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Research Article

Clinical Features and CSF Profile of Adults Bacterial Meningitis: A Retrospective Analysis Of 173 Cases

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Abstract

Background: Adult Bacterial Meningitis (ABM) is a widespread neurological illness worldwide.

Methods: The study retrospectively collected 173 clinical cases, and involved analysis of pathogenic bacterial composition and drug sensitivity tests, as well as a comparison of clinical and Cerebrospinal Fluid (CSF) features between sub-groups.

Results: The predominant pathogenic bacterium identified was Streptococcus pneumoniae. Male and elderly patients presenting with seizures, shivering, or altered consciousness were more likely to yield positive CSF cultures. Incidence rates of altered consciousness, shivering, and seizure attacks were higher in the group with positive cultures compared to the group with negative cultures. Furthermore, the group with positive cultures exhibited higher blood neutrophil counts, CSF white cell counts, and CSF protein levels than those with negative cultures. Additionally, the gram-positive bacillus group showed a higher incidence of seizure attacks, hydrocephalus, and brain edema than the gram-negative bacillus and gram-positive coccus groups.

Conclusion: The predominant pathogen identified in CSF was Streptococcus pneumoniae. Male and older patients presenting with seizures, shivering, and altered consciousness were more prone to yield positive CSF culture results. Those with positive CSF cultures exhibited elevated levels of inflammatory markers. Gram-positive bacilli were associated with a higher likelihood of causing seizure, hydrocephalus, and brain edema.

Keywords: Adult bacterial meningitis, Cerebrospinal fluid, CSF culture, Clinical Features

Background

Adult Bacterial Meningitis (ABM), also known as adult purulent meningitis, poses a significant healthcare challenge due to its high mortality and disability rates, often exceeding 20% [1-3]. Globally, approximately 1.2 million people suffer from bacterial meningitis annually, with developing countries bearing the most significant burden [4]. Timely diagnosis and treatment are crucial for improving patient outcomes. The primary approach to managing ABM involves promptly administering antibiotics targeting specific pathogens. However, identifying these pathogens can be challenging and time-consuming, often requiring several days [5,6]. Consequently, clinicians often rely on empiric antibiotic selection based on clinical presentation, laboratory findings, and epidemiological data during the initial stages of treatment. Furthermore, the landscape of bacterial infections is continually evolving. New strains emerge through genetic mutations, leading to variations in the predominant pathogens and their antibiotic susceptibilities across different geographical region [1,2,7]. These dynamic changes present significant challenges for healthcare

providers when selecting appropriate antibiotic therapies [8]. In this retrospective study, we aimed to address these challenges by analyzing 173 cases of ABM patients admitted to the General Hospital of Ningxia Medical University. By elucidating common patient characteristics and gaining insights into the evolving epidemiology of ABM in our region, we aimed to inform clinical practice and optimize patient management strategies for this life-threatening condition. Through our comprehensive analysis, we aim to contribute to the growing body of knowledge on ABM and facilitate the development of evidence-based guidelines for its management.

Materials and Methods

Patients

One hundred seventy-three patients diagnosed with ABM were retrospectively included in this study, comprising 173 cases from the General Hospital of Ningxia Medical University over the past 15 years. The inclusion criteria for a definitive ABM diagnosis were: 1) age ≥18 years; 2) clinical symptoms of meningitis such as headache, fever, altered consciousness, seizures, and signs of meningeal irritation; 3) purulent Cerebrospinal Fluid (CSF) features meeting at least one of the following parameters: leukocytosis with a leukocyte count > 0.25 ×109/L and predominantly polymorphonuclear cells, lactate concentration > 3.5 mmol/L, CSF glucose/serum glucose ratio < 0.4, or CSF glucose level < 2.5 mmol/L if simultaneous blood glucose level was not available. The Ethics Committee of the respective hospitals approved the study. Exclusion criteria: (1) Those who did not meet the above inclusion criteria; the first cerebrospinal fluid examination was not performed at our hospital; (2) Those who did not undergo cerebrospinal fluid examination during hospitalization due to patient refusal; (3) Those whose patients abandoned treatment without a sufficient course of treatment.

