Children With Meningeal Signs

Predicting Who Needs Empiric Antibiotic Treatment

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Background: Since delayed diagnosis and treatment of bacterial meningitis worsens patient prognosis, clinicians have a low threshold to perform a lumbar puncture or to start empiric antibiotic treatment in patients suspected of having meningitis.

Objective: To develop a decision rule, including cerebrospinal fluid (CSF) indices and clinical characteristics, to determine whether empiric antibiotic treatment should be started in children with meningeal signs.

Design: Multivariable logistic regression analysis of retrospectively collected data. Bacterial meningitis was defined as a CSF leukocyte count of more than 5/μL with positive bacterial culture findings from CSF or blood specimens.

Setting: Pediatric emergency department of a pediatric university hospital.

Patients: A total of 227 children (aged 1 month to 15 years) with meningeal signs.

Main Outcome Measure: The diagnostic value of adding early obtainable CSF indices to clinical characteristics to predict bacterial meningitis.

Results: Independent predictors of bacterial meningitis from early obtainable CSF indices were the CSF polymorphonuclear leukocyte count and the CSF–blood glucose ratio. The diagnostic value (area under the receiver operating characteristic curve) of this CSF model was 0.93. Application of the model together with clinical characteristics could predict early the absence of bacterial meningitis in 69 (30%) of the 227 patients so that empiric antibiotic treatment could be safely withheld.

Conclusion: A diagnostic decision rule that uses clinical characteristics at admission, the CSF polymorphonuclear leukocyte count, and the CSF–blood glucose ratio is a useful tool for deciding whether to start empiric antibiotics in children with meningeal signs.

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DELAYED DIAGNOSIS and treatment of bacterial meningitis worsen the prognosis of patients with this condition. Consequently, physicians have a low threshold to perform a lumbar puncture in patients suspected of having meningitis. Moreover, patients with an increased cell count in the cerebrospinal fluid (CSF) are commonly treated for bacterial meningitis until the CSF culture result becomes available (after 48-72 hours).[1-3] Patients with meningeal signs, however, may have diseases other than bacterial meningitis.[4-6] Early discrimination of bacterial meningitis from other diseases can prevent unnecessary hospitalization and potential adverse effects of empiric antibiotic treatment.

Previous studies[7-12] have assessed several characteristics from clinical evaluation or laboratory tests that may predict bacterial meningitis. These studies, however, selected patients on the diagnosis (proven bacterial, viral, and/or aseptic meningitis) or presence of a lumbar puncture. Such a patient selection may lead to bias toward the more evident cases of meningitis and thus to an overestimation of the diagnostic value of tests that in practice will be applied to all patients *suspected* of having meningitis.[13-15] Moreover, in practice the physician is faced with a patient with meningeal signs in whom the diagnosis is not known yet.[13] In accordance with clinical practice, we therefore selected to study children by their clinical presentation (ie, meningeal signs).

In a previous study,[16] we examined 360 children with meningeal signs to derive and validate a prediction rule based on clinical signs and symptoms, which enables physicians to determine whether lumbar puncture is indicated. The aim of the present study was to evaluate, in those patients with an indication for lumbar

puncture, whether early available CSF indices can predict the presence or absence of bacterial meningitis before the CSF culture becomes available. Such predictors could then be used to determine whether empiric antibiotic treatment should be started.

METHODS

PATIENTS

Eligible patients included all patients aged 1 month to 15 years who had visited the emergency department of the Sophia Children's Hospital in Rotterdam, the Netherlands, between January 1, 1988, and December 31, 1998, with meningeal signs. This selection of patients was based on a prospective, problem-oriented patient classification system, by which the main reason (complaint or symptom, abnormal laboratory results, or presumed diagnosis) for visiting the emergency department is prospectively coded.[17] Patients could have more than one complaint or symptom, but the most important one is coded. Meningeal signs, as documented by this coding system, were defined as presence of neck pain as reported in the medical history or presence of meningeal irritation as assessed by either the general practitioner or the pediatrician. Meningeal irritation was defined as presence of Brudzinski sign I or II, Kernig sign, tripod phenomenon, or neck stiffness in children older than 1 year. In children 1 year or younger, signs of meningeal irritation were the signs mentioned herein or irritability during manipulation of head or legs by the pediatrician or a bulging fontanel.[6,16,18] Patients with a history of severe neurologic disease or ventricular drain were excluded. Patients referred from other hospitals were also excluded because in these patients treatment may have been initiated already and influenced the clinical signs at presentation.

