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Original Research Article

Neonatal septicemia: bacteriological profile in a tertiary level hospital in South India

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ABSTRACT

Background: Early onset bacterial sepsis remains a major cause of neonatal morbidity and death. The choice of antibiotic for an infant with sepsis depends on the predominant bacterial pathogens and the antibiotic susceptibility profiles for the microorganisms causing disease in a particular geographic region. The purpose of this study was to analyze the bacteriological profile and antibiotic sensitivity pattern of neonatal septicemia in our neonatal unit.
Methods: A descriptive cross sectional study carried was out at the NICU of a tertiary level hospital in South India for a period of one year.
Results: Clinically suspected septicemia comprised 18.14% of total NICU admissions. Organism was isolated by blood culture in 14.9% of cases. The most common organisms causing septicemia were *Coagulase negative Staphylococci*, *Klebsiella* and *Staphylococcus aureus*. Gram positive isolates were most sensitive to Vancomycin (100%) while the gram negative isolates were most sensitive to Amikacin. Resistance to Crystalline Penicillin, Ampicillin and 3rd generation cephalosporins was high.
Conclusions: The most common organism isolated in septicemia was Coagulase negative staphylococcus in our NICU. Gram positive isolates were most sensitive to Vancomycin (100%) while the gram negative isolates were most sensitive to Amikacin. High resistance to commonly used antibiotics is worrisome. There should be a constant surveillance of the common microbes and their sensitivity pattern in each NICU and the antibiotic protocols should be periodically reviewed. Rational use of antibiotics and preventive measures like hand washing is the need of the hour.

Keywords: Antibiotic, Blood culture, Neonatal septicemia, Organism

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia. Early onset bacterial sepsis remains a major cause of neonatal morbidity and death. The incidence of early onset bacterial infection is variable and ranges from 1-5 per 1000 live births in developed countries.[1] According to pooled hospital data based on neonatal-perinatal data (NNPD 2002-2003) the incidence of neonatal sepsis in India is around 30 per 1000 live births.[2]

Early onset sepsis (EOS) is defined as the onset of symptoms before 7 days of age, although some experts limit the definition to infections occurring within the first 72 hours of life. Early onset infections are acquired before or during delivery.[3] Late onset sepsis (LOS) is defined as occurring from 7 days of life. Late onset infections develop after delivery from organisms acquired in the hospital or the community.[3,4]

The gold standard for detection of bacteremia in newborns with suspected sepsis is a positive blood culture result. The choice of antibiotic for an infant with early onset sepsis depends on the predominant bacterial pathogens and the antibiotic susceptibility profiles for the microorganisms causing disease in a particular geographic region.[1] It is important to remember that bacterial flora is dynamic, different from one place as compared to the other and it changes in the same place over a period of time. It is essential to closely monitor the bacterial flora of the NICU and the antibiotic sensitivity pattern of the pathogens to evolve rational antibiotic policy which is most suitable and specific for a particular NICU.[2]

The purpose of the study was to analyze the bacteriological profile and antibiotic sensitivity pattern of neonatal septicemia in our NICU.

METHODS

The study was a descriptive cross sectional study**,** it was carried out at the Neonatal Intensive Care Unit (NICU), Institute of Maternal and Child Health, Government Medical College, Kozhikode, a tertiary level hospital in Kerala, South India for a period of one year (1st September 2003 to 31st August 2004).

Inclusion criteria

Neonates with proven sepsis i.e. having a clinical picture suggestive of sepsis with isolation of pathogens from blood were included in final analysis.

Exclusion criteria

Neonates with gross congenital anomalies, or those with blood culture showing two or more organisms were excluded from final analysis.

All neonates admitted in the NICU (both inborn and outborn) with clinical features suggestive of septicemia were considered for the study. Early onset septicemia was defined as septicemia occurring in the first 7 days of life and late onset that occurring after 7 days of life. The presenting complaints were recorded. A detailed antenatal, natal and postnatal history was taken with special emphasis on the risk factors for septicemia. A detailed physical examination was done. Important clinical manifestations looked for included poor suck, lethargy, hypotonia, fast breathing, incessant cry, fever, loose stools, vomiting, jaundice, abdominal distension, seizures, apnoea, bulging anterior fontanelles, bleeding manifestations, sclerema and evidence of superficial infection (skin pustules, umbilical sepsis).

