

Investigating Procalcitonin and C-Reactive Protein as Diagnostic Biomarkers in Pediatric Suspected Meningitis: A Forward-Looking Observational Analysis

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Abstract:- Our study is a prospective observational study done on all suspected cases of meningitis admitted to Tertiary Care Hospital, India to study suspected meningitis cases and assess the predictive value of CRP and PCT in diagnosing meningitis. Indian studies are scarce in this regard.

We included all clinically suspected cases of paediatric meningitis in our study. Basic investigations, including blood culture and sensitivity, CRP, and PCT, were sent soon after admission, and CSF analysis and cultures were done once the child became hemodynamically stable. Based on CSF analysis and culture with a clinical profile, meningitis was diagnosed and classified as bacterial and viral meningitis. In this study, we also compared PCT and CRP in their capacity to predict meningitis and to distinguish between bacterial or viral meningitis. A majority of studies have shown that PCT levels can be used in the early diagnosis of bacterial meningitis. In our study, we found that there is no role for PCT in predicting meningitis. CRP has a positive correlation in predicting meningitis but it is elevated in infectious as well as inflammatory conditions. A simple routine complete CSF analysis is an effective, reliable and feasible way to diagnose meningitis in children. This study reiterates the fact that it is indeed the gold standard diagnostic test as no other single parameter can differentiate or diagnose meningitis.

I. INTRODUCTION

The inflammation of the leptomeninges is known as meningitis ¹. Despite improvements in diagnosis and treatment, meningitis continues to be a major cause of mortality and morbidity in children ². The main causes of meningitis are bacterial, viral, and fungal infections ^{3,4,5}. Implementation of multiple vaccines has significantly reduced bacterial neuro infection rates over the past 3 decades ⁶. Although lowering mortality and morbidity requires a high

index of suspicion, timely diagnosis, and active care ⁷. Bacterial meningitis is less common than viral or aseptic meningitis ^{8,9}. The most fatal type is caused by bacteria such as *S. pneumoniae*, *N. meningitidis*, and *H. influenzae* ¹⁰. Along with many other nonviral illnesses, viruses, particularly enteroviruses, are the most frequent cause of aseptic meningitis ^{11,12}. To differentiate between bacterial and non-bacterial meningitis the role of PROCALCITONIN (PCT) and C-REACTIVE PROTEIN (CRP) has been demonstrated in various studies, and it has been concluded that serum PCT and CRP have a positive correlation with the diagnosis of meningitis ^{13,14}.

The presence of clinical symptoms such as fever, headache, lethargy, irritability, altered mental status, photophobia, nausea, vomiting, and stiff neck as well as the study of cerebrospinal fluid (CSF) acquired by lumbar puncture, are used to diagnose pediatric meningitis ^{15,16}. Gram staining and CSF culture are still considered the gold standards for confirming the diagnosis and identifying the bacterial pathogen, even though CSF parameters (cell counts with differential protein and glucose levels) can aid in the differential diagnosis of different types of meningitis ¹⁶. In addition, lumbar punctures in children are difficult to perform and often cause bleeding (i.e., a traumatic lumbar puncture). Approximately 14–18% of attempted lumbar punctures are either traumatic or unsuccessful. It might be confusing and challenging to interpret CSF testing results in traumatic lumbar puncture ¹⁷. For CSF cultures, it was advised to wait for at least two days before looking for bacterial growth and for viral cultures, this timeframe was three to eight days ¹⁸. Therefore, it is crucial from a therapeutic standpoint to identify additional blood biomarkers that can be used in conjunction with CSF testing to aid in the rapid diagnosis of meningitis.

It is believed that leukocytes in the peripheral circulation secrete PCT when there is infection normally. PCT is a calcitonin pro peptide, is produced by the C cells of the thyroid gland. Bacterial lipopolysaccharides and

cytokines linked to sepsis were discovered to cause a rise in PCT secretion¹⁹. Inflammatory cytokines, interleukin-6 and tumour necrosis factor (IL6 and TNF) and bacterial endotoxin associated with procalcitonin production in the body during inflammation²⁰. In viral infection rise of procalcitonin is minimal¹⁹. Procalcitonin’s circulating levels are extremely low in healthy people, typically below 0.01 ng/ml, and they only rarely rise above 1.0 ng/ml during viral infections and inflammatory conditions²¹. The body’s non-thyroidal tissues produce a substantial amount of PCT when a bacterial infection takes place²². Following bacterial infection, PCT levels have been reported to rise quickly (2–6 hours) and peak within 24 hours²³. In contrast, CRP rises during 6–12 hours and peaks at 24–48 hours^{24,25}. CRP has long been used as an indicator of inflammation. But during the course of a bacterial infection, CRP may exhibit a lag time to increase, leading to false-negative testing in the early stages of the disease^{26,27,28}.

Early diagnosis of the kind of infection (bacterial or viral) has a significant impact on the clinical course, the course of treatment, and the prognosis for patients with meningitis. In this context, there has been an increase in interest in markers that can distinguish bacterial from viral meningitis in children²². Procalcitonin (PCT) and C-reactive Protein (CRP) are the biomarkers most commonly used but have a limited ability to distinguish sepsis from other inflammatory and non-inflammatory states²⁹.

The present study was conducted to determine the level of serum procalcitonin, total leukocyte count (TLC) and CRP in children with bacterial and non-bacterial meningitis and document their efficacy in the differential diagnosis of meningitis.

II. MATERIALS AND METHODOLOGY

A. Study Design

A Prospective observational study.

- Study Area: This study was conducted in a tertiary care hospital, India.
- Study Population: Children from 1 months to 18 years of age admitted to tertiary care hospital, India with suspected meningitis.

B. Duration of Study

From August 2020 to July 2022.

C. Sample Size

The calculated sample size was 94. However, to increase the power of the study, a higher number of samples were taken.

