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Research Article

A Study of Bacteriological Profile and Their Sensitivity Pattern in Neonatal Sepsis at Tertiary Care Hospital in Mysore, Southern India

Dr Vinay BS, Dr Kruthi BN, Dr Girish GN
Apollo Bgs Hospital, Adichunchanagiri Road, Kuvempunagar, Mysore 570023, Karnataka, India

***Corresponding author**
Dr Vinay BS
Email: vny_mys@yahoo.com

Abstract: Epidemiology and surveillance of neonatal sepsis helps in implementation of rational empirical antibiotic strategy. 60 consecutive babies over 1year period with suspected sepsis based on risk factors and clinical presentation were included in this study. All the babies underwent blood culture. Blood culture sample included a single sample from peripheral vein or artery. Blood culture report and sensitivity pattern was noted. In total, 80% (48 of 60) of the clinically suspected cases were culture-proven cases of neonatal sepsis, which isolated 9 pathogens. Gram negative organisms were isolated from 31 (64.5%). Klebsiella pneumoniae (19 out of 48, 40%) was the most common gram negative organism and most common causative agent of neonatal sepsis. Gram positive organisms were isolated from 15 (31.2%). Coagulase-negative staphylococci 10 (20.8%) were the most common gram-positive agent. The 19 Klebsiella pneumoniae isolates were 100% susceptible to Amikacin, Ciprofloxacin, Ofloxacin and Meropenem; and 100% resistant to Amoxyclav, ampicillin, Ceftazidime and Cefotaxime. Other Gram negative organisms isolated (Pseudomonas, E.coli, and Acinetobacter) were 100% sensitive to Amikacin, Ciprofloxacin, Levofloxacin, Piperacillin Tazobactum and Meropenem. E.coli was totally sensitive for Ceftriaxone, Ceftazidime, and Cefotaxime. All isolated E.coli were resistant to Amoxyclav and Ampicillin. All the gram positive isolates were 100% susceptible for Linezolid and Vancomycin. Bacteriological profile in neonatal sepsis in our locality is dominated by Gram negative bacteria, Klebsiella pneumoniae. Second commonest bacteria isolated are Staphylococcus, with 61.5% being Coagulase Negative strain. Ciprofloxacin and Amikacin would be appropriate as empirical first line antibiotic for suspected neonatal sepsis in our locality.
Keywords: Bacteriological profile**, N**eonatal sepsis, Blood culture, Antibiotic sensitivity, Gram negative organisms, Gram positive organism.

INTRODUCTION

Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries [1, 2] and approximately 1% die of sepsis related causes. It is estimated that up to 20% of neonates develop sepsis. Sepsis related mortality is largely preventable with early diagnosis, rational antimicrobial therapy and aggressive supportive care [2].

The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births. The database comprising 18 tertiary care neonatal units across India found sepsis to be one of the commonest causes of neonatal mortality contributing to 19% of all neonatal deaths.3 Septicaemia was the commonest clinical category with an incidence of 23 per 1000 live births while the incidence of meningitis was reported to be 3 per 1000 live births. Among intramural births, Klebsiella pneumoniae was the most frequently isolated pathogen (32.5%), followed by Staphylococcus aureus (13.6%). Among extramural neonates (referred from community/other hospitals), Klebsiella pneumoniae was again the commonest organism (27%), followed by Staphylococcus aureus (15%) and Pseudomonas (13%) [3].

Neonatal septicaemia with its high incidence and its bad prognosis, in spite of adequate treatment with modern antibiotics, has been a challenge all the times. Optimal diagnosis and treatment strategies are difficult to define. Early diagnosis of NNS has remained a frustrating experience even in the developed countries. Prompt and correct diagnosis of NNS is difficult because of its subtle and non-specific symptoms and signs. The gold standard for diagnosis is blood culture but has a high cost and delay of at least 48 hours before preliminary results are received. Antibiotics have major role in the treatment of sepsis and it should be initiated early as possible to improve the outcome, hence it is very essential to know the bacteriological profile and

their sensitivity pattern for early initiation of appropriate antibiotics before we get the blood culture. Hence this study was conducted.

Aims & Objectives of the Study:

To study the bacteriological profile and its sensitivity pattern in tertiary care centre.

METHODOLOGY

Study Design: Prospective Observational Study.

