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## Validity of Hematological scoring system in diagnosis of neonatal sepsis at Birat Medical College Teaching Hospital

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### ABSTRACT

**Introduction:** Newborns are vulnerable to infections. Timely diagnosis of neonatal sepsis can avoid major morbidity and mortality. Neonates with sepsis present with non-specific signs and symptoms. Timely diagnosis is important. Though blood culture is gold standard, it consumes time. Hematological scoring system (HSS) using hematological parameters can be effective in early diagnosis of sepsis.

**Objectives:** To evaluate the effectiveness (Sensitivity, specificity, Positive Predictive value (PPV), Negative Predictive value (NPV) of HSS and their individual parameters in diagnosis of neonatal sepsis.

**Methodology:** This was the cross-sectional study done at tertiary care hospital for period of six months. Neonates with clinical suspicion of sepsis were included in the study. Blood was drawn from neonate in two vials, one was sent for culture and other for calculation of hematological parameters as per Rodwell Hematological scoring system. Diagnostic study parameters were calculated.

**Result:** Total of 143 neonates clinically suspected of sepsis were included in the study with 83 having positive blood culture. Highest sensitivity (86.7%) was recorded for Total Polymorph neutrophil (PMN) while highest specificity (93.3) and PPV (81.8) for I: T PMN ratio. A sensitivity of 67.5% and specificity of 91.7% was seen along with PPV of 91.8% and NPV of 67.1% with HSS greater than or equal to 5.

**Conclusion:** HSS of greater than or equal to 5 can be considered to be the reliable screening tool for diagnosis of sepsis.

### INTRODUCTION

"Sepsis is life threatening organ dysfunction caused by dysregulated host response to infection."<sup>1</sup> Because of weaker immune system the new born are more vulnerable to infections and premature babies are even more vulnerable than older children.<sup>2</sup>

Being major cause of morbidity and mortality among neonates, timely diagnosis of sepsis is important to avoid morbidities like seizures, neurodevelopmental disorders, sensorineural hearing loss, visual disturbances and death. The signs and symptoms of sepsis in neonates are non-specific, hence clinical diagnosis is difficult.<sup>3</sup> Bacterial infection in new born is still the major cause of sepsis which is treatable if diagnosed early.<sup>5</sup> The bacterial infection can be transmitted from mother by transplacental route, ascending infection, in infected birth canal or during birth.<sup>4</sup> Hence can be treated by use of antibiotics. Having nonspecific symptoms sometimes sepsis results in injudicious use of antibiotic which may result in side effects and emergence of resistance.

Though blood culture is considered to be gold standard but it is time consuming and may take upto 48 to 72 hours.<sup>6</sup> Procalcitonin, interleukin, interferon gamma, tumour necrosis factor alpha, CD64 and soluble intercellular adhesion molecules are more sophisticated and costly markers for diagnosis.<sup>7</sup> The Rodwell scoring system utilizes the parameters like total count, total Polymorph neutrophil (PMN) count, immature PMN

count, Immature to total PMN ratio, Immature to mature PMN ratio, degenerative changes in PMN and platelets count which can be done during complete hemogram and is cost effective and easily available technique. Hence this scoring system can be used to for early diagnosis and to avoid unnecessary use of antibiotic in neonatal sepsis and has good sensitivity and specificity.<sup>8 6</sup> Thus the current study is done to evaluate the sensitivity, specificity, positive predictive value and negative predictive value of hematological scoring system in diagnosis of neonatal sepsis.

## METHODOLOGY

This was the hospital based cross sectional study done at Birat Medical College Teaching hospital (BMCTH), Tankisinuwari, Nepal from March to August, 2022 with duration of 6 months. All the neonates, age ranging from 0 to 28 days, presenting to pediatric OPD and emergency with the clinical features suspicious of sepsis were included in this study. Under aseptic condition blood samples of these neonates were collected in EDTA vial for hematological parameters analysis and in plain vial for blood culture. Neonates with major congenital abnormality, inborn error of metabolism, receiving prior antibiotic therapy, receiving blood transfusion, history of meconium aspiration, intrapartum

or neonatal death in sibling with similar presentation were excluded from the study.

Blood sample in EDTA vial were analyzed by hematological analyzer (Beckman coulter DxH500) and after that an air-dried slide was prepared which was stained by Wright Giemsa stain. Hematological parameters like total leucocyte count (TLC), Total PMN count, immature PMN count, I: T PMN count, I:M PMN count, degenerative changes in PMN and platelets count were done accordingly. Hematological scoring system score (HSS) were calculated as per Rodwell scoring system (Table no 1).<sup>6</sup> Each of the parameters based on the standard value were be given score of 1 or 0 with one exception, abnormal total count was given score 2, instead of 1 if no mature polymorphs were seen to compensate for low immature to mature ratio. Based on total score further classification of Sepsis (score>=5), Probable sepsis (score 3,4) and No sepsis (score 1,2) were made. Blood collected in the plain vial were sent for culture and antimicrobial growth was observed for at least 72 hours. The data were entered in MS excel and later analyzed using SPSS 20 to compare Culture status with hematological score. Thus sensitivity, specificity, Positive predictive Value (PPV) and Negative Predictive Value (NPV) of HSS was calculated.

