

# Effectiveness of Tollner's Score and Procalcitonin for Diagnosing Neonatal Sepsis

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## Abstract:-

**Background:** Gold standard for diagnosing neonatal sepsis is blood culture, but it takes time to get results. Procalcitonin is an acute phase reactant which increases 2 hours after infection. The Tollner's score, include clinical and laboratory tests, maybe useful for diagnosing sepsis in limited health care facilities. **Objective:** To determine the effectiveness of Tollner's score and procalcitonin for diagnosing neonatal sepsis. **Methods:** This cross-sectional study was conducted at Perinatology Haji Adam Malik Hospital Medan from March to July 2021. The sample was neonates who were clinically suspected sepsis. Patients went clinical examination, laboratory, and blood culture and then the Tollner's score was calculated. The analysis used receiver operating characteristic (ROC) curve to get the cut-off value. Diagnostic tests were performed to assess the effectiveness of the Tollner's score and procalcitonin. **Result:** Of 40 neonates, 24 (60%) neonates with positive blood culture. With a cut-off value is 11.8, Tollner's score obtained a sensitivity value 91.7%, specificity 87.5%, and with a cut-off of 8.5, procalcitonin obtained a sensitivity value 83.3%, specificity 81.2%. There was no significant difference in the Tollner's score in early and late onset sepsis. Procalcitonin in late-onset sepsis had a statistically significant result ( $p < 0.001$ ) compared to early-onset sepsis ( $p = 0.132$ ). The most common pathogen causing neonatal sepsis in this study was *Acinetobacter baumannii* as much as 16.7%. **Conclusion:** Tollner's score and procalcitonin have good sensitivity and specificity for diagnosing neonatal sepsis so it can be used in limited health care facilities.

**Keywords:-** Tollner's score, procalcitonin, neonatal sepsis, effectivity.

## I. INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by bacteremia and occurs in the first month of life.<sup>1</sup> Neonatal sepsis was divided into two groups based on the onset of presentation after birth, early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS refers to sepsis in neonates <72 hours after birth, whereas LOS refers to sepsis in neonates >72 hours after birth.<sup>2</sup>

The gold standard for diagnosing neonatal sepsis is blood culture. However, to get the results of blood culture takes time. Other blood tests that can be used in diagnosis are

complete blood count and acute phase reactants such as procalcitonin (PCT) and C-reactive protein (CRP).<sup>3</sup> Procalcitonin is an acute-phase reactant in response to inflammatory stimuli, especially bacteria.<sup>4</sup> Procalcitonin is more sensitive than CRP assays in the early diagnosis of neonatal sepsis due to bacterial infection, but with lower specificity.<sup>5</sup>

Tollner created a score to determine the initial diagnosis of neonatal sepsis. The scoring system consists of clinical examination of the patient as well as laboratory tests. This scoring examination can also be carried out by general practitioners by assessing all the scoring criteria. This scoring can be done in places with limited health care facilities, especially for blood cultures.<sup>5</sup>

The aim of our study was to determine the effectiveness of Tollner's score and procalcitonin for diagnosing neonatal sepsis.

## II. MATERIAL AND METHODS

This cross-sectional study was done to assess the effectiveness of Tollner's score and procalcitonin for diagnosing neonatal sepsis. This study was held in the Neonatology Unit of Haji Adam Malik Hospital, Medan, North Sumatera, from March to July 2021. The sample was neonates (<28 days) who were clinically suspected sepsis. Subject who had antibiotics 48 hours prior to the study were excluded.

Subject's demographic data were collected consisting of gender, methods of delivery, birth weight, gestational age, and congenital anomaly. Clinical evaluation was performed. Blood specimen, such as complete blood count, blood gas analysis, procalcitonin, were drawn at the time of the initial sepsis evaluation and conducted in Clinical Pathology Laboratory. Blood cultures were done in the Microbiology Laboratory. Tollner's score was calculated based on the results of clinical and laboratory examinations (Table 1). Neonates with positive blood culture were classified as having neonatal sepsis.

