Hypothesis

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Importance of CSF Glucose: Protein Ratio in Diagnosis of Tuberculous Meningitis

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Abstract

Background: Tuberculous meningitis (TBM) is the most severe manifestation of extrapulmonary tuberculosis with a high mortality and morbidity rates. As per the global tuberculosis (TB) report of 2017, the estimated incidence of TB in India was approximately 2,800,000 accounting for about a quarter of the world's TB cases. Many a times differentiating tuberculous meningitis from pyogenic meningitis becomes very difficult. The diagnosis depends upon clinical manifestation and cytochemical analysis of cerebrospinal fluid (CSF). Many researchers found that the CSF glucose: protein ratio less than 0.5 is useful to differentiate tubercular disease from non-tubercular meningitis.

Methods: A total of Sixty-two patients admitted to this tertiary hospital with symptoms and signs of meningitis, were selected and divided into two groups: tubercular (n=39) and pyogenic (n=23), depending upon the accepted criteria. Clinical features and CSF parameters noted in each patient.

Results: The mean age of patients with tubercular meningitis was 39.07 ± 16.67 years and that of pyogenic meningitis 34.35 ± 16.73 years. On CSF cytological and biochemical analysis the mean total white blood cell count was 256.74 ± 184.03 / cmm, mean protein 182.22 ± 113.12 mg/ dl and mean sugar 52.85 ± 19.3 in TBM whereas in pyogenic meningitis 106.17± 185.18/cmm, 88.78 ±114.35 mg/ dl, and 63.47 ±19.48 mg/ dl respectively. The CSF glucose: protein ratio in TBM was 0.29 and 0.71 in pyogenic meningitis.

Conclusion: It was found that the CSF glucose: protein ratio of ≤ 0.5 may be useful in differentiating tuberculous from pyogenic meningitis high sensitivity and specificity. The cutoff value is highly statistically significant.

Keywords: CSF; Tuberculous Meningitis; Glucose: Protein ratio; Central nervous system

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Introduction

Tuberculosis (TB) of the central nervous system is the most severe manifestation of extrapulmonary tuberculosis. As per the global tuberculosis (TB) report of 2017, the estimated incidence of TB in India was approximately 2,800,000 accounting for about a quarter of the world's TB cases, 15,000 being multidrug-resistant TB with mortality of 42,000 patients [1]. The incidence and prevalence of central nervous system-TB (CNS-TB) are unknown but roughly accounts for 1%–10% of all TB cases [1]. Tubercular meningitis (TBM) is characterised by a slowly progressive granulomatous inflammation of the basal meninges. Delay in diagnosis and so in the start of effective treatment results in poor prognosis and sequel in up to 25% of cases [2]. Rapid diagnosis and initiation of treatment is therefore necessary to reduce the high mortality and morbidity associated with the disease. The objective of this study is to find out the role of CSF glucose: protein ratio as diagnostic marker for tuberculous meningitis.

Materials and Methods

The study conducted between January to Decrember 2020 at Patna Medical College and Hospital, Patna, Bihar, a tertiary care centre, in 62 patients with meningitis after prior consent and ethical approval. The diagnosis of meningitis was made on the basis of clinical symptoms and signs like headache, fever, nausea,

vomiting, neck rigidity, presence of Kernig's and/or Brudzinski's sign, altered sensorium, any focal neurological deficit with no other general medical condition explaining them. Patients were divided into two groups:

- **Group A** - Tubercular Meningitis (n=39)
- **Group B** - Pyogenic Meningitis (n =23)

Presence of above signs and symptoms with one or more of the following criteria was adopted to label a case as tuberculous meningitis:

1. Bacteriological proof of presence of Mycobacterium tuberculosis in CSF.
2. Biopsy showing caseating granulomas.
3. Suspected active pulmonary tuberculosis based on chest X ray.
4. Acid fast bacilli found in any sample apart from the CSF,
5. Clinico- radiological findings consistent with Tuberculosis.
6. Predominance of lymphocytes in the CSF, CSF glucose: protein ratio < 0.5, Raised CSF Protein.
7. Definite clinical and radiological improvement in one month after specific anti-tubercular treatment.

For pyogenic meningitis presence of above signs and symptoms for a short period of time and typical CSF findings were elevated pressure, neutrophilic pleocytosis, i.e., cell count > 100 WBC/ cu. mm consisting of more than 90% polymorphs, elevated protein > 40 mg%, sugar ≤ 50% of the blood sugar, cloudy or turbid appearance, culture and gram staining may be positive for bacteria and full recovery without anti-tuberculosis therapy.

Lumbar puncture was done in each case and at least 2ml of CSF was collected in a sterile vial. Hemorrhagic CSF was excluded from the study. This CSF was subjected to biochemical and microscopic examination.

SPSS 19.0 was used for statistical analyses. Patient's ages were described as mean ± standard deviation. Continuous variables were compared by the t-test and dichotomous variables were compared by Fisher's exact test for two by two comparisons or Pearson χ^2 for greater than two responses.