In a previous study of 360 children with meningeal signs, the following prediction rule was derived and validated, using clinical signs and symptoms and blood laboratory tests for the presence and absence of bacterial meningitis[16]:

$$
\begin{aligned}
\text{Total Score} &= [1 \times \text{Duration of Main Problem} \\
&\quad (1 \text{ Point for Each Day})] + [2 \times \text{Vomiting in History} \\
&\quad (\text{Yes}=1; \text{No}=0)] + [7.5 \times \text{Meningeal Irritation (Yes}=1; \\
&\quad \text{No}=0)] + [6.5 \times \text{Cyanosis (Yes}=1; \text{No}=0)] + [4 \times \text{Petechiae} \\
&\quad (\text{Yes}=1; \text{No}=0)] + [8 \times \text{Disturbed Consciousness (Yes}=1; \\
&\quad \text{No}=0)] + [0.1 \times \text{Serum C-reactive Protein (CRP)} \\
&\quad (\text{per } 10 \text{ mg/L})].
\end{aligned}
$$

Using this algorithm, a risk score could be computed for each patient by assigning points for each variable present. In all 360 patients (of whom 99 [28%] had bacterial meningitis), the score ranged from 0.5 to 31 points, and the risk of bacterial meningitis increased with the score. In those with a risk score of less than 9.5 points (approximately 35% of the patients), bacterial meningitis seemed always to be absent. In the remaining 227 patients (score, ≥9.5), the risk of bacterial meningitis was 44%.[16] In these 227 patients, the present study assessed the additional predictive value of CSF indices to the presence or absence of bacterial meningitis and the indices use in making the decision of whether to start empiric treatment.

DATA COLLECTION

Demographic data and information on presenting signs and symptoms were retrospectively collected from the pediatric medical record, which has a standard format. Data from laboratory tests of CSF, blood, stool, and urine specimens were retrieved from the computer-documented hospital information system. The following CSF indices were analyzed: the total CSF leukocyte count, the percentage of polymorphonuclear leukocytes (PMNs), the

absolute number of PMNs, protein and glucose concentration, and the gram-stained smear of CSF specimen. The CSF–blood glucose ratio was computed by dividing the CSF glucose level by the serum glucose level (both samples obtained at the same time) and analyzed as a separate variable.

DIAGNOSTIC OUTCOME

The diagnostic outcome was the presence or absence of bacterial meningitis. Its presence was defined as a CSF leukocyte count greater than 5/µL and positive bacterial culture findings from CSF or blood specimens.[2,16] Patients using antibiotics before the lumbar puncture were considered to have pretreated bacterial meningitis if they had an increased CSF leukocyte count and negative bacterial culture results but subsequently were hospitalized and treated with antibiotics for at least 7 days.[9] Final diagnoses other than bacterial meningitis were based on either bacteriologic or viral culture findings from CSF, blood, urine, stool, and ear, nose, or throat specimens or based on a consensus diagnosis.[6] In absence of a lumbar puncture, presence or absence of bacterial meningitis was assessed by follow-up, involving an outpatient department visit or telephone call by one of the pediatricians (R.O.) (in training) within 14 days after presentation.

