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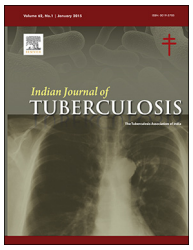

Original Article

Predictors of adverse outcome in patients of tuberculous meningitis in a multi-centric study from India

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ABSTRACT

Introduction: This study aimed to investigate the factors which may predict mortality and neurological disability at one year follow up in patients of tuberculous meningitis (TBM) in India.
Methodology: Patients with TBM were prospectively enrolled from July 2012 to September 2014 from four tertiary care hospitals of Delhi. The demographic characteristics, clinical features and laboratory findings were collected and patients were followed up till 1 year. These were analyzed by univariate and multivariate multinomial logistic regression analysis to identify predictors of adverse patient outcome at 1 year follow up.
Results: Out of 478 patients enrolled, 391 patients could be followed up to 1 year. Sixty-four patients (16.3%) died and 150 patients (39%) survived with one or more neurological disability. Altered sensorium, motor deficit, cranial nerve palsy, seizures, isolation of *M. tuberculosis* and presence of multi-drug resistance were independently associated with any adverse outcome (death or disability) but by multivariate analysis only motor deficit, altered sensorium and isolation of *M. tuberculosis* on culture produced a statistically significant model for prediction of patient outcome.
Conclusion: The three-predictor model with motor deficit, altered sensorium and isolation of *M. tuberculosis* produced a statistically significant model with correct prediction rate of 60.4%. These three variables predicted death with odds ratio of 39.2, 6.7 and 2.1 respectively in comparison to recovery whereas only motor deficit and isolation of *M. tuberculosis* predicted neurological disability at 1 year with odds ratio of 3.9, 2.4 respectively.

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1. Introduction

Tuberculous meningitis (TBM) is the most severe clinical manifestation of tuberculosis and leads to significant mortality and morbidity in spite of many advances in diagnosis and treatment modalities.[1] Timely initiation of chemotherapy and active management of complications of TBM has reduced the mortality rate but morbidity is still unacceptably high.[1,2] Though TBM is endemic in India but there is limited data on patient outcome after initiation of anti-tubercular drug treatment (ATT) and there are very few studies which have followed up the patients till treatment completion. British Medical Research Council (BMRC) staging for evaluation of disease severity is extensively used to predict patient outcome but is not built on multivariable approach.[3,10] It is still challenging to predict patient outcome on the basis of different clinical and laboratory parameters exhibited by the patients.[3–11] Some earlier studies have evaluated the association of different combinations of clinical, neuro-imaging and laboratory variables in limited number of patients (19–100) with prediction of disease outcome as either good or poor, death or recovery, neurological sequelae or no sequelae with clubbing of neurological sequelae in recovery or poor patient outcome depending upon scoring systems. The clubbing of neurological sequelae with either the recovery or death may lead to some degree of bias, e.g. patients with focal neurological deficit like optic atrophy cannot be clubbed with either recovery or death.[3,11]

This multicentric study aimed to analyze the demographic, clinical and laboratory variables in patients diagnosed as TBM on prediction of mortality and neurological sequelae separately at 1 year follow up by multinomial logistic regression technique so as to determine the effect of each predictor variable on the outcome with and without controlling for confounding.

2. Methodology

2.1. Settings

The patients for this study were prospectively recruited (purposive sampling) from Department of Neurology, Institute of Human Behaviour and Allied Sciences and GB Pant Hospital, Dept of Medicine and paediatrics, Guru Tegh Bhadur Hospital and Department of Paediatrics, Chacha Nehru Bal Chikitsalaya, Delhi, India from July 2012 to September 2014 after obtaining ethical approval from all the Institutes (IHBAS/ethics/2011/010, MAMC/(30)/2/2012/197, MAMC/(35)/1/2013/70, UCMS/2012/23/3). Informed written consent was obtained from all patients recruited in the study. All the diagnostic testing was done in Dept. of Microbiology, Institute of Human Behaviour and Allied Sciences, Delhi.

The consecutive patients diagnosed as TBM according to consensus TBM criteria of Marais et al. and decided for initiation of ATT were included in the study ($n = 520$).[12] The patients with absolute contraindications to lumbar puncture, with significant pre-existing neurological deficit, seizure disorder, mental retardation, cerebral palsy were not included in the study. A total of 42 patients were excluded later because of the reasons mentioned in Fig. 1.

2.2. Clinical evaluation and diagnosis

2.2.1. Clinical history

The history for duration of illness, fever, signs of meningeal irritation (headache vomiting, neck stiffness), altered sensorium and seizures was taken. All the patients were subjected to detailed neurological examination which included assessment of level of consciousness by Glassgow Coma Scale, signs of meningeal irritation, cranial nerve involvement, fundus examination, motor, sensory deficits and any other neurological signs. Screening was done to rule out the dissemination of tuberculosis to other parts of the body. All the clinical details were recorded in pre-designed performa.

All the patients were staged according to disease severity as per BMRC guidelines: Stage 1 included patients in prodromal phase with no definite neurological symptoms, Stage 2 included patients with signs of meningeal irritation with slight or no clouding of sensorium and minor (cranial nerve palsies) or no neurological deficit, Stage 3 included patients with severe clouding of sensorium, convulsions, focal neurological deficit and/or involuntary movements.[3]

Other medical details included history of past tuberculosis, contact with TB patients, human immuno deficiency virus (HIV) co infection and any other chronic illness.

2.2.2. Laboratory investigations

Besides routine laboratory investigations, lumbar puncture was done in all the clinically suspected patients and 2 ml of cerebro spinal fluid (CSF) was collected and subjected to cytology, biochemistry, smear microscopy, bacterial cultures ((BACTEC MGIT 960, Becton Dickinson, Sparks, MD, USA)) and conventional polymerase chain reaction (PCR) (IS6110 gene, PalmCycler, Genetix Biotech Asia Pvt. Ltd).[13]

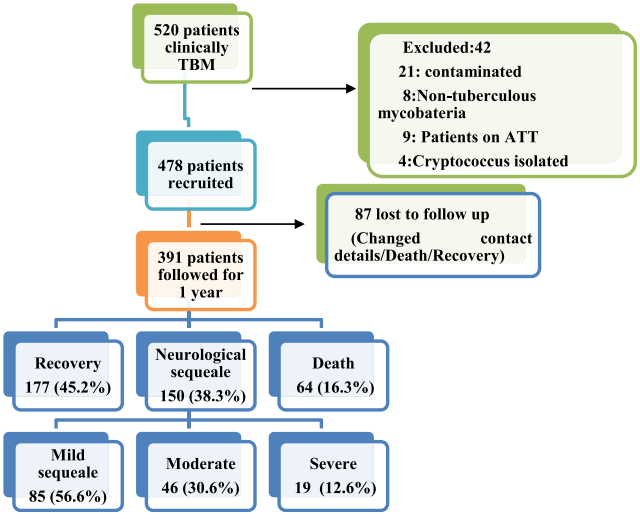

Fig. 1 – Flow chart of patients recruited in the study with clinical outcome.

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