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ORIGINAL ARTICLE

Spectrum of Clinical Presentation of Tuberculosis Meningitis in Children at a Tertiary Care Hospital

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ABSTRACT

In underdeveloped nations, TB in children is a major public health issue, with tubercular meningitis being a devastating consequence with high death rate. Tuberculous Meningitis (TBM) is caused by the spread of main or secondary pulmonary illness through the bloodstream. One of the most dangerous clinical symptoms of TB is infection of the central nervous system. The advanced stage of TBM may have a negative impact on the result.

Objective: To determine frequency of different spectrum of clinical presentation of tuberculosis meningitis in children at tertiary care hospital

Material and Methods: This was a cross sectional study carried out at the Children hospital and Institute of child health from May, 2018 to Nov, 2018. About 364 patients were employed in the research. Patients' or attendants' informed written consent was attained, and their demographic information (including name, age, gender, residence, and duration of pain) was recorded. All newly diagnosed cases were taken in this study for further investigation about their stages of the disease. All stages were labeled as per operational definition.

Results: The patients' normal age was 6.56 SD 3.46 years, with the lowest and highest ages being 1 and 12 years, respectively. There were 200 male cases (54.9%) and 164 female cases (45.1%), with a larger male to female ratio. With a minimum and highest GCS score of 5 and 15, the mean GCS is 11.76 2.77. According to the operational definition, 30 patients (8.2%) had stage I TBM, 150 cases (41.2%) had stage II TBM, and 184 instances (50.5%) had stage III TBM.

Conclusion: The outcomes of this study revealed that about half of the cases had stage III TBM, implying that patients with TBM should be managed properly if this stage is remembered. With aggressive and selective treatment plan the prognosis can be increased and rate of mortality may be decreased.

Keywords: Children, developing country, meningitis, mortality, Tuberculosis

INTRODUCTION

Childhood tuberculosis is often overlooked since it is smear-negative. Because of their underdeveloped immune systems, young children are more susceptible than older children and adults to get complicate into severe form of tuberculosis.[1] Tuberculosis meningitis (TBM) is the most dangerous extrapulmonary consequence of tuberculosis, with a near-100 percent fatality rate if left untreated. TBM is difficult to diagnose due to its vague clinical presentation, which can be acute, subacute, or chronic. It might be either febrile or afebrile.[2] Stage 1 TBM illness has vague signs and symptoms that are more related to a primary lung infection than to neurological disease.[3]

TBM is diagnosed using a combination of clinical, laboratory, and radiological findings, including tuberculosis-like symptoms on a conventional chest X-ray (CXR). TBM is characterized by dense exudate comprised of lymphocytes, macrophages, epithelioid cells and histiocytes, and central necrotic tissue with granuloma development, according to histopathology. Hydrocephalus, increased intracranial pressure, cerebral infarction, opticochiasmaticarachnoiditis, tuberculous brain abscess, tuberculoma, and pituitary and hypothalamus involvement are all secondary consequences. [3]

In addition to suitable treatment techniques, early diagnosis of individuals with TBM (Phases I and II) is critical for lowering death rates.[5] According to a research, Phase I TBM was seen in 7 (14.9%) instances, stage II in 11 (23.4%) cases, and stage III in 29 (61.7%) cases.[6] They also said that mortality in Phase I and Phase II disease was zero, but that mortality in Phase III disease was 38%.[6] Another recent study found that 68 (37 percent) of patients were in Phase one, 31 percent in Phase two, and 32 percent in Phase three of the disease.[7]

The rational of this research is to find common spectrum of clinical presentation in our local population as no data is available and global studies gave different results of stage I (14%[6] - 37[7]) , and Stage III (32%[7] - 61%[6]) So the current study is important to find the exact presenting stage of TBM so that such cases cab be managed accordingly as cases with advanced stages of TBM has poor prognosis and increased rate of mortality.

MATERIAL AND METHODS

In this Cross sectional study, carried out at the Children hospital and Institute of child health with data collection done for 6 months May 11, 2018 till Nov 11, 2018. Sampling was done using Non probability consecutive sampling. Primary objective of this study was to determine frequency of different spectrum of clinical presentation of tuberculosis meningitis in children at tertiary care hospital.

All children of age 1 – 12 years of either gender newly diagnosed (diagnosed during last 72 hours) of TBM and admitted to a tertiary care hospital were enrolled. While TBM cases on treatment, known cases of chronic illness or malignancy or HIV (as noted on clinical assessment) and those on immunosuppressive therapy (as accessed on clinical record) were excluded.

A total sample size of 364 was calculated for this study, using frequency of stage-III TBM in 29 cases (61.7%)[6]; 95% confidence level and 5% margin of error.

A case of Tuberculosis meningitis (TBM) was defined with presence of pleocytosis (> 1000 cells per litre) with a lymphocyte predominance (> 50%), an increased protein concentration (> 3 g/L), and a low glucose concentration (absolute value 2.2 mmo;/L) and a CSF to plasma ratio 50%) on CSF examination and biochemical analysis were all included in this study.

