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ORIGINAL ARTICLE

Diagnostic Value of Cerebrospinal Fluid Procalcitonin in Differentiating Bacterial and Aseptic Meningitis: A Cross-Sectional Study

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ABSTRACT

Background: In adults, procalcitonin (PCT) has been the focus of various investigations about its diagnostic accuracy in differentiating between bacterial and aseptic meningitis in adults. This study set out to determine whether procalcitonin is a good diagnostic tool for distinguishing between bacterial and non-bacterial meningitis.

Methods: We performed a cross-sectional study with 32 patients: 16 in Group A, who had bacterial meningitis (ascertained by positive cerebrospinal fluid culture and/or Gram stain), and 16 in Group B, who had aseptic meningitis (ascertained by negative cerebrospinal fluid culture and Gram stain). We measured CSF procalcitonin, C-reactive protein (CRP), blood glucose, and complete blood counts (CBCs) before antibiotic treatment began.

Results: A CSF procalcitonin cutoff of 0.5 ng/mL demonstrated excellent diagnostic accuracy, with 87.5% sensitivity and 93.75% specificity (AUC 0.887) in distinguishing between the two groups. Several inflammatory indicators were positively correlated with CSF procalcitonin levels. The following variables were taken into consideration: total leukocyte count (TLC) ($r=0.493$, $p=0.004$), C-reactive protein (CRP) ($r=0.779$, $p<0.001$), cerebrospinal fluid pressure ($r=0.579$, $p<0.001$), total cell count ($r=0.359$, $p=0.04$), protein concentration ($r=0.515$, $p=0.003$), and neutrophil count ($r=0.744$, $p<0.001$). On the other hand, insulin levels ($r=-0.622$, $p<0.001$) and the number of lymphocytes ($r=-0.766$, $p<0.001$) were inversely associated with CSF procalcitonin levels. In a multivariate linear regression analysis that considered other variables, CSF procalcitonin remained strongly associated with TLC ($\beta=0.128$, $p<0.001$), CRP ($\beta=0.012$, $p=0.04$), and neutrophil count ($\beta=0.056$, $p=0.02$).

Conclusion:
This study demonstrates that cerebrospinal fluid procalcitonin is a reliable and highly accurate biomarker for distinguishing bacterial meningitis from aseptic meningitis in adults. With a diagnostic cutoff value of 0.5 ng/mL, CSF procalcitonin exhibited 87.5% sensitivity and 93.75% specificity, underscoring its utility as a rapid and effective diagnostic tool. Furthermore, significant positive correlations with inflammatory markers such as CRP, neutrophil count, and total leukocyte count (TLC), alongside inverse associations with glucose and lymphocyte levels, strengthen its role as an indicator of bacterial etiology.

Keywords: Cerebrospinal Fluid, Bacterial Meningitis, Procalcitonin.

INTRODUCTION

The etiology of bacterial meningitis varies depending on the patient's age and location; it is a severe infectious condition affecting the leptomeninges. Important microorganisms comprise, among others, Listeria monocytogenes, Group B Streptococcus, Neisseria meningitidis, and Streptococcus pneumoniae. Vaccination programs that aim to prevent the spread of disease have significantly reduced the number of cases of this illness around the world. Two examples of these programs are the heptavalent pneumococcal conjugate vaccine (2000) and the Hib conjugate vaccine (1990) [1].

When bacterial meningitis is suspected, a lumbar puncture is performed to collect cerebrospinal fluid (CSF). The CSF undergoes a comprehensive analysis, including Gram stain, culture, cell count (typically showing a neutrophilic predominance), glucose, and protein levels. Absolute CSF glucose levels can be influenced by the patient's blood glucose concentration, making the CSF-to-serum glucose ratio a more dependable diagnostic indicator than the low CSF glucose and high protein levels that are characteristic of bacterial meningitis [2].

Acute bacterial meningitis, unlike the usually self-limiting aseptic form, demands prompt diagnosis and treatment with intravenous antibiotics to avoid severe complications. Early diagnosis can be difficult because initial symptoms are often nonspecific, and standard CSF analysis has limitations. Although Gram staining and CSF culture are considered the gold standard for confirmation, these methods suffer from relatively low sensitivity, and culture results may take considerable time [3].

