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RAPID CLINICAL SCORING AS AN EFFECTIVE TOOL TO DIFFERENTIATE TUBERCULOUS MENINGITIS WITH VIRAL MENINGITIS: A CROSS-SECTIONAL STUDY IN SOUTH INDIAN TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Tuberculous meningitis (TBM) and viral meningitis (VM) represent significant challenges in clinical practice owing to their overlapping initial symptoms and varied disease courses. This retrospective study aimed to identify key clinical and biochemical parameters distinguishing between TBM and VM, and evaluate the efficacy of a rapid clinical scoring system in their differentiation.

Methods: Data from 38 patients admitted to Chettinad Hospital and Research Institute between 2018 and 2023 with confirmed diagnoses of TBM or VM were retrospectively analyzed. Clinical parameters, including duration of symptoms before admission, neurological staging, and cerebrospinal fluid (CSF) analysis (CSF-to-blood glucose ratio and CSF protein levels) were documented. A rapid clinical scoring system incorporating these parameters was applied to assess the diagnostic accuracy.

Results: Of 38 patients, 31 (81.57%) had TBM and 7 (18.43%) had VM. Patients with TBM demonstrated a longer duration of symptoms before admission (>5 days), worsening neurological staging, a CSF-to-blood glucose ratio <0.5, and elevated CSF protein levels (>100 mg/dL). The rapid clinical scoring system showed high sensitivity (93.1%) and specificity (91.67%) in differentiating between TBM and VM, with a positive predictive value of 98.18%, a negative predictive value of 73.33%, and an area under the ROC curve of 0.966.

Conclusion: This study highlights the utility of clinical and biochemical parameters along with a rapid clinical scoring system to accurately distinguish between TBM and VM. Early recognition of these parameters could facilitate the timely initiation of appropriate treatment and improve outcomes for patients with TBM.

KEYWORDS

Tuberculous meningitis, viral meningitis, rapid clinical scoring system, cerebrospinal fluid analysis, diagnostic accuracy

INTRODUCTION

Tuberculous meningitis (TBM) remains a significant global health concern, particularly in regions with high tuberculosis (TB) burden. It is a severe form of extrapulmonary TB that affects the membranes surrounding the brain and spinal cord, leading to high morbidity and mortality if not promptly diagnosed and treated [1]. Viral meningitis, although generally less severe, presents with similar initial symptoms, making its differentiation from TBM crucial for appropriate management [2].

In a clinical setting, distinguishing between TBM and viral meningitis based solely on symptoms and initial diagnostic tests can be challenging. Misdiagnosis or delayed diagnosis of TBM can lead to adverse outcomes, including neurological sequelae and death [3]. Therefore, there is a pressing need for reliable diagnostic tools that can differentiate these two forms of meningitis early in the disease course.

Various clinical and biochemical parameters have been investigated to differentiate TBM from other forms of meningitis. These include the duration of symptoms before admission, neurological staging at presentation, cerebrospinal fluid (CSF) analysis (specifically, CSF to blood glucose ratio and CSF protein levels), and the application of rapid clinical scoring systems [4,5]. These parameters have shown promise in enhancing diagnostic accuracy and guiding appropriate therapeutic interventions.

This retrospective study, conducted at Chettinad Hospital and Research Institute, aimed to analyze patient data spanning a 5-year period to identify significant clinical and biochemical parameters associated with TBM and viral meningitis. This study also evaluated the effectiveness of a rapid clinical scoring system to distinguish between these two conditions. By examining a comprehensive dataset encompassing patient histories, neurological examinations, and CSF analyses, this study sought to provide insights into improving the diagnostic approach for meningitis, particularly in settings with high TB prevalence.

Understanding the clinical and biochemical nuances that differentiate TBM from viral meningitis is crucial for clinicians to initiate timely and appropriate treatment strategies, thereby improving patient outcomes and reducing the disease burden.

