# Diagnostic Accuracy of Clinical Symptoms and Signs in Children With Meningitis

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**Background:** The diagnostic accuracy of the classic symptoms and signs of meningitis in infants and children has not been established.

**Methods:** All children aged 2 months to 16 years with clinically suspected meningitis were eligible for this prospective cohort study at 2 large medical centers between February 2006 and October 2007. Exclusion criteria were severe chronic disease, severe immune deficiency, or idiopathic intracranial hypertension. The emergency department physician obtained information on clinical symptoms and signs and cerebrospinal fluid analysis. Meningitis was defined as white blood cell count of 6 or higher per microliter of cerebrospinal fluid.

**Results:** A total of 108 patients with suspected meningitis were enrolled. Meningitis was diagnosed in 58 patients (53.7%; 6 bacterial and 52 aseptic). Sensitivity and specificity were 76% and 53% for headache (among the verbal patients) and 71% and 62% for vomiting, respectively. Photophobia was highly specific (88%) but had low sensitivity (28%). Clinical examination revealed nuchal rigidity (in patients without open fontanel) in 32 (65%) of the patients with meningitis and in 10 (33%) of the patients without meningitis. Brudzinski and Kernig signs were present in 51% and 27% of the patients with meningitis, respectively, and had relatively high positive predictive values (81% and 77%, respectively). Bulging fontanel in patients with open fontanel was present in 50% of the patients with meningitis but had a positive predictive value of only 38%.

**Conclusions:** Classic clinical diagnostic signs have limited value in establishing the diagnosis of meningitis in children and should not be the sole determinants for referral to further diagnostic testing and lumbar puncture.

**Key Words:** meningitis, nuchal rigidity, Brudzinski sign, Kernig sign, lumbar puncture

(*Pediatr Emer Care* 2011;27: 196–199)

A definitive diagnosis of meningitis is dependent on examination and culture of cerebrospinal fluid (CSF), and a lumbar puncture (LP) should be undertaken whenever the physician suspects meningitis.[1] Rapid and accurate clinical evaluation is required to determine the risk of meningitis and the need for LP in children with suspected meningitis. Several studies have tried to establish rules for the management of children with meningeal signs,[2–6] but the implementation of some of these methods in actual clinical practice has been questioned.[7] We conducted this prospective to determine the diagnostic accuracy of common signs and symptoms for the diagnosis of meningitis in children.

## METHODS

The study population was composed of all patients (aged 2 months to 16 years) admitted with clinically suspected meningitis to the emergency departments of Dana Children's Hospital of the Tel-Aviv Medical Center and the Assaf-Harofe Medical Center between February 1, 2006, and October 31, 2007. "Suspected meningitis" was defined as the presence of clinical symptoms compatible with meningitis (ie, fever, headache, stiff neck, photophobia, nausea, and vomiting), according to the impression of the resident or the attending physician in the emergency department, which warranted referral for LP to determine whether CSF inflammation was present. Meningitis was defined as a white blood cell count of 6 or higher per microliter of CSF. Excluded were children who experienced a neurological condition (eg, epilepsy, cerebral palsy, hydrocephalus, Chiari malformation, brain tumor) or a severe chronic disease, those who received immunosuppressive treatment or chemotherapy, and children with idiopathic intracranial hypertension. Also excluded were children who were eligible but who did not undergo LP for any reason. All clinical information and physical examination were gathered by the emergency department physician.

Statistical analysis was performed by using the $\chi^2$ (of Fisher exact test) for categorical variables. A 1-way analysis of variance was used for continuous variables. In addition, the sensitivity, specificity, and positive predictive value (PPV) of each clinical sign and symptom were assessed. Sensitivity was defined as the proportion of true positives that are correctly identified by the test. Specificity was defined as the proportion of true negatives that are correctly identified by the test. Positive predictive value was defined as the proportion of positive test results that are true positive. Negative predictive value was defined as the proportion of negative test results that are true negative. SPSS v11.0.0 (SPSS Inc, Somers, NY) was used for all statistical analyses. This study was approved by the institutional review board.