Infants and children can have fatality rates as low as 2% from this condition, while neonates and adults can have rates of 20-30%. Any potential diagnostic tool for bacterial meningitis has to be very sensitive, if not 100% sensitive, to avoid the potentially fatal repercussions of a delayed diagnosis. Serum procalcitonin (PCT) level appears to be a highly sensitive and specific indicator for differentiating bacterial infections from non-bacterial ones, among other emerging markers [4].

As a precursor to the hormone calcitonin, procalcitonin is among the most extensively studied indicators of sepsis [5]. Thyroid C cells produce PCT, which, under normal circumstances, is converted to calcitonin before entering the bloodstream. The normal range for PCT in healthy people is less than 0.10 ng/mL. The body's non-thyroidal tissues produce a substantial amount of PCT when a bacterial infection happens. After bacterial infection, PCT levels rise fast (2-6 hours) and reach a maximum (24 hours later). [6].

In terms of sensitivity and specificity, blood PCT has shown extremely high values in previous systematic evaluations for bacterial meningitis in both adults [8] and children [7]. Other research has shown that PCT levels in CSF are similar in meningitis patients and those with non-inflammatory CNS diseases.

To what extent procalcitonin can distinguish between aseptic and bacterial meningitis in adult patients has been the subject of multiple studies. Conclusions about Procalcitonin's diagnostic utility in meningitis remain conflicting due to the heterogeneity of the studies' reported outcomes.

The topic is highly relevant and addresses an important gap in the diagnostic approach to meningitis. While previous studies have explored the utility of serum PCT in diagnosing bacterial infections, fewer studies have specifically investigated the diagnostic accuracy of CSF PCT in differentiating bacterial from aseptic meningitis in adults. This study contributes to reducing diagnostic delays, which is critical for improving patient outcomes in bacterial meningitis.

Therefore, the main question addressed by this research is whether cerebrospinal fluid (CSF) procalcitonin (PCT) can serve as a reliable diagnostic marker to differentiate between bacterial and aseptic meningitis in adult patients.

METHODS

A cross-sectional study was performed at Zagazig University Hospitals' Internal Medicine Department between December 2023 and June 2024. The study included 32 adults, 16 from each of the two groups: Group A, which included patients with bacterial meningitis as confirmed by positive cerebrospinal fluid (CSF) culture and/or Gram stain, and Group B, which included patients with aseptic meningitis as indicated by negative CSF culture and Gram stain. Detailed explanations of the study's procedures and aims were presented to all participants before they supplied signed informed consent. Institutional Review Board approval (IRB#22-21-1-2024) ensured that the study adhered to the ethical standards laid out in the World Medical Association's Declaration of Helsinki.

Cases with the following criteria were included: those individuals between the ages of 16 and 75

who exhibited symptoms consistent with meningitis, such as a headache, fever, vomiting that spews projectiles, nuchal ligament rigidity, Kernig's sign, Brudzinski's signs, and positive results from cerebrospinal fluid examination.

Cases with the following characteristics were excluded: patients who had epilepsy, intracranial hemorrhage, malignancy, brain tumor, multi-system pyogenic infections, who were treated with antibiotics before admission, or meningitis caused by fungi or tuberculosis.

A complete medical history, including the patient's age, name, sex, and any relevant family medical history, was taken from each patient. A comprehensive general clinical assessment and a focused abdominal examination were performed, emphasizing symptoms commonly associated with meningitis. Symptoms such as Brudzinski's and Kernig's symptoms, as well as headaches, fevers, projectile vomiting, and nuchal stiffness, were among them. The study of cerebrospinal fluid provided further evidence for the diagnosis.

Sixteen individuals with bacterial meningitis (defined as a positive cerebrospinal fluid (CSF) bacterial culture and/or Gram stain) made up Group A. There were sixteen patients in Group B who had aseptic meningitis, which was defined as a negative cerebrospinal fluid bacterial culture and Gram stain.

