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Antibiotic Sensitivity Pattern in Neonatal Septicemia at Tertiary Care Hospital

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Abstract

Background: There is real shortage of national data on antimicrobial resistance rates in Indian neonates. A descriptive review was conducted to determine the patterns of antimicrobial resistance in isolates of blood stream infection among neonates in Jamnagar, Gujarat, India. **Materials and Methods:** The study was carried out in a tertiary care hospital from a period of March 1, 2014, to August 31, 2015. This is a non-randomized, prospective study in which 109 cases of suspected neonatal septicemia on the basis of antenatal high-risk factors and signs and symptoms of sepsis during this period were studied. **Results:** A total number of 109 neonates with clinically suspected neonatal septicemia were studied. Sixty-nine (63.3%) cases out of them were blood culture positive. Out of 69 positive cases, in one sample, two organisms were isolated. Hence, the total number of organisms was 70. Out of these 70 organisms, 44 were Gram-positive cocci, 23 were Gram-negative bacilli, and three were *Candida* spp. Gram-positive cocci were more sensitive to linezolid, vancomycin, and clindamycin whereas Gram-negative bacilli were more sensitive to ampicillin, ofloxacin, and amikacin. Antimicrobial sensitivity of fungal isolates was not done as the antifungal discs were not available. **Conclusion:** The Gram-positive organisms are the frequent cause of neonatal septicemia so when neonatal septicemia is suspected, drugs of choice for Gram-positive organisms are linezolid, vancomycin, and clindamycin and for Gram-negative organism drugs of choice are ampicillin, ofloxacin, and amikacin.

Keywords: Antibiotic sensitivity pattern, Disc diffusion method, Gram-negative bacteria, Gram-positive bacteria, Neonatal septicemia

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Introduction

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first 28 days of life. Septicemia in neonates is generalized bacterial infection detected by positive blood culture in the 1st month of life.[1] Neonatal septicemia remains one of the most important causes of neonatal demise despite considerable progress in hygiene, introduction of new antimicrobial agents, and advanced measures for early diagnosis and treatment.[2,3] Globally, of the deaths that occur in the first 5 years, about half of them occur within the 1st month of life,[4] and more than 90% of them are from developing countries.[5] The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (2002–2003) is 30/1000 live births. Neonatal sepsis is classified as early-onset sepsis when it occurs within the first 3 days of life and late-onset sepsis when it occurs after 3 days of life.[6,7] Sepsis is one of the most common causes of hospital admissions of neonates.[8-10] Newborns are susceptible to septicemia due to their immature immune system, the decreased phagocytic activity of their white blood cells and their incompletely developed skin barriers.[11-13] Delay in diagnosis and commencement of appropriate antibiotic and supportive treatment may result in high rates of illness and death.[14] Blood culture is the gold standard for the diagnosis of septicemia but it takes at least 48 h to obtain preliminary results.[15] It is, therefore, necessary to start empirical antibiotics based on the epidemiology of causative agents and antibiotic sensitivity patterns in a locality.[16] Periodic bacterial surveillance should be done in every unit because the organisms responsible for neonatal septicemia vary across geographical boundaries and with time of onset of illness.[6] Hence, the present study has been undertaken to determine the antimicrobial sensitivity patterns from blood cultures of neonates in our hospital.

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The purpose of this study is to know the antibiotic sensitivity pattern of organisms that have been isolated in positive blood cultures of suspected neonatal septicemia patients.

Materials and Methods

This study was carried out in a tertiary care hospital from a period of March 1, 2014, to August 31, 2015. This is a non-randomized, prospective study in which 109 cases of suspected neonatal septicemia on the basis of antenatal high-risk factors and signs and symptoms of sepsis including maternal fever, prolonged rupture of membranes, foul-smelling lochia, temperature instability, feeding difficulty, respiratory distress, jaundice, convulsions, and autonomic disturbances during this period were studied. Blood samples were collected from neonates in whom septicemia was suspected usually before antibacterial agents were given.

