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Original Article

Bacterial Profile and Antibiotic Sensitivity Pattern of Neonatal Septicemia In NICU at a Tertiary care Set up

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Abstract
Background: *Neonatal septicemia signifies a generalized bacterial infection documented by a positive blood culture and is one of the leading causes of neonatal mortality and morbidity in India.*
Aim: *To isolate and identify the bacterial etiological agents responsible for neonatal sepsis and to determine their susceptibility pattern in a tertiary care hospital.*
Materials and Methods: *108 blood culture positive neonatal cases admitted from 1st December 2016 to 1st December 2017 were included in the study.*
Results: *Out of a total of 108 blood culture positive cases, the majority were Gm negative bacteria comprising 75 (69.44%), Gm positive bacteria comprised 31(28.7%) and 2(1.85%) were positive for fungal organisms (Candida other than C.albicans). Among the Gm negative organisms, most common were Enterobacter spp. comprising 44(40.74%) [Enterobacter cloacae forming 23(21.30%) and Enterobacter aerogenes forming 21(19.44%)], followed by Acinatobacter 13(12.04%), Klebsiella spp. 7(6.48%), Pseudomonas aeruginosa 6(5.56%), E.coli 2(1.85%), Burkholderia capacia 2(1.85%) and Citrobacter 1(0.93%). Among Gm positive organisms, most common was Coagulase negative Staphylococcus forming 24(22.22%) followed by Enterococcus 4(3.7%), Streptococci 2(1.85%) and Coagulase positive Staphylococcus 1(0.93%).*
Conclusion: *Gm negative organisms are the leading cause of neonatal sepsis in our study with most being resistant to multiple antibiotics. Enterobacter septicemia is a cause of concern with its rising incidence. A regular antibiotic surveillance is a necessity in every hospital to reduce antibiotic resistance.*
Keywords: *Neonatal septicemia, susceptibility, surveillance, resistance.*

Introduction

Neonatal Septicemia defined as a systemic bacterial infection in neonates[1] proved by a positive blood culture is an important cause of neonatal morbidity and mortality in developing countries[2,3,4,5]. The gold standard for the diagnosis of neonatal septicemia is the isolation of the bacterial agent from a blood culture. The micro-organism isolated with its antibiotic susceptibility varies from place to place and over time in the same place[1-6].

Neonatal septicemia is a life threatening emergency and delays in diagnosis and treatment with appropriate antibiotics may have a devastating consequence. Also true is the antibiotic drug resistance of micro-organisms which is a rapidly emerging and potentially dangerous problem in developing nations. There is thus a need of periodic bacterial surveillance to identify the common pathogens of the disease as well as their antibiotic susceptibility profile in a particular area as the organisms vary across geographical boundaries and with the time of onset of the illness. This also helps to formulate an empirical choice of antibiotics based on the epidemiology of causative agents and antibiotic sensitivity pattern in a locality which can be started before the results of the blood culture arrive.

The present study was designed to evaluate the common pathogens associated with neonatal septicemia seen in the NICU in our hospital and their antibiotic sensitivity pattern. The results of the study will help in guiding therapy, influence the infection control practices and rational antibiotic use.

Materials and Methods

The present study was conducted at the NICU, Mahila Chikitsalaya, SMS Medical College and Hospitals, Jaipur, Rajasthan. 108 blood culture positive cases of newborns admitted from 1stDecember 2016 to 1st December 2017 were included in the study. Blood for culture was taken under strict aseptic conditions. Standard procedures were followed for sample collection, isolate identification and studying the antibiotic sensitivity pattern[7,8,9]. All the blood samples were collected on D1 of life. A detailed information of all the cases was recorded including antenatal, natal and postnatal history with the maternal and neonatal risk factors associated. It was a descriptive observational study.

Results

Table 1 Various isolates obtained from neonatal septicemia patients.

