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IP International Journal of Medical Microbiology and Tropical Diseases

Journal homepage: https://www.ijmmtd.org/

Original Research Article

Neonatal septicemia and current scenario of antibiotic sensitivity pattern – A study of blood culture isolates in a tertiary care hospital, Rajkot

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ARTICLE INFO

Article history:
Received 18-09-2021
Accepted 22-10-2021
Available online 18-11-2021

Keywords:
Coagulase negative Staphylococcus (CONS)
Neonatal Septicemia
BACTEC

ABSTRACT

Background: Neonatal sepsis is one of the leading causes of neonatal mortality in developing countries. Neonatal sepsis can be classified into two subtypes depending upon onset of symptoms- before 72 hours of life (early-onset neonatal sepsis—EONS) or later (late-onset neonatal sepsis—LONS). Bacteriological profile and antibiotic susceptibility pattern in neonatal septicemia are changing time-to-time and place-to-place. This study is aimed to know the current scenario of neonatal septicemia and antibiotic susceptibility pattern for determining effective treatment, hence reducing burden of antibiotic resistance.

Materials and Methods: This is a Retrospective study. Data was collected from Bacteriology lab, PDUMC Rajkot (May 2020 – May 2021). Blood cultures were performed on suspected neonates. Both BACTEC and conventional methods were used. Organisms were isolated by standard microbiological protocols and antibiotic sensitivity was performed by Kirby-Bauer disc diffusion method as per CLSI- 2020/2021 guidelines.

Results: Total 1402 samples were screened. 326 were positive (23.25%). 214(65.64%) were male and 112(34.36%) were female. CONS (32.21%) was found to be the predominant pathogen followed by Klebsiella (19.63%), Staphylococcus aureus (18.10%), E. coli (15.95%), Acinetobacter (12.27%) and Enterococcus spp. (1.84%). EONS was seen in 195(59.82%) cases and LONS was seen in 131(40.18%) cases. Gram-negative bacteria are predominant in EONS (76.28%) and gram-positive bacteria is predominant in LONS (64.12%). Gram negative isolates are mostly susceptible to Meropenem, Piperacillin-tazobactam, Cefepime, Ceftazidime. Gram positive isolates mostly showed sensitivity to Vancomycin, Linezolid.

Conclusion: Multi-drug resistant organism are emerging in neonatal septicemia. Strict antibiotic stewardship should be practiced to avoid the upcoming treatment difficulties.

1. Introduction

Neonatal sepsis can be defined as systemic and generalized bacterial infection of the newborn with positive blood culture in the first four weeks of life. It is one of the leading causes of neonatal mortality in developing countries. The overall incidence of culture-proven sepsis varies between 1-8 cases per 1000 live births.[1–4] There are two classifications of neonatal sepsis that are based upon the onset of symptoms- early-onset neonatal sepsis-EONS (before 72 hours of life) and late-onset neonatal sepsis-LONS (after 72 hours of birth).[5] Organisms in the maternal genital tract are the main causative agents in early-onset neonatal sepsis. Organisms thriving in the external environment of the home or the hospital are the cause of late-onset septicemia.[6] Bacteriological profile and antibiotic susceptibility pattern in neonatal septicemia are changing time-to-time and place-to-place.[7] The organisms commonly

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https://doi.org/10.18231/j.ijmmtd.2021.046

associated with EONS are group B streptococcus and E Coli in the West, while in India most cases are due to Gram-negative organisms especially E. coli, Klebsiella, and Enterobacter spp.[8,9] Organisms that have been implicated in LONS are coagulase-negative Staphylococci (CONS), Staphylococcus aureus, Klebsiella pneumonia, Escherichia coli, Enterobacter spp., Pseudomonas aeruginosa and anaerobes.[9,10] Mortality from neonatal sepsis can be prevented by early diagnosis and effective treatment. The blood culture remains the "Gold Standard" for the diagnosis of neonatal sepsis though its sensitivity is 50-80 percent.[10] It is essential to initiate empirical treatment of suspected cases as the results of blood culture take hours to days. This study is designed to know the present picture of neonatal septicemia and antibiotic susceptibility pattern in this region, so that empirical treatment can be determined, hence preventing mortality, morbidity and reducing the burden of antibiotic resistance.[11]

2. Aim

This study is aimed to know the current scenario of neonatal septicemia and antibiotic susceptibility pattern in Western part of Gujarat for determining effective treatment, hence reducing burden of antibiotic resistance.