Observations

Out of 62 patients with meningitis admitted to our hospital, 50 were male **(Table 1)**. Thirty-nine patients (62.9%) with tubercular meningitis and twenty-three (37.1%) pyogenic meningitis. The mean age of patients with tubercular meningitis was 39.07 ± 16.67 years (19-76 years) and that of pyogenic meningitis 34.35 ± 16.73 years (21-45 years). Overall fever was present in 60 (96.77%), headache in 49 (79.03%), and vomiting in 44 (70.96%) patients. The symptom duration range from 7 to 98 days with a median of 28 days and clinically fever was present in 37 (94.8%), headache in 29 (74.3%), and vomiting in 22 (56.4%) patients with TBM. Four patients (10.25%) with tuberculous meningitis had symptom duration of ≤ 7 days. Among tubercular meningitis, 6 (15.38%) had seizure. None with pyogenic meningitis had seizure. In pyogenic meningitis group, the symptom duration range from 2 to 21 days with a median of 3 days and clinically fever was present in 23 (100%), headache in 20 (86.9%), and vomiting in 22 (95.7%) patients. Twenty patients (86.9%) had symptom duration of ≤ 7 days. On CSF cytological and biochemical analysis the mean total white blood cell count was 256.74 ± 184.03 /cmm, mean protein 182.22 ± 113.12 mg/ dl and mean sugar 52.85 ± 19.3 mg/dl in TBM whereas in pyogenic meningitis 106.17 ± 185.18/cmm, 88.78 ± 114.35 mg/ dl, and 63.47 ± 19.48 mg/ dl respectively **(Table 2)**. The average CSF glucose: protein ratio in TBM was 0.29 and 0.71 in pyogenic meningitis. Among tuberculous meningitis patients, 28 (71.8%) and among pyogenic meningitis only one (4.3%) had the CSF glucose: protein ratio ≤ 0.5. The P value is highly significant (P <0.001) **(Table 3)**. The odd ratio was 0.018. The sensitivity and specificity for the cutoff value of CSF glucose: protein ratio ≤ 0.5 is high, 71.8% and 95.65% respectively **(Table 4)**.

Table 1 Demography and clinical features of all patients with meningitis.

Characteristics	Tubercular meningitis (Group A), N = 39 (%)	Pyogenic meningitis (Group B), N = 23 (%)	All (Group A+B), N = 62 (%)
Sex			
Male	36 (92.3 %)	14 (60.9 %)	50 (80.6 %)
Female	03 (7.7 %)	09 (39.1 %)	12 (19.4 %)
Age (Mean ± SD), Years	39.07 ± 16.67	34.35 ± 16.73	37.32 ± 16.67
Fever	37 (94.8 %)	23 (100 %)	60 (96.8 %)
Headache	29 (74.3 %)	20 (86.9 %)	49 (79.0 %)
Vomiting	22 (56.4 %)	22 (95.7 % %)	44 (71.0 %)
Seizure	06 (15.4 %)	00 (0.0 %)	06 (9.7 %)
Neck rigidity	31 (79.5 %)	15 (65.2 %)	46 (74.2 %)
Kernig's sign	17 (43.6 %)	20 (86.9 %)	37 (59.7 %)
Brudzinski's sign	06 (15.4 %)	12 (52.2 %)	18 (29.0 %)
Cranial CT or MRI			
Tuberculoma	03 (7.6 %)	--	--
Hydrocephalous	11 (28.2 %)	--	--
Arachnnoiditis	02 (5.1 %)	--	--

Table 2 Cerebrospinal fluid results in TBM (n=39) and Pyogenic meningitis (n=24) patients.

Variables	TBM (n=39)	Pyogenic Meningitis (n=24)
WBC /cm^2, Mean ± SD	256.74 ± 184.03	106.17± 185.18
CSF protein (mg/dl), Mean ± SD	182.22 ± 113.12	88.78 ±114.35
CSF sugar (mg/dl), Mean ± SD	52.85 ± 19.3	63.47 ±19.48
CSF glucose : protein ratio	0.41	0.54

Table 3 CSF glucose: Protein ratio.

CSF glucose: Protein Ratio	TBM (N =39)	PYOGENIC (N =23)	P-value
> 0.5	11 (28.2%)	22 (95.7 %)	<0.001
≤ 0.5	28 (71.8 %)	01 (04.3 %)	
Odd Ratio	0.018		

Table 4 CSF glucose: Protein ratio with a cut off value of ≤ 0.5 for differentiating tubercular meningitis.