## RESULTS

A total of 112 pediatric patients with suspected meningitis underwent an LP during the study period and 108 of them were enrolled. Four patients were excluded owing to insufficient data. Demographic characteristics of the study groups are presented in Table 1. Meningitis was diagnosed in 58 patients (53.7%): it was bacterial in 6 (specific description of these patients is outlined in Table 2) and aseptic in 52. Eight patients had evidence of CSF infection (positive results of either CSF culture or polymerase chain reaction test). The causative pathogens included *Streptococcus pneumoniae* (3 patients), *Nisseria meningitides* (2 patients), *Listeria monocytogenes* (1 patient), Enterovirus (1 patient), and Herpes simplex virus type 1 (1 patient). The patients who were finally diagnosed as having meningitis were significantly older than the other group ($P < 0.026$). There were no sex differences between the groups (Table 1).

The presenting signs and symptoms of the study groups on admission are outlined in Table 3. The most common presenting symptoms were fever (93%), headache (84%), and vomiting (71%). The sensitivity and specificity were 76% (confidence interval [CI], 60%–87%) and 53% (CI, 29%–74%) for headache (among the verbal patients) and 71% (CI, 57%–81%) and 62% (CI, 47%–75%) for vomiting or complaints of nausea (among the verbal patients), respectively. Photophobia was highly

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ISSN: 0749-5161

**TABLE 1.** Demographic Characteristics of the Study Groups

| | Total | Meningitis* | Meningitis† | *P* |
|---|---|---|---|---|
| Age, mean ± SD, yr | 4.1 ± 4.5 | 5.08 ± 4.8 | 3.1 ± 3.9 | 0.026 |
| Sex, % | | | | |
| Male | 55.7 | 65 | 64.6 | 0.96 |
| Female | 55.3 | 35 | 35.4 | |

*Final diagnosis of meningitis.
†Final diagnosis not meningitis.

specific (88%; CI, 69%–97%) but had low sensitivity (28%; CI, 16%–44%). Motor deficiency (defined as presence of focal motor abnormalities on neurologic examination) was rare and present in only 3 patients. Seizures yielded low sensitivity (19%; CI, 10%–32%) and specificity of 64% (CI, 49%–77%). The PPV was the highest in photophobia and headaches as presenting symptoms, although the maximal values were only 80% and 78%, respectively.

Fever was a nonspecific sign, and it was present in more than 90% of both the meningitis and nonmeningitis groups. A low Glasgow Coma Scale (<13) was highly specific but had low sensitivity. Nuchal rigidity (in patients without open fontanel) was present in 32 (65%) of the patients with meningitis and in 10 (33%) of the patients without meningitis ($P = 0.02$). Of the 30 patients without meningitis, 20 did not have nuchal rigidity (specificity, 76%; PPV, 80%).

Results of an examination for Brudzinski and Kernig signs performed before the LP procedure were available in 79 patients (73%). Brudzinski sign was present in 25 of the 49 patients with meningitis (sensitivity, 51%; CI, 36%–65%) and absent in 24 of the 30 patients without meningitis (specificity, 80%; CI, 63%–92%). Kernig sign was present in 13 of the 49 patients with meningitis (sensitivity, 27%; CI, 15%–41%) and absent in 26 of 30 patients without meningitis (specificity, 87%; CI, 68%–96%). From our 30 study patients who were found not to have meningitis and who were assessed for meningeal signs, 10 (33%) had nuchal rigidity, 6 (20%) had a positive Brudzinski sign, and 4 (13%) had a positive Kernig sign.

This study included 31 children who were 1 year or younger. Bulging fontanel was present in 5 of the 10 patients with meningitis in this age group (sensitivity, 50%; CI, 20%–80%) and absent in 13 of 21 patients without meningitis, yielding a specificity of 62% (CI, 39%–81%) and a PPV of only 38%.

We also analyzed the probability for meningitis for patients with different combinations of signs and symptoms (Table 4). The sensitivity of these combined signs and symptoms was, of course, lower compared with each symptom alone, but the specificity and the PPV values were increased.

