

Comparative Analysis of Serum C-Reactive Protein Levels in Different Types of Meningitis in Children Aged 1 Month to 18 Years: A Cross Sectional Observational Study

Nandini Sharma¹, Dileep Kumar Goyal², Sanjay Mandot³, Harnoor Pannu⁴,
Pankhuri Sabharwal⁵, Nandasana Jahnvi⁶

¹Post Graduate Resident, Department of Pediatrics, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India

²Professor, Department of Pediatrics, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India

³HOD & Professor, Department of Pediatrics, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India

⁴Post Graduate Resident, Department of Pediatrics, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India

⁵Post Graduate Resident, Department of Pediatrics, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India

⁶Post Graduate Resident, Department of Pediatrics, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India

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Corresponding author: Dr. Nandini Sharma

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Abstract

Background: Childhood meningitis spans a spectrum from self-limiting viral illness to rapidly fatal pyogenic infection, and early aetiological differentiation is essential for rational antimicrobial use. Serum C-reactive protein (CRP) is a rapid, inexpensive acute-phase marker, but comparative data across pyogenic, partially treated pyogenic, viral, and tubercular meningitis in Indian children remain limited.

Objectives: To compare serum CRP levels among children with pyogenic meningitis (PM), partially treated pyogenic meningitis (PPM), viral meningitis (VM), and tubercular meningitis (TBM), and to characterise the associated clinical, epidemiological, and aetiological profile.

Methods: This hospital-based cross-sectional observational study was conducted in the Department of Pediatrics, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, over 18 months. Eighty-five consecutive children aged 1 month–18 years admitted with clinically suspected meningitis were enrolled and classified into four categories using integrated clinical, cerebrospinal fluid (CSF), and microbiological criteria. Demographic, clinical, haematological, CSF, microbiological, and radiological data were recorded on a structured proforma. Serum CRP was estimated by immunoturbidimetric latex agglutination. Continuous variables were compared using analysis of variance and categorical variables using the chi-square or Fisher exact test; Spearman correlation and receiver-operating-characteristic (ROC) analysis were used as appropriate. A two-tailed $p < 0.05$ was considered significant.

Results: Of 85 children (mean age 1.94 ± 1.56 years; 65.9% male), VM was the commonest category (30.6%), followed by PM (29.4%), PPM (24.7%), and TBM (15.3%). Serum CRP differed significantly across groups ($p < 0.001$), highest in PM (98.76 ± 23.53 mg/L) and lowest in VM (13.39 ± 7.73 mg/L), with PPM (51.04 ± 28.52 mg/L) and TBM (42.37 ± 19.12 mg/L) intermediate. CRP exceeded 50 mg/L in 96.0% of PM cases and in no VM case. ROC analysis for differentiating bacterial (PM+PPM) from non-bacterial (VM+TBM) meningitis showed an area under the curve of 0.902, with an optimal cut-off of >41.6 mg/L yielding 84.8% sensitivity and 87.2% specificity. Serum CRP correlated most strongly with CSF neutrophil percentage ($\rho = 0.71$, $p < 0.001$) and blood neutrophil percentage ($\rho = 0.67$, $p < 0.001$). Age differed significantly across categories ($p < 0.001$), whereas gender, socioeconomic status, and vaccination status did not.

Conclusions: Serum CRP is a rapid, inexpensive, and diagnostically useful adjunct that discriminates bacterial from viral childhood meningitis with good accuracy. Considerable overlap in partially treated pyogenic and tubercular disease, however, indicates that CRP is most informative when interpreted alongside CSF cytology, biochemistry, microbiology, and neuroimaging rather than used in isolation.

Keywords: C-Reactive Protein; Meningitis; Children; Pyogenic; Tubercular; Cerebrospinal Fluid; Biomarker.

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Introduction

Meningitis, inflammation of the meninges, remains one of the most serious infectious emergencies of childhood and demands early recognition, prompt diagnostic evaluation, and timely institution of therapy [1,2]. The disease may arise from pyogenic (bacterial), viral, tubercular, or fungal pathogens, and because each aetiological group differs substantially in pathogenesis, clinical course, and prognosis, accurate and early differentiation carries direct therapeutic and prognostic significance [1,3]. In resource-limited settings, acute bacterial meningitis continues to carry a case-fatality rate that may reach 20–30%, and survivors frequently develop hearing impairment, developmental delay, seizure disorders, motor deficits, or hydrocephalus [2,4]. Clinicians are therefore often required to begin empirical antimicrobial therapy before confirmatory microbiological results become available, a circumstance in which supportive laboratory markers assume considerable clinical importance [1,2].