Source of Data: 60 neonates admitted to our NICU with clinical suspicion of sepsis during Nov 2012 to Nov 2013.

Method of Collection of Data:

Clearance from the Institutional Ethical committee was taken prior to the study.

Sample Size: Based on our hospital admission of neonatal sepsis incidence, we took 60 as sample size.

Inclusion Criteria

1. Neonates (<30 days) admitted to NICU of Apollo BGS Hospital with clinically suspected neonatal sepsis.

Exclusion Criteria

1. Neonates who received antibiotics before.
2. Neonates who die before work up were complete.
3. Neonates who underwent surgery.

The study included neonates who were suspected of having sepsis, based on the presence of risk factors and/or clinical features that were consistent with sepsis.

Risk factors for sepsis include: Prematurity, Low birth weight, Maternal fever, Chorioamnionitis, Foul smelling liquor, Prolonged rupture of membranes (>18hours) and maternal urinary tract infection (UTI).

Clinical features include: Fever, Hypothermia, Weight loss, Decreased activity, Convulsions, Respiratory distress, Apnea, Cyanosis, Skin mottling, Sclerema, Refusal to feed, Feed intolerance, Abdominal distension. A detailed antenatal, natal and postnatal history was taken. The birth weight, sex and day of onset of sepsis were noted. Depending on the age at admission, babies were divided in to two groups:

- Early onset sepsis: babies <72hrs old
- Late onset sepsis: babies 72hrs-30 days old.

All the babies underwent sepsis screen and blood culture. Blood samples were obtained from peripheral venepuncture in all neonates within 24 hrs of admission, before initiation of antibiotic therapy.

Sepsis screen included following tests:

Total Leucocyte Count (TLC), Absolute Neutrophil Count (ANC), Platelet Count (PC), Immature: Total Neutrophil ratio (I: T ratio), Micro Erythrocyte Sedimentation Rate (mESR), C-reactive protein (CRP).

Blood culture was performed under strict sterile precautions. A single blood sample (2ml) was inoculated into the culture bottle. The BacT alert microbial detection system was used for blood culture. The susceptibility of the clinical isolates to some routinely used antibiotics was determined by the Kirby-Bauer disk diffusion method according to Clinical Laboratory Standards Institute guidelines. The isolates were identified based on standard bacteriological techniques. All the babies with blood culture positive undergone CSF analysis.

Bacterial isolates and their sensitivity patterns were noted.

RESULTS

A total of 60 neonates admitted to our NICU on first come first serve basis were included in the study. No neonates were excluded from the study. The demographic data of these 60 cases are summarized in the Table-1.

Our study population consisted of more male babies (40) than females (20). There were more number of preterm babies (41) and LBW babies (42). Nearly 70% of the total cases were referred to us (out born) and only 30% were inborn babies. Of the 60 clinically suspected cases of neonatal sepsis, 54 (90%) were early-onset and only 6 (10%) were late-onset sepsis.

In total, 80% [48 of 60] of the clinically suspected cases were culture-proven cases of neonatal sepsis, which isolated 9 pathogens. Gram negative organisms were isolated from 31 (64.5%) out of 48 culture proven sepsis. Klebsiella pneumoniae (19 out of 48, 40%) was the most common gram negative organism and most common causative agent of neonatal sepsis. K. pneumoniae was followed by Pseudomonas aeroginosa, Escherichia coli 5 (10.4%) and Acineto bacterbaumani 2 (4.1%). Gram positive organisms were isolated from 15 (31.2%) out of 48 cases. Coagulase-negative staphylococci 10 (20.8%) were the most common gram-positive agent, followed by Staphylococci aureus 3 (6.25%) and Group B Streptococci 2 (4.1%). Candida was isolated from 2 (4.1%) cases. Blood culture positive rate in EOS was 77.8% (42) and 100% in LOS. Klebsiella was the most common pathogen isolated from both EOS and LOS group followed by CONS.