ANALYSIS

The association between the CSF indices and the presence or absence of bacterial meningitis was quantified using univariate logistic regression analyses. Continuous variables were analyzed without categorization, but various cutoff levels and transformations (square root, log) were evaluated.[19] Subsequently, multivariate logistic regression analysis was used to evaluate the independent value of all CSF indices in the prediction of bacterial meningitis. Model reduction was performed by excluding predictors from the model with $P>.10$, since variables with a $P\leq.10$ were considered to be independently related to bacterial meningitis only.[19] Reliability (goodness of fit) of all models was estimated using the Hosmer and Lemeshow test[20] and the ability to discriminate between patients with and without bacterial meningitis using the area under the receiver operating characteristic curve (ROC area). Differences in the discriminative value between the overall and reduced models were estimated using the ROC areas with 95% confidence intervals (CIs), taking into account the correlation between the models since they were based on the same cases.[21,22]

Since multivariate analysis requires all data to be present in all patients,[19] imputation techniques as available in SOLAS statistical software (version 1.1; Statistical Solutions, Saugus, Mass) were used to fill in missing values of some variables by a (theoretical) value, without disturbing the relationship between the variables as observed in the data. This allowed all patients to be included in the analysis (increased statistical efficiency) and reduced bias since missing data may not occur at random (eg, a record of a seriously sick patient may be more complete than that of a less sick patient), such that the complete cases would reflect a selected sample of children with meningeal signs.[23,24] To account for uncertainties in imputed data,[23,24] the imputation was repeated 5 times (ie, multiple imputation), and 1 prediction model was estimated as described herein from each of the 5 imputed data sets.

Next, to validate each model obtained from each data set and to adjust for too optimistic estimates of the predictors' regression coefficients, random bootstrapping techniques were used.[19,25] Bootstrapping involves taking numerous samples with replacement from the study population sample and is an internal validation technique (ie, it estimates the future performance of the model without using new data). The 5 adjusted regression coefficients and SEs (ie, from each of the 5 imputed

data sets) were then averaged according to standard statistical techniques to obtain one final (adjusted) model.[24] This adjusted final model was then transformed into a CSF prediction rule by rounding the coefficients of the included variables to the nearest half integer. A total CSF score was computed for each individual patient by assigning points for each variable present. The ROC area of this score was estimated. Finally, the discriminative ability of the CSF prediction rule combined with the previously obtained clinical risk score[16] was evaluated.

RESULTS

General characteristics of the 227 included patients are given in **Table 1**. Bacterial meningitis was present in 44% (95% CI, 37%-50%) of patients, among whom 5 had pretreated meningitis. Four children with negative CSF culture findings were diagnosed as having bacterial meningitis due to pleocytosis as evident from a CSF leukocyte count of more than 1000/µL and *Neisseria meningitidis* detected in nose (n=1) or throat (n=1) culture results or by antigen detection (n=2). In 3 children with mild pleocytosis (CSF leukocyte count, 7-48/µL), bacterial meningitis was diagnosed based on *N meningitidis* present in blood culture findings and a clinical course of bacterial meningitis. In 211 children (93%), a lumbar puncture had been performed; 186 children (82%) were hospitalized.

Table 2 presents the values of CSF indices among children with and without bacterial meningitis. The total CSF cell count, percentage of PMNs, absolute PMN count, and CSF protein concentration were significantly higher in patients with bacterial meningitis, whereas CSF glucose concentration and CSF–blood glucose ratio were significantly lower. Because of substantial overlap in values of CSF indices between children with and without bacterial meningitis, a threshold value could not be found for any of the CSF variables to discriminate a meaningful number of patients without from those with bacterial meningitis. The gram-stained smear was negative in 29 (29%) of the 99 patients with bacterial meningitis and positive in 2 (2%) of the 128 patients without and thus did not fully discriminate either. In 1 of these 2 false-positive cases, *Staphylococcus epidermidis* was identified in the CSF culture results, which was considered to be contamination; in the other one, the CSF culture findings remained negative.