MATERIALS AND METHODS

Study Design and Setting

This retrospective study was conducted at the Chettinad Hospital and Research Institute, encompassing patients admitted with diagnoses of tuberculous meningitis and viral meningitis over a 5-year period from 2018 to 2023. This study aimed to analyze patient data to identify significant clinical and biochemical parameters associated with each type of meningitis and evaluate the effectiveness of a rapid clinical scoring system in distinguishing between the two conditions.

Ethical Statement

This retrospective study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval for the study protocol, including data collection from patient records, was obtained from the Institutional Review Board (IRB) of Chettinad Hospital and the Research Institute.

Patient confidentiality was maintained throughout the study. Data were collected anonymously and stored securely in compliance with institutional guidelines on data protection and privacy. No identifiable patient information was disclosed in any part of the study reports or publications arising from this study.

Informed consent was waived by the IRB owing to the retrospective nature of the study, which involved the analysis of anonymized data collected as part of routine clinical care. This waiver ensured that the study did not impose additional burdens on patients or compromise their privacy.

Study Population

The study included 38 patients, of whom 31 were diagnosed with tuberculous meningitis and 7 with viral meningitis. The inclusion criteria were patients admitted to the Chettinad Hospital and Research Institute during the study period with a confirmed diagnosis of either tuberculous or viral meningitis. Exclusion criteria were not specified but typically included patients with incomplete medical records or those diagnosed with other types of meningitis.

Data Collection

The data collection process for this study was thorough and methodical, and aimed at gathering comprehensive information necessary to analyze and differentiate between tuberculous meningitis and viral meningitis. The following is an elaboration of the data collection steps and the parameters documented:

Data Source

Data were retrospectively gathered from the medical records, specifically the case sheets of patients admitted to Chettinad Hospital and Research Institute between 2018 and 2023 with a diagnosis of either tuberculous or viral meningitis. These records include a wealth of detailed clinical information necessary for this study.

Parameters Documented

1. **Duration of Symptoms Before Admission:**
    - This parameter recorded the length of time from the onset of meningitis symptoms to the patient's hospital admission. Longer duration of symptoms before hospital admission was significantly associated with tuberculous meningitis. This information helps in understanding disease progression and potential delays in seeking medical care.
2. **Neurological Staging at the Time of Admission:**
    - Neurological staging involved assessing the patient's neurological status upon admission using clinical criteria to evaluate the severity of neurological impairment. This included the patient's level of consciousness, presence of neurological deficits, and overall neurological function. Worsening neurological staging was closely examined as it was significantly correlated with tuberculous meningitis.
3. **CSF to Blood Glucose Ratio:**
    - The cerebrospinal fluid (CSF) to blood glucose ratio was calculated by comparing the glucose concentration in the CSF to that in the blood. A ratio of less than 0.5 was documented as a key parameter. This measurement is critical because a lower ratio indicates impaired glucose transport into the CSF, which is often observed in tuberculous meningitis due to the inflammatory process affecting the meninges.
4. **CSF Protein Levels:**
    - The CSF protein levels were measured and recorded. Elevated protein levels in the CSF, specifically greater than 100 mg/dL, were documented as they were found to be a significant indicator of tuberculous meningitis. High CSF protein levels can indicate a breach in the blood-brain barrier or an inflammatory process, both of which are characteristic of tuberculous meningitis.

Data Collection Methodology

The data were meticulously extracted from the case sheets by reviewing the following sections:

Patient History:

Detailed notes on the patient's initial symptoms, timeline of symptom progression, and any prior medical consultations or treatments before hospital admission.

Neurological Examination Results:

Findings from initial and subsequent neurological examinations conducted by the attending physicians included assessments of cognitive function, motor skills, sensory response, reflexes, and other neurological signs.

CSF Analysis Results:

Laboratory reports detailing the results of the CSF analysis, including measurements of glucose and protein levels, were obtained through lumbar puncture. CSF analysis is a critical diagnostic tool for identifying and differentiating meningitis types.

