



Study of Blood Culture and Sensitivity in Neonatal Septicemia

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ABSTRACT

Background: Septicemia remains to be the commonest cause for mortality and morbidity among neonates all over the world, especially in developing countries. The trend in bacterial spectrum causing sepsis is changing over last few decades. Emergence of resistant strains has worsened the scenario. Hence this study was planned to study blood culture and sensitivity in neonatal septicemia.

Objectives: To study blood culture and sensitivity in neonatal septicemia

Methodology: The present study was a prospective analysis of 80 cases of suspected neonatal septicemia who were admitted in NICU. Blood samples of suspected cases of septicemia were sent to the laboratory for culture and sensitivity.

Results: Incidence of early onset septicemia is marginally higher than the late onset septicemia. Low birth weight babies are more prone for septicemia than normal birth weight babies. Gram negative organisms are more commonly isolated from blood culture than gram positive organisms. Klebsiella pneumoniae is the most common organism isolated. There is emergence of multidrug resistant organisms in neonatal septicemia, Klebsiella Pneumoniae topping the list which is becoming resistant to penicillin group of drugs and some of the cephalosporins. ESBL Klebsiella Pneumoniae is a major concern to be looked upon in NICU.

Conclusion: Blood culture and sensitivity can be used in clinical suspected cases of neonatal septicemia for better treatment and hence better prognosis.

KEYWORDS :

Introduction

Septicemia remains to be the commonest cause for mortality and morbidity among neonates all over the world, especially in developing countries. We have achieved considerable progress in hygiene, newer antibiotics and many advanced methods for early diagnosis of infection and treatment, but despite of this neonatal mortality due to septicemia is still considerably high.

Current neonatal mortality rate of India is 39 deaths per 1000 live births and among these early neonatal mortality rate is 30 per 1000 live births.^{1,2}

Early onset sepsis is defined as that occurs within first 7 days of life, usually 72 hours after birth and is due to microbes acquired before or during delivery. Late onset sepsis is defined as that occurring from 8 to 90 days of life and occurs due to microbes acquired after delivery.³ According to National Neonatal Perinatal Database 2002-03, overall incidence of neonatal systemic infection was 3%, i.e. 30 per 1000 live births. Out of those 67% were early onset and 31.6% were of late onset variety.^{2,4}

Clinical features with which generally neonates present are nonspecific and diagnosis is not easy which has led to both underdiagnosis and overdiagnosis. Various diagnostic tests available have low predictive value and low sensitivity and specificity. Antibiotic abuse has further complicated the situation by emergence of new antibiotic resistant strains making diagnosis a tough job. High degree of clinical suspicion is what really needed for diagnosis.

The trend in bacterial spectrum causing sepsis is changing over last few decades. Emergence of resistant strains has worsened the scenario. Incidence of septicemia and deaths due to it are decreasing in developed countries. But these values are hardly showing any changes in some developing countries and slowly improving in few countries like India. In India according to the studies conducted by NNPD 2002-03, the incidence of neonatal septicemia is 30 per 1000 live births and 16% of total neonatal deaths are due to neonatal septicemia alone.² These values indicate there is lot to be done in this regard. Over the last century mortality due to sepsis has significantly decreased. However, in spite of giving good antenatal and intranatal care, availability of modern well equipped Neonatal Intensive Care Units, newer antibiotics, newer diagnostic and treatment modalities,

septicemia remains to be the major killer.^{1,5}

To curb down the mortality and morbidity due to neonatal septicemia early diagnosis and prompt treatment of sepsis is needed. This study will definitely help to achieve this goal.

Aims and Objectives

To study blood culture and sensitivity in neonatal septicemia.

Materials and Methods

Total numbers of patients admitted in NICU of Niramay Hospital & Research Center, Satara, in the year January 2013 to December 2013 were 212. Out of those, we suspected 80 neonates having septicemia based on clinical presentation.

After admission a detailed history was taken in detail as per the following proforma

Day to day follow up of these various clinical symptoms and signs was kept in detail and studied.

As neonate presents with vague and nonspecific signs and symptoms in septicemia, with presence of any signs and symptoms clinical diagnosis of septicemia was suspected. Sample was sent to the laboratory for blood culture and sensitivity.

After sending blood for investigation, the neonate was immediately put on appropriate antibiotics.

Collection of blood for cultures:

Skin preparation and obtaining blood for culture specimen:-

The preparation of skin prior to venipuncture was done with utmost care. Rigid antiseptic techniques were required to guard against contamination from the skin and air.