Table 1: Demographic and maternal data of all cases

Parameters	Values (%)
Sex	
No. of males	40 (66.6)
No. of females	20 (33.4)
Gestational age	
Term	19 (31.6)
Preterm	41 (68.4)
Birth Weight	
Low birth weight	42 (70)
Normal birth weight	18 (30)
Age at onset	
Earl onset sepsis	54 (90)
Late onset sepsis	6 (10)
Place of delivery	
No. of inborn babies	19 (31.6)
No. of out born babies	41 (68.4)
Maternal data	
No. of cases with PROM > 24 h	15 (25)
No. of cases with meconium stained liquor	5 (8.3)
No. of cases with foul smelling liquor	5 (8.3)
No. of cases with maternal fever	5 (8.3)

Table 2: Etiological agents of early-onset and late-onset neonatal sepsis

Organism	Early onset sepsis	Late onset sepsis
Klebsiella	17 (40.4%)	2 (33.3%)
CONS	8 (19%)	2 (33.3%)
Pseudomonas	4(9.5%)	1(16.6%)
E coli	4 (9.5%)	1(16.6%)
Staphylococcus	3 (7.1%)	___
Streptococci	2 (4.7%)	___
Acinetobacter	2 (4.7%)	___
Candida	2 (4.7%)	___

Among 41 out born babies, 37 cases (90%) were culture positive with 13 (35.1%) cases being positive for Klebsiella followed by 8 (21.6%) cases of CONS sepsis. 11 (57.8%) out of 19 inborn cases were culture proven sepsis with Klebsiella (6 of 19, 54.5% as most common organism.

Table 3: Etiological agents of sepsis in inborn and out born neonates

Organism	Inborn (%)	Out born (%)
Klebsiella.	6 (54.5)	13(35.1)
CONS	0	8(21.6)
Pseudomonas	1 (9)	4(10.8)
E coli	2 (18.1)	3(8)
Staphylococcus	2 (18.1)	3(8)
Streptococci	0	2(5.4)
Acinetobacter	0	2(5.4)
Candida	0	2(5.4)

The 19 Klebsiella pneumoniae isolates were 100% susceptible to Amikacin, Ciprofloxacin, Ofloxacin and Meropenem; and 100% resistant to Amoxyclav, ampicillin, Ceftazidime and Cefotaxime. However, Klebsiella was variably sensitive to Piperacillin Tazobactum (79%) and Ceftriaxone (10%). Other Gram negative organisms isolated (Pseudomonas, E.coli, and Acinetobacter) were 100% sensitive to

Amikacin, Ciprofloxacin, Levofloxacin, Piperacillin Tazobactum and Meropenem. Further, Pseudomonas showed 100% susceptibility to Gentamicin and variable susceptibility towards Ceftazidime (40%) and Cefixime (60%). E.coli was totally sensitive for Ceftriaxone, Ceftazidime, Cefotaxime and Gentamicin; variable sensitive to Cotrimoxazole (40%). All isolated E.coli were resistant to Amoxyclav and Ampicillin. Acinetobacter isolated were completely resistant to Ceftriaxone and Ceftazidime.

Out of 15 cases of Gram positive sepsis, 13 were from Staphylococcus and only 2 were Streptococci. Of the 13 cases of Staphylococci, 8 were Coagulase negative and 5 were Coagulase positive. All the gram positive isolates (CONS, Staphylococcus and Streptococcus) were 100% susceptible for Linezolid and Vancomycin. Most common gram positive organism isolated, CONS was further 100% sensitive to Ciprofloxacin, Ofloxacin and Levofloxacin. It was variably sensitive to Cotrimoxazole (25%). Coagulase Positive Staphylococci isolated was sensitive to Levofloxacin (60%), Erythromycin (60%), Clindamycin (40%) and Co trimaxozle (20%). All of the Staphylococci isolated were 100% resistant to Amoxyclav, Penicillin and Oxacillin. CONS were completely resistant to Clindamycin. There were 2 cases of Group B Streptococci sepsis, which were totally sensitive to Ampicillin and totally resistant to Levofloxacin, Clindamycin and Erythromycin. There was one death recorded among study population, which grew Staphylococcus.