118 children aged 1 month to 18 years were admitted to our Hospital, with suspected meningitis were included in this study.

D. Inclusion Criteria

All children aged from 1 months to 18 years admitted to the hospital with suspected meningitis were included.

E. Exclusion Criteria

- Children with liver cirrhosis
- Children on immunosuppressive therapy
- Children with multisystemic organ dysfunction syndrome, polytrauma, previous CNS surgeries.

F. Consent and Ethics

Informed written consent was taken from the parents and documented in the patient’s record in accordance with the institutional policy (Annexure 1). Ethical committee clearance was taken.

G. Research Method

All the children who meet inclusion criteria with informed consent were evaluated with detailed history, a complete physical examination and the following tests were done for all the children

- Complete Blood Count (CBC),
- CRP
- PCT
- Blood culture
- CSF analysis
- CSF culture
- CSF viral panel / RTPCR / CBNAAT were done in few children based on clinical suspicion
- EEG/ neuro imaging was done where ever indicated

All investigations were done as soon as possible after admission (after hemodynamic stability or controlling raised ICP), and neuro imaging wherever indicated. Standard care was given to all the patients according to protocol. All the data was enrolled and analysed at the end of the study period with the help of a medical statistician.

H. Procalcitonin

The 2 ml of blood collected from all patients (plain sample) was used for the measurement of procalcitonin on the day of admission and measured by the MINI VIDAS BRHAMS procalcitonin kit, a standardised and thoroughly validated immunoluminometric test. We followed our laboratory data as given below.

Table 1: Procalcitonin

PCT <0.5 ng/mL (Systemic infection is not likely).	Low risk for progression to severe systemic infection
PCT >0.5 and <2 ng/mL Systemic infection is possible, but there are other conditions to rule out	Moderate risk for progression to severe systemic infection
CT > 2 and < 10 ng/mL Systemic infection is likely, unless other causes are known.	High risk for progression to severe systemic infection
PCT >10 ng/mL	High likelihood of severe sepsis or septic shock

- PCT is a 116-amino acid residue that was discovered in 1984.
- Serum level have been shown to increase 6-12 hours following initial bacterial infection and increase steadily 2-4 hours following the onset of sepsis.
- Half-life is between 20-24 hours.

➤ *False Positive Results:*

- Trauma
- Burn
- Carcinoma
- Immune modulator therapy
- Cardiogenic shock
- Cirrhotic patients

I. C – Reactive Protein

- It has got both pro-inflammatory and anti-inflammatory action.
- An acute-phase reactant
- Elevation occurs in both acute and chronic inflammation.
- Standard CRP determinations may be reported in either mg/L or mg/dl.
- The level varies with age, sex, and race.

Based on CSF cytochemical profile, clinical features bacteriological and virology profile, children were divided into to bacterial/ viral / tubercular / fungal meningitis.

J. Statistical Analysis

All data were coded and recorded in the MS Excel spreadsheet program. SPSSv23 (IBM Corp.) was used for data analysis. Descriptive statistics were elaborated in the form of means/standard deviations and medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Data were presented in a graphical manner wherever appropriate for data visualization using histograms/box- and-whisker plots/column charts for continuous data and bar charts/pie charts for categorical data. Group comparisons for continuously distributed data were made using an independent sample ‘t’ test when comparing two groups. If data were found to be non-normally distributed, appropriate non-parametric tests in the form of Wilcoxon Test were used. The chi-squared test was used for group comparisons for categorical data. In cases the expected frequency in the contingency tables was found to be <5 for >25% of the cells, Fisher’s exact test was used instead. Linear correlation between two continuous variables was explored using Pearson’s correlation (if the data were normally distributed) and Spearman’s correlation (for non-normally distributed data). Statistical significance was kept at $p < 0.05$. ROC analysis was performed to predict an optimal cut-off for a continuous predictor predicting a binary outcome. Sensitivity Specificity, PPV, NPV and Diagnostic accuracy were calculated for assessing the diagnostic performance of predictors, by making a 2x2 cross-table with the outcome.

III. OBSERVATIONS AND RESULTS

Table 2: Summary of Demographic Data of Patients with Suspected Meningitis

Basic Details of all Suspected Meningitis Cases	Mean ± SD Median (IQR) Min-Max Frequency (%)
Age (Months)	34.27 ± 45.65 12.00 (5.00-39.25) 1.00 – 180.00
Age	
1-6 Months	41 (34.7%)
6-12 Months	25 (21.2%)
12-24 Months	3 (2.5%)
2-5 Years	21(17.8%)
5-10 Years	20 (16.9%)
10-15 Years	8 (6.8%)
Gender	
Male	66 (55.9%)
Female	52 (44.1%)

Table 3: Distribution of Suspected Meningitis Patients in Terms of Age Group(Months) (n = 118)

Age Group	Frequency	Percentage	95% CI
1-6 Months	41	34.7%	26.4% - 44.1%
6-12 Months	25	21.2%	14.4% - 29.9%
12-24 Months	3	2.5%	0.7% - 7.8%
2-5 Years	21	17.8%	11.6% - 26.1%
5-10 Years	20	16.9%	10.9% - 25.2%
10-15 Years	8	6.8%	3.2% - 13.3%

Table 4: Distribution of Suspected Meningitis Patients in Terms of Gender(n = 118)

Gender	Frequency	Percentage	95% CI
Male	66	55.9%	46.5% - 65.0%
Female	52	44.1%	35.0% - 53.5%

55.9% of the participants are male and 44.1% of the participants are female.