S.NO	Organism Isolated	Number (Percentage)
1.	Acinatobacter	13(12.04%)
2.	Burkholderia Cepecia	2(1.85%)
3.	Candida other than Candida Albicans	2(1.85%)
4.	Citrobacter	1(0.93%)
5.	**Coagulase negative Staphylococcus**	**24(22.22%)**
6.	Coagulase Positive Staphylococcus aureus	1(0.93%)
7.	E Coli	2(1.85%)
8.	**Enterobacter Aerogenes**	**21(19.44%)**
9.	**Enterobacter Cloacae**	**23(21.30%)**
10.	Enterococcus	4(3.70%)
11.	Klebsiella	7(6.48%)
12.	Pseudomonas Aeruginosa	6(5.56%)
13.	Streptococci	2(1.85%)
	Grand Total	**108**

Table 2 Antibiotic sensitivity and antibiotic resistance of the most commonly isolated bacteria from positive cultures in neonates.

Microorganism	Number/proportion of resistant isolates	Number/proportion of sensitive isolates
Acinatobacter (n= 13)		
Piperacillin + Tazobactem	2 (15.38%)	11(84.62%)
Cefotaxim	8 (61.54%)	5 (38.46%)
Ceftriaxone	7 (53.85%)	6 (46.15%)
Cefipime	8 (61.54%)	5 (38.46%)
Ceftazidime	8 (61.54%)	5 (38.46%)
Cefoparazone + sulbactem	2 (15.38%)	11 (84.62%)
Ofloxacin	5 (38.46%)	8 (61.54%)
Ciprofloxacin	10 (76.92%)	3 (23.08%)
Amikacin	4 (30.77%)	9 (69.23%)
Meropenem	4 (30.77%)	9 (69.23%)
Colistin	0 (0%)	13 (100%)
Polymixin B	0 (0%)	13 (100%)
Fosfomycin	0 (0%)	13 (100%)
Burkholderia cepecia (n=2)		
Piperacillin + Tazobactem	0 (0%)	2 (100%)
Ceftazidime	2 (100%)	0 (0%)
Cefoparazone + sulbactem	1 (50%)	1 (50%)
Tobramycin	1 (50%)	1 (50%)
Gentamycin	1 (50%)	1 (50%)
Imipenem	2 (100%)	0 (0%)
Colistin	2 (100%)	0 (0%)
Polymyxin B	2 (100%)	0 (0%)
Carbenicillin	1 (50%)	1 (50%)
Aztreonam	2 (100%)	0 (0%)
Citrobacter (n=1)		
Ofloxacin	0 (0%)	1 (100%)
Amikacin	0 (0%)	1 (100%)
Meropenem	0 (0%)	1 (100%)
Imipenem	0 (0%)	1 (100%)
Polymyxin B	0 (0%)	1 (100%)
Coagulase Positive Staph aureus (n=1)		
Vancomycin	0 (0%)	1 (100%)
Linezolid	0 (0%)	1 (100%)
Meropenem	0 (0%)	1 (100%)
Coagulase negative staph aureus (n=24)		
Ampicillin	7 (29.17%)	17 (70.83%)
Amox-clav	9 (37.5%)	15 (62.5%)
Piperacillin + Tazobactem	6 (25%)	18 (75%)
Cefotaxim	8 (33.33%)	16 (66.67%)
Ceftazidime	9 (37.5%)	15 (62.5%)
Cefoxitin	15 (62.5%)	9 (37.5%)
Cefoparazone + sulbactem	6 (25%)	18 (75%)
Azithromycin	16 (66.67%)	8 (33.33%)
Vancomycin	0 (0%)	24 (100%)
Linezolid	0 (0%)	24 (100%)
Teicoplanin	0 (0%)	24 (100%)
Levofloxacin	10 (41.67%)	14 (58.33%)

