# Research Article

## OOSTENBRINK SCORE FOR DETECTING BACTERIAL MENINGITIS IN CHILDREN AT DR. MOEWARDI HOSPITAL

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## ABSTRACT

**Background**: The clinical symptoms of bacterial meningitis are various and non-specific as there are no obvious symptoms. Establishing diagnosis of meningitis and finding its etiology with limited health facility areas is still constrained by several factors. However several clinical predictors can help predict the incidence of bacterial meningitis in children. One of them is Oostenbrink score.

**Aim**: this study aimed to analyze Oostenbrink score as clinical predictor to detect bacterial meningitis in children.

**Methods**: A Cross-sectional diagnostic study was conducted in children aged 1 month-18 years old from September 2018- June 2019 in Dr.Moewardi hospital, Surakarta. The data were analyzed with SPSS version 20 for statistical analysis of diagnostic tests. The cut-off point of Oostenbrink score was obtained from the best AUC (Area Under Curve) from sensitivity and specificity sides. A diagnostic test was performed by calculating sensitivity and specificity, positive predictive value, negative predicted value, positive likelihood ratio and negative likelihood ratio to the Oostenbrink score.

**Results** : Among the 40 children of the study subjects, 25 were boys. All subjects presented with fever, some of the subjects also came with seizures (75%), decreased consciousness (50%), and meningeal signs (30%). Of the overall study subjects, 27.5% had of bacterial meningitis. Oostenbrink cut-off score of 9.75 had a sensitivity value of 90.9%, specificity of 69% with AUC 0.813.

**Conclusion**: Oostenbrink score is a good clinical predictor for screening detection bacterial meningitis in children.

**Keywords**: Oostenbrink score, bacterial meningitis, children, diagnostic

## INTRODUCTION

Acute meningitis in children is generally aseptic meningitis and does not require specific treatment. About 4%-6% of acute meningitis cases are bacterial meningitis. Bacterial meningitis is one of the potentially severe infections in a pediatric population.[1,2,3] The clinical symptoms of bacterial meningitis are very broad and not specific. Sometimes a child has meningitis, but there are no obvious symptoms. Clinical symptoms vary depending on the patient's age, duration of illness, and the body's response to infection.[4]

Distinguishing etiological diagnosis of meningitis is often difficult as many factors affect it. Longer time needed to collect cerebrospinal fluid (CSF), runs CSF culture and gram staining examination are parts of the obstacles. Antibiotics administration before lumbar puncture procedure disguise the final result. Several contraindication lumbar puncture procedures also make it more difficult to distinguish bacterial meningitis from other etiologies of meningitis.

There are number of clinical decision rules derived from identification of variable predictors in bacterial meningitis to predict bacterial meningitis in order to determine further examinations that are required and to consider immediate antibiotics administration. Several clinical decision rules have been reported to distinguish bacterial from viral meningitis including Boyer, Chavanet, Oostenbrink, Bacterial meningitis score, Freedman, Bonsu, Spanos.[5]

Almost all clinical decision rules need CSF examination to predict bacterial meningitis. Oostenbrink score is the only clinical predictor score for meningitis which does not require cerebrospinal fluid examination data.[6]

Further study needed to evaluate the difference in cut-off point of this score and limited prospective cohort studies evaluating predictor of this clinical decision rules on wider population.[7]

In Indonesia, there are many health care facilities especially in remotes area which have difficulties to perform CSF examination because of limited resources. Therefore, we evaluated Oostenbrink score potential to detect bacterial meningitis in children in less-invasive simple way.