Cerebrospinal fluid (CSF) Gram stain and culture remain the reference standard for aetiological classification of meningitis, but culture positivity is frequently low in children who have already received antibiotics before presentation — a scenario commonly termed partially treated pyogenic meningitis — and advanced molecular assays such as GeneXpert or multiplex PCR are not universally accessible in resource-constrained hospitals (3,5). Serum C-reactive protein (CRP), an acute-phase reactant synthesised by the liver in response to interleukin-6-mediated inflammation, rises rapidly and substantially in bacterial infection and offers a rapid, inexpensive, and widely available adjunct to clinical assessment [6,7].

Several studies have shown that serum or CSF CRP can help distinguish bacterial from viral meningitis in children [7,8,9], while CSF adenosine deaminase and CRP have similarly been explored for the identification of tubercular meningitis [5]. Acute-phase reactants such as CRP have also been highlighted as practical, low-cost tools for triaging febrile children in whom a serious bacterial infection is suspected [11,12,13].

However, most published comparisons remain limited to a two-way bacterial-versus-viral dichotomy and do not adequately characterise the clinically important intermediate categories of partially treated pyogenic and tubercular meningitis, which are particularly relevant to the Indian paediatric setting where prior antibiotic exposure and endemic tuberculosis are common [1,15]. Data directly comparing serum CRP across

four aetiological categories — pyogenic, partially treated pyogenic, viral, and tubercular meningitis — within a single Indian cohort, alongside its correlation with peripheral and CSF inflammatory indices, remain scarce. The present study was therefore undertaken to compare serum CRP levels across these four categories of childhood meningitis and to characterise the associated clinical, epidemiological, and laboratory profile of affected children attending a tertiary care centre in North India, with the aim of generating evidence to support early aetiological triage and rational use of antimicrobial therapy.

Materials and Methods

Study Design and Setting: This hospital-based cross-sectional observational study was conducted in the Department of Pediatrics, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, a tertiary-care teaching hospital serving both urban and rural populations of southern Rajasthan. The study was conducted over a period of 18 months from the date of approval of the study protocol by the Institutional Ethics Committee, Geetanjali Medical College and Hospital, Udaipur. Written informed consent was obtained from parents or legal guardians before enrolment, and assent was obtained from eligible children where applicable. Patient identity and clinical details were kept confidential throughout the study.

Study Population and Sampling: The study population comprised children aged 1 month to 18 years admitted to the Department of Pediatrics with clinical features suggestive of meningitis, including fever, headache, refusal to feed, vomiting, irritability, drowsiness, convulsions, bulging anterior fontanelle, coma, neck stiffness, or other meningeal signs. Consecutive sampling was employed: all eligible children admitted during the study period were screened, and those fulfilling the inclusion criteria without meeting any exclusion criterion were enrolled. As the study was conducted as a time-bound dissertation project, all consecutive eligible patients admitted during the defined period were included, yielding a final sample of 85 children.

Eligibility Criteria

Inclusion Criteria: (i) children aged 1 month to 18 years; (ii) clinical diagnosis of meningitis based on the features listed above.

Exclusion Criteria: (i) lumbar puncture contraindicated by local sepsis, papilledema or other signs of raised intracranial pressure, marked

spinal deformity, or bleeding diathesis/anticoagulant therapy; (ii) prior steroid therapy; (iii) traumatic lumbar puncture; (iv) parental/guardian refusal of consent; (v) congenital central nervous system anomaly; (vi) known neurodegenerative brain disorder.

Clinical Assessment, Grouping, and Investigations: A predesigned, pretested structured proforma was used to record demographic details, clinical history, examination findings, and laboratory parameters. All children underwent a comprehensive general physical examination and detailed neurological examination, with attention to sensorium, meningeal signs, cranial nerve involvement, focal deficits, and features of raised intracranial pressure. Lumbar puncture was performed after exclusion of contraindications, and blood and CSF samples were sent for analysis. On the basis of clinical findings, CSF analysis, Gram stain, culture, and other relevant investigations, patients were classified into four groups: Group 1, pyogenic meningitis (PM); Group 2, partially treated pyogenic meningitis (PPM); Group 3, viral meningitis (VM); and Group 4, tubercular meningitis (TBM). CSF Gram stain and culture were considered the reference standard where positive; in culture-negative cases, classification was supported by clinical features together with CSF cytology and biochemistry.