**Table 1: Hematological Scoring System**

S.NO	Criteria	Abnormality	Score
1.	Total WBC count (TLC)	<5000/μl	1
		>25,000 at birth	1
		>30,000 at 12-48hrs	
		>21000 from day 2 onwards	
2.	Total PMN ratio	1800-5400/μl	0
		No mature PMN seen	1
		Increased/Decreased	2
3.	Immature PMN count	<600/μl	0
		Increased	1
4.	Immature: Total PMN count (I: T)	<0.12	0
		>0.12	1
5.	Immature to mature PMN ratio (I:M)	<0.3	0
		>0.3	1
6.	Degenerative changes in PMN	Toxic granules/Cytoplasmic Vacuolization	1
7.	Total platelet count	<150000/μl	1

## RESULT AND OBSERVATION

This study included 143 neonates clinically suspected of sepsis of age ranging from 0 days (10 hour) to 28 days. Among these neonates 38(26.6%) were females and 105(73.4%) were males with male to female ratio of 2.7:1.

**Table 2: Correlation of HSS parameters with blood culture status**

HSS parameters	Blood culture positive n=83(%)	Blood culture negative n=60(%)	Total n=143(%)
TLC count	69(83.1)	23(38.3)	92(64.3)
Total PMNs	72(86.7)	50(83.3)	122(85.3)
Immature PMN	66(79.5)	22(36.6)	88(61.5)
I: T PMN ration	50(60.2)	11(18.3)	61(42.7)
I:M PMN ration	18(21.7)	4(6)	22(15.4)
Degenerative changes in PMN	67(80.7)	18(30)	85(59.4)
Platelets count	64(77.1)	20(33.3)	84(58.7)

Table 2 shows comparison of different hematological score parameters with blood culture status. Our study showed 83(58%) culture positive neonates and 60(42%) culture negative ones.

Maximum number of cases (85.3%) has abnormal Total PMN count in which 72 cases were culture positive which comprises 86.7% of all culture positive cases. This was followed by abnormal

TLC and Immature PMN count. Immature cells like bands, myelocytes and metamyelocytes were noted and included in immature PMN count. Similarly degenerative changes were noted in the form of toxic granules and vacuolization. Total PMN count, TLC count and degenerative changes in PMN were positive in higher proportion in culture positive cases.

**Table 3: Performance of individual hematological parameters in culture proven cases in comparison to various studies**

Parameters	Authors	Sensitivity%	Specificity%	PPV%	NPV%
TLC count	Bhalodi <sup>9</sup>	66.7	74.5	48	87
	Derbala <sup>10</sup>	90	93.3	93.3	92
	Dey <sup>2</sup>	97.56	47.85	32	98.73
	Our study	83.1	61.7	75	72.5
Total PMNs	Tushar <sup>11</sup>	52.75	91.04	80	73.94
	Rajshree <sup>8</sup>	89.1	32.1	41.8	84.3
	Our study	86.7	16.7	59	47.6
Immature PMN	Tushar <sup>11</sup>	55.49	92.91	84.17	75.45
	Rajshree <sup>8</sup>	67.3	63	50	77.9
	Our study	79.5	63.3	75	69.1
I: T PMN ratio	Tushar <sup>11</sup>	35.82	72.76	39.17	59.09
	Aparna <sup>5</sup>	63.15	75	88.88	39.13
	Our study	60.2	81.7	82	59.8
I:M PMN ratio	Tushar <sup>11</sup>	25.8	74.1	26.5	60.2
	Rajshree <sup>8</sup>	13	100	100	67.7
	Our study	21.7	93.3	81.8	46.3
Degenerative changes	Tushar <sup>11</sup>	45.60	86.19	69.17	70
	Aparna <sup>5</sup>	68.42	66.66	66.66	40
	Our study	80.7	70	78.8	72.4
Platelets count	Makkar <sup>4</sup>	70.45	93.93	93.9	72.4
	Hassan <sup>12</sup>	55.6	59.5	70	44
	Our study	77.1	66.7	76.2	67.8

Performance of individual HSS parameters among investigated neonates along with comparisons of different studies is shown in Table 3. The highest sensitivity was recorded for total PMNs

count (86.7%), highest specificity for I:M PMN ratio (93.3%), Highest PPV for I:M ratio (81.8%) and highest NPV for TLC count and degenerative changes (72.5%).

