The Efficacy of Bacterial Meningitis Score in Predicting Bacterial Meningitis at Mansoura Fever Hospital

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Background and study aims: Despite the advances in the diagnosis and treatment of infectious diseases, the meningitis and the encephalitis are still considered to be important causes of mortality and morbidity. Early diagnosis and starting immediate empirical therapy are the key factors of decreasing morbidity and mortality. We aimed to detect the frequency of bacterial meningitis among the suspected cases and to evaluate bacterial meningitis score (BMS) for detection the bacterial meningitis cases.

Methods: This study was a cross-sectional included 48 patients admitted to the Mansoura Fever Hospital with clinical pictures suspected of meningitis. Full medical history, clinical examination, laboratory investigations and lumber puncture with CSF examination were provided to the participant patients. They were classified according to the results of CSF culture into two groups. The first group: included 12 patients with confirmed septic meningitis. The second group: included 36 patients with aseptic meningitis. The Application of bacterial meningitis score (BMS) was applied.

Results: The incidence of the bacterial meningitis in our study was 25% (12 from 48 patients).

The aspect of CSF was turbid among all the patients of septic meningitis, while was turbid only in in (8.3%) of aseptic meningitis cases. The total leucocytes count, polymorphs, and protein were significantly higher in patients with septic meningitis. The bacterial meningitis score has high sensitivity (91.7%), specificity (97.2%), PPV (91.7%) and NPV (97.2%) in the diagnosis of the septic meningitis cases.

Conclusion: The BMS is a quick, simple score, and highly accurate, which could be used for the diagnosis of the septic meningitis .

INTRODUCTION

Bacterial meningitis is a serious illness that causes more than 300 000 deaths worldwide. It is an acute purulent infection of the meninges, subarachnoid space, and the brain parenchyma all are involved in the inflammatory reaction [1]. Symptoms may include fever, headache, stiff neck, eye discomfort, confusion, drowsiness, seizures, nausea, and vomiting [2].

Bacterial meningitis is predominately caused by three pathogens, Streptococcus pneumoniae, Neisseria meningitides and Haemophilus influenza type B. Additionally, Listeria monocytogenes, Group B Streptococci, and Gram-negative bacteria such as *Escherichia coli* and *Klebsiella pneumoniae*, cause meningitis in specific groups, including neonates, pregnant women, transplant recipients and older adults [3].

In Egypt, meningitis is endemic and occasional instances can be seen at any time of the year. The winter and spring months of January to April have the highest prevalence of bacterial meningitis [4]. Streptococcus pneumonia is a leading causative agent of bacterial meningitis infections In Egypt [5]. It affects males slightly more than females. The incidence and the proportion of deaths among diagnosed cases of bacterial meningitis are dependent on area and

Country, the causative micro-organism and age. **[6]**.

Positive Kerning's and Brudzinski's signs of meningeal irritation are seen in many of patients. A meta-analysis of several studies revealed sensitivities of 51% for neck stiffness, 53% for Kernig sign and 66% for Brudzinski sign for the diagnosis of bacterial meningitis, as well as poor test characteristics of other common signs and symptoms in the differentiation between bacterial and viral/aseptic or no meningitis [7].These data indicate that clinical characteristics cannot be used to rule out bacterial meningitis [8]. With progression of the disease other symptoms develop such as cardiorespiratory arrest, focal CNS signs, and seizures may frequently occur [9].

Many guidelines recommend early diagnosis and starting immediate empiric antibiotics for cases suspected to be bacterial meningitis based on age and type of microorganism and can be modified once the results are available [10]. The bacterial meningitis score (BMS) is a validated clinical score to detect high-risk patients with bacterial meningitis for better diagnosis and to start early empirical antibiotics which leads to improved outcome. BMS consists of positive Gram-stain of Cerebrospinal Fluid (CSF), CSF protein >80mg/dl, peripheral absolute neutrophil count >10,000 cells/mm^3, CSF neutrophil count >1000cells / mm^3 and seizure before or at time of presentation [11, 12].