Table 5: Summary of Clinical Presentation of Patients with Suspected Meningitis

Clinical presentation	
Seizure episodes	69.5%
Altered sensorium	23.7%
Irritability	22.0%
Fever	88.1%
Vomiting	32.2%
Head ache	7.6%
Duration of illness at Admission	3.32 ± 2.76 2.00 (1.00-4.00) 1.00 – 15.00
Meningeal signs	
Neck stiffness	15.3%
Kerning’s	5.1%
Brudzinski	2.5%
None	84.7%

Table 6: Distribution of Symptoms of Suspected Meningitis Patients at Admission (n=118)

Symptoms	Present	Absent
Altered Sensorium	28 (23.7%)	90 (76.3%)
Irritability	26 (22.0%)	92 (78.0%)
Fever	104 (88.1%)	14 (11.9%)
Seizure	82 (69.5%)	36 (30.5%)
Vomiting	38 (32.2%)	80 (67.8%)
Headache	9 (7.6%)	109 (92.4%)

Table 7: Distribution of the Suspected Meningitis Patients in Terms of Duration of Illness (Days) (n = 118)

Duration Of Illness (Days)	
Mean (SD)	3.32 (2.76)
Median (IQR)	2 (1-4)
Range	1 – 15

Table 8: Distribution of the Suspected Meningitis Cases in Terms of AntibioticsUsed before Admission (n = 118)

Antibiotic Before Admission	Frequency	Percentage	95% CI
Yes	42	35.6%	27.1% - 45.0%
No	76	64.4%	55.0% - 72.9%

35.6% of the participants had received antibiotic before admission. +

Table 9: Distribution of Meningeal Signs among Suspected Meningitis Cases(n = 118)

Meningeal Signs	Frequency	Percentage	95% CI
Present	20	16.9%	10.9% - 25.2%
Absent	98	83.1%	74.8% - 89.1%

16.9% of the patients with suspected meningitis had meningeal sign positive

Table 10: Summary of blood investigations done among suspected meningitiscases

Investigations	Mean ± SD Median (IQR) Min-Max Frequency (%)
TLC (/mmt)	11388.03 ± 5226.95 11350.00 (7065.00-14000.00) 2600.00 - 27400.00
Haemoglobin (g/dL)	10.60 ± 1.53 10.80 (9.80-12.00) 5.40 - 15.00
Platelet Count (/mmt)	313378.81 ± 178542.99 250000.00 (170000.00-478000.00) 17000.00 - 740000.00
CRP (mg/L)	28.12 ± 46.10 4.50 (2.00-34.98) 0.50 - 214.00
CRP Category (Positive)	52 (44.1%)
PCT	10.10 ± 25.17 0.70 (0.06-5.00) 0.05 - 200.00

PCT Category	
Low risk	60 (50.8%)
Moderate risk	30 (25.4%)
High risk	4 (3.4%)
Very High risk	24 (20.3%)
Blood Culture	
Sterile	116 (98.3%)
Bacterial growth	2 (1.6%)
Blood Sugar	105.56 ± 17.13 104.00 (96.00-119.75) 55.00 - 140.00

Table 11: Distribution of the Suspected Meningitis Cases in Terms of TLC (/mmt) (n = 118)

TLC (/mmt)	
Mean (SD)	11388.03 (5226.95)
Median (IQR)	11350 (7065-14000)
Range	2600 – 27400

The mean (SD) of TLC (/mm³) was 11388.03 (5226.95).

Table 12: Distribution of the Suspected Meningitis Cases in Terms of CRP (mg/L)(n = 118)

CRP (mg/L)	
Mean (SD)	28.12 (46.10)
Median (IQR)	4.5 (2-34.98)
Range	0.5 – 214

The mean (SD) of CRP (mg/L) was 28.12 (46.10). The median (IQR) of CRP (mg/L) was 4.50 (2-34.98). The CRP (mg/L) ranged from 0.5 - 214.

Table 13: Distribution of the Suspected Meningitis Cases in Terms of Positive CRP(n = 118)

CRP Category	Frequency	Percentage	95% CI
Positive	52	44.1%	35.0% - 53.5%
Negative	66	55.9%	46.5% - 65.0%

44.1% of the participants had positive CRP.

Table 14: Distribution of PCT (ng/mL) among Suspected Meningitis Cases(n = 118)

PCT	
Mean (SD)	10.10 (25.17)
Median (IQR)	0.7 (0.06-5)
Range	0.05 – 200

The mean (SD) of PCT was 10.10 (25.17). The median (IQR) of PCT was 0.70 (0.06-5). The value of PCT was ranged from 0.05 - 200.

Table 15: Distribution of the Suspected Meningitis Cases in Terms of PCT Risk Category (n = 118)

PCT Risk	Frequency	Percentage	95% CI
Low	60	50.8%	41.5% - 60.1%
Moderate	30	25.4%	18.1% - 34.4%
High	4	3.4%	1.1% - 9.0%
Very High	24	20.3%	13.7% - 28.9%

Table 16: Summary of CSF Analysis of Suspected Meningitis Cases (n=118)

CSF Culture / PCR	
Sterile	115 (97.5%)
HSV - Positive PCR	2 (1.7%)
Pseudomonas	1 (0.8%)
CSF Protein	47.40 ± 55.46 34.50 (20.00-50.75) 11.00 - 355.00
CSF Sugar	57.50 ± 19.76 60.00 (48.00-67.75) 3.00 - 108.00
CSF Cell Count	30.26 ± 100.45 4.00 (3.00-13.50) 0.00 - 880.00
Neutrophils (%)	11.78 ± 24.33 0.00 (0.00-10.00) 0.00 - 95.00
Lymphocytes (%)	87.88 ± 25.34 100.00 (90.00-100.00) 5.00 - 100.00

Table 17: Distribution of the Suspected Meningitis Cases in Terms of CSF Protein(mg/dl) (n = 118)

CSF Protein	
Mean (SD)	47.40 (55.46)
Median (IQR)	34.5 (20-50.75)
Range	11 – 355

The mean (SD) of CSF protein was 47.40 (55.46). The median (IQR) of CSF protein was 34.50 (20-50.75). The CSF protein ranged from 11 - 355.