Ciprofloxacin	13 (54.17%)	11 (45.83%)
Imipenem	2 (8.33%)	22 (91.67%)
Fosfomycin	0 (0%)	24 (100%)
Cefoxitin	10 (41.67%)	14 (58.33%)
Ticarcillin clavulonic acid	12 (50%)	12 (50%)
Cotrimox/IMP	3 (12.5%)	21 (87.5%)
E coli (n=2)		
Piperacillin + Tazobactem	1 (50%)	1 (50%)
Cefotaxim	1 (50%)	1 (50%)
Ceftriaxone	0 (0%)	2 (100%)
Cefipime	1 (50%)	1 (50%)
Ceftazidime	1 (50%)	1 (50%)
Cefoparazone + sulbactem	0 (0%)	2 (100%)
Ofloxacin	2 (100%)	0 (0%)
Amikacin	1 (50%)	1 (50%)
Meropenem	0 (0%)	2 (100%)
Colistin	0 (0%)	2 (100%)
Polymyxin B	0 (0%)	2 (100%)
Fosfomycin	0 (0%)	2 (100%)
Enterobacter aerogenes (n=21)		
Piperacillin + Tazobactem	6 (28.57%)	15 (71.43%)
Cefotaxim	14 (66.67%)	7 (33.33%)
Ceftriaxone	12 (57.14%)	9 (42.86%)
Cefipime	12 (57.14%)	9 (42.86%)
Ceftazidime	18 (85.71%)	3 (14.29%)
Cefoparazone + sulbactem	8 (38.10%)	13 (61.90%)
Ofloxacin	5 (23.81%)	16 (76.19%)
Ciprofloxacin	16 (76.19%)	5 (23.81%)
Amikacin	7 (33.33%)	14 (66.67%)
Meropenem	3 (14.29%)	18 (85.71%)
Colistin	2 (9.52%)	19 (90.48%)
Polymyxin B	2 (9.52%)	19 (90.48%)
Fosfomycin	3 (14.29%)	18 (85.71%)
Microorganism	Number/proportion of resistant isolates	Number/proportion of sensitive isolates
Enterobacter Cloacae (n=23)		
Piperacillin + Tazobactem	20 (86.96%)	3 (13.04%)
Cefotaxim	20 (86.96%)	3 (13.04%)
Ceftriaxone	21 (91.30%)	2 (8.70%)
Cefipime	23 (100%)	0 (0%)
Cefoparazone + sulbactem	21 (91.30%)	2 (8.70%)
Ofloxacin	3 (13.04%)	20 (86.96%)
Amikacin	17 (73.91%)	6 (26.09%)
Meropenem	10 (43.48%)	13 (56.52%)
Colistin	0 (0%)	23 (100%)
Polymyxin B	0 (0%)	23 (100%)
Fosfomycin	0 (0%)	23 (100%)
Enterococcus (n=4)		
Ampicillin	2 (50%)	2 (50%)
Amox-clav	2 (50%)	2 (50%)
Piperacillin + Tazobactem	3 (75%)	1 (25%)
Cefotaxim	4 (100%)	0 (0%)
Ceftazidime	4 (100%)	0 (0%)
cefoxitin	4 (100%)	0 (0%)
Cefoparazone + sulbactem	2 (50%)	2 (50%)
Azithromycin	3 (75%)	1 (25%)
Vancomycin	3 (75%)	1 (25%)
Linezolid	0 (0%)	4 (100%)
Meropenem	2 (50%)	2 (50%)

