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Original Research Article

Bacteriological profile and antimicrobial sensitivity pattern in neonatal sepsis: a study from North India

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ABSTRACT

Background: Neonatal sepsis is a leading cause of neonatal mortality and continues to be a formidable problem for neonatologists and pediatricians world over. Knowledge of microbial flora and their susceptibility will help us to decide empirical treatment for the neonatal sepsis. The objective of this study was to determine the bacteriological flora prevalent in NICU and the antimicrobial sensitivity pattern.
Methods: The blood culture reports of all the neonates with culture proven neonatal sepsis during the period July 2010 to September 2013 were reviewed retrospectively. A retrospective review in tertiary care teaching medical college. The data was entered in Excel sheets and percentages of various outcomes were calculated.
Results: A total of 28,927 babies were born during the study period and 336 among them had positive blood culture. The incidence of neonatal sepsis was 11.62 per 1,000 live births. Three hundred fifty- six microbes were isolated, out of which 50% presented as early onset sepsis and remaining as late onset sepsis. *Pseudomonas aeruginosa* was the most common organism encountered in both early (43.82%) and late onset sepsis (51.35%). Gram negative bacilli were sensitive to carbapenems (92%) followed by piperacillin-tazobactam (90%) whereas linezolid (90%) was most sensitive antimicrobial for gram positive cocci.
Conclusions: *Pseudomonas* was most commonly isolated in both early and late onset sepsis. Gram negative bacilli were most sensitive to piperacillin-tazobactam and the carbapenems whereas linezolid and vancomycin were most effective against the gram-positive cocci. Resistance to third generation cephalosporins was rampant. Continuous surveillance for microbial flora, their antibiotic susceptibility, rational use of antibiotics and the strategy of antibiotic cycling may be of help to curtail emerging antimicrobial resistance.

Keywords: Antibiotic sensitivity, Microbial flora, Neonatal sepsis, Resistance

INTRODUCTION

Sepsis is one of the leading causes of neonatal mortality accounting for 18.6% neonatal deaths.[1] According to the data from National Neonatal Perinatal Database 2002-03, incidence of neonatal sepsis was 30 per 1000 live births.[1] Multidrug antibiotic resistance is an emerging problem in NICU's particularly in developing countries. The choice for the empirical therapy should be based upon recent flora and their sensitivity pattern. Knowledge of microbial flora and their antimicrobial susceptibility would help decide the best empirical treatment plan for neonatal sepsis. Antibiotics should be re-viewed once the results of the cultures and sensitivity are available.

METHODS

This retrospective study was conducted in Neonatal intensive care unit of a tertiary care teaching medical college from July 2010 to September 2013. Details of obstetric history, maternal risk factors, and physical examination, all were recorded.

Sepsis screen including CRP, I/T ratio, micro ESR, ANC, TLC were done for all neonates with clinical suspicion of sepsis. Blood cultures from neonates were collected as per standard guidelines before starting empirical antibiotics.[2] The local site was cleansed with 70% alcohol and povidone iodine (1%) followed by 70% alcohol again. Under stringent aseptic conditions, 1 ml of blood was collected and inoculated into 10 ml brain heart infusion broth and incubated at 37°C for 24 hours. Subcultures were carried out on blood agar and MacConkey agar and incubated aerobically overnight at 37°C. Bacterial isolates were identified and antibiotic susceptibility test was performed using modified Kirbey Bauer disc diffusion method.

RESULTS

A total of 28,927 neonates were born during this period and 336 among them had culture proven sepsis accounting for the incidence of neonatal sepsis of 11.62 per 1,000 live births. A total of 356 microbes were isolated with half of them (178) accounting for early onset sepsis. Gram negative organisms were isolated in 81.18% cases whereas 18.82% cases were with gram positive organisms. *Pseudomonas aeruginosa* was the most common organism isolated in both early (43.82%) (Figure 1) and late onset sepsis (51.35%) (Figure 2). *Staphylococcus aureus* was the most common gram positive organism in both early (7.3%) and late onset sepsis (17.41%).

Table 1: Antibiotic sensitivity pattern of gram positive microorganisms prevalent in NICU. ND = not done.