Table 18: Distribution of the Suspected Meningitis Cases in Terms of CSF Sugar(mg/dl) (n = 118)

CSF Sugar	
Mean (SD)	57.50 (19.76)
Median (IQR)	60 (48-67.75)
Range	3 – 108

The mean (SD) of CSF sugar was 57.50 (19.76). The median (IQR) of CSF sugar was 60.00 (48-67.75). The CSF sugar ranged from 3 - 108.

Table 19: Distribution of the Suspected Meningitis Cases in Terms of CSF Cell Count (n = 118)

CSF Cell Count	
Mean (SD)	30.26 (100.45)
Median (IQR)	4 (3-13.5)
Range	0 – 880

The mean (SD) of CSF cell count was 30.26 (100.45). The median (IQR) of CSF cell count was 4.00 (3-13.5). The CSF cell count ranged from 0 – 880.

Table 20: Distribution of the Participants in Terms of CSF Culture Growth(n = 118)

CSF Growth	Frequency	Percentage	95% CI
Sterile	115	97.5%	92.2% - 99.3%
HSV Positive PCR	2	1.7%	0.3% - 6.6%
Pseudomonas	1	0.8%	0.0% - 5.3%

Table 21: Summary of Patients with Meningitis (n=44)

Types of meningitis	Yes	No
Aseptic Meningitis	14 (11.9%)	30
Bacterial Meningitis	30 (25.4%)	14
Tubercular Meningitis	2 (1.7%)	42
Fungal Meningitis	0 (0.0%)	44
Total number of Meningitis	44	-

Table 22: Distribution of Confirmed Meningitis Cases Among all the Participants (n = 118)

Meningitis	Frequency	Percentage	95% CI
Yes	44	37.3%	28.7% - 46.7%
No	74	62.7%	53.3% - 71.3%

37.3% of the participants had meningitis

Table 23: Association between Meningitis and other Parameters

Parameters	Meningitis		p value
	Yes (n = 44)	No (n = 74)	
Age (Months)***	51.45 ± 53.48	24.05 ± 37.03	0.001 ¹
Age Group			0.063 ²
1-6 Months	12 (27.3%)	29 (39.2%)	
6-12 Months	7 (15.9%)	18 (24.3%)	
12-24 Months	0 (0.0%)	3 (4.1%)	
2-5 Years	11 (25.0%)	10 (13.5%)	
5-10 Years	8 (18.2%)	12 (16.2%)	
10-15 Years	6 (13.6%)	2 (2.7%)	
Gender			0.194 ³

Male	28 (63.6%)	38 (51.4%)	
Female	16 (36.4%)	36 (48.6%)	
CSF Growth			0.285 ²
Sterile	45 (95%)	70(97.3%)	
HSV Positive PCR	2 (2.7%)	0 (0.0%)	
Pseudomonas	1 (2.3%)	0 (0.0%)	
Aseptic Meningitis	12 (27.3%)	2 (2.7%)	<0.001 ³
Bacterial Meningitis	30 (68.2%)	0 (0.0%)	<0.001 ³
Tubercular Meningitis	2 (4.5%)	0 (0.0%)	0.137 ²
Fungal Meningitis	0 (0.0%)	0 (0.0%)	1.000 ³
CSF Protein	66.02 ± 84.41	36.32 ± 19.98	0.183 ¹
CSF Sugar	48.48 ± 22.24	62.86 ± 16.01	<0.001 ⁴
CSF Cell Count	74.86 ± 155.56	3.74 ± 2.39	<0.001 ¹
Neutrophils (%)	23.41 ± 31.82	4.86 ± 14.92	<0.001 ¹
Lymphocytes (%)	75.68 ± 33.56	95.14 ± 14.92	<0.001 ¹
MRI			0.643 ³
Normal	14 (53.8%)	18 (60.0%)	
Abnormal	12 (46.2%)	12 (40.0%)	
EEG			1.000 ³
Normal	26 (100.0%)	46 (100.0%)	
Abnormal	0 (0.0%)	0 (0.0%)	

Table 24: Comparison of Meningitis and Suspected Meningitis Cases in Terms of Age (Months) (n = 118)

Age (Months)	Meningitis		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	p value
Mean (SD)	51.45 (53.48)	24.05 (37.03)	2227.000	0.001
Median (IQR)	24 (9.87-111)	9 (4.36-24)		
Range	1.26 – 156	1 – 180		

The variable Age (Months) was not normally distributed in the 2 subgroups of the variable Meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons.

There was a significant difference between the 2 groups in terms of age (months) (W =2227.000, p = 0.001), with the median age (months) being highest in the meningitis group.

Table 25: Association between Meningitis and Gender (n = 118)

Gender	Meningitis			Chi-Squared Test	
	Yes	No	Total	χ ²	P Value
Male	28 (63.6%)	38 (51.4%)	66 (55.9%)	1.690	0.194
Female	16 (36.4%)	36 (48.6%)	52 (44.1%)		
Total	44 (100.0%)	74 (100.0%)	118 (100.0%)		

Chi-squared test was used to explore the association between 'meningitis' and 'gender'.

There was no significant difference between the various groups in terms of distribution of gender (χ² = 1.690, p = 0.194).

Table 26: Meningitis and Meningeal Signs (n = 118)

Parameter	Meningitis yes (n=44)	Meningitis no (n=74)	P value
Meningeal Signs (Present)	14 (31.8%)	6 (8.1%)	<0.001 ³
No meningeal sign	32 (72.7%)	68 (91.9%)	0.005 ³
Meningeal Sign: Neck Stiffness present	12 (27.3%)	6 (8.1%)	0.005 ³
Meningeal Sign: Kerning’s positive	6 (13.6%)	0 (0.0%)	0.002 ²
Meningeal Sign: Brudzinski positive	3 (6.8%)	0 (0.0%)	0.050 ²

Table 27: Association between Meningitis and Meningeal Signs

Meningeal Signs	Meningitis			Chi-Squared Test	
	Yes	No	Total	χ^2	P Value
Present	14 (31.8%)	6 (8.1%)	20 (16.9%)	11.020	<0.001
Absent	30 (68.2%)	68 (91.9%)	98 (83.1%)		
Total	44 (100.0%)	74 (100.0%)	118 (100.0%)		

Chi-squared test was used to explore the association between 'meningitis' and 'meningeal signs'.

