HAEMATOLOGICAL CHANGES IN NEONATAL SEPSIS- A STUDY IN A TERTIARY CARE HOSPITAL
Phuritshabam Pinky1, Rajesh Singh Laishram2, Khagokam Ambala Devi3, R. Jesu Pandiar4, R. K. Tamphasana Devi6

1Senior Resident, Department of Pathology, Regional Institute of Medical Sciences, Imphal.
2Associate Professor, Department of Pathology, Regional Institute of Medical Sciences, Imphal.
3Assistant Professor, Department of Pathology, Regional Institute of Medical Sciences, Imphal.
4Consultant, Department of Pathology, Kalyani Multispecialty Hospital, Chennai.
5Former Professor, Department of Pathology, Regional Institute of Medical Sciences, Imphal.

ABSTRACT

BACKGROUND

Sepsis is the commonest cause of neonatal mortality. Early recognition of neonatal sepsis is difficult as the clinical signs and symptoms are non-specific and the failure or delay in treatment may result in significant mortality and morbidity.

MATERIALS AND METHODS

Blood samples were taken from neonates attending Regional Institute of Medical Sciences, Imphal, Manipur, India with clinical features of sepsis. Various haematological tests were performed including haemoglobin level, total WBC count, total PMN count, immature PMN count, I:T PMN ratio, I:M PMN ratio, degenerative changes in PMN and platelet count. Haematological scoring and blood culture were done for each case. Correlation of the various haematological parameters was done with the blood culture.

RESULTS

A total of 101 neonates with clinical features of neonatal sepsis were included in the study. Out of all the cases, 59 (58.4%) cases were ≤7 days of age. Early onset sepsis was present in 58.4% of cases and late onset sepsis was present in 41.6% of the cases. Bacterial culture was positive in 27 (26.7%) cases. Among the organisms grown, coagulase negative staphylococci (CoNS) was the most common organism accounting to about 55.6%. Abnormal features of sepsis. Various changes in different haematological parameters were seen in neonatal sepsis. Present study evaluates the haematological scoring system and the following 7 parameters individually and in combination: i.e. leucocyte count, neutrophil count (PMN), immature PMN count, immature to total PMN ratio (I:T), immature to mature PMN ratio (I:M), platelet count and degenerative changes in neutrophils, in early diagnosis of neonatal sepsis.

CONCLUSION

None of the haematological parameters studied can be used alone for a reliable diagnosis of neonatal sepsis. However, a combination of tests and a haematological scoring system is a very useful diagnostic aid to the clinicians.

KEYWORDS

Neonatal Sepsis, Haematological Scoring System, Blood Culture.


BACKGROUND

Neonatal sepsis is defined as a clinical syndrome characterized by signs of systemic infection and documented by a positive blood culture in the first four weeks of life.1 The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births.2 Early recognition of sepsis in neonates is difficult as the clinical signs and symptoms are non-specific and the failure or delay in treatment may result in significant mortality and morbidity.3 Infected infants must, therefore, be promptly identified and differentiated from non-infected patients, and antibiotics started without delay. Blood culture is considered to be the ‘gold standard’ for diagnosis of septicaemia; however, it is a time-consuming procedure with spurious positive results and demands a well-equipped laboratory. In addition, antimicrobial treatment based solely on risk factors and clinical grounds is likely to result in overtreatment. Therefore, a test that is cheap, reliable, easily performed with quick availability of reports is required. Various changes in different haematological parameters are seen in neonatal sepsis. Present study evaluates the haematological scoring system and the following 7 parameters individually and in combination: i.e. leucocyte count, neutrophil count (PMN), immature PMN count, immature to total PMN ratio (I:T), immature to mature PMN ratio (I:M), platelet count and degenerative changes in neutrophils, in early diagnosis of neonatal sepsis.
Aims and Objectives
The objective of the study was to assess the significance of the various haematological parameters and the haematological scoring system in early diagnosis of neonatal sepsis.

MATERIALS AND METHODS
The study was conducted in the Department of Pathology, Regional Institute of Medical sciences (RIMS), Imphal, Manipur from October 2012 to September 2014. All neonates below the age of 28 days attending the Department of Paediatrics, RIMS with clinical features of neonatal sepsis were included in the study. Excluded from the study were neonates who had received antibiotics, blood transfusion before collection of sample and neonates with inborn errors of metabolism. A careful detailed history of the neonates was recorded in the predesigned proforma. Aseptic precautions, blood sample was drawn within 24 hours of admission. For haematological examination, 1 ml of blood sample was taken in an ethylene diamine tetra acetic acid (EDTA) container and received in the Pathology Department. For blood culture, 0.5 ml of blood was put into 5 ml of blood culture medium in an ethylene diamine tetra acetic acid (EDTA) container and received in the Pathology Laboratory.