This study aimed to detect the frequency of bacterial meningitis among suspected cases and to evaluate bacterial meningitis score in detecting bacterial meningitis cases.

PATIENTS AND METHODS

Study design and Participants

This cross-sectional study included 48 patients with acute meningitis admitted to the Mansoura Fever Hospital, Dakahlia Governorate, Egypt in the period from October 2018 to March 2019. Patients with clinical pictures suspected of meningitis (fever, headache, projectile vomiting, neck rigidity, positive Kernig's and Brudzinski's signs) at any age, gender, and acute onset in equal or less than 10 days were included.

Exclusion criteria: onset of symptoms in more than 10 days prior to presentation, post neurosurgery, post- traumatic, cerebrovascular accidents, and patient refusing to share in the study

Patients' assessments:All patients in the current study were subjected to full medical history and complete clinical examination. Routine laboratory investigations including complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein, Kidney function tests (Serum creatinine, blood urea), liver biochemistry (ALT, AST albumin, prothrombin time), and blood glucose level.

All patients suspected of acute meningitis underwent lumber puncture for CSF analysis for confirmation of diagnosis once the patients admitted to the hospital and no contraindication for lumber puncture.

Bacterial meningitis was defined for patients who had a lumbar puncture with CSF leucocytosis and positive bacterial culture of CSF [13].

The technique of Lumbar puncture:Lumber puncture was done for all patients by expertise once the patients came to the hospital with clinical picture suggestive of acute meningitis. The patient assumed either the lateral recumbent position or a sitting position. The needle under complete aseptic technique was inserted in the interspace between L3 and L4 or L4 and L5, in the midline, approximately 15 degrees cephalic. The amount of CSF withdrawn was 3 to 5 ml enough for analysis [14, 15].

CSF analysis

We examined CSF for Physical appearance (color, aspect,), chemical (glucose, protein), cell count, gram's stain and culture. According to the results of the CSF examination, meningitis cases were divided into:

Septic meningitis (positive CSF culture) and **aseptic meningitis** (negative CSF culture)

Application of bacterial meningitis score

Bacterial meningitis score predictors	**criteria**
CSF gram stain	Positive (2 points)
CSF protein	≥ 80 mg/dl (1 point)
CSF absolute neutrophil count	≥ 1000 cells/ mm^3 (1 point)
Peripheral blood neutrophil count	≥ 10 000 cells / mm^3 (1 point)
Seizure	Before or at the time of presentation (1 point)

If the score 2-6 points, the bacterial meningitis is most likely **[16].**

Statistical analysis

The collected data was revised, coded, and tabulated using the Statistical package for Social Science (SPSS Statistics for Windows, Version 25.0.). Data were presented and a suitable analysis was done according to the type of data obtained for each parameter. Shapiro test was done to test the normality of data distribution. Mean, Standard deviation (± SD) were used for numerical data. Frequency and percentage of non-numerical (qualitative) data. Student T test was used to assess the statistical significance of the difference between the two study group means. The Chi-Square test was used to examine the relationship between two qualitative variables. Sensitivity, specificity, PPV, NPV, and accuracy to differentiate the patient and healthy cases correctly. P values is significant if <0.05 at confidence interval 95%.

RESULTS

Patient characteristics

This cross-sectional study recruited patients with symptoms suggestive of acute meningitis, their ages ranged from 4 to 73 years, 47.9% were less than 18 years, and predominantly there were males (n= 32, 66.7%).

Their residence was predominantly rural 52.1%, 66.7% had low socioeconomic status. All cases presented with fever, 91.7% with headache and in 75% neck rigidity was evident **(Table 1- Figure 1).**

Results of CSF examination and culture

According to the results of CSF culture, cases were classified into septic (positive culture growth) and aseptic (negative bacterial growth) **(Figure 2)**. Septic cases were significantly associated with urban residence, low socioeconomic status, and family history of smoking (**Table 1**). There were no significant differences in the clinical presentation between septic and aseptic cases.