Neonates with proven sepsis i.e. having a clinical picture suggestive of sepsis with isolation of pathogens from blood were included in final analysis. When the blood culture showed a possible contaminant like Coagulase negative staphylococcus (CONS), it was included only if the baby had clinical sepsis and at least one abnormal hematology test in the septic screen.

Investigations done with:

1. Septic work up – total white blood cell (WBC) count, absolute neutrophil count (ANC), IT ratio, C reactive protein (CRP), platelet count
2. Blood culture and sensitivity - 0.5 ml of blood collected under strict aseptic precautions (in brain heart infusion broth 5 ml) was sent in all cases. Antibiotic sensitivity was tested by disc diffusion method
3. Lumbar puncture was done in all cases of clinically suspected meningitis and blood culture positive cases
4. Urine culture and sensitivity and swabs taken from sites of superficial infection were sent in indicated cases
5. Repeat blood culture and sensitivity was sent in cases not responding to treatment.
6. Other investigations as needed.

Treatment

All patients were treated with a third generation cephalosporin (Cefotaxime) and an aminoglycoside (Amikacin) as per Unit protocols. The dosage of antibiotics was according to the gestational age and weight of the neonate. Antibiotics were later modified according to blood culture and sensitivity reports and if no clinical improvement occurred. Antibiotics were given for atleast 14 days in cases of septicemia and 21 days in meningitis. Other supportive measures like maintenance of temperature, control of seizures, fluid and electrolyte balance, correction of hypoglycemia, blood transfusion, phototherapy and exchange transfusion were provided. All patients were followed up in the hospital for clinical evidence of recovery and for development of complications including death.

Analysis was done using Chi-Square test. The difference was considered significant if probability (P) value was less than 0.05.

RESULTS

During the study period of one year there were a total of 3699 inpatients in the NICU of which clinically suspected cases of sepsis (671) comprised 18.4%. Of the 671 cases pathogen was isolated by blood culture in 100 cases (14.9%). The blood culture positive cases comprised 2.7% of the total admissions.

Of the blood culture positive cases 65 were inborn and 35 out born. 69 were male and 31 were female babies. Onset of disease was within 72 hours of life in 58 babies, from 72 hours to 1 week in 22 babies; after one week of life in 20 babies.

Table 1: Microorganisms in neonatal septicemia.

Organisms	IB (n= 65)		OB (n= 35)		Total		Total %
	EOS	LOS	EOS	LOS	EOS (N=80)	LOS (N=20)	N=100
CONS	14	4	8	1	22	5	27
Klebsiella	13	3	7	1	20	4	24
S. aureus	11	3	3	1	14	4	18
E.coli	1	1	6	3	7	4	11
Acinetobacter	4	1	2	0	6	1	7
Enterobacter	3	0	1	0	4	0	4
Enterococci	3	0	0	0	3	0	3
Proteus	0	1	1	0	1	1	2
Pseudomonas	1	0	0	1	1	1	2
Flavobacterium	2	0	0	0	2	0	2

IB – Inborn OB – Outborn CONS – Coagulase negative staphylococcus

Table 2: Sensitivity of Gram positive organisms (n=48).

Organism	Vancomycin	Cloxacillin	Cefazolin	GM	CP
CONS (N=27)	100%	62%	55%	40%	48%
S. aureus (n=18)	100%	56%	53%	50%	13%
Enterococci (n=3)	100%	-	0%	0%	-

GM – Gentamicin CP – Crystalline Penicillin

Table 3: Sensitivity of the Gram negative organisms (n=52).

Organism	Cefazolin	GM	Amikacin	Ampicillin	Cefotaxime	Ceftazidime	Cefriaxone
Klebsiella (n=24)	17%	40%	75%	6%	33%	0%	63%
E. Coli (n=11)	11%	18%	100%	0%	0%	-	0%
Acinetobacter (n=7)	33%	85%	75%	40%	0%	-	-
Enterobacter (n=4)	0%	25%	33%	33%	-	-	-
Proteus (n=2)	50%	0%	0%	-	-	0%	-
Pseudomonas (n=2)	-	0%	0%	-	-	0%	-
Flavobacterium (n=2)	100%	100%	100%	100%	-	-	-

GM - Gentamicin

The most common organism isolated in EOS, LOS and overall was *CONS* (27%). This was followed by *Klebsiella* (24%), *Staphylococcus aureus* (18%) and *E. coli* (11%). Group B *Streptococcus* was not isolated in any of the cases. Gram positive isolates were 48% while Gram negative isolates comprised 52% (Figure 1) and (Table 1).

