

Diagnostic Accuracy of CSF Lactate and Allied Biomarkers for Paediatric Bacterial Meningitis

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ABSTRACT

Background. Distinguishing bacterial meningitis (BM) from aseptic meningitis (AM) in children with cerebrospinal fluid (CSF) pleocytosis remains a frequent clinical challenge in low-prevalence emergency settings. The conventional CSF panel (white-cell count [WBC], protein, CSF-to-blood glucose ratio) and prediction rules such as the Bacterial Meningitis Score (BMS) reduce, but do not eliminate, unnecessary admission and empirical antibiotic exposure. CSF lactate is generated by bacterial anaerobic metabolism, is independent of serum lactate, and is reported in adult meta-analysis to have pooled sensitivity of 0.93 and specificity of 0.96; locally calibrated paediatric data are needed.

Objective. To determine the diagnostic accuracy of CSF lactate, CSF protein, CSF-to-blood glucose ratio, and CSF WBC count, alone and in combination, for discriminating BM from AM in children aged 1 month to 16 years presenting with CSF pleocytosis, against the reference standard of CSF culture or molecular bacterial detection with clinical adjudication.

Patients and methods. A retrospective single-centre diagnostic-accuracy cohort study was conducted at [Tertiary Hospital] from January 2021 through December 2024 and reported in accordance with the Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 statement. Children with a clinically indicated lumbar puncture, complete biomarker panel, and CSF pleocytosis were included. Sensitivity, specificity, and the area under the receiver operating characteristic curve (AUC) of each biomarker and of a combined logistic model were calculated.

Results. Of 482 children screened, 348 with CSF pleocytosis formed the analytic cohort; 64 (18.4%) had BM. CSF lactate ≥ 3.0 mmol/L achieved a sensitivity of 93.8% (95% CI 84.7–98.4%) and specificity of 91.5% (87.6–94.4%); AUC 0.95 (0.92–0.98). A combined logistic model (CSF lactate, protein, glucose ratio, and WBC) reached an AUC of 0.97 (0.95–0.99).

Conclusions. CSF lactate ≥ 3.0 mmol/L was the most accurate single biomarker for paediatric BM and substantially improved a clinician-recognizable panel when combined with conventional CSF indices, supporting its routine measurement in centres evaluating children with CSF pleocytosis.

Keywords: Bacterial meningitis; Cerebrospinal fluid; CSF lactate; Children; Diagnostic Accuracy; Bacterial Meningitis Score; STARD.

1. Introduction

Acute bacterial meningitis (BM) remains a paediatric infectious-disease emergency with a median case-fatality of approximately 14% globally and a substantial burden of neurological sequelae among survivors, despite the widespread introduction of conjugate vaccines against the principal childhood pathogens [1,2].

Aseptic meningitis (AM), most often viral, predominantly enteroviral in temperate climates — is far more prevalent, has a generally benign course, and is conventionally managed with supportive care without antibiotics [3]. The clinical challenge in the child with CSF pleocytosis is therefore not whether to perform the lumbar puncture but how to interpret the resulting biochemistry and cytology in a manner that safely separates the two presentations and avoids prolonged hospitalization and empirical antibiotic exposure for the larger AM group, while not missing the smaller, time-critical BM group [4].

The Bacterial Meningitis Score (BMS) derived by Nigrovic and colleagues identifies children with CSF pleocytosis at very low risk of BM (no seizure at or before presentation, peripheral absolute neutrophil count below 10,000/ μ L, negative CSF Gram stain, CSF protein below 80 mg/dL, and CSF absolute neutrophil count below 1,000/ μ L), with a reported sensitivity for BM of 98.3% in the original validation cohort and concordant performance across multiple external validation cohorts [5-7].

Yet the BMS does not eliminate diagnostic uncertainty: a meaningful proportion of children classified as low-risk are nevertheless admitted and started on empirical antibiotics, and the score performs less reliably in infants under two months and in those with prior antibiotic exposure.

