IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 13, Issue 5 Ver. V. (May. 2014), PP 52-56
www.iosrjournals.org

Study on Correlation between Sepsis Screening and Blood Culture in Neonatal Sepsis

Rajarshi Basu[1], Syamalkumar Bandyopadhyay[2]
[1](*RMO cum Clinical Tutor, Department of Pediatric Medicine, NRS Medical College and Hospital, Kolkata, India)*
[2](*Professor, Department of Pediatric Medicine, NRS Medical College and Hospital, Kolkata, India)*

Abstract : *Objective: Neonatal septicemia is a major cause of morbidity and mortality in newborn inborn. As the clinical manifestations are vague and nonspecific, it is pertinent that an early diagnosis is made to prevent serious morbidity and mortality. So, an attempt was made to establish correlation between sepsis screening & blood culture in neonate presenting with features of sepsis to accelerate the diagnostic process. Research and Methods: In our study we tried to study (1) early indicators of sepsis screen & their statistical correlation with blood culture (considered as gold standard); (2) different aspects of outcome in neonatal sepsis. Results: Though individual sepsis screen parameters showed little correlation with blood culture status, yet on combination it was found that specificity and positive predictive accuracy increased while sensitivity decreased them individual tests. Also combination of tests yield better results than single tests. Conclusion: The combination of parameters yielded better results than single tests and proved to be an invaluable aid for early diagnosis of neonatal sepsis.*

Keywords : *Blood culture, CRP, neonatal sepsis, sepsis screen*

I. Introduction

Neonatal period is defined as the first 28 days of life. Before birth the baby remains well protected in his/her mother's womb. After birth, the baby has to face all adverse conditions of outer world; i.e. temperature difference, large number of microorganisms, lack of nutrition supply etc.

Neonatal period is the most hazardous period of life because of various problems / diseases which a neonate faces.

Neonatal septicemia is defined as a bacterial infection documented by a positive blood culture in the first four weeks of life.

Systemic bacterial infection during this period have remained a major cause of infant morbidity and mortality.

According to National Neonatal Perinatal Database (NNPD) 2000 neonatal sepsis is the most common cause of deaths in the country followed by prematurity & birth asphyxia [1,2].

To prevent serious morbidity and mortality it is important that the diagnosis is made early and treatment started within the shortest possible time frame.

Even though a positive blood culture, is gold standard for diagnosis of neonatal sepsis the technique is time consuming, demands a proper laboratory setup and is positive in only 40% cases.[3]

Early treatment with antibiotics is possible with the help of certain indirect markers such as neutropenia (<1800 cells/mm^3), leucopenia (<5000 cells/mm^3), band cells, micro ESR and C-reactive protein (CRP). All these investigations are collectively known as sepsis screen and aids in early diagnosis of neonatal sepsis in absence of negative blood cultures.[4,5]

Thus in presence of predisposing factors; early clinical suspicion, coupled with sepsis screen will detect neonatal septicemia earlier which will enable the clinician to treat the infection timely and thus reduce neonatal morbidity and mortality.[6,7]

II. Aims And Objectives

Specific Objectives were

1. To study the early indicators of sepsis screen and their statistical correlation with blood culture (considered as gold standard) in neonatal septicemia.[8,9]
2. To study the different aspects of outcome in neonatal sepsis.

All these will help in early diagnosis of neonatal septicemia and its speedy management and ultimately lead to timely intervention thus leading to reduced mortality and morbidity amongst neonates afflicted with neonatal sepsis.[10,11]

III. Materials And Methods

1. Study area

This study was conducted in the baby nursery ward and adjacent NICU of Pediatric Medicine department, Nilratan Sircar Medical College and Hospital, Kolkata with active collaboration of Department of Microbiology of the same institution.

2. Study population

Neonates being admitted to baby nursery with signs and symptoms of sepsis or presence of predisposing factors for development of sepsis.[12]

3. Period of study: 1st April 2011 to 31st March 2012

4. Target sample size: 300 subjects

5. Study design: Descriptive prospective study with cross sectional design.

6. Sample design

A. Inclusion criteria

Neonates were enrolled on the basis of signs and symptoms of clinical sepsis (as per NNF criteria)[11,13] after through clinical examination and proper history taking.

The clinical criteria considered (NNF criteria) were – poor feeding, irritability / excessive cry, lethargy poor cry and reflexes, fever, hypothermia, jaundice, vomiting, abdominal distension, tachypnoea and grunting, convulsions, diarrhea, pustules, sclerema, cyanosis, bulged fontanalle, DIC/bleeding, poor perfusion / shock, apnea.

Also significant predisposing factors for presumed early onset sepsis was taken into consideration (according to NNF guidelines)[11,14] during inclusion of cases.

