Abstract

Background: Neonatal sepsis is one of the major causes of morbidity & mortality in the newborn, more so in the developing countries.

Objective: The objective of this study was to evaluate the applicability of Haematological Scoring System (HSS) in early diagnosis of sepsis and its compatibility with C-reactive protein (CRP) and blood culture.

Materials and methods: This prospective study consisted of 205 neonates admitted at neonatal intensive care unit of Chattogram Maa-shishu-o General Hospital with clinical suspicion of neonatal sepsis, from July 2017 to December 2017. The neonatal hematological parameter was measured in all cases. Blood culture and CRP estimation were also performed. Blood culture is considered as gold standard for diagnosis of sepsis. Score ≥3 and more was considered as positive.

Results: Out of 205 neonates of our study population, forty one (20%) had proven sepsis according to culture. Total leukocyte count showed high sensitivity & least specificity, immature to mature neutrophil ratio showed high sensitivity and high specificity. Platelet count showed high negative predictive value and least positive predictive value. The HSS was found to have a sensitivity of 82.9%, specificity of 79.8%, positive predictive value was 50.74% and negative predictive value was 94.92%. Considering the high sensitivity and negative predictive value, this study implies that score ≥3 were more reliable as a screening tool for sepsis than any of the individual hematological parameter.

Conclusion: HSS is a simple, easy and rapid adjunct for the diagnosis of clinically suspected cases of neonatal sepsis. It also provides an effective guideline to make decisions regarding judicious use of antibiotic therapy.

Key words : Neonatal sepsis; Blood culture; Hematological scoring system.

INTRODUCTION

Neonatal sepsis is a clinical syndrome resulting from pathophysiological effects of local & systemic infection in the 1st month of life. Septicemia refers to bacteremia along with signs and symptoms resulting from the microorganisms or their toxic products in the blood1. Sepsis has been reported in upto 25% children in intensive care units2. About 4 million deaths occur worldwide annually from neonatal sepsis and 99% of them occur in developing countries3. Sepsis not only causes mortality but also causes some serious morbidities such as seizures, neuro-developmental disorders, sensory neural hearing loss, ocular disturbances etc4. The newborns can acquire the infection from mother through transplacental routes, ascending infection, during passage through an infected birth canal or exposure to infected blood at delivery5. In comparison to older children or adults, newborns have weaker immune system, therefore are more susceptible to bacterial invasion, premature babies being even more vulnerable6.
With early diagnosis, it is possible to treat sepsis and prevent its life-threatening complications. But the early clinical features of sepsis are often non-specific that makes it difficult for the physician to come to a definite diagnosis. Therefore, often empirical use of antibiotics are seen with a little doubt of sepsis. Though earliest administration of antibiotics is effective in combating acute infections, it also increases the emergence of antibiotic resistant organisms which is a great concern nowadays. The gold standard for diagnosis of sepsis is blood culture, but the technique is time consuming and requires an well-equipped laboratory, which is not available in most of the hospitals of developing countries. A disadvantage of culture based diagnosis is the assay time of up to 48-72 hours, yields a positive result in 10-60% of causes.

Various studies have been done regarding the early diagnosis of neonatal sepsis, which have shown that hematological parameters are simple, quick and cost-effective tools for this purpose. Both sensitivity and specificity are increased when the hematological parameters were studied together as a combination of tests. By early prediction of sepsis, these parameters help to start early treatment using appropriate antibiotics. A diagnostic test is considered ideal, when it is quick, cost-effective, having high sensitivity, specificity, positive and negative predictive value. Considering above criteria Hematological Scoring System of Rodwell is reliable for early diagnosis of neonatal sepsis as it includes all parameters, and shown to be significantly associated with sepsis.

Hematological Scoring System (HSS) that we studied includes Total leucocyte count, Absolute neutrophil count, Immature to Total neutrophil ratio (I:T), Degenerative change in PMN (eg: toxic granulation, vacuolation), Platelet count. Measurement of CRP and blood culture was also done. This study was done to evaluate the utility of the HSS in the early diagnosis of neonatal sepsis.

MATERIALS AND METHODS

It was a prospective cross sectional study which was done at the Neonatology Department of Chattogram Maa-Shishu-O General Hospital, Chattogram from July 2017 to December 2017 in co-ordination with Pathology Department. Following were the inclusion criteria: Maternal history of prolong rupture of membrane, maternal foul smelling vaginal discharge, intrapartum fever, maternal urinary tract infection or clinical feature of sepsis, such as, reluctance to feed, poor activity, fever ≥101°F. All the neonates with perinatal asphyxia, history of passage of meconium in utero, gross congenital anomaly, any prior administration of antibiotic, history of sibling death were excluded from the study. The study population were scored as per as the Hematological scoring system. Blood Culture and CRP estimation were also done. Score of more than 3 was considered as positive (Table I).

| Criteria | Abnormality | Score |
|----------|-------------|-------|
| Total Leucocyte Count (Cells/cumm) | <5,000 or > 20,000 | 1 |
| Absolute Neutrophil Count (Cells/cumm) | <1,800 or ≥ 5,400 | 1 |
| IT Ratio | ≥ 0.2 | 1 |
| Degenerative Changes In Neutrophil | Toxic-granules, cytoplasmic vacuoles | 1 |
| Platelet Count (Cells/cumm) | <1,50,000 | 1 |

Findings of HSS were recorded in a proforma and later compared with results of CRP and Blood Cultures.