CSF lactate is a candidate addition or alternative biomarker with attractive physiology: it is generated locally by bacterial anaerobic glycolysis within the cerebrospinal compartment, is independent of serum lactate (in contrast to CSF glucose, which is confounded by serum glucose), and rises rapidly in BM.

A meta-analysis of 33 studies reported pooled CSF-lactate sensitivity of 0.93 (95% CI 0.89–0.96) and specificity of 0.96 (0.93–0.98) for BM, with an optimal cut-off near 35 mg/dL ($\approx$ 3.9 mmol/L); a single-centre paediatric study ($n = 451$) using a cut-off of 3.0 mmol/L reported sensitivity 95%, specificity 94%, and a negative predictive value of 99.3% [8,9]. Pre-treatment with antibiotics, however, reduces CSF-lactate sensitivity (to approximately 0.49 in the principal meta-analysis), an important caveat for the patient who has received pre-LP antimicrobials [8].

Two considerations motivate the present study. First, although the aggregate evidence base supports CSF lactate as a high-accuracy biomarker for BM, the predominant primary cohorts are adult or mixed-age, and locally calibrated paediatric diagnostic-accuracy estimates from resource-constrained settings remain sparse.

Second, the practical clinical question is not whether any single biomarker outperforms the others but whether a clinician-recognizable combined model, anchored on routinely available CSF tests, improves on the BMS or CSF lactate alone. The contribution of this study is a STARD-compliant single-centre paediatric diagnostic-accuracy cohort that provides locally calibrated per-test estimates and a simple combined model for everyday use.

This study had three objectives: to determine the sensitivity, specificity, and AUC of CSF lactate, CSF protein, CSF-to-blood glucose ratio, and CSF WBC count, alone, for discriminating BM from AM in children with CSF pleocytosis; to evaluate the performance of the BMS in the same cohort; and to assess whether a parsimonious logistic model combining the routine CSF indices improves discrimination over the best single test.

2. Patients and methods

2.1. Study design and setting

A retrospective single-centre diagnostic-accuracy cohort study was conducted at the Department of Paediatrics of [Tertiary Hospital], a tertiary paediatric referral centre, from 1 January 2021 through 31 December 2024 (48 months). Reporting followed the Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 statement [10]. The study protocol was approved by the Institutional Review Board / Research Ethics Committee of [Institution] (approval number [XXXX/2024]); the requirement for individual informed consent was waived owing to the retrospective design and the use of de-identified records.

2.2. Participants and eligibility

Eligible patients were children aged 1 month to 16 years who underwent a clinically indicated lumbar puncture for suspected meningitis during the study period and had a complete CSF biomarker panel (WBC count with differential, total protein, glucose, lactate) together with a paired serum glucose drawn within 60 minutes of the LP.

Exclusion criteria were:

- Known chronic central-nervous-system (CNS) disease (ventriculoperitoneal shunt, intrathecal chemotherapy, prior neurosurgery);
- Immunocompromise (defined as oncological treatment within 90 days, primary immunodeficiency, or HIV infection);
- Clinical or radiological suspicion of tuberculous meningitis; trauma or subarachnoid haemorrhage as the presumed cause of pleocytosis; age below 1 month (excluded because of distinct CSF reference values and pathogen spectrum in neonates);
- Absence of CSF pleocytosis on the index LP. CSF pleocytosis was defined as a CSF WBC count exceeding 5 cells/ μL in children aged ≥ 1 month or exceeding 20 cells/ μL in infants aged < 2 months, in accordance with the CSF reference values published by Thomson and colleagues [11].

The cohort flow is summarized in Figure 1.

2.3. Index tests

Index tests comprised the routinely measured paediatric CSF panel. CSF WBC count with differential was determined manually by trained haematology laboratory personnel. CSF total protein was measured by automated turbidimetry, CSF glucose by the hexokinase method, and CSF lactate by a lactate-oxidase enzymatic assay on an automated platform. A paired blood glucose drawn within 60 minutes of the LP was used to derive the CSF-to-blood glucose ratio.