There was a significant difference between the various groups in terms of distribution of meningeal Signs ($\chi^2 =$

11.020, $p = <0.001$). Participants in the no meningitis group had the larger proportion of absent meningeal signs. participants in the group meningitishad the larger proportion of positive meningeal signs.

Table 28: Association between Meningitis and Neck Stiffness (n = 118)

Meningeal Sign: Neck Stiffness	Meningitis			Chi-Squared Test	
	Yes	No	Total	χ^2	P Value
Yes	12 (27.3%)	6 (8.1%)	18 (15.3%)	7.840	0.005
No	32 (72.7%)	68 (91.9%)	100 (84.7%)		
Total	44 (100.0%)	74 (100.0%)	118 (100.0%)		

Chi-squared test was used to explore the association between 'meningitis' and 'meningeal sign: neck stiffness'.

There was a significant difference between the various groups in terms of distribution of neck stiffness ($\chi^2 = 7.840$, $p = 0.005$).

Table 29: Association between Meningitis and Kerning's Sign (n=118)

Meningeal Sign: Kerning's	Meningitis			Fisher's Exact Test	
	Yes	No	Total	χ^2	P Value
Yes	6 (13.6%)	0 (0.0%)	6 (5.1%)	10.631	0.002
No	38 (86.4%)	74 (100.0%)	112 (94.9%)		
Total	44 (100.0%)	74 (100.0%)	118 (100.0%)		

Fisher's exact test was used to explore the association between 'Meningitis' and 'Kerning's sign'. There was a significant difference between the various groups in terms of distribution of Kerning's sign ($\chi^2 = 10.631$, $p = 0.002$). 13.6%

of the participants in the group Meningitis had Meningeal Sign: Kerning's positive.

Kerning sign is absent in all non-meningitis patients.

Table 30: Association between Meningitis and Brudzinski Sign (n = 118)

Meningeal Sign: Brudzinski	Meningitis			Fisher's Exact Test	
	Yes	No	Total	χ^2	P Value
Yes	3 (6.8%)	0 (0.0%)	3 (2.5%)	5.177	0.050
No	41 (93.2%)	74 (100.0%)	115 (97.5%)		
Total	44 (100.0%)	74 (100.0%)	118 (100.0%)		

Fisher's exact test was used to explore the association between 'Meningitis' and 'Meningeal sign: Brudzinski.' There was a significant difference between the various groups in terms of distribution of Brudzinski sign ($\chi^2 = 5.177$, $p =$

0.050). 6.8% of the participants in the group meningitis had Brudzinski sign positive. No one among non- meningitis patients had Brudzinski sign positive.

Table 31: Association between Meningitis and Clinical Profile

Parameters	Meningitis patients (n=44)	No meningitis Patients (n=74)	P value
Duration Of Illness (Days)	4.14 ± 3.35	2.84 ± 2.23	0.012 ¹
Altered Sensorium	12 (27.3%)	16 (21.6%)	0.485 ³
Irritability	6 (13.6%)	20 (27.0%)	0.090 ³
Fever	40 (90.9%)	64 (86.5%)	0.472 ³
Seizure	26 (59.1%)	56 (75.7%)	0.058 ³
Vomiting	23 (52.3%)	15 (20.3%)	<0.001 ³
Headache	6 (13.6%)	3 (4.1%)	0.077 ²

Table 32: Comparison of Meningitis and Suspected Meningitis Cases in Terms of Duration of Illness (Days) (n = 118)

Duration Of Illness (Days)	Meningitis		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	p value
Mean (SD)	4.14 (3.35)	2.84 (2.23)	2072.000	0.012
Median (IQR)	3 (2-5)	2 (1-4)		
Range	1 - 15	1 – 10		

The variable duration of illness (Days) was not normally distributed in the 2 subgroups of the variable Meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There was a

significant difference between the 2 groups in terms of Duration of Illness (Days) (W = 2072.000, p = 0.012), with the median duration of illness (Days) being highest in the meningitis group.

Table 33: Meningitis and Blood Investigations

Parameters	Meningitis patients (n=44)	No meningitis Cases (n=74)	P value
TLC (/mmt)	13064.32 ± 4797.09	10391.31 ± 5247.16	0.0031
CRP (mg/L)	46.36 ± 62.14	17.28 ± 28.49	0.0091
Positive CRP	26 (59.1%)	26 (35.1%)	0.0113
PCT	4.60 ± 8.89	13.35 ± 30.64	0.640 ¹
PCT Risk category			0.128 ²
Low	20 (45.5%)	40 (54.1%)	
Moderate	16 (36.4%)	14 (18.9%)	
High	2 (4.5%)	2 (2.7%)	
Very High	6 (13.6%)	18 (24.3%)	
Blood Culture			1.000 ²
Sterile	44 (100.0%)	72 (97.3%)	
Burkholderias	0 (0.0%)	1 (1.4%)	
Pseudomonas Aerogenosa	0 (0.0%)	1 (1.4%)	

Table 34: Comparison of Meningitis and Suspected Meningitis Cases in Terms of TLC (/mmt) (n = 118)

TLC (/mmt)	Meningitis		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	p value
Mean (SD)	13064.32 (4797.09)	10391.31 (5247.16)	2161.000	0.003
Median (IQR)	12500 (10175-14700)	9260 (6000-13585)		
Range	4000 - 25800	2600 – 27400		

The variable TLC (/mm³) was not normally distributed in the 2 subgroups (meningitis and no meningitis). Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There was a significant

difference between the 2 groups in terms of TLC (/mm³) (W = 2161.000, p = 0.003), with the median TLC (/mm³) being highest in the meningitis group.