Only those neonates were enrolled in the study whose parents / guardians agreed to the informed consent. The decision of consultant (guide) was final while considering inclusion of cases.

B. Exclusion criteria

The following category were excluded from the study

a. Congenital anomalies of GI system, e.g. tracheoesophageal fistula, malrotation of the gut.
b. Congenital anomalies of respiratory system, e.g. lobar agenesis
c. Congenital anomalies of the cardiovascular system, e.g. TGA, complex heart diseases.
d. Inborn errors of metabolism
e. Congenital anomalies of central nervous system, e.g. microcephaly, anencephaly, other neural tube defects etc.

7. Parameters to be studied

Each patients will be studied in a methodical manner using a well designed proforma (given at the back) to find out

a. The varied clinical profile of neonatal septicemia amongst all cases of neonatal sepsis (especially amongst sepsis screen positive and/or bacteriologically positive i.e. blood culture positive cases).[11]
b. To study the early indicators of sepsis screen and their statistical correlation with blood culture (considered as gold standard) in neonatal septicemia.
c. To study the various aspects of outcome in neonatal septicemia.

8. Study tools

A. To ascertain demographic details, relevant maternal history and to note the findings of clinical examinations of neonates, a well designed structural proforma was used (given at the back) where all requisite details were filled up pertaining to the study.
B. Investigations:
   i. Sepsis screen (according to NNF criteria) [22]
      a. Total leukocyte count
      b. I/T ratio (band cell ratio)
      c. Absolute neutrophil count
      d. m-ESR
      e. C reactive protein
   ii. Blood culture

9. Study techniques

The neonates who were enrolled on the basis of signs and symptoms of clinical sepsis (NNF guidelines) after thorough clinical examination and history taking. Also any predisposing factors for septicemia

presumed early onset sepsis (according to NNF criteria) was considered while inclusion of cases. Relevant laboratory investigations were done. All these were systematically entered in a predesigned structural proforma.

The sepsis screen parameters were taken as per NNF guidelines. If any two of the following parameters are positive or significant, the sepsis screen is said to be positive as per NNF guidelines[11]

Components	Abnormal value
a) Total leukocyte count	< 5000 cells/mm^3
b) I/T ratio	> 0.2
c) ANC	< 1800 cells/mm^3
d) m-ESR	> 15 mm at the end of 1st hour
e) C reactive protein	> 1 mg/dl

The initial sepsis screen was done at the time of admission and if found to be negative was repeated after 12-24 hours.

The operating definition of septicemia was taken as per NNF guidelines and the following categories were chosen for inclusion under neonatal septicemia category.

a) Blood culture positive cases
b) Blood culture negative but sepsis screen positive cases
c) Blood culture negative and sepsis screen negative cases, but with a clinical course compatible with sepsis

All the above groups were considered for final statistical analysis.

10. Statistical analysis and Ethical Clearance

It was done as per standard statistical tools. 'p' value was calculated according to Fisher's Exact test. A 'p' value less than 0.05 was considered to be statistically significant. Some help was taken from statistical package for social sciences (SPSS, Version 15) software.

For ethical issues confidentiality of patients information was considered and ethical clearance was duly taken from institutional ethics committee and progress of study was duly intimated to the ethics committee time to time.

IV. Results & Analysis And Discussion

This study was conducted at baby nursery ward and adjacent neonatal intensive care unit (NICU) of Department of Pediatric Medicine, Nilratan Sircar Medical College and Hospital, Kolkata with the help of Microbiology Department of the same institute.

The study period was for one year from 1/4/2011 to 31/3/2012. Three hundreds neonates with clinical suspicion of septicemia were included in this study.

Distribution of cases

1) Bacteriologically positive cases were found in 119 (39.66%) neonates.
2) Bacteriologically negative but sepsis screen positive cases were found in 102 (34%) neonates.
3) Bacteriologically negative, sepsis screen negative but clinical course compatible with sepsis were found in 54 (18%) neonates.
4) Bacteriologically negative, sepsis screen negative and clinical course not compatible with sepsis were found in 25 (8.34%) neonates. After investigations and clinical follow up, this group was hence excluded from study as it did not confirm to either clinically compatible course and / or sepsis screen or blood culture positivity (according to NNF criteria).

Thus ultimately 275 subjects were finally considered for evaluation out of total 300 neonates originally enrolled. Hence n = 275.