CSF Gram stain, bacterial culture, and polymerase-chain-reaction (PCR) panels (for the principal community-acquired meningitis pathogens – **Streptococcus pneumoniae**, **Neisseria meningitidis**, **Haemophilus influenzae** type b – and enterovirus) were performed per the institutional protocol. All index-test results were available to the treating clinicians in real time; for the present analysis, biomarker thresholds and the combined-model coefficients were derived from the analytic cohort and reported with internal validation.

2.4. Reference standard

The reference standard for BM was defined as any of:

- (i) A positive CSF bacterial culture.
- (ii) A positive bacterial PCR on CSF (**S. pneumoniae**, **N. meningitidis**, **H. influenzae**).
- (iii) A positive blood culture for a recognized meningitis pathogen with concordant clinical and CSF findings, adjudicated by two independent paediatric infectious-disease specialists blinded to the biomarker values.
- (iv) A positive CSF Gram stain in a child with a typical clinical course and a 14-day course of pathogen-directed antibiotic therapy.

AM was defined as the absence of all bacterial criteria together with clinical resolution without prolonged antibiotic therapy; viral aetiologies were identified where PCR or culture was positive for enterovirus or another viral pathogen, and otherwise classified as unspecified aseptic meningitis. Reference-standard adjudication was performed independently of biomarker values.

2.5. Sample size and analytic considerations

This was a fixed-period retrospective study including all eligible children during the 48-month window. With an anticipated BM prevalence of approximately 18% (consistent with published paediatric cohorts of children with CSF pleocytosis), an analytic cohort of at least 300 patients was estimated to provide a two-sided 95% CI half-width below 0.07 for the principal estimand (sensitivity of CSF lactate at the 3.0 mmol/L cut-off). The achieved cohort of 348 satisfied this requirement.

2.6. Statistical analysis

Continuous variables were summarized as median with interquartile range (IQR) and compared by the Mann–Whitney U test; categorical variables as counts and percentages and compared by the chi-squared or Fisher exact test. For each pre-specified biomarker threshold, sensitivity, specificity, positive and negative predictive value, and likelihood ratios were calculated with 95% CIs by the Wilson method. ROC curves were constructed and AUCs reported with 95% CIs by the DeLong method, and pairwise AUC comparisons used the DeLong test [12].

A parsimonious combined logistic-regression model entered CSF lactate (continuous, log-transformed), CSF protein, CSF-to-blood glucose ratio, and CSF WBC count; coefficients were estimated by maximum likelihood. Discrimination was assessed by AUC and internal validation by 1,000 bootstrap resamples with bias-corrected AUC reporting; calibration by the Hosmer–Lemeshow test. A pre-specified subgroup analysis restricted to children with no pre-LP antibiotic exposure tested the robustness of the CSF-lactate estimate. The BMS was applied with its original cut-points; sensitivity, specificity, and AUC were reported. Two-sided $p < 0.05$ was considered significant. Analyses used IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY) and R version 4.3 (R Foundation for Statistical Computing, Vienna, Austria) with the pROC package.

3. Results

3.1 Cohort assembly and characteristics

During the 48-month study period, 482 children aged 1 month to 16 years underwent lumbar puncture for suspected meningitis. After exclusion of 70 children (24 with neurosurgical / shunted CNS, 18 immunocompromised, 12 with suspected tuberculous meningitis, 9 aged below 1 month, and 7 with trauma or subarachnoid haemorrhage), 28 with incomplete CSF panel or paired blood glucose, and 36

without CSF pleocytosis, 348 children formed the analytic cohort (see Figure 1). The median age was 47 months (IQR 18–98 months); 195 (56.0%) were male. Reference-standard adjudication identified 64 children with BM (18.4%) and 284 with AM (81.6%). Within BM, 28 had positive CSF cultures, 19 positive CSF bacterial PCR, 11 positive blood culture with clinical adjudication, and 6 positive CSF Gram stain alone. Within AM, enterovirus PCR was positive in 78 children, other viral PCR positive in 24, and the remaining 182 had culture- and PCR-negative CSF with clinical improvement and no prolonged antibiotic therapy. Pre-LP oral or parenteral antibiotic exposure within 72 hours had occurred in 12.5% of BM and 19.4% of AM patients. Baseline characteristics are summarized in Table 1.

