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Cerebrospinal fluid C-reactive protein estimation as a rapid bedside diagnostic tool for pyogenic meningitis in children

Hiba Saher *, Sadashiva. B. Ukkali, Safoora Umaima and Asfiya Iram

Junior Resident (JR-3), Department of Paediatrics, Al-Ameen Medical College Hospital, Bijapur – 586108, Karnataka, India.

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Abstract

Background: Pyogenic meningitis is a leading cause of childhood morbidity and mortality in developing countries. Rapid and accurate differentiation of bacterial from non-bacterial central nervous system (CNS) infections remains a significant clinical challenge, particularly in resource-limited settings. C-reactive protein (CRP), an acute-phase reactant, has been proposed as a simple, rapid, and cost-effective bedside test for diagnosing bacterial meningitis.

Methods: A case-control study was conducted in the Department of Paediatrics, Al-Ameen Medical College Hospital, Bijapur, from November 2024 to October 2025. One hundred children (50 culture-positive cases and 50 culture-negative controls) were enrolled. CSF CRP was assessed using the latex agglutination method. CSF culture served as the gold standard. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results: CSF CRP was positive in 41 of 50 (82%) culture-proven pyogenic meningitis cases and negative in all 50 controls. Sensitivity was 82%, specificity 100%, PPV 100%, and NPV 85%, with an overall diagnostic accuracy of 91%. *Klebsiella pneumoniae* was the most frequently isolated organism (56%), followed by *Escherichia coli* (18%) and *Pseudomonas aeruginosa* (14%). Amikacin (66%) and ciprofloxacin (56%) demonstrated the highest sensitivity profiles.

Conclusions: CSF CRP estimation by latex agglutination is a rapid, reliable, and highly specific bedside test for pyogenic meningitis in children. When combined with standard CSF biochemistry and cell count, diagnostic sensitivity improves to 90%. It is particularly valuable in settings where conventional microbiological facilities are limited.

Keywords: Pyogenic meningitis; CSF C-reactive protein; Latex agglutination; Bacterial meningitis; Paediatrics; Bedside diagnosis

1. Introduction

Acute bacterial meningitis (ABM) is one of the most devastating neurological emergencies in paediatric practice, carrying substantial risks of mortality and long-term neurological sequelae. Despite advances in antimicrobial therapy and preventive immunisation, pyogenic meningitis continues to exert a disproportionate burden in low- and middle-income countries (LMICs), where incidence may reach 20 per 100,000 population, compared to 1.5 per 100,000 in developed nations.[1,2]

The central challenge in managing bacterial meningitis is timely and accurate diagnosis. The classical triad of fever, neck stiffness, and altered mental status is frequently absent or incomplete, particularly in neonates and young infants.[3] A

* Corresponding author: Hiba Saher

significant proportion of children presenting to tertiary centres have already received parenteral antibiotics prior to admission, markedly altering CSF findings.[4]

CSF culture remains the gold standard but requires 24–48 hours, with sensitivity reduced in partially treated cases.[5] Gram staining is rapid but highly operator-dependent with reported sensitivity of only 46–60%.[6] Latex agglutination tests for bacterial antigens offer faster results but are expensive and limited to specific pathogens.[7]

C-reactive protein (CRP), a member of the pentraxin superfamily, is synthesised in the liver in response to interleukin-1, interleukin-6, and tumour necrosis factor-alpha released by activated macrophages.[8] Under physiological conditions serum CRP is below 8 mg/L; in bacterial infection levels rise dramatically within 6–8 hours, peaking within 24–48 hours.[9] CRP detected in CSF is thought to occur via passive diffusion through an inflamed blood–brain barrier rather than local intrathecal synthesis.[10] Several studies have demonstrated a strong correlation between elevated CSF CRP and microbiologically confirmed bacterial meningitis, and importantly, CSF CRP tends to remain elevated even in partially treated cases.[11,12]

Qualitative CRP detection using the latex agglutination method represents a particularly attractive point-of-care approach: results are available within two to three minutes, no sophisticated laboratory infrastructure is required, and the test is cost-effective even in resource-constrained settings.[13] This is especially relevant to district and peripheral hospitals across India where microbiological services are often limited.

The bacteriological profile of pyogenic meningitis in Indian tertiary centres differs considerably from that of high-income countries, where *Neisseria meningitidis*, *Haemophilus influenzae* type b, and *Streptococcus pneumoniae* predominate globally. Gram-negative enteric bacilli such as *Klebsiella pneumoniae* and *Escherichia coli* are frequently isolated in Indian children, especially after prior antibiotic exposure.[14,15] This has significant implications for empirical antibiotic prescribing.