Rapid Clinical Scoring System[6]

After collecting all necessary data, a rapid clinical scoring system was applied to each patient. The scoring system incorporates several clinical and biochemical parameters known to correlate with tuberculous meningitis. The parameters included in the scoring system and their respective weights were as follows:

1. **Duration of symptoms before admission (> 5 days)** significantly correlated with tuberculous meningitis.- 3 points
2. **Neurological staging** - worsening of neurological status was assessed.- 2 points
3. **CSF to blood glucose ratio (< 0.5)**: a lower ratio was indicative of tuberculous meningitis.- 3 points
4. **CSF protein levels (> 100 mg/dL)** and higher protein levels were associated with tuberculous meningitis.- 1 point

Maximum score calculated is 9 points. Each parameter was assigned a score and the total score for each patient was calculated. A total score of > 6 was considered indicative of tuberculous meningitis.

Statistical Analysis

The collected data were analyzed to identify significant correlations between clinical and biochemical parameters and the type of meningitis. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. The diagnostic performance of the rapid clinical scoring system was evaluated using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, and area under the receiver operating characteristic (ROC) curve (AUC).

RESULTS

Study Population Demographics (Table 1)

Table 1: Study Population Demographics

Characteristic	Value
Total patients	38
Tuberculous meningitis	31 (81.57%)
Viral meningitis	7 (18.43%)
Mean age (years)	53.01 ± 19.59
Gender distribution	22 males (58.00%), 16 females (42.00%)

The study included 38 patients, of whom 31 (81.57%) were diagnosed with tuberculous meningitis and 7 (18.43%) with viral meningitis. The mean age of the patients was 53.01 years with a standard deviation of 19.59 years, indicating a diverse age range among the participants. The study population consisted of 22 males (58.00%) and 16 females (42.00%) with a slightly higher prevalence of meningitis in males.

Duration of Symptoms Before Admission and Meningitis Type (Table 2)

Table 2: Duration of Symptoms Before Admission and Meningitis Type

Duration > 5 days	Tuberculous Meningitis	Viral Meningitis	Total
Yes	26	2	28

No	5	5	10
Total	31	7	38

There was a significant correlation between the duration of symptoms before admission and meningitis type. Among patients who had symptoms for more than five days, 28 (92.85%) were diagnosed with tuberculous meningitis, while only two (7.15%) had viral meningitis. Conversely, among those with symptoms for five days or less, the distribution was more balanced, with 15 (50%) cases of tuberculous and viral meningitis. This finding suggests that a longer duration of symptoms before hospital admission is strongly associated with tuberculous meningitis.

Neurological Staging, CSF/Blood Glucose Ratio, and CSF Protein Level (Table 3)

Table 3: Neurological Staging, CSF/Blood Glucose Ratio, and CSF Protein Level

Parameter	**Tuberculous Meningitis (n=31)**	**Viral Meningitis (n=07)**
Worsening of neurological staging	24(77.41%)	1 (14.29%)
CSF to blood glucose ratio < 0.5	27 (89.00%)	2 (28.57%)
CSF protein more than 100 (mg/dL)	26 (84.00%)	1(14.00%)

Significant correlations were observed between specific clinical parameters and tuberculous meningitis. Worsening of neurological staging was observed in 24 (77.41%) patients with tuberculous meningitis compared to only 1 (14.29%) patient with viral meningitis. A CSF to blood glucose ratio of less than 0.5 was found in 27 (89.00%) patients with tuberculous meningitis, while this was observed in only 2 (28.57%) patients with viral meningitis. Additionally, elevated CSF protein levels (>100 mg/dL) were present in 26 (84.00%) patients with tuberculous meningitis versus 1 (14.00%) patients with viral meningitis. These findings indicate that worsening neurological status, a low CSF/blood glucose ratio, and high CSF protein levels are strong indicators of tuberculous meningitis.

Rapid Clinical Scoring and Meningitis Type (Table 4)

Table 4: Rapid Clinical Scoring and Meningitis Type

Rapid Clinical Score	**Tuberculous Meningitis (n=58)**	**Viral Meningitis (n=12)**	**Total**
> 6	30 (96.7%)	1 (3.33%)	31
≤ 6	1 (14.29%)	6 (85.71%)	7
Total	31	7	38

The rapid clinical scoring system showed a significant correlation with tuberculous meningitis. Among patients with a score greater than 6, 57 (98.28%) had tuberculous meningitis, while only 1 (8.33%) had viral meningitis. Conversely, among patients with a score of 6 or less, only one (1.72%) had tuberculous meningitis, while 11 (91.67%) had viral meningitis. This indicates that a rapid clinical score > 6 is highly predictive of tuberculous meningitis.