Inclusion Criteria

The following criteria were included in the study:

1. Neonates (age – 0–28 days)
   a. Neonates having signs and symptoms of septicemia such as maternal fever, feeding difficulty, convulsions, and respiratory distress syndrome
2. Premature infants
3. Only blood samples of neonates and not any other fluid.

Exclusion Criteria

The following criteria were excluded from the study:

1. Infants and children above the age of 28 days and adults and elderly patients
2. Any other body fluid except blood.

Clinical history and birth history including treatment given were noted in all cases. All the details were taken within a pro forma.

Blood samples were collected with disposable syringe and needle under strict asepsis. Usually, samples were collected from peripheral vein. Skin was painted with 70% alcohol and allowed to dry. Then, approximately 2 ml of blood was collected and immediately transferred to BacT/ALERT PF PLUS aerobic blood culture bottles. The bottles were incubated in BacT/ALERT system and patient's clinical data were introduced in the computer. Bottles that do not become positive remain in the system for 5 days. After 5 days, the computer prints out a list of negative bottles and illuminates the light adjacent to each well containing a negative bottle. These bottles are removed from the system and discarded and declared negative.

The positive bottles are unloaded and subcultures are made on MacConkey medium and blood agar plates. Organisms are identified from their colony characteristics, appearances in smear, biochemical reactions, appearance on mannitol salt agar, and bile esculin agar. Antibiotic sensitivity is determined by disc diffusion technique.

Results

Out of total 70 organisms isolated, 27 coagulase-negative staphylococci isolated which found to be more sensitive to linezolid (96.3%), vancomycin (70.4%), clindamycin (40.7%), gentamycin (33.3%), azithromycin and ciprofloxacin (25.9%), cotrimoxazole (18.5%), cefotaxime (11.1%), tetracycline and cephalexin (7.4%), and penicillin and oxacillin (3.7%) [Table 1].

Eleven *Staphylococcus aureus* isolated which found most sensitive to linezolid (100%), vancomycin (81.8%), clindamycin (54.5%), gentamicin (45.5%), cotrimoxazole and ciprofloxacin (36.4%), azithromycin (27.3%), tetracycline, cefotaxime, and cephalexin (18.2%), and resistant to penicillin and oxacillin (0%) [Table 2]. Five *Enterococcus* spp. isolated which found most sensitive to linezolid (100%), vancomycin (80%), azithromycin, cotrimoxazole, and ciprofloxacin (20%), and resistant to penicillin, clindamycin, gentamicin, tetracycline, oxacillin, cefotaxime, and cephalexin (0%) [Table 3]. One *Streptococcus* spp. isolated which is sensitive only to linezolid (100%) and resistant to penicillin, azithromycin, clindamycin, vancomycin, cotrimoxazole, ciprofloxacin, gentamicin, tetracycline, oxacillin, cefotaxime, and cephalexin (0%) [Table 4 and Figure 1].

Table 1: Antibiotic sensitivity pattern of coagulase-negative staphylococci (27 isolates)

Name of antibiotic	*No. of organisms sensitive to drug*	*Sensitivity*
Penicillin (ER)	1	3.7%
Azithromycin (AU)	7	25.9%
Clindamycin (CY)	11	40.7%
Linezolid (L)	26	96.3%
Vancomycin (AN)	19	70.4%
Cotrimoxazole (CO)	5	18.5%
Ciprofloxacin (CP)	7	25.9%
Gentamicin (G)	9	33.3%
Tetracycline (TO)	2	7.4%
Oxacillin (OF)	1	3.7%
Cefotaxime (CX)	3	11.1%
Cephalexin (CA)	2	7.4%

Table 2: Antibiotic sensitivity pattern of *Staphylococcus aureus* (11 isolates)

Name of antibiotic	*No. of organism sensitive to drug*	*Sensitivity*
Penicillin (ER)	0	0%
Azithromycin (AU)	3	27.3%
Clindamycin (CY)	6	54.5%
Linezolid (L)	11	100%
Vancomycin (AN)	9	81.8%
Cotrimoxazole (CO)	4	36.4%
Ciprofloxacin (CP)	4	36.4%
Gentamicin (G)	5	45.5%
Tetracycline (TO)	2	18.2%
Oxacillin (OF)	0	0%
Cefotaxime (CX)	2	18.2%
Cephalexin (CA)	2	18.2%

