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BACTERIOLOGICAL PROFILE OF NEONATAL SEPSIS IN NEONATAL INTENSIVE CARE UNIT (NICU) IN A TERTIARY CARE HOSPITAL: PREVALENT BUGS AND THEIR SUSCEPTIBILITY PATTERNS

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ABSTRACT

Introduction: Neonatal sepsis remains an important cause of neonatal morbidity & mortality in NICU setup and a major challenge for the neonatologists. The prevalent organisms & their antibiotic resistance patterns evolve with time and with the usage of antimicrobials. Knowledge of the causative bacteria & their antibiotic resistance patterns is pivotal for better therapeutic results. **Aims & Objectives:** To analyze the bacteriological profile and antibiotic resistance patterns of proven neonatal sepsis cases in NICU setup of a tertiary care Hospital. **Materials and Methods**: The study is Prospective obervational study. The study Conducted at Pt. Jawahar Lal Nehru Memorial (JNM) Medical College and Hospital, Raipur, Chhattisgarh, India. The Duration of study was from January 2013 to December 2013 (12 months). All proven neonatal sepsis cases in NICU with positive blood culture reports (141 cases) were included in the study. Clinically suspected cases of neonatal sepsis admitted to NICU were further evaluated with blood cultures & antibiotic susceptibility testing using the Kirby Bauer disc diffusion method. Data was collected for the following variables: Demographic profile, gestational age, age of onset of sepsis (early versus late), culture results & antibiotic resistance patterns. **Results:** Out of 841 cases of clinically suspected neonatal sepsis, 141 were culture positive. *Klebsiella pneumoniae* was the most common isolate accounting for 49.64% cases followed by *Escherichia coli* 26.95%, *Pseudomonas aeruginosa* 7.80%, and *Staphylococcus aureus* 7.09%. High level of resistance was found against various antibiotics such as ampicillin(58-63%),Third generation cephalosporins(9-41%) and combination drugs such as piperacillin-tazobactum(7.8-32.8%). Meropenem is most sensitive antibiotics. **Conclusion**: Gram negative bacteria were the most common cause of neonatal sepsis. Increased level of resistance was found to penicillins, 3rd generation cephalosporins & piperacillin-tazobactum in the present study thus suggesting judicious use of these antibiotics in NICU setup.

KEYWORDS: Neonatal sepsis, Bacterial isolates, antibiotic sensitivity, NICU.

Key Message: Emergence of multi-drug resistant strains in NICU is a potential challenge to the pediatrician and neonatologists. This study aims to guide the clinicians about the antibiotic resistance patterns of bacterial isolates in neonatal sepsis cases so as to modify the empirical therapy of such cases and take preventive measures for a better therapeutic outcome.

INTRODUCTION

Neonatal sepsis is the most common infection encountered in the Neonatal Intensive Care Unit (NICU)[2] and forms the basis for most of the studies conducted in NICU[3]. The causative organisms vary from region to region and from time to time. Group B Streptococcus (GBS) and *Escherichia coli (E. Coli)* have been implicated in > 70% cases in the Western countries whereas in developing countries, gram negative organisms form the major culprits[4].

Neonatal sepsis is defined as systemic inflammatory response syndrome caused by suspected or proven infection occurring within the first 28 days of life[1]. It is further classified into early onset sepsis if the patient presents within 72 hours of birth and late onset sepsis if the presentation is after 72 hours of birth[2].

Proper management of these cases in NICU requires a thorough knowledge of the prevailing causative organisms and their antibiotic resistance patterns. This in turn may guide the neonatologist regarding empirical therapy and a better therapeutic outcome. In the absence of such a data from the Central India (Chhattisgarh State), we tried to analyze the prevalent causative

organisms in neonatal sepsis and their antibiotic susceptibility patterns in NICU setup**.**

MATERIAL AND METHODS

This was a prospective observational study conducted in the Department of Pediatrics, Pt. Jawahar Lal Nehru Memorial (JNM) Medical College and Hospital, Raipur, Chhattisgarh, India. Pt. JNM Medical College and Hospital is a 700 bedded Multispecialty Tertiary care Urban Hospital with 24 bedded Level II NICU setups. All the clinically suspected cases of Neonatal Sepsis admitted to the NICU from January 2013 to December 2013 were included in the study. Neonatal sepsis was clinically suspected if a neonate presented with the clinical signs and symptoms of Neonatal sepsis **(Table 1)** and with positive history of high risk factors in mother such as chorioamniotis, prolonged rupture of membrane> 24 hours, meconium stained or foul smelling liquor during labour, presence of urinary tract infection, more than 3 or unclean vaginal examination during labour and those babies who needed active resuscitation at the time of birth.