Procedure:-

1. Apply tourniquet and select optimal venipuncture site usually.
2. Release tourniquet and proceed to prepare skin.
3. Prepare skin as follows
 - Vigorously clean skin with 70% alcohol soaked gauze.

- Then swab concentrically with 2% tincture of iodine soaked gauze and lastly again with isopropyl alcohol.
 - Allow to dry.
 - Once skin is disinfected, cover site with sterile gauze.
 - Venipuncture site should not be probed unless fingers are similarly decontaminated or sterile gloves are worn.
1. Disinfect the top of culture bottle with alcohol and allow to dry.
 2. With plastic sterile syringe and needle, withdraw 2-3 ml blood.
 3. Collect blood in sterile culture bottle.

Result & observations

Out of 80 neonates, 32 cases showed positive blood culture report, i.e. blood culture positivity rate was 40%.

Out of total 32 culture positive cases, 19 (59.37%) patients presented within 7 days of life suggesting EOS (early onset sepsis) was much commoner than late onset sepsis. 13 (40.62%) cases were of LOS (late onset sepsis).

Out of total 32 blood culture positive cases in our study, 25 cases were males and 7 were female with male: female ratio being 3.57:1. Thus study shows incidence of septicemia is almost 4 times higher in male neonates than female neonates in both early as well as late onset neonatal septicemia.

Table 1
Distribution of blood culture positive cases admitted in our NICU according to weight

| Weight (Grams) | Suspected septicemia cases (N=80) | Culture positive cases (N=32) | EOS (N=19) | LOS (N=13) |
|----------------|-----------------------------------|-------------------------------|-------------|------------|
| <2500 | 57 (71.25%) | 21 (65.62%) | 14 (73.68%) | 8 (61.54%) |
| >=2500 | 23 (28.75%) | 11 (34.37%) | 5 (26.32%) | 5 (38.46%) |

Above table shows that overall incidence of neonatal septicemia was higher in low birth weight babies (<2,500gms) than babies with good birth weight. Similar trend can be seen in both early as well as late onset neonatal septicemia.

Table 2
Distributions of pathogens in blood culture positive cases

| Organisms | Culture positive Cases (n=32) | | EOS (n=17) | | LOS (n=15) | |
|-------------------------|-------------------------------|-------|------------|-------|------------|-------|
| | N | % | N | % | N | % |
| Klebsiella | 9 | 28.12 | 3 | 17.64 | 6 | 40 |
| Klebsiella ESBL | 2 | 6.25 | 2 | 11.76 | 0 | 0 |
| E. Coli | 6 | 18.75 | 4 | 23.53 | 2 | 13.33 |
| Staphylococcus aureus | 4 | 12.5 | 1 | 5.88 | 3 | 20 |
| Streptococcus viridians | 2 | 6.25 | 2 | 11.76 | 0 | 0 |
| CONS | 2 | 6.25 | 2 | 11.76 | 0 | 0 |
| Streptococcus pneumonia | 1 | 3.12 | 0 | 0 | 1 | 6.66 |
| Enterobacter | 2 | 6.25 | 2 | 11.76 | 0 | 0 |
| Acenatobacter | 1 | 3.12 | 0 | 0 | 1 | 6.66 |
| Pseudomonas | 1 | 3.12 | 0 | 0 | 1 | 6.66 |
| Candida | 2 | 6.25 | 1 | 5.88 | 1 | 6.66 |

Table 2 shows that most common organism isolated in our study was Klebsiella pneumonia with 9 cases of total 32 cases. It was the most common cause of sepsis in LOS and second most common cause in EOS. In EOS the most common cause was E. Coli, with total 4 cases out of 17. Thus gram negative organisms top the list followed by gram positive organisms. Fungal sepsis was present in 2 cases and the organism isolated was candida.