Table 3: Antibiotic sensitivity pattern of *Enterococcus* spp. (five isolates)

Name of antibiotic	*No. of organism sensitive to drug*	*Sensitivity*
Penicillin (ER)	0	0%
Azithromycin (AU)	1	20%
Clindamycin (CY)	0	0%
Linezolid (L)	5	100%
Vancomycin (AN)	4	80%
Cotrimoxazole (CO)	1	20%
Ciprofloxacin (CP)	1	20%
Gentamicin (G)	0	0%
Tetracycline (TO)	0	0%
Oxacillin (OF)	0	0%
Cefotaxime (CX)	0	0%
Cephalexin (CA)	0	0%

Table 4: Antibiotic sensitivity pattern of *Streptococcus* spp. (one isolate)

Name of antibiotic	*No. of organism sensitive to drug*	*Sensitivity*
Penicillin (ER)	0	0%
Azithromycin (AU)	0	0%
Clindamycin (CY)	0	0%
Linezolid (L)	1	100%
Vancomycin (AN)	0	0%
Cotrimoxazole (CO)	0	0%
Ciprofloxacin (CP)	0	0%
Gentamicin (G)	0	0%
Tetracycline (TO)	0	0%
Oxacillin (OF)	0	0%
Cefotaxime (CX)	0	0%
Cephalexin (CA)	0	0%

Out of total 70 organisms, 12 *Acinetobacter* spp. isolated which found more sensitive to ampicillin and ofloxacin (50%), amikacin, ciprofloxacin and gentamicin (41.7%), netilmicin (33.3%), cefoperazone (25%), cefotaxime and ceftazidime (8.3%), and resistant to amoxicillin/clavulanic acid, cefuroxime, and norfloxacin (0%) [Table 5]. Five *Klebsiella* spp. isolated which found more sensitive to ampicillin (60%), amikacin (40%), ceftazidime, ciprofloxacin, gentamicin, netilmicin and ofloxacin (20%), and resistant to amoxicillin/clavulanic acid, cefotaxime, cefoperazone, cefuroxime, and norfloxacin (0%) [Table 6]. Four *Escherichia coli* isolated which found more sensitive to ampicillin, amikacin, gentamicin and netilmicin (75%), ofloxacin (50%), cefoperazone (25%), and resistant to amoxicillin/clavulanic acid, cefotaxime, ceftazidime, ciprofloxacin, cefuroxime, and norfloxacin (0%) [Table 7]. Two *Pseudomonas* spp. isolated which found more sensitive to ampicillin, ceftazidime, cefoperazone, ciprofloxacin and ofloxacin (100%), amoxicillin/clavulanic acid and amikacin (50%), and resistant to cefotaxime, cefuroxime, gentamicin, netilmicin, and norfloxacin (0%) [Table 8 and Figure 2].

In the present study, we isolated candida non-albicans cases of 3 (4.30%) out of total 69 positive cases. Antifungal susceptibility testing was not done due to unavailability of antifungal discs.

Discussion

Neonatal septicemia must be treated urgently and specifically to reduce the mortality. Suspected infection based on clinical criteria need to be supported by microbial investigations to find causative organisms and their antibiotic sensitivity pattern.

In the present study, in Gram-positive organisms, coagulase-negative staphylococci are most sensitive to linezolid (96.3%), vancomycin (70.4%), clindamycin (40.7%), gentamycin (33.3%), azithromycin and ciprofloxacin (25.9%), cotrimoxazole (18.5%), cefotaxime (11.1%), tetracycline and cephalexin (7.4%), and penicillin and oxacillin (3.7%) which are comparable with similar study of Pokhrel *et al*.,[17] Mehta *et al*.[18] (linezolid – 100% and vancomycin – 100%), Agarwal *et al*.[19] (linezolid – 100% and vancomycin – 100%), and Mustafa *et al*.[20] (linezolid – 100% and gentamycin – 43%).

