

Evidence-Based Case Report

## Diagnostic Test of The Hematologic Scoring System in Neonatal Sepsis

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### Abstract

Neonatal sepsis remains a major challenge in neonatal care, particularly because early detection and clinical severity categorization are not always effectively achieved. The hematologic scoring system (HSS) has been proposed as a useful tool for assessing the presence or absence of infection. This study aimed to compare the HSS with blood culture in diagnosing neonatal sepsis. A cross-sectional study was conducted at Ulin Hospital, Banjarmasin, in September 2019, involving 43 neonates aged 0–30 days with clinical or suspected neonatal sepsis. Neonatal sepsis was assessed using HSS, supported by a hematology analyzer. The Leishman-stained peripheral blood smear was evaluated according to Rodwell's hematological criteria. Diagnostic performance was evaluated by calculating sensitivity, specificity, positive predictive value, and negative predictive value using blood culture as the reference standard. The chi-square test was used to assess the association between HSS and blood culture results. The HSS results did not associate with blood culture results in patients ( $p = 0.850$ ). The HSS demonstrated a sensitivity of 59.09%, a specificity of 38.10%, a positive predictive value of 50%, and a negative predictive value of 47.06%. The HSS showed limited diagnostic performance and should not replace blood culture. However, it may be considered as an adjunctive tool in the initial assessment of neonatal sepsis.

**Keywords:** diagnostic test, hematologic scoring system, neonatal sepsis.

## Uji Diagnostik Sistem Skoring Hematologi pada Sepsis Neonatal

### Abstrak

Sepsis neonatus masih menjadi tantangan dalam perawatan dan pelayanan neonatus, terutama karena deteksi dini dan kategorisasi pasien berdasarkan tingkat keparahan klinis belum efektif. Sistem skoring hematologi (HSS) dianggap sebagai alat penilaian yang bermanfaat untuk menentukan ada atau tidaknya infeksi. Penelitian ini bertujuan membandingkan HSS dengan kultur darah dalam mendiagnosis sepsis neonatus. Penelitian potong lintang dilakukan di Rumah Sakit Ulin, Banjarmasin, pada September 2019, melibatkan 43 neonatus berusia 0–30 hari dengan sepsis neonatus klinis atau suspek sepsis neonatus. Sepsis neonatus dinilai menggunakan HSS dengan analisis hematologi. Apusan darah perifer dengan pewarnaan Leishman dievaluasi berdasarkan kriteria Rodwell. Performa diagnostik dinilai dengan menghitung sensitivitas, spesifisitas, nilai prediksi positif, dan nilai prediksi negatif, menggunakan kultur darah sebagai standar acuan. Uji chi-square digunakan untuk menilai hubungan antara hasil HSS dan hasil kultur darah. Hasil HSS tidak menunjukkan hubungan yang bermakna dengan hasil kultur darah pada pasien ( $p = 0,850$ ). HSS menunjukkan sensitivitas sebesar 59,09%, spesifisitas sebesar 38,10%, nilai prediksi positif sebesar 50%, dan nilai prediksi negatif sebesar 47,06%. HSS menunjukkan performa diagnostik yang terbatas dan tidak dapat menggantikan kultur darah. Namun demikian, HSS dapat dipertimbangkan sebagai alat tambahan dalam penilaian awal sepsis neonatus.

**Kata kunci:** tes diagnostik, sistem skoring hematologi, sepsis neonatus.

## Introduction

Neonatal sepsis remains a major problem in neonatal care and services.<sup>1</sup> Globally, the estimated incidence of neonatal sepsis reached 2,824 per 100,000 live births in 2021, reflecting a rising trend compared with prior years.<sup>2,3</sup> The morbidity and mortality were high, especially in low- and middle-income countries.<sup>4</sup> In several referral hospitals in Indonesia, neonatal sepsis rates range from 1.5% to 3.72%, with a mortality rate of 94,050 neonates annually.<sup>5</sup> The most common factors were premature rupture of membranes. Low birth weight (LBW) babies and prematurity are associated with mortality in neonates.<sup>6</sup>