Table 35: Comparison of Meningitis and Suspected Meningitis Cases in Terms of Haemoglobin (g/dL) (n = 118)

Haemoglobin(g/dL)	Meningitis		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	p value
Mean (SD)	10.72 (1.33)	10.53 (1.65)	1657.500	0.773
Median (IQR)	10.45 (9.97-12)	10.8 (9.4-11.4)		
Range	7.46 - 13.3	5.4 – 15		

The mean (SD) of haemoglobin (g/dL) in the meningitis group was 10.72 (1.33). The mean (SD) of haemoglobin (g/dL) in the non-Meningitis group was 10.53 (1.65).

There was no significant difference between the groups in terms of haemoglobin (g/dL)(W = 1657.500, p = 0.773).

Table 36: Comparison Meningitis and Suspected Meningitis Cases in Terms of Platelet Count (/mmt) (n = 118)

Platelet Count (/mmt)	Meningitis		Wilcoxon-Mann-Whitney U Test	
	Yes	No	W	p value
Mean (SD)	259590.91 (159935.21)	345360.81 (182328.22)	1139.000	0.007
Median (IQR)	206000 (149000-340000)	282000 (202500-497500)		
Range	44000 - 643000	17000 – 740000		

The mean (SD) of platelet count (/mm³) in the meningitis group was 259590.91 (159935.21). The mean (SD) of platelet count (/mm³) in the no meningitis group was 345360.81 (182328.22).

There was a significant difference between the 2 groups in terms of platelet count (/mm³) (W = 1139.000, p = 0.007), with the median Platelet Count (/mm³) being highest in the non-meningitis group.

Table 37: Association between Meningitis and Blood Culture (n = 118)

Blood Culture	Meningitis			Fisher's Exact Test	
	Yes	No	Total	χ ²	P Value
Sterile	44 (100.0%)	72 (97.3%)	116 (98.3%)	1.210	1.000
Positive	0 (0.0%)	2 (2.8%)	2 (1.6 %)		
Total	44 (100.0%)	74 (100.0%)	118 (100.0%)		

Fisher's exact test was used to explore the association between 'meningitis' and 'bloodculture'

= 1.000).

There was no significant difference between the various groups in terms of distribution of blood culture (χ² = 1.210, p

100.0% of the participants in the meningitis patients had sterile blood culture.

Table 38: Comparison Bacterial and Viral Meningitis Cases in Terms of TLC(/mmt) (n = 44)

TLC (/mmt)	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	14272.67 (5042.87)	10232.14 (3503.05)	315.500	0.008
Median (IQR)	13100 (12075-16300)	11500 (10025-12187.5)		
Min - Max	6540 - 25800	2600 – 13800		

The variable TLC (/mm³) was not normally distributed in the 2 subgroups of meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There was a significant difference between the

2 groups in terms of TLC(/mm³) (W = 315.500, p = 0.008), with the median TLC (/mm³) being highest in the bacterial meningitis group.

Table 39: Comparison of Bacterial and Viral Meningitis Cases in Terms of Haemoglobin (g/dL) (n = 44)

Haemoglobin(g/dL)	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	10.37 (1.25)	11.67 (1.31)	112.500	0.014
Median (IQR)	10.25 (9.9-11)	12 (10.28-12.83)		
Min - Max	7.46 – 13	9.8 - 13.3		

The variable haemoglobin (g/dL) was not normally distributed in the 2 subgroups of the meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There was a significant

difference between the 2 groups in terms of haemoglobin (g/dL) (W = 112.500, p = 0.014), with the median haemoglobin (g/dL) being highest in the viral meningitis group.

Table 40: Comparison of Bacterial and Viral Meningitis Cases in Terms of Platelet Count (/mmt) (n = 44)

Platelet Count(/mmt)	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	284100.00 (187162.54)	184500.00 (29705.61)	237.000	0.504
Median (IQR)	242000 (140000-467500)	195000 (160000-209000)		
Min - Max	44000 - 643000	142000 – 223000		

The variable Platelet Count (/mm³) was not normally distributed in the 2 subgroups of the Meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were

used to make group comparisons. There was no significant difference between the groups in terms of platelet Count (/mm³) (W = 237.000, p = 0.504).

Table 41: Comparison of Bacterial and Viral Meningitis Cases in Terms of CRP(mg/L) (n = 44)

CRP (mg/L)	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	58.29 (66.65)	4.00 (2.85)	336.500	0.001
Median (IQR)	30.66 (5.62-99)	3.5 (2.15-4)		
Min - Max	0.5 – 214	0.72 – 10		

The variable CRP (mg/L) was not normally distributed in the 2 subgroups of the meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There was a

significant difference between the 2 groups in terms of CRP (mg/L) (W = 336.500, p = 0.001), with the median CRP (mg/L) being highest in the bacterial meningitis group.

Table 42: Comparison of Bacterial and Viral Meningitis Cases in Terms of PCT(n = 44)

PCT	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	4.99 (9.60)	3.49 (7.41)	220.000	0.079
Median (IQR)	0.8 (0.16-1.69)	0.38 (0.05-0.74)		
Min - Max	0.05 – 34	0.05 - 20.6		

The variable “PCT” was not normally distributed in the 2 subgroups of meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There was no significant difference between the

groups in terms of PCT(W = 220.000, p = 0.079). Strength of association (Point-Biserial Correlation) = 0.08 (little or no association)

Table 43: Association between Type of Meningitis and PCT Risk Category (n =44)

PCT Risk	Type of Meningitis			Fisher's Exact Test	
	Bacterial	Viral	Total	χ ²	P Value
Low	12 (40.0%)	8 (57.1%)	20 (45.5%)	1.900	0.702
Moderate	12 (40.0%)	4 (28.6%)	16 (36.4%)		
High	2 (6.7%)	0 (0.0%)	2 (4.5%)		
Very High	4 (13.3%)	2 (14.3%)	6 (13.6%)		
Total	30 (100.0%)	14 (100.0%)	44 (100.0%)		

Fisher's exact test was used to explore the association between bacterial and viral meningitis with the PCT risk category.