Clinical Index

The clinical data of 173 patients with ABM were gathered, encompassing gender, age, initial symptoms, physical signs, initial intracranial pressure upon admission, CSF cytology, CSF biochemistry, CSF culture results, and drug sensitivity tests, hemanalysis, blood culture results, imaging signs, treatment, and outcomes.

CSF cytology: CSF specimens of 3-5mL were routinely taken by lumbar puncture and sent for examination immediately. According to the results of routine counting of CSF, 0.2~0.5mL of CSF was added to a Cytospin-4 slide centrifuge and centrifuged (900r-min-1, 5min). The slides with cells were stained with Raget staining (8min), dried, and then classified cytologically by light microscope. Each specimen was categorized and counted 100 cells, and the proportion of each type of cell was calculated. A leukocyte counts of >10 cells/mm~3 was considered abnormal, and 0-10 cells/mm~3 was considered normal. Cell image acquisition was performed using a M99 I cell image analysis system.

CSF culture results of pathogenic microorganisms were proceeded along with a record of the patient's antibiotic use (type and duration of antibiotic). BACT/ALBRT 3D automatic blood culture instrument and VITEK 2 COMPACT automatic microbial identification system of Bio Merieux Company of France were used, and the culture and identification of strains were carried out in accordance with the National Clinical Laboratory Operation Procedures. The drug sensitivity test was performed by K-B method, and the operation and judgment of the results were in strict accordance with the standards of the Committee for Clinical Laboratory Standardization (CLSI) of the United States of America.

Comparison Between Groups According to CSF Cultures

We analyzed 173 cases, focusing on their clinical features, the composition of pathogenic bacteria, and the results of antibiotic sensitivity tests. Patients were categorized into two groups based on the results of CSF culture: the CSF Culture-Positive Group (CP) and the CSF Culture-Negative Group (CN). A comparison of clinical features and laboratory examination results was then made between these two groups. Subsequently, the 66 patients in the CP group were further subdivided into three subgroups: gram-positive coccus group, gram-positive bacilli group, and gram-negative bacilli group, and comparisons of clinical data and laboratory examination results were conducted among these subgroups.

Statistical Analysis

The data were presented as the number of cases or means ± standard deviation. Statistical analysis was conducted using the SPSS (version 17.0) software package, and Chi-Square and corrected Chi-square tests were performed. The significance level was set at 0.05.

Results

Clinical Features of 173 ABM

The study included 173 cases, with an age range of 18 to 83 years (mean 39.1±17.1), comprising 123 males (71.1%) and 50 females (28.9%). The most prevalent symptoms were fever (166 patients, 95.95%), headache, nausea, and vomiting (141, 81.50%), altered consciousness (56, 32.37%), and shivering (38, 21.97%). Additional symptoms included psychiatric symptoms (27, 15.61%), seizure attacks (20, 11.56%), limb weakness (9), speech disability (2), diplopia (2), and hypoplasia (1). The primary pathological indicator was meningeal irritation signs, such as stiff neck, positive Kernig's sign, and Brudzinski's sign (135 cases, 78.03%). Positive CSF bacterial culture was found in 66 cases, while 107 had negative findings. Imaging examinations revealed cerebral edema or hydrocephalus in 15 cases. Following active treatment, 131 cases showed significant improvement or were cured, while 42 patients either died or refused treatment. (Table 1) provides a summary of the clinical features of the 173 ABM patients.

Table 1: Clinical features of 173 patients with ABM.

Clinical Features	Number of Cases	Occurrence Rate
Fever	166	95.95%
Headache, nausea, vomit	141	81.50%
Shiver	38	21.97%
Conscious disturbance	56	32.37%
Psychiatric symptom	27	15.61%
Seizure attack	20	11.56%
Limb weakness	9	5.2%
Speech disorder	2	1.16%
Diplopia	2	1.16%
Hypopsia	1	0.58%
Meningeal irritation sign	135	78.03%
Cerebral edema or hydrocephalus	15	8.67%
Cured or improved	131	75.72%

Pathogenic Bacteria and Drug Sensitivity Analysis

Among the 173 cases of ABM, pathogenic bacterial strains were cultured from the CSF of 66 patients (38.15%). These comprised 43 cases of gram-positive cocci (65.15%), 11 cases of gram-negative bacilli (16.67%), and 12 cases of gram-positive bacilli (18.18%). The predominant gram-positive cocci were *Streptococcus pneumoniae*, followed by *Staphylococcus aureus*. The primary gram-negative bacillus was *Escherichia coli*, and the major gram-positive bacillus was *Listeria monocytogenes*. The specific bacteria identified in CSF cultures are listed in (Figure 1).