Neonatal sepsis is difficult to diagnose because its clinical features are nonspecific. Early diagnosis and appropriate treatment can minimize mortality and morbidity in patients; hence, to assist clinical assessment, investigations must be conducted.<sup>7,8</sup> Blood culture examination is the gold standard for diagnosing neonatal sepsis.<sup>9</sup> The World Health Organization (WHO) recommends that the diagnosis of neonatal sepsis should be based on a combination of clinical signs, risk factors, and laboratory investigations, with blood culture remaining the gold standard. Biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) are recognized as supportive tools; however, no single biomarker is considered sufficiently accurate for definitive diagnosis, and their use should be interpreted in conjunction with clinical findings and other investigations.<sup>10</sup> Neonatal sepsis markers can also be assessed using procalcitonin testing. A procalcitonin value of 2–2.5 ng/mL indicates a systemic infection with bacteria or fungi, with sensitivities and specificities of 85% and 54%, respectively.<sup>11</sup>

Early diagnosis of neonatal sepsis is currently preferred using the hematologic scoring system (HSS), which comprises all parameters. Therefore, this method is believed to accurately determine whether an infection is present.<sup>12,13</sup> The HSS based on Rodwell assigns a score of 1 for each significant hematological finding, except for the number of polymorphonuclear leukocyte(s) (PMNs): if no mature PMN is found in peripheral blood, the score is 2. If the score is  $\leq 2$ , the

probability of not having sepsis is 99%; 3–4, sepsis is probable; and  $\geq 5$ , sepsis or another infection is probable.<sup>12</sup>

Recent studies indicate that no single biomarker is sufficient for the early diagnosis of neonatal sepsis, and a combined approach is increasingly recommended. A systematic review by Sundara et al<sup>14</sup> reported that PCT rises earlier and is more sensitive for early detection, whereas CRP is more useful for serial monitoring and exclusion of sepsis. In comparison, the HSS remains a rapid and cost-effective screening tool, particularly in resource-limited settings. Jethani et al<sup>15</sup> demonstrated that combining hematological parameters with CRP improves diagnostic accuracy, while Kumar et al.<sup>16</sup> found a significant correlation between HSS and CRP levels. Overall, these findings support the complementary roles of HSS, CRP, and PCT in improving the early diagnosis of neonatal sepsis.

Abnormal hematological counts, acute phase reactants, and inflammatory cytokines, especially at the outset of illness, are neither sensitive nor specific. Furthermore, microbiological culture findings are typically unavailable for 48 to 72 hours after the sample arrives at the laboratory.<sup>17</sup> Consequently, there is a need for a rapid and easy test; HSS is a simple, inexpensive, and quick adjunct for diagnosing clinically suspected newborn sepsis.<sup>18</sup>

Although the diagnosis of neonatal sepsis has developed scientifically, such as blood culture and other immunoserological marker examinations such as CRP and PCT, HSS as a simple examination method which includes the calculation of scoring from the hematology examination section through routine blood tests at hospitals or health services in peripheral communities with limited sophisticated equipment and limited examination skills will be very helpful as a supporting additional diagnosis of suspected of neonatal sepsis. Thus, HSS, as a simple, basic method, can be used to help establish a diagnosis in rural areas with limited equipment, such as in Indonesia.

A case–control study has reported the diagnostic value of hematological sepsis scores and presepsin. The study comprised two groups.