Table 3
Antibiotic sensitivity pattern among different organisms

| Antibiotic | Organisms | | | | |
|------------------------|------------|------------|-----------------|------------|------------|
| | CONS | ENTERO. | STREPT. PNEUMO. | ACENATO. | PSEUDO. |
| Ampicillin | 0/2*(0%)** | 0/2 (0%) | 1/1 (100%) | 0/1 (0%) | 0/1 (0%) |
| amox-clav acid | 2/2 (100%) | 0/2 (0%) | 1/1 (100%) | 0/1 (0%) | 1/1 (100%) |
| Ceftriaxone | 2/2 (100%) | 0/2 (0%) | 1/1 (100%) | 1/1 (100%) | 1/1 (100%) |
| Cefotaxime | 2/2 (100%) | 0/2 (0%) | 1/1 (100%) | 0/1 (0%) | 0/1 (0%) |
| Cefazolin | 0/0 | 0/0 | 0/0 | 0/1 (0%) | 0/0 |
| Cefuroxime | 0/0 | 0/0 | 0/0 | 0/1 (0%) | 0/0 |
| Ceftazidime | 0/0 | 0/0 | 0/0 | 0/1 (0%) | 0/0 |
| Cefipime | 0/0 | 0/0 | 0/0 | 0/1 (0%) | 0/0 |
| Cefperazone | 2/2 (100%) | 1/2 (50%) | 1/1 (100%) | 0/0 | 1/1 (100%) |
| co-trimoxazole | 0/2 (0%) | 0/2 (0%) | 0/1 (0%) | 0/1 (0%) | 0/1 (0%) |
| Chloramphenicol | 2/2 (100%) | 2/2 (100%) | 1/1 (100%) | 0/0 | 0/1 (0%) |
| piperacilin-tazobactam | 2/2 (100%) | 0/2 (0%) | 1/1 (100%) | 1/1 (100%) | 1/1 (100%) |
| Meropenem | 2/2 (100%) | 2/2 (100%) | 1/1 (100%) | 0/1 (0%) | 1/1 (100%) |
| Imipenem | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| Amikacin | 2/2 (100%) | 2/2 (100%) | 1/1 (100%) | 1/1 (100%) | 1/1 (100%) |
| Netilmycin | 2/2 (100%) | 2/2 (100%) | 1/1 (100%) | 0/0 | 0/1 (0%) |
| Gentamycin | 0/0 | 0/0 | 0/0 | 0/1 (0%) | 0/1 (0%) |
| Ciprofloxacin | 1/2 (50%) | 2/2 (100%) | 1/1 (100%) | 0/1 (0%) | 1/1 (100%) |
| Ofloxacin | 2/2 (100%) | 2/2 (100%) | 0/0 | 0/1 (0%) | 0/1 (0%) |
| Levofloxacin | 0/0 | 2/2 (100%) | 0/0 | 0/1 (0%) | 0/1 (0%) |
| Sparfloxacin | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| Vancomycin | 2/2 (100%) | 0/0 | 0/0 | 0/0 | 0/0 |

* no of isolates studied for that antibiotic
**% sensitivity to the antibiotic

Table 3 shows that, Coagulase Negative Staph. Aureus (CONS) are sensitive to amoxiclav combination, cephalosporins, aminoglycosides, piperacilin-tazobactam combination, meropenem, vancomycin and to some extent fluoroquinolones.

Only one enterobacter group organism was isolated, but it showed multidrug resistance with sensitive to chloramphenicol, meropenem, aminoglycosides, and ciprofloxacin.

Only one of each streptococcus pneumoniae, acenatobacter and pseudomonas organisms were isolated with much less data to comment about their sensitivity pattern.

Discussion

Among suspected cases of neonatal septicemia, 32 (40%) patients showed culture positivity.

In a study done by A.S.M. Nawshad Uddin Ahmed et al in Bangladesh showed culture positivity rate in septicemia suspected neonates were 35%.⁶ In another study by Shrestha P et al conducted in Nepal showed culture positivity rate to be 20%.⁷ In another retrospective study done in India at AIIMS by Upadhyay A et al showed the culture positivity rate was found to be 18.6%.⁸ Thus culture positivity rate in our institute is comparable to other institutes. A low blood culture isolation rate could be due to administration of antibiotic before blood collection from the primary centers or the possibility of infection with anaerobes. A negative blood culture does not exclude sepsis

and about 26% of all neonatal sepsis could be due to anaerobes.⁹

In the study incidence of early onset sepsis was slightly higher than late onset sepsis. This data is comparable with data from National Neonatal-Perinatal database 2000 by National Neonatology Forum.²

In a study done by Shrestha P et al conducted in Nepal showed the incidence of LOS was higher as compared to EOS.⁷ In AIIMS study done by Upadhyay A et al showed LOS to be more common than EOS.⁸ The reason why we had less incidence of late onset sepsis may be due to better sterile techniques while handling babies, strict aseptic precautions, separate compartments and attending staff for septic babies.

Study showed that, males are more prone for septicemia than females. Similar observations were made in study done by Shrestha P et al which showed male:female ratio being 3.1: 1.⁷ Another study done by A.S.M. Nawshad Uddin Ahmed et al showed male preponderance with male to female ratio being 1.7: 1.⁶ Higher male to female ratio is definitive indicative of males being more prone for septicemia, but the fact that male neonates are better cared than female neonates in our society should also be kept in mind while interpreting these results.