According to physical appearance of CSF sample, septic group was significantly associated with whitish color, turbid aspect, and high pressure ($p<0.001$ for each) **(Table 3).** Total leucocytes count, neutrophil, lymphocytes, protein, ESR, and CRP were significantly higher in CSF of septic cases, while CSF glucose was significantly low **(Table 2).**

One-quarter of patients show bacterial growth (12 patients), 8 of them (66.7%) were Gram-positive cocci (Streptococcus pneumoniae), while 4 cases (33.3%) were Gram-negative bacilli (3 cases of H Influenza and one case was Pseudomonas) **(Figure 3).**

Bacterial meningitis score:

We calculate bacterial Meningitis Scores for all cases. Gram stain was positive in 12 samples, 31.3% of cases had CSF protein >80 mg/d1, 20.8% had peripheral absolute neutrophils count ≥ 10000/ mm^3, 18.8% had CSF neutrophils ≥ 1000 cells/mm^3, 16.7% had seizure at or before the presentation. The total score in all studied cases was 1.7, with range from 0 to 6 **(Table 4)**.

BMS was significantly higher in septic cases, it ranged from 3 to 6, comparing to that of aseptic cases which ranged from 0 to 2. (**Table 4**)

Bacterial meningitis score detected 11 out of the 12 cases diagnosed with bacterial meningitis with PPV of 91.7% and only missed one case which has a score of less than 2. Moreover, 35 cases from the 36 aseptic meningitis cases had a score ≤ 2 with a NPV of 97.2%. Sensitivity was 91.7%, and specificity was 97.2%. The overall accuracy of the test is 95.8% **(Table 5)**.

Table (1): Sociodemographic data of all septic and aseptic cases.

Parameter	Aseptic n=36 N %	Septic n= 12 N %	P value
Ages in years			
Mean±SD	25.3±3.4	19.1±4.4	0.397
Ages in groups			
≤ 18 years	17 47.2%	6 50%	0.558
19-40	11 30.6%	5 41%	
>40	8 22.2%	1 8.3%	
Gender:			
Male	23 63.9%	9 75%	0.725
female	13 36.1%	3 25%	
Resident			
Urban	13 36.1%	10 83.3%	0.005
Rural	23 63.9%	2 16.7%	
Socioeconomic status			
Low	21 58.3 %	11 91.7 %	
high	15 41.7%	1 8.3 %	0.04
Smoker in the family			
Yes	12 33.3 %	9 75 %	
No	14 66.7 %	3 25 %	0.012

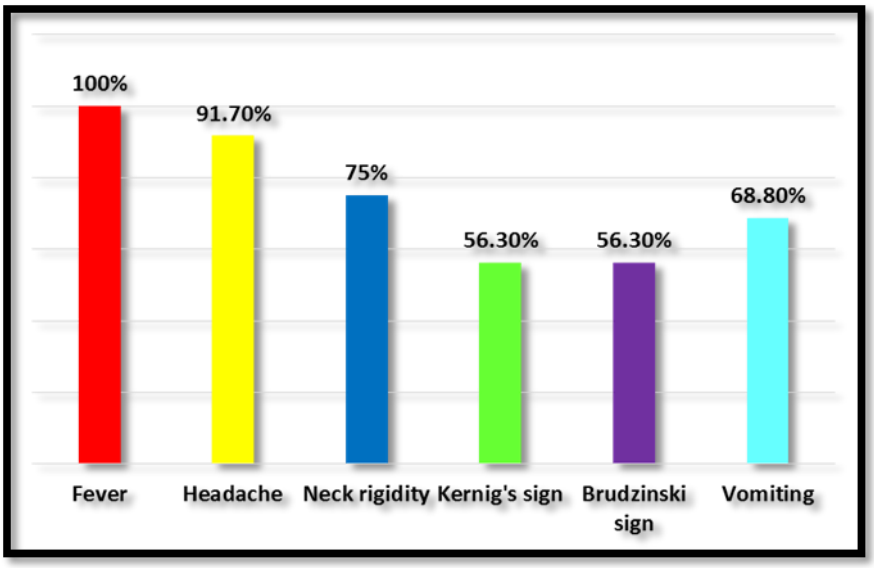

Figure (1): Clinical presentation of all studied cases.