Parameter	Score
<b>Skin coloration</b>	
Normal	0
Moderate change	2
Considerable change	4
<b>Microcirculation</b>	
Normal	0
Impaired	2
Considerably impaired	3
<b>Metabolic acidosis</b>	
Normal	0
pH $\geq 7,2$	1
pH $< 7,2$	2
<b>Muscular hypotonic</b>	
No	0
Hypotonic	1
Floppy	2
<b>Bradycardias</b>	
No	0
Yes	1
<b>Apneic spells</b>	
No	0
Yes	1
<b>Respiratory distress</b>	
No	0
Yes	2
<b>Liver enlargement</b>	
0-2cm	0
2-4cm	0,5
>4cm	1
<b>Gastrointestinal symptoms</b>	
No	0
Yes	1
<b>White blood cell count</b>	
Normal	0
Leukocytosis	1
Leukocytopenia	2
<b>Shift to the left</b>	
No	0
Moderate	2
Considerable	3
<b>Trombositopenia</b>	
No	0
Yes	2

Table 1: Tollner's score

#### A. Research ethics

The parents or guardians of the research subjects were given explanations about the research and were asked for consent to be involved in the research. This research was approved by the Health Research Ethical Committee, Faculty of Medicine of Universitas Sumatera Utara and Haji Adam Malik hospital, Medan, Indonesia.

#### B. Data Analysis

Data collected was processed and analyzed with SPSS v20.0. Univariate analysis was done to describe the characteristics of research subjects. To determine the cut off point of Tollner's score and procalcitonin in diagnosing neonatal sepsis, receiver operating characteristic (ROC)

curve analysis and measurement area under curve (AUC) was used. Diagnostic tests were performed to assess sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), positive likelihood ratio (LR+), negative likelihood ratio (LR-), and accuracy of Tollner's score and procalcitonin for diagnosis neonatal sepsis.

### III. RESULTS

#### A. Research subject data characteristic

Forty neonates fulfilled the inclusion criteria. Out of which, 24 neonates (60%) were proven neonatal sepsis with positive blood culture. Twenty-two cases (55%) were male and 18 neonates (45%) were female. The proportion of vaginal delivery and caesarian section among the study population were 15 neonates (37,5%) and 25 neonates (62.5%) had sectio-caesarian delivery. Among 40 cases of neonatal sepsis, 15 neonates (37,5%) were diagnosed with early-onset sepsis, and 25 neonates (62.5%) cases were late-onset sepsis.

#### B. Diagnostic value of Tollner's score and procalcitonin

The value of Tollner's score in this study was obtained by ROC analysis (Figure 1), and the AUC was 96,9% (95%CI 0,91 to 0,99) and based on that we found the cut off value of the Tollner's score for diagnosing neonatal sepsis was 11,8. The value of procalcitonin in this study was obtained by ROC analysis (Figure 2), and the AUC was 88,7% (95%CI 0,80 to 0,90) and based on that we found the cut off value of the procalcitonin for diagnosing neonatal sepsis was 8,5.

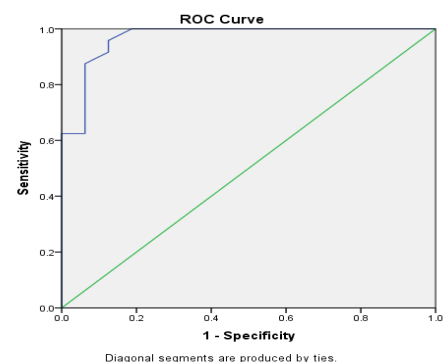


Fig. 1: Receiver operating characteristic (ROC) curve for Tollner's score

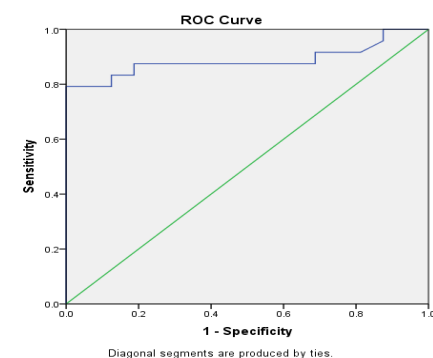


Fig. 2: Receiver operating characteristic (ROC) curve for Procalcitonin

Tollner's score and procalcitonin had high sensitivity and specificity for diagnosis neonatal sepsis. By using the cut-off value for Tollner's score of 11.8, the sensitivity value was 91.7%, specificity was 87.5%, PPV was 91.7%, NPV was 87.5%, LR+ was 7.3, LR- was 0.09. The accuracy of the

Tollner's score is 90%. By using a cut-off value for procalcitonin of 8.5, the sensitivity value was 83.3%, specificity was 81.2%, PPV was 87%, NPV was 76.5%, LR+ was 4.4, LR- 0.29. The accuracy of procalcitonin levels was 82.5%. Data shown in Table 2.