Sensitivity of *CONS*, *S. aureus* and *Enterococci* to Vancomycin was 100%. Sensitivity to Cloxacillin, Gentamicin and Cefazolin was only moderate and sensitivity to Crystalline Penicillin was low (Table 2).

Gram negative isolates were most sensitive to Amikacin. Only *Flavobacterium* was found to be 100% sensitive to commonly used antibiotics. The resistance to Cefazolin, Gentamicin and 3rd generation cephalosporins was high (Table 3). 89 of the babies were cured, one baby was lost for follow up and 10 babies expired in the hospital (Figure 2). Of the 10 babies that expired 7 had EOS(mortality of EOS was 8.75%) and 3 had LOS (mortality of LOS was 15%). *Klebsiella* was responsible for 5 deaths (15% deaths), *E. coli* for 2 deaths (20%), *CONS* for 2 deaths (20%) and *Acinetobacter* for 1 death (10%) (Figure 3). Case fatality rate was also highest for *Klebsiella* (20.8%) (Table 4).

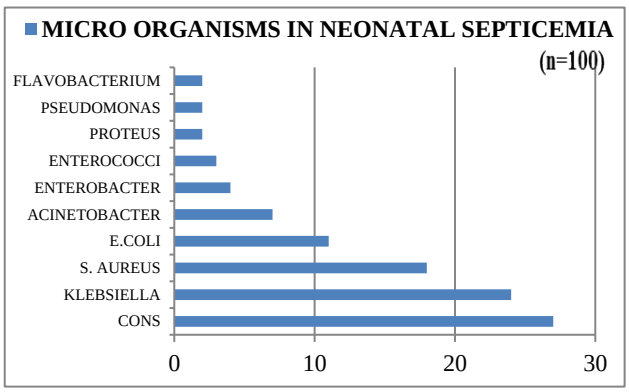

Figure 1: Microorganisms isolated in neonatal septicemia.

Table 4: Organisms and case fatality rate.

Organism	CFR %
Klebsiella	20.8
E. coli	18.2
Acinetobacter	14.3
CONS	7.4

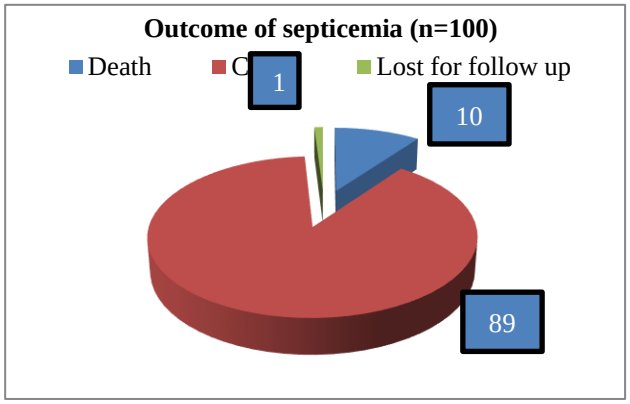

Figure 2: Outcome of blood culture positive septicemia.

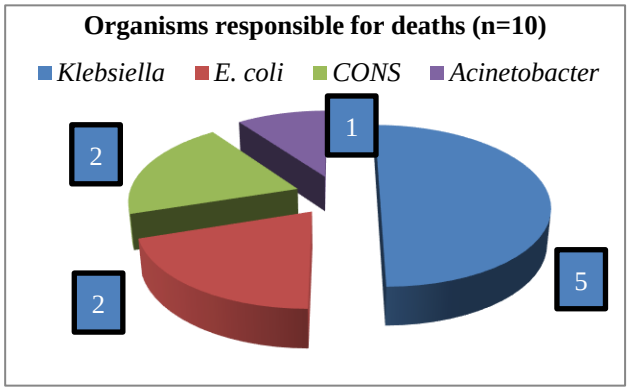

Figure 3: Organisms responsible for deaths.