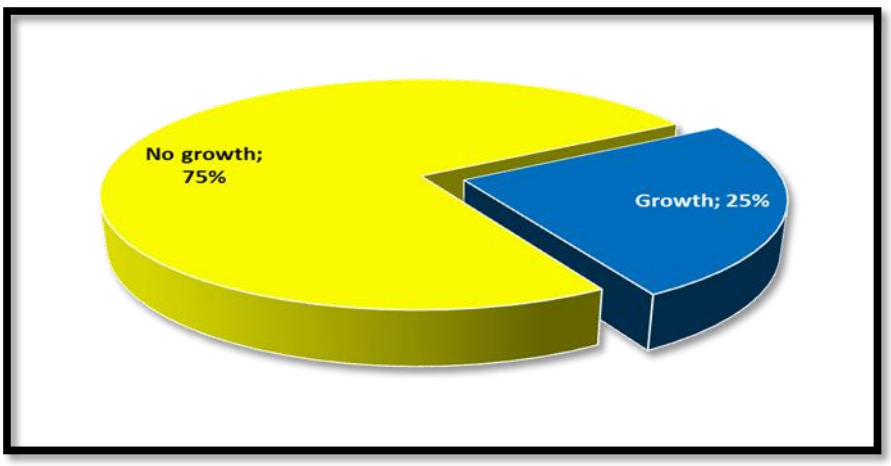

Figure (2): Results of CSF culture for all cases.

Table (2): Comparison of blood laboratory data between septic and aseptic cases.

variables	Aseptic group n= 36 Mean ± SD	Septic group n= 12 Mean ± SD	P value
WBCs (10^9/L)	9.6 ± 0.6	14.6 ± 2	0.003
Neutrophiles ($X10^9$/L)	3.4 ± 0.5	10.9 ± 1.5	0.001
Lumphocytes ($X10^9$ /L)	6.2 ± 2	3.5 ± 1.1	0.001
Hemoglobin (g/dl)	11.1± 0.2	10.4 ± 0.4	0.177
Plateletes ($X10^9$/L)	258.5 ± 15.5	296.4 ± 40.5	0.290
ESR at second hour (mm/h)	37.8 ± 2.3	75.7 ± 8.2	0.001
CRP (mg/dl)	14.9 ± 1.7	111.6 ± 28.5	0.001
Blood glucose (mg/dl)	152.2 ± 6.9	151.5 ± 17.5	0.915

CRP: C reactive protein.

Table (3): Comparison of CSF examination between septic and aseptic cases.

Physical apperance	**Aseptic group** n= 36 N %	**Septic group** n= 12 N %	P value
Color:			
Watery (colorless, clear)	33 91.7 %	0	<0.001
Whitish(purulent)	0	12 100 %	
Reddish	3 8.3%	0	
Aspect :			
Clear	33 91.7 %	0	<0.001
Turbid	3 8.3%	12 100 %	
Pressure:			
Normal	31 86.1 %	0	
High	5 13.9 %	12 100%	<0.001
Laboratory data	Mean ± SD	Mean ± SD	
TLC (cells/mm^3)	30.1 ± 6.6	11258.3 ± 4262.9	<0.001
Neutrophils (cells/mm^3)	9.9 ± 4.5	9179.5 ± 3453.3	<0.001
lymphocytes (cells/mm^3)	20.2 ± 5.4	2078.5 ± 647.3	<0.001
Glucose (mg/dL)	72 ± 3.2	40.3 ± 3.3	<0.001
Protein (mg/dL)	47.9 ± 11	211.4 ± 24.8	<0.001

TLC: total leucocytes count.