Multivariate regression analysis of all CSF indices identified the absolute PMN cell count and CSF–blood glucose ratio as independent determinants of presence of bacterial meningitis. The second column of **Table 3** presents the contents of this final model before bootstrapping. With the final model, the probability of bacterial meningitis could be computed by $e^{score}/(1+e^{score})$, where score indicates $[3 \times {}^{10}\log(\text{CSF absolute PMN count})] + [0.6 \times (\text{CSF–blood glucose ratio})]$. The diagnostic value (ROC area) of this CSF model was 0.93 (95% CI, 0.89-0.96). The third column shows the odds ratios and the ROC area of this model after adjustment for overfitting (bootstrapping). Both models had a good fit (ie, Hosmer and Lemeshow test $P=.45$) (data not shown).

From the regression coefficients of the predictors in the adjusted model, corresponding scores were derived (regression coefficients rounded to the nearest half integer), such that a prediction rule was developed (fourth column, Table 3). A total score was computed for each patient by assigning 1 point for each increase of the absolute PMN count (on ${}^{10}\log$ scale) and –0.5 point for each tenth increase of the CSF–blood glucose ratio. For instance, a patient with a leukocyte count of 1500/µL with

Table 1. General Characteristics of 227 Patients With Indication for Lumbar Puncture*

Characteristic	No. (%) of Patients*
Age, mean (SD), y	3.6 (3.6)
Male	139 (61)
Fever	220 (97)
Vomiting	165 (73)
Duration of main problem, mean (SD), d	2.1 (2.0)
Disturbed consciousness	82 (36)
Meningeal irritation	221 (97)
Petechiae	37 (16)
Cyanosis	10 (4)
Bacterial meningitis, No.	99 (44)
Neisseria meningitidis	49
Streptococcus pneumoniae	8
Haemophilus influenzae	32
Pretreated or other	10
Lumbar puncture performed	211 (93)
Hospitalization	186 (82)

*Data are presented as number (percentage) of patients unless otherwise indicated.

Table 2. Cerebrospinal Fluid Laboratory Findings in 227 Patients With and Without Bacterial Meningitis*

Component	Bacterial Meningitis Present (n = 99)	Bacterial Meningitis Absent (n = 128)	OR (95% CI)
Total leukocyte count, median (25th-75th percentiles), µL	3333 (907-7000)	4 (1-70)	4.1 (3.0-5.7)†
Absolute PMN count, median (25th-75th percentiles), µL	2097 (347-4333)	0 (0-33)	3.4 (2.6-4.4)†
PMNs, median (25th-75th percentiles), %	80 (60-90)	0 (0-42)	1.5 (1.3-1.6)‡
Glucose concentration, mg/dL§	32 (23)	67 (18)	0.3 (0.2-0.4)
Protein concentration, g/dL	0.19 (0.16)	0.06 (0.06)	5.6 (3.3-9.4)
CSF–blood glucose ratio	0.29 (0.22)	0.65 (0.21)	0.4 (0.3-0.5)‡
Positive gram-stained smear, No. (%)	70 (70)	2 (2)	144.9 (33.6-624.5)

*Data are presented as mean (SD) unless otherwise indicated. OR indicates odds ratio; CI, confidence interval; PMN, polymorphonuclear cells; and CSF, cerebrospinal fluid.
†Odds ratio on ${}^{10}\log$ scale.
‡Odds ratio per 100% increase.
§To convert milligrams per deciliter to millimoles per liter, multiply by 0.0555.