	Neonatal sepsis Yes	Neonatal sepsis No	Sensitivity	Specificity	PPV	NPV	LR+	LR -	Accuracy
Tollner's score ≥ 11,8	22	2	91,7%	87,5%	91,7 %	87,5%	7,3	0,09	90%
< 11,8	2	14							
Procalcitonin ≥ 8,5	20	3	83,3%	81,2%	87%	76,5%	4,4	0.29	82,5%
< 8,5	4	13							

Table 2: Diagnostic value of Tollner's score and procalcitonin

#### IV. DISCUSSION

Neonatal sepsis is a clinical syndrome consisting of non-specific symptoms and signs of infection accompanied by bacteremia in the first 28 days of life.<sup>3</sup> Risk factors for sepsis in neonates can be divided into infant risk factors and maternal risk factors.<sup>6</sup> This study was a cross-sectional study to assess the effectiveness of Tollner's score and procalcitonin for diagnosing neonatal sepsis.

In our study, most of the subjects were male. This is similar to the study conducted by Ramadanti *et al.*, from 94 neonates there were 56 (59%) male neonates and 38 (41%) female neonates with suspected neonatal sepsis.<sup>7</sup> This can be multifactorial, such as genetics, immunology, and hormones.<sup>8</sup> However, there are no adequate studies to demonstrate an association between sex as a risk factor for the development of neonatal sepsis.

The most common type of causative microorganism in this study was *Acinetobacter baumannii* in 4 neonates (16.7%) and followed by *Enterobacter aerogenes*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* in 3 neonates each (12.5%). A study by Wen *et al.* suggested that 60% of microorganisms causing neonatal sepsis in developing countries are gram-negative bacteria. It was found that *Acinetobacter spp.* was higher in Asia, especially South Asia. This could be because neonates admitted to the NICU are at high risk for invasive interventions, especially in preterm infants. Another risk factor is the high rate of cesarean delivery in South Asia, resulting in the acquisition of maternal-neonatal infection with *Acinetobacter spp* during hospitalization.<sup>9</sup>

Tollner created a scoring system using clinical examination and laboratory tests to establish early diagnosis of neonatal sepsis. It said that sepsis if the Tollner score >10.<sup>3</sup> In our study, the cut-off of the Tollner's score was 11.8 with a sensitivity value was 91.7% and specificity was 87.5.

A study by Harsanti *et al.* compared modified Tollner scores before and after antibiotics. Tollner's modified score in this study was to replace the blood gas analysis level with the value of C-reactive protein. The median value of

Tollner's score in this study before giving empirical antibiotics was 11.5 and after giving empirical antibiotics was 5.5 with p value = 0.001. A decrease in the sepsis score after 48 hours of empiric antibiotics was <10 indicating clinical improvement.<sup>10</sup> However, in our study there was no re-examination of the Tollner's score after giving empiric antibiotics.

In our study, the cut-off value of procalcitonin was 8.5ng/mL with a sensitivity 83,3% and specificity 81,2%. According to a study by Handayani *et al.*, the cut-off level of procalcitonin was found to be higher in gram-negative bacteria than in gram-positive bacteria.<sup>11</sup> In this study, the most microorganisms found were gram-negative bacteria.

A study compared the Tollner's score and procalcitonin found that Tollner's score is statistically significant to the procalcitonin value where the higher of Tollner score which indicates the presence of neonatal sepsis, the higher of procalcitonin value with p = 0.01. This can explain that Tollner's score can be carried out as a diagnostic tool in areas with limited facilities, especially if there is no procalcitonin examination and blood culture examination.<sup>12</sup>

#### V. CONCLUSION

The Tollner's score ≥11,8 and procalcitonin ≥8,5 could be use as early diagnostic tools for neonatal sepsis without waiting for the results of blood culture examination. The Tollner's score and procalcitonin have good sensitivity and specificity for diagnosis neonatal sepsis so it can also be used in areas with limited facilities.

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