The present study was designed to evaluate the diagnostic utility of CSF CRP as a rapid bedside test for pyogenic meningitis in children aged 1 month to 12 years, with concurrent analysis of prevailing bacterial pathogens and their antibiotic susceptibility profiles.

2. Methods

2.1. Study design and setting

This prospective case-control study was conducted in the Department of Paediatrics, Al-Ameen Medical College Hospital, Bijapur, Karnataka, India, over twelve months from November 2024 to October 2025. Ethical clearance was obtained from the Institutional Ethics Committee (Al-Ameen Medical College Hospital, Bijapur), and written informed consent was obtained from parents or legal guardians of all participating children.

2.2. Study population and sample size

Children aged 1 month to 12 years admitted with clinical features suggestive of meningitis or CNS infection were screened for eligibility. Sample size was calculated for estimation of sensitivity of CSF CRP using the standard formula for diagnostic studies ($n = Z^2 \times S \times (1 - S) / d^2$), where Z = 1.96 (95% CI), S = expected sensitivity (0.90), and d = absolute precision (0.10). The minimum required sample size was 35. To improve study validity and account for potential exclusions, 50 cases were enrolled along with 50 controls.

2.3. Case definitions

Cases (n=50): Children with clinically suspected pyogenic meningitis whose CSF yielded a positive bacterial culture.

Controls (n=50): Age- and sex-matched children who underwent lumbar puncture for non-meningitic indications (febrile seizures, acute respiratory tract infection with meningismus, and acute flaccid paralysis) and whose CSF culture was negative.

2.4. CSF CRP estimation (bedside latex agglutination)

Lumbar puncture was performed under strict aseptic precautions. CSF samples were collected simultaneously for cell count, biochemical analysis, CRP estimation, and culture. Qualitative CRP assessment was performed at the bedside using the slide latex agglutination method. One drop of fresh CSF was placed on a glass slide, one drop of CRP latex

reagent was added, and the slide was rocked for two minutes. Macroscopic agglutination indicated a positive result. Positive and negative controls were included with each batch.

2.5. Microbiological culture

CSF specimens were inoculated onto blood agar, chocolate agar, and MacConkey agar and incubated at 37°C for 18–24 hours. Organisms were identified using standard biochemical reactions. Antibiotic sensitivity testing was performed on Mueller-Hinton agar by the Kirby-Bauer disc diffusion method.

2.6. Statistical analysis

Data were analysed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean ± standard deviation; categorical variables as frequencies and percentages. Diagnostic performance of CSF CRP was assessed by calculating sensitivity, specificity, PPV, NPV, and overall accuracy. Chi-square and Mann-Whitney U tests were used for comparative analysis. A p-value <0.05 was considered statistically significant.

3. Results

A total of 100 children were enrolled: 50 with culture-proven pyogenic meningitis and 50 culture-negative controls.

3.1. Age and sex distribution

The majority of pyogenic meningitis cases occurred in infants aged 1 month to 1 year (50%). Mean age in the pyogenic meningitis group was 29 months and in the control group 33 months. The difference in age distribution between groups was not statistically significant (p=0.73) (Table 1).

3.2. Clinical features

Altered sensorium (92%), seizures (90%), and fever (88%) were the most common presenting features in the pyogenic meningitis group. Shock was present in 46% of cases and was a highly significant discriminating feature compared to controls (p<0.001). Classical meningeal signs — neck rigidity and Kernig's sign — were present in only 22% and 24% of cases respectively, highlighting the frequent absence of classical examination findings in children (Table 2).

3.3. CSF analysis

CSF was clear in 70% of pyogenic meningitis cases, reflecting the high proportion of partially treated cases at this referral centre. Cellular pleocytosis with predominant polymorphonuclear cells was present in 50% of cases. Elevated CSF protein (>45 mg/dL) was found in 70% and hypoglycorrhachia in 40% of cases (Table 3).

3.4. Bacteriological profile

Gram-negative organisms dominated the bacteriological profile. *Klebsiella pneumoniae* was the most frequently isolated pathogen (56%), followed by *Escherichia coli* (18%) and *Pseudomonas aeruginosa* (14%). *Streptococcus pneumoniae* accounted for 8%; *Haemophilus influenzae*, *Staphylococcus aureus*, and *Proteus* species each contributed 2% (Table 4).

3.5. Antibiotic susceptibility pattern

Amikacin demonstrated the highest overall sensitivity (66%), followed by ciprofloxacin (56%). Together these two agents covered approximately 96% of isolated organisms. Cefotaxime, which forms the backbone of current empirical meningitis protocols, demonstrated sensitivity in only one case (2%) (Table 5).