Statistics	P-value
Sensitivity	71.79%
Specificity	95.65%
Positive predictive value	96.55%
Negative predictive value	66.67%
Positive Likelihood Ratio	16.51
Negative Likelihood Ratio	0.29

Discussion

Sixty-two patients with meningitis analyzed. On the basis of clinical features and cerebrospinal fluid examination findings patients were divided into two groups: Tubercular meningitis (n= 39) and Pyogenic meningitis (n=23). The most common clinical manifestation was fever in 96.8% followed by headache and vomiting in 79% and 71% respectively. In some studies headache was more common than fever [3,4]. Seizure was found in 15.4% of patients. In one study convulsions occurred in 15.6% where as in another study it was only 1% [3,4] History of seizures on presentation were common in TBM group but none in other group. This is similar to prior reports [5]. Overall about two - third of the patients had neck rigidity (74.2%), but Kernig's and Brudzinski's signs were present in 59.7% and 29% of patients, respectively. A study by Aminzadeh Z and Mahmoodi T, found that about 50% of the patients had neck stiffness, but Kernig and Brudzinski's signs were found in 45.5% and 23% of patients, respectively [6]. A review by Pehlivanoglu F et al. in 160 patients noted that 88% had neck stiffness [4]. On cranial CT or MRI of patients with TBM, 28.2% had hydrocephalous, 7.6% tuberculoma and 5.1% had spinal arachnoiditis presenting as paraparesis. Around 36% patients had tuberculoma, 20% hydrocephalous and 2% arachnoiditis in one study [4]. Cranial CT or MRI was normal in cases of pyogenic meningitis. On CSF analysis, in TBM, the mean WBC count was 256.74 ± 184.03/ cmm with lymphocyte predominance, mean protein was 182.22 ± 113.12 mg/ dl which was more as compared to pyogenic meningitis, 106.17 ± 185.18/cmm and 88.78 ± 114.35 mg /dl respectively. In TBM the average CSF glucose: protein ratio was less than 0.5 (0.29). The value of CSF protein and glucose, although well known to be different from bacterial meningitis, has rarely been reported to be significant in cases of TBM [7,8]. It was found that 28/39 (71.8%) patients with tubercular meningitis had CSF glucose: protein ratio ≤ 0.5. When these data compared with 23 pyogenic meningitis patients, the cut off value of CSF glucose: protein ratio ≤ 0.5 is found to be highly significant (P<0.001). A ratio of ≤ 0.5 was found to be significant because of very high protein and moderately low glucose levels found in cases of TBM, in contrast to very low glucose and moderately high protein in cases of bacterial meningitis (ratio > 0.5). In this study the sensitivity and specificity for the cutoff value of CSF glucose: protein ratio ≤ 0.5 is high, 71.8% and 95.65% respectively. A study by Qumar NF, et al. found that 39/44 (86.6%) patients with tubercular meningitis had CSF glucose: protein ratio ≤ 0.5 [9]. The sensitivity and specificity were 80% and 88% respectively in the same study. A study done in children, found that absolute CSF glucose values of < 2.2 mmol/L and protein values of >1 g/L differentiated between TBM and non-bacterial meningitis with good specificity, although sensitivity was poor [10].

Conclusion

In this study, it was found that the CSF glucose: protein ratio of ≤ 0.5 may be useful in differentiating tuberculous from pyogenic meningitis high sensitivity and specificity. The cutoff value is highly statistically significant. A large number of patients need to study to validate the result of the findings.

References

1 https://www.who.int/tb/publications/global_report/MainText_13Nov2017.pdf

2 Garcia-Monco JC (1999) Central nervous system tuberculosis. Neurol Clin 17: 737-759.

3 Ersöz M, Yildirmak MT, Gedik H, Şimşek F, Kantürk A, et al. (2012) Tuberculous meningitis: a report of 60 adult cases. West Indian Med J 61: 592.

4 Pehlivanoglu F, Kart Yasar K, Sengoz G (2012) Tuberculous meningitis in adults: a review of 160 cases. Sci World J 2012: 1-7.

5 Yaramiş A, Gurkan F, Elevli M, Söker M, Haspolat K, et al. (1998) Central nervous system tuberculosis in children: a review of 214 cases. Pediatrics 102: e49.

6 Aminzadeh Z, Mahmoodi Z (2011) Tuberculous meningitis in adults in the terms of tertiary prevention: A review of 22 cases. Int J Prev Med 4: 496-497.

7 Youssef FG, Afifi SA, Azab AM, Wasfy MM, Abdel-Aziz KM, et al. (2006) Differentiation of tuberculous meningitis from acute bacterial meningitis using simple clinical and laboratory parameters. Diagnostic microbiology and infectious disease 55: 275-278.

8 Hooker JA, Muhindi DW, Amayo EO, McOligeyo SO, Bhatt KM, et al. (2003) Diagnostic utility of cerebrospinal fluid studies in patients with clinically suspected tuberculous meningitis. Int J Tuberc Lung Dis 7: 787-796.

9 Qamar FN, Rahman AJ, Iqbal S, Humayun K (2013) Comparison of clinical and CSF profiles in children with tuberculous and pyogenic meningitis; role of CSF protein: glucose ratio as diagnostic marker of tuberculous meningitis. J Pak Med Assoc 63: 206.

10 Solomons RS, Visser DH, Donald PR, Marais BJ, Schoeman JF, et al. (2015) The diagnostic value of cerebrospinal fluid chemistry results in childhood tuberculous meningitis. Childs Nerv Syst 31: 1335-1340.