Table 5 summarizes the CSF analysis findings. As expected, there were significant group differences in leukocytes, glucose, and protein values.

## DISCUSSION

The era of conjugate bacterial vaccines has made bacterial meningitis a relatively rare disease, as may be well reflected from our results. Various prediction models were developed in the past to diagnose promptly bacterial meningitis and to distinguish it from aseptic meningitis[8,9]; however, a definitive diagnosis of meningitis is still dependent on examination and culture of CSF, and LP should be undertaken whenever the physician suspects meningitis.

**TABLE 2.** Bacterial Meningitis—Description of 6 Patients

| Patients | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Age, yr | 1.25 | 1.5 | 5 | 1 | 0.5 | 15 |
| Sex | Female | Male | Male | Female | Female | Female |
| Anamnesis | | | | | | |
| Headaches | − | − | − | Irrelevant | Irrelevant | + |
| Vomiting | + | − | − | − | + | + |
| Photophobia | − | − | + | Irrelevant | Irrelevant | − |
| Motor deficiency | − | − | Irrelevant | − | + | − |
| Sensory deficiency | − | − | Irrelevant | − | Missing data | − |
| Seizures | − | + | − | − | − | + |
| Clinical signs | | | | | | |
| Fever | + | + | + | + | + | − |
| GCS < 13 | − | + | + | − | + | Missing data |
| Nuchal rigidity | − | − | + | + | − | + |
| Kernig sign | − | − | − | + | Irrelevant | + |
| Brudzinski sign | − | − | + | + | Irrelevant | + |
| CSF—laboratory | | | | | | |
| WBC | 312 | 7800 | 3600 | 980 | 478 | 2700 |
| RBC | 20 | 83 | Many | Many | 0 | 0 |
| Protein | 40 | 215 | 200 | 120 | 169 | 105 |
| Glucose | 54 | 1 | 50 | 1 | 2 | 45 |
| Positive smear | + | + | − | Missing | + | − |
| Bacterial culture | *Streptococcus pneumoniae* | *Nisseria meningitides* | *Nisseria meningitides* | *Streptococcus pneumoniae* | *Streptococcus pneumoniae* | *Listeria monocytogenes* |

GCS indicates Glasgow Coma Scale; RBC, red blood cell; WBC, white blood cell.

**TABLE 3.** Presenting Symptoms and Signs of the Study Groups on Admission (n = 108)

| | No. Patients* | Meningitis† Sensitivity, % | 95% CI (Sensitivity) | Meningitis‡ | Specificity | 95% CI Specificity | PPV | Odds Ratio | 95% CI | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| Headaches | 61 (56%) | 32§/42 (76%) | 0.6–0.86 | 9‖/19 (47%) | 0.53 | 0.29–0.74 | 0.78 | 3.5 | 1.1–11.1 | 0.026 |
| Vomiting, nausea | 108 (100%) | 41/58 (71%) | 0.57–0.81 | 19/50 (38%) | 0.62 | 0.47–0.75 | 0.68 | 4.1 | 1.8–9.4 | 0.01 |
| Photophobia | 69 (64%) | 12/43 (28%) | 0.16–0.44 | 3/26 (12%) | 0.88 | 0.69–0.97 | 0.8 | 2.9 | 0.75–11.7 | 0.11 |
| Motor deficiency | 108 (100%) | 2/58 (3%) | 0–0.13 | 1/50 (2%) | 0.98 | 0.88–0.99 | 0.67 | 1.7 | 0.14–19 | 0.67 |
| Seizures | 108 (100%) | 11/58 (19%) | 0.1–0.32 | 18/50 (36%) | 0.64 | 0.49–0.77 | 0.38 | 0.37 | 0.15–0.9 | 0.028 |
| Fever¶ | 108 (100%) | 54§/58 (93%) | 0.82–0.98 | 46‖/50 (92%) | 0.08 | 0.02–0.2 | 0.54 | 1.1 | 0.22–6 | 0.86 |
| GCS < 13 | 108 (100%) | 5/58 (9%) | 0.03–0.2 | 4/50 (8%) | 0.92 | 0.8–0.97 | 0.56 | 1.05 | 0.26–4.1 | 0.94 |
| Nuchal rigidity | 79 (73%) | 32/49 (65%) | 0.5–0.77 | 10/30 (33%) | 0.67 | 0.47–0.82 | 0.8 | 4.8 | 2–11.4 | 0.01 |
| Brudzinski sign | 79 (73%) | 25/49 (51%) | 0.36–0.65 | 6/30 (20%) | 0.8 | 0.63–0.92 | 0.81 | 4.3 | 1.5–12.3 | 0.004 |
| Kernig sign | 79 (73%) | 13/49 (27%) | 0.15–0.41 | 4/30 (13%) | 0.87 | 0.68–0.96 | 0.77 | 2.3 | 0.66–7.8 | 0.19 |
| Bulging fontanel | 31 (29%) | 5/10 (50%) | 0.2–0.8 | 8/21 (38%) | 0.62 | 0.39–0.81 | 0.38 | 0.6 | 0.13–2.8 | 0.54 |