3.6. CSF CRP results

CSF CRP was positive in 41 of 50 (82%) culture-proven cases and negative in all 50 controls. The difference in CRP positivity between groups was highly statistically significant (p<0.01, Mann-Whitney U test). No false-positive results were recorded in the control group (Table 6).

3.7. Diagnostic accuracy

CSF CRP demonstrated sensitivity 82%, specificity 100%, PPV 100%, and NPV 85%, with overall diagnostic accuracy of 91%. Abnormal CSF biochemistry had sensitivity 74% and specificity 80%; abnormal cell count had sensitivity 56% and specificity 92%. Combining all three parameters improved sensitivity to 90%, confirming that CSF CRP is the single most specific parameter for differentiating pyogenic from non-pyogenic meningitis (Table 7).

Table 1 Age distribution of the study population**.**

Age Group	Pyogenic Meningitis (n=50)	%	Control Group (n=50)	%	p-value
1 month – 1 year	25	50	25	50	0.73 (NS)
1 – 3 years	13	26	9	18	–
3 – 6 years	8	16	11	22	–
6 – 12 years	4	8	5	10	–

NS: not significant.

Table 2 Clinical presentation of children with acute CNS infection.

Clinical Feature	Pyogenic (n=50)	%	Control (n=50)	%	Significance
Fever	44	88	27	54	p<0.001
Altered Sensorium	46	92	24	48	p<0.001
Seizures	45	90	44	88	NS
Shock	23	46	4	8	p<0.001
Altered Level of Consciousness	48	96	20	40	p<0.001
Vomiting	17	34	5	10	p<0.01
Headache	9	18	3	6	p<0.05
Neck Rigidity	11	22	4	8	p<0.05
Kernig's Sign	12	24	4	8	p<0.05
Bulging Fontanelle	5	10	1	2	p<0.05
Focal Neurological Deficit	19	38	10	28	NS
Papilloedema	6	12	1	2	p<0.05

NS: not significant.

Table 3 CSF findings in pyogenic meningitis vs. control group.

Parameter	Finding	Pyogenic (n=50)	%	Control (n=50)	%
CSF Colour	Clear	35	70	50	100
	Turbid	12	24	0	0
	Purulent	3	6	0	0
CSF Cells	Polymorphs predominant	25	50	1	2
	Lymphocytes predominant	3	6	3	6
	No cells	22	44	46	92
CSF Protein	<45 mg/dL	15	30	40	80
	45–100 mg/dL	27	54	7	14
	>100 mg/dL	8	16	3	6
CSF Glucose	<2/3 of blood glucose	20	40	10	20
	≥2/3 of blood glucose	30	60	40	80

Table 4 Bacterial organisms isolated from CSF culture (n=50).

Organism Isolated	Number of Cases	Percentage (%)
Klebsiella pneumoniae	28	56
Escherichia coli	9	18
Pseudomonas aeruginosa	7	14
Streptococcus pneumoniae	4	8
Haemophilus influenzae	1	2
Staphylococcus aureus	1	2
Proteus species	1	2

Table 5 Antibiotic sensitivity of isolated organisms (n=50).

Antibiotic	Sensitive Cases (n=50)	Sensitivity (%)
Amikacin	33	66
Ciprofloxacin	28	56
Ceftazidime	2	4
Gentamicin	2	4
Cefotaxime	1	2
Vancomycin	1	2
Ampicillin	1	2
Cloxacillin	1	2
Erythromycin	1	2
Multidrug Resistant	1	2

Table 6 CSF CRP (latex agglutination) results in study and control groups.

Group	CSF CRP Positive	CSF CRP Negative	Total	p-value
Pyogenic Meningitis (Culture +ve)	41 (82%)	9 (18%)	50	<0.01
Control (Culture –ve)	0 (0%)	50 (100%)	50	–
Total	41	59	100	

Table 7 Diagnostic performance of CSF CRP vs. conventional CSF parameters.

Diagnostic Parameter	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CSF CRP (Latex Agglutination)	82	100	100	85
Abnormal CSF Biochemistry	74	80	79	75
Abnormal CSF Cell Count	56	92	88	68
Cell Count + Biochemistry	80	78	78	80
CRP + Biochemistry + Cell Count	90	76	79	88