DISCUSSION

During the observation period of one year clinically suspected septicemia comprised a major portion (18.14%) of total NICU admissions. Organism was isolated by blood culture in 14.9% of the cases. Similar blood culture positivity of 19.2% was obtained in another study done in South India.[5] Higher rate of culture positivity of 28.3% was observed in a study from Nepal and 42% in a study from North India.[6,7]

The low blood culture positivity in our unit was possibly due to increased use of maternal antibiotics. The use of maternal antibiotics has reduced the rate of positive blood culture in early onset sepsis.[8] Of the blood culture positive cases 65% were inborn and 35% were out born. 69% were males and 31% females. High male to female ratio was found in other studies also.[5,7]

Gram negative isolates were slightly more common (52%) than Gram positive isolates (48%). Predominance of Gram negative isolates (55.7%) has been reported by Jyothi P et al, in India and in a recent study from Cameroon, Africa (56%).[5,9] The most common organisms causing EOS were *CONS* (22 cases), *Klebsiella* (20 cases) and *Staphylococcus aureus* (18 cases). The most common organisms causing LOS were *CONS* (5 cases) followed by *Klebsiella*, *Staphylococcus aureus* and *E. coli* (4 cases each). Overall the most common organism isolated was *CONS* (27%) followed by *Klebsiella* (24%), *Staphylococcus aureus* (18%) and E coli (11%). In none of the cases GBS was isolated. In developing countries GBS is extremely rare.[10] Organisms most commonly isolated in India in other studies were *Klebsiella* (30.5%) and *CONS* (27.5%) from a centre in South India.[5] However Gram positive *Staphylococcus aureus* (40%) and *CONS* (16%) were more common in a study in North India.[7] *Klebsiella* (33.3%) was commonest isolated in a Nepal study.[6] A study in Ethiopia found *Klebsiella* (39.2%) and *Staphylococcus aureus* (29.2%) the commonest.[11] According to the NNPD 2002-2003 *Klebsiella* was the most common cause of neonatal sepsis.[12] In the United States, the most common pathogens responsible for early-onset neonatal sepsis are *GBS* and *Escherichia coli.*[13] The increasing incidence of *CONS* as the etiology for LOS was studied in Australia (51% of LOS).[14] *CONS* was also found to be the most common pathogen in a study in Taiwan by Lee NC et al, where *CONS* was isolated in 34% cases.[15] The increased incidence of *CONS* has been associated with increased survival of small premature infants with immature immune systems.

Gram positive isolates were most sensitive to Vancomycin (100%) while the gram negative isolates were most sensitive to Amikacin.100% sensitivity of *CONS* to Vancomycin was seen in a recent study from Nepal and from India.[7,16]

High sensitivity of Gram negative isolates to Amikacin was also seen in the studies in Cameroon but some studies from India showed only 50% sensitivity.[5,7] Resistance to Crystalline Penicillin, Ampicillin and 3rd generation cephalosporins was high. Resistance to commonly used antibiotics noted in the study has been reported from developed and developing countries.[1,3-5-7,9,11] In vitro resistance however does not always mean in vivo resistance.

The overall case fatality rate was 10%. This is similar to mortality of 11.7% reported by Thakur et al, but lesser than that reported by Chacko B et al, of 19.4% and Kemeze et al (33.6%).[7,9,17]

This was probably because of the use of maternal antibiotics and early use of appropriate antibiotics in sick babies who were inborn. The reported mortality rates of neonatal sepsis in various studies in India range between 15 and 50%.[2] The mortality in case of EOS was 8.75%

and LOS was 15% in our study. The organism responsible for most deaths was *Klebsiella* (50%). Case fatality rate was also highest for *Klebsiella* (20.8%). High mortality with *Klebsiella* (27.7%) was also reported by Thakur et al.[7]

CONCLUSION

Neonatal septicemia contributes to a significant proportion of NICU admissions (18.14%). In clinically suspected cases blood culture positivity was only 14.9%. The most common organisms causing sepsis were *Coagulase negative staphylococci* (27%), *Klebsiella* (24%) and *Staphylococcus aureus* (18%). Gram positive organisms were most sensitive to Vancomycin while Gram negative isolates were most sensitive to Amikacin. High resistance to commonly used antibiotics is worrisome.

There should be a constant surveillance of the common microbes and their sensitivity pattern in each NICU and the antibiotic protocols should be periodically reviewed. Rational use of antibiotics and preventive measures like hand washing is the need of the hour.

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