Distribution of cases according to sex

Observation: out of 275 patients, 162 (58.91%) were males and 113 (41.09%) were females. Thus male babies were more affected by neonatal septicemia than female babies.[11,15]

Distribution of cases according to age of onset of septicemia

Observation: early onset septicemia was found in 191 (69.45%) cases. Late onset septicemia was present in 84 (30.55%) cases. Thus early onset septicemia was more common than late onset septicemia.[16]

Distribution of cases according to Birth Weight

Observation: Birth weight less than 2500 gms (low birth weight) was present in 179 (65.09%) cases. Birth weight greater than equal to 2500 gms (normal birth weight) was present in 96 (34.91%) cases. Hence septicemia is more common in LBW neonates.[16]

Distribution of cases according to Maturity

Observation: 173 (62.91%) preterm babies were affected by septicemia. 102 (37.09%) term babies were affected by septicemia. Hence preterm babies were more affected by septicemia.

Relation of age of onset of septicemia with maturity

Observation: EOS affected 137 (71.73%) of preterm babies and only 54 (28.27%) of term babies. Thus early onset sepsis was overwhelmingly common in preterm babies.

Relation of age of onset with birth weight

Observation: EOS affected 143 (74.87%) of low birth weight infants (<2500 gms) and only 48 (25.13%) of infants with body weight ≥2500 gms. Thus EOS was much more common in LBW babies than normal birth weight babies.

Table 1: Outcome of Mortality

Outcome	Death	Survival	Total
No. of Cases	55 (20%)	220 (80%)	275

Relation of mortality according to age of onset of septicemia

Observation: 40 (72.73%) infants died due to early onset of sepsis (EOS). Only 15 (27.27%) infants died due to late onset of sepsis (LOS). Thus mortality in EOS was relatively much more common.

Relation of mortality according to maturity

Observation: Mortality occurred in 39 (70.91%) preterm infants and only in 16 (29.09%) term infants. Thus mortality was much higher for preterm babies.[15,17]

Relation of mortality according to birth weight

Observation: Mortality occurred in 30 (54.55%) low birth weight infants and only 25 (45.45%) normal birth weight infants. Thus mortality was more common in low birth weight infants.

Distribution of mortality according to culture positivity

Observation: Death occurred in 46 culture positive cases (83.64%) and only 9 (16.36%) culture negative cases. Thus mortality was overwhelmingly higher for culture positive cases.

Table 2: Shows the sensitivity, specificity, positive predictive value, negative predictive value and p-value of sepsis screen parameters in correlation with blood culture status.

Sepsis screen parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P value
Single Test					
Neutropenia (ANC <1800 cells/mm^3)	55.46	53.85	47.83	61.31	0.1446
Leucopenia (TLC <5000 cells/mm^3)	54.62	50.64	45.77	59.40	0.3932
IT Ratio (>0.2)	56.30	53.85	48.20	61.76	0.1136
mESR (>15 mm in 1^{st} hour)	64.71	80.77	71.96	75.00	<0.001
CRP Positive (>1 mg/dl)	79.83	83.97	79.17	84.52	<0.001
Two tests					
CRP + mESR	49.58	91.67	81.94	70.44	<0.001
CRP + TLC	54.62	88.46	78.31	71.86	<0.001
CRP + IT ratio	31.13	96.15	87.76	66.37	<0.001
TLC + mESR	49.58	84.62	71.08	68.75	<0.001
mESR + IT Ratio	21.01	96.15	80.65	61.48	<0.001
Three tests					
CRP+TLC+mESR	49.57	91.67	81.94	70.44	<0.0001

Significant observations were

1. Of the single tests of sepsis screen parameter CRP had the highest sensitivities (79.83%), specificity (83.97%) and positive predictive value (79.17%)
2. Of the single tests, only mESR and CRP had significant statistical correlation with blood culture status and hence proven sepsis (p value < 0.001). The other 3 tests namely Leucopenia, Neutropenia and IT ratio had statistically insignificant association with blood culture status (hence proven sepsis, $p > 0.05$)[18,19]
3. When 2 tests were combined and 3 tests were combined, all the tests had significant statistical correlation with blood culture status (gold standard for diagnosis of sepsis).[20]
4. Specificity and positive predictive accuracy were increased at the cost of sensitivity when combinations of tests were done.

Clinical features (EOS & LOS) amongst blood culture positive &/or sepsis screen positive cases of sepsis
Observation: Tachypnoea, Grunting (73.91%) and poor feeding (77.64%) to be the most common clinical features amongst EOS. Amongst LOS lethargy (78.33%), poor feeding (68.33%) and fever (60%) were most common clinical features observed.