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

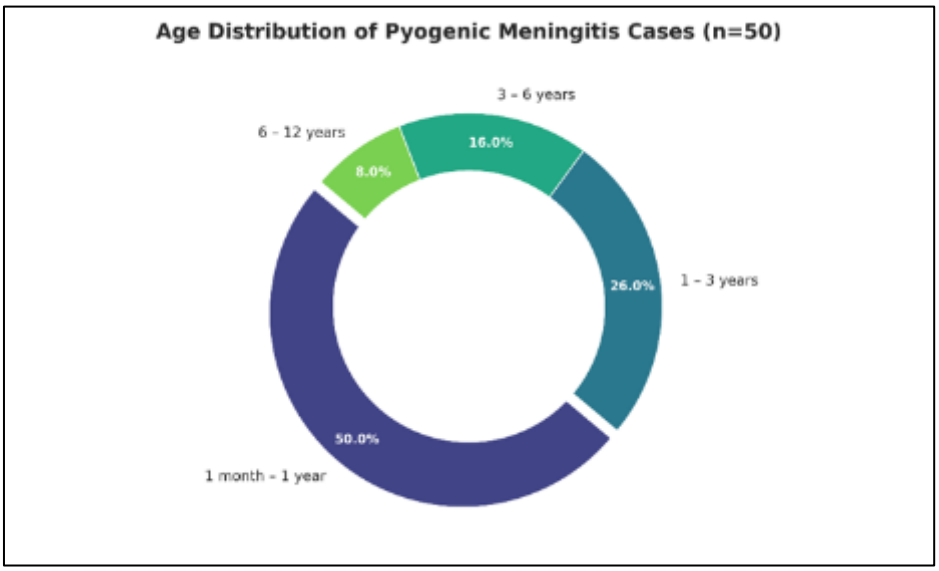

Figure 1 Age distribution of the study population. Bar chart depicting the percentage of pyogenic meningitis cases and controls in each age group.

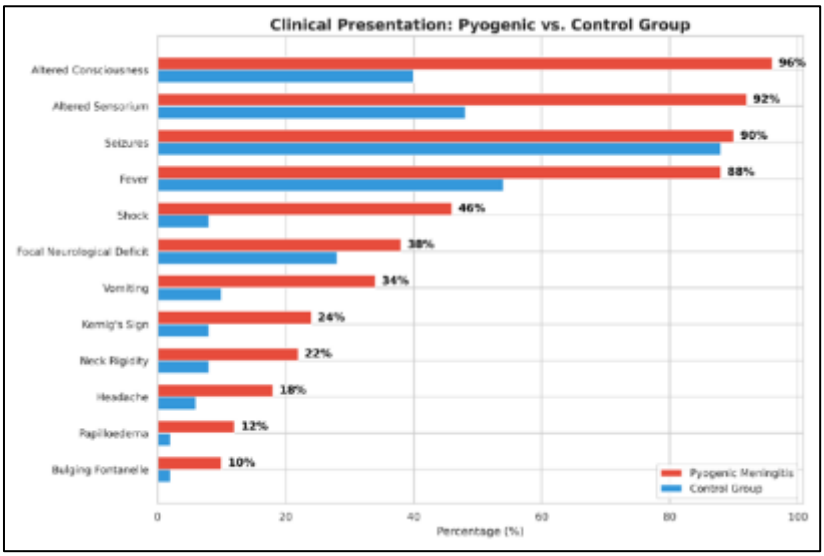

Figure 2 Clinical presentation of children with acute CNS infection. Bar chart comparing the frequency of clinical features between pyogenic meningitis cases and controls.