Prior to beginning the first course of antibiotic treatment, blood, and cerebrospinal fluid samples were obtained in a completely aseptic manner in accordance with the established protocols. Each individual had three milliliters of blood drawn from their veins using a sterile, clean separator tube in an effort to isolate their serum. The collection process was carried out under strict aseptic conditions. The serum was extracted by centrifugation, which was carried out for 20 minutes at a speed of 2000-3000 r.p.m. On the day of the investigation, the serum was transferred to an eppendorf tube and kept at a temperature of -4^{o} C. Repeat centrifugation is performed if precipitation is observed.

Routine laboratory investigation:

Blood was examined for routine laboratory investigations at admission in all participants, including Complete blood count (CBC): CBC performed on automated cell counter (XN330-Sysmex-Japan) with differential count on Leishman-Gemsia stained peripheral. Erythrocyte sedimentation rate (ESR) was performed on an automated ESR analyzer (VB0125). C reactive protein (CRP) and random blood sugar were done using Cobas 6000-C502 Modular Analyzer (Roche, Germany).

CSF analysis included the assessment of physical characteristics (appearance and pressure), total and differential leukocyte counts (using a hemocytometer), and the measurement of glucose and protein concentrations. All were performed on Cobas 6000-C502 Modular Analyzer (Roche, Germany). Bacteriological analysis culture using Vitek 2 compact system (biomerieux) (France). Gram stain of the sample [8].

CSF samples were examined for PCT using the ELISA method: PCT was performed using Finecare™ Rapid Quantitative Test (Catalog No. W210). A FinecareTM FIA Meter can measure PCT concentrations in blood samples, and the strength of the detection antibody's fluorescence signal indicates the amount of PCT collected. When using a FinecareTM FIA Meter, the default unit of display for the results of the PCT Rapid Quantitative Test is XXX ng/mL. The PCT Test system allowed concentrations between 0.1 and 100 ng/mL to be measured, with a detection limit of 0.1 ng/mL [8].

Statistical analysis

In order to analyze the data, SPSS version 24 was used. Data normality was evaluated using the Shapiro-Wilk test. We utilized chi-square or Fisher's exact tests for group comparisons as needed, as well as descriptive statistics like percentages and frequencies for categorical data summarization. Parametric independent samples t-tests and non-parametric Mann-Whitney U tests were used to assess continuous data based on the distribution of the data. The Pearson's and Spearman's correlation coefficients were used to evaluate the interrelationships of the variables. In order to model the relationship between the outcome and predictor factors, multiple linear regression was employed.

RESULTS

No statistically significant differences were found in the demographic profiles of the two groups, bacterial meningitis (Group A) and aseptic meningitis (Group B) ($P > 0.05$). On the other hand, 81.3% of Group A patients and 18.8% of Group B patients, respectively, had neck rigidity ($P = 0.001$). Similarly, Brudzinski's sign and Kernig's sign were also substantially more common in Group A than in Group B (43.8% vs. 6.3%, $P = 0.04$) (Table 1).

Notable variations among the categories are seen in Table 2. Group A, which was affected by bacterial meningitis, had significantly higher levels of total lipids ($P = 0.01$) and C-reactive protein (CRP) ($P <$

0.001). Group B's cerebrospinal fluid was constantly clear, in contrast to Group A's persistently murky CSF (P < 0.001). In addition, Group B, which was affected by aseptic meningitis, had a considerably higher CSF-to-serum glucose ratio (P < 0.001).

The levels of CSF procalcitonin were much more significant in Group A, which had bacterial meningitis than in Group B, which had aseptic meningitis. This difference was highly significant (P < 0.001), as shown in Table 3.

Inflammation and bacterial infection markers were significantly associated with cerebrospinal fluid procalcitonin levels (Table 4). Protein concentration (r=0.515, p=0.003), total leukocyte count (r=0.493, p=0.004), C-reactive protein (r=0.779, p<0.001), CSF pressure (r=0.579, p<0.001), total cell count (r=0.359, p=0.04), and neutrophil count (r=0.744, p<0.001) were some of the markers that showed significant positive correlations with CSF procalcitonin levels. In contrast, there were notable inverse relationships demonstrated by glucose levels (r=-0.622, p<0.001) and lymphocyte count (r=-0.766, p<0.001).