Variable	Model (Unadjusted)	Model (Adjusted)	Risk Score†
CSF absolute PMN count‡	3.0 (2.2-4.2)	3.0 (2.1-4.1)	1.0
CSF–blood glucose ratio per 0.1 increase§	0.6 (0.5-0.8)	0.6 (0.5-0.8)	−0.5
ROC area	0.93 (0.89-0.96)	0.93 (0.89-0.97)	0.93 (0.89-0.97)

*CSF indicates cerebrospinal fluid; PMN, polymorphonuclear cells; and ROC, receiver operating characteristic. Scoring algorithm: Total score = [1.0 × (absolute PMN count in CSF)] − [0.5 × (CSF–blood glucose ratio)].
†The score per variable is obtained by rounding the regression coefficients (=ln [OR]) to the nearest half integer.
‡Included in the model on a ^{10}log scale in score coded as 0 (0-9/µL of PMNs), 1 (10-99/µL of PMNs), 2 (100-999/µL of PMNs), 3 (1000-9999/µL of PMNs), and 4 (≥10 000/µL of PMNs).
§In score coded as 0 (ratio <0.10), 1 (ratio 0.10-0.19), 2 (ratio 0.20-0.29), 3 (ratio 0.30-0.39), and so on, up to 10 (ratio ≥1.00).

Table 4. Distribution of Patients With and Without Bacterial Meningitis According to the CSF Score*

CSF Score	Incidence of Bacterial Meningitis, No. (%)	Total No. of Patients	Bacterial Meningitis Present, No. (%)	Bacterial Meningitis Absent, No. (%)
−5 to −3	3	48	3 (3)	45 (35)
−2.5 to −1.5	13	62	8 (8)	54 (42)
−1 to 1.5	55	62	34 (34)	28 (22)
2 to 4	98	55	54 (55)	1 (1)
All		**227**	**99 (100)**	**128 (100)**

*CSF indicates cerebrospinal fluid.

CSF Score	Clinical Risk Score			
	9.5-10.4	10.5-12.9	13-19.9	≥20
−5 to −3.5				
−3 to −2.5				
−2 to 0.5				
1 to 4				

Combination of the clinical risk score with cerebrospinal fluid (CSF) score (n=227). Gray-shaded boxes indicate no indication for treatment, including 69 children without bacterial meningitis; black-shaded boxes, indication for treatment, including 59 children without and 99 with bacterial meningitis.

80% PMNs (1200/µL of PMNs) and a CSF–blood glucose ratio of 0.2 received 2 points (3−1). When applied to all patients, the score ranged from −5 to +4. The ROC area of this CSF rule was 0.93 (95% CI, 0.89-0.97).

Next, we evaluated the incidence of bacterial meningitis and the number of patients across selected categories of the score (**Table 4**). The CSF score identified groups with increasing probability of true bacterial meningitis. However, no threshold value could be defined for the CSF score that selected a substantial group of patients without bacterial meningitis in whom treatment could be withheld without missing one case of bacterial meningitis.

A lumbar puncture is only one step in the diagnostic process and is usually performed after obtaining patient history and conducting a physical examination. Therefore, we evaluated the CSF model combined with the clinical patient characteristics, such as vomiting and

duration of complaints in history, meningeal signs, disturbed consciousness, petechiae, or cyanosis at examination as included in the previously derived clinical risk score.[16] The **Figure** shows that combined use of both rules can discriminate well between patients with and without bacterial meningitis. Again, in an attempt not to miss any patient with bacterial meningitis, the required threshold for the CSF score varied among groups of patients with different clinical risk scores. In patients with a clinical score between 9.5 and 10.4, a threshold CSF score of less than 1 identified patients without meningitis. For patients with a clinical score of 10.5 to 12.9 and 13 to 19.9, the CSF thresholds were less than −2 and less than −3, respectively. In patients with a very high clinical risk score (≥20), the CSF score could not additionally discriminate the patients with bacterial meningitis from those without. Similarly, in patients with a CSF score of 1 or more, the clinical score could not further select patients with and without bacterial meningitis. Using the thresholds (Figure), a 30% reduction of empiric treatment could be achieved by excluding bacterial meningitis in 69 patients (30%; 95% CI, 24%-36%).

As presented in Table 1, our study included 32 children with bacterial meningitis caused by *Haemophilus influenzae*, a pathogen that has almost been eradicated by vaccination. We therefore repeated the analysis excluding these meningitis cases. No substantial differences were found, and a similar prediction rule was derived.