Imipenem	2 (50%)	2 (50%)
Fosfomycin	0 (0%)	4 (100%)
Cefoxitin	4 (100%)	0 (0%)
Ticarcillin clavulonic acid	4 (100%)	0 (0%)
Cotrimox/IMP	4 (100%)	0 (0%)
Klebsiella (n=7)		
Piperacillin + Tazobactem	2 (28.57%)	5 (71.43)
Cefotaxim	7 (100%)	0 (0%)
Ceftriaxone	7 (100%)	0 (0%)
Cefipime	7 (100%)	0 (0%)
Ceftazidime	7 (100%)	0 (0%)
Cefoparazone + sulbactem	7 (100%)	0 (0%)
Ofloxacin	0 (0%)	7 (100%)
Amikacin	4 (57.14%)	3 (42.86%)
Meropenem	0 (0%)	7 (100%)
Polymyxin B	0 (0%)	7 (100%)
Fosfomycin	0 (0%)	7 (100%)
Pseudomonas Aerugenosa (n=6)		
Piperacillin + Tazobactem		
Ceftazidime	2 (33.33%)	4 (66.67%)
Cefoperazone	0 (0%)	6 (100%)
Cefoparazone + sulbactem	2 (33.33%)	4 (66.67%)
Tobramycin	0 (0%)	6 (100%)
Gentamycin	0 (0%)	6 (100%)
Imipenem	0 (0%)	6 (100%)
Colistin	3 (50%)	3 (50%)
Polymyxin B	0 (0%)	6 (100%)
Fosfomycin	0 (0%)	6 (100%)
Carbenicillin	3 (50%)	3 (50%)
Aztreonam	1 (16.67%)	5 (83.33%)
	2 (33.33%)	4 (66.67%)
Streptococci (n=2)		
Ampicillin	0 (0%)	2 (100%)
Amox-clav	0 (0%)	2 (100%)
Piperacillin + Tazobactem	0 (0%)	2 (100%)
Cefotaxim	1 (50%)	1 (50%)
Ceftazidime	2 (100%)	0 (0%)
cefoxitin	2 (100%)	0 (0%)
Cefoparazone + sulbactem	2 (100%)	0 (0%)
Azithromycin	1 (50%)	1 (50%)
Vancomycin	0 (0%)	2 (100%)
Linezolid	0 (0%)	2 (100%)
Teicoplanin	0 (0%)	2 (100%)
Levofloxacin	2 (100%)	0 (0%)
Ciprofloxacin	0 (0%)	2 (100%)
Imipenem	0 (0%)	2 (100%)
Fosfomycin	0 (0%)	2 (100%)
Cefoxitin	2 (100%)	0 (0%)
Ticarcillin clavulonic acid	2 (100%)	0 (0%)
Cotrimox/IMP	2 (100%)	0 (0%)

Discussion

Neonatal septicemia remains an important public health problem in developing countries despite considerable progress in hygiene, introduction of new anti-microbial agents and advanced measures for early diagnosis and treatment. The correct and timely identification of infectious agents and their antibiotic sensitivity patterns are essential to guide the clinicians regarding both empirical and definitive treatment. The most common organisms associated with neonatal sepsis vary with time of infections and geographical location. Therefore

information on bacteriological profile of neonatal sepsis and effective antimicrobials for its treatment are important to combat neonatal morbidity and mortality.

In our study, out of a total of 108 blood culture positive cases, Gm negative bacteria comprised 75 (69.44%), Gm positive bacteria comprised 31(28.7%) and 2(1.85%) were positive for fungal organisms (Candida other than C.albicans). Among the Gm negative organisms, most common were Enterobacter spp. comprising 44(40.74%) [Enterobacter cloacae forming 23(21.30%) and Enterobacter aerogenes forming 21(19.44%)], followed by Acinatobacter 13(12.04%), Klebsiella spp. 7(6.48%), Pseudomonas aeruginosa 6(5.56%), E.coli 2(1.85%), Burkholderia capacia 2(1.85%) and Citrobacter 1(0.93%). Among Gm positive organisms, most common was Coagulase negative Staphylococcus forming 24(22.22%) followed by Enterococcus 4(3.7%), Streptococci 2(1.85%) and Coagulase positive Staphylococcus 1(0.93%). Fungal infection comprised 2(1.85%) cases.

The study conducted by Mahapatra et al showed similar results – Gm negative bacilli isolated in maximum number of cases (88.45%) whereas Gm positive bacteria in 11.6% cases. E.cloacae (39.5%) was maximally isolated among the pathogenic bacteria followed by K.pneumoniae (23.2%), E.coli (11.6%) and others like Acinetobacter spp.(6.9%), Citrobacter (4.6%) and P.mirabilis(2.3%). All the Gm negative bacilli isolates showed 100% susceptibility to amikacin, whereas 85% of E.cloacae isolates were sensitive to the same.

Similar results were seen in the study conducted by Kaistha N which showed Gm negative bacilli preponderance in 80.4% cases (most common being Klebsiella 28.3%) and Gm positive cocci in 20.6% cases[10]. The study by Ullah O had Gm negative organisms as 78.6% (most common being E coli 52.8%) and Gm positive organisms as 21.4% (most common being Staphylococcus aureus 19.5%)[11]. Study by Kumhar GD showed Gm negative bacilli sepsis in 60% cases (most common Klebsiella 33.8%) and Gm positive sepsis in 40% cases (most common Staphylococcus aureus 24.4%)[12]. Agnihotri et al in their study reported Gm negative sepsis in 58.5% and Gm positive sepsis in 41.5% cases[13]. The study by P Jyothi showed Gm negative bacilli comprising 55.7% (most common Klebsiella) and Gm positive cocci making 44.3% (most common Coagulase negative Staphylococcus)[14]. Waheed in his study had a preponderance of sepsis by Gm negative bacilli making 47.8% cases (most common being E.coli)[15].