The ROC curve analysis revealed that a CSF procalcitonin cut-off of 0.5 ng/mL was the most effective in differentiating between bacterial and aseptic meningitis, with an area under the curve (AUC) of 0.887, sensitivity of 87.5%, and specificity of 93.75 percent (Table 5, Figure 1).

A multiple linear regression analysis was conducted with CSF procalcitonin as the dependent variable and age, neck stiffness, Kernig's sign, Brudzinski sign, total lipid profile, C-reactive protein, cerebrospinal fluid pressure, cells, protein, glucose, neutrophils, and lymphocytes as the independent variables. Table 6 shows that regardless of the variables indicated earlier, CSF procalcitonin had a positive association with TLC (β =0.128, P<0.001), CRP (β =0.012, P=0.04), and neutrophils (β =0.056, P=0.02).

Table 1: Demographic and clinical data among the studied groups

Variables		**Group A (n=16)**	**Group B (n=16)**	**Test**	**P Value**
Age *(years)*	*Mean ± SD*	54.6 ± 10.4	55.6 ± 11.9		
	Range	(38 – 75)	(33 – 76)	-0.237	0.81[1]
Sex *(n. %)*	Male	10 (62.5%)	9 (56.3%)		
	Female	6 (37.5%)	7 (43.8%)	0.130	0.72[2]
Variables *(n. %)*		**Group A (n=16)**	**Group B (n=16)**	**Test**	**P Value**
Fever		16 (100%)	15 (93.8%)	F	1.00[2]
Headache		12 (75%)	8 (50%)	2.13	0.14[1]
Projectile vomiting		6 (37.5%)	9 (56.3%)	1.13	0.29[1]
Convulsions		5 (31.3%)	10 (62.5%)	3.14	0.08[1]
Neck rigidity		13 (81.3%)	3 (18.8%)	F	**0.001[2]**
Kernig's sign		7 (43.8%)	1 (6.3%)	F	**0.04[2]**
Brudzinski sign		7 (43.8%)	1 (6.3%)	F	**0.04[2]**
Irritability		2 (12.5%)	1 (6.3%)	F	1.00[2]
Disturbed conscious level		9 (56.3%)	7 (43.8%)	0.500	0.48[1]

**[1]Student T-test, [2]Chi-square test, Non-significant: P >0.05, Significant: P ≤0.05*

Table 2: Laboratory data and CSF findings among the studied groups

Variables		**Group A (n=16)**	**Group B (n=16)**	**Test**	**P Value**
TLC *($10^3/mm^3$)*	*Mean ± SD*	16.6 ± 8.09	10.4 ± 4.3		
	Range	(4.6 – 33)	(4.2 – 17)	2.703	**0.01[1]**
Hb *(g/dL)*	*Mean ± SD*	10.4 ± 2.31	10.9 ± 1.74		
	Range	(7.9 – 16.7)	(7.8 – 13.6)	-0.701	0.49[1]
PLT *($10^3/mm^3$)*	*Median (IQR)*	178 (96)	173 (85)		
	Range	(101 – 354)	(100 – 387)	118	0.71[2]
Creatinine	*Mean ± SD*	1.32 ± 0.54	1.51 ± 0.67		

