Hematologic scoring system (hss); a simple diagnostic tool to detect early neonatal sepsis in a resource limited setup.

Dr.Beela Siddiqui MBBS, MCPS. *,Dr. Kashif Abbas a, Dr. Fatima Asif b, Dr.Beela Musib c, Dr samina shamim d

Registrar Paediatric Medicine*, Department of Pediatrics , Liaquat National Hospital , Karachi, Pakistan, Department of Hematology, Liaquat National Hospital, Karachi, Pakistan.

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Corresponding Author:
Dr.Beela Siddiqui

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ABSTRACT

Introduction: Over past two decades neonatal morbidity associated with sepsis has increased due to changing microbial spectrum. To establish early diagnosis of neonatal sepsis is a challenge because of varied clinical presentations. For definite diagnosis of sepsis culture results are gold standard which are time consuming. The other recent available markers are sensitive but expensive. Hence they have limited use in financially constrained setup. Therefore there is always a need for an infallible cost-effective test to detect bacteremia that could be easily performed. In this study we have evaluated the effectiveness of the hematological scoring system (HSS) of Rod well et al suggested in 1988 which is based on CBC report

Material and Methods: A prospective study was conducted in NICU of Liaquat National Hospital from October 2015 to March 2016. All Neonates with predisposing perinatal risk factors for sepsis or clinical index of suspicion were enrolled in the study. A baseline CBC and bloods C/S were sent. The hematological findings were analyzed according to the hematologic scoring system (HSS) of Rod well et al. A score of 2 or above out of 7 was consider to be indicative of sepsis

Results: 109 neonates were enrolled in the study, 63 were male and 46 were female. Of total 62(56.8) % were culture positive, in which 45 (41.2%) had positive blood culture, 13 (11.9%) had positive urine culture only 4 (3.6%) with positive tracheal culture isolated. The sensitivity of HSS detecting neonatal sepsis is 90.3%, specificity is 85.1%, positive predictive value (PPV) is 88.89% and negative predictive value (NPV) is 86.96%.

Conclusion: Rod wells’ hematological scoring system is a feasible and cost effective method in detecting early neonatal sepsis for the resource limited countries. However the emphasis for a well-equipped laboratory and a trained hematologist is of much value

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Introduction:
It has been explained that neonates are at the highest risk for bacterial sepsis, with the prevalence at 1 to 10 per 1000 live births worldwide. 1, 2. Mortality due to sepsis has increased by approximately 13.7% each year over the past two decades. 3. Neonatologists who supervise neonatal intensive care unit (NICU) always face a challenge in managing the neonatal infections due to the changing patterns of the microbial flora and their antibiotic sensitivity. A gradual decrease in susceptibility to routine antibiotic is more highlighted in infants with lower birth weight and premature infants .4, 5

Neonatal sepsis is a systemic infection occurring in infants at ≤28 days of life and is an important cause of morbidity and mortality of newborns. Early-onset neonatal sepsis (EOS) has been variably defined based on the age at onset, with bacteremia or bacterial meningitis occurring at ≤72 h in infants hospitalized in the NICU versus <7 days in term infants. In preterm infants, EOS is most consistently defined as occurring in the first 3 days of life and is caused by bacterial pathogens transmitted vertically from mother to infant before or during delivery .6

Therefore, the early detection of neonatal sepsis is a vexing problem. A definite diagnosis is made by blood culture. However, the procedure is time consuming (takes 48-72 h), yield is low (8-73%) [7-8, 9, 10] So, the significance of various screening tests, either singly or in combination is observed. Recently there has an emergence of new, sensitive and specific markers of sepsis but are expensive. Due to limitation of resources it become impossible to perform these test. Therefore the need for an infallible test for bacteremia that is easily and routinely performed and also quick, simple, and especially cost-effective. The cost difference is around 4 to 5 times higher for new markers as compare to complete blood count required for Rodwell scoring system.