V. Conclusion

1. Though most of the individual sepsis screen parameters showed little statistical correlation with blood culture status, yet CRP had highest sensitivity, specificity, positive predictive value and proved to be a sensitive and responsive indicator of neonatal sepsis.
2. On combination of the sepsis screen parameters it was found that specificity and positive predictive accuracy increased, while sensitivity decreased than the individual test.
3. The combination of tests also yielded statistically significant correlation with blood culture status than individual test. Thus, the combination of parameters (sepsis screen) yielded better results than single test and proved to be an invaluable aid for early diagnosis of neonatal sepsis.
4. Amongst early onset sepsis the predominant clinical features were respiratory distress (manifested by tachypnoea and grunting) followed by poor feeding.
5. Amongst late onset sepsis poor feeding and lethargy were the most common clinical features followed by meningeal signs like irritability and convulsions.
6. Blood culture is the gold standard for diagnosis of neonatal sepsis and should be done in all cases of suspected neonatal septicemia.
7. Mortality in early onset of sepsis was relatively more common. Mortality was higher for preterm, low birth weight and bacteriologically positive babies.
8. Male, preterm and low birth weight neonates were more prone for septicemia.
9. Early onset sepsis was commoner than late onset sepsis.
10. The common predisposing neonatal factors for early onset sepsis are prematurity and low birth weight.
11. The common predisposing maternal factors for early onset sepsis are foul smelling liquor, poor maternal health (maternal fever), premature rupture of membranes and multiple vaginal examination.

References

[1]. National Neonatology Forum. Report of National Neonatal Perinatal Database 2000, New Delhi.
[2]. Singh Meherban. Perinatal Infections. In: *Care of Newbown*. 7th Edition. Sagar Publication, New Delhi; 2010: p 223-233.
[3]. Buetow KC. Septicemia in premature infant. *American Journal of Diseased Child* 1965; 110-29.
[4]. Bhakoo ON. Neonatal bacterial infections at Chandigarh. A decade of experience. *Indian Journal of Pediatrics* 1980; *47* : 419-424.
[5]. Waaga A, Brandtzaeg P, Hatstensen P. The complex patter of cytokines in serum from patients with meningococcal septic shock. *J Exp Med 1989; 169*: 333-8.
[6]. Jeevasankar M, Agarwal R, Deorari A, Paul VK. Sepsis in Newborn. *Indian Journal of Pediatrics* 2008; *75(3):* 261-266.
[7]. Stoll Barbara J. Infections of the neonatal infant. In: Kliegman RM, Behrman RE, Jenson HB editors. *Nelson's Textbook of Pediatrics. 18th edition.* Philadelphia, Saunders; 2007: p 794-811.
[8]. Mathur NB. Neonatal Sepsis. *Indian Pediatr 1996; 33*: 663-74.
[9]. Lokeshwar MR, Bharat Rao, Raksha Dalal, Niranjan V, Shah N, Chirla D, Manglani M. Immuno-haematology of neonatal sepsis. Recent advances in the management of haematological disorders of childhood. National workshop 1988; 96-110.
[10]. Singh M, Narang A, Bhakoo ON. Predictive perinatal score in the diagnosis of neonatal sepsis. *J Trop Pediatr 1994; 40*: 365-368.
[11]. NNF Teaching Aids. Newborn Care. Neonatal Sepsis. www.newborn.whocc.Org/pdf. accessed on 10/08/2012.
[12]. Bhakoo ON, Aggarwal KC, Mohini Mahajan C, Walia BN. Septicemia in infants and children, a bacterialogical study. Indian Pediatrics 1968; 05: 518-523.
[13]. Fanaroff AA, Korones SB, Wright LL, Verter J, Poland RL, Bauer CR. et al. Incidence, presenting features, risk factors and significance of late – onset septicemia in very low birth – weight infants. *Pediatr. Infect. Dis J 1998; 17(7)*: 593 – 8.
[14]. Al-Harthi AA, Dagriri KA, Asindi AA, et al. Neonatal meningitis. *Saudi Med J 2000; 2*: 550-53.
[15]. Berger A, Salzer HR, Weninger M, Sageder B, Aspock C. Septicemia in an Austrian neonatal intensive care unit, a 7-year analysis. *Act a Paediatr 1998; 87 (10)*: 1066-9.
[16]. Basavaraja M, Kerur B, Bhat V, Harish BN, Habeebullah S, Uday Kumar C. Maternal Genital Bacteria and surface colonization in early neonatal sepsis. *Indian Journal of Pediatrics 2006; 73*: 29-32.
[17]. Steigbigel. NST Vs conventional hematology in diagnosis of bacterial infection. *New Eng Journal of Medicine 1974*: 210-235.
[18]. Xanthou M. Leucocyte blood picture in healthy full-term and premature babies during neonatal period. *Archives of Disease in Childhood 1970; 45*: 242-249.
[19]. Zipursky A, Phalko J, Milner R, Akenzua GI. The hematology of bacterial infection in premature infants. *Pediatrics 1976; 57*: 839-853.
[20]. Rodwell RL, Kerry F, Tudehope TDI, et al. Haematologic scoring system in early diagnosis of sepsis in neutropenic newborn. *Pediatr Infect Dis J 1993; 12*: 372-76.