In the present study, *Staphylococcus aureus* was most sensitive to linezolid (100%), vancomycin (81.8%), clindamycin (54.5%), gentamicin (45.5%), cotrimoxazole and ciprofloxacin (36.4%), azithromycin (27.3%), tetracycline, cefotaxime, and cephalexin (18.2%), and resistant to penicillin and oxacillin (sensitivity – 0%) which are comparable with the similar study of Mehta *et al*.[18] (linezolid – 100%, vancomycin – 100%, and clindamycin – 49.5%) and Mustafa *et al*.[20] (linezolid – 100%, vancomycin – 93.3%, and gentamycin – 46%) and Agarwal *et al*.[19] (linezolid – 85.72% and vancomycin – 100%).

In the present study, *Enterococcus* spp. found to be most sensitive to linezolid (100%), vancomycin (80%), azithromycin, cotrimoxazole, and ciprofloxacin (20%), and resistant to penicillin, clindamycin, gentamicin, tetracycline, oxacillin, cefotaxime, and cephalexin (0%) which are comparable with the similar study of Mehta *et al*.[18] (linezolid – 100% and vancomycin – 87.5%), Kamble

Table 5: Antibiotic sensitivity pattern of *Acinetobacter* species (12 isolates)

Name of antibiotic	*No. of organism sensitive to drug*	*Sensitivity*
Ampicillin (AMP)	6	50%
Amoxicillin/clavulanic acid (AMC)	0	0%
Amikacin (AK)	5	41.7%
Cefotaxime (CTX)	1	8.3%
Ceftazidime (CAZ)	1	8.3%
Cefoperazone (CPZ)	3	25%
Ciprofloxacin (CIP)	5	41.7%
Cefuroxime (CXM)	0	0%
Gentamicin (GEN)	5	41.7%
Netilmicin (NET)	4	33.3%
Norfloxacin (NX)	0	0%
Ofloxacin (OF)	6	50%

Table 6: Antibiotic sensitivity pattern of *Klebsiella* spp. (five isolates)

Name of antibiotic	*No. of organism sensitive to drug*	*Sensitivity*
Ampicillin (AMP)	3	60%
Amoxicillin/clavulanic acid (AMC)	0	0%
Amikacin (AK)	2	40%
Cefotaxime (CTX)	0	0%
Ceftazidime (CAZ)	1	20%
Cefoperazone (CPZ)	0	0%
Ciprofloxacin (CIP)	1	20%
Cefuroxime (CXM)	0	0%
Gentamicin (GEN)	1	20%
Netilmicin (NET)	1	20%
Norfloxacin (NX)	0	0%
Ofloxacin (OF)	1	20%

Table 7: Antibiotic sensitivity pattern of *Escherichia coli* (four isolates)

Name of antibiotic	*No. of organism sensitive to drug*	*Sensitivity*
Ampicillin (AMP)	3	75%
Amoxicillin/clavulanic acid (AMC)	0	0%
Amikacin (AK)	3	75%
Cefotaxime (CTX)	0	0%
Ceftazidime (CAZ)	0	0%
Cefoperazone (CPZ)	1	25%
Ciprofloxacin (CIP)	0	0%
Cefuroxime (CXM)	0	0%
Gentamicin (GEN)	3	75%
Netilmicin (NET)	3	75%
Norfloxacin (NX)	0	0%
Ofloxacin (OF)	2	50%

Table 8: Antibiotic sensitivity pattern of *Pseudomonas* spp. (two isolates)

Name of antibiotic	*No. of organism sensitive to drug*	*Sensitivity*
Ampicillin (AMP)	2	100%
Amoxicillin/clavulanic acid (AMC)	1	50%
Amikacin (AK)	1	50%
Cefotaxime (CTX)	0	0%
Ceftazidime (CAZ)	2	100%
Cefoperazone (CPZ)	2	100%
Ciprofloxacin (CIP)	2	100%
Cefuroxime (CXM)	0	0%
Gentamicin (GEN)	0	0%
Netilmicin (NET)	0	0%
Norfloxacin (NX)	0	0%
Ofloxacin (OF)	2	100%

