Original Article

Criteria indicating morbidity in tuberculous meningitis

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Abstract

Objective: To work out a criterion that may indicate morbidity in tuberculous meningitis.

Methods: The retrospective study was conducted at the Medical Unit of the Liaquat University of Health Sciences, Jamshoro, Pakistan, and included cases related to a period between January 2006 and June 2011. Record of 50 patients were evaluated for clinical features, chest radiograph, Mantoux test, sputum for acid fast bacilli, routine investigations, cerebrospinal fluid studies, computerised tomography scan and magnetic resonance imaging of head. All the patients in the study had been treated with conventional approach. The severity of the condition was classified in stages, I, II and III. Clinical features, laboratory findings and imaging reports were analysed through SPSS 10 to find out the criteria indicating morbidity. Mean, median, standard deviation were calculated. Student t-test was applied on variables.

Results: Of the 50 patients, 26 (52%) were male and 24 (48%) were female. Their ages ranged from 12 to 70 years. Mean age was 37.72 ±19.65 years. Median age was 35.54 years. Of the total, 17 (34%) patients recovered completely without any complications. Their mean age was 24±8.98 years and their mean time interval from onset of illness to presentation in the hospital was 21.75±9.75 days. Besides, 30 (60%) patients persisted with neurological sequelae, including cranial nerve palsies, hemiplegia, and hydrocephalus. Patients with neurological sequelae had mean age of 48±17.48 years and their mean time interval from onset of illness to presentation in the hospital was 41.33±14.14 days. Hydrocephalus was seen in 10 (20%) patients. Three (6%) patients expired. Clinical features, laboratory findings and imaging reports analysis showed that the criteria indicating morbidity were increasing age of the patient (p=0.037), late diagnosis (p=0.044), advancing stage of disease, and development of hydrocephalus.

Conclusion: Increasing age of the patient, late diagnosis, advancing stage of the disease and the development of hydrocephalus indicate morbidity in tuberculous meningitis.

Keywords: Tubercculous meningitis, Morbidity, Criteria. (JPMA 62: 1137; 2012)

Introduction

All aspects of tuberculous meningitis (TBM) are dominated with uncertainty and doubt. Changing natural history and accompanying clinical features of TBM make the diagnosis difficult. Ziehl-Neelsen staining lacks sensitivity; and culture results are not timely enough to aid clinical judgment. New rapid diagnostic methods are incompletely evaluated, and many are not suitable for laboratories in under-developed countries.[1] Tuberculosis is the most common and important infectious diseases causing morbidity and death around the world. One-third of the world's population is infected with mycobacterium tuberculosis. The World Health Organisation estimates that about 8 to 10 million new cases occur annually worldwide and the incidence is currently increasing. Tuberculosis, malaria and HIV are the leading causes of death from a single infectious agent, and approximately two million deaths are due to tuberculosis annually.[2] TBM is the most severe form of the disease in which the infection spreads to membranes enveloping the brain and the spinal cord. Tuberculous infection rate in population is one every second. However, only one in 10 infected persons will develop symptoms; and that usually happens when their immune systems are already weak.[3] Africa is facing the worst tuberculosis epidemic.[4] Mycobacterium Tuberculosis has infected man since the time in memory. It can damage every organ of the body. TBM continues to be a serious infection in many developing countries, including Pakistan. It is the most dangerous form of extra-pulmonary tuberculosis. Delay in diagnosis is directly related to poor outcome.[5] Neurological sequelae are commonly present. In India 2% to 5% of patients admitted in paediatric hospitals suffer from TBM.[4] Its incidence has increased in developed countries because of Acquired Immuno-Deficiency Syndrome (AIDS); such patients are more likely to have mycobacterimia.[6] TBM was the prime type of meningitis associated with patients of injecting

drug abuse.[7] Genetic factors play a role in host response to infection with mycobacterium tuberculosis.[8] It has been observed that mannose binding protein B allele confers protection against TBM.[9]

Complications of TBM are due to development of hydrocephalus, arteritis and organisation of exudates at base of brain causing cranial nerve palsies, leading to disability and epilepsy. In patients with altered sensorium motor and somatosensory, evoked potentials may be helpful in objective documentation of respective motor and sensory functions.[10] It is now accepted that anti-tuberculous drug therapy for 12 to 18 months is necessary to achieve cure. The use of steroids remains selective. High-dose predinisolone should be carefully considered in current treatment regimen of TBM.[11] Acute onset syringomylia should be suspected in any patient being treated for TBM who subsequently develops limb weakness and/or sphinteric dysfunction. Inflammatory oedema and cord ischaemia appeared to be underlying mechanism in these early onset cases rather than arachnoiditis which is important in late onset cases.[12] Considering the high morbidity due to this disease, it was decided to search the criteria indicating morbidity in TBM.