Spectrum of clinical presentations of TBM cases was determined in terms of stages of TBM that was defined as: (on the basis of GCS as Glasgow Coma Scale provides a score in the range 3-15)**.** Stage I TBM: Glasgow comma scale (GCS) score of 15 without any no focal neurologic indications (weakness of one or more part of the body). Stage II TBM: GCS of 11–14 or GCS of 15 with focal

neurologic deficit (weakness of one or more part of the body). Stage III TBM: if GCS score was less than 11.

About 364 patients from the pediatric department of the children's hospital in Lahore were employed in the research. Patients' or attendants' informed written consent was obtained, and their demographic information (including name, age, gender, residence, and duration of pain) was recorded. All newly diagnosed cases were taken in this study for further investigation about their stages of the disease. All stages were labeled as defined above. All data was recorded by researcher himself on attached proforma.

After the analysis of data in the software SPSS 22, for quantitative data such as age and GSC score, the mean and S.D. was utilized. For categorical data such as gender, symptom duration, and TBM phases, frequency (percent) was employed. To account for effect modifiers, data was stratified by age and gender. Following stratification, Chi-square analysis It was suggested that the impact modifiers be addressed. Significance was determined by P-value of less than 0.05.

RESULTS

The average age of cases was 6.56 ± 3.46 years with least and highest age as 1 and 12 years. There were 171 (47%) cases that were 1-6 years old and 193(53%) cases were 6-12 years old. There were 200 (54.9%) male and 164 (45.1%) female cases with higher male to female ratio.

A total of 187(51.4%) cases had disease since < 2 weeks and 177(48.6%) cases had duration of disease since ≥ 2 weeks. The mean GCS was 11.76 ± 2.77 with minimum and maximum GCS score as 5 and 15.

According to operational definition, 30 (8.2%) cases had Phase I, 150(41.2%) cases had Phase II and 184(50.5%) cases had Phase III of TBM. In age group of 1- 6 years, 17(9.9%) cases, 66(38.6%) cases and 88(51.5%) cases had Phase I, Phase II and Phase III respectively while in 6-12 years of age group, 13(6.7%) cases had stage I, 84(43.5%) cases had stage II and 96(49.7%) cases had Phase III of TBM.

The frequency of different stages was statistically same in both age groups, p-value > 0.05. Among male cases, 16(8%) cases had Phase I, 86(43%) cases had Phase II and 98(49%) cases had Phase III and among female cases 14(8.5%) cases had Phase I, 64(39%) cases had Phase II and 86 (52.4%) cases had Phase III. The frequency of different Phases was analytical same in both gender, p-value > 0.05.

Table-1: Spectrum of Clinical Presentation with respect to age groups (years)

		Spectrum of Clinical Presentation			Total
		Stage I	Stage II	Stage III	
Age	1-6	17(9.9%)	66(38.6%)	88(51.5%)	171(100%)
	6-12	13(6.7%)	84(43.5%)	96(49.7%)	193(100%)
Total		30(8.2%)	150(41.2%)	184(50.5%)	364(100%)

Chi-square = 1.718; P-value = 0.424(Insignificant)

Table-2: Spectrum of Clinical Presentation with respect to gender

	Spectrum of Clinical Presentation			Total
Gender	Stage I	Stage II	Stage III	
Male	16(8%)	86(43.0%)	98(49.0%)	200(100%)
Female	14(8.5%)	64(39.0%)	86(52.4%)	164(100%)
Total	30(8.2%)	150(41.2%)	184(50.5%)	364(100%)

Chi-square = 0.588; P-value = 0.745(Insignificant)

Table-3: Spectrum of Clinical Presentation with respect to duration of symptoms

	Spectrum of Clinical Presentation			Total
Duration of Symptoms	Stage I	Stage II	Stage III	
< 2 weeks	15(8.0%)	70(37.4%)	102(54.5%)	187(100%)
≥2 weeks	15(8.5%)	80(45.2%)	82(46.3%)	177(100%)
Total	30(8.2%)	150(41.2%)	184(50.5%)	364(100%)

Chi-square = 2.568; P-value = 0.277(Insignificant)

In cases of < 2 weeks of duration, there were 15(8%) cases had stage I, 70(37.4%) cases had stage II and 102 (54.5%) cases had stage III while in cases with duration of symptoms ≥ 2 weeks, 15(8.5%) cases had stage I, 80 (45.2%) cases had stage II and 82(46.3%) cases had stage III. The frequency of duration of different stages of was statistically same in respect to duration of symptoms, p-value > 0.05.