Variables		Group A (n=16)	Group B (n=16)	Test	P Value
(mg/dL)	*Range*	(0.3 – 2.3)	(0.5 – 2.8)	-0.873	0.39[1]
CRP *(mg/dL)*	*Median (IQR)*	218 (52)	46.5 (13.3)	1.1	**<0.001**[2]
	Range	(71 – 334)	(21 – 62)		
ALT *(U/L)*	*Median (IQR)*	14.5 (16)	23.5 (20)	85	0.11[2]
	Range	(2 – 83)	(11 – 73)		
AST *(U/L)*	*Median (IQR)*	25.5 (37)	36.5 (44.3)	98	0.27[2]
	Range	(8 – 202)	(8.7 – 220)		
RBS *(mg/dL)*	*Mean ± SD*	106 ± 22.7	119 ± 25.9	-1.53	0.14[1]
	Range	(80 – 160)	(80 – 150)		
CSF findings					
Variables		**Group A (n=16)**	**Group B (n=16)**	**Test**	**P Value**
Aspect	Clear	0 (0%)	16 (100%)	F	**<0.001**[3]
	Turbid	16 (100%)	0 (0%)		
Pressure *(cmH_2O)*	*Median (IQR)*	25 (10.25)	14 (4)	1.5	**<0.001**[2]
	Range	(20 – 45)	(5 – 20)		
Cells *(µl)*	*Median (IQR)*	530 (575)	29 (29)	0.00	**<0.001**[2]
	Range	(200 – 5000)	(8 – 70)		
Protein *(mg/dL)*	*Median (IQR)*	153 (132.5)	100 (83.8)	42.0	**0.001**[2]
	Range	(111 – 400)	(25 – 250)		
Glucose *(mg/dL)*	*Mean ± SD*	32.4 ± 8.65	74.6 ± 24.95	-6.39	**<0.001**[1]
	Range	(16 – 45)	(25 – 110)		
Neutrophils *(%)*	*Mean ± SD*	76.2 ± 8.67	29.4 ± 6.74	17.1	**<0.001**[1]
	Range	(62 – 90)	(20 – 40)		
Lymphocytes *(%)*	*Mean ± SD*	24.4 ± 9.69	74.5 ± 8.76	-15.3	**<0.001**[1]
	Range	(8 – 40)	(60 – 90)		
CSF/serum glucose ratio	*Mean ± SD*	0.32 ± 0.09	0.66 ± 0.28	-4.66	**<0.001**
	Range	(0.17 – 0.5)	(0.27 – 1.24)		

***[1]Student T-test, [2]Mann-Whitney U test, [3]Fisher exact test, Non-significant: P >0.05, Significant:P ≤0.05*TLC=Total leukocytic count, Hb=Hemoglobin, PLT=Platelets, CRP=C-reactive protein, ALT=alanine aminotransferase, AST=aspartate aminotransferase, RBS=Random blood sugar*

Table 3: CSF procalcitonin among the studied groups

Variables		Group A (n=16)	Group B (n=16)	Test	P Value
CSF procalcitonin *(ng/ml)*	*Mean ± SD*	4.71 ± 1.86	0.13 ± 0.02	9.86	**<0.001**
	Range	(3.12 – 9.3)	(0.1 – 0.16)		

**Student T-test, Non-significant: P >0.05, Significant: P ≤0.05*

Table 4: Correlation of CSF procalcitonin with different parameters among studied patients

Variable	CSF procalcitonin	
	r	***P***
Age	-0.142	0.437[1]
TLC	0.493	**0.004**[1]
Hb	-0.097	0.59[2]
PLT	-0.182	0.32[2]
Creatinine	-0.112	0.54[1]
CRP	0.779	**<0.001**[2]

Variable	CSF procalcitonin	
	r	***P***
ALT	-0.182	0.32[1]
AST	-0.164	0.37[1]
RBS	-0.214	0.24[1]
Pressure	0.579	**<0.001**[2]
Cells	0.359	**0.04**[2]
Protein	0.515	**0.003**[2]
Glucose	-0.622	**<0.001**[1]
Neutrophils	0.744	**<0.001**[1]
Lymphocytes	-0.766	**<0.001**[1]

*[1]*Pearson correlation,* [2]*Spearman rank correlation test, Non-significant: P >0.05, Significant: P ≤0.05*

Table 5: ROC curve analysis of CSF procalcitonin in detecting bacterial meningitis diagnosis

Variables	Cut point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (%)
CSF procalcitonin	**0.5**	87.5%	93.75%	93.33%	88.24%	0.887

Table 6: Multiple linear regression analysis of CSF procalcitonin and different predictors of bacterial meningitis

