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Outcome of tuberculous meningitis patients requiring mechanical ventilation

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ABSTRACT

Purpose: There is paucity of information about the outcome of tuberculous meningitis (TBM) patients on mechanical ventilation (MV). In this communication, we report the clinical characteristics, predictors of MV, and outcome of TBM patients requiring MV.
Method: Thirty-eight (18%) of 205 patients with TBM requiring MV were included; and their demographic, clinical, cerebrospinal fluid, and magnetic resonance imaging finding at admission and follow-up were noted. The ventilator-related and systemic complications, hospital death, and 3-month functional outcome were noted. The predictors of need of MV were derived by multivariate regression analysis.
Results: There were 38 MV and 36 non-MV TBM patients who were matched for age, sex, and stage of meningitis on admission. The requirement of MV was independently related to leukocytosis, seizure, and cerebrospinal fluid pleocytosis on admission. Patients on MV had higher frequency of septicemia (9 vs 2), bedsores (6 vs 0), and gastric hemorrhage (4 vs 0) compared with non-MV patients. Only 29% of MV patients survived and had poor outcome at 3 months; but in the non-MV group, all the patients survived, and only 11% had poor outcome.
Conclusion: Mechanical ventilation was needed in 18% TBM patients because of TBM-related or systemic complications. Those requiring MV had high mortality and may be categorized separately.

1. Introduction

Tuberculosis is an important public health problem. It is estimated that more than 2 billion people are infected with *Mycobacterium tuberculosis*, and 10% of them develop active tuberculosis [1]. Tuberculosis results in 2 million deaths annually, and 90% of these deaths occur in the developing countries of Asia and Africa. About 50% of new cases are from Bangladesh, Pakistan, India, China, Indonesia, and the Philippines [2]. Tuberculous meningitis (TBM) constitutes about 5% of extrapulmonary tuberculosis and is the most severe form of tuberculosis with high mortality and morbidity. About 10% to 30% of patients with TBM die, one third of the surviving patients have long-term functional deficit, and 78% have neurological sequelae [3–7]. In TBM, there may be vasculitis, exudates, hydrocephalous, and tuberculoma which contribute to increased intracranial pressure, altered sensorium, and brain herniation with ominous consequences [4,8]. Intensive care management of these patients can be challenging but lifesaving. There is a paucity of information regarding intensive care unit (ICU) management of TBM patients. In this communication, we report our experience of management of TBM patients in a neurology ICU and evaluate the predictors of mechanical ventilation (MV) and their outcome.

2. Subjects and methods

Patients with TBM admitted to neurology ICU during 2010-2014 were included. These patients were retrospectively analyzed from a prospectively maintained TBM registry. The diagnosis of TBM was based on clinical, cerebrospinal fluid (CSF), and magnetic resonance imaging (MRI) findings. The essential diagnostic criteria were symptoms of meningitis (fever, headache, vomiting) for at least 2 weeks in which malaria, septic meningitis, and fungal meningitis were excluded. The supportive criteria included (*a*) CSF cells greater than 2×10^9/L with lymphocyte predominance, protein greater than 1 g/L, sterile bacterial and fungal culture, and negative cryptococcal antigen; (*b*) computed tomography (CT) or MRI showing exudate, hydrocephalous, tuberculoma, or infarction; and (*c*) extra central nervous system (CNS) tuberculosis.

Presence of essential criteria with 2 supportive criteria was considered TBM. Presence of acid-fast bacilli (AFB) in CSF, smear or BACTEC culture, polymerase chain reaction (PCR), or immunoglobulin M enzyme-linked immunosorbent assay was considered as definite and the remaining as probable TBM [5].

2.1. Evaluation

Clinical history including demographic information, symptoms of meningitis and its duration, alteration in sensorium, seizure, focal weakness, and respiratory symptoms were noted. Consciousness was assessed by Glasgow Coma Scale (GCS). The patients were considered

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Table 1A
Comparison of demographic and clinical characteristics of tubercular meningitis patients with and without MV

	Ventilated (n = 38)	Non ventilated (n = 36)	*P* value
Sex (female/male)	15/23	13/23	.81
Age (y)	35.9 ± 12.6	37.1 ± 16.6	.72
Stage of TBM, I/II/III	1/15/22	1/18/17	.65
Duration of illness (d)	74.3 ± 65.5	68.5 ± 66.6	.71
GCS score	9.8 ± 3.3	11.0 ± 2.7	.11
Focal motor deficit	24	18	.35
Seizures	24	11	.004
Status epilepticus	7	3	.21
Hypertension	9	20	.005
Diabetes mellitus	5	4	1.00
Coronary artery disease	1	2	.61
Renal failure	5	0	.02
Liver dysfunction	0	1	.49
Diagnosis			.78
Definite/probable	14/24	11/25	
PCR+	9/27	7/28	
AFB+	3/35	2/34	
Culture+	8/30	7/29	

+, present.

to have raised intracranial pressure based on extensor posturing, hyperventilation, and pupillary asymmetry. Cranial nerve palsies and papilloedema were noted. Muscle weakness was recorded as monoplegia, hemiplegia, paraplegia, or quadriplegia. The severity of weakness was graded as complete or partial. Muscle tone and tendon reflexes were graded as absent, normal, or increased. Stage of meningitis was categorized as follows [7]:

Stage I: meningitis only
Stage II: meningitis with focal neurological signs or GCS score 11 to 14
Stage III: meningitis with altered sensorium; GCS score less than 11.