*Patients for whom all required data were available.

†Final diagnosis of meningitis.

‡Final diagnosis not meningitis.

§Number of patients with a positive sign in the meningitis group.

‖Number of patients with a positive sign in the nonmeningitis group.

¶Fever was defined as rectal temperature higher than 38°C.

Meningitis was diagnosed in 58 (53.7%) of a total of 108 patients with suspected meningitis who underwent LP and were enrolled in this study. As noted before, 6 (5.6%) of these patients were diagnosed as having bacterial meningitis and the other 52 (48%) as having aseptic meningitis. Other studies on children who underwent LP have reported a 40% prevalence of meningitis (bacterial in 8% and aseptic in 32%)[2,3,7,8]; figures that are close to our current findings.

Our data clearly show that the classic meningeal signs and symptoms have limited clinical diagnostic value for children with suspected meningitis. None of these signs and symptoms could accurately discriminate between patients with meningitis from those without it. Sixty-five percent of the children with meningitis had nuchal rigidity, and 51% and 27% had Brudzinski and Kernig sign, respectively. Current data on the diagnostic accuracy of Kernig and Brudzinski signs are limited. Other pediatric studies showed that signs of meningeal irritation are missing in approximately 20% of the children with meningitis.[8–12] One study on adults reported sensitivity values for Kernig sign (36%) and Brudzinski sign (39%)[13] that are close to the sensitivity observed in our study. In that study, however, only a few patients (n = 36) were tested for the presence of meningeal signs, and the study's retrospective data collection was subject to bias because tests for meningeal signs may have been performed after the LP results were known. A second smaller study, which prospectively evaluated 54 patients with fever and recent-onset headache[14] reported sensitivity and specificity values for Kernig sign as being 8.8% and 100%, respectively, demonstrating much lower sensitivity and higher specificity than the values calculated in our current study. In another study on adults that prospectively evaluated 297 patients, the sensitivity of both Kernig sign and Brudzinski sign was 5%, which suggests that these bedside diagnostic tools did not reliably identify the need for LP among patients with meningitis.[15] Although the specificity of both Kernig and Brudzinski signs was high in our study (87% and 80%, respectively) as well as in the other above-cited studies, the high specificity values are a result of the overall paucity of positive results of examination for Kernig sign and Brudzinski sign rather than a reflection of the discriminating ability of these indicators. Taken together, these results indicate that none of the classic meningeal

**TABLE 4.** Analysis of Patients With Different Combinations of Clinical Signs and Symptoms (n = 108)

| | No. Patients* | Meningitis† Sensitivity, % | 95% CI Sensitivity | Meningitis‡ | Specificity | 95% CI Specificity | PPV |
|---|---|---|---|---|---|---|---|
| He + NR | 79 (73%) | 25§/49 (51%) | 0.37–0.65 | 6‖/30 (20%) | 0.8 | 0.6–0.92 | 0.81 |
| He + Vo + NR | 79 (73%) | 21/49 (43%) | 0.29–0.58 | 9/30 (30%) | 0.7 | 0.5–0.84 | 0.7 |
| He + NR + BS | 79 (73%) | 19/49 (39%) | 0.26–0.54 | 3/30 (10%) | 0.9 | 0.72–0.97 | 0.86 |
| He + NR + BS + KS | 79 (73%) | 7/49 (14%) | 0.06–0.28 | 1/30 (3%) | 0.97 | 0.8–0.99 | 0.875 |

*Patients for whom all required data were available.