Antimicrobials	*Staphylococcus aureus* (44)	*Coagulase negative staphylococcus* (15)	*Enterococcus* (8)
Erythromycin, n (%)	15 (34%)	9 (60%)	2 (25%)
Penicillin, n (%)	7 (16%)	2 (13%)	1 (13%)
Cefoxitin, n (%)	11 (25%)	2 (13%)	0 (0%)
Co-trimoxazole, n (%)	21 (48%)	9 (60%)	ND
Linezolid, n (%)	40 (91%)	13 (87%)	7 (88%)
Doxycycline, n (%)	18 (41%)	6 (40%)	ND
Clindamycin, n (%)	32 (73%)	3 (20%)	ND
Vancomycin, n (%)	36 (82%)	12 (80%)	4 (50%)
Amoxyclav, n (%)	13 (30%)	4 (27%)	3 (37%)
Piperacillin- tazobactam, n (%)	ND	ND	3 (38%)
Teicoplanin, n (%)	4 (100%)	ND	ND
Quinopristin, n (%)	4 (100%)	ND	1 (50%)

Carbapenems (92%) and piperacillin-tazobactam (90%) were the most sensitive antimicrobials against gram negative organisms. Among aminoglycosides, gentamycin and amikacin revealed 62% and 67% sensitivity for gram negative organisms, respectively. Sensitivity pattern of amikacin was more favourable for *E. coli* (70%) and *Klebsiella* (73%) when compared to *Pseudomonas* (66%) and *Acinetobacter* (67%). Resistance to cephalosporins, ciprofloxacin and aztreonam was rampant although ciprofloxacin revealed increased sensitivity to *E. coli* (75%) and *Klebsiella* (73%). Colistin sensitivity was done only when the organisms were resistant to other antimicrobials. It was found sensitive in 10 out of 11 cultures of *Pseudomonas* and in all 7 cases of *Acinetobacter*.

Most of the gram-positive organisms were found to be sensitive to linezolid (90%) and vancomycin (78%). Four out of eight *enterococci* (50%) were resistant to vancomycin. Resistance against amoxyclav (70%) and pencillin (85%) was seen frequently. Teicoplanin and quinopristin were sensitive in all 4 cases of *Staphylococcus aureus* where it was done.

Table 2: Antibiogram of *Staphylococcus aureus* in early and late onset sepsis.

Antimicrobials	Early onset sepsis (13)	Late onset sepsis (31)
Erythromycin, n (%)	6 (46%)	7 (23%)
Penicillin, n (%)	4 (31%)	3 (10%)
Cefoxitin, n (%)	6 (46%)	5 (16%)
Co-trimoxazole, n (%)	7 (54%)	14 (45%)
Linezolid, n (%)	13 (100%)	27 (87%)
Doxycycline, n (%)	7 (54%)	11 (35%)
Clindamycin, n (%)	11 (85%)	21 (68%)
Vancomycin, n (%)	12 (92%)	24 (77%)
Amoxyclav, n (%)	8 (62%)	5 (16%)
Teicoplanin, n (%)	ND	4 (100%)
Quinopristin, n (%)	ND	4 (100%)

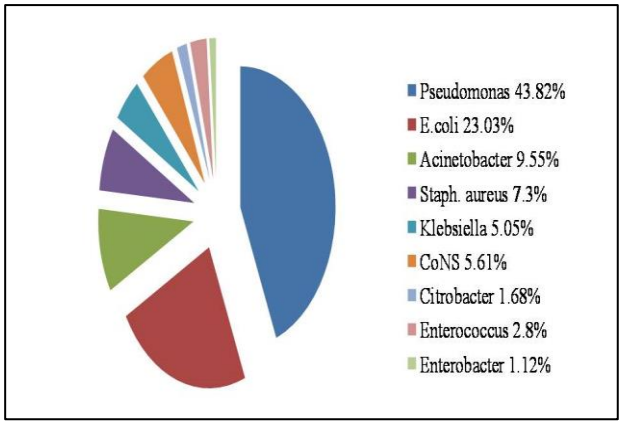

Figure 1: Profile of microorganisms seen in early onset sepsis.

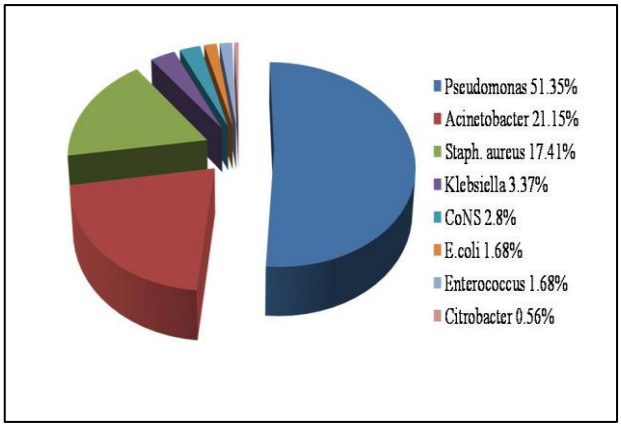

Figure 2: Profile of microorganisms isolated in late onset sepsis.