Model fit measures	R=0.947	R^2=0.897	P Value
Model coefficients	**Estimate**	**t**	
Age	-0.012	-0.269	0.79
Neck rigidity	0.347	0.592	0.56
Kernig's sign	-0.827	-1.386	0.18
Brudzinski sign	-0.849	-1.552	0.14
TLC	0.128	3.893	**<0.001**
CRP	0.012	2.103	**0.04**
CSF pressure	-0.069	-1.905	0.07
Cells	-0.426	-1.625	0.12
Protein	0.262	0.086	0.93
Glucose	0.587	0.051	0.96
Neutrophils	0.056	2.658	**0.02**
Lymphocytes	-0.018	-0.811	0.43

TLC=Total leukocytic count, CRP=C-reactive protein, CSF: Cerebrospinal fluid

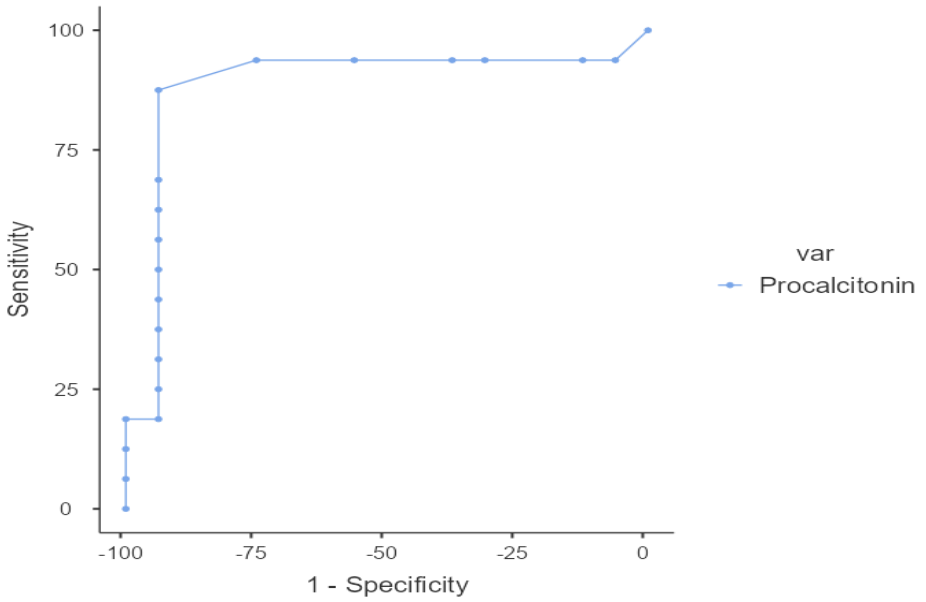

Figure 1: ROC curve analysis of CSF procalcitonin in detecting bacterial meningitis diagnosis

DISCUSSION

Meningitis is still a significant health concern because of its exceptionally high mortality and morbidity rates, even if medical treatment standards, earlier diagnosis, and immunizations have all contributed to a decline. When comparing procalcitonin to C-reactive protein, interleukin-6, and interferon-alpha in children, numerous research from different regions of the globe has shown that it has superior specificity, sensitivity, predictive value, and likelihood ratio for differentiating between viral and bacterial diseases. [8:11].

The bacterial invasion and subsequent immune response cause the blood-brain barrier to be more permeable, leading to an increased CSF protein level. Bacterial meningitis causes hypoglycemia (CSF glucose < 45 mg/dl) because the infection interrupts glucose diffusion and causes the body to consume more glucose. As part of the standard procedure for diagnosing meningitis, measuring CSF PCT can aid in the wait for culture findings, which can be helpful in determining if the infection is bacterial or not [11].

Procalcitonin is helpful for the early identification of meningitis since it starts to rise at 4 hours, peaks at 6 hours, and stays elevated for 24 hours. Contrast this with CRP, which spikes between 24 and 48 hours after it begins to climb (6-12 hours). Patients typically end up on empiric antibiotic treatment because of the delay in diagnosis and the conventional 72-hour wait for Gram stain results. Possible side effects, higher healthcare expenses, and an uptick in nosocomial infections may result from this [11].