3. Materials and Methods

1. This is a Retrospective study. Data was collected from Bacteriology lab, PDUMC Rajkot (May 2020 - May 2021). Blood cultures were performed on suspected neonates. Both BACTEC and conventional methods were used for detection of positive cultures. Organisms were isolated by standard microbiological protocols and antibiotic sensitivity was performed by Kirby-Bauer disc diffusion method as per CLSI-2020/2021 guidelines.
2. The study population consists of 1402 neonates (less than 28 days age) with clinical presentation of septicemia. Neonates with signs and symptoms such as fever, poor feeding, respiratory distress, irritability, vomiting, diarrhea, cyanosis, cold clammy skin, grunt, tachycardia, tachypnea, seizures, bulging fontanelle etc.
3. Sample Processing: - About 2 ml of blood was drawn aseptically before starting antimicrobial therapy and directly inoculated into Brain Heart Infusion broth (BHIB) (both BD BACTEC Peds plus bottle and conventional bottle) in a ratio of blood: BHIB of 1:5. The blood culture bottles were immediately sent to the microbiology laboratory.
   (a) BACTEC bottles were loaded in BACTEC machine and sub-cultured on MacConkey agar, blood agar, and chocolate agar after showing red-alert in machine. Significant growths were processed for isolation by standard biochemical reactions and microbiological methods. Bottles showing a green light on 5^{th} day were reported negative.
   (b) Conventional bottles were incubated at 37◦ C for 24 hours and sub-cultured on MacConkey agar, blood agar, and chocolate agar daily for 5 days. Positive growths were processed accordingly for culture and isolation by standard biochemical reactions and microbiological methods. Conventional blood culture bottles showing no growth on subculture done after incubation of 5 days were reported as negative.
4. Antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method as recommended by Clinical Laboratory Standard Institute (CLSI) guidelines. Antibiotic disks (Hi-Media) were used. For quality control of antimicrobial susceptibility testing, E. coli ATCC 25922, S. aureus ATCC 25923, Enterococcus faecalis ATCC 29212 were used.

Fig. 1: Conventional BHIB

4. Results

Total 1402 samples were screened out of which 326 were positive (23.25%). Out of these, 214(65.64%) were male and 112(34.36%) were female. CONS (32.21%) was found to be the predominant pathogen followed by Klebsiella (19.63%), Staphylococcus aureus (18.10%), E. coli (15.95%), Acinetobacter (12.27%) and Enterococcus spp. (1.84%). EONS was seen in 195(59.82%) cases and LONS was seen in 131(40.18%) cases. Gram-negative

Fig. 2: BD BACTEC Peds plus bottle

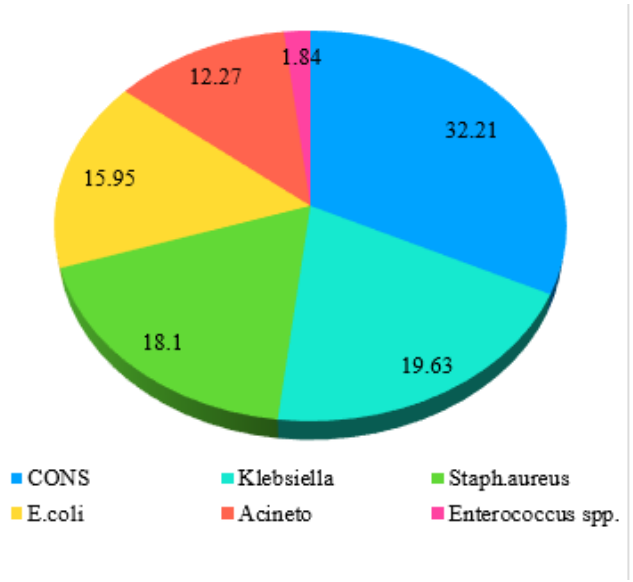

Fig. 3: Pathogens isolated from Blood culture samples (in %)