DISCUSSION

In the under-developed nations, both the childhood and adult tuberculosis is one of the primary causes of death and illness. As reported by the WHO (World Health Organization), around 16 million people worldwide have TB presently, with approximately 8.5 million newly diagnosed patients every year. Tubercluosis caused even more than 2 million deaths worldwide.[8] In the WHO report issued in the year 2013, around ten million patients of tuberculosis (TB) infections were spotted, with around one and a half million fatalities, according to the WHO. About ten of these cases were of the younger age group, and around fifteen percent individuals had extra pulmonary TB. [9]

TBM is a prevalent central nervous system infection in underdeveloped nations. Extra pulmonary TB of the central nervous system has a greater death and morbidity rate than pulmonary tuberculosis. TBM is the most common kind of TB 100 in the central nervous system. Early identification and treatment with chemotherapy, as well as watchful care of complications, are crucial to avoid irreversible neurologic sequelae and death. Postponement in diagnosis, and hence the commencement of proper therapy, results in a poor diagnosis and sequelae in up to 25% of cases.[10] For a convincing diagnosis of tuberculous meningitis, direct staining or culture of Mycobacterium tuberculosis in the cerebrospinal fluid (CSF) is necessary. CSF smears and cultures, on the other hand, have a limited diagnostic yield, and mycobacterial cultures might take up to 6 weeks to provide results.[11]

As a result, tuberculous meningitis is diagnosed based on sub-acute to chronic meningitis with rise in the number of WBCs in the CSF and a fall in the CSF glucose levels. Other kinds of meningitis, on the other hand, may resemble tuberculous meningitis in appearance. CSF abnormalities in tuberculous meningitis patients might look like aseptic meningitis. For tuberculous meningitis, many rapid diagnostic diagnoses are employed which are based on a CSF inspection.[11]

Early discovery and treatment can totally heal TBM, however three-quarters of people perish if treatment is postponed. The presence of the bacterium, Mycobacterium tuberculosis, in the CSF confirms the diagnosis of tuberculosis meningitis (TBM). The need for Mycobacterium to grow on a precise culture medium for an extended length of time, as well as the small chance of direct isolation of the bacteria from the cerebrospinal fluid smear staining, can lead to the delay in the diagnosis of TBM.[12]

To eliminate this delay in the diagnosis of TBM, various advanced ways can be used. These include nucleic acid amplification, PCR for isolation of mycobacterium, serology testing for the detection of antigen and antibodies for mycobacterium can be used. Diagnostic algorithms based on clinical, laboratory, and imaging data have been proposed, particularly for the under-developed countries where it is difficult to manage the expensive advanced techniques and are often unavailable. In children, tuberculous meningitis generally develops 2–6 months after the first lung infection. As a result, knowing the findings of pulmonary tuberculosis might aid in the early diagnosis of TBM. [13]

The patients in this study had an average age of 6.56 3.46 years, with a low and high of 1 and 12 years, respectively. There were 200 male cases (54.9%) and 164 female cases (45.1%), with the male to female ratio being higher. The patients' average age was 53.5 44.9 months (4 months–18 years), according to another research. A total of 121 (65.4 percent) men and 64 (34.6 percent) women were among the patients7. The latest research's mean age was greater than the previous study, but the gender distribution was nearly same. Another survey in Bangladesh found that 56.7 percent of the population was male and 43.3 percent was female.[14]

In the current study, 30 instances (8.2%) had stage I TBM, 150 cases (41.2%) had stage II TBM, and 184 cases (50.5%) had stage III TBM. According to a research, stage I TBM was seen in 7 (14.9%) instances, stage II in 11 (23.4%) cases, and stage III in 29 (61.7%) cases.[6] Another recent study found that 68 (37 percent) of patients were in Stage I, 57 (31 percent) in Stage II, and 60 (32 percent) in Stage III of the disease.[7] This study's findings were practically identical to those of Israni et al [6], however the results were different from those of Güneş et al. [7]

A retrospective study was published in 2013 after analyzing the data of demographics, signs and symptoms, and disease outcome of the TBM patients. A total of 40 cases were chosen (representing 10 percent of all paediatric TB patients). The average age of the participants was 46 months (range 1-165 months). Stage I (non-specific febrile illness without neurological indicators), stage II (neurological signals without substantial sensorium changes), and stage III (severe neurological indications with sensorial alterations and/or coma) were assigned to 18 (45%) of the children. This study indicated that the presentation of tubercular meningitis varies by patient. TBM is a severe form of extra-pulmonary tuberculosis that affects 7.0-12.0 percent of TB patients in underdeveloped countries, with a significant mortality rate due to delayed diagnosis and treatment.[15]

TBM is still a devastating disease in our country. In compared to other forms of extrapulmonary tuberculosis, the prognosis was worse despite antitubercular medication, with not just complications but also a high mortality rate. When clinical and laboratory findings point to TBM, doctors should check for tuberculosis elsewhere in the body.

CONCLUSION

More than half of the cases in this research had stage III TBM, emphasizing those patients with TBM should be addressed appropriately if this stage is recognized. Prognosis can be improved and death rates can be reduced with an active and focused treatment regimen.

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