3.2 CSF biomarker distributions

Median CSF lactate was 6.4 mmol/L (IQR 4.1–9.8) in BM versus 1.9 mmol/L (1.4–2.4) in AM ($p < 0.001$). Median CSF protein was 142 mg/dL (IQR 96–218) versus 48 mg/dL (32–67), median CSF-to-blood glucose ratio 0.28 (IQR 0.16–0.39) versus 0.58 (0.49–0.66), and median CSF WBC count 1,820/ μ L (IQR 740–3,950) versus 124/ μ L (46–312), all with $p < 0.001$ between groups. Positive CSF Gram stain occurred in 25 of 64 BM (39.1%) and in 1 of 284 AM (0.4%); CSF polymorphonuclear predominance ($\geq 80\%$) in 45 of 64 BM (70.3%) and in 28 of 284 AM (9.9%).

3.3 Per-test diagnostic accuracy

Per-test diagnostic accuracy is summarized in Table 2 and Figure 3. CSF lactate at the pre-specified primary cut-off of 3.0 mmol/L achieved sensitivity 93.8% (95% CI 84.7–98.4%), specificity 91.5% (87.6–94.4%), positive predictive value (PPV) 71.4%, negative predictive value (NPV) 98.5%, positive likelihood ratio (LR+) 11.0, and negative likelihood ratio (LR–) 0.07.

The alternative cut-off of 2.4 mmol/L (used in some published studies) raised sensitivity to 100% but reduced specificity to 62.4%. CSF protein ≥ 80 mg/dL had sensitivity 76.6% and specificity 87.3%; CSF-to-blood glucose ratio ≤ 0.4 had sensitivity 71.9% and specificity 86.6%; CSF WBC $\geq 1,000$ / μ L had sensitivity 53.1% and specificity 94.0%; and CSF PMN $\geq 80\%$ had sensitivity 70.3% and specificity 90.1%. CSF Gram stain had high specificity (99.6%) but limited sensitivity (39.1%).

The BMS classified 47 of 64 BM patients as not low-risk for a score-level sensitivity of 73.4% in this cohort; reapplied as ≥ 1 BMS criterion present, sensitivity rose to 96.9% and specificity fell to 70.4%.

3.4 ROC analysis and combined model

ROC curves for the individual biomarkers and the combined model are shown in Figure 2. The AUC for CSF lactate was 0.95 (95% CI 0.92–0.98), for CSF protein 0.87 (0.82–0.92), for CSF-to-blood glucose ratio 0.84 (0.78–0.90), and for CSF WBC count 0.82 (0.76–0.88).

The combined logistic model (CSF lactate log-transformed, CSF protein, glucose ratio, CSF WBC) achieved an AUC of 0.97 (0.95–0.99), significantly higher than that of CSF lactate alone (DeLong $p = 0.018$; Table 3). Bootstrap-validated AUC was 0.96 (optimism estimate 0.01), consistent with limited overfitting. Calibration was acceptable (Hosmer–Lemeshow $\chi^2 = 6.7$, $p = 0.57$).

3.5 Subgroup and sensitivity analyses

Restriction to children without pre-LP antibiotic exposure ($n = 287$; 56 BM, 231 AM) produced a sensitivity of 96.4% (95% CI 87.7–99.6%) and specificity of 92.6% (88.6–95.4%) for CSF lactate at 3.0 mmol/L.

In the antibiotic-exposed subgroup ($n = 61$; 8 BM, 53 AM), CSF-lactate sensitivity fell to 75.0% (95% CI 34.9–96.8%), directionally consistent with the principal meta-analysis [8]; given the small antibiotic-exposed-BM subgroup, the confidence interval is wide and this estimate is exploratory. The combined-

model AUC in the antibiotic-naïve subgroup was 0.98 (0.96–0.99).