One group comprised 51 neonates who were further subgrouped into suspected and proven sepsis, along with 30 uninfected neonates as the control group. The results showed that hematological sepsis scores and presepsin were useful diagnostic tools for neonatal sepsis, with presepsin a good predictor of mortality, comparable to CRP.<sup>19</sup>

In another study, a prospective study included 150 neonates, found that HSS is a simple, easy, cheap, and rapid adjunct for the diagnosis of clinically suspected cases of neonatal sepsis.<sup>18</sup> Additionally, a study involving 450 neonates with clinical suspicion of sepsis, followed for 1.5 years, showed that the hematological scoring system is a rapid, simple, inexpensive, and reliable test for the early diagnosis of neonatal sepsis compared with the gold standard, blood culture, in differentiating infected from non-infected neonates. Absolute neutrophilia showed high specificity (91.04%), positive predictive value (80%), negative predictive value (73.94%), sensitivity (52.75%), and a significant p-value (<0.001).<sup>20</sup> While in some studies, neutropenia was more significant.<sup>21,22</sup>

Despite the increasing use of biomarkers in diagnosing neonatal sepsis, no single biomarker has demonstrated optimal diagnostic accuracy. Yadav et al.<sup>23</sup> reported that PCT shows high accuracy as an early marker of neonatal sepsis, whereas Chaurasia et al.<sup>24</sup> found that its sensitivity and specificity remain limited when used as a standalone test. Similarly, CRP and hematological parameters, including the HSS, have limitations in detecting all cases of neonatal sepsis, particularly in resource-limited settings. These inconsistencies indicate a gap in the current literature, as the combined diagnostic value of HSS, CRP, and procalcitonin has not been comprehensively evaluated, especially in developing countries such as Indonesia. Therefore, this study is expected to provide supporting data on the role of HSS examination in early diagnosis of neonatal sepsis and in strengthening clinical considerations for early therapeutic decisions.

## Methods

This cross-sectional study was conducted at Ulin Hospital, Banjarmasin, Indonesia, in September 2019. Inclusion criteria are neonates aged 0–30 days diagnosed with clinical neonatal sepsis by a pediatric neonatology consultant. Exclusion criteria were as follows: conjoined twins, vascular disorders, immune deficiencies or disorders, previous blood transfusion at the time of sample collection, parents' refusal to participate (lack of informed consent), and failure in blood drawing. Based on the inclusion and exclusion criteria, 43 patients were recruited as subjects.

Neonatal sepsis was assessed using the hematologic scoring system (HSS) based on complete blood count (CBC) parameters and peripheral blood smear findings. Blood samples were collected for CBC examination, HSS assessment, and blood culture. Hematological parameters were measured using a hematology analyzer. Leishman-stained peripheral blood smears from the neonates were evaluated and scored according to the seven hematological criteria proposed by Rodwell et al.<sup>25</sup> The values of micro-erythrocyte sedimentation rate (ESR), CRP, and PCT were included in the calculation of HSS from a complete blood count (CBC).

The HSS score was calculated based on the Rodwell scoring system. Each abnormal hematological parameter was assigned a score of 1 or 0 based on the established reference values. As an exception, an abnormal total leukocyte count was assigned a score of 2 when no mature polymorphonuclear cells were observed, to compensate for a low immature-to-mature neutrophil ratio. Based on the total HSS score, neonates were classified as having sepsis (score  $\geq 5$ ), probable sepsis (score 3–4), or no sepsis (score 1–2). Blood culture was performed in all suspected cases and used as the reference standard. Blood specimens were collected aseptically and sent for culture, with microbial growth observed for at least 72 hours.

Data were extracted from medical records, including maternal and neonatal characteristics, medical record numbers, major and minor risk

factors, diagnoses upon admission and at birth, and administered therapies. Major and minor risk factors were examined based on references from the WHO and the American College of Obstetricians and Gynecologists (ACOG) guidelines.<sup>26,27</sup> Major maternal risk factors included premature rupture of membranes, intrapulmonary fever in the mother, clinical chorioamnionitis, untreated urinary tract infection in the last trimester, colonization or infection of group B Streptococcus in the mother, history of non-aseptic birth or invasive manipulation, and birth with action (forceps, vacuum, etc.) without adequate sterile indications. Minor maternal risk factors included maternal leukocytosis, maternal tachycardia, feculent or smelly amniotic fluid, pathological vaginal discharge in late pregnancy, low socio-economic status, and repeated internal examinations without antiseptics.