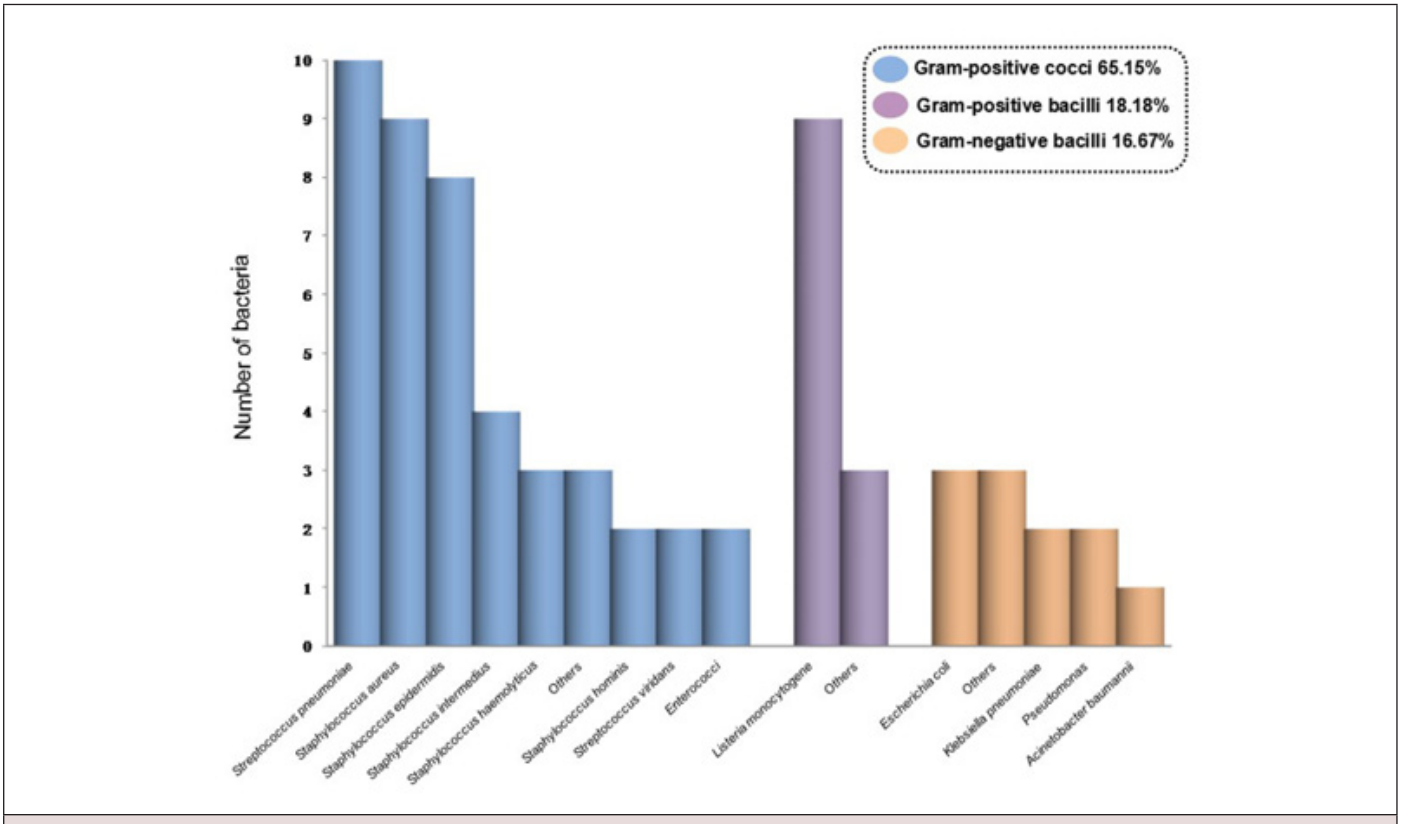

Figure 1: The pathogenic bacterial distribution of 66 CSF culture-positive cases.