Table 3: Antibiotic sensitivity pattern of gram negative microorganisms prevalent in NICU. ND = not done.

Antimicrobials	*E. coli* (44)	*Klebsiella* (15)	*Pseudomonas* (169)	*Enterobacter* (2)	*Citrobacter* (4)	*Acinetobacter* (55)
Ceftazidime,	23 (52%)	5 (33%)	92 (54%)	1 (50%)	1 (25%)	30 (55%)
Ceftizoxime	21 (47%)	4 (27%)	96 (57%)	1 (50%)	1 (25%)	28 (51%)
Gentamycin	28 (64%)	10 (67%)	103 (61%)	1 (50%)	2 (50%)	35 (63%)
Amikacin	31 (70%)	11 (73%)	112 (66%)	1 (50%)	3 (75%)	37 (67%)
Aztreonam	27 (61%)	11 (73%)	81 (48%)	ND	1 (25%)	23 (42%)
Cefepime	22 (50%)	4 (27%)	76 (45%)	1 (50%)	1 (25%)	18 (33%)
Ciprofloxacin	33 (75%)	11 (73%)	79 (47%)	2 (100%)	1 (25%)	10 (18%)
Carbapenem	40 (91%)	13 (87%)	162 (96%)	2 (100%)	4 (100%)	46 (84%)
Piperacillin-tazobactam	41 (93%)	14 (93)	158 (93%)	2 (100%)	3 (75%)	41 (75%)
Doxycycline	8 (18%)	3 (20%)	32 (19%)	0 (0%)	0 (0%)	8 (15%)
Amoxyclav	18 (41%)	2 (13%)	22 (13%)	0 (0%)	1 (25%)	18 (33%)
Cefuroxime	2 (4%)	1 (6%)	4 (2%)	0 (0%)	0 (0%)	4 (8%)
Cotrimoxazole	37 (84%)	2 (13%)	27 (16%)	1 (50%)	0 (0%)	11 (20%)
Colistin	ND	ND	10 (91%)	ND	ND	7 (100%)

Table 4: Antibiogram of pseudomonas aeruginosa in early and late onset sepsis.

Antimicrobials	Early onset sepsis (78)	Late onset sepsis (91)
Ceftazidime,	49 (63%)	43 (47%)
Ceftizoxime	48 (62%)	48 (53%)
Gentamycin	57 (73%)	46 (51%)
Amikacin	62 (79%)	50 (55%)
Aztreonam	46 (59%)	35 (38%)
Cefepime	42 (54%)	34 (37%)
Ciprofloxacin	42 (54%)	37 (41%)
Carbapenem	78 (100%)	84 (92%)
Piperacillin-tazobactam	77 (99%)	81 (89%)
Doxycycline	30 (33%)	2 (2%)
Amoxyclav	20 (26%)	2 (2%)
Cefuroxime	4 (5%)	0 (0%)
Cotrimoxazole	17 (22%)	10 (11%)
Colistin	ND	10 (91%)

DISCUSSION

Neonatal infection is a major problem in developing countries including India. Early diagnosis and prompt institution of empirical antimicrobials pending culture sensitivity reports may be life-saving. The spectrum of organisms that cause neonatal sepsis changes over time and also varies from region to region. The uncertainty regarding the clinical approach to treatment of neonatal sepsis can be minimized by periodic surveillance for bacteriological flora and susceptibility pattern so that appropriate choice of antimicrobials for empirical therapy can be outlined and re-evaluated in timely manner.

Gram negative bacteria (81.2%) were the most common organisms isolated in the present study. Similar observations have been made by others; Bhat et al (90.8%) and Shrestha et al (60.64%).[3,4] The low incidence of gram positive sepsis in present study can be attributed to low infection rates with CoNS which is usually associated with central lines and rarity of Group B *Streptococcus* infection in India.[5]

Among the early onset neonatal sepsis, *Pseudomonas aeruginosa* (43.82%) was the commonest organism in our study. Similar results were also seen in another study (33.2%) from south India.[3] Whereas, many studies reported *Klebsiella* to be the most common organism.[4,6-9] Some authors had found *Staphylococcus aureus* as the most common organism.[10,11] Intrapartum antibiotic prophylaxis has also led to a substantial change in the bacterial flora responsible for early onset neonatal sepsis.