This case-control study included 32 individuals. Group A (bacterial meningitis) comprised patients aged 38-75 years (mean ± SD: 54.6 ± 10.4 years), with 62.5% male and 37.5% female. Group B (aseptic meningitis) included patients aged 33-76 years (mean ± SD: 55.6 ± 11.9 years), with 56.3% male and 43.8% females. All studied groups were matched in terms of demographic data. These findings were in accordance with those of Abro et al. [12] as well as Alkholi et al. [13].

A statistically significant was revealed between both studied groups as regards neck rigidity, Kernig's sign, and Brudzinski sign, as (81.3%) of group A had neck rigidity in comparison to (18.8%) of group B (P=0.001). Also, (43.8%) of group A had a positive Kernig's sign in comparison to (6.3%) of group B (P=0.04). Also, (43.8%) of group A had a positive Brudzinski sign in comparison to (6.3%) of group B (P=0.04).

Chekrouni et al. [14] observed among patients with bacterial meningitis. Five hundred eighty-five episodes (47% of the total) had the trifecta of neck stiffness (866 out of 1216, or 71% of the total), fever (979 out of 1325, or 74% of the total), and reduced awareness (a Glasgow Coma Scale score of 14 or lower, 1155 out of 1360, or 85% of the total).

Group A (bacterial meningitis) showed significantly higher total leukocyte count (TLC) and C-reactive protein (CRP) levels than Group B (aseptic meningitis). All patients in Group A had turbid CSF, while all in Group B had clear CSF. Group A

also exhibited higher CSF pressure, total cell count, protein, and neutrophil levels, while Group B showed higher glucose and lymphocyte levels.

These results align with previous research [15] demonstrating significant differences in CRP, erythrocyte sedimentation rate (ESR), and TLC between bacterial and aseptic meningitis. This is attributable to the hematological response elicited by bacterial infection [16]. The elevated CSF protein, TLC, and polymorphonuclear leukocytes (PMNs) in bacterial meningitis, alongside lower CSF glucose and lymphocyte counts, reflect increased blood-brain barrier permeability due to bacterial invasion and the subsequent immune response [17].

Bacterial meningitis causes hypoglycemia (CSF glucose < 45 mg/dl) because the infection disrupts glucose diffusion and causes an increase in glucose intake [18].

When comparing bacterial and viral meningitis patients, Alnomasy et al. [19] found that CSF-leucocytosis, protein levels, and glucose levels were significantly different.

The results of the case studies corroborated the previous finding, showing that more than half of the patients with bacterial meningitis had cerebrospinal fluid glucose levels below 10 mg/dl, in contrast to zero individuals with viral meningitis who exhibited such a low level. [12,20].

The current study findings were consistent with previous studies that reported that this ratio was decreased among patients with bacterial meningitis. [21,22].

This study demonstrates significantly higher CSF procalcitonin levels in bacterial meningitis, likely due to infection-induced CGRP upregulation and subsequent procalcitonin release from multiple tissues [23]. This aligns with procalcitonin's established role as a bacterial infection marker [24, 25]. Furthermore, elevated CSF procalcitonin and lactate have been reported in post-neurosurgical bacterial meningitis [26], supporting its diagnostic utility in distinguishing bacterial from aseptic meningitis. Importantly, elevated serum procalcitonin levels are observed even in patients with acute bacterial meningitis who received brief courses of oral antibiotics before admission [26].

A meta-analysis has shown that procalcitonin is highly effective in differentiating between bacterial and viral meningitis, with a sensitivity of 90% and specificity of 98%. Taken together, these results lend credence to the idea that cerebrospinal fluid procalcitonin is helpful as a diagnostic indicator for distinguishing between bacterial and viral meningitis [27].

A positive correlation between CSF leukocyte count and CSF procalcitonin (PCT) levels has been documented, aligning with our findings [28]. It is well-known that blood leukocytes are a key biological source of serum PCT in sepsis. Studies using flow cytometry, immunoluminometric assays, Western blotting, and reverse transcription-PCR have confirmed that PCT is expressed in the three main leukocyte types found in human peripheral blood: monocytes, granulocytes, and lymphocytes. Moreover, bacteria-associated substances like lipopolysaccharides (LPS) and proinflammatory cytokines, including IL-1β, IL-6, TNF-α, and IL-2, significantly stimulate PCT production in peripheral blood monocytes. Notably, serum PCT levels show a strong correlation with PCT secretion from peripheral blood monocytes ($r = 0.76$; $p < 0.001$) [29].