DISCUSSION

The etiological agents of neonatal sepsis vary between developed and developing countries [4]. Klebsiella pneumoniae and other Gram-negative organisms were the common causes of sepsis in the present study as well other studies from India and Nigeria [5]. However, in the developed countries Group B Streptococcus and coagulase negative staphylococci (CONS) are the predominant causes of sepsis [6]. The bacteriological profile of early-onset sepsis differs from that of late-onset sepsis as the mode of infection is different [7]. Early-onset neonatal sepsis is acquired transplacental or as an ascending infection from cervix or during passage of the baby through a colonized birth canal. In the present study, Klebsiella pneumonia was the common agent implicated in early-onset sepsis, while Group B Streptococcus was isolated from only 2 neonates. Although Group B Streptococcus was considered as an important agent associated with early onset sepsis, the recent studies are showing a decreasing trend in the incidence of this pathogen [7]. Late-onset neonatal sepsis is usually acquired from the care-giving environment and coagulase-negative staphylococci (CONS), Staphylococcus aureus, Escherichia coli and Klebsiella species are the common agents involved. In the present study, Klebsiella pneumoniae and CONS were the common etiological agents of late-onset sepsis. In an epidemiological study performed to observe the long term trends in the agents causing neonatal sepsis, CONS were showing an increasing trend [7].

Table 4.Organisms isolated in different studies.

Sl.no.	Study Group	Year	Culture +Ve rate	Commonest isolate
1	Tallur *et al.;* [8]	2000	64.87%	Klebsiella (53%)
2	Roy *et al.;* [9]	2002	47.5%	Klebsiella (24.1%)
3	Madhu Sharma *et al.;* [10]	2002	33.94%	Klebsiella (61%)
4	NNPD 2002-034	2002	28.6%	Klebsiella (32%)
5	Present study	2013	80%	Klebsiella (39.5%)

In this study, the authors compared the etiological agents of neonatal sepsis in babies born in their hospital and those born outside. Klebsiella pneumoniae was significantly implicated in sepsis occurring among both in-born babies and out born babies. Klebsiella pneumoniae is commonly found in the environment of the neonatal intensive care units and nursery. It can also be present as colonizers on the hands of the health care workers. There are also frequent reports of neonatal septicaemia outbreaks due to Klebsiella pneumoniae in nursery and NICUs [11].

In our study, 100% of K pneumoniae isolates were resistant to third generation cephalosporins, except for 2 cases which were sensitive to ceftriaxone. In a similar study, 50–100% of the Klebsiella pneumoniae isolates were observed to be resistant to commonly used antibiotics especially gentamicin and the second and third generation cephalosporins [12]. In another study from North India, 30–80% of the Gram negative isolates were resistant to third-generation cephalosporin [5]. This suggests that the third-generation cephalosporins cannot be used alone for empirical treatment of neonatal sepsis and Amikacin which shows good activity against the gram negative bacteria should always be included in the empirical regimen. This also emphasizes the need to routinely test for cephalosporin resistance and ESBL production among the gram-negative bacterial isolates. In the present study, all the Klebsiella and other gram negative isolates were

sensitive to Amikacin, Ciprofloxacin and Meropenem. This would suggest that Amikacin and Ciprofloxacin as the empiric antibiotic of choice in suspected sepsis neonate in our locality. Meropenem is a good second line drug if there is no response for the above.

Staphylococcus was isolated in 13 cases, the second commonest isolated organism in our study. Out of 13 cases, 8 (61.5%) were Coagulase negative and 5 (38.5%) were Coagulase Positive. Both strains were completely sensitive to Ciprofloxacin, Linezolid and Vancomycin. Both were resistant to Amoxyclav, Penicillin and Oxacillin. Hence, choice of Ciprofloxacin as first line drug would be justified, with Vancomycin reserved for the unresponsive cases. Fortunately, there were no VRSA documented. Nonetheless, with VRSA strain in rise, one needs to reduce the unnecessary Vancomycin use to keep VRSA in check.

We had only death among 60 cases, which was septic screen positive and blood culture grew Staphylococcus aureus, It was a case of early onset sepsis, referred from outside.

CONCLUSION

Bacteriological profile in neonatal sepsis in our locality is dominated by Gram negative bacteria, Klebsiella pneumoniae. Second commonest bacteria isolated are Staphylococcus, with 61.5% being Coagulase Negative strain. The entire Gram negative bacteria isolated were sensitive to Ciprofloxacin, Amikacin and Meropenem; and most Klebsiella isolated were resistant to third generation cephalosporins. All the Staphylococci isolated were sensitive to ciprofloxacin, Linezolid and Vancomycin. Ciprofloxacin and Amikacin would be appropriate as empirical first line antibiotic for suspected neonatal sepsis in our locality, with big guns like Meropenem and Vancomycin reserved for unresponsive cases only.

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