Here, in this study, we undertake to evaluate the performance of the hematological scoring system (HSS) of Rodwell et al. (1988)11 based on complete blood count, in 110 neonates for the early detection of sepsis. Therefore the aim of this study is to evaluate the diagnostic accuracy of the complete blood cell count as a screening test for neonatal sepsis.

Material and methods:
This is a prospective study, conducted in NICU of LIAQUAT NATIONAL HOSPITAL within a time period of six months, October 2015 to march 2016.

Inclusion criteria: Neonates were enrolled in the study if there were predisposing perinatal factors or if there was clinical suspicion of sepsis.

Exclusion criteria: Neonates who were severely jaundiced due to blood group incompatibilities were excluded from this study.

After taking a careful history specified questionnaire was designed and the detailed information was recorded by the investigator. Blood sample was obtained by peripheral venipuncture in an ethylenediaminetetraacetic acid (EDTA) vial. The total leukocyte counts were counted on a Sysmex counter (Sysmex K21) and corrected for nucleated red blood cells. Differential counts were performed on Leishman stained blood smears by counting at least 200 cells.

A band was defined as a neutrophil in which the nucleus was indented by more than one half, but in which the isthmus between the lobes was wide enough to reveal two distinct margins with nuclear material between. All films were reviewed by a pathologist blinded to the infection status of the infants. Degenerative morphologic changes in neutrophils were graded 0 to 4+ according to Zipursky et al 12. Immature neutrophils include promyelocyte, myelocyte, metamyelocytes, and band form. Degenerative changes in neutrophils include vacuolization, toxic granulations, and Dohle bodies.

The hematological findings were analyzed according to the hematologic scoring system (HSS) of Rodwell et al.11 The HSS assigns a score of one for each of the seven criteria found to be significantly associated with sepsis [Table 1] with one exception. A score of ≤ 2 indicates “sepsis which is unlikely”, 3/4 indicates “suspected sepsis” and ≥ 5 sepsis is very likely.
Results: Of 109 neonates enrolled in the study, 63 were male and 46 were female babies which constitute about 57.7% and 42.2% respectively. Moreover, a total of 62 out of 109 babies were found to have positive culture which is about 56.8% of total, in which 45 (41.2%) had positive blood culture, 13 (11.9%) had positive urine culture only 4 (3.6%) with positive tracheal culture was found in our study.

Furthermore, Acinetobacter MDR is the most common organism being found in this study, out of 62 cultures positive neonates, 27 was found to have acinetobacter MDR, 11 with Pseudomonas, 10 with E.coli, 8 with acinetobacter, 4 with Burkholderia Cepacia, , and only 2 babies with MRSA was found in our study.

Maternal fever was found as the leading risk factor which causes sepsis in neonates in our study. Of 109 neonates enrolled in study, 36 had been associated with Maternal fever as risk factor developing sepsis in neonates which constitute 33.0% of total. Other risk factors includes High maternal TLC with 27 (24.8%), PROM (prolong rupture of membrane) which comprises 17(15.6%), leaking 16(14.7%), urinary tract infection 10 (9.2%), and maternal positive culture constitute 3 (2.8%) respectively.

HSS is found to be a good indicator for detecting early neonatal sepsis. It detects early neonatal sepsis depending upon criteria by which baby condition is assessed. Certain risk factors influence the criteria which include both fetal and maternal conditions. ≤2 indicates “sepsis which is unlikely”, 3/4 indicates “suspected sepsis” and ≥ 5 sepsis is very likely.

In our study, a total of 46 babies which constitute about 42.2% were found to have hematologic score ≤ 2. For our convenience; to determine the diagnostic accuracy, we have categorized babies into septic and non-septic on the basis of hematologic score in our study. Those who have scores ≤ 2 are non-septic and those who have scores ≥2 are septic neonates.