**Table 4: Hematological scoring system comparisons with Culture**

Hematological score	Culture		Total
	Positive	Negative	
No sepsis (Score 0,1,2)	3	31	34
Probable sepsis (Score 3,4)	24	24	48
Sepsis (Score 5,6,7)	56	5	61
Total	83	60	143

Table 4 shows classification of neonates as per HSS and comparison with blood culture status

1. Sepsis (42.7%) with score of greater than or equal to 5
2. Probable sepsis (33.6%) with score of 3 and 4
3. No sepsis (23.8%) with score of 1 and 2.

Out of 34 cases in category of no sepsis (score of 0,1,2) only 3 were culture positive and 31 were culture negative. Similarly, out of 61 cases in category sepsis (score 5,6,7), 56 were culture positive and 5 were negative. Considering culture positivity as the standard, HSS of greater than or equal to 5 (sepsis) were compared. A sensitivity of 67.5% and specificity of 91.7% was seen along with PPV of 91.8% and NPV of 67.1% was observed in our study.

Similarly taking cutoff value of HSS as 3 (probable sepsis and sepsis) the sensitivity of 96.1%, Specificity of 51.6%, PPV of 73.4% and NPV of 91.2% was observed in our study.

## DISCUSSION

Neonatal sepsis is one of the major problems in developing world due to high morbidity and mortality. Undiagnosed sepsis results in rapid deterioration and death.<sup>9,10</sup> Early empirical antibiotic therapy can be lifesaving, hence early diagnosis is very important.<sup>13</sup> Although blood culture is the most definitive diagnosis of neonatal sepsis, it takes time and sometimes results in judicious use of antibiotics. Hence lack of rapid laboratory tests results in difficulty to clinicians.<sup>10</sup> Early HSS is practically possible in all laboratories and even in resource poor settings. Therefore, this study was done to assess the performance of HSS for early detection of neonatal sepsis.

This study showed male preponderance with male outnumbering females by 2.7 times which was similar to the study done by Rajshree et al, Heena et al and Dipika et al.<sup>8,12,2</sup> The findings in this study was in contrast to study done by Manoj et al and Makkar et al where there was female predominance.<sup>6,4</sup> The male preponderance is due to fact that that the development of thymus and antibody production is X-linked hence contributing to the susceptibility to infections in male.

In our present study 69 neonates were culture positive, with culture positivity rate of 58% which is similar to the study done by Heena where culture positivity rate was 63%.<sup>12</sup> The culture positivity depends upon the time of sampling, bacterial overload and prior antibiotic therapy was excluded from this study.

Table 3 shows the performance of individual HSS parameters in diagnosing neonatal sepsis comparison with various other studies. Leucopenia and leukocytosis depending upon age were taken into the consideration in TLC count. Our study shows higher sensitivity whereas moderate specificity, PPV and NPV in TLC count. Comparing TLC count with other studies, TLC alone is of little clinical use in diagnosis of neonatal sepsis because of wide variation of values according to age.

Neutropenia and neutrophilia (Total PMN count) has highest sensitivity and lowest specificity in our study similar to study done by Tussar and Rajshree.<sup>11,8</sup> Immature cell count of more than 600/  $\mu$ l was considered in our study. Interobserver variations are seen in counting immature cells like myelocytes, metamyelocytes and band cells and time of sample collection also affects this value. Hence variation was seen among different studies in immature PMN count, I:T ratio and I:M ratio. I:M ratio has lowest sensitivity and highest specificity in our study similar to Tussar and Rajshree.<sup>11,8</sup>

Degenerative changes like cytoplasmic vacuolization and toxic granules of neutrophils are due to continuous stimulation of neutrophils production resulting in rapidly maturing neutrophils.<sup>14</sup> Sensitivity and specificity of the degenerative changes of our study was similar to study done by Aparna and Tussar.<sup>5,11</sup>

Thrombocytopenia (platelets count <1,50,000/ $\mu$ l) in sepsis is due to increased platelets destruction, sequestration secondary to infections and reduced megakaryocyte production to damaging effect of endotoxin. This is correlated with our study along with other study as shown in Table 3.

In our study among the neonates with culture positivity and hematological score of greater than or equal to 5 (sepsis) has high specificity (91.7%) and PPV (91.8%) with moderate sensitivity (67.5%) and NPV (67.1%). The score of greater than or equal to 3 (sepsis and probable sepsis) has higher sensitivity (91.6%) and NPV (91.2%) in our study. Hence score of greater than or equal to 5 is considered to be the reliable screening tool for diagnosis of sepsis which is similar to the findings by study done by Majumdar and Fathia.<sup>15,14</sup>

Sepsis markers like CRP, cytokines and prolactin will give better results if combined together but these are expensive and not available at every health care centre.<sup>14</sup>

## CONCLUSION

Hence hematological scoring system with score of greater than or equal to 5 can be utilized in the resource poor setting in diagnosis of neonatal sepsis as it is feasible, cost effective and rapid.

**LIMITATIONS OF THE STUDY** Correlation with other parameters like CRP, ESR, interleukin was not done in our study.

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**CONFLICTS OF INTEREST** NONE

**FINANCIAL DISCLOSURE** NONE

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