Neonatal Sepsis: Clinical Spectrum, Bacteriological Profile and Antibiotic Sensitivity Patterns in Neonatal Intensive Care Unit in a Tertiary Care Hospital

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ABSTRACT

Introduction: Neonatologists face a perpetual challenge in managing neonatal septicaemia due to changing patterns of the microbial flora and their antibiotic sensitivity. The present study was designed to evaluate the clinical spectrum, bacteriological profile, antibiotic sensitivity patterns in neonates with suspected septicaemia in a tertiary care teaching hospital.

Material and Methods: This prospective observational study was carried out in neonatal intensive care unit for a period of nine months. All the neonates with suspected septicaemia, were evaluated by sepsis screen (C- reactive protein). C-reactive protein positive neonates were subjected to blood culture for isolation of microorganisms. Antibiotic sensitivity testing was done with disc diffusion method. The data was analyzed using descriptive statistics.

Results: Among 519 neonates, blood culture was positive in 183 (35.2%). Most of the neonates presented with early onset sepsis(65%), were preterm(59%) and of low birth weight (58.5%). Major clinical presentation was respiratory distress (31.2%). Gram negative bacteria were frequently isolated (68.3%). Most common isolates were Klebsiella pneumonia (34.70%) and staphylococcus aureus (21.8%) respectively. Gram negative organisms were sensitive to imipenem, followed by piperacillin tazobactam and amikacin. Gram positive organisms showed good sensitivity to vancomycin, teicoplanin and imipenem. High resistance was observed to ampicillin and ceftriaxone in both gram positive and gram negative organisms.

Conclusions: Preterm and low birth weight neonates were more susceptible to neonatal sepsis. Gram negative organisms were frequently isolated. The present study would suggest rational use of empirical antibiotic therapy and to review the antibiotic policy periodically basing on the microbial flora detected in their region time to time.

Keywords: Antibiotics, Klebsiella, Neonatal Septicaemia

INTRODUCTION

Neonatal sepsis is a worldwide problem that presents a dynamic challenge to paediatricians. Globally, it is estimated that 2.6 million neonatal deaths were reported in 2015.[1] Globally, the major causes of neonatal death are prematurity (28%), sepsis (26%), and asphyxia (23%).[2] South Asia and Sub Saharan Africa have the highest burden of neonatal sepsis in the world. Of the total sepsis related neonatal deaths in 2013, 38.9% occurred in South Asia.[3]

Nearly, 0.75 million neonates died in India in 2013.[4] The current Indian neonatal mortality rate is 24 per 1000 live births and in Andhra Pradesh, it is 23 per 1000 live births.[5] Septicaemia is the one of the major cause of neonatal mortality and morbidity in India. It can be defined as "a clinical syndrome characterized by systemic signs and symptoms of bacteraemia during the first 28 days of life".[6] It is labeled as "early onset (first 72 hours of life)" and "late onset" (beyond 72 hours of life) sepsis. This classification has clinical importance, as early onset neonatal sepsis is generally acquired from pathogens of maternal genital tract, whereas late onset sepsis has its origin either from the community or from hospital. About 62% of the infections in South Asia occur in the first 72 hours of life, roughly translating into an incidence of 9.8 per 1000 live births.[7]

Multidrug antibiotic resistance is an emerging problem in neonatal intensive care units particularly in developing countries. Neonatologists who supervise neonatal intensive care unit (NICU) always face a continuous challenge in managing the neonatal infections due to the changing patterns of the microbial flora. The knowledge of bacteriological profile and its antibiotic sensitivity pattern is of great use to paediatricians in choosing antibiotics optimally to treat neonates with septicaemia. In suspected clinical septicaemia, rational empirical therapy has to be started. Antibiotics should be re-evaluated when the results of the cultures and sensitivity are available.

This study was carried out to determine the clinical spectrum, bacteriological profile and antibiotic sensitivity pattern of neonatal sepsis in NICU in a tertiary care hospital, so that appropriate antimicrobial policy could be made for effective management of neonatal sepsis.