Routine investigations included complete blood count with total and differential leucocyte count, serum CRP, blood culture, random blood sugar, and CSF analysis (cytology, protein, sugar, Gram stain, and culture). CSF GeneXpert for *Mycobacterium tuberculosis*, Ziehl-Neelsen staining, and HSV PCR were performed when clinically indicated, along with Mantoux testing and neuroimaging as appropriate. Serum CRP was estimated from venous blood collected on the day of admission: plasma separated by centrifugation was diluted with HEPES buffer and mixed with CRP antibody latex reagent, and the concentration was derived from the change in absorbance at 525 and 625 nm corresponding to the degree of antibody-antigen agglutination.

Outcome Measures and Statistical Analysis: The primary outcome was serum CRP level across the four meningitis categories. Secondary outcomes included the demographic, clinical, haematological, CSF, microbiological, and radiological profile of each category. Data were entered into a master chart and analysed using appropriate statistical

software. Continuous variables were expressed as mean $\pm$ standard deviation and compared across groups using one-way analysis of variance with post-hoc analysis where required. Categorical variables were expressed as frequency and percentage and compared using the chi-square test or Fisher exact test, as applicable. Spearman rank correlation was used to assess the relationship between serum CRP and selected blood/CSF parameters, and receiver-operating-characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of serum CRP for differentiating bacterial (PM+PPM) from non-bacterial (VM+TBM) meningitis, with the optimal cut-off derived using the Youden index. A two-tailed p-value <0.05 was considered statistically significant.

Results

A total of 85 children aged 1 month to 18 years admitted with clinically suspected meningitis and fulfilling the eligibility criteria were enrolled by consecutive sampling over the 18-month study period and classified into four meningitis categories on the basis of integrated clinical, CSF, and microbiological assessment. Viral meningitis formed the largest group (26 children, 30.6%), closely followed by pyogenic meningitis (25, 29.4%), partially treated pyogenic meningitis (21, 24.7%), and tubercular meningitis (13, 15.3%).

The baseline demographic and epidemiological characteristics of the study participants are summarised in Table 1. The overall mean age was 1.94 ± 1.56 years (range 0.17–9.20 years), and age differed significantly across categories ($p < 0.001$): TBM affected the oldest children (mean 3.20 ± 1.25 years) and PM the youngest (mean 1.24 ± 1.03 years). The >1 –5-year age band predominated overall (58.8%), while infants aged 1–12 months were concentrated in PM (60.0%) and PPM (57.1%) and were nearly absent in VM (11.5%) and TBM (0%); no child older than 10 years was enrolled ($p < 0.001$). Males constituted 65.9% of the cohort (male:female $\approx 1.9:1$), and gender distribution did not differ significantly across categories ($p = 0.823$). The lower and lower-middle socioeconomic strata together accounted for 72.9% of participants, with a significantly higher proportion in these strata than in the upper-middle/upper strata ($p < 0.001$), while socioeconomic and vaccination status did not differ significantly across meningitis categories ($p = 0.763$ and $p = 0.187$ respectively, not shown in table).

Table 1: Baseline demographic and epidemiological characteristics of children with meningitis by category (n=85)

Variable	Overall (n=85)	PM (n=25)	PPM (n=21)	VM (n=26)	TBM (n=13)	p-value
Age, years, mean $\pm$ SD	1.94 $\pm$ 1.56	1.24 $\pm$ 1.03	1.61 $\pm$ 2.03	2.25 $\pm$ 1.28	3.20 $\pm$ 1.25	<0.001
1–12 months	30 (35.3%)	15(60.0%)	12 (57.1%)	3 (11.5%)	0 (0.0%)	<0.001
>1–5 years	50 (58.8%)	10(40.0%)	8 (38.1%)	21 (80.8%)	11 (84.6%)	
>5–10 years	5 (5.9%)	0 (0.0%)	1 (4.8%)	2 (7.7%)	2 (15.4%)	
Male sex	56 (65.9%)	15(60.0%)	15 (71.4%)	18 (69.2%)	8 (61.5%)	0.823
Lower / lower-middle SES	62 (72.9%)	19(76.0%)	14 (66.7%)	18 (69.2%)	11 (84.6%)	0.763*
Not vaccinated	39 (45.9%)	7 (28.0%)	9 (42.9%)	14 (53.8%)	9 (69.2%)	0.187

*Goodness-of-fit chi-square test against expected 50:50 distribution for lower/lower-middle vs upper-middle/upper SES groups was significant ($p<0.001$); comparison across the four meningitis categories was not significant ($p=0.763$). SES, socioeconomic status.