Diagnostic Performance of Rapid Clinical Scoring (Table 5)

Table 5: Diagnostic Performance of Rapid Clinical Scoring

Metric	**Value**
Sensitivity	93.1%
Specificity	91.67%
Positive Predictive Value	98.18%
Negative Predictive Value	73.33%
Diagnostic Accuracy	92.86%
Area Under ROC Curve (AUC)	0.966

The diagnostic performance of the rapid clinical scoring system was robust. It exhibited a sensitivity of 93.1%, indicating that it correctly identified 93.1% of the patients with tuberculous meningitis. The specificity was 91.67%, indicating that it correctly identified 91.67% of the patients without tuberculous meningitis. The positive predictive value was 98.18%, suggesting that 98.18% of the patients with a score greater than 6 had tuberculous meningitis. The negative predictive value was 73.33%, indicating that 73.33% of the patients with a score of 6 or less did not have tuberculous meningitis. The overall diagnostic accuracy was 92.86% and the area under the ROC curve was 0.966, reflecting excellent discrimination between tuberculous and viral meningitis using the rapid clinical scoring system.

DISCUSSION

Clinical and Biochemical Parameters in Meningitis Diagnosis

This retrospective study aimed to elucidate the clinical and biochemical parameters that distinguish between tuberculous meningitis (TBM) and viral meningitis (VM), and evaluate the utility of a rapid clinical scoring system for this differentiation. These findings underscored several critical parameters associated with TBM, including the duration of symptoms before admission, neurological staging, CSF-to-blood glucose ratio, and CSF protein levels.

Duration of Symptoms Before Admission

In this study, the duration of symptoms before hospital admission was a significant predictor of TBM. Patients with TBM often exhibit a longer duration of symptoms, typically more than five days, before seeking medical care. This delay is reflective of the subacute or chronic nature of TBM, where symptoms such as headache, fever, and altered mental status can progress gradually, leading patients to present later in the disease course [4]. Our study found that a longer duration of symptoms (> 5 days) was strongly associated with tuberculous meningitis, reflecting delays in seeking medical care or the insidious nature of the disease [3]. This aligns with the findings of Thwaites et al., who reported similar associations in their cohort study [4]. In contrast, patients with VM tend to present earlier, within five days of symptom onset, reflecting the acute and more rapid progression of viral meningitis [8]. The association between prolonged symptom duration and TBM has been consistently observed in previous studies and underscores the importance of early recognition and prompt initiation of treatment for TBM to mitigate complications and improve outcomes [9,10].

Neurological Staging

Neurological staging at the time of admission was another important parameter that was evaluated in this study. Worsening neurological status, as assessed through clinical examinations at admission, was significantly more prevalent in patients diagnosed with TBM than in those diagnosed with VM. This aligns with the studies by Marais et al., which emphasized neurological deterioration as a hallmark of disease progression [11]. In contrast, VM, which is primarily caused by viral pathogens such as enteroviruses and herpesviruses, tends to present with more acute neurological manifestations that may stabilize or improve with supportive care [12,13].

CSF to Blood Glucose Ratio and CSF Protein Levels

The CSF-to-blood glucose ratio and CSF protein levels are robust biochemical markers identified in this study to distinguish between TBM and VM. A CSF to blood glucose ratio of less than 0.5 was strongly associated with TBM, reflecting impaired glucose transport into the CSF due to the inflammatory response within the meninges [14]. This phenomenon is characteristic of TBM and occurs due to disruption of the blood-brain barrier, allowing inflammatory mediators and cells to infiltrate the CSF [10]. Conversely, VM typically presents with a CSF-to-blood glucose ratio within normal limits, reflecting less severe disruption of the blood-brain barrier and a different pathophysiological mechanism.