The antibiotic sensitivity test revealed that the majority of Staphylococci were resistant to penicillin, while most *Listeria Monocytogenes* were sensitive to it. Additionally, almost all Escherichia Coli showed resistance to cephalosporin. *Streptococcus pneumoniae* exhibited partial sensitivity to penicillin and cephalosporin but were resistant to macrolide antibiotics. Notably, all cultured bacteria demonstrated sensitivity to vancomycin, imipenem, linezolid, and furantoin (Table 2).

Table 2: Drug sensitivity analyses of bacterial strains in the CSF.

Antibiotics	*Staphylococcus aureus* n=9		*staphylococcus epidermidis* n=8		*Streptococcus pneumoniae* n=10		*Listeria monocytogenes* n=9		*E. coli* n=3	
	S	R	S	R	S	R	S	R	S	R
Penicillin	1	8	1	7	8	2	7	2	-	-
Ampicillin/sulbactam	1	8	2	6	9	1	8	1	0	3
Amoxicillin	4	5	5	3	1	9	-	-	-	-
Oxacillin	3	6	2	6	-	-	-	-	-	-
Piperacillin/Tazobactam	4	5	2	6	-	-	-	-	3	0
Cephazolin	4	5	4	4	-	-	8	1	0	3
Cefuroxime	-	-	4	4	-	-	-	-	0	3
Ceftriaxone	-	-	-	-	10	0	8	1	2	1
Ceftazidime	-	-	-	-	-	-	-	-	0	3
Cepoperazon	-	-	2	6	1	9	-	-	-	-
Imipenem	4	5	7	1	-	-	-	-	3	0
Levofloxacin	8	1	5	3	10	0	8	1	2	1
Ciprofloxacin	6	3	3	5	-	-	-	-	0	3
Erythromycin	1	8	1	7	2	8	8	1	-	-
Azithromycin	-	-	-	-	0	10	-	-	-	-
Cidomycin	4	5	5	3	-	-	-	-	2	1
Vancocin	8	1	8	0	10	0	8	1	-	-
Linezolid	8	1	7	1	9	1	9	0	-	-
Furantoin	3	6	2	6	-	-	-	-	1	2

***Note:** S, sensitive; R, drug resistance; -, not tested.

Comparison of the Clinical Features Between CN And CP Groups

Among the 173 cases of CSF culture in this study, 66 cases yielded positive results for bacterial culture (CP), while 107 tested negatives (CN). Both CP and CN groups presented common symptoms such as fever, headache, nausea, vomiting, and psychiatric symptoms without any statistical variance. Similar observations were made regarding hospitalization duration, brain edema, and prognosis. However, conscious disturbance, shivering, and seizure attacks were significantly more prevalent in the CP group than in the CN group ($P<0.05$). Furthermore, the average age in the CP group (42.6) exceeded that of the CN group (35.7). Male patients constituted 82% of the CP group and 64.5% of the CN group ($p<0.05$) (Table 3).

Comparison of the laboratory features between CN and CP patients

The study conducted a comparison of blood cell counts, intracranial pressure on the first day of hospitalization, CSF cytology, and CSF biochemistry between the CN and CP groups (Table 4). The CP group showed a significantly higher proportion of peripheral blood neutrophils than the CN group ($p<0.05$). Additionally, the CP group exhibited elevated CSF white cell counts and protein content compared to the CN group ($p<0.05$). However, no differences were observed in peripheral white blood cell counts, intracranial pressure, and other CSF indices between the two groups.

Table 3: Comparison of the Clinical features between CN and CP.