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MATERIAL AND METHODS

A cross sectional prospective study was conducted at Government General Hospital, Guntur Medical College, Guntur, Andhra Pradesh. The study was conducted from January 2018 to September 2018 after obtaining Institutional Ethics Committee approval. Neonates between the age of 0–28 days admitted to NICU with suspected neonatal sepsis were included in the study. Antibiotics used prior to admission to the hospital, neonates who died before reports of blood culture sensitivity were excluded from the study

Sepsis was suspected from the clinical presentation of one or more of the symptoms like respiratory distress (tachypnea, grunting, chest retractions,), refusal of feeds, lethargy, fever, neonatal seizures, absent cry,vomiting, neonatal Jaundice, hypothermia, cyanosis, apnea, and excessive crying,etc.

For all clinical suspected cases of neonatal septicaemia, laboratory screening for sepsis was done with C-reactive protein (CRP). All clinically suspected neonatal sepsis cases with CRP positive result were sent for blood cultures and antibiotic susceptibility testing. Samples for blood culture were obtained before the commencement of antibiotics under strict asepsis, and were sent to the microbiological laboratory.Antimicrobial susceptibility of bacterial isolates was done by disc diffusion method. Other investigations were done as required. The neonates with suspected sepsis were started empirically on antibiotics, which were changed according to the sensitivity pattern once the culture report was available.

category		Number (percentage)
Sex	Males	94 (51.4%)
	Females	89 (48.6%)
Onset of sepsis	Early onset sepsis	119(65%)
	Late onset sepsis	64 (35%)
Gestational age	Preterm	108 (59%)
	Term	75 (41%)
Birth weight	Extremely low birth weight	6 (3.3%)
	Very low birth weight	21 (11.5%)
	Low birth weight	107 (58.5%)
	Normal birth weight	49 (26.8%)

Table-1 : Distribution of culture positive sepsis of neonates according to onset of sepsis, sex gestational age and birth weight

Isolated microorganism	EOS	LOS	Total (%)
Klebsiella pneumoniae	31	15	46(25.1)
Citrobacter species	10	4	14(7.65)
Pseudomonas aeruginosa	11	6	17 (9.28)
Proteus sps	4	2	6(3.27)
Klebsiella oxytoca	4	1	5(2.73)
E.coli	9	6	15(8.1)
Acinetobacter sps	12	6	18(9.83)
Burkholderia cepacia	1	1	2(1.09)
Candida sps	0	2	2(1.09)
Coagulase negative staphylococci	13	5	18(9.83)
Staphylococcus aureus	24	16	40(21.8)
Total	119	64	183(100)

Table-2: Distribution of the isolated microorganisms

STATISTICAL ANALYSIS

The collected data was analyzed using descriptive statistics with the help of statistical package for the social science (SPSS) version 16.0.

RESULTS

During the study period a total of 1314 neonates were admitted in NICU. Out of these, 519 neonates were suspected with clinical septicaemia. Among them, 237 (45.7%) were female babies and 282 (54.3%) were male babies. Among them, 285 (54.9%) presented with early onset sepsis (EOS) and 234 (45.1%) presented with late onset sepsis (LOS).

Respiratory distress (31.2%) was the major presenting symptom, followed by refusal of feeds(23.7%), prematurity (16%) and neonatal seizures (14.3%). Absent cry, lethargy, neonatal jaundice,abdominal distension and excessive cry were the other presenting symptoms. (figure 1)

Out of 519 neonates, blood culture was positive in 183 (35.2%) cases. Female babies represented 89 (48.6%) and male babies represented 94(51.4%) cases. Basing

Antibiotics	Gram negative organisms (%)					Gram positive organisms (%)	
	Klebsiella pneumonia (46)	Acinetobacter species (18)	Pseudomonas aerugonisa (17)	E.coli (15)	Citrobacter species (14)	Staphylococcus aureus (40)	Coagulase negative staphylococci (18)
Ampicillin	4 (8.6)	2 (11.1)	0 (0)	2 (13.3)	1 (7.1)	3 (7.5)	2 (11.1)
Ceftriaxone	5 (10.8)	3(16.6)	0 (0)	7 (46.6)	3 (21.4)	0(0)	0 (0)
Amikacin	23 (50)	7 (38.8)	2 (11.7)	4 (26.6)	8 (57.1)	3 (7.5)	1 (5.5)
Imipenem	42 (91.3)	16 (88.8)	12 (70.5)	13 (86.1)	12 (85.7)	20 (50)	6 (33.3)
Piperacillin tazobactam	28 (60.8)	11 (61.1)	6 (35.2)	4 (26.6)	6 (42.8)	23 (57.5)	3 (16.6)
ciprofloxacin	14 (30.4)	8 (44.4)	3 (17.6)	5 (33.3)	8 (57.1)	0 (0)	5 (27.7)
Vancomycin	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	30 (80)	16 (88.8)
Teicoplanin	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	28 (70)	10 (55.5)
Ceftazidime	0 (0)	0 (0)	13 (76.4)	0 (0)	0 (0)	0 (0)	0 (0)
Ofloxacin	6 (13.1)	5 (27.7)	7 (41.7)	5 (33.3)	4 (28.5)	4 (10)	2 (11.1)