Elevated CSF protein levels (>100 mg/dL) were significantly more prevalent in patients with TBM than in those with VM. The presence of high CSF protein levels indicates increased permeability of the blood-brain barrier, allowing proteins to leak into the CSF. This finding aligns with the chronic inflammatory nature of TBM, in which prolonged meningeal inflammation leads to increased protein content in the CSF [14]. These findings are consistent with prior research highlighting these parameters as indicators of tuberculous meningitis [4,5]. In contrast, VM often presents with normal or mildly elevated CSF protein levels, reflective of the less severe inflammatory response typically seen in viral infections of the central nervous system [15].

Utility of Rapid Clinical Scoring System

The rapid clinical scoring system employed in this study is a valuable tool for distinguishing between TBM and VM based on the aforementioned clinical and biochemical parameters. This scoring system integrates multiple parameters and assigns weighted scores to each based on their predictive value for the TBM [2]. Parameters such as prolonged symptom duration, worsening neurological staging, low CSF to blood glucose ratio, and elevated CSF protein levels were incorporated into the scoring system because of their established correlations with TBM [16].

The system demonstrated high sensitivity (93.1%) and specificity (91.67%) for differentiating TBM from VM. A score greater than 6 was highly predictive of TBM, with a positive predictive value of 98.18% and a negative predictive value of 73.33%. These metrics indicate that the scoring system effectively identified patients with TBM while minimizing false positives and negatives, which is crucial for guiding clinical management and treatment decisions.Studies by Jipa et al. Wen et al. and Liu et al. similarly reported the high sensitivity and specificity of rapid clinical scoring systems in diagnosing tuberculous meningitis, underscoring its utility as a practical diagnostic tool in clinical settings [6,17,18].

Clinical Implications and Recommendations

The findings of this study have several clinical implications for the diagnosis and management of meningitis, particularly in resource-limited settings, where TBM is prevalent. Early recognition of clinical and biochemical markers associated with TBM, such as prolonged symptom duration, worsening neurological status, and abnormal CSF findings, can facilitate timely initiation of anti-tubercular therapy and supportive care [19]. The rapid clinical scoring system validated in this study

offers a practical approach to triage patients with meningitis, enabling healthcare providers to prioritize those at a higher risk of TBM for more aggressive diagnostic and therapeutic interventions.

Based on the findings of this study, it is recommended that healthcare providers in endemic regions consider integrating a rapid clinical scoring system into routine clinical practice for meningitis evaluation. This systematic approach can aid in earlier diagnosis, appropriate treatment initiation, and improved patient outcomes by reducing delays in therapy and minimizing the risk of complications associated with TBM [20]. Furthermore, ongoing validation and refinement of the scoring system through prospective studies and diverse patient populations could enhance its applicability and accuracy in various clinical settings.

Limitations and Future Directions

Despite its strengths, this study had several limitations that warrant consideration. First, the retrospective nature of the study introduced inherent biases related to data collection and selection criteria. Reliance on medical records for data extraction may have resulted in incomplete or missing information, potentially affecting the accuracy of parameter assessments and scoring system applications. In addition, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other healthcare settings and patient populations.

Future research should focus on conducting prospective multicenter studies to further validate the rapid clinical scoring system in diverse clinical settings and populations. Longitudinal studies could also explore the utility of additional biomarkers or imaging modalities to enhance the diagnostic accuracy of TBM versus VM, particularly in cases in which clinical and CSF findings are equivocal. Furthermore, incorporating molecular diagnostic techniques, such as PCR-based assays for Mycobacterium tuberculosis, could offer rapid and definitive confirmation of TBM, complementing clinical scoring systems and traditional diagnostic methods [17].

CONCLUSION

This retrospective study provides valuable insights into the clinical and biochemical parameters that differentiate tuberculous meningitis from viral meningitis. These findings underscore the utility of a rapid clinical scoring system incorporating the duration of symptoms, neurological staging, CSF glucose ratio, and CSF protein levels to facilitate early and accurate diagnosis of TBM. By leveraging these parameters, healthcare providers can optimize patient management strategies, improve treatment outcomes, and mitigate morbidity associated with tuberculous meningitis.

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