Items	CSF culture results		P value
	CN (n=107)	CP (n=66)	
Symptoms			
Hyperthermia (T≥39.0°C)	72	48	0.451
Headache, nausea and vomiting	87	54	0.933
Shiver	18	20	0.037*
Conscious disturbance	28	28	0.026*
Psychiatric symptom	14	13	0.244
Seizure attack	8	12	0.032*
Imaging examination			
Hydrencephalus or brain edema	6	9	0.068
Prognosis			
Cured or relieved	82	49	0.721
Male gender	69	54	0.015*
Age	35.67±14.85	42.58±19.53	0.028*
Days of Hospitalization	27.72±25.76	34.49±26.97	0.137

***Note:** Data were expressed as means ± s.d. or number of cases. CN, CSF culture-negative group; CP, CSF culture positive group.

Table 4: Comparison of the laboratory features between CN and CP.

Items	Groups		P value
	CN (n=107)	CP (n=66)	
White blood cell counts ($x10^9$/L)	12.50±7.60	13.67±6.75	0.356
Blood neutrophil proportion (%)	78.13±13.25	82.52±9.43	0.022*
Intracranial pressure (mmH_2O)	240.33±66.15	250.62±67.72	0.374
CSF white cell counts ($x10^6$/L)	2181.61±4440.87	4078.13±5739.24	0.010*
CSF neutrophil proportion (%)	54.34±34.51	62.58±34.17	0.168
CSF leukomonocyte proportion (%)	35.28±31.39	26.13±29.22	0.087
CSF protein (g/L)	2.18±2.01	2.99±2.67	0.041*
CSF glucose (mmol/L)	2.16±0.96	1.98±1.03	0.289
CSF chloridate (mmol/L)	117.88±8.12	115.35±9.92	0.101

***Note:** Data were expressed as means ± s.d. CN, CSF culture negative group; CP, CSF culture positive group.

Comparison of the Clinical Data and Laboratory Features Among Three Kinds of Pathogenic Bacteria Classified According to Gram's Stain

Based on the bacterial culture results, the 66 patients testing positive for pathogens were categorized into gram-positive bacillus, gram-negative bacillus, and gram-positive coccus subgroups. A comparison of clinical data among these groups indicated a higher likelihood of seizure attack and brain edema associated with gram-positive bacillus infections ($P<0.05$). However, no disparities in other clinical symptoms and prognosis were observed among the three subgroups (Table 5).

Table 5: Comparison of the clinical data among three pathogenic subgroups.

	G+ bacillus	G- bacillus	G+ coccus	P value
	N=12	N=11	N=43	
Symptoms				
Hyperthermia (T≥39°C)	8	9	37	0.322
Headache, nausea and vomiting	10	6	33	0.274
Shiver	4	2	14	0.730
Conscious disturbance	7	3	16	0.307
Psychiatric symptom	3	2	8	0.900
Seizure attack	5	1	5	0.043*
Imaging examination				
Hydrencephalus or brain edema	4	2	3	0.041*
Prognosis				
Cured or relieved	9	6	34	0.251

Discussion

Bacterial meningitis in adults is a significant public health concern, with an annual incidence of 5 per 100,000 in developed countries and ten times higher in developing countries [7,9,10]. A retrospective study by Proulx [11] found a strong correlation between the timing of antibiotic initiation and patient prognosis. Administering antibiotics within 6 hours of hospitalization resulted in a mortality rate of 5%-6%, while delays of 6-8 hours increased mortality to 45%, and further delays to 8-10 hours raised mortality to 75%. Therefore, early and effective antibiotic treatment is crucial for the prognosis of ABM. However, early diagnosis is challenging due to atypical symptoms, delays in obtaining CSF test results, and low pathogenic bacteria detection rates in cultures. Various factors, including patient age, pathogenic bacteria, immune status, and prior therapy, impact both the clinical presentation and the results of CSF examination [12]. Retrospective studies of ABM cases can assist physicians in identifying typical and atypical clinical features, thereby facilitating early antibiotic selection.