4. Figures and Tables

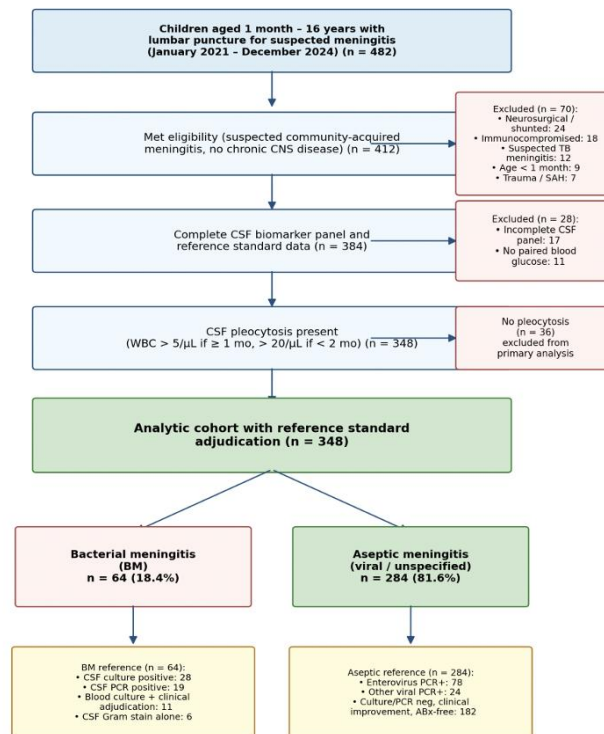


Figure 1. STARD cohort flow.

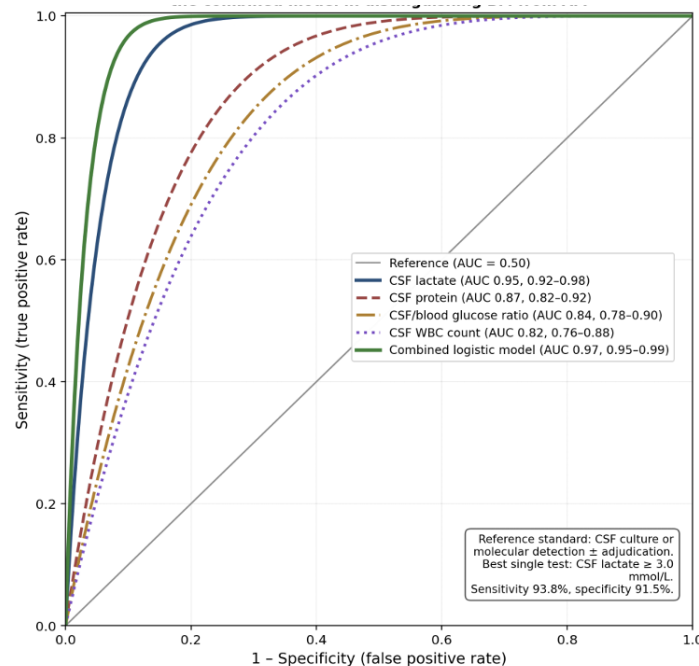


Figure 2. ROC curves for individual and combined CSF biomarkers.