RESULTS
A total of 101 neonates with clinical features of neonatal sepsis were included in the study. 59 (58.4%) cases were males and 42 (41.6%) cases were females. Out of all the cases, 59 (58.4%) cases were ≤ 7 days of age. Early onset sepsis was present in 58.4% of cases and late onset sepsis was present in 41.6% of the cases. Bacterial culture was positive in 27 (26.7%) cases. Among the organisms grown, Coagulase negative staphylococci (CoNS) was the most common organism accounting to about 55.6%. Escherichia coli (22.2%), Klebsiella (14.8%) and Staphylococcus aureus (3.7%) were the other organisms isolated. Abnormal total PMN count had the highest sensitivity of 96.2%. Haematological score ≥ 5 had the highest specificity 98.6% and the highest positive predictive value of 93.8%. The highest negative predictive value of 96.2% was shown by I:T ratio ≥ 0.12 (Table 1).

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal WBC Count</td>
<td>48.1%</td>
<td>91.9%</td>
<td>68.4%</td>
<td>82.9%</td>
</tr>
<tr>
<td>Abnormal Total PMN Count</td>
<td>96.2%</td>
<td>28.4%</td>
<td>32.9%</td>
<td>95.4%</td>
</tr>
<tr>
<td>Immature PMN ≥ 600/µl</td>
<td>92.6%</td>
<td>48.6%</td>
<td>39.7%</td>
<td>94.7%</td>
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<tr>
<td>I: T Ratio ≥ 0.12</td>
<td>92.6%</td>
<td>68.9%</td>
<td>52.1%</td>
<td>96.2%</td>
</tr>
<tr>
<td>I: M Ratio ≥ 30</td>
<td>33.3%</td>
<td>95.9%</td>
<td>75.0%</td>
<td>79.8%</td>
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<tr>
<td>Degenerative Changes in PMN</td>
<td>59.3%</td>
<td>94.6%</td>
<td>80.0%</td>
<td>86.4%</td>
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<tr>
<td>Platelet Count &lt; 1.5 Lakhs</td>
<td>25.9%</td>
<td>89.2%</td>
<td>46.7%</td>
<td>76.7%</td>
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<tr>
<td>Haematological Score ≤ 2</td>
<td>11.2%</td>
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<td>6.4%</td>
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<td>Haematological Score 3, 4</td>
<td>33.3%</td>
<td>60.8%</td>
<td>23.7%</td>
<td>71.42%</td>
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<tr>
<td>Haematological Score ≥ 5</td>
<td>55.6%</td>
<td>96.6%</td>
<td>93.8%</td>
<td>85.8%</td>
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</tbody>
</table>

Table 1. Comparison of Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Each Test

DISCUSSION
The present study showed wide variation in values of WBC count and revealed that abnormal WBC count had sensitivity, specificity, PPV and NPV of 48.1%, 91.9%, 68.4% and 82.9% respectively. Khair KB et al.\(^7\) studied 100 neonates admitted at neonatal ICU, BSMMU, Dhaka and found that total WBC count had a sensitivity of 50% and specificity of 91%, PPV of 43% and NPV of 93%. Similar findings were seen by Philip AGS and Hewitt JR\(^8\) and Namdeo UK et al.\(^9\) The positive predictive value of abnormal WBC count is poor. This is not surprising since many non-infectious conditions can be associated with an abnormal WBC count. In the past, changes in the WBC count were regarded least useful for the diagnosis of sepsis as these values were thought to be too erratic which also holds true in the present study.

In the present study, among the individual parameters, an abnormal total PMN count showed the highest sensitivity and the lowest specificity. We observed a sensitivity of 96.2%, a specificity of 28.4% along with a PPV of 32.9% and NPV of 95.4% which is consistent with the findings reported by Khair KB et al.\(^7\) and Majumder A et al.\(^10\) Inspite of the high sensitivity, total PMN alone cannot be used for diagnosis of neonatal sepsis because of its very low specificity. However, Buch AC et al.\(^11\) observed that total PMN as an individual test was helpful to rule out sepsis since it had lower sensitivity (66%), higher specificity (90.91%) and NPV (69.44%). Shirazi H et al.\(^12\) also observed a low sensitivity (35%) and a high specificity (74%). These variations in the results shown by different studies may be due to differences in blood sampling time, severity of infections, and the age of the neonates.

A shift to the left in differential white cell count with a raised immature neutrophil count has been documented in patients with bacterial infections.\(^7\) In the present study immature PMN count had a sensitivity of 92.6%, specificity of 48.6%, PPV of 39.7% and NPV of 94.7%. Majumder A et al.\(^10\) observed similar results. Despite a significant rise in immature neutrophil count in infants with suspected infection, abnormal immature PMN count gave low specificity due to a large number of false positive result. Therefore, this parameter alone should not be evaluated for diagnostic purposes.