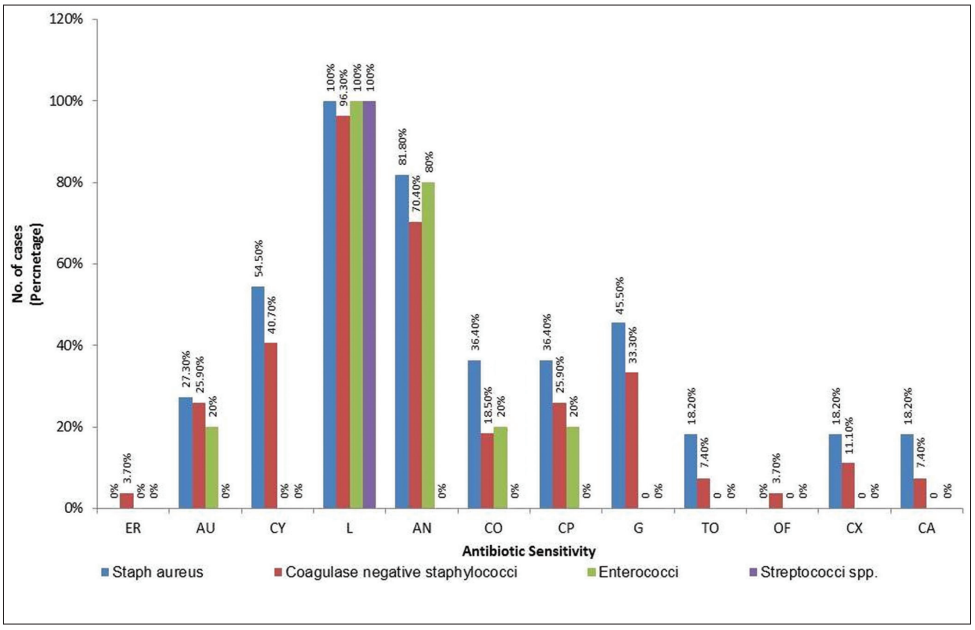

Figure 1: Antibiotic sensitivity pattern of Gram-positive Cocci

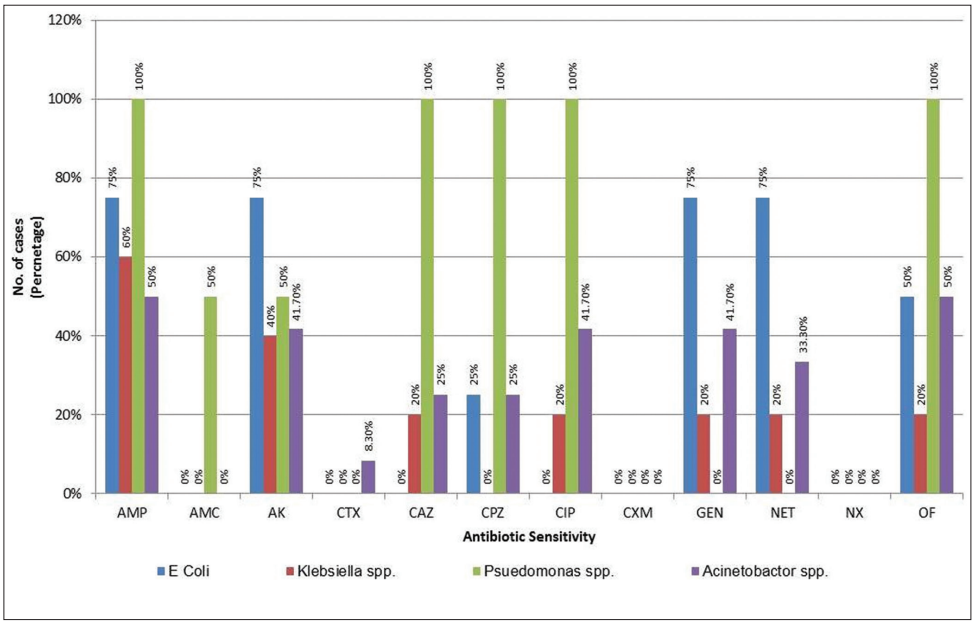

Figure 2: Antibiotic sensitivity pattern of Gram-negative Bacilli

et al.[21] (linezolid – 100% and vancomycin – 100%), and Shrestha *et al.*[22] (vancomycin – 100%).