Data were analyzed using a chi-square test for each variable in SPSS version 27. The results were tabulated to determine their significance. Diagnostic test data were analyzed using a 2 × 2 table, and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and likelihood ratios were calculated, with statistical significance set at p <0.05. The study was approved by Ulin Hospital, Banjarmasin, with an ethical clearance No. 223/VIII-Reg/RSUDU/19.

### Results

This cross-sectional study was conducted at Ulin Hospital, Banjarmasin, in September 2019. A total of 43 neonates with clinically suspected neonatal sepsis were consecutively enrolled. All diagnoses were established by a pediatric neonatology consultant, and participants met predefined eligibility criteria.

**Table 1. Subjects Characteristics (n=43)**

Characteristics	n (%)
Gender	
Male	19 (44.2)
Female	24 (55.8)
Mean birth weight (gr)	2747
Mean birth length (cm)	47
APGAR score	
≤5	7 (16.3)
>5	36 (83.7)
Ways of birth	
Spontaneous	26 (60.5)
Sectio Cesaria	15 (34.9)
Vacuum	2 (4.6)
Sepsis Risk Factor	
Positive	35 (81.4)
Negative	8 (18.6)

Table 2 shows that the sensitivity and specificity of HSS were 59.09% and 38.10%, respectively, with PPV and NPV of 50% and 47.06%, respectively. The data were then

collected into two groups. The first group comprised nonsepsis, suspected sepsis, and confirmed sepsis; the second group comprised cultures that were positive or negative.

**Table 2. Diagnostic Accuracy of Hematologic Scoring System**

Parameter	Value	CI 95%	
		Min	Max
Sensitivity	59.09%	38.55%	79.64%
Specificity	38.10%	17.32%	58.87%
Positive predictive value	50.00%	30.78%	69.22%
Negative predictive value	47.06%	23.33%	70.79%

**Table 3. Comparison of Hematologic Scoring System with Blood Culture Results**

HSS Category	Culture (+)	Culture (-)	Total
Nonsepsis	8	9	17
Suspected sepsis + confirmed sepsis	13	13	26
Total	21	22	43

Chi-square test:  $\chi^2 = 0.036$ ;  $df = 1$ ;  $P = 0.850$

In Table 3, among neonates categorized as “nonsepsis” by the HSS, eight tested positive for sepsis by culture, whereas nine tested negative. Conversely, for neonates categorized under “Suspected sepsis + confirmed sepsis” using HSS, 13 tested positive and 13 tested negative in the culture tests.

The distribution of blood culture results did not differ significantly between HSS categories ( $\chi^2 = 0.036$ ;  $df = 1$ ;  $P = 0.850$ ). This indicates that there was no association between HSS classification and blood culture results in this study population.

## Discussion

Many studies have explored the significance and diagnostic accuracy of the HSS in neonatal sepsis. In this study, the significance of the HSS in the early detection of neonatal sepsis was assessed. Although HSS is widely considered a useful tool for neonatal sepsis screening, this study found its diagnostic accuracy to be lower than previously reported.<sup>13</sup> In contrast to the findings of this study, which demonstrated low diagnostic accuracy of HSS in identifying neonatal sepsis, previous studies have reported more favorable results.<sup>28</sup> This finding is consistent with the study by Makkar et al.<sup>22</sup> HSS was found to be a simple, rapid, and effective tool with high sensitivity and specificity in detecting neonatal sepsis.<sup>22</sup>

HSS combines several hematological parameters, such as total leukocytes, total neutrophils, immature neutrophils, I/T Ratio (immature/total neutrophil count), I/M Ratio (immature/mature neutrophil count), and thrombocytopenia (low platelet count). Each parameter is scored against a predetermined threshold. The total score is calculated by summing the scores of each parameter. This total score is used to assess the possibility of neonatal sepsis.