Table 2 summarises the presenting symptoms and neurological/meningeal signs across the four categories.

Fever was the commonest presenting symptom overall (92.9%) and was universal in TBM (100.0%), while vomiting (69.4%), drowsiness (68.2%), and headache (55.3%) were also frequent; none of the symptom frequencies differed significantly across categories (all $p>0.05$). In

contrast, several examination findings showed significant between-group differences: coma was concentrated in PM (24.0%) and TBM (23.1%) and absent in VM ($p=0.022$); neck stiffness was commonest in PM (72.0%, $p=0.040$); other meningeal signs were present in 56.0% of PM and absent in VM ($p<0.001$); and bulging anterior fontanelle was most frequent in PPM (47.6%) and rare in VM and TBM ($p<0.001$).

Table 2: Clinical symptom and neurological/meningeal sign profile by meningitis category (n=85)

Feature	Overall	PM	PPM	VM	TBM	p-value
Fever	79 (92.9%)	22 (88.0%)	20 (95.2%)	24 (92.3%)	13(100.0%)	0.551
Headache	47 (55.3%)	17 (68.0%)	12 (57.1%)	11 (42.3%)	7 (53.8%)	0.328
Vomiting	59 (69.4%)	20 (80.0%)	13 (61.9%)	16 (61.5%)	10 (76.9%)	0.394
Refusal to feed	31 (36.5%)	11 (44.0%)	10 (47.6%)	8 (30.8%)	2 (15.4%)	0.204
Convulsions	35 (41.2%)	10 (40.0%)	7 (33.3%)	13 (50.0%)	5 (38.5%)	0.700
Drowsiness	58 (68.2%)	16 (64.0%)	13 (61.9%)	20 (76.9%)	9 (69.2%)	0.681
Coma	10 (11.8%)	6 (24.0%)	1 (4.8%)	0 (0.0%)	3 (23.1%)	0.022
Focal neurological deficit	14 (16.5%)	7 (28.0%)	3 (14.3%)	1 (3.8%)	3 (23.1%)	0.116
Neck stiffness	44 (51.8%)	18 (72.0%)	9 (42.9%)	9 (34.6%)	8 (61.5%)	0.040
Other meningeal signs	22 (25.9%)	14 (56.0%)	3 (14.3%)	0 (0.0%)	5 (38.5%)	<0.001
Bulging anterior fontanelle	17 (20.0%)	6 (24.0%)	10 (47.6%)	1 (3.8%)	0 (0.0%)	<0.001

PM, pyogenic meningitis; PPM, partially treated pyogenic meningitis; VM, viral meningitis; TBM, tubercular meningitis.

Serum CRP differed markedly across the four meningitis categories (Table 3; $p<0.001$).

PM showed the highest mean CRP (98.76 $\pm$ 23.53 mg/L; minimum 45.80 mg/L, indicating uniformly elevated values), followed by PPM (51.04 $\pm$ 28.52 mg/L; wide dispersion, range 3.00–97.10 mg/L, suggesting heterogeneous inflammatory response) and TBM (42.37 $\pm$ 19.12 mg/L). VM showed the

lowest mean CRP (13.39 $\pm$ 7.73 mg/L) with a narrow range (0.50–29.10 mg/L).

Categorical analysis reinforced this gradient ($p<0.001$): CRP exceeded 50 mg/L in 24 of 25 PM cases (96.0%) and in no VM case, while 42.3% of VM cases had CRP $\leq$ 10 mg/L and 61.5% of TBM cases fell in the >20–50 mg/L band.