Table-3: Antibiotic sensitivity pattern of isolates.

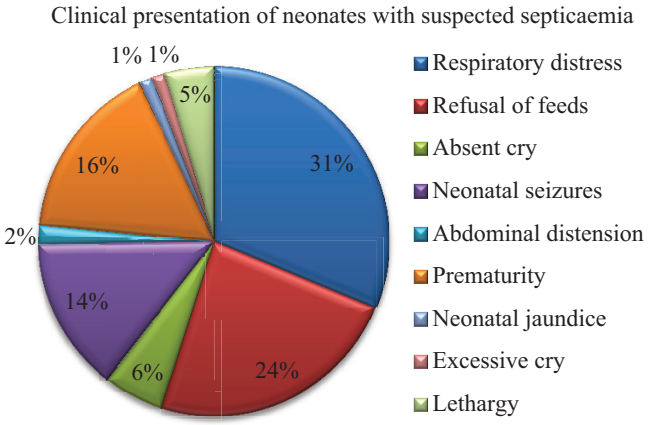

Figure-1 : Clinical presentation of neonates with suspected septicaemia

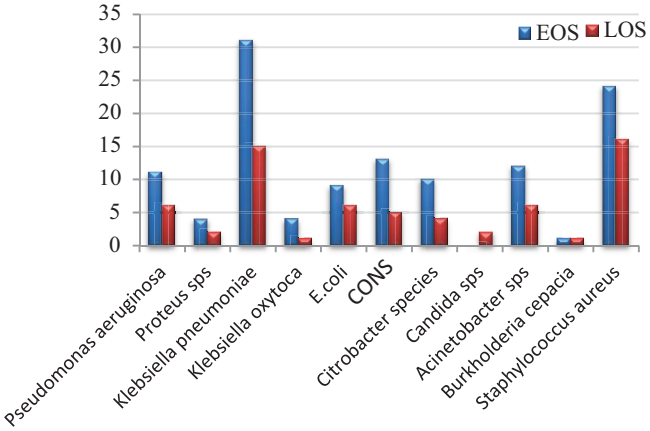

Figure-2: Distribution of the isolated microorganisms based on onset of sepsis

on gestational age, 108 (59%) were preterm, remaining 75(41%) were term babies. Out of 183 cases, 6 (3.3%) were of extremely low birth weight (elbw), 21 (11.5%) were of very low birth weight (vlbw), 107 (58.5%) were of low birth weight(lbw) and 49 (26.8%) were normal birth weight. Most of the neonates admitted presented with early onset sepsis (65%), and 35% presented with late onset sepsis.(fig 2)

Of 183 (35.2%) positive blood cultures, Gram negative bacteria and Gram positive bacteria accounted for (68.3%) and (31.7%) respectively.It indicates Gram negative organisms were the most frequent cause of septicaemia. The most common isolated microorganism was Klebsiella pneumonia (34.70%), followed by acinetobacter species (9.83%), pseudomonas aeruginosa (9.23%), E.coli (8.10%). Less frequent gram negative organisms isolated were klebsiella oxytoca, burkholderia cepacia, Proteus sps. Among gram positive organisms, staphylococcus aureus (21.8%) was the most common organism isolated, followed by coagulase negative staphylococci (9.83%). Very few candida species were also isolated.