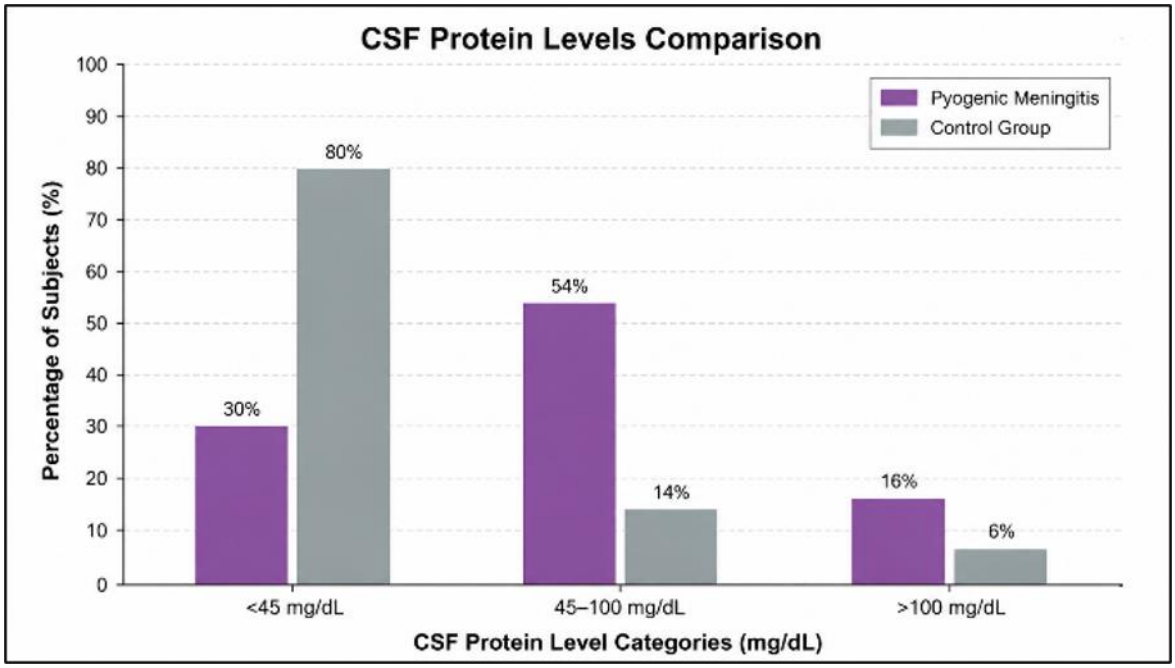

Figure 3 CSF findings in pyogenic meningitis vs. control group. Bar chart illustrating CSF protein level distribution. X-axis: CSF protein level categories (<45, 45–100, and >100 mg/dL). Y-axis: Percentage of subjects (%). Purple bars represent the pyogenic meningitis group, and grey bars represent the control group.

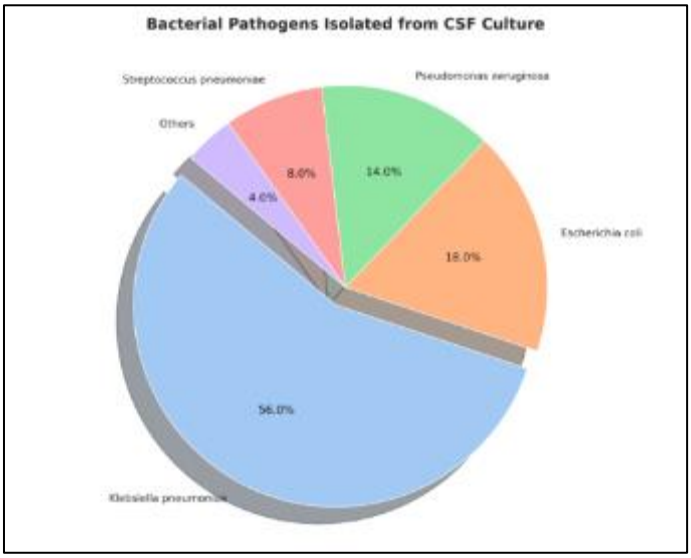

Figure 4 Bacterial organisms isolated from CSF culture (n=50). Pie chart depicting the relative proportion of each organism.

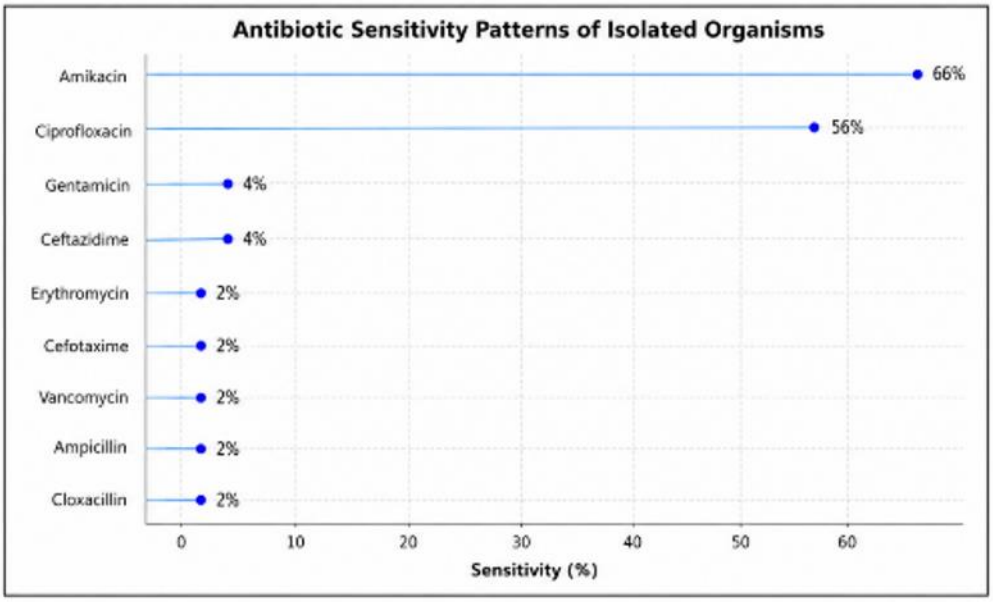

Figure 5 Antibiotic sensitivity of isolated organisms (n=50). Bar chart showing sensitivity rates for each antibiotic tested.