## METHODS

A cross-sectional diagnostic study was conducted in pediatric ward, pediatric high care units and pediatric intensive care unit of Dr. Moewardi hospital, Surakarta between September 2018- June 2019. The samples were taken from all children aged 1 moths-18 years old with acute meningitis clinical symptoms. The samples were selected by consecutive sampling after fulfilling inclusion and exclusion criteria. The inclusion criteria were: all children aged 1 months-18 years old with acute meningitis clinical symptoms such as fever followed by altered mental status or positive meningeal sign (bulging fontanel, neck stiffness, kernig or brudzinski sign), or fever followed by seizure without clear source of infection. Pediatric patient with history of antibiotic use with intracranial dose > 48 hours, head trauma, cerebral tumor, post intracranial surgery, sepsis, any contraindication of spinal tap procedure, intracranial bleeding, failed to attempt spinal tap procedure were excluded from this study. The ethical clearance was obtained from the ethical commitee review board of faculty of medicine of Sebelas Maret University and Dr. Moewardi hospital, Surakarta, Indonesia. Permission to collect data was granted from hospital authorities

Oostenbrink score parameters are assessed in subjects with suspected acute meningitis. Oostenbrink score range from 0-40. This score consists of several clinical criteria and CRP serum examination as described in table 1. CRP serum examination used ADVIA 1800 clinical chemistry with immunoturbidimetry method in Clinical Pathology laboratory of Dr. Moewardi hospital. Based on Oostenbrink score, we assigned the subjects into two groups, namely Oostenbrink scores over and below the cut-off point which obtained from the ROC curve analysis.

**Table 1. Oostenbrink score.[8]**

| Variable | Point |
|---|---|
| **Duration of main problem (1.0 per day, maximum 7)** | 1.0 |
| **History of vomiting** | 2.0 |
| **Physical examination findings:** | |
| • Cyanosis | 6.5 |
| • Disturbed consciousness | 8.0 |
| • Meningeal irritation | 7.5 |
| • Petechiae | 4.0 |
| **Serum C-reactive protein level (mg/dL)** | |
| • < 5.0 | 0 |
| • 5.0 - 9.9 | 0.5 |
| • 10.0 - 14.9 | 1.0 |
| • 15.0 - 19.9 | 1.5 |
| • > 20.0 | 2.0 |

Case classification of bacterial meningitis according to WHO:

1. **Suspected**: Any child with sudden onset of fever (> 38.5 °C rectal or 38.0 °C axillary) and one of the following signs: neck stiffness, altered consciousness or other meningeal signs.
2. **Probable**: A suspected case with CSF examination showing at least one of the following:
   a. turbid appearance CSF,
   b. Leucocytosis (> 100 cells/mm3);
   c. Leucocytosis (10-100 cells/ mm3) and either an elevated protein (> 100 mg/dl) or decreased glucose (< 40 mg/dl).
3. **Confirmed**: A case that is laboratory-confirmed by culture of bacterial pathogen in the CSF in a child with a clinical syndrome consistent with bacterial meningitis

For the study purpose, we used probable case and confirmed case criteria to establish bacterial meningitis diagnosis. CSF analysis used ADVIA 120 in Clinical Pathology laboratory of Dr. Moewardi hospital while CSF culture was perform in Microbiology laboratory of Dr. Moewardi hospital. The subjects who didn't meet the criteria for bacterial meningitis classified as non-bacterial meningitis group.

The data were analyzed with SPSS version 20 for statistical analysis of diagnostic tests. The cut-off point of Oostenbrink score was obtained from the best AUC (Area Under Curve) from sensitivity and specificity sides. A diagnostic test was performed by calculating sensitivity and specificity to the Oostenbrink score.

## RESULTS

Of the 40 pediatric patients with acute meningitis criteria, 11 (27.5%) of them were diagnosed as bacterial meningitis. Most patients were in the age range 1-5 years old, boys were more common than girls. All patients presented with fever, some of the subjects also came with seizures (75%), decreased consciousness (50%), and meningeal signs (30%). Of the bacterial meningitis group, we found positive nonne/pandy result in 8 (72.7%) subjects, CSF protein level $\geq$ 100mg/dl in 7 (63.6%) subjects, CSF glucose <40 mg/dl in 10 (90.9%) subjects. Serum CRP levels in bacterial meningitis group were 3.31 $\pm$ 2.54 mg/dl. Positive CSF culture were obtained in 4 (36.4%) patients of bacterial meningitis group patients.