Table 1: Clinical Signs and Symptoms of Neonatal sepsis

Poor feeding and lethargy
Respiratory problems such as respiratory rate > 60 /min
Apnea, grunting, cyanosis and retraction
Temperature instability for longer than 1 h : hyperthermia (axillary temperature: >37.5) or hypothermia (axillary temperature: <36.5)
Gastrointestinal problems including vomiting, abdominal distension, diarrhea and abnormal gastric residual, thermal and autonomic instability, bleeding manifestation, pathological jaundice and post exchange transfusion
Central nervous system symptoms such as convulsion, hypotonia and irritability.

Blood cultures were taken in all the clinically suspected cases. Empirical antibiotic therapy were started in all the cases. Demographic profile (age, sex and birth weight), clinical features etc. were properly recorded and tabulated in a chart.

The Blood samples were collected from peripheral vein or artery using strict aseptic precautions. Sampling site was cleansed with 70 % alcohol and 1% povidone iodine followed by alcohol. 2 ml of blood was collected in a single blood culture bottle (20 ml of brain heart infusion broth with 0.025 % sodium polyanethol sulfonate as anticoagulant) and sent for microbiological analysis.

The Samples were incubated at 37^0C for 7 days. Subcultures were done on blood agar, Mac Conkey and Chocolate medium on appearance of turbidity on days 1, 2, 3 and 7.[5] Organisms were identified according to the standard microbial procedures including gram stain, colony morphology, motility, and biochemical reactions.[6] Antimicrobial susceptibility testing was done using Kirby Bauer disc diffusion method on Mueller Hinton agar as per CLSI guidelines[7].

All the data was analyzed by graph prism 4. The mean were calculated for quantitative variables and frequency and percentages were calculated for all qualitative variables.

RESULTS

A total of 840 blood cultures were taken from clinically suspected cases of neonatal sepsis admitted to NICU over a period of 1 year. Only 141 cases (16.78 %) showed bacterial growth. Majority of neonates -118 (83.68%) were delivered vaginally and rest 23- (16.31%) by cesarean. 49 preterm, 81 term and 11 post term cases were found. Male (76) to female (65) ratio was 1.16:1. 125 cases (88.65%) were classified as early onset sepsis and rest 16 cases (11.35%) as late onset sepsis. Characteristics of neonatal sepsis cases are briefed in Table 2.

Table 2. Characteristic of Neonatal sepsis cases

	(N=141)	**EOS(N=125)**	**LOS(16)**
Gender			
Male	76	67	9
Female	65	58	7
Gestation			
Preterm	49	41	8
Term	81	75	6
Post term	11	9	2
Mode of delivery			
VD	118	108	10
LSCS	23	17	6

Organisms isolated: 84.39% gram negative (119/141) and 15.61 % gram positive (22/141) organisms were isolated. Most common isolate was *Klebsiella* pneumoniae (K. pneumoaniae) accounting for 49.65% cases (70) followed by *Escherichia. coli* (E.coli)26.95% (38), *Pseudomonas. aeruginosa* (P. aeruginosa) 7.80% (11), *Staphylococcus aureus* (S. aureus) 7.09% (10), *Coagulase negative staphylococci* (CONS) 4.96% (7) and *Enterococci* 3.55% (5).

Table 3 Distribution of organisms and Type of Neonatal sepsis

	Early onset (N=125)	Late onset (N=16)	Total
Klebsiellae pneumoniae	61(87.14)	9(12.86)	70
Escherichia coli	33(86.84)	5(13.16)	38
Pseudomonas aeruginosa	10(90.91)	1(9.09)	11
Staphylococcus aureus	10(100)		10
Coagulase negative staphylococci	7(100)		7
Enterococci	4(80)	1 (20)	5

( ) percentage

Antibiotic susceptibility patterns: Most sensitive antimicrobials against *K. pneumoniae* were meropenem (100%), amikacin (85.71%), and ciprofloxacin (81.43%). Antimicrobials sensitive against *E. coli* were meropenem (100%), ciprofloxacin (97.37%), and amikacin (94.74%). *P. aeruginosa* were highly susceptible to meropenem (100%), ceftazidime (100%), and piperacillin-tazobactum (90.91%). In conclusion, all the gram negative isolates were sensitive to amikacin and ciprofloxacin with additional susceptibility of *E.coli* , *P. aeruginosa to* piperacillin -tazobactum and *P. aeruginosa* to ceftazidime. Majority of the gram negative isolates were 100% sensitive to meropenem thus warranting use of this antibiotic as a reserve drug so as to avoid emergence of resistant strains **(Table 4, Fig.1).** Most of the gram negative isolates were resistant to the commonly used antibiotics such as ampicillin. Increased resistance of gram negative organisms was found against 3rd generation cephalosporins, thus limiting the use of these antibiotics in neonatal sepsis. High level of resistance was also reported to combination drugs like piperacillin tazobactum in *K. pneumoniae isolates*.

