article

Complications of Tuberculous Meningitis in Patients

Prevalence of Complications of Tuberculous Meningitis in Patients Presenting to Paediatric Department

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ABSTRACT

Objective: To determine the prevalence of complications in patients presenting with tuberculous meningitis.
Study Design: Descriptive / case series study.
Place and Duration of Study: This study was conducted at the Pediatrics Unit, Mardan Medical Complex, Mardan from 22 February 2015 to 21 February 2017.
Materials and Methods: A total of 50 diagnosed cases of tuberculous meningitis were enrolled. Common presenting clinical features and Complications of TBM were recorded and analyzed.
Results: Out of 50 patients 32 (64 %) were male and 18 (36%) were females. Mean age was 07.35±3.0208 S.D years. Presenting features included fever, vomiting, meningism, neurological deficits, altered level of consciousness and failure to thrive. Only 33 (66%) had available records on immunization and they all had received BCG vaccination. Common complications of TBM included Neurological sequelae 26 (52%), Hyponatraemia 25 (50%), Hydrocephalus 24 (48%) Epileptic seizure 24 (48%) Stroke 16 (32%) Cranial nerve palsies 13 (26%), Diabetes insipidus 04 (08%) Tuberculoma 03 (06%) Myeloradiculopathy 02 (04%), Hypothalamic syndrome 01 (02%) and Mortality 06 (12%),
Conclusion: Tubercular meningitis is associated with significant neurological and systemic complications. Early diagnosis, timely recognition of complications and institution of antituberculous treatment strategies may reduce mortality and morbidity

Key Words: Tuberculosis meningitis, complications. Central nervous system tuberculosis,

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INTRODUCTION

Tuberculosis (TB) is an important cause of morbidity and mortality worldwide.[1] The World Health Organization (WHO) estimated the prevalence of tuberculosis to be 442 per 100,000 population and incidence to be 234 per 100,000 population. Estimated mortality rate was 46 per 100,000 population.[2] Tuberculous meningitis (TBM) accounts for approximately 1% of all forms of tuberculosis and 5.1% of extrapulmonary tuberculosis.[3, 4]

Tuberculous meningitis (TBM) is the most severe complication of tuberculosis and frequently occurs in childhood.[5] TBM is the most severe form of tuberculosis, with high rates of disability and death.[6] It carries a risk of fatal outcome or severe neurological deficit, especially when the diagnosis and treatment are delayed.[7] TBM is a chronic serious illness with varied presentation and relatively high mortality and morbidity.[9] It is commonly considered a disease of developing nations, the burden of disease in developed nations is increasing. Young children, in particular, are the most susceptible to tuberculous meningitis (TBM).[8, 9]

A study showed common characteristics i.e. young age (<5 years), nonspecific symptoms existing for >1 week, stage II or III tuberculous meningitis, loss of consciousness, poor weight gain or weight loss, , meningeal irritation, motor deficit, raised intracranial pressure, cranial nerve palsies and brainstem dysfunction. Common features of tuberculous meningitis on CT scan of the brain were hydrocephalus, basal meningeal enhancement, infarctions, and periventricular lucency.[5]

The objective and rationale behind doing this study was to determine the frequency of complications of TBM in patients presenting with illness duration of > 4 weeks, hydrocephalus, cranial nerve palsy, Glasgow coma score of < 7, and hemiplegia. This study gave us insight to the local trend of complications of TBM in the pediatric population and on the basis of results of this study, recommendations were suggested regarding regular screening and in time management of all patients with TBM as these complications act as

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markers of poor outcome in patients with TBM and this study was also open more research questions regarding complications associated with disease.

MATERIALS AND METHODS

This descriptive case series was conducted in the Paediatrics Unit, Mardan Medical Complex, Mardan; a tertiary care hospital and was completed in One year period. A total of 50 patients were selected for the study with convenient (non-probability) sampling technique following the inclusion criteria; all patients with diagnosed tuberculous meningitis (diagnosed on clinical examination and were confirm on CT Scan) presenting with illness duration of > 4 weeks, hydrocephalus, cranial nerve palsy, Glasgow coma score of < 7 and hemiplegia, of both sexes, aged from 01 to 12 years. Already diagnosed cases of tuberculous meningitis, cases having bacterial, viral meningitis and cerebral malaria, cases having co-morbid conditions like acute respiratory infections, urinary tract infections, and enteric fever, which require antibiotic therapy were excluded from the study.

Data Collection Procedure: After getting approval from the hospital ethical committee to conduct the study, data was collected of all those patients with tuberculous meningitis (diagnosed on clinical examination and were confirm on CT Scan) presenting with illness duration of > 4 weeks, hydrocephalus, cranial nerve palsy, Glasgow coma score of < 7 and hemiplegia, to the Out-patient department (OPD) or Emergency department were admitted in Paediatrics Unit, of Mardan Medical Complex, Mardan. Patients who were fulfilling the inclusion criteria were included in the study. An informed written consent was taken from parents or relatives of the patients for further evaluation. After inclusion in the study, the patients were evaluated by clinical examination and laboratory tests including cerebrospinal fluid (CSF) analysis findings, tuberculin skin test; and other clinical specimens positive for acid-fast bacilli and computed tomography (CT) scan brain. Radiological evaluation was included CT scan compatible with TBM; and chest radiography compatible with primary tuberculosis. Complications of TBM in patients presenting with illness duration of > 4 weeks, hydrocephalus, cranial nerve palsy, Glasgow coma score of < 7 and hemiplegia were recorded and then these were noted down into the proforma of the study.

