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Original Research Article

A study to evaluate the diagnostic value investigations in early diagnosis of septicemia in newborn

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ABSTRACT

Background: The early diagnosis of neonatal septicemia still poses great difficulties. Early clinical symptomatology of neonatal septicemia is mimicked by a lot of other disorders affecting the newborn. To study the diagnostic value of the combination of CRP, absolute neutrophil count, band form count to the total neutrophil ratio in early diagnosis of neonatal septicemia.
Methods: A total 75 babies who got admitted to Mahavir institute of medical sciences between October 2018 to September 2019 (12) months were included in the study medical college hospital in a newborn with age less than 3 days and with well-defined maternal risk factors or clinical evidence of sepsis are included in the study. In all neonates, the blood sample was collected from a peripheral vein with all aseptic precautions, before administration of any antibiotic therapy.
Results: A total 20 preterm babies (62.5%) were affected by septicemia.12 full-term babies (37.5%) were affected by septicemia. The sensitivity of a lab test is defined as the proportion of infants with proven sepsis in whom the result is abnormal. Specificity is the proportion of healthy infants in whom the result is normal.
Conclusions. When both CRP and band form to mature neutrophil counts were positive the sensitivity and the negative predictive value were high compared to other combinations of two.

Keywords: Differential count, Band form to neutrophil ratio, C-reactive protein, Micro erythrocyte sedimentation rate

INTRODUCTION

In recent year's improvement in neonatal intensive care resulted in increased survival. However neonatal survivors of sepsis can have severe neurologic sequel due to CNS infection as well as from secondary hypoxemia resulting from septic shock, persistent pulmonary hypertension, and severe parenchymal lung disease.[1] Extremely low birth weight babies who had neonatal infection were more likely to have cerebral palsy and a range of adverse neurodevelopmental sequel. Early recognition of neonatal sepsis is vital to the optimal outcome of this serious illness. The early diagnosis of neonatal septicemia still poses great difficulties.[2]

Neonatal sepsis can be divided into two subtypes depending upon whether the onset of symptoms is during the first 72 hours of life or later.[3] Although the term early-onset sepsis had been used to refer to neonatal infections occurring as late as one week of age, it should be restricted to those infections with perinatal pathogenesis, the usual onset of which occurs within 72 hours. Early-onset sepsis is caused by organisms prevalent in the genital tract or the labor room. Ascending infection, transplacental hematogenous spreads are important mechanisms of early-onset sepsis. The organisms enter the body through the umbilicus, skin, or mucosa.[4] Due to the poor immunological defense of the newborn, even local infections tend to become generalized. Early-onset sepsis can manifest as a fulminant disease with

immediate onset of respiratory distress soon after delivery or on days one to three of postnatal life after an asymptomatic period. Infections are more commonly met with preterm and low birth weight babies.[5] Early treatment with rational antibiotic therapy is possible with the help of certain indirect markers such as total leukocyte count, band form to neutrophil ratio, absolute neutrophil count, micro-ESR, and C-reactive protein.[6,7]

METHODS

75 babies who got admitted to Mahavir institute of medical sciences between October 2018 to September 2019 (12) months were included in the study medical college hospital in a newborn with age less than 3 days and with well-defined maternal risk factors or clinical evidence of sepsis are included in the study. In all neonates, the blood sample was collected from a peripheral vein with all aseptic precautions, before administration of any antibiotic therapy.

Inclusion criteria

Inclusion criteria for study included, PROM>18 hours, intrapartum temperature≥100.4(38.^{0}C), a vaginal examination did> 3 times in labor, foul-smelling liquor, untreated maternal UTI in the last trimester.

Exclusion criteria

Exclusion criteria for study excluded, the babies with RDS, perinatal asphyxia, meconium aspiration syndrome, babies weighing <1500 gm, babies with congenital malformation. The following investigations were done in all the selected babies. Total WBC count, absolute neutrophil count, band form (band form neutrophil ratio) CRP, blood culture. All these details were recorded in a special proforma after obtaining informed consent from the parent/guardian for registering the required data.

Statistical analysis

Data entry was made in the Microsoft excel software in codes and analysis was done with an SPSS-20 computer package. Categorical variables are expressed as percentages whereas continuous variables are expressed as mean ± standard deviation. Association between the categorical variable was found by the chi-square test and the relationship between the continuous variable was assessed by student's t-test.

RESULTS

All the 75 babies were subjected to these three investigations along with blood culture. Positive blood culture was taken as the gold standard. The diagnostic value of these three tests individually and in combinations was analyzed against blood culture. The following results were observed.

Table 1: Risk factors.