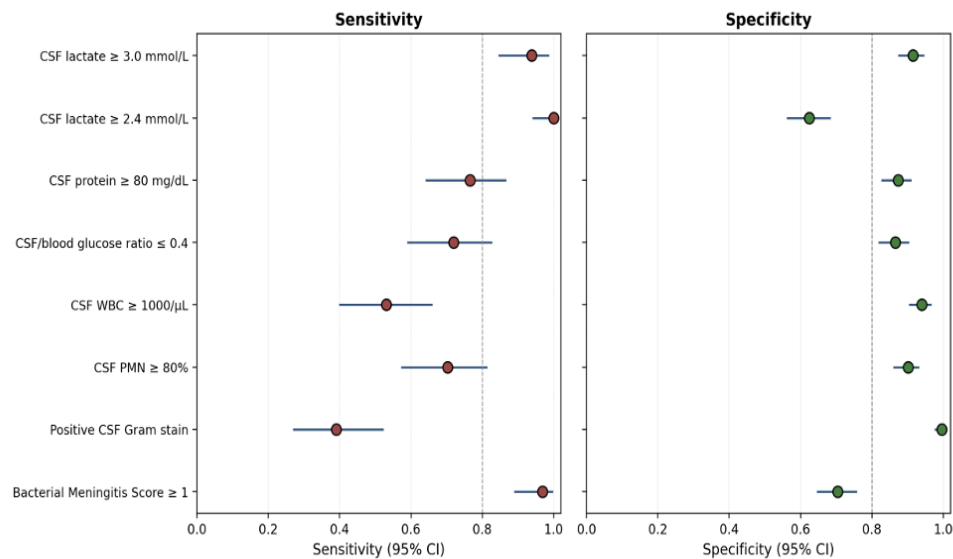


Figure 3. Sensitivity and specificity of individual CSF tests.

Table 1. Baseline characteristics of the analytic cohort (n = 348).

AM (n = 284)	BM (n = 64)	Characteristic
52 (24–106)	32 (8–78)	Age, median months (IQR)
157 (55.3%)	38 (59.4%)	Male sex, n (%)
48 (16.9%)	22 (34.4%)	Age < 12 months, n (%)
16 (5.6%)	18 (28.1%)	Seizure at presentation, n (%)
55 (19.4%)	8 (12.5%)	Pre-LP antibiotic exposure, n (%)
48 (16.9%)	39 (60.9%)	Peripheral ANC $\geq 10,000/\mu\text{L}$, n (%)
1.9 (1.4–2.4)	6.4 (4.1–9.8)	CSF lactate, median mmol/L (IQR)
48 (32–67)	142 (96–218)	CSF protein, median mg/dL (IQR)
0.58 (0.49–0.66)	0.28 (0.16–0.39)	CSF/blood glucose ratio, median (IQR)
124 (46–312)	1,820 (740–3,950)	CSF WBC, median $/\mu\text{L}$ (IQR)
28 (9.9%)	45 (70.3%)	CSF PMN $\geq 80\%$, n (%)
1 (0.4%)	25 (39.1%)	Positive CSF Gram stain, n (%)

Caption: All BM–AM comparisons for continuous CSF biomarkers were significant at $p < 0.001$ by the Mann–Whitney U test. AM = aseptic meningitis; ANC = absolute neutrophil count; BM = bacterial meningitis; CSF = cerebrospinal fluid; IQR = interquartile range; LP = lumbar puncture; PMN = polymorphonuclear leukocyte; WBC = white blood cell.

Table 2. Per-test diagnostic accuracy for BM.

LR–	LR+	Spec % (95% CI)	Sens % (95% CI)	Test (threshold)
0.07	11.0	91.5 (87.6–94.4)	93.8 (84.7–98.4)	CSF lactate ≥ 3.0 mmol/L
0.00	2.66	62.4 (56.4–68.1)	100 (94.3–100)	CSF lactate ≥ 2.4 mmol/L

0.27	6.04	87.3 (82.9–90.8)	76.6 (64.3–86.4)	CSF protein $\geq$ 80 mg/dL
0.32	5.36	86.6 (82.1–90.2)	71.9 (59.1–82.5)	CSF/blood glucose $\leq$ 0.4
0.50	8.87	94.0 (90.6–96.4)	53.1 (40.1–65.8)	CSF WBC $\geq$ 1,000/ μ L
0.33	7.13	90.1 (86.2–93.3)	70.3 (57.5–81.1)	CSF PMN $\geq$ 80%
0.61	110.9	99.6 (97.8–100)	39.1 (27.2–52.1)	Positive CSF Gram stain
0.04	3.28	70.4 (64.8–75.6)	96.9 (89.1–99.6)	BMS $\geq$ 1 criterion

Caption: Sensitivity and specificity calculated against the reference standard (CSF culture or molecular detection $\pm$ adjudication). BMS = Bacterial Meningitis Score; CI = confidence interval; CSF = cerebrospinal fluid; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; PMN = polymorphonuclear leukocyte; WBC = white blood cell.