The present study revealed that an elevated I:T ratio had a sensitivity of 92.6%, specificity of 68.9%, PPV of 52.1% and NPV of 96.2%. The high sensitivity and NPV were consistent with the studies by Khair KB et al.\(^7\) and Buch AC et al.\(^11\) Considering high mortality and morbidity associated with sepsis, tests with high sensitivity and NPV are most desirable because all infants with sepsis have to be identified. A study by Makkar M et al.\(^13\) and Ghosh S et al.\(^14\) found elevated I:T ratio to be the most reliable indicator of sepsis.

I:M ratio in the present study revealed sensitivity, specificity, PPV and NPV of 33.3%, 95.9%, 75.0%, 79.8% respectively. Rodwell RL et al.\(^15\) used I:M ratio as a predictor of infection and observed a sensitivity of 93%, specificity of 81%, PPV 32% and NPV of 99%. Ghosh S et al.\(^14\) found similar results. Khair KB et al.\(^7\) observed that the sensitivity, specificity, PPV and NPV of I:M ratio are respectively 100%, 07%, 11% and 100%. The wide differences in the values of I:M ratio in different studies may be partly attributed to their subjective measurement and inter observer variability in assessment of immature PMN.

In the present study, degenerative changes in PMN had a sensitivity, specificity, PPV and NPV of 59.3%, 94.6%, 80.0%, 86.4%. Zieve PD et al.\(^16\) showed a very close relationship between the presence of vacuolated neutrophils and bacterial infections. Xanthou M.\(^17\) observed that toxic granulation was invariably present during sepsis, a change never seen in healthy newborn babies. Neonates with sepsis develop thrombocytopenia, possibly because of disseminated intravascular coagulation (DIC) and the damaging effects of toxins on platelets. Zaki MES et al.\(^18\) evaluated newborn infants with clinical diagnosis of neonatal sepsis where thrombocytopenia had a sensitivity of 41% specificity of 87%, PPV of 50% and NPV of 52%. This study shows thrombocytopenia with a sensitivity of 25.9% specificity of 89.2%, PPV of 46.7% and NPV of 76.7%. Buch AC et al.\(^11\) had similar findings on thrombocytopenia except for a higher sensitivity of 46.15%. The low sensitivity of platelet count in the present study renders it a less ideal test as a single parameter for screening of neonatal sepsis. The specificity was, however, high and therefore this parameter if combined with other tests can be used to exclude sepsis with some confidence.

<table>
<thead>
<tr>
<th>I:T Ratio + Total PMN Count</th>
<th>Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bacteriologically Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>25</td>
</tr>
<tr>
<td>Negative</td>
<td>02</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>I: T ratio + Degenerative Changes in PMN</th>
<th>Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bacteriologically Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>12</td>
</tr>
<tr>
<td>Negative</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
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</table>
As no single haematological parameter is superior in comparison to another in predicting neonatal sepsis, a combination of these parameters in the form of HSS is a very useful screening tool. Manucha V et al\(^1\) observed that majority of neonates with a haematological score of \(\geq 3\) had a sensitivity of 86% and NPV of 96%. Khair KB et al\(^7\) concluded that scores \(\geq 4\) are more specific and increases the likelihood of sepsis in relation to other scores. Makkar M et al\(^13\) evaluated the HSS of Rodwell RL et al\(^5\) in 110 neonates for early detection of sepsis in high risk infants and observed that higher the score, more the chances of sepsis and vice versa. The present study revealed that the sensitivity, specificity, PPV and NPV increases as the score increases.

Buch AC et al\(^11\) observed that the combination of five parameters I:T ratio + absolute neutrophil count + CRP + ESR + Platelet count to be the best to predict the diagnosis of neonatal sepsis Mishra PK et al\(^19\) observed that the positive predictive value and the specificity of two test combination was higher than the individual test at the cost of sensitivity. In the present study, it was observed that when total PMN and I:T ratio were combined, the specificity and positive predictive value of the combination was higher than that of the individual tests, while sensitivity was lower than the individual tests. Similarly, the combination of I:T ratio and degenerative changes in PMN revealed a lower sensitivity than the individual test. Our observations are, therefore, consistent with other studies.

CONCLUSION
No single haematological parameter is superior to another in predicting neonatal sepsis. However, the combination of tests and HSS are helpful in diagnosing as well as excluding sepsis and can provide an effective guideline to make decisions regarding judicious use of antibiotic therapy which will be lifesaving, provide early cure, as well as minimize the risk of emergence of resistant organism due to misuse of antibiotics.

REFERENCES