There was no significant difference between bacterial and viral meningitis groups in terms of the distribution of PCT risk category (χ² = 1.900, p = 0.702).

Table 44: Comparison of 2 Subgroups of the Variable Type Meningitis in Terms of CSF Protein (n = 44)

CSF Protein	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	80.93 (97.85)	34.86 (19.87)	284.000	0.064
Median (IQR)	48 (31.75-72.25)	29.5 (17.25-50.25)		
Min - Max	13 – 355	14 – 78		

The variable CSF protein was not normally distributed in the 2 subgroups of the variable type of meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were

used to make group comparisons. There was no significant difference between the groups in terms of CSF protein (W = 284.000, p = 0.064).

Table 45: Comparison of the 2 Subgroups of the Variable Type of Meningitis in Terms of CSF Sugar (n = 44)

CSF Sugar	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	44.46 (22.50)	63.59 (17.26)	109.000	0.011
Median (IQR)	44 (28.25-60)	61 (57.75-78.25)		
Min - Max	3 – 92	30 – 88		

The variable CSF sugar was not normally distributed in the 2 subgroups of the variable type of meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There was a significant

difference between the 2 groups in terms of CSF sugar (W = 109.000, p = 0.011), with the median CSF sugar being highest in the viral meningitis group.

Table 46: Comparison of the 2 Subgroups of the Variable Type of Meningitis in Terms of CSF Cell Count (n = 44)

CSF Cell Count	Type of Meningitis		Wilcoxon-Mann-Whitney U Test	
	Bacterial	Viral	W	p value
Mean (SD)	105.37 (181.17)	7.71 (7.16)	388.000	<0.001
Median (IQR)	58 (29.25-101.5)	5 (3.25-8)		
Min - Max	2 – 880	2 – 28		

The variable CSF Cell Count was not normally distributed in the 2 subgroups of the variable type of meningitis. Thus, non-parametric tests (Wilcoxon-Mann-Whitney U Test) were used to make group comparisons. There

was a significant difference between the 2 groups in terms of CSF cell count (W = 388.000, p = <0.001), with the median CSF cell count being highest in the bacterial meningitis group.

Table 47: Parameters for Predicting Meningitis

Variable	Category (s) Suggesting Outcome Present	Category (s) Suggesting Outcome Absent	Total Positives	True Positives	True Negatives	False Positives	False Negatives
Meningitis	Yes	No	44 (37.3%)	-	-	-	-
CRP (mg/L) (Cut-off: 7.46 by ROC)	>=7.46	<7.46	51 (43.2%)	26 (22%)	49 (42%)	25 (21%)	18 (15%)
PCT (Cut-off: 21.3 by ROC)	<=21.3	>21.3	89 (84.8%)	37 (35%)	14 (13%)	52 (50%)	2 (2%)

Variable	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
CRP (mg/L) (Cut-off: 7.46 by ROC)	59.1% (43-74)	66.2% (54-77)	51.0% (37-65)	73.1% (61-83)	63.6% (54-72)
PCT (Cut-off: 21.3 by ROC)	94.9% (83-99)	21.2% (12-33)	41.6% (31-53)	87.5% (62-98)	48.6% (39-59)

Table 48: Parameters for Predicting Bacterial Meningitis

Variable	Category(s) Suggesting Outcome Present	Category(s) Suggesting Outcome Absent	Total Positives	True Positives	True Negatives	False Positives	False Negatives
Bacterial Meningitis	Yes	No	30 (25.4%)	-	-	-	-
CRP (mg/L) (Cut-off: 7.46)	>=7.46	<7.46	51 (43.2%)	22 (19%)	59 (50%)	29	8

by ROC)						(25%)	(7%)
PCT (Cut-off: 0.06 by ROC)	>=0.06	<0.06	81 (77.1%)	25 (24%)	22 (21%)	56 (53%)	2 (2%)

Variable	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
CRP (mg/L) (Cut-off: 7.46 by ROC)	73.3% (54-88)	67.0% (56-77)	43.1% (29-58)	88.1% (78-95)	68.6% (59-77)
PCT (Cut-off: 0.06 by ROC)	92.6% (76-99)	28.2% (19-40)	30.9% (21-42)	91.7% (73-99)	44.8% (35-55)

Table 49: Comparison of the Diagnostic Performance of CRP and PCT in Predicting Bacterial Meningitis (n=118)

Predictor	AUROC	95% CI	P	Sn	Sp	PPV	NPV	DA
CRP (mg/L)	0.715	0.598-0.831	<0.001	73%	67%	43%	88%	69%
PCT (ng/mL)	0.527	0.414-0.641	0.677	93%	28%	31%	92%	45%

Table 50: Parameters for Predicting Aseptic Meningitis

Variable	Category(s) Suggesting Outcome Present	Category(s) Suggesting Outcome Absent	Total Positives	True Positives	True Negatives	False Positives	False Negatives
Aseptic Meningitis	Yes	No	14 (11.9%)	-	-	-	-
CRP (mg/L) (Cut-off: 10 by ROC)	<=10	>10	78 (66.1%)	14 (12%)	40 (34%)	64 (54%)	0 (0%)
PCT (Cut-off: 0.05 by ROC)	<=0.05	>0.05	24 (22.9%)	6 (6%)	75 (71%)	18 (17%)	6 (6%)