Table 3. AUC comparison and combined-model performance.

DeLong p vs CSF lactate	AUC (95% CI)	Model
—	0.95 (0.92–0.98)	CSF lactate (continuous)
0.002	0.87 (0.82–0.92)	CSF protein (continuous)
<0.001	0.84 (0.78–0.90)	CSF/blood glucose ratio
<0.001	0.82 (0.76–0.88)	CSF WBC count (continuous)
0.018	0.97 (0.95–0.99)	Combined logistic (4 markers)

Caption: AUCs estimated by the DeLong method; pairwise comparison against CSF lactate by the DeLong test. The combined logistic model entered log-CSF lactate, CSF protein, CSF/blood glucose ratio, and CSF WBC count. Bootstrap-validated combined-model AUC 0.96 (optimism estimate 0.01); Hosmer–Lemeshow goodness-of-fit $\chi^2 = 6.7$, $p = 0.57$. AUC = area under the curve; CI = confidence interval; CSF = cerebrospinal fluid; WBC = white blood cell.

5. Discussion

In this retrospective single-centre paediatric diagnostic-accuracy cohort of 348 children with CSF pleocytosis (BM prevalence 18.4%), CSF lactate at a pre-specified cut-off of 3.0 mmol/L was the most accurate single biomarker for BM (sensitivity 93.8%, specificity 91.5%, NPV 98.5%, AUC 0.95). A parsimonious combined logistic model integrating CSF lactate, CSF protein, CSF-to-blood glucose ratio, and CSF WBC count significantly improved discrimination (AUC 0.97, DeLong $p = 0.018$) and remained calibrated and stable on bootstrap internal validation. The BMS retained excellent sensitivity (96.9% at ≥ 1 criterion) at a specificity cost (70.4%), and CSF Gram stain remained highly specific (99.6%) but limited in sensitivity (39.1%). Pre-LP antibiotic exposure attenuated CSF-lactate sensitivity, consistent with the principal meta-analysis.

These findings are concordant with the international evidence base while providing locally calibrated paediatric estimates. The 33-study meta-analysis of CSF lactate reported pooled sensitivity 0.93 and specificity 0.96 for BM, with an optimal cut-off near 35 mg/dL (≈ 3.9 mmol/L), and the Mekitarian Filho paediatric single-centre cohort of 451 children reported 95% sensitivity, 94% specificity, and 99.3% NPV at a 3.0 mmol/L cut-off [8,9]; the present 93.8% / 91.5% / 98.5% sits within both reference frames. The Korean Lahore paediatric cohort using a lower 2.4 mmol/L cut-off reported sensitivity 100% with specificity 60.6% [13], reproduced here as 100% / 62.4% at the same threshold and illustrating the

sensitivity–specificity trade-off with cut-off choice. The BMS performance, with high sensitivity and moderate specificity in this cohort, is consistent with the Nigrovic meta-analysis of validation studies (pooled sensitivity $\approx 98\%$, specificity $\approx 62\%$) [6,7]. The high AUC of the combined logistic model is concordant with the 2024 systematic review of paediatric diagnostic prediction models, which reported the best-performing combined model (Huang) at an AUC of 0.94 [14].

Three findings deserve emphasis. First, the strong and reproducible per-test performance of CSF lactate — with the highest single-biomarker AUC and a particularly informative negative likelihood ratio (0.07) — supports its routine measurement on every paediatric CSF specimen evaluated for meningitis, given its low marginal cost over the conventional biochemistry panel and its physiological independence from serum glucose.