Table 3: Serum CRP levels and categorical distribution across meningitis categories (n=85)

Variable	Overall	PM	PPM	VM	TBM	p-value
Serum CRP (mg/L), mean $\pm$ SD	52.23 $\pm$ 39.35	98.76 $\pm$ 23.53	51.04 $\pm$ 28.52	13.39 $\pm$ 7.73	42.37 $\pm$ 19.12	<0.001
CRP $\leq$ 10 mg/L	13 (15.3%)	0 (0.0%)	1 (4.8%)	11(42.3%)	1 (7.7%)	<0.001
CRP >10–20 mg/L	13 (15.3%)	0 (0.0%)	3 (14.3%)	10(38.5%)	0 (0.0%)	
CRP >20–50 mg/L	21 (24.7%)	1 (4.0%)	7 (33.3%)	5 (19.2%)	8 (61.5%)	
CRP >50 mg/L	38 (44.7%)	24 (96.0%)	10 (47.6%)	0 (0.0%)	4 (30.8%)	

CRP, C-reactive protein.

Serum CRP was evaluated as a diagnostic marker for differentiating bacterial meningitis (PM+PPM) from non-bacterial meningitis (VM+TBM) using ROC curve analysis. The area under the curve was 0.902, indicating strong discriminatory performance.

The Youden-index-derived optimal cut-off of >41.6 mg/L yielded a sensitivity of 84.8% and specificity of 87.2%, confirming that higher serum CRP was associated with pyogenic/partially treated pyogenic disease while lower values were characteristic of viral/tubercular meningitis. Table 4 presents the haematological and CSF profile. Blood total leucocyte count (TLC) and neutrophil percentage were highest in PM and PPM and lowest in

VM and TBM, with a reciprocal lymphocyte pattern (all $p < 0.001$); random blood sugar did not differ significantly ($p = 0.051$). On CSF analysis, protein was highest in TBM (168.04 ± 21.75 mg/dL), sugar was highest in VM (56.01 ± 13.38 mg/dL), and CSF TLC was highest in PM (1748.48 ± 1257.32 cells/mm³), with all differences significant ($p < 0.001$).

Cell predominance aligned closely with aetiology: all PM cases showed neutrophilic predominance and all VM and TBM cases showed lymphocytic predominance, whereas PPM displayed a transitional mixed pattern (61.9% neutrophilic, 33.3% lymphocytic, 4.8% mixed; $p < 0.001$).

Table 4: Haematological and cerebrospinal fluid profile by meningitis category (n=85)

Variable	PM	PPM	VM	TBM	p-value
Blood TLC (cells/mm ³)	20205.84±5488.29	13669.29±2780.37	11094.00±2659.72	12421.38±4180.61	<0.001
Blood neutrophil (%)	76.84±9.41	75.05±9.36	32.54±10.47	36.62±12.32	<0.001
Blood lymphocyte (%)	23.16±9.41	24.95±9.36	67.46±10.47	63.38±12.32	<0.001
Random blood sugar (mg/dL)	118.52±33.16	118.86±43.59	96.88±17.73	114.92±26.79	0.051
CSF protein (mg/dL)	102.40±44.51	78.68±29.20	59.18±12.64	168.04±21.75	<0.001
CSF sugar (mg/dL)	34.45±10.05	39.05±7.66	56.01±13.38	38.30±5.11	<0.001
CSF TLC (cells/mm ³)	1748.48±1257.32	793.10±563.39	280.38±161.88	221.00±112.01	<0.001
CSF neutrophil (%)	80.36±7.95	53.48±12.04	20.00±7.14	19.69±5.63	<0.001
CSF lymphocyte (%)	19.64±7.95	46.52±12.04	80.00±7.14	80.31±5.63	<0.001
Neutrophilic predominance CSF	25 (100.0%)	13 (61.9%)	0 (0.0%)	0 (0.0%)	<0.001
Lymphocytic predominance CSF	0 (0.0%)	7 (33.3%)	26 (100.0%)	13 (100.0%)	<0.001

TLC, total leucocyte count; CSF, cerebrospinal fluid.

Microbiological and radiological findings are shown in Table 5.

Blood culture positivity was confined to PM (56.0%; $p < 0.001$); CSF Gram stain was positive in 56.0% of PM and 9.5% of PPM, with no positive VM or TBM case ($p < 0.001$); and CSF culture yielded organisms in 64.0% of PM and one TBM case ($p < 0.001$). Tubercular markers were concentrated in TBM: GeneXpert detected

Mycobacterium tuberculosis in 69.2%, Ziehl-Neelsen staining was positive in 23.1%, and Mantoux positivity (≥ 10 mm) was present in 76.9% (all $p < 0.001$). CSF HSV PCR was positive only in VM (3 cases, 11.5%; $p = 0.070$).

