Available online at www.sciencedirect.com
ScienceDirect
journal homepage: http://www.journals.elsevier.com/indian-journal-of-tuberculosis/

Original Article

Tuberculosis versus pyogenic meningitis in a Pakistani population

Shujah Saleem Khan [a,*], Zawar Ali [b]

[a] Medecins Sans Frontieres (MSF), Pakistan
[b] Northwest General Hospital & Research Centre, Peshawar, Pakistan

ARTICLE INFO

Article history:
Received 10 October 2016
Accepted 4 January 2017
Available online xxx

Keywords:
Tuberculosis
Meningitis
CSF analysis
TB meningitis
Bacterial meningitis

ABSTRACT

Background: Research has been going on to formulate diagnostic criteria for TBM. Two criteria that have been studied and validated in high TB prevalence areas are the Youssef criteria (Rule 1) and Thwaites criteria (Rule 2). In our study we aimed to compare the different features of TBM and acute bacterial meningitis.

Methods: This retrospective study was done at Northwest General Hospital & Research Centre (NWGH&RC), Peshawar, Pakistan. Patients who were clinically diagnosed with TB meningitis or bacterial meningitis at the time of presentation were included in the study.

Results: Lab parameters for both groups were compared using independent sample *T* tests.

We plotted ROC curves for Rule 1 and Rule 2. For Rule 1, at cut off value 2 it has a sensitivity of 97.5% and a specificity of 47.2%. For Rule 2, area at cut off value 3.5, sensitivity was 95% and specificity was 23.5%.

We also plotted CSF protein to glucose ratio of our sample on an ROC curve and looked for measures of sensitivity and specificity. At cut off point 2 the sensitivity was 93% and specificity was 66.66%.

Conclusion: It should be noted that although sensitivity for all three indices were high, specificity of all three tests was not very encouraging. We would like to emphasize that these indices can be useful in screening for patients with suspected TBM but they do not have the specificity to act as the sole test for initiation and continuance of therapy.

1. Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. Although it typically affects the lungs (pulmonary TB) it can affect any other organ in the body (extra pulmonary TB). TB is a major global health problem with 1.3 million deaths worldwide in 2012. An estimated 8.6 million people developed TB in the same year.[1] TB ranks as the second leading cause of death from an infectious disease worldwide after HIV.[1]

Pakistan has a high TB-burden and ranks sixth among countries worldwide in terms of TB prevalence. Pakistan has an estimated prevalence and incidence of 420,000 and 231 per 100,000 populations, respectively.[1]

Although pulmonary TB is an easily identified disease, the manifestations of extra pulmonary TB are often inconspicuous. Extra pulmonary TB (EPTB) is probably underreported and

* *Corresponding author.*
E-mail address: sskmsf@gmail.com (S.S. Khan).
http://dx.doi.org/10.1016/j.ijtb.2017.01.001

prevalence varies by geographical location and is thought to be related to several factors such as ethnicity and HIV status.[2–4]

It is estimated that central nervous system (CNS) TB constitutes ~1–10% of all forms of TB.[5–7] It accounts for 6.3% of patients with EPTB.[8] Amongst all the different clinical phenotypes of TB, tuberculous meningitis (TBM) is the most severe, with a high mortality and morbidity.[9,10] TBM results from the haematogenous dissemination of *M. tuberculosis* from the primary pulmonary site of infection to the meninges or brain parenchyma, where it forms small tubercles. The tuberculous (Rich) foci may remain asymptomatic for an unspecified period. The bursting, presumably preceded by an unknown immune stimulus of these foci into the arachnoid space, may lead to the development of TBM.[11] Untreated TBM is fatal, and even with treatment, the mortality rate is high.[12] Approximately half of the survivors suffer from long-term neurological sequelae including cognitive impairment, motor deficits, optic atrophy and other cranial nerve involvement.[13–15] Therefore early recognition and treatment of the disease is essential.