Patients and Methods

Fifty diagnosed TBM patients were retrospectively studied from January 2006 to June 2011. The descriptive and analytical study was carried out at the Medical Unit of Liaquat University of Medical and Health Sciences, Jamshoro, Hyderabad, Pakistan. After the record files were managed, the diagnostic criteria for TBM for the study were defined as: clinical features of subacute meningitis, including headache, fever and neck stiffness; clear cerebro spinal fluid (CSF) with high protein, low glucose and lymphocyte pleocytosis; no response to standard anti-bacterial drugs and no evidence of brain abscess; and evidence of tuberculosis outside the central nervous system.

Patients' records were evaluated for clinical features, chest radiograph, Mantoux test, sputum for acid fast bacilli, routine investigations, cerebrospinal fluid (CSF) studies, computerized tomography (CT) scan and magnetic resonance imaging (MRI) of head. All the patients had been treated with conventional treatment. Drugs given were isoniazid, rifampicin, streptomycin and pyrazinamide. In case of toxicity, drugs were changed. Steroids were used in all of the patients. Severity of TBM was classified in stages, I, II and III — conscious; drowsy, and in coma respectively.

Clinical features, laboratory findings and imaging reports were analysed by SPSS 10. Mean, median, and standard deviation were calculated, while student t-test was applied on variables. P value less than 0.05 was considered to be statistically significant.

Results

Of the 50 TBM patients in this study, 26 (52%) were male and 24 (48%) were female. Their ages ranged from 12 to 70 years. Mean age was 37.72±19.65 years. Median age was 35.54 years. Besides, 19 (38%) were <40 years, and 31 (62%) were >40 years of age. Two (4%) patients presented in conscious stage (stage I), and recovered completely; 30 (60%) patients presented in drowsy and/or with focal neurological sign (stage II), and 15 of them improved completely while the remaining 15 persisted with neurological sequelae; and 18 (36%) patients presented in deep coma (stage III), and 3 (6%) of them expired of brain stem compression, while the remaining persisted with neurological sequelae.

Of the total, 17 (34%) patients recovered completely without any complications. Their mean age was 24±8.98 years and their mean time interval from the onset of illness to presentation in the hospital was 21.75±9.75 days. They were in stage I and II of the disease and none had hydrocephalus.

Leaving the 3 (6%) deaths aside, 30 (60%) patients persisted with neurological sequelae, including cranial nerve palsies, hemiplegia, and hydrocephalus. Patients with neurological sequelae had mean age of 48±17.48 years and their mean time interval from the onset of illness to presentation in the hospital was 41.33±14.14 days. They were in stage II and III of the disease and seven patients had

Table: Criteria indicating morbidity in Tuberculous meningitis.

Variable	Recovered 17(34%)	Morbidity 30 (60%)	P value
Mean Age years	24±8.98	48±17.4	0.037
Mean Time since illness days	21.8±9.74	41.3±14.1	0.044
Mean CSF Glucose mg/dl	32.3±6.55	30.2±6.5	0.63
Mean CSF Protein mg/dl	53±9.21	51.5±7.71	0.77
Mean CSF WBC/cmm	242±172	228±155	0.90
Mean Blood WBC/cmm	13000±5500	13800±6100	0.83
Stage of disease	I,II	II,III	
Hydrocephalus Patients	0	7	

CSF: Cerebro Spinal Fluid. WBC: White Blood Cells.

hydrocephalus.

Among all patients hydrocephalus was seen in 10 (20%) patients. Three (6%) patients expired. Clinical features, laboratory findings and imaging reports analysis showed that the criteria indicating morbidity in TBM are increasing age of the patient (p=0.037), late diagnosis (p=0.044), advancing stage of disease, and development of hydrocephalous. Peripheral white blood cell (WBC) count (p=0.83), CSF glucose (p=0.63), CSF protein (p=0.77) and CSF WBC count (p=0.0.90) were not statistically significant (Table).

Discussion

The study revealed that the best criteria indicating morbidity in TBM are increasing age of the patient (p<0.037), late diagnosis (p<0.044), advancing stage of disease and development of hydrocephalous. But peripheral WBC count (p=0.83), CSF glucose (p=0.63), CSF protein (p=0.77) and CSF WBC count (p=0.90) were not statistically significant factors indicating morbidity of disease.

This study is comparable with other national and international studies. One study has shown that significant prognostic factors were the patient's age, the severity of TBM, and effective treatment of hydrocephalus and corticosteroid therapy.[13] Another study observed that the most important predictors of mortality for TBM were older age, altered mental status on admission, underlying co-morbidities and leukocytosis.[14] Further studies revealed that the presence of hydrocephalus and severity of TBM was strongly associated with therapeutic outcome.[15] Recently it has been found that initial isoniazid resistance is associated with poor clinical outcomes in TBM.[16] TBM is still quite common around the world with high mortality. In this study the morbidity was 60% and mortality was 6%, while in other studies mortality has remained high.[17] In this study clinical features and CSF findings were not associated criteria indicating morbidity in TBM, but other studies have shown that these variables are also predictors of outcome.[18] A study carried out at Karachi showed that among 40 cases of TBM, 40% patients fully recovered without complications, 35% had partial recovery with complications and 25% expired.[19]

Conclusion

The study revealed that increasing age of patient, late diagnosis and start of treatment, advancing stage of disease and the development of hydrocephalous indicate morbidity in TBM.

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