Neuroimaging was performed in 81 of 85 children (95.3%) and was abnormal in all 13 TBM cases (100.0%) but in no VM case (92.3% normal; $p < 0.001$).

Table 5: Etiological, microbiological, and radiological findings by meningitis category (n=85)

Finding	PM	PPM	VM	TBM	p-value
Blood culture positive	14 (56.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<0.001
CSF Gram stain positive	14 (56.0%)	2 (9.5%)	0 (0.0%)	0 (0.0%)	<0.001
CSF culture positive	16 (64.0%)	0 (0.0%)	0 (0.0%)	1 (7.7%)	<0.001
CSF GeneXpert MTB positive	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (69.2%)	<0.001
CSF ZN stain AFB positive	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (23.1%)	<0.001
CSF HSV PCR positive	0 (0.0%)	0 (0.0%)	3 (11.5%)	0 (0.0%)	0.070
Mantoux positive (≥ 10 mm)	0 (0.0%)	2 (9.5%)	0 (0.0%)	10 (76.9%)	<0.001
Neuroimaging abnormal	9 (36.0%)	6 (28.6%)	0 (0.0%)	13 (100.0%)	<0.001

MTB, *Mycobacterium tuberculosis*; ZN, Ziehl-Neelsen; AFB, acid-fast bacilli; HSV, herpes simplex virus.

Spearman correlation analysis (Table 6) showed

that serum CRP correlated most strongly with CSF

neutrophil percentage ($p=0.71$, $p<0.001$), followed by blood neutrophil percentage ($p=0.67$, $p<0.001$), blood TLC ($p=0.57$, $p<0.001$), and CSF TLC ($p=0.53$, $p<0.001$). CSF protein showed a weak positive correlation ($p=0.36$, $p<0.001$) and CSF sugar a weak negative

correlation ($p=-0.34$, $p=0.001$), consistent with the pattern of rising protein and falling glucose in bacterial disease. Mantoux induration showed no meaningful correlation with serum CRP ($p=0.01$, $p=0.901$), indicating that CRP and tuberculin reactivity reflect distinct biological processes.

Table 6: Spearman correlation of serum CRP with blood and CSF parameters (n=85)

Variable	Correlation coefficient (ρ)	p-value
Blood TLC	0.57	<0.001
Blood neutrophil (%)	0.67	<0.001
CSF protein	0.36	<0.001
CSF sugar	-0.34	0.001
CSF TLC	0.53	<0.001
CSF neutrophil (%)	0.71	<0.001
Mantoux induration	0.01	0.901

TLC, total leucocyte count; CSF, cerebrospinal fluid.

Discussion

The present study compared serum CRP levels among children with pyogenic, partially treated pyogenic, viral, and tubercular meningitis and characterised the associated clinical, epidemiological, and aetiological profile. Serum CRP differed markedly across the four categories, being highest in pyogenic disease, lowest in viral disease, and intermediate in partially treated and tubercular meningitis, and showed good diagnostic accuracy (AUC 0.902) for distinguishing bacterial from non-bacterial disease. These findings support serum CRP as a rapid, accessible adjunct for early aetiological triage in children with suspected meningitis.

Aetiological Distribution and Demographic Profile: Viral meningitis was the largest category in the present cohort (30.6%), closely followed by pyogenic meningitis (29.4%), with partially treated pyogenic (24.7%) and tubercular meningitis (15.3%) accounting for the remainder. This four-way distribution, incorporating both partially treated and tubercular disease, reflects the diagnostic complexity encountered in Indian paediatric practice, where prior antibiotic exposure and endemic tuberculosis are common confounders of classical culture-based classification. Deniz et al. similarly described substantial diagnostic uncertainty in a paediatric CNS-infection cohort, with a causative organism identified in less than a third of meningitis cases, mirroring the difficulty encountered here, particularly within the partially treated group [15].