**Tabel 12. The baseline characteristics of the study subjects subjects**

| Variable | Bacterial Meningitis | | Total |
|---|---|---|---|
| | Bacterial meningitis group (n=11) | Non-bacterial meningitis group (n=29) | |
| **Sex** | | | |
| **Boy** | 6 (54.5%) | 19 (65.5%) | 25 (62.5%) |
| **Girl** | 5 (45.5%) | 10 (34.5%) | 15 (37.5%) |
| **Age** | | | |
| **<1 y.o** | 3 (27.3%) | 7 (24.1%) | 10 (25%) |
| **1-5 y.o** | 5 (45.5%) | 16 (55.2%) | 21 (52.5%) |
| **>5 y.o** | 3 (27.3%) | 6 (20.7%) | 9 (22.5%) |
| **Fever** | | | |
| **Present** | 11 (100%) | 29 (100%) | 40 (100%) |
| **Absent** | 0 (0%) | 0 (0%) | 0(0%) |
| **Seizure** | | | |
| **Present** | 11 (100%) | 20 (69.0%) | 31 (77.5%) |
| **Absent** | 0 (0%) | 9 (31.0%) | 9 (22.5%) |
| **Consciousness** | | | |
| **Fully alert** | 4 (36.4%) | 16 (55.2%) | 20 (50.0%) |
| **Altered consciousness** | 7 (63.6%) | 13 (44.8%) | 20 (50.0%) |
| **Meningeal irritation signs** | | | |
| **Positive** | 6 (54.5%) | 6 (20.7%) | 12 (30%) |
| **Negative** | 5 (45.5%) | 23 (79.3%) | 28 (70%) |
| **Petechie** | 0 (0%) | 0 (0%) | 0 (0%) |
| **Routine CSF analysis** | | | |
| **Nonne/Pandy CSF** | | | |
| **Positive** | 8 (72.7%) | 3 (10.3%) | 11 (27.5%) |
| **Negative** | 3 (27.2%) | 26 (89.6%) | 29 (65.9%) |
| **CSF Protein (mg/dl)** | | | |

| | | | |
|---|---|---|---|
| **>100** | 7 (63.6%) | 5 (17.2%) | 12 (30%) |
| **<100** | 4 (36.3%) | 24 (82.7%) | 28 (70%) |
| **CSF Glucose (mg/dl)** | | | |
| **<40** | 10 (90.9%) | 2 (6.9%) | 12 (30%) |
| **>40** | 1 (9%) | 27 (93.1%) | 28 (70%) |
| **CSF Culture** | | | |
| **Positive** | 4 (36.4%) | 0 (0.0%) | 4 (10%) |
| **Negative** | 7 (63.6%) | 29 (100%) | 36 (90%) |
| **Serum CRP (mg/dl)** | | | |
| **Mean+ Standard deviation** | 3.31 + 2.54 | 3.48 + 4.18 | 3.43 + 3.76 |

Based on ROC curve analysis, cut-off of score Oostenbrink 9.75 had the best sensitivity and specificity of area under the curve (AUC) 0.813 (95% CI = 0 .684- 0.943) p-value = 0.002. The cut-off of 9.75 had a sensitivity of 90.9%, specificity 69.0%, with an AUC value of 0.813,  Thus AUC value which is indicating that oostenbrink score fairly good for screening detection of bacterial meningitis in children.
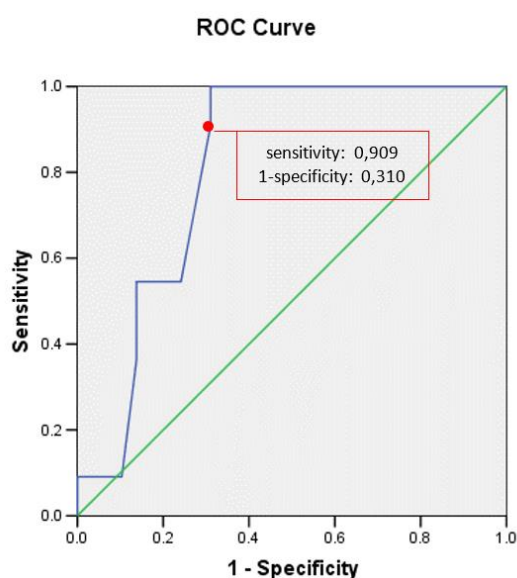