All the qualitative variables like illness duration of > 4 weeks, hydrocephalus, cranial nerve palsy, Glasgow coma score of < 7, hemiplegia and death were analyzed for percentages and frequencies. Mean ± standard deviation was calculated for quantitative variables like age. For gender, male to female ratio was calculated. The results were presented through tables, graphs and charts. All the data was stored and analyzed by statistical program SPSS version 12 for windows.

RESULTS

A total of 50 children with TBM admitted to Pasediatrics Unit, Mardan Medical Complex, Mardan during the study period. The mean age was 07.3500±3.02083 (S.D) years, ranging from 01 to 12 years. The male to female ratio was 1.77:1 (Table 1).

Table No. 1: Various demographic features of cases (n=50)

Variables	Frequency	Percentage
Age:		
01 - 05 years	09	18%
06 - 10 years	26	52%
11 - 12 years	15	30%
Sex:		
Male	32	64%
Female	18	36%

Table No. 2: Various features at presentation (n=50)

Presentation	Frequency	%age
History of Fever	50	100%
Temperature above 37.50 ºC	44	88%
Altered level of consciousness	19	38%
Convulsions	38	76%
Irritability	39	78%
Poor feeding	37	74%
TB contact	25	50%
Headache	49	98%
Vomiting	39	78%
Cough	41	82%
Difficulty in breathing	15	30%
Failure to thrive	44	88%
Meningism	37	74%
Bulging fontanelle	28	56%
Neurological deficits	38	76%
TBM stage 1	31	62%
TBM stage 2	14	28%
TBM stage 3	05	10%
History of BCG immunization done	33	66%

Common features included vomiting, neurological deficits, meningism, altered level of consciousness fever, and failure to thrive. Although 45 (90%) had a history of fever, and 05 (10%) had a normal temperature at admission. Of the 50, 19 (38%) with data on level of consciousness, only 31 (62%) had a record on the Glasgow coma scale. Out of these 50, 31 (62%) had TBM stage 1, 13 (26%) had TBM stage 2 and 06 (12%) had TBM stage 3.

According to the patient's attendants, only 33 (66%) had received BCG vaccination as they had records of immunization (Table 2).

The CSF protein concentration was done in 50 (100%) children. CSF glucose below 3.0 mmol/l was in 46 (92%) patients. To make a diagnosis of tuberculosis,

other tests including sputum smear and culture, chest X-rays, Mantoux test, CT and MRI are detailed in table 3.

Complications of TBM i.e. neurological sequelae, hyponatraemia, hydrocephalus, stroke, cranial nerve palsies, epileptic seizures, diabetes insipidus, tuberculoma, myeloradiculopathy, and hypothalamic syndrome are mentioned in table 4.

Table No. 3: Cerebrospinal fluid findings and other TB investigations (n=50)

Cerebrospinal fluid findings	Freq-uency	%age
CSF TB culture positive	14	28%
AAFBs negative	50	100%
Raised proteins concentration >0.4g/l	46	92%
Increased cell count >5cells/mm3	45	90%
Lymphocyte predominance	46	83%
Neutrophil predominance	11	22%
Other TB Investigation		
Mantoux test reactive	31	62%
Chest X-ray suggestive of TB.	35	70%
TB sputum culture positive.	09	18%
TB sputum smear negative	50	100%
CT/MRI results		
Basal meningeal enhancement	28	56%
Hydrocephalus	24	48%
Cerebral infarcts	19	38%
Cerebral oedema	17	35%
Normal	13	16%

Table No. 4: Complications of TBM (n=50)

Complications	Frequency	%age
Neurological sequelae	26	52%
Hyponatraemia	25	50%
Hydrocephalus	24	48%
Epileptic seizure	24	48%
Stroke	16	32%
Cranial nerve palsies	13	26%
Mortality	06	12%
Diabetes insipidus	04	08%
Tuberculoma	03	06%
Myeloradiculopathy	02	04%
Hypothalamic syndrome	01	02%

DISCUSSION

Tuberculous meningitis (TBM) is usually a progressive disorder and the diagnosis is difficult especially in regions with poor resources.[10]

TBM risk is greatest for infants and children under 2 years of age, probably due to the immaturity of the immune system.[11] The disease can occur at any age but is uncommon in children younger than 6 months and rare in those who are younger than 3 months of age. The peak incidence in a study was found during adolescence in the age group of 11 to 16 years (43%), followed by 31.8% cases in the age group of 6-10 years. Youngest was 3 months old. Higher incidence was observed by Malla et al[12] in the similar age group 10-16 years (70%). Similarly in our study peak incidence was found in 06-10 years with mean age of 07.35$\pm$3.02 (S.D.) which could be due to reason that we have selected children from 01 year to 12 years old.