According to table no. 1, 21 babies are having birth weight less than 2500 grams as compared to 11 babies with birth weight more than 2500 grams. Thus 65.62 % newborns were of low birth weight which suggest higher incidence of septicemia in low birth weight babies. Similar trends are seen in both early as well as late onset septicemia. Similar trends are seen in study done by Shrestha P et al.⁷, A.S.M. Nawshad Uddin Ahmed et al⁶ and study done by Upadhyay A et al.⁸ Thus it is very clear from our study that low birth weight babies are more prone for septicemia than babies having good birth weight.

From table 2 it is very much clear that Klebsiella tops the list among all organisms. Total numbers of cases isolated with Klebsiella are 9 cases out of 32 cases i.e. 28.12%. The very important thing to note that, distribution among early versus late onset septicemia showed very high occurrence of Klebsiella in late onset septicemia. These results are in concordance with the results obtained in National Neonatal Perinatal Database (NNPD).²

Another important thing to note is, we had 2 successive cases of ESBL (extended spectrum beta lactamase inhibitor) Klebsiella isolated in our NICU. These were very resistant organisms sensitive to only imipenem group of drugs, aminoglycosides and chloramphenicol. Both were the cases of early onset septicemia.

E.coli was the second most common organism isolate (6/32, 18.75%). In contrast to Klebsiella, E.Coli predominated as early onset septicemia with 4 cases being of EOS. Other organisms isolated are Staphylococcus aureus, Streptococcus viridians, CONS, Streptococcus pneumonia, Enterobacter, Acenatobacter and Pseudomonas.

Gram negative organisms dominated the list among all organisms.

2 cases of fungal septicemia were isolated, Candida albicans was the organism isolated.

The pattern of organisms varies according to place, NICU flora. In Bangladesh, study done by A.S.M. Nawshad Uddin Ahmed et al

showed, E.Coli and Klebsiella to be commonest organisms and gram negative organisms topping the list.⁶ In contrast study done by Shrestha P et al, gram positive organisms like Staph. Aureus dominated the list.⁷ In AIIMS sepsis study done by Upadhyay A. et al, showed most common isolate to be S. aureus(25.3%) followed by K. pneumoniae(17%) and CONS(11.3%).⁸

Thus overall experience is organism spectra varies according to place, but overall gram negative organisms are still dominating the list and klebsiella pneumoniae being on the top.

Table no. 3 shows, antibiotic sensitivity patterns for various organisms in this study. Most of the klebsiella pneumoniae organisms are susceptible to piperacillin-tazobactam combination, meropenem, netilmycin, ceftazidime, amikacin, chloramphenicol and less sensitive to gentamycin, ciprofloxacin, ofloxacin, levofloxacin, co-trimoxazole, amoxiclav and ceftriaxone.

(Extended Spectrum Beta Lactamase) ESBL Klebsiella are very much resistant organisms with sensitivity to fluoroquinolones, meropenem, imipenem, amikacin and gentamycin. E.coli is sensitive to aminoglycosides, piperacillin-tazobactam combination and many of the third generation cephalosporins.

Staph. Aureus and Streptococcus viridians are sensitive to the most of the third generation cephalosporins, aminoglycosides and fluoroquinolones.

Coagulase Negative Staph. Aureus (CONS) are sensitive to amoxiclav combination, cephalosporins, aminoglycosides, vancomycin, piperacillin-tazobactam combination, meropenem and to some extent fluoroquinolones.

Only one Enterobacter group organism was isolated, but it showed multidrug resistance with sensitive to chloramphenicol, meropenem, aminoglycosides, and ciprofloxacin.

Only one of each Streptococcus pneumoniae, Acenatobacter¹⁰ and Pseudomonas organisms were isolated with much less data to comment about their sensitivity pattern.

These data are correlating with data obtained in National Neonatal Perinatal Database 2002-03.^{2,11}

Conclusions

The culture positivity rate in clinically suspected cases of neonatal septicemia was 40%. Gram negative organisms are more commonly isolated from blood culture than gram positive organisms. Klebsiella pneumoniae is the most common organism isolated.

There is emergence of multidrug resistant organisms in neonatal septicemia, Klebsiella Pneumoniae topping the list which is becoming resistant to penicillin group of drugs and some of the cephalosporins. ESBL Klebsiella Pneumoniae is a major concern to be looked upon in NICU.

In nutshell, culture and sensitivity can be used in clinical suspected cases of neonatal septicemia for better treatment and hence better prognosis.

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