Noteworthy among the other groups was the BM group, whose lower CSF/serum PCT ratios were a result of their substantially higher serum PCT levels. The fact that sepsis (affecting 38.8% of BM patients) and pneumonia (affecting 69.4% of BM patients) are known to raise serum PCT levels may explain this. [30] .

The best CSF procalcitonin threshold for distinguishing bacterial meningitis from aseptic meningitis was found to be 0.5 ng/mL, according to the ROC curve study. The test's sensitivity was 87.5%, and specificity was 93.75% at this cutoff, indicating excellent diagnostic performance. Its high potential as a trustworthy clinical indicator for bacterial meningitis was demonstrated by its area under the curve (AUC) of 0.887.

Previous research has similarly found a CSF procalcitonin cutoff of 0.5 ng/mL, with specificities ranging from 0.93 to 1.0 and sensitivity from 0.55 to 1.0; our results are consistent with these earlier investigations [15, 31, 32]. Although the precise reason for increased cerebrospinal fluid procalcitonin levels in bacterial meningitis is still unknown, a study conducted by Konstantinidis et al. [32] found that higher levels of CSF PCT are linked to more severe disease, a longer duration of illness, and a higher risk of fatality.

Serum procalcitonin (S-PCT) showed remarkable diagnostic performance in differentiating bacterial meningitis (BM) from viral meningitis (VM) at a cutoff of 0.28 ng/mL, according to research by Viallon et al. [33]. S-PCT had a positive predictive value of 97%, a specificity of 100%, and a

sensitivity of 95% (AUC 0.99, 95% CI 0.99-1.0) in their investigation, which included 64 patients with PAM and 14 patients with PBM.

In a study of meningitis patients with negative Gram stains, Ray et al. [34] compared the diagnostic performance of various laboratory tests. While CSF analysis provided some discriminatory value, serum procalcitonin (S-PCT) and C-reactive protein (CRP) proved more effective in identifying bacterial meningitis, with S-PCT demonstrating significantly superior diagnostic accuracy ($p<0.05$).

Age, neck stiffness, Kernig's sign, Brudzinski's sign, total lymphocyte count, hyperglycemia, C-reactive protein, cerebrospinal fluid pressure, and total cell count were all analyzed in a multiple linear regression analysis using C-reactive protein as the outcome variable. The results showed that CSF procalcitonin was still linked to TLC, CRP, and neutrophils separately. These results are consistent with those of Alnomasy et al. [19], who demonstrated that neurological signs, meningeal irritation symptoms, protein and glucose levels in CSF, and the possibility of using these markers to distinguish between viral and bacterial meningitis might be utilized.

While the study design and methodology are generally robust, the following improvements could be considered:

Limitations and Future recommendations: The sample size (n=32) is relatively small. A larger cohort would increase the generalizability of the findings. Control Group: Including healthy control subjects (without meningitis) as a reference group could help clarify baseline CSF PCT levels. Longitudinal Data: Following up with patients to correlate CSF PCT levels with clinical outcomes and treatment responses would add depth to the findings. Antibiotic Influence: Although antibiotic-naïve patients were included, some additional sensitivity analyses could explore how prior antibiotic exposure might affect CSF PCT levels. Future studies with larger sample sizes and longitudinal follow-ups are warranted to validate these findings and explore their applicability across diverse clinical settings.

Conclusion

This study demonstrates that cerebrospinal fluid procalcitonin is a reliable and highly accurate biomarker for distinguishing bacterial meningitis from aseptic meningitis in adults. With a diagnostic cutoff value of 0.5 ng/mL, CSF procalcitonin exhibited 87.5% sensitivity and 93.75% specificity, underscoring its utility as a rapid and effective diagnostic tool. Furthermore, significant positive correlations with inflammatory markers such as CRP, neutrophil count, and total leukocyte count (TLC), alongside inverse associations with glucose and lymphocyte levels, strengthen its role as an indicator of bacterial etiology.

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