COMMENT

This study provides physicians with a rational basis for estimating the risk of bacterial meningitis in patients presenting to the emergency department with meningeal signs. We have found the absolute number of PMNs in CSF and the CSF–blood glucose ratio to be independent predic-

tors of bacterial meningitis in patients with meningeal signs. However, if only these early CSF indices are used, cases of bacterial meningitis can be missed. Combination of these 2 CSF indices with patient characteristics, such as the duration of the main problem, vomiting, meningeal irritation, cyanosis, petechiae, disturbed consciousness, and serum CRP, however, can discriminate well between the absence or presence of bacterial meningitis such that unnecessary treatment can be withheld. Application of this CSF rule in combination with these patient characteristics will reduce unnecessary antibiotic treatment and unnecessary adverse effects of this treatment (allergy, gastrointestinal complaints, infusion problems, hospital infections) and increase clinical efficiency. Hence, empiric antibiotic treatment can correctly be withheld in 30% of the children. Of course, this reduction in treatment should be considered in view of the actual number of treatments in current practice (n=186). The net reduction of empiric treatment as achieved by the decision rule is 28 (16%; 95% CI, 10%-21%). This net benefit, however, depends on the actual number of empiric treatments and will vary among hospitals.

The combined use of the clinical risk score[16] with the CSF rule in predicting bacterial meningitis agrees with common practice, in which laboratory tests usually are evaluated in view of the present clinical signs and symptoms. As illustrated in the Figure, both the intermediate clinical risk score and the CSF score contribute to the assessment of the risk of bacterial meningitis; therefore, the decision rule is valuable in patients with both scores in particular. In patients with a very high clinical risk score (≥20), who are the most obvious cases of bacterial meningitis, the CSF score does not contribute to therapeutic decisions, and empiric treatment will be started anyway; the CSF culture result, however, will guide specific antimicrobial treatment.[2,3] Similarly, patients with a very high CSF score are evident cases of bacterial meningitis, and the clinical profile does not contribute much to therapeutic decisions.

The diagnostic process is a stepwise procedure that uses diagnostic tests subsequent to obtaining patient history and conducting a physical examination.[13] Following this usual order of testing in clinical practice, we selected from the total group of 360 patients suspected of having bacterial meningitis (because of meningeal signs) those with an indication for lumbar puncture as defined by a prediction rule based on clinical symptoms.[16] In these patients (n=227), we derived a rule to decide whether empiric treatment is necessary. One may question whether the decision rule, including the CSF score and the clinical score together, may also be applicable in a clinical setting where lumbar punctures are performed without using the clinical prediction rule. Therefore, we repeated the analyses on all 360 patients with meningeal signs who underwent a lumbar puncture (n=256). The same CSF and clinical scoring rule was found, and the same number of patients was selected for empiric treatment. This indicates that our CSF rule can be applied in both patients undergoing lumbar puncture was selected by our clinical rule and patients undergoing a lumbar puncture based on the pediatrician's decision. Nevertheless, in this latter clinical setting, more unnecessary lumbar punctures will be performed,

since clinical symptoms contribute to the prediction of the risk of bacterial meningitis as well.[16]

That CSF indices alone cannot discriminate well between absence or presence of bacterial meningitis has been mentioned previously.[7,26] This underlines the diagnostic problem when evaluating a child suspected of having bacterial meningitis. Given the increased risk of mortality and morbidity in a delayed diagnosis and treatment of bacterial meningitis, clinicians preferably treat children who have increased CSF leukocyte counts empirically, until the CSF culture result is available.[2,3] Although a safe strategy, a large group of patients without bacterial meningitis will be unnecessarily treated with antibiotics, with unnecessary costs and risk for potential adverse effects of treatment.[27] Our finding that total CSF PMN count and the CSF–blood glucose ratio are independent predictors of bacterial meningitis has also been reported by previous studies.[7,8,10] In contrast to others,[7] serum glucose was not an independent predictor in our study, although the CSF–blood glucose ratio in our rule indirectly includes this variable. The diagnostic value of CSF CRP and lactate concentration has not been evaluated in this study. Although their diagnostic value has been reported,[28,29] these highly advanced tests are not available in every hospital emergency department. Since our aim was to develop a rule widely applicable in general pediatric practice, we have decided not to include these advanced tests in the study. The final CSF model also does not contain the gram-stained CSF smear. Its addition to the CSF model with PMN count and CSF–blood glucose ratio only significantly increased the ROC area from 0.93 to 0.95 (95% CI, 0.92-0.98). Despite this increase in ROC area, however, the gram stain smear did not improve the discrimination of patients without bacterial meningitis such that more unnecessary treatments could be withheld.