RESULTS

**Table II : Presentation profile of study cohort**

| Variable          | Frequency | Percentage |
|-------------------|-----------|------------|
| Age               |           |            |
| * 0-7             | 121       | 59         |
| * 8-14            | 19        | 9.26       |
| * 15-21           | 45        | 21.9       |
| * ≥21             | 20        | 9.7        |
| Gender            |           |            |
| * Male            | 134       | 65         |
| * Female          | 71        | 35         |
| Place of birth    |           |            |
| * Home            | 54        | 26.3       |
| * Hospital        | 151       | 73.6       |
| Gestation         |           |            |
| * Term            | 146       | 71.2       |
| * Preterm         | 59        | 28.78      |
| Mode of delivery  |           |            |
| * Vaginal         | 126       | 61.4       |
| * Cesarean section| 79        | 38.5       |
| Birth weight      |           |            |
| * 1.5             | 9         | 4.3        |
| * 1.5-2.5         | 62        | 30.24      |
| * 2.5             | 134       | 65.36      |
| Risk factors      |           |            |
| * PROM             | 56        | 27.3       |
| * Maternal fever  | 38        | 18.5       |
| * Poor Neonatal feeding | 159 | 77.5 |
| * Depressed neonatal reflexes | 136 | 66.3 |

Figure 1 : Distribution of Neonates according to the hematological parameters
Role of Hematological Score in Early Diagnosis

**Table III : Comparison of HSS with CRP**

| CRP         | Positive | Negative | Correct Total |
|-------------|----------|----------|---------------|
| Sepsis on HSS Positive | 44       | 23   | 67           |
| Negative    | 8        | 130  | 138          |
| Total       | 52       | 153  | 205          |

Sensitivity = 84% Specificity = 85%

**Table IV : Comparison of HSS with blood culture**

| SEPSIS ON BLOOD CULTURE | Positive | Negative | Correct Total |
|-------------------------|----------|----------|---------------|
| Sepsis on HSS Positive  | 34       | 33   | 67           |
| Negative                | 7        | 131  | 138          |
| Total                   | 41       | 164  | 205          |

Sensitivity = 82.9% Specificity = 79.8%

**Table V : Distribution of hematological score by blood culture & sensitivity**

| Blood CS Score | Positive Number(%) | Negative Number(%) | P value |
|----------------|--------------------|-------------------|---------|
| Score 1        | 3(7.3%)            | 71(43.2%)         | 0.017   |
| Score 2        | 4(9.75%)           | 60(36.58%)        | 0.594   |
| Score 3        | 14(34.1%)          | 20(12.10%)        | 0.000   |
| Score 4        | 20(48.78%)         | 13(7.92%)         | 0.000   |

*Chi square test was done to measure the level of significance. Figure within parentheses indicates in percentage.

**Table VI : Comparison between hematological parameters and blood culture**

| Blood CS Parameters | Positive | Negative | Sensitivity | Specificity | PPV | NPV |
|---------------------|----------|----------|-------------|-------------|-----|-----|
| Leucocytosis/Leukopenia | 40       | 85       | 97.56%      | 47.85%      | 32% | 98.73% |
| Thrombocytopenia    | 19       | 17       | 95.12%      | 89.63%      | 69.64% | 98.65% |
| IT Ratio (T:L)      | 40       | 8        | 97.56%      | 95.12%      | 83.33% | 99.36% |
| ANC (High/Low)      | 40       | 80       | 97.56%      | 51.21%      | 33.33% | 98.8%  |
| Toxic Granules(+)   | 38       | 60       | 92.68%      | 63.41%      | 38.77% | 97.19% |

**DISCUSSION**

Neonatal sepsis due to its high mortality rate, still a diagnostic and treatment challenge for the neonatal health care providers. Early diagnosis helps the clinician in instituting antibiotic therapy at the earliest, which in turn reduces the mortality rates in the neonates.

205 newborns were included in this study. Among them 20% (41) newborns were diagnosed as proven sepsis by blood culture. However suspected sepsis groups 32.68% (67) comprises a difficult diagnostic group & count not be ignored as negative blood culture does not rule out fatal infection. Among the infected newborns, male (65%) were found predominant. It may be due to the factors regulating the synthesis of a globulin are situated on the X-Chromosome. Males have only one X-Chromosome, that’s why less immunologically protected than the females. Premature Rupture of Membrane (PROM) is an important risk factor for neonatal sepsis as it poses of ascending infection to the fetus and it was found in 27.3% cases in our study.

In this present study, sensitivity of Total Leukocyte Count (TLC) was found to be 97.56%, specificity 47.85% with PPV 32% and NPV 98.73%. This result was consistent with other studies. So it can be said that total leucocyte count acts as a good parameter for confirmation of sepsis.

The mortality and morbidity associated with sepsis is high, that’s why tests with high sensitivity and Negative Predictive Value (NPV) are most desirable because all infants with sepsis have to be identified. HSS is a combination of different parameters, which makes it a better diagnosis tool, because no individual parameter was found more accurate than another. Although the chance of sepsis is more with higher score on HSS, it is still a necessity to simplify & standardize this test. Globally different rapid diagnostic test such as automated blood culture system, DNA probes, fluorometric detection system are available for detection of micro-organisms, but still HSS may be considered as a good screening test for early differentiation of the septicemic groups from the non-septicemic ones. Moreover, HSS has high sensitivity & specificity with increasing score increasing certainty of sepsis.

**CONCLUSION**

HSS in an effective tool for early diagnosis of neonatal sepsis which makes it possible to start antibiotic rationally and prevent irrational use of antibiotic, thereby minimizes the emergence of resistant organism. It is also a simple, cost-effective tool that can be done at the primary health care center as a routine screening procedure.

**LIMITATIONS**

- Single center study
- Short duration of the study.

**DISCLOSURE**

All the authors declared no competing interest.
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