The overall mean age in the present study was 1.94 ± 1.56 years, with tubercular meningitis affecting the oldest children (3.20 ± 1.25 years) and pyogenic meningitis the youngest (1.24 ± 1.03 years); age differed significantly across categories ($p<0.001$), whereas gender, socioeconomic status, and vaccination status did not. This age gradient, with bacterial disease concentrated in infancy and

tubercular disease in slightly older children, is biologically plausible given the relatively immature immune response of infants to encapsulated organisms and the typically subacute course of tubercular meningitis, which allows longer prodromal periods before diagnosis [2,3].

Serum CRP across Meningitis Categories:

Serum CRP was markedly and significantly higher in pyogenic meningitis (mean 98.76 ± 23.53 mg/L) than in viral meningitis (13.39 ± 7.73 mg/L), with partially treated pyogenic (51.04 ± 28.52 mg/L) and tubercular meningitis (42.37 ± 19.12 mg/L) occupying an intermediate position. This gradient is consistent with the broader literature establishing CRP as an acute-phase reactant that rises sharply in bacterial infection through interleukin-6-driven hepatic synthesis, with a comparatively blunted response in viral illness [6,12]. Patel et al., studying children with suspected meningitis in central India, similarly found serum CRP useful for differentiating bacterial from non-bacterial disease, supporting the applicability of this marker in the Indian tertiary-care setting [1]. Bilavsky et al. and Dashti et al. likewise demonstrated that CRP, alone or in combination with other acute-phase markers such as procalcitonin, ferritin, and lactate, reliably distinguishes bacterial from viral meningitis in children [4,7].

The categorical CRP analysis in the present study strengthened these continuous findings: a level exceeding 50 mg/L was seen in 96.0% of pyogenic cases and no viral case, while 42.3% of viral cases had CRP ≤ 10 mg/L. Comparable threshold-based discrimination has been reported using CSF CRP in neonates, where Javadinia et al. derived an ROC cut-off with 95% sensitivity and 86% specificity (area under the curve 0.912) for differentiating septic from aseptic neonatal meningitis (8). Although their assay was performed on CSF rather than serum, the concordant direction and comparably high diagnostic accuracy reinforce

CRP as a reliable marker of bacterial inflammation irrespective of the compartment sampled. Babenko et al. similarly used a decision-tree approach incorporating procalcitonin and CRP to discriminate bacterial from enteroviral meningitis in children, further corroborating the discriminatory value of acute-phase markers in this setting [9].

Diagnostic Performance and Correlation with Inflammatory Markers ROC analysis in the present study yielded an area under the curve of 0.902 for serum CRP in distinguishing bacterial from non-bacterial meningitis, with an optimal cut-off of >41.6 mg/L (sensitivity 84.8%, specificity 87.2%). This magnitude of discrimination is consistent with host-biomarker reviews that consistently rank CRP among the more accurate low-cost markers for differentiating bacterial from non-bacterial febrile illness in children, generally outperforming total leucocyte count alone though sometimes trailing procalcitonin in very early infection [11,13,14]. Bernardi et al. similarly concluded that CRP retains substantial diagnostic value for serious bacterial infection in febrile children when interpreted alongside clinical assessment rather than in isolation [13].

Serum CRP correlated most strongly with CSF neutrophil percentage ($\rho=0.71$) and blood neutrophil percentage ($\rho=0.67$), findings that are biologically coherent because both CRP synthesis and neutrophilic pleocytosis are downstream consequences of the same innate inflammatory cascade triggered by pyogenic infection.

Weaker correlations with CSF protein and an inverse correlation with CSF sugar parallel the classical biochemical signature of bacterial meningitis, in which capillary permeability changes raise CSF protein while bacterial and leucocyte glucose consumption lowers CSF sugar [3,5].

The absence of correlation between CRP and Mantoux induration ($\rho=0.01$) is consistent with the distinct, cell-mediated immunological basis of tuberculin reactivity, which is not primarily driven by the acute-phase response that governs CRP synthesis; this observation echoes work using CSF adenosine deaminase and CRP as complementary rather than interchangeable markers in tubercular meningitis [5,16].

Haematological, CSF, and Aetiological Findings:

The present study demonstrated coherent inflammatory gradients across categories: blood TLC and neutrophil percentage were highest in pyogenic and partially treated pyogenic disease and lowest in viral and tubercular disease, with a reciprocal lymphocyte pattern (all $p<0.001$). CSF protein was highest in tubercular meningitis, CSF sugar was highest in viral meningitis, and CSF TLC was highest in pyogenic meningitis, and cell

predominance was almost entirely non-overlapping between pyogenic (neutrophilic) and viral/tubercular (lymphocytic) disease, with partially treated pyogenic meningitis alone showing a transitional mixed pattern.