In our study, in general among Gm negative bacilli (Enterobacter spp, Acinatobacter, Klebsiella, Citrobacter), maximum sensitivity was seen with piperacillin- tazobactum, ofloxacin, meropenem, colistin, polymyxin b, fosfomycin and resistance with third generation cephalosporins and ciprofloxacin.As for aminoglycosides, those sensitive to amikacin were Enterobacter aerogenes, Acinatobacter and Citrobacter. Resistance to amikacin was seen with Enterobacter cloacae (73.9%). E coli showed samesensitivity as in above but it had resistance to ofloxacin in 100% cases. Pseudomonas showed sensitivity to Piperacillin-tazobactum, aminoglycosides, carbenicillin, polymyxin b, colistin, third generation cephalosporins (ceftazidime, cefoperazone and cefoperazone-sulbactum) and resistance to imipenem and fosfomycin.

Among Gm positive organisms (coagulase positive and negative Staphylococcus, Streptococci) sensitivity was seen to vancomycin, linezolid and teicoplanin. Resistance was seen with third generation cephalosporins (Enterococci and Streptococci). Enterococci showed 100% sensitivity to linezolid and fosfomycin; resistance was also seen with vancomycin and azithromycin. Coagulase negative staphylococcus showed resistance to azithromycin and ciprofloxacin.

Kaistha N in their study found Gm negative bacteria showing sensitivity to imipenem, amikacin and cefoperazone-sulbactum ; resistance to third generation cephalosporins. Gm positive

bacteria were sensitive to vancomycin[10]. In the study by Ullah O the Gm negative bacteria showed high sensitivity to imipenem and fluoroquinolones; Gm positive cocci had sensitivity to imipenem and fluoroquinolones[11]. In study by Kumhar GD, Gm positive isolates were sensitive to vancomycin; Gm negative isolates were sensitive to ciprofloxacin and amikacin[12]. In the study by Agnihotri et al amikacin was found to be the most effective drug against Gm negative bacteria. For staphylococcus aureus and pseudomonas netilmicin and ciprofloxacin were the most effective drugs[13]. Waheed in their study found a high resistance to third generation cephalosporins, amikacin and ciprofloxacin for both Gm positive and Gm negative isolates[14].P Jyothi in their study found best overall sensitivity among Gm negative isolates to imipenem followed by amikacin and netilmicin ; Gm positive isolates had sensitivity to linezolid, tetracycline, piperacillin- tazobactum, erythromycin and ciprofloxacin[15]. In the study by Poonam Marwah the Gm negative isolates showed high sensitivity to imipenem, aminoglycosides and polymyxin b with a low sensitivity to ciplrofloxacin and ampicillin; Staphylococcus aureus isolates showed good sensitivity to vancomycin, linezolid and aminoglycosides[16].

Thus overall, sepsis in newborns is a life-threatening emergency and its rapid treatment with antibiotics is necessary. The correct and timely identification of infectious agents and their antibiotic sensitivity patterns are essential to guide the clinicians regarding both empirical and definitive treatment.

Conclusion

Our study shows that Gm negative organisms are the leading cause of septicemia in admitted newborns with most of them being resistant to multiple antibiotics. Therefore periodic bacterial surveillance is necessary in each unit as the organisms vary across geographical boundaries and with the time of onset of illness. Antibiotics should be used depending on the antibiotic sensitivity pattern of the isolates. Also needed are stress on effective hand washing, rational use of antibiotics and training of healthcare personnel so that we can decrease the indiscriminate use of antibiotics, prevent the development of resistance to common antibiotics and thus be successful in controlling the menace of neonatal sepsis.

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