**Figure 1. ROC curve Oostenbrink score in detecting bacterial meningitis**

**Table 3. Diagnostic Test of Oostenbrink score in Detecting Bacterial Meningitis**

| Oostenbrink Score | Bacterial Meningitis | | Total |
|---|---|---|---|
| | **Yes** | **No** | |
| **>9.75** | 10 | 9 | 19 |
| **< 9.75** | 1 | 20 | 21 |
| **Total** | 11 | 29 | 40 |

## DISCUSSION

One of the host factors that influence the incidence of bacterial meningitis is male sex. In our study, of all subjects with suspected acute meningitis, 25 (62.5%) were boys, and the remaining 15 (37.5%) were girls. Although there is no significant difference in the population with bacterial meningitis from the proportion based

on sex, we found more boys affected than girls. This is in line with Ardyna et al study which reported that 51.6% patient with suspected meningitis were male.[2] Another study in Korea by Lee et al also found that sex-linked factors played role in host susceptibility to infection. The gene located on the x chromosome influences function of tymus gland and synthesis of female immunoglubulin has two x genes which make it more resistant to infection.[10]

Although the incidence of meningitis can occur in all ages, the age group below 5 years old are mostly affected by meningitis as their immune system is still low and susceptive to infectious diseases.[11]

All patients in our study came with fever. Thirty-one patients came with fever accompanied by seizures, 12(30%) of all subjects came with meningeal irritation signs, whereas 6 of them were from bacterial meningitis group. Our study also found similar finding to previous study by Chavez et al revealed signs of meningeal irritation were only found in one third of children with meningitis. Oostenbrink study also reported that signs of meningeal irritation appeared in 30% of children with bacterial meningitis, whereas in cases of viral meningitis it was only 13% .[6] Study by Berkley et al showed that seizures was one of the symptoms used as a screening criteria for acute bacterial meningitis with the sensitivity value of 59% and the specificity of 94%. In addition, signs of neck stiffness as meningeal sign and bulging fontanel have a sensitivity value 41% and specificity of 98%.[12]

Other clinical signs such altered of consciousness, in the group of bacterial meningitis, 7 out of 11 patients came with this symptom. This result conformed Karanika et al study which stated only 70% of bacterial meningitis cases appeared with altered of conciousness. [13]

An increase of CSF protein level and decrease of CSF glucose level are usually found in bacterial meningitis. This can be distinguished bacterial meningitis from aseptic meningitis, although this representation can resemble tuberculous meningitis. Predicted factors that make low CSF glucose levels are pathogenic microorganisms which require a significant amount of glucose for metabolism, more cell counts, glucose transport defects in cerebrospinal fluid, and may be an increase in brain glucose uses due to glycolysis process.[14]

The increase in serum levels of CRP between groups of bacterial meningitis and not bacterial meningitis does not vary much. CRP production increases rapidly and this is induced by cytokines due to response of infections, malignancies, inflammation and tissue damage such in cases of trauma or surgery. Increased CRP level can be detected within 6-12 hours of the onset of inflammatory stimulus, and its concentration reaches to peak in 24-48 hours. The increase can be up to 1000 times. CRP was found to reflect the activity, the extent and severity of the disease. Along with resolution and the process of inflammation and infection, CRP levels in the blood fall according to its half-life (19 hours). Most of our study subjects were referral patients, so that the early onset of the disease could not be clearly described when the patient arrived, whereas along with the resolution of inflammation CRP levels fell rapidly within 19 hours.[15,16]