In our study, the sensitivity of HSS detecting neonatal sepsis is 90.32%, specificity is 85.11%, positive predictive value (PPV) = 88.89% and negative predictive value (NPV) is 86.96%. This can be done by the table-2 given below.

### Table - 1: Spectrum of organism in NICU

<table>
<thead>
<tr>
<th>Organism</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinobacter MDR</td>
<td>27</td>
<td>24.8</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>11</td>
<td>10.1</td>
</tr>
<tr>
<td>E.coli</td>
<td>10</td>
<td>9.2</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>8</td>
<td>7.3</td>
</tr>
<tr>
<td>Burkholderia cepacia</td>
<td>04</td>
<td>3.7</td>
</tr>
<tr>
<td>MRSA</td>
<td>02</td>
<td>1.8</td>
</tr>
<tr>
<td>No growth</td>
<td>47</td>
<td>43.1</td>
</tr>
</tbody>
</table>

### Table - 2: Sensitivity= TP/TP+FN, Specificity= TN/TN/FP, Positive predictive value (PPV) = TP/TP+FP×100, Negative predictive value (NPV) = TN/TN+FN×100

<table>
<thead>
<tr>
<th>Blood Culture</th>
<th>Septic Neonates (HSS Scores)</th>
<th>Non-Septic Neonates (HSS Scores)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>True positive 56</td>
<td>False positive 7</td>
</tr>
<tr>
<td>Negative</td>
<td>True negative 6</td>
<td>False negative 40</td>
</tr>
</tbody>
</table>

Discussion:

Neonatal sepsis remains a leading cause of mortality and morbidity, and also challenging and time consuming in terms of diagnosis. Empiric treatment is usually started in all clinically suspicious cases, as gold standard diagnostic test for sepsis is blood culture which requires a minimum of 48-72 hours for initial report and sometimes more time is required for slow growing organisms. To rule out neonatal sepsis is difficult and can result in prolong and unnecessary exposure to antibiotics. Thus need for a quick, cheap and easily available laboratory test that assists in early diagnosis is required.
Hematologic scoring system (HSS) has emerged as an important tool in early diagnosis of sepsis, it relies on complete blood count report, which is easily accessible and is part of routine baseline investigations. It takes into account WBC count, I:M,(Immature to mature neutrophils ) I: T ratio (immature to total neutrophilic count ), degenerative changes of neutrophils and platelet count. Males were predominant in our study which is consistent with other studies, in study by munaza saleem attributed male predominance to globulin synthesizing factors on X chromosome thus making males more susceptible to infections.

In our study 56.88% of neonates were found to be culture proven sepsis with acinatobacter MDR being common organism. Maternal fever was found as the leading risk factor for sepsis in neonates (33.0 %) of total in our study this is related to study done by Khalida binte khair et al in which PROM was found to be the major risk factor.

Categorization was done for diagnostic accuracy into septic and non-septic on the basis of hematologic score in our study, scores ≤ 2 are non-septic and those who have scores ≥2 are septic neonates.

In our study, the sensitivity of HSS detecting neonatal sepsis is comparable to study done by Manisha makkar which divided the result in preterm and term babies. Moreover the presence of toxic granules indicates the production of unusual PMNs during infection and stress induced leucopoiesis. They are never seen in healthy babies. Their presence invariably indicates sepsis, but their count is not always increased. In our study, the sensitivity of HSS detecting neonatal sepsis is 90.32%, specificity is 85.11%, positive predictive value (PPV) is 88.89 % and negative predictive value (NPV) is 86.96%.

Conclusion:
The feasibility and the cost effectiveness of Hematological scoring system increase the usefulness of this test. This helps the clinicians to reach a probable diagnosis, decreasing the death toll and institute a rational approach towards the patient medication, i.e., avoiding unnecessary instillation of antibiotics and preventing the development of resistance to these drugs.

References:
10. Gladstone IM, Ehrenkrantz RA, Edberg SC, Baltimore RS. A ten-year review of neonatal sepsis and comparison with the previous