Risk factors	No. of babies
Prolonged rupture of membrane >18 hours	30
Untreated UTI at the time of delivery	3
Vaginal examination >3 in labor	10
Foul-smelling liquor	6
Maternal fever at the time of delivery	4
Clinical evidence of sepsis in the baby	22

Table 1 shows 49% of infection with GBS and 79% of other infants with sepsis had one more of three major maternal risk factors like signs and symptoms of chorioamnionitis PROM>18 hours, colonization of GBS. Microbial pathogens can be recovered from the amniotic cavity in 10- 15% of cases of spontaneous preterm labor and 32-35% of women with PPROM and chances of neonatal infection increase by threefold in prolonged rupture of membrane. Prolonged labor was found to be increasingly associated with neonatal sepsis. Organisms that inhabit the cervix, vagina, and rectum can spread upward in the amniotic cavity through intact or ruptured membranes and causes amnionitis. Intra amniotic infections are usually polymicrobial in etiology. Those were meconium staining of liquor and multiple vaginal examinations.

Table 2: Culture.

Culture	Bacteriologically positive	Bacteriologically negative
No. of cases	32	43
Total		75

Table 2 shows blood culture was bacteriologically positive in 42.6% of cases (32). Blood culture was bacteriologically negative in 57.33% of cases (43). 20 preterm babies (62.5%) were affected by septicemia. 12 full-term babies (37.5%) were affected by septicemia. Preterm babies were more affected by septicemia than full-term babies.

Table 3: Band neutrophil ratio and absolute neutrophil count.

B/N ANC	Blood culture		Total
	Positive (%)	**Negative (%)**	
Both positive	21 (65.62)	6 (16.95)	27
Negative	11 (34.37)	37 (86.04)	48
Total	32	43	75
Band neutrophil ratio and absolute neutrophil count (%)			
Sensitivity	Specificity	PPV	NPV
65.62	86.04	77.77	77.08

Table 3 shows the absolute neutrophil count varies considerably in the immediate neonatal period. It has increased the utility of this test through the establishment of normal reference ranges for the absolute neutrophil count and indices for immature neutrophils. Those babies who were falling outside these values were taken as positive. The sensitivity, specificity, positive predictive value, negative predictive value was 78.12%, 72.09%, 67.56%, 81.51% respectively.

Table 4: Band neutrophil ratio, C-reactive protein, and absolute neutrophil count.

B/N CRP ANC	Blood culture		Total
	Positive (%)	Negative (%)	
ALL positive	20 (62.5)	2 (4.6)	22
Negative	12 (37.5)	41 (95.34)	53
Total	32	43	75
Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
62.5	95.34	90.90	77.35

Table 4 shows the ratio of immature to mature neutrophils is a sensitive indicator of sepsis, as observed in our study has also been documented by other authors. The observation was as follows. Sensitivity was 84.37%, specificity was 72.09%, positive predictive value and negative predictive values were 69.23% and 86.11% respectively.

DISCUSSION

All the 75 babies were subjected to these three investigations along with blood culture. Positive blood culture was taken as the gold standard. The diagnostic value of these three tests individually and in combinations was analyzed against blood culture. The following results were observed the incidence of septicemia among male babies was 65.33%, Dawodu et al observed ale predominance (64.7%) in neonatal septicemia.[8,9] Prematurity and low birth weights are the two important risk factors for septicemia. In our study, it was observed that Preterm and low birth weight babies had a high incidence of septicemia 62.5%. Berger et al observed that refusal to suck, sluggish activity, fever, jaundice were common clinical features.[10] Our study and many other studies like these show that clinical features of neonatal septicemia are highly nonspecific and can mimic various common conditions that may occur in the newborn period.[11] Due to these reasons the blood cultures, most of the time has low sensitivity.[12] The ratio of immature to mature neutrophils is a sensitive indicator of sepsis, as observed in our study has also been documented by other authors. The observation was as follows. Sensitivity was 84.37%, specificity was 72.09%, positive predictive value and negative predictive values were 69.23% and 86.11% respectively. The absolute neutrophil count varies considerably in the immediate neonatal period.[13] The work of Monroe et al has increased the utility of this test through the establishment of normal reference ranges for the absolute neutrophil count and indices for immature neutrophils.[14] Those babies who were falling outside these values were taken as positive. The sensitivity, specificity, positive predictive value, negative predictive value was 78.12%, 72.09%, 67.56%, and 81.51% respectively. CRP levels were found to be more useful in screening neonatal septicemia through various studies.[15] Jaswal et al reported no recurrence of infection within 7 days of discontinuation of antibiotics based on three normal CRP determinations within 48 hours and negative cultures in 147 low birth infants at risk for early-onset infection.[16]

CONCLUSION

Even though blood culture is the gold standard for diagnosis of septicemia, the technique of blood culture is time-consuming (It takes 48-72 hours for the results to be available) and the success rate is only around 40%. The culture result may be influenced by previous antibiotic exposure and also the bacteremia phase will be missed by poor timing and blood sample size. So certain indirect markers of sepsis are being used for screening the neonates with sepsis. Among them, the well-known, most useful, and widely used tests include total WBC count, absolute neutrophil count, Immature to total WBC ratio (I:T ratio), ESR, and CRP. Furthermore, the greatest predictability usually results from a combination of assays. Ultimately, application of the various tools of molecular biology, such as MicroArray chip technology, should allow rapid identification of potential pathogens together with antimicrobial resistance markers.

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