The results of another study showed that majority (67 %) of children were less than 5 years old.[13]In a study from India, out of 44 patients with TBM it has been observed that 45% were male and 55% were female with a male to female ratio of 0.8:1.[14] In another study, 56% of patients were males.[13] Results of our study also showed that majority (67%) children were males, with a male o female ratio of 01.77:01. This may be due to reasons that the socio-cultural customs and rules of the region are against the female children, which are neglected in every aspect even if they are very sick they are not brought to male doctors for treatment.

In a study fever was present in 100% of patients followed by altered sensorium, present in 54.5%. Vomiting in 50%, headache in 45.4%, seizures 40.9% cases. Cough present in only 27.2% patients. Abdominal pain (11.3%), altered bowel habits (2.2%), loose motion (2.2%). Other neurological deficit found was loss of speech in 6.8%, right sided weakness 4.5%, diplopia 2.2%, blurred vision 2.2%.[14] Similarly in our study common features like vomiting, meningism, fever, neurological deficits, failure to thrive and altered levels of consciousness were present with more or less percentages were present in patients having TBM.

In a study,[14] in 93% patients consciousness was altered at presentation, out of which 40.9% were drowsy at presentation, 36.3% patients were unconscious at presentation, 15.9% were irritable. Signs of meningeal irritation were present in 79.5%. Cranial nerve involved in the referenced study was optic (4.5%), ophthalmic (9%), abducens (31.8%), facial (13.6%), glossopharyngeal and vagus nerve (2.2%). Abducens nerve involvement was most common. Fundus was normal in 45.4% patients, Edema was found in 29.5%, atrophy in only 2.2%. Motor involvement in form of hemiplegia was found in only 2 patients. No case with quadriplegia was found. Tender lymphadenopathy was present in 2 patients. Same or more or less percentages of signs were also present in our patients at presentation.

In a study[15] TBM was present in only 15% cases. Results of our study showed that CSF TB culture was positive in 29% cases, AAFBs was negative in 100% patients, while raised proteins concentration of >0.4g/l was found in 91% patients of TBM. Other tests for the diagnosis of tuberculosis i.e. chest X-rays, sputum smear and culture, Mantoux test, MRI and CT scan were done to confirm the TBM as early as possible.

There are three main factors in delay of diagnosis and treatment of TBM. First, poverty is a barrier to

accessing health care in resources scarce countries. Secondly, TBM presents in a distracted method and it is uncommon to verify the diagnosis microbiologically even in high resource settings.[13]Improving laboratory training and infrastructure, and improving access to WHO endorsed technologies such as the GeneXpert, would potentially reduce this delay but will not alter the fact that clinical specimens from children are limited both by their volume and their paucibacillary nature.[16] An adequate volume of CSF significantly affects the likelihood of confirming the diagnosis and appropriate sampling for TB at other sites should be performed. Moreover, while TB diagnostic tests remain poorly sensitive, increasing the capacity to recognize and keep out other central nervous system pathogens, is key in giving clinicians the confidence to initiate a timely treatment and which reduce unnecesssary prescription of lengthy TB regimens.[17]

Tuberculous meningitis in children carries significant morbidity and mortality.[13] The mortality ranges from 13% to 69% even in developed countries.[18-21] In the aforesaid study, the better outcome may be because all 37 patients had the records of date of starting anti-TB treatment (ATT) and had started treatment within 3 days of admission. Early initiation of treatment has been recognized as the main predictive factor which predicts disease lethality and sequelae.[20] The another study[22] showed that overall mortality was 28% in cases of TBM. In our study mortality rate was 11%, which is within the range as mentioned in the literature.

Seizure is one of the clinical feature or complication of meningitis. In the first

few days of bacterial meningitis, seizures occur in about 25% cases.[23]

Common and important causes of mortality and long-term morbidity were neurological and systemic complications of tuberculous meningitis.Hydrocephalus is a common complication of TBM; prevalence has been reported in more than 75% of cases in literature review.[24]

Hyponatremia occurs in 35-65% of patients with tuberculous meningitis and is an independent predictor of death or severe disability.[25] There are many factors which are responsible for the complications of TBM like delay presentation to specialist hospitals of city, our illiterate and uneducated peoples first contact hakeems, quacks, non-qualified, and spiritual heelers and peers. Poverty is another factor which hinders for seeking medical treatment in this poor part of the country. There are no facilities of diagnosis of TBM in many districts and agency headquarters hospitals in the province of KPK. Which enhances the burden of the TBM in this poor resources province of the country.

CONCLUSION

Earlier investigations and diagnosis of TBM and treatment may be able to prevent these complications. If left untreated, TBM can be life threaten. The proper BCG vaccination can help to prevent TBM in young children living in places where this disease is more common.

Author's Contribution:

Concept & Design of Study:	Muhammad Qasim Khan
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Revisiting Critically:	Muhammad Qasim Khan, Kiramat Ullah Wazir
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