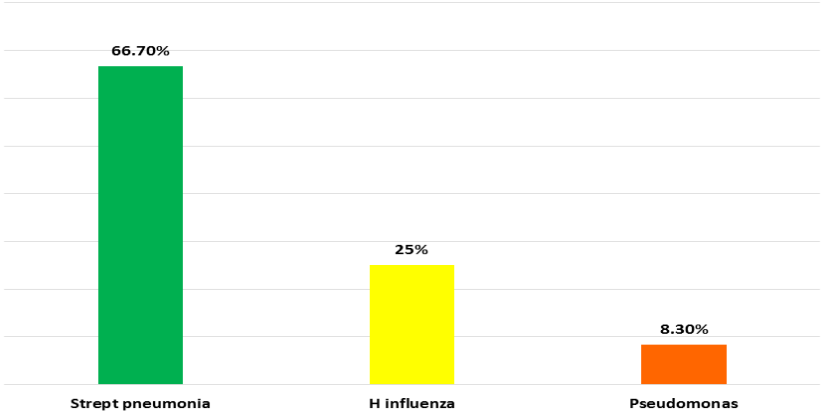

Figure (3): Identification of isolated organisms in septic group.

Table (4). Comparison of total score between septic and aseptic cases.

Bacterial meningitis score	**Aseptic** N=36	**Septic** N=12	*P*
Mean±SD	**0.4 ± 0.1**	**4.3 ± 0.3**	**<0.001**
range	**0 - 2**	**3 - 6**	
≤2	35	1	
>2	1	11	

Table (5): Bacterial meningitis score items and efficacy.

Items	Absent	Present
Positive Gram stain	36 75%	12 25 %
CSF protein >80 mg/d1	33 68.8%	15 31.3 %
blood neutrophils count ≥ 10000 cells/ mm3	38 79.2%	10 20.8 %
CSF neutophils counts ≥ 1000 cells/mm^3	39 83.3 %	9 18.8 %
Seizure at or before presentation	40 83.3 %	8 16.7 %
Total score: Means± SD Range	1.7±0.3 0 – 6	
Sensitivity	91.7%	
Specificity	97.2%	
PPV	91.7%	
NPV	97.2%	
Accuracy	95.8%	

PPV: positive predictive value, NPV: negative predictive value.

DISCUSSION

Bacterial meningitis is life-threatening inflammation of the meninges and cerebrospinal fluid (CSF) that surrounds and protects the brain and spinal cord. Some people with the infection die and death can occur in a few hours. Patients who do recover can have permanent disabilities, such as brain damage, hearing loss, and learning disabilities [17-19]. The incidence and fatality rates for bacterial meningitis vary by region, country, pathogen, and age group. Without treatment, the fatality rate can be as high as 70 percent [20].

Meningitis can affect any age and gender, affecting more children and the elderly. The association seems to be related to poor immunity in younger children and a combination of other diseases and immunosuppression in the elderly. [21].

The current study was designed to determine the frequency of acute bacterial meningitis and identify some risk factors and for evaluation of bacterial meningitis score to detect high risk patients with acute bacterial meningitis.

In this study, we recruited 48 patients (32 male and 16 female). Males account for 66.7% of patients, with no significant difference between patients with septic meningitis and aseptic meningitis. These results less than with those of Abro et al. [22] who found that males predominance (84%). However, these results are close to that reported by Alkholi et al., and Moradi et al. [23, 24] who found that 57.5% and 59.6% of patients with meningitis were men, respectively. There were no variations in terms of gender, age groupings, or age. These findings support other research findings [25, 26].

A low socioeconomic state has an important role in the increased incidence of bacterial meningitis. These factors include poverty, household crowding, limited access to health care, and lower educational level [27]. Overcrowding and poor households, facilitate the transmission of respiratory droplets from the carrier or symptomatic patients to healthy individuals [28]. Tobacco seems to increase the risk of bacterial meningitis among both active and passive smokers [29-31]. The results of the current study as shown above are in agreement with these demographic variables.

All cases with bacterial meningitis in the current study presented with fever. It is clear from the available literature that fever is the most commonly reported symptom in bacterial meningitis, with an occurrence rate of 92–93%. Vomiting is reported in 55–67% of children with bacterial meningitis [32- 34], figures emphasized by the current study.