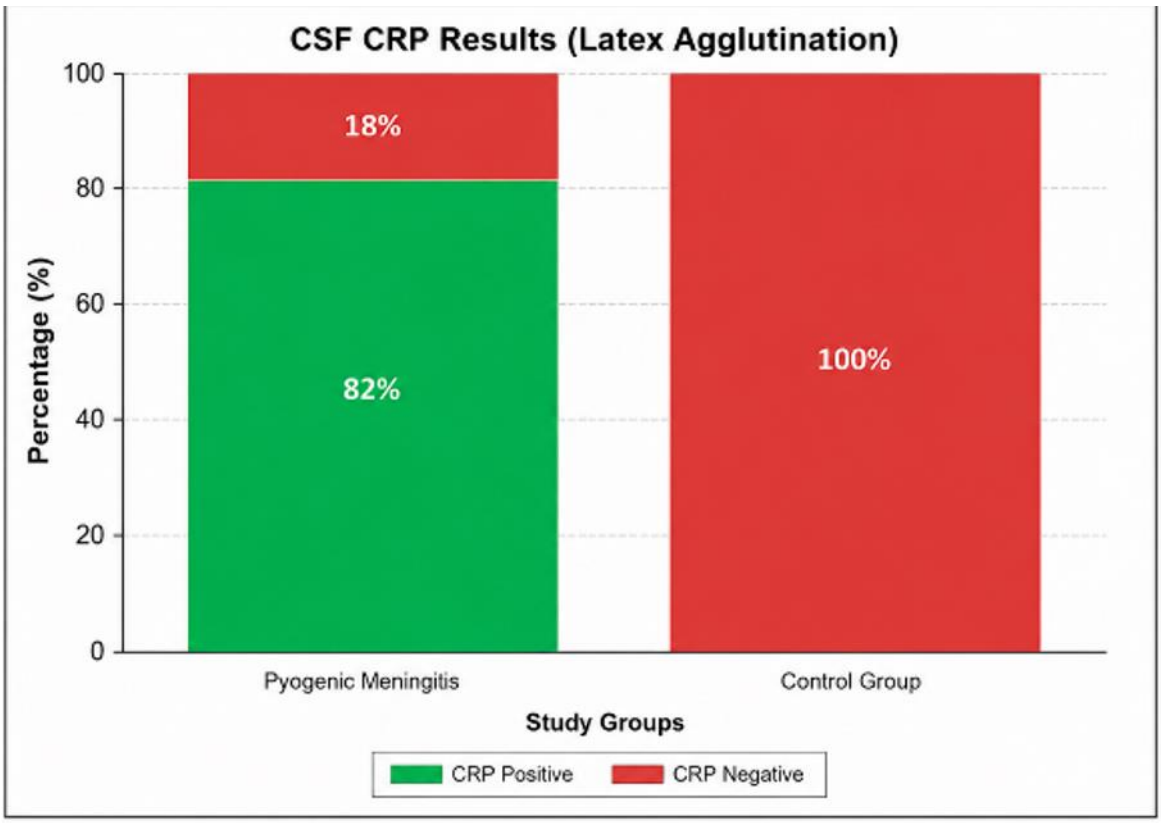

Figure 6 CSF CRP (latex agglutination) results in study and control groups. Bar chart showing proportions of CRP-positive and CRP-negative results.