Pseudomonas (51.35%) and *Acinetobacter* (21.15%) were the most common organisms attributing to late onset sepsis in the present study as compared to other studies which found *Klebsiella* and *Acinetobacter* as the leading organisms.[4,8,10]

Although the gram-negative organisms were most common in both early as well as late onset sepsis, but the incidence of gram positive sepsis was higher in late onset sepsis (21.89%) when compared to early onset sepsis (15.7%). *Staphylococcus aureus* was the most common gram positive microbe in both early (7.3%) and late onset sepsis (17.41%). A low rate of *enterococci* infection in present study (2.24%) is similar to the observations of Bhat et al (2.2%).[3]

The association of two different organisms did not occur in any particular pattern in polymicrobial sepsis. A neonate already infected with one microbe may have acquired the second one from the hospital environment, or both the bacteria could be hospital acquired. Most previous studies failed to document polymicrobial sepsis, either because of unawareness of its significance or disregard for the second organism in an already positive culture.[12] Incidence of polymicrobial sepsis was 5.95% in our study. While it was reported to be 5.2% by Shrestha, 6.8% by Kumhar et al and 3.92% by Viswanathan.[4,12.13] Nepal et al did not find any case of polymicrobial sepsis.[10] There is a need to correlate the occurrence of polymicrobial sepsis with clinical outcome in neonatal septicemia.

Antibiotic resistance is a widespread problem. In the present study too, a large number of Gram positive and Gram negative bacteria exhibited variable resistance to many of the clinically useful antibiotics. The greater prevalence of resistance to commonly used antibiotics has also been reported in recent studies.[11,14]

Gram negative isolates were most frequently susceptible to carbapenems and piperacillin-tazobactam followed by aminoglycosides in the index study. Although, studies in the past have shown favorable sensitivity pattern of 3rd generation cephalosporins but our study revealed higher resistance of gram negative isolates to 3rd generation cephalosporins varying from 47% to as high as 96%. Third generation cephalosporin resistance is now rampant and has been widely reported by recent studies.[3,4,7,8,10,15,16,17] Ceftizoxime revealed better sensitivity pattern against *Pseudomonas aeruginosa* (57%) in index study when compared to a recent study (25%).[18] *Pseudomonas* was sensitive to ciprofloxacin in only 47% isolates in our study as against reported sensitivity of 75% by Kumhar.[12] Recent studies reported increased resistance of *Pseudomonas* to ciprofloxacin varying from 10% to 40.8%.[13,14]

High resistance of gram negative isolates to piperacillin-tazobactam has been reported recently by Bhat et al (76.3%) and Shrestha et al (87.5%).[3,4] *Pseudomonas* and *Acinetobacter* were the most common isolated flora in the index study and they were mostly sensitive to piperacillin-tazobactam and amikacin. So, the first line empirical therapy comprising of piperacillin-tazobactam and amikacin is justified at our institute.

The analysis showed that, among gram-positive *isolates*, maximum numbers were sensitive to linezolid (90%) followed by vancomycin (78%) and Clindamycin (59%). However, all gram-positive organisms were less sensitive to erythromycin (39%), amoxyclav (30%) and rarely sensitive to penicillin (15%). Favorable susceptibility pattern of vancomycin and linezolid has been reported in recent studies.[3,4,8,12] Index study reported 50% (4/8) incidence of vancomycin resistant enterococci in contrast to 18.2% incidence reported by Kumhar et al.[12] One of vancomycin resistant enterococci was resistant to linezolid also but was found to be sensitive to quinopristin.

Carbapenems, colistin, linezolid, teicoplanin and quinopristin, although revealed maximum sensitivity but these drugs should not be used indiscriminately and be kept as reserve drugs. Development of resistance to these drugs may leave us with no option in life threatening infections by resistant organisms.

CONCLUSION

Pseudomonas was the most common organism isolated in both early and late onset sepsis. Piperacillin-tazobactam and the carbapenems were the most effective antibiotics for the gram-negative bacilli whereas linezolid and vancomycin were the most effective against the gram-positive cocci. Resistance to a list of commonly used antimicrobials including third generation cephalosporins is rampant. Continuous surveillance for microbial flora, their antibiotic susceptibility, rational use of antibiotics and the strategy of antibiotic cycling may be of help to curtail emerging antimicrobial resistance.

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