Gram positive isolates were resistant to commonly used antibiotics specially ampicillin but showed good sensitivity to third generation cephalosporins - cefotaxime (90%), meropenem (90%), and vancomycin (100%). *CONS* and *Enterococci* were largely resistant to 3rd generation cephalosporins but showed high level of sensitivity to ciprofloxacin (80%), meropenem and vancomycin (100%) **(Table 5, Fig.2).** No single case of *Vancomycin resistant Stap. Aureus(VRSA)/Vancomycin resistant Enterococcus* (VRE) was reported.

Table 4: Antibiotic susceptibility pattern of gram negative isolates:percentage

	Klebsiella pneumoniae	E.coli	Pseudomonas
Ampicillin	41.43	36.85	NT
Cefotaxime	68.58	84.22	90.91
Ceftazidime	58.58	86.85	100
Ciprofloxacin	81.43	97.37	81.82
Amikacin	85.71	94.74	90.90
Meropenem	100	100	100
Pipercillin-Tazobactum	67.15	92.11	90.91
Cotrimoxazole	80	94.74	NT

NT=(Not Tested)

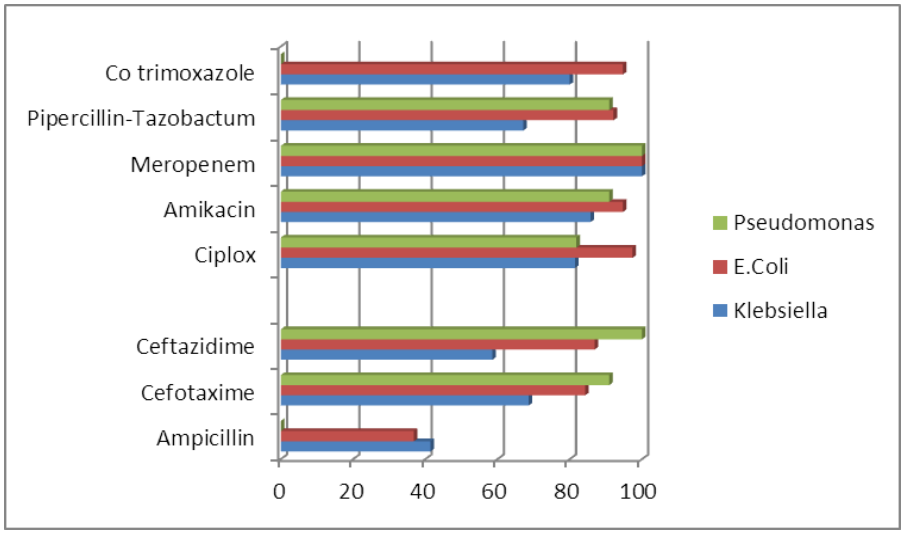

Fig. 1 – Bar Chart depicting the percentage of Antibiotic sensitivity pattern of Gram Negative isolates in percentage

Table 5. Antibiotic Sensitivity Pattern of gram positive isolates in percentage.

	Staph aureus	CONS	Enterococci
Ampicillin	20	14.28	60
Cefotaxime	90	57.15	40
PipercillinTazobactum	NT	NT	60
Ciprofloxacin	80	71.43	80
Vancomycin	100	100	100
Meropenem	90	85.72	80
Co-trimoxazole	40	28.57	80
Amikacin	100	100	60

NT=(Not Tested)