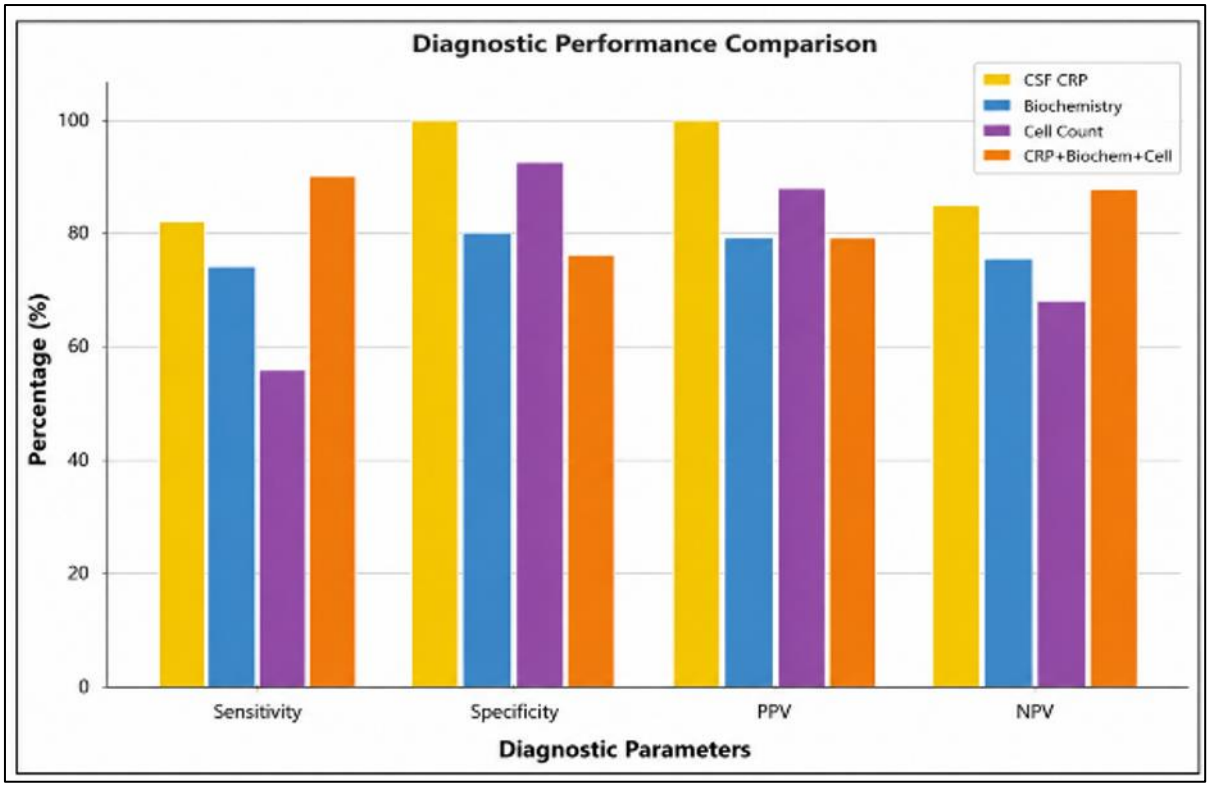

Figure 7 Diagnostic performance of CSF CRP vs. conventional CSF parameters. Comparative bar chart of sensitivity, specificity, PPV, and NPV.

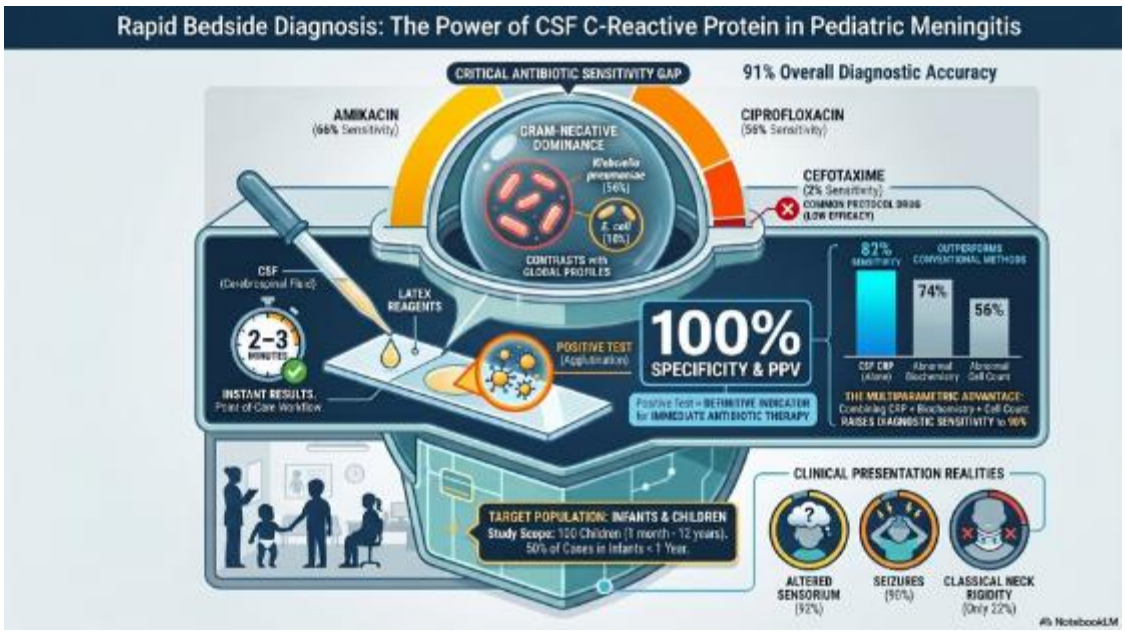

Figure 8 Clinical decision-making workflow for CSF CRP as a point-of-care bedside test in children with suspected pyogenic meningitis. The flow diagram illustrates the 2–3-minute latex agglutination test pathway, interpretation, and recommended clinical response based on results.