2.2. Investigations

Blood counts, hemoglobin, erythrocyte sedimentation rate at first hour, blood glucose, serum creatinine, albumin, bilirubin, transaminases, and electrolytes were measured. Chest radiograph, electrocardiogram, and HIV serology were also done. Cranial MRI was done using a 3-T MRI scanner (Signa; GE Medical Systems, Milwaukee, WI). T1, T2, fluid attenuated inversion recovery, diffusion weighted image, and T1 contrast images were obtained in axial, coronal, and sagittal plain. Presence of exudates, hydrocephalus, infarction, and granuloma was noted. Lumbar CSF was examined for cell, protein, and glucose. Cerebrospinal fluid smear and culture (BD BACTEC TM, BD, Sparks, MD) were done for AFB. Cryptococcal antigen, immunoglobulin M enzyme-linked immunosorbent assay for *M tuberculosis*, and PCR were also carried out. The patients were treated with rifampicin (10 mg/kg, ~450 mg), isoniazid (5 mg/kg, ~300 mg), pyrazinamide (20-25 mg/kg, ~1500 mg), and ethambutol (15-20 mg/kg, ~800 mg) with prednisolone 0.5 mg/kg (~40 mg) and aspirin 150 mg daily [9]. Prednisolone was tapered after 1 month and stopped at the end of the second month. All the antitubercular drugs were given for 6 months followed by rifampicin and isoniazid for an additional 1 year. Drug-induced hepatitis was diagnosed on the basis of 3- to 5-fold rise in transaminase level after at least 3 days of antitubercular treatment (ATT) without any other apparent cause for liver dysfunction whose baseline liver function was normal. After discontinuation of hepatotoxic ATT, there was more than 50% improvement in liver functions. In these patients, ATT was modified and was restarted sequentially when the transaminase level was less than 2 times the normal [10]. Patients with obstructive hydrocephalus with deteriorating consciousness were subjected to ventriculoperitoneal shunt.

Table 1B
Comparison of baseline laboratory profile of tubercular meningitis patients with and without MV

Parameters	Ventilated (n = 38)	Non ventilated (n = 36)	*P* value
Hemoglobin (g/dL)	10.7 ± 2.4	11.5 ± 1.8	.11
Leucocyte count/mm^3	13805.3 ± 6798.3	9713.9 ± 3838.8	.002
Sodium (mEq/L)	132.4 ± 8.0	133.49 ± 7.3	.53
Creatinine at admission (mg/dL)	1.1 ± 0.9	0.9 ± 0.8	.44
Serum albumin (g/dL)	3.2 ± 0.8	3.5 ± 0.6	.05
ALT (mEq/L)	120.0 ± 119.2	101.1 ± 135.2	.53
AST (mEq/L)	117.7 ± 118.2	88.5 ± 91.6	.25
Serum bilirubin (mg/dL)	0.8 ± 0.4	1.0 ± 0.9	.26
CSF total cells/mm^3	210.9 ± 251.7	78.4 ± 94.4	.005
CSF proteins (mg/dL)	222.0 ± 243.7	171.5 ± 174.7	.34

Table 1C
Baseline MRI findings of TBM patients who required MV and those who did not

	Mechanically ventilated n = 38	Not ventilated N = 36	*P* value
Infarct	20	15	.51
Tuberculoma	13	17	.46
Hydrocephalus	15	19	.46
Meningeal enhancement	11	14	.55
Brainstem lesion	4	3	.68
Posterior fossa lesion	6	6	.74
Midline shift/herniation	1	1	.74

The TBM patients were intubated and artificially ventilated if unable to maintain oxygen saturation by Ventimask or if there was respiratory acidosis (pH <7.3), carbon dioxide retention ($Paco_2$ >50 mm Hg), or hypoxia (Pao_2 <60 mm Hg) [11]. Blood pressure, pulse, and oxygen saturation were monitored continuously. Arterial blood gas analysis (ABG) was done daily or more frequently if indicated. Chest radiograph, blood counts, and blood culture were done as indicated. The duration of MV, ventilator-related complications (ventilator-associated pneumonia, pneumothorax), and other complications (deep vein thrombosis, pressure sores, urinary tract infection, sepsis) were also noted.

From our TBM registry, 36 age- and stage-matched TBM patients on admission who did not require artificial ventilation were included as controls.

2.3. Outcome

Complications during hospital stay were noted. Death during hospital stay and 3-month functional outcome of the surviving patients were categorized on the basis of activity of daily living (ADL) as complete (independent for ADL), partial (partially dependent for ADL), and poor (bed ridden or wheel chair bound) recovery [12].

2.4. Statistical analysis

The baseline clinical, laboratory, and MRI findings between the TBM patients with and without MV were compared using χ^2 for categorical variables and independent *t* test or Mann-Whitney *U* test for continuous variables. The predictors of MV were derived using logistic regression analysis including the variables with a *P* value of <.10. The patients with MV who died were compared with the surviving group with respect to their clinical, demographic, radiological, and ventilator-related and systemic complications using χ^2, Mann-Whitney *U* test, or Student *t* test. The predictors of death of MV patients were analyzed using logistic regression analysis. The variable was considered significant if the 2-tailed *P* value was less than .05. The statistical analysis was done using SPSS (Chicago, IL) 16 version software.

3. Results

During the study period, 205 patients with TBM were admitted and 38 (18.5%) of them needed MV. The median age of the MV patients was 32.5 (range, 17-65) years, and 15 (39.5%) were female. On admission,

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