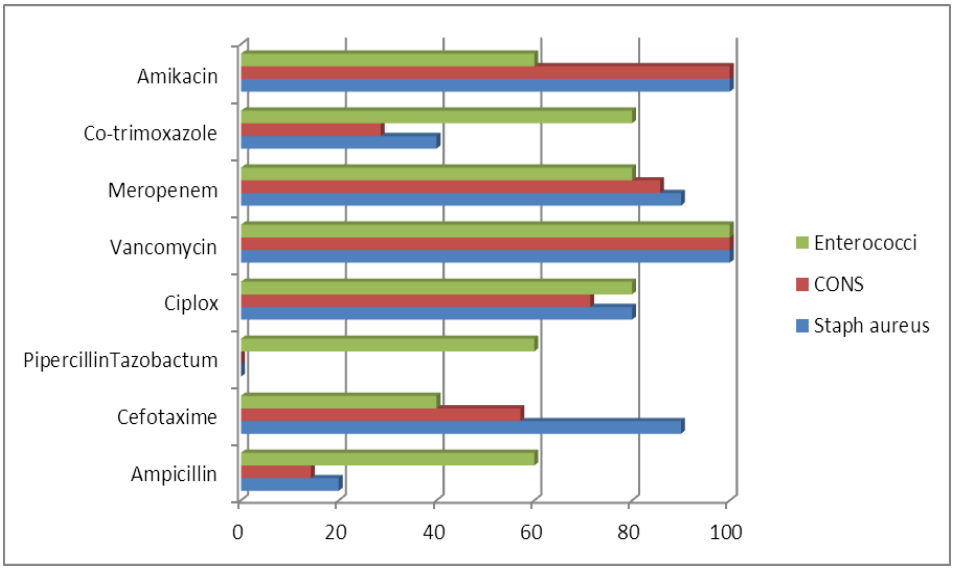

Fig.2: Bar Chart depicting the percentage of Antibiotic sensitivity pattern of Gram Positive isolates in percentage

DISCUSSION

Neonatal septicemia remains an important cause of neonatal morbidity and mortality in NICU and a major challenge for the clinicians. Careful selection of antimicrobials helps in early recovery, reduced stay and consequently decreased risk for emergence of multidrug resistant strains in NICU. Causative organisms and their ever changing antibiotic susceptibility patterns warrant for continuous monitoring and research in NICU.

In our study, positive blood cultures were found in 16.78 % of clinically suspected neonatal sepsis cases, similar to the results of previous studies by Khan et al[8] and Kenneth C Iregbu et al[9]. About 88.65% cases were of early onset sepsis and 11.35% cases were of late onset sepsis, alike to the results of studies by Jain NK[10], Kumar V[11] and Shrestha R et al[12]. Gram negative organisms were isolated in >60 % of cases, comparable to the results of the other studies[12,13]. Most common isolate among gram negative organisms was *K. pneumoniae* (49.6%) followed by *E.coli* (26.95%) and *P. aeruginosa* (7.80%), same as the results of earlier studies.[9,11,14] The common isolate among Gram positive organisms was *S. aureus* similar to the findings of Kairavi et al[16]. Enterococci were also isolated in our study, congruous to the results of few of the former studies[15]. Group B streptococcus was not isolated consistent with the study results from the developing countries[17,18]. We did not find any Vancomycin resistant S. Aureus (VRSA) resembling the results of prior studies[19].

Most of the gram negative organisms were found to be resistant against 3rd generation cephalosporins. High level of resistance was found against cefotaxime (31.42%) and ceftazidime (41.42%) suggesting cautious use of these drugs. Most of the gram negative isolates were highly sensitive to amikacin consistent with results of other studies[19].

S. aureus showed high resistance to ampicillin (80 %) similar to the results of other studies[19]. Varying levels of resistance was also found against co-trimoxazole (60%) and 3rd generation Cephalosporins (10%). All of the *S.* aureus strains were susceptible to vancomycin, thus warranting its judicious use in NICU setup to avoid emergence of resistance to this drug.

Most of the organisms (gram positive as well as gram negative) remained highly sensitive to fluoroquinolones). Fluoroquinolones can thus serve as a cheap alternative to the 3rd generation cephalosporins and carbapenems in the

NICU setup in developing countries due to their good sensitivity profile, good CSF penetration, good oral bioavailability and reasonably acceptable safety profile in infants[20].

Piperacillin-tazobactum was found to highly sensitive combination antibiotic against most of the gram negative bacteria, similar to the findings of Kairavi et al[16]. The commonly used drug combinations were Cefotaxime and Amikacin followed by Piperacillin- Tazobactum.

WHO recommends empirical treatment of neonatal sepsis with a combination of ampicillin and aminoglycoside. In the present study, high level of resistance was found against ampicillin, 3rd generation cephalosporins and combination drugs such as piperacillin-tazobactum. Thus, WHO recommended empirical combination regimen may no longer be valid in neonatal sepsis cases in our setup.

CONCLUSION

Gram negative bacteria were the most common cause of early and late onset sepsis in NICU setup with K. pneumoniae being the most common pathogen. Proper and judicious use of antibiotics along with regular monitoring in sensitivity pattern is need of modern day practice to decrease morbidity and mortality from neonatal sepsis.

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