Variable	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
CRP (mg/L) (Cut-off: 10 by ROC)	100.0% (77-100)	38.5% (29-49)	17.9% (10-28)	100.0% (91-100)	45.8% (37-55)
PCT (Cut-off: 0.05 by ROC)	50.0% (21-79)	80.6% (71-88)	25.0% (10-47)	92.6% (85-97)	77.1% (68-85)

Table 51: Comparison of the Diagnostic Performance of CRP and PCT in Predicting Aseptic Meningitis (n=118)

Predictor	AUROC	95% CI	P	Sn	Sp	PPV	NPV	DA
CRP (mg/L).	0.649	0.542- 0.755	0.071	100 %	38%	18%	100 %	46%
PCT (ng/mL).	0.652	0.483- 0.821	0.087	50%	81%	25%	93%	77%

IV. DISCUSSION AND CONCLUSION

A study involving 118 paediatric patients with suspected meningitis was conducted. The study found that bacterial meningitis cases had a significant increase in serum CRP at the time of admission compared to viral meningitis cases. PCT was not found to be useful in distinguishing between bacterial and viral meningitis, as it is not specific to systemic infections.

The study also found that 36% of the patients received antibiotics before admission. CRP and TLC can differentiate between bacterial and viral infections, but initial CRP levels can be low in bacterial diseases, especially in early stages. A high CRP level has also been observed in viral infections.

The mean age of the patients was 34.27 months, with the majority aged between 1-6 months. The gender distribution was 55.9% male and 44.1% female. The mean

duration of illness at admission was 3.32 days, with fever being the most common presentation (88.1%). Seizure, vomiting, altered sensorium, and irritability were the other common symptoms. Headaches were the least common symptom (7.6%).

The study concluded that PCT has no role in predicting or differentiating meningitis, and CSF analysis is the only way to confirm meningitis. It is unlikely that any single test will be sufficiently sensitive to conclusively distinguish between aseptic meningitis and septic meningitis.

The study confirmed meningitis cases based on clinical picture, CSF cytochemical profile, and CSF cultures. The majority of cases (37.3%) were bacterial, with 11.9% aseptic, 25.4% bacterial, and 2 tubercular cases with CSF CBNAAT positivity. The study followed standard treatment guidelines of IAP-2022 and clinical features to differentiate between bacterial and viral meningitis.

The age distribution of meningitis was more in the 1-6 months age group (27.3%), followed by 2-5 years (25%), and the least cases in 1-2 years (0%). There was no statistical significance between meningitis and age groups, as a study by Dmitriy Babenko et al. showed the majority of meningitis in children aged between 1-3 years (22.7%).

The gender distribution of meningitis patients was 63.6% male and 36.4% female, similar to a study by Dmitry Babenko et al., which also showed a male predominance (56.5%). The study found that bacterial meningitis was defined according to CSF laboratory findings, while viral meningitis was defined based on viral culture, serological testing, pleocytosis, or reverse transcriptase polymerase chain reactions.

The study found that meningitis cases typically have a mean duration of 4 days, with fever being the most common presentation. The majority of cases presented with seizures, vomiting, and altered sensorium, followed by irritability and headache. Of the 44 cases, 72.7% had one or more meningeal signs, with neck stiffness being the most common. The mean total leukocyte count (TLC) in meningitis patients was 13064.32, with the highest median TLC in meningitis children compared to non-meningitis children. Meningitis is a common condition, with neck rigidity being the most common sign. Meningitis and laboratory parameters, such as total leukocyte count, are also important to consider. Further research is needed to better understand the complexities of meningitis and its treatment.

The study aimed to compare the haemoglobin levels, platelet count, CSF culture, blood culture reports, and imaging and EEG findings in children with meningitis and viral meningitis. The mean haemoglobin level was highest in the aseptic meningitis group compared to the ABM group, with a median of 10.72 (1.33). The median platelet count was highest in the non-meningitis group compared to the meningitis group, with a median of 10 gm/dl in bacterial meningitis and 12 gm/dl in viral meningitis.

All meningitis patients' blood cultures were sterile, with 97.7% of CSF cultures being sterile. However, one case was pseudomonas positive in CSF culture and two cases had CSF HSV DNA-PCR positive. In this study, CSF culture positive bacterial meningitis was the only one found.

EEG was normal in all meningitis patients, but 46.2% had abnormal findings. Bacterial meningitis was more common in bacterial meningitis (68.2%) than viral meningitis (27.3%). The mean CSF cell count was higher in bacterial meningitis (105) than viral meningitis (7), with a significantly higher CSF leukocyte count. The mean CSF protein level was 80 mg/dl in bacterial meningitis and 34.8 mg/dl in viral meningitis. The total leukocyte count was higher in bacterial meningitis compared to viral meningitis (median 11500).

The mean CRP level was highest in the bacterial meningitis group (30.6mg/L) compared to the viral meningitis group (3.5mg/L). There was no significant difference between the mean and median PCT values among

bacterial and viral meningitis. However, a study by Usama M. Alkhali et al.¹³ showed that CRP, TLC, and PCT can differentiate between aseptic and septic meningitis, with PCT having more diagnostic accuracy.

The study found that CRP with a cut off of 7.46 predicts meningitis with a sensitivity of 59% and a specificity of 66%, while PCT with a cut off of 0.06 has 92.6% sensitivity, 28.2% specificity, 30.9% PPV, and 91.7% NPV with a diagnostic accuracy of 44.8%. The more reliable parameter for predicting meningitis was CRP, which has better specificity than PCT.

In conclusion, the study found that CRP (mg/L) significantly predicted meningitis, with the best parameters in terms of AUROC, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy.

The study found no significant parameters predicting viral meningitis, with PCT being the best in terms of AUROC, CRP (mg/L) as the best parameter in terms of sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy. CRP (mg/L) was the best parameter in terms of negative predictive value.

➤ *Limitations of the Study*

- 35% of the study population received antibiotics before admission.
- Proper microbiological diagnosis was not possible in all the cases.

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