Diagnosis should be based on a culture-positive specimen, histological or strong clinical evidence consistent with active extra pulmonary disease, followed by a clinical decision to treat with a full course of anti-TB chemotherapy.[16]

TBM has remained a diagnostic dilemma. It has a spectrum of non-specific and vague symptoms. Discriminating TBM from other forms of meningitis by clinical features alone is often difficult due to overlapping clinical presentations. The evaluation of cerebrospinal fluid (CSF) is therefore an important parameter.

The standard for diagnosis of TBM is isolation of *M. tuberculosis* from CSF.[17,18] These methods are operator and laboratory expertise dependant and thus have a highly variable sensitivity. Newer methods have been developed such as PCR, ELISA and CSF adenosine deaminase and lactic acid, but these techniques are expensive and usually not available in most hospital settings of a developing country. In practice, in a developing country like Pakistan, the clinical diagnosis and initial treatment of TBM is based on strong clinical suspicion based on clinical features and simple laboratory tests of CSF and blood.

Research has been going on to formulate diagnostic criteria for TBM. There are a few criteria that have been developed. Two criteria that have been studied and validated in high TB prevalence areas are the **Youssef criteria (Rule 1)** and **Thwaites criteria (Rule 2)**.[19,20]

In a recent study from a large tertiary care centre in Pakistan, it was suggested that **CSF protein to glucose (CSF P/G) ratio** could help in establishing a diagnosis of TBM in children.[12]

A CSF P/G ratio of less than 2 was suggestive of TBM.

In this study our primary objective was to compare the different features clinical, radiological and diagnostic laboratory indices of TBM and acute bacterial meningitis. Our secondary objective was to compare the previously validated criterion (Youssef & Thwaites criteria) to our clinical diagnosis and check their validity in our population. A tertiary objective was to assess the potential of CSF protein to glucose ratio as a diagnostic tool in TBM.

2. Methodology

This retrospective study was carried out at the Neurology department of Northwest General Hospital & Research Centre (NWGH & RC), Peshawar, Pakistan. NWGH is a 220 bedded tertiary care hospital in the north of Pakistan, close to the Afghanistan border that receives patients from both countries.

2.1. *Inclusion criteria*

Patients who were clinically diagnosed with TB meningitis or bacterial meningitis at the time of presentation were included in the study. Clinical diagnosis was based on the duration of the illness, previous exposure to TB, previous history of TB, physical examination, blood culture and radiological findings (such as basal enhancement, hydrocephalus and presence of tuberculomas on CT). Patients admitted between August 2011 and September 2013 were included in the study.

2.2. *Bacterial meningitis group*

Patients diagnosed with bacterial meningitis/pyogenic (PM) were started on Ceftriaxone IV and steroids and response to treatment after 72 h was checked in patient files. Patients without a positive response were excluded from the study. Patients in whom a response was not recorded or left the hospital before 72 h were also excluded.

2.3. *TBM group*

Patients with a clinical diagnosis of TBM were included in this group. They were started on a four drug regimen along with steroids according to WHO criteria. Response to treatment at 1 month or more in patient files was checked and only patients with a positive response were included.

3. Results

A total of 72 cases were identified; 42 in the TBM group and 30 in the PM group.

The mean age of the TBM group was 33.07 (standard deviation {s.d.} 19.14) years and that of the PM group were 37.93 (s.d. 22.49) years. Both groups had more male patients with 64% ($n = 27$) in the TBM group and 53% ($n = 16$) in the PM group.

3.1. *Clinical features*

Table 1 compares the different clinical signs and symptoms of patients recorded during the first 24 h of admission.

Headache, fever, neck stiffness & vomiting were the commonest features in both groups.

History of weight loss was more common in the TBM group compared to the PM group (47% vs 23%). Patients with TBM were also more likely to report diplopia (16.7% vs 3.3%).

Patients with TBM tested positive more frequently when Brudzinski (40.5%) and Kernig (38.1%) were tested as compared to the PM group (16.7% and 13.3%, respectively).

Please cite this article in press as: Khan SS, Ali Z. Tuberculosis versus pyogenic meningitis in a Pakistani population, *Indian J Tuberc.* (2017), http://dx.doi.org/10.1016/j.ijtb.2017.01.001