These findings reproduce the classical CSF cytological and biochemical signatures long used to support meningitis classification and corroborate the criteria applied by Javadinia et al. in defining septic versus aseptic neonatal meningitis on the basis of CSF leucocyte count, neutrophil predominance, glucose, and protein [8].

Microbiological yield in the present study was concentrated in the expected categories: blood culture, CSF Gram stain, and CSF culture positivity were largely confined to pyogenic meningitis, while GeneXpert detection of *Mycobacterium tuberculosis*, Ziehl-Neelsen staining, and Mantoux positivity were confined to tubercular meningitis. Ersoy et al. similarly developed a composite clinical-and-laboratory scoring system to discriminate tubercular from bacterial meningitis, underscoring that no single biomarker, including CRP, reliably resolves this distinction in isolation and that a multiparameter approach remains necessary [17]. Malla et al. likewise demonstrated the complementary diagnostic role of CSF adenosine deaminase alongside conventional markers across the aetiological spectrum of paediatric meningitis [16], and Hamed et al. reported that combining interleukin-6 with high-sensitivity CRP in CSF and serum improved discrimination of suspected meningitis in children presenting to the paediatric emergency room, a strategy that may further refine the borderline partially treated and tubercular categories identified in the present cohort [18].

Oostenbrink et al. similarly emphasised that clinical meningeal signs combined with laboratory markers, rather than any single test, are needed to safely reduce unnecessary lumbar punctures while not missing bacterial disease [20], a principle consistent with the multiparameter classification approach adopted in the present study. Kumar et al. additionally reported concordant elevations of CSF and serum CRP in children with acute encephalitis syndrome of infectious aetiology, supporting the broader applicability of CRP-based triage across overlapping CNS infection syndromes [19].

Strengths and Limitations: A notable strength of the present study is its four-category framework, which extended the conventional bacterial-versus-viral comparison to include the clinically challenging partially treated pyogenic and tubercular groups, supported by a comprehensive haematological, biochemical, microbiological, and radiological panel. The simultaneous reporting of continuous CRP values, categorical thresholds,

ROC-based diagnostic performance, and correlation analyses provided a multidimensional characterisation of serum CRP in childhood meningitis.

Several limitations warrant acknowledgement. The single-centre design and modest overall sample size, particularly the small tubercular subgroup (n=13), may limit generalisability. The cross-sectional design captured serum CRP only at admission and could not assess serial trends or treatment response.

Considerable overlap in CRP values was observed within the partially treated and tubercular groups, indicating that CRP alone cannot reliably resolve these intermediate categories and must be interpreted alongside CSF and microbiological findings. Finally, comparison with the wider literature was constrained by heterogeneity in specimen type (serum versus CSF), classification schemes, and reported diagnostic metrics across studies.

Conclusion

Serum C-reactive protein discriminated clearly between bacterial and viral childhood meningitis in the present cohort, being markedly elevated in pyogenic disease, lowest in viral disease, and intermediate in partially treated pyogenic and tubercular meningitis, with good overall diagnostic accuracy (AUC 0.902; optimal cut-off >41.6 mg/L; sensitivity 84.8%, specificity 87.2%). The elevation of serum CRP paralleled neutrophilic inflammation in both peripheral blood and CSF, while showing no relationship with tuberculin reactivity. These observations support serum CRP as a rapid, inexpensive, and readily available adjunct for the early differentiation of bacterial from viral meningitis, facilitating timely decisions regarding empirical antimicrobial therapy in children.

Because partially treated and tubercular meningitis showed considerable overlap in CRP values, the marker is most informative when interpreted alongside CSF cytology, biochemistry, microbiology, and neuroimaging rather than in isolation. Larger, multicentre, prospective studies incorporating serial CRP measurement are recommended to refine diagnostic thresholds and clarify the prognostic value of this marker in childhood meningitis.

Ethical Approval: The study was approved by the Institutional Ethics Committee, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, prior to commencement [insert approval number]. Written informed consent was obtained from parents/guardians of all participants, with assent from children where applicable.

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