Regarding symptoms and signs of septic and aseptic meningitis, there is no statistically significant difference between both groups. Our results are matched with Singhi& Bansal **[35].** On the other hand Zhang et al., found that headache was statistically significantly higher in bacterial meningitis **[26].**

The diagnosis of bacterial meningitis cannot be proven without CSF examination. A positive CSF culture is diagnostic for bacterial meningitis and enables testing of the antimicrobial susceptibility patterns, after which antibiotic

treatment can be optimized **[36]**, and this was followed in the current study.

In our study, CSF was turbid among all patients with septic meningitis and in 8.3% among patients with aseptic meningitis, due to excessive cells (pus, inflammatory cells, WBCs; mainly neutrophils, and RBCs) and proteins. As usual WBCs, neutrophils, and protein were significantly higher in CSF samples of septic cases when compared to samples of aseptic cases. These results are in agreement with many studies **[25, 26, 37, 38]**. The white blood cell count in bacterial meningitis is typically greater than 1000 cells/mL; mainly neutrophils predominate, but about 10% of patients present with lymphocyte predominance **[39-42]**. The CSF glucose concentration is < 40 mg/dL In more than half of BM patients. Low CSF glucose concentration virtually excludes viral meningitis. In BM, the CSF protein concentration is elevated usually to 1,000 to 5,000 mg/L **[43, 44]**.

According to CSF culture, 8 cases out of the 12 were gram positive cocci (Strept. Pneumonia), while Gram negative bacilli (H influenza) were isolated in 3 cases and one isolate was due to Pseudomonas. These results are in agreement with many reports in the literature [45-47]. These reports stated that S. pneumonia was the leading cause of bacterial meningitis among adults in Egypt and Neisseria meningitides was described as the second or third leading cause. Reflecting a change in the epidemiology of the disease where *N. meningitides* was for a long time the main etiological agent **[48]**. The decrease in the number of meningococcal meningitis may be due to the introduction of school-based vaccination program, vaccination for all persons before travelling to the Hajj in addition to the immunization programs of military recruits **[49]**.

While in a large European study conducted on children presented with sepsis and admitted to ICU, the common clinical illnesses were meningitis/encephalitis. *Neisseria meningitides* was the most commonly identified pathogen (n = 131, 31%) followed by *S. pneumonia* (n = 78, 18%) **[50]**.

CSF sterility is achieved rapidly after IV antibiotics, within 15 minutes to 2 hours for meningococcal, 4–6 hours for pneumococcal and 8 hours for neonatal GBS infection **[51, 52]**.

This study determines high-risk patients of bacterial meningitis for recognition and immediate antibiotic administration and hospitalization, and therefore better outcomes and improved morbidity and mortality in this serious disease. Patients with a bacterial meningitis score of less than 2 can be considered to be at very low risk of bacterial meningitis. Bacterial meningitis score in our study detected 11 cases from 12 cases with proven bacterial meningitis in whom medicines were appropriately commenced, with PPV; 91.7%., NPV; 97.2%, and the accuracy of the test was 95.8%. These results are in agreement with many studies **[53-55]**. Furthermore, one large European multicenter study showed BMS NPV was 100% (95% CI, 98.8-100%) **[56]**.

This study had its own limitation; which is not only small number of the patients recruited, but also and being single center study which consequently don't allow for better recognition of microbiological patterns of acute meningitis.

Funding: None.

Conflicts of interest: None.

Informed consent and ethical approval :

The study was carried out following the ethical principles of the Declaration of Helsinki, and it was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Zagazig University, Egypt (approval no. **4086**). Informed consent has been obtained from every participant, verbal explanations were done to all children in front of their parents and misunderstanding was clarified and written consent was then signed by the parents.

Research Highlights:

- Acute bacterial meningitis is common in Egypt.
- Acute bacterial meningitis is a serious infection with high morbidity and mortality.
- Gram positive cocci mainly *strept. Pneumonia* is the most causative pathogen.
- Incidence of bacterial meningitis in our study is 25%.
- The bacterial meningitis score has high sensitivity (91.7%), specificity (97.2%), PPV (91.7%) and NPV (97.2%) in the diagnosis of the septic meningitis cases.

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