To appreciate the present results, certain issues need to be discussed. First, our study partly includes a period in which bacterial meningitis caused by *H influenzae* type b was still present, although today it has almost been eradicated by vaccination.[30] Modifying the group to exclude patients with *H influenzae* type b (n=32), however, did not alter the results and yielded the same CSF and clinical scoring rule. Second, the CSF rule has been developed in a population of patients with meningeal signs as the main problem. This rule does not apply to all patients suspected of having meningitis, since patients with a prominence of other symptoms of meningitis (such as convulsions and coma) but without meningeal signs at presentation are not included in our study population.[2,3,31] To our knowledge, however, this is the first study in a pediatric emergency department based on the patient's clinical presentation. Third, in some children the reference standard (lumbar puncture) for the outcome bacterial meningitis was missing (n=18). In these children, absence of bacterial meningitis has been assessed using follow-up data. Although this could have introduced some diagnostic verification bias,[32] we think this did not occur in our study, since bacterial meningitis is a serious and fatal disease without adequate treatment[2] and all children without a lumbar puncture were followed up and recovered uneventfully. We may, how-

What This Study Adds

Previous studies have assessed several characteristics from clinical evaluation or laboratory tests that may predict bacterial meningitis in patients selected on the diagnosis (proven bacterial, viral, and/or aseptic meningitis) or the presence of a lumbar puncture. In practice, however, the physician is faced with a patient suspected of having bacterial meningitis, in whom the diagnosis is not known yet. In accordance with clinical practice, we selected children by their clinical presentation (ie, meningeal signs). Previously, we had derived and validated a prediction rule for the presence and absence of bacterial meningitis using clinical signs and symptoms and laboratory blood tests. In the present study, we define independent predictors of bacterial meningitis obtained from CSF analysis, in addition to the previous prediction rule. Use of the absolute number of PMNs in CSF and the CSF–blood glucose ratio together with patient characteristics, such as the duration of the main problem, vomiting, meningeal irritation, cyanosis, petechiae, disturbed consciousness, and serum CRP, can discriminate well between the absence or presence of bacterial meningitis and could achieve a 30% reduction of (unnecessary) empiric antibiotic treatments.

ever, have misdiagnosed some cases of viral or aseptic meningitis. Since we aimed to distinguish between the presence or absence of bacterial meningitis, this will not affect our results. Fourth, the aim of our rule was to define patients in whom empiric treatment for bacterial meningitis could be safely omitted. However, after bacterial meningitis has been ruled out, some of these children may require antibiotic treatment for other conditions, such as septicemia, urinary tract infections, or pneumonia, pending the results of further investigations. Fifth, our study was performed at a pediatric university hospital. Ninety percent of patients visiting the emergency department of this hospital, however, require basic pediatric care.[17] Therefore, we think that the derived prediction rule is applicable both to academic and general hospitals. Finally, internal validation of the CSF model by bootstrapping demonstrated that the rule is robust. Before implementation of this decision rule in clinical practice, however, a prospective validation in similar future patients is necessary and currently being performed in our hospital. Subsequently, impact analysis is necessary to see how the rule really functions in practice and if a reduction of lumbar punctures and hospitalizations for empiric treatment will be achieved.

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