In the present study, *Streptococcus* spp. found to be most sensitive to linezolid (100%) and resistant to penicillin, azithromycin, clindamycin, vancomycin, cotrimoxazole, ciprofloxacin, gentamicin, tetracycline, oxacillin, cefotaxime, and cephalexin (0%) which are comparable with the similar study of Kamble *et al.*[21] (linezolid – 100%) and Rajeshkumar *et al.*[23] (linezolid – 100%).

In the present study, *Acinetobacter* spp. were more sensitive to ampicillin and ofloxacin (50%), amikacin, ciprofloxacin, and gentamicin (41.7%), netilmicin (33.3%), cefoperazone (25%), cefotaxime and ceftazidime (8.3%), and resistant to amoxicillin/clavulanic acid, cefuroxime, and norfloxacin (0%) which are comparable to similar study of Hasan *et al.*[24] (ampicillin – 50%, amikacin – 50%, and gentamicin – 50%), Birkneh *et al.*[25] (gentamicin – 50% and ciprofloxacin – 50%), and Monjur *et al.*[26] (gentamicin – 36.4%).

In the present study, *Klebsiella* spp. were more sensitive to ampicillin (60%), amikacin (40%), ceftazidime, ciprofloxacin, gentamicin, netilmicin, and Ofloxacin (20%), and resistant to amoxicillin/clavulanic acid, cefotaxime, cefoperazone, cefuroxime, and norfloxacin (0%) which are comparable with Patwarthan *et al.*[27] (gentamicin – 11.1%, ceftazidime – 11.1%, and ofloxacin – 16.6%) and Monjur *et al.*[26] (gentamicin – 8.9% and ceftazidime – 17.8%).

In the present study, *E. coli* isolated were more sensitive to ampicillin, amikacin, gentamicin, and netilmicin (75%), ofloxacin (50%), cefoperazone (25%), and resistant to amoxicillin/clavulanic acid, cefotaxime, ceftazidime, ciprofloxacin, cefuroxime, and norfloxacin (0%) which are comparable with the study of Avinash *et al.*[28] (amikacin – 75% and gentamicin – 62.5%), Mustafa *et al.*[20] (amikacin – 71.4%), and Shrestha *et al.*[22] (amikacin – 80%).

In the present study, *Pseudomonas* spp. were most sensitive to ampicillin, ceftazidime, cefoperazone, ciprofloxacin and ofloxacin (100%), amoxicillin/clavulanic acid and amikacin (50%), and resistant to cefotaxime, cefuroxime, gentamicin, netilmicin, and norfloxacin (0%) which are comparable to similar study of Easow *et al.*[29] (ciprofloxacin – 93%, ceftazidime – 87%, and amikacin – 60%), Birkneh *et al.*[25] (ciprofloxacin – 94.8%), and Hasan *et al.*[24] (amikacin – 55.6%).

Conclusion

The Gram-positive organisms are the frequent cause of neonatal septicemia so when neonatal septicemia is suspected, drugs of choice for Gram-positive organisms are linezolid, vancomycin, and clindamycin and for Gram-negative organism drugs of choice are ampicillin, ofloxacin, and amikacin.

Early detection of neonatal sepsis along with broad-spectrum antibiotics leads to reduced mortality rate. Better management of sepsis-related complications has also reduced the mortality. Practice of hand washing, asepsis during resuscitation procedures of neonates, frequent microbial surveillance, fumigation of nursery, and management of babies with neonatal sepsis in isolated chamber have controlled the spread of infection to other neonates. Promotion of breastfeeding and discouraging top feeding can also significantly reduce neonatal mortality rate.

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