A retrospective analysis of 173 cases of ABM showed that the predominant symptoms included fever (95.95%), headache, nausea, and vomiting (81.50%). A relatively high proportion of patients experienced altered consciousness (32.37%). Psychiatric symptoms and seizure attacks were observed in approximately 10% of the cases. The primary physical examination findings indicated meningeal irritation signs, consistent with earlier studies [7,13,14]. The CSF culture accurately detected pathogenic bacteria in 66 cases, with Gram-positive bacteria being the most prevalent. These included *Staphylococcus aureus* (9 cases), *Listeria monocytogenes* (9 cases), *Streptococcus pneumoniae* (10 cases), and Escherichia coli (3 cases). Previous research has shown that pathogen prevalence can vary based on time, geographical location, and patient age [15,16]. Several studies have identified *Streptococcus pneumoniae* as the primary pathogen in ABM [17-19]. Furthermore, other studies have indicated that most Staphylococcus ABM cases are linked to craniocerebral trauma, surgery, and conditions leading to blood-brain barrier impairment [20,21]. Our findings further corroborate that *Streptococcus pneumoniae* is the predominant pathogen in ABM.

Drug sensitivity tests revealed that the majority of Staphylococci exhibited resistance to penicillin, while most *listeria monocytogenes* were susceptible to penicillin, which is consistent with previous research by Aral and Clauss [22,23]. Our study also identified partial sensitivity of *Streptococcus pneumoniae* to penicillin, in line with Mengistu's report of 34.3% resistance, but maintained high susceptibility to cephalosporin [10,24]. Additionally, our observation of all three cases of Escherichia coli being resistant to cephalosporin contrasts with Mengistu's findings [24], possibly due to the limited number of cases (3 out of 66 patients). Notably, all cultured pathogenic bacteria demonstrated sensitivity to vancomycin, imipenem, linezolid, and furantoin, suggesting these antibiotics are viable last-line therapeutic options if other treatments are ineffective.

The primary means of diagnosing bacterial meningitis is through the examination of CSF and CSF bacterial cultures. Our retrospective analysis revealed a CSF culture positivity rate of 38.15%, lower than that reported by *Khorasani et al.* [25]. Various factors, such as sample contamination, delays in sample analysis, prior antibiotic use, bacterial culture methods, and bacterial characteristics, can influence CSF culture results [26,27]. Our data suggests that older male patients presenting with seizures, shivering, and altered consciousness are more likely to have positive CSF culture results. In the present investigation, the comparison between the CN and CP groups revealed that CP patients had a higher incidence of altered mental status, shivering, and seizures compared to CN patients.

Laboratory examination showed elevated white blood cell counts and protein levels in the CSF in the CP group compared to the CN group. The lower levels of inflammatory markers in the blood and CSF in CN meningitis may be due to infection by hypotoxic bacteria or early antibiotic treatment. The symptoms among the three pathogenic subgroups were broadly similar, except that Gram-positive bacillus was more likely to cause seizures and cerebral edema than Gram-negative bacillus and Gram-positive coccus, a correlation not previously reported. However, further validation through large-scale case analysis is necessary due to the small number of patients in each subgroup.

In conclusion, the typical symptoms and clinical indicators of ABM have remained consistent. Patients in the CP group, particularly those with Gram-positive bacillus infection, exhibited a higher propensity for altered mental status, seizures, and cerebral edema. *Streptococcus pneumoniae* was the predominant pathogen, while penicillin and cephalosporin demonstrated efficacy against *Listeria monocytogenes*. Male patients of advanced age were more prone to yielding positive CSF culture results.

Conflict of Interest

The authors declare no conflicts of interest.

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Ethical Approval and Consent to Participate

The Ethics Committee of the respective hospitals approved the study.

Consent to Publication

All authors involved in this study have provided their agreement to publish the research findings.

Data Availability Statement

The data supporting the findings of this study are accessible from the corresponding author upon reasonable request.

Author Contributions

Xiaoyan Niu: Conceptualization, Methodology, Validation, Investigation, Data curation, Resources, Writing original draft, Review & editing, Project administration. Qiang Liu: Conceptualization, Formal analysis, Investigation, Data curation, Writing original draft, Review & editing, Visualization. Weimin Qi: Validation, Formal analysis, Investigation, Data curation, Review & editing. Jianhang He: Validation, Formal analysis, Investigation, Data curation, Review & editing. Xiaoyan Chen: Validation, Methodology, Investigation, Data curation, Resources, Review & editing, Visualization. Zhenhai Wang and Haining Li: Conceptualization, Formal analysis, Investigation, Data curation, Writing original draft, Review & editing, Resources.

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