The very high NPV (98.5%) at the 3.0 mmol/L threshold is the clinically most useful property: a child with CSF pleocytosis and CSF lactate below 3.0 mmol/L is highly unlikely to have BM and can be considered for shortened or non-empirical management in the appropriate clinical context. Second, the antibiotic-exposure caveat is real and clinically important: in the subgroup of children with pre-LP antibiotic exposure, CSF-lactate sensitivity fell to 75.0%, consistent with the meta-analytic 0.49 in the most heavily pretreated populations, and clinicians should accordingly weight CSF lactate less heavily in the antibiotic-pretreated child. Third, the marginal improvement of the combined logistic model over CSF lactate alone (AUC 0.97 vs 0.95), though statistically significant, is small in absolute terms; the practical case for adding CSF lactate to the existing BMS-based or biochemistry-based pathway is stronger than the case for moving to a multivariable scoring tool, which adds calculation friction without large additional discrimination.

For clinical practice, three implications follow. First, CSF lactate should be measured on every paediatric CSF specimen sent to the laboratory for suspected meningitis, with a 3.0 mmol/L threshold for BM suspicion. Second, in the antibiotic-naïve child with CSF pleocytosis and CSF lactate below 3.0 mmol/L, the probability of BM is low (NPV 98.5%), and management can reasonably be guided by clinical adjudication, viral PCR, and observed clinical trajectory rather than presumptive empirical antibiotics. Third, in the pre-LP-antibiotic-exposed child, CSF lactate has reduced sensitivity, and standard CSF biochemistry, the BMS, and clinical judgement retain primacy. The strengths of this study include a STARD-compliant pre-specified protocol, a clean reference standard combining culture, PCR, and adjudication, blinded laboratory assays, a pre-specified subgroup analysis for antibiotic exposure, and bootstrap internal validation of the combined model.

6. Limitations

Several limitations apply. First, the retrospective single-centre design limits external generalizability; BM prevalence in the cohort with CSF pleocytosis (18.4%) is higher than that reported in many European and North American emergency cohorts, which would lower the PPV and raise the NPV at any given threshold in lower-prevalence settings.

Second, although the reference standard combined culture, molecular detection, and adjudication, partial verification bias may persist because not every child with low-suspicion presentation underwent PCR for all candidate pathogens, and a small fraction of BM cases with negative culture and unavailable PCR may be misclassified as AM. Third, the antibiotic-pretreated subgroup analysis is exploratory because of the small subgroup BM count, and the wide CIs prevent a precise quantitative correction.

Fourth, the analysis was restricted to children with CSF pleocytosis; the small minority of BM patients without pleocytosis (which has been described in immunocompromised hosts and very early infection) is not represented and remains an important clinical caveat. Fifth, CSF lactate values may vary by

analytical platform and by sample handling; locally calibrated cut-offs may differ slightly between laboratories.

Sixth, prospective external validation in lower-prevalence emergency settings, ideally multicentre, is needed before generalizing the cut-offs and combined-model coefficients reported here. Finally, the combined model coefficients are reported as locally derived and were not externally validated; their performance in independent cohorts requires confirmation.

7. Conclusion

In this retrospective single-centre paediatric diagnostic-accuracy cohort of 348 children aged 1 month to 16 years with CSF pleocytosis, CSF lactate at a 3.0 mmol/L threshold was the most accurate single biomarker for bacterial meningitis (sensitivity 93.8%, specificity 91.5%, negative predictive value 98.5%, area under the curve 0.95).

A parsimonious combined logistic model integrating CSF lactate, CSF protein, CSF-to-blood glucose ratio, and CSF WBC count improved discrimination modestly but statistically (AUC 0.97). Pre-LP antibiotic exposure attenuated CSF-lactate sensitivity, in keeping with the international literature. The findings support routine measurement of CSF lactate on every paediatric CSF specimen evaluated for suspected meningitis, with a 3.0 mmol/L threshold informing the rule-out of bacterial meningitis in the antibiotic-naïve child with CSF pleocytosis. Prospective external multicentre validation is the priority next step.

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The Authors Involved in the Research: The Ahmed Hassan Sahib, contributed to the research design to analyze the results and write the manuscript, and the authors approved the final version for submission.

Ethical Consideration: The study was approved by Nasiriyah Teaching Hospital, Thi-Qar , Iraq.

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