†Final diagnosis of meningitis.

‡Final diagnosis not meningitis.

§Number of patients with a positive sign in the meningitis group.

‖Number of patients with a positive sign in the nonmeningitis group.

BS indicates Brudzinski sign; He, headache; KS, Kernig sign; NR, nuchal rigidity; Vo, Vomiting.

**TABLE 5.** Cerebrospinal Fluid Analysis of the Study Groups on Admission (n = 108)

| | Meningitis* | Meningitis† | *P* |
|---|---|---|---|
| Leukocytes count ($\times 10^3/\mu L$) | 719 ± 1344 | 0.87 ± 1.5 | <0.001 |
| Red blood cells ($\times 10^3/\mu L$) | 88.4 ± 419 | 0.14 ± 0.79 | 0.182 |
| Glucose, mmol/L | 59.7 ± 19.4 | 70.2 ± 12.5 | <0.001 |
| Protein, mmol/L | 50.8 ± 46 | 21 ± 20 | <0.002 |
| Bacterial culture | 6/58 (10%) | 0/50 (0%) | <0.03 |

*Meningitis (+).

†Meningitis (-).

Values are mean ± SD.

Meningitis was defined as a white blood cell count of 6 or higher per microliter.

signs were clinically discriminating indicators of the presence or absence of meningitis.

Part of our 30 study patients who were found not to have meningitis had positive meningeal signs. The presence of meningeal irritation in children without meningitis can be explained by cervical lymphadenitis that can cause nuchal spam or torticollis. Pneumonia is known to elicit meningism by pleural irritation.[10,16] Surprisingly, bulging fontanel, practically the only relevant sign in infants with open fontanel, had very low sensitivity (21%), specificity (62%), and PPV (38%). This is probably because many infants who have bulging fontanel are finally diagnosed with other diseases, such as simple viral ones like roseola infantum.

Other symptoms and signs were rare but highly specific (eg, Glasgow Coma Scale <13) or were common but not specific (eg, fever, headaches). When trying to create a set of representative clinical sign and symptoms, we found that a child who presents with headaches and is found to experience nuchal rigidity and positive Brudzinski and Kernig signs will have the highest probability to be experiencing meningitis (PPV value of 87.5%). However, only a few of our patients actually had this set of symptoms and signs.

Some limitations of our study need to be discussed when interpreting our results. First, physical examination findings are subject to individual interpretation and interobserver variability, and the manner in which meningeal signs were evaluated was not standardized. Second, the presence or absence of the signs of meningeal irritation was not always documented for each patient. Documentation of nuchal rigidity and of Kernig and Brudzinski signs was complete for 73% of the patients. We could not know whether the missing data resulted from the sign having been negative or if it had not been evaluated. A third limitation is our small sample size and the small number of patients with bacterial meningitis.

In conclusion, this study provides data on the diagnostic accuracy of classic physical examination findings in children aged 2 months to 15 years who presented with suspected meningitis and who were evaluated at a pediatric emergency department. Although the results of our study substantiate the general conclusion that meningeal signs can identify patients with severe meningial inflammation, they also demonstrate that the presence of clinical diagnostic classic signs has limited value in predicting a final diagnosis of meningitis. Clinical decisions on whether to refer to further diagnostic testing and the need for an LP should not rely solely on the presence or the absence of these signs. Better bedside diagnostic tests are needed as are further studies for standardizing examinations and interpretations of these diagnostic signs and for evaluating interobserver reliability.

## ACKNOWLEDGMENT

*Esther Eshkol is thanked for editorial assistance.*

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