Gram negative organisms were sensitive to imipenem (84%), followed by piperacillin-tazobactam (45.3%) and amikacin(36.8%),ciprofloxacin (36.4%). Gram positive organisms showed good sensitivity to vancomycin (84.4%), teicoplanin (62.7%) and imipenem (41.6%). Gram negative organisms were resistant to ampicillin (89.4%), followed by cefotaxim (68.2%) and ceftriaxone (66.6%). Gram positive organisms were resistant to ampicillin (86.2%), followed by ceftriaxone (60.3%), azithromycin (41.3%). Among gram negative organisms, klebsiella pneumonia showed good sensitivity to imipenem (91.3%) followed by piperacillin-tazobactam(60.8%) and high resistance was observed to ampicillin(67.4%) and cefotaxime(43.5%). Among gram positive organisms, staphylococcus aureus showed good sensitivity to vancomycin (80%) followed by teicoplanin(70%),imipenem (50%) and high resistance was observed to ampicillin(90%). (Table 3)

DISCUSSION

Antibiotic resistance has become a global threat. Reports of multidrug-resistant bacteria causing neonatal sepsis in developing countries are increasing, particularly in neonatal intensive care units. There is a constant change of bacterial flora and sensitivity patterns in different regions from time to time. For effective management of neonatal septicemia, study of bacteriological profile along with the antimicrobial sensitivity pattern plays a crucial role. The correct and timely identification of microorganisms and their antibiotic sensitivity patterns are essential to guide the paediatricians regarding both the empirical and definitive treatment.

In the present study, 519 neonates were suspected with clinical septicaemia. Respiratory distress (31.2%) was the major presenting symptom in the present study which was similar to studies done by Khante SV et al[8] and Satyamurthi et al.[9] In the present study, blood culture positivity in neonatal septicaemia was 35.2%. These findings were similar to the prevalence rate of 36.2%, 37.69% and 35% reported by Khante SV et al[8], Sharma CM et al[10] and Gandhi S et al[11] respectively.

In the present study, (65%) cases presented with early onset sepsis (EOS). Our findings were in accordance with Peterside O et al[12] and Muley VA et al[13], who found EOS in 66% and 66.7% cases respectively and LOS in 34% and 33.3% cases respectively. The incidence of sepsis was found to be more in preterm babies and low birth weight babies in the present study. This is in accordance with other studies that have been done previously in india.

In the present study, the Gram negative bacteria and Gram positive bacteria accounted for (68.3%) and (31.7%) respectively. This is in comparable with the studies done by Tak SK et al[14], Shrestha et al[15], Rajana R et al[16] which also showed that gram-negative organisms were more common causes of neonatal sepsis. The probable reasons being, newborns most probably acquire these Gram-negative organisms from the maternal genital tract. Importance of both vertical transmission from the mother and postnatal acquisition of infection from the environment has been suggested in the literatures for pathogenesis of neonatal sepsis. Two of the isolates were candida albicans which was similar to the study done by Gandhi S et al.[11]

The most common organism isolated was Klebsiella followed by staphylococcus aureus which are similar to the studies done by Tak sk et al[14], Shrestha et al[15] and Natasha

Sawhney et al.[17] The Gram-negative organisms showed good sensitivity to imipenem, piperacillin-tazobactam and amikacin,ciprofloxacin and high resistance to ampicillin. This finding is similar to another study done by Satyamurthi et al[9], Pooja et al.[18] The Gram-positive organisms showed good sensitivity to vancomycin, teicoplanin and imipenem and high resistance to pencillins. Studies done by Pooja et al[18], and Gandhi s et al[11] also showed similar findings.

CONCLUSION

Preterm and low birth weight neonates are more susceptible to neonatal sepsis. Gram negative organisms were the commonly isolated organisms. This study emphasises that empirical therapy for suspected neonatal septicaemia should cover both Gram-negative and Gram-positive organisms particularly Klebsiella pneumoniae and Staphylococcus aureus which were more prevalent in this region. There is also need for regular periodic surveillance of the causative organisms of neonatal sepsis as well as their antibiotic susceptibility patterns to curtail the inappropriate use of antibiotics and emergence of resistant strains and review the hospital antibiotic policy from time to time.

There is a need to implement Antimicrobial stewardship programmes to rationalise antibiotic usage to reduce neonatal mortality due to sepsis. Early detection of sepsis and judicial use of antibiotics are useful to decrease neonatal mortality and the emergence of multidrug resistant bacteria.

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