In our study, positive CSF culture was obtained in 36,4% subjects with bacterial meningitis. Factors affecting CSS culture result include the use of antibiotics before CSF culture samples and the presence of CSS autolysis enzymes. Because most of our subjects were referral patients, we only excluded patients who had received intracranial antibiotic therapy 48 hours earlier. Thus, there was a possibility that this factor caused low isolation of CSF bacteria.[17]

Several studies reported that CSF culture as the gold standard in meningitis was only positive for 6%-50% of cases of meningitis.[18] Culture sensitivity decreases by 30% if antibiotics have been given before lumbar puncture is performed.[19]

Culture delays, inadequate storage and CSF transport, unavailability of CSF culture facilities and prior antibiotic treatment are the main causes of low report on positive CSF culture results from countries with limited resources.[20] Therefore other examinations that are easy, less-invasive, affordable and fast are needed in these limited resources area. Oostenbrink score helps distinguish bacterial meningitis from other etiologies of meningitis in children by using a combination of clinical criteria include history taking, physical examination and CRP serum examination that are easily and quickly examined.

In the first study of Oostenbrink, a univariate analysis of clinical signs obtained in patients, physical examination and laboratory examinations. There are several independent predictors of bacterial meningitis. This score consists of patient's symptoms and physical examination include: duration of the main complaint, history of vomiting, signs of meningeal irritation, cyanosis, petechiae and altered of consciousness on physical examination. CRP serum is the only laboratory predictor that has added value to previous clinical predictors, adding serum CRP increases AUC from 0.92 to 0.95. [8] Patients with score >9.5 must undergo lumbar puncture

to confirm exact etiological diagnosis of bacterial meningitis. A prospective validation study at four hospitals in the Netherlands applied this clinical score to 226 pediatric patients. The authors used lower cut-off of a total score of 8.5 which was then applied to the initial study population (360 children) and the population in the study (226 children). The predictive value of bacterial meningitis increased along with determination of the new cut-off value. Their study showed none of 205 children with clinical score less than 8.5 were diagnosed as bacterial meningitis, about 13% of children with score range 8.5-14.9 clearly diagnosed as bacterial meningitis.[7] The ROC area for this study was 0.90, slightly lower than the initial research data with an ROC area of 0.94.[7]

AUC was considered poor in diagnosing with < 0.7 score. Otherwise, it was considered good with 0.7-0.9 score, and very good with 0.9-1. Our study obtained that Oostenbrink scores with cut-off 9.75 had sensitivity 90.9%, specificity 69.0%, AUC value 0.813 with p-value < 0.05. Hence, the diagnostic ability of Oostenbrink score based on AUC 0.813 was fairly good for screening bacterial meningitis in children.

The difference of Oostenbrink score cut-off in this study is not much different from the first study which found 9.5. Whereas in our study, only one patient had cut-off value below 9.75. The impact of likelihood ratio to possibility of the disease has a fairly good diagnostic value. AUC values obtained in our study were lower than previous studies had. This could be due to the limited sample size, this study was conducted in referral hospital, so it can't be compared with actual prevalence of bacterial meningitis in children population.

Oostenbrink score of >9.75 can be used as a predictor for screening detection of bacterial meningitis in children. This predictor is easier and cheaper because it doesn't need any CSF laboratory examination. Oostenbrink score can be an alternative screening tool that helps medical personnel in limited resources to determine the necessity of a lumbar puncture procedure or further CSF examination in children with bacterial meningitis. Although it can not replace CSF culture examination as a gold standard for bacterial meningitis. Further studies for validation of this scoring system are needed.

Several limitations of this study include the sample sizes used in the study is small and only conducted in referral hospitals, this study did not use other diagnostic examination that ensure non-bacterial meningitis such as PCR viruses and other methods which ensure etiological bacteria in CSF such latex agglutination or PCR.

## CONCLUSION

Oostenbrink score is a good clinical predictor for screening detection of bacterial meningitis in children. Oostenbrink score with a cut-off value 9.75 has a sensitivity value 90.9%, specificity 69.0 and AUC 0.813 with p-value <0.05.

## CONFLICTS OF INTEREST

None declared.

## FUNDING ACKNOWLEDGEMENT

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