4. Discussion

This study evaluated CSF CRP as a bedside diagnostic tool in 100 children, demonstrating sensitivity 82%, specificity 100%, PPV 100%, and NPV 85% against the gold standard of CSF culture. These findings carry meaningful implications for managing paediatric CNS infections in resource-limited environments.

The high specificity and PPV of CSF CRP (both 100%) are its most clinically valuable attributes. A positive result in a child with clinical features of meningitis should be treated as confirmatory evidence of bacterial infection, mandating immediate empirical antibiotic therapy irrespective of culture results or CSF cell count. This is especially pertinent when CSF appears clear, cells are absent, or the child has received antibiotics prior to presentation. A negative CRP should prompt careful re-evaluation rather than reassurance (NPV 85%).

The sensitivity of 82% in this study aligns with comparable Indian studies. Gaur and Seshan reported 80% sensitivity in children with meningitis in India,[16] while Pemde et al. found 100% sensitivity in their prospective study at a different cut-off titre.[17] The somewhat lower sensitivity in bedside qualitative studies likely reflects the dilutional effect seen in CSF of partially treated patients.[18]

The absolute specificity is consistent with multiple investigators. Vaidya et al. demonstrated that CSF CRP was more sensitive and selective than conventional CSF parameters.[19] Similarly, John et al. found CRP a better indicator than Gram staining, with a sensitivity of 91%, and noted its value in distinguishing bacterial meningitis from tubercular meningitis, viral encephalitis, and febrile convulsions.[20]

The comparative analysis reveals important observations. Abnormal cell count, a cornerstone diagnostic indicator, showed sensitivity of only 56%, consistent with evidence that a normal cell count does not exclude bacterial meningitis in immunocompromised patients or those pre-treated with antibiotics.[21] The combination of all three parameters (CRP, biochemistry, and cell count) improved sensitivity to 90%, suggesting that a multiparametric bedside approach is the most diagnostically robust strategy.[22]

Klebsiella pneumoniae dominated at 56%, followed by *E. coli* (18%) and *Pseudomonas aeruginosa* (14%), while *S. pneumoniae* and *H. influenzae* contributed only 8% and 2% respectively. This pattern contrasts starkly with global epidemiological data but is consistent with tertiary-centre reports from India, as documented by Tankhiwale et al. and Panjarathinam et al., particularly in children referred after prior antibiotic therapy.[23,24]

The antibiotic susceptibility data present a critical clinical message. Cefotaxime — a third-generation cephalosporin forming the backbone of empirical meningitis protocols — showed sensitivity in only one case (2%). This finding strongly advocates for revisiting empirical antibiotic policies in tertiary Indian centres treating gram-negative meningitis. Given poor CSF penetration of aminoglycosides, fluoroquinolones such as ciprofloxacin with documented CNS penetration may represent a more appropriate empirical choice.[25]

Several limitations should be acknowledged. This is a single-centre study, and the bacteriological profile may not be representative of all Indian settings. The qualitative technique limits the ability to define optimal cut-off thresholds. Additionally, prior antibiotic exposure in a number of cases may have lowered CSF CRP titres and contributed to observed false-negative results. Future multicentre studies employing quantitative CRP measurement alongside procalcitonin and serum lactate would further enhance diagnostic precision.[28]

5. Conclusion

CSF CRP estimation by latex agglutination is a rapid, simple, inexpensive, and highly specific bedside test for the diagnosis of pyogenic meningitis in children. A positive CSF CRP result should be treated as diagnostic of bacterial meningitis, warranting immediate antibiotic therapy irrespective of other findings. Gram-negative organisms — particularly *Klebsiella pneumoniae* — dominate the bacteriological profile in this referral-centre setting, with amikacin and ciprofloxacin showing the highest susceptibility rates. Empirical antibiotic protocols should be re-evaluated in light of local bacteriology. The multiparametric approach combining CSF CRP, biochemistry, and cell count achieves 90% sensitivity and is recommended for comprehensive bedside assessment.

Compliance with ethical standards

Disclosure of conflict of interest

The author sincerely acknowledges the Department of Paediatrics, Al-Ameen Medical College Hospital, Bijapur, for providing clinical support and laboratory facilities for this study. The author is grateful to the patients and their guardians for their participation.

Statement of ethical approval

Ethical clearance was obtained from the Institutional Ethics Committee of Al-Ameen Medical College Hospital, Bijapur, prior to commencement of the study.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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