The sensitivity of HSS in this study was 59.09%. Meanwhile, the specificity of HSS in this study was 38.10%. This result is still lower than that in previous studies. Research from Soneta et al.<sup>29</sup> and Derbala et al.<sup>30</sup> had sensitivity values of 76.4% and 95%, and specificity values of 62.2% and 96.7%, respectively.<sup>24,25</sup> The study's low sensitivity and specificity results may be caused by differences in patient populations, sample size, methods, cutoffs used to determine HSS scores, and deviations in blood culture examination techniques.

Besides its diagnostic accuracy, the HSS has been compared with other diagnostic methods for neonatal sepsis. However, in this study, the HSS demonstrated low diagnostic accuracy, indicating limited reliability as a standalone diagnostic tool. Although previous studies have reported that HSS is a valuable tool for early diagnosis with good diagnostic performance and correlation with other markers, these findings were not consistent with the results of the present study.

The HSS is a simple and cost-effective tool that can aid in the early identification of neonatal sepsis. However, the relatively low sensitivity and specificity observed in this study indicate a substantial risk of false-negative and false-positive results, potentially leading to missed diagnoses or unnecessary antibiotic treatment. Therefore, HSS should be interpreted cautiously and used as an adjunct rather than a standalone diagnostic tool.

The clinical implication of this study is the need for rapid detection of neonatal sepsis. Neonatal sepsis requires rapid diagnosis to prevent high morbidity and mortality. HSS with high sensitivity can help doctors recognize this condition faster than waiting for blood culture results, which take 7 to 10 days longer. With accurate use of HSS, doctors can immediately start or stop antibiotics based on the level of suspicion of sepsis, reducing antibiotic overuse

that contributes to antimicrobial resistance. Although this study did not directly evaluate the combination of HSS with other biomarkers, previous studies have reported that combining HSS with biomarkers such as CRP and procalcitonin may improve diagnostic accuracy. This supports the potential role of a multimodal diagnostic approach for a more comprehensive assessment of neonatal sepsis. Therefore, HSS may still be considered in hospitals as a practical tool to screen for sepsis in newborns, especially in resource-limited settings. Another implication of this study is the need for further validation in different populations to ensure HSS remains relevant and can be widely applied in clinical practice. However, given its limited diagnostic accuracy in this study, HSS should be used cautiously and not as a standalone diagnostic tool. HSS is expected to help fill the gap in diagnosing and managing neonatal sepsis, accelerate early detection, and optimize antibiotic therapy when used in combination with other diagnostic methods.

This study, while providing valuable insights into the diagnostic capabilities of the HSS in neonatal sepsis, has certain limitations. First, the sample size may not be representative of the broader neonatal population, potentially limiting the generalizability of the findings. Moreover, the study relied heavily on the HSS's categorizations, which, as observed, showed discrepancies compared with the gold standard of blood culture results. The study did not account for potential external factors that might influence the HSS readings or the blood culture results, such as the timing of the tests, the health status of the neonates beyond sepsis, or the potential for human error in recording or interpreting results. Additionally, the study was conducted in a specific setting, and the findings might differ across healthcare environments or regions. Future research must address these limitations to provide a more comprehensive understanding of the HSS method's diagnostic capabilities.

## Conclusions

The study found that the hematologic scoring system (HSS) demonstrated low-to-moderate

sensitivity and specificity. Nevertheless, discrepancies emerged in the categorizations when juxtaposed with actual culture results. This underscores that although the HSS provides certain diagnostic insights, it may not be as reliable as blood culture results in definitively diagnosing neonatal sepsis. Combining HSS with C-reactive protein, IL-6, PCT, or I/T ratio is necessary to improve diagnostic accuracy.

## Conflict of interest

None.

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## Contributors

Dewi Indah Noviana Pratiwi conceptualized, analyzed the data, and wrote a draft of the manuscript, and Dastin Andre contributed to the methodology and data curation and reviewed the manuscript. Pandji Winata Nurikhwan was involved in methodology, data analysis, and reviewing the manuscript. All of the authors agreed on the final manuscript.

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## Data Availability Statement

The data supporting this study's findings are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

## Declaration of the Use of AI in Scientific Writing

During the preparation of this work, the author(s) did not use AI in Scientific Writing.

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