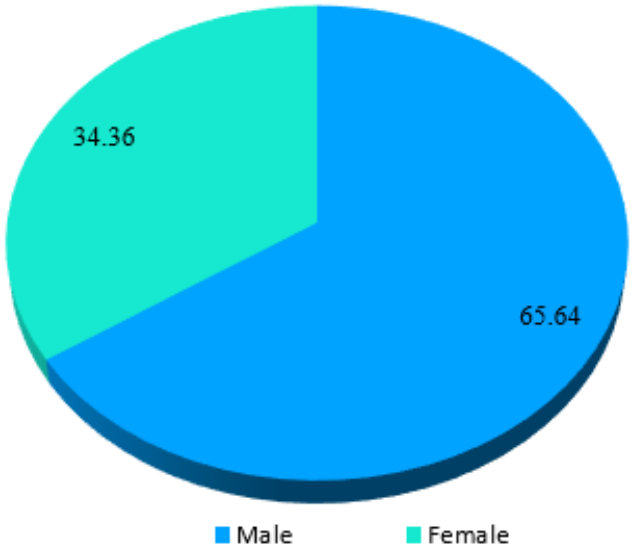

Fig. 4: Sex-wise distribution of positive samples (in %)

bacteria are predominant in EONS (76.28%) and gram-positive bacteria is predominant in LONS (64.12%). Gram negative isolates are mostly susceptible to Meropenem, Piperacillin-tazobactam, Cefepime, Ceftazidime. Gram positive isolates mostly showed sensitivity to Vancomycin, Linezolid.

5. Discussion

In India, neonatal sepsis is one of the four leading causes of neonatal mortality.[12] The isolation of bacterial agents from blood culture is the gold standard for the diagnosis of septicemia. The prevalence of bacterial profile of blood culture and their susceptibility pattern in an area, guides to start empirical treatment which is the cornerstone in the management of sepsis.[12] In this study, the incidence of neonatal sepsis was 28.6/1000 neonatal admissions which is consistent with studies done by Chacko et al,[1] National Neonatal, Perinatal Database,[13] and Sharma et al.[14] In our study, the blood culture positivity rate in neonatal sepsis cases was 23.5%, which was less as observed by Chacko et al.[1] However, some studies have reported higher blood culture positivity rates.[13,15]

In this study, the gram-positive organisms constituted the major group of isolates (52.11%) from neonatal septicemia cases, which is similar to the findings of Desai et al.[16] which had more gram-positive (67.85%). CONS were the predominant pathogen of neonatal sepsis in our study (32.21%) followed by Klebsiella (19.6%) and Staphylococcus aureus (18.1%) which is different from observations made by Deorari, and the National Neonatal Perinatal Database.[17–19] The observations by

Table 1: Distribution of Organisms

Gram Positive isolates				Gram negative Isolates			
Organism	**No. of isolates**	**EOS**	**LOS**	**Organism**	**No. of isolates**	**EOS**	**LOS**
CONS	105	31	74	**Klebsiella**	64	55	9
S.aureus	59	28	31	**E. coli**	52	50	2
Enterococcus spp.	6	2	4	**Acinetobacter spp.**	40	14	26
Total	170	61	109	**Total**	156	119	37

Table 2: Sensitivity of Gram-Negative Isolates (In%)

Drugs	**E. coli (n=52)**	**Klebsiella (n=64)**	**Acinetobacter (n=40)**
Ampicillin	11.54(n=6)	-	-
Ampicillin-sulbactam	44.23(n=23)	31.25(n=20)	62.50(n=25)
Piperacillin-tazobactam	86.54(n=45)	79.68(n=51)	75(n=30)
Cefuroxime	25(n=13)	31.25(n=20)	-
Cefotaxime	61.54(n=32)	45.31(n=29)	12.50(n=5)
Ceftazidime	73.08(n=38)	54.68(n=35)	22.50(n=9)
Cefepime	86.54(n=45)	71.88(n=46)	25(n=10)
Meropenem	100(n=52)	100(n=64)	100(n=40)
Amikacin	71.15(n=37)	59.37(n=38)	45(n=18)
Gentamicin	73.08(n=38)	62.50(n=40)	45(n=18)
Ciprofloxacin	38.46(n=20)	17.19(n=11)	40(n=15)
Levofloacin	38.46(n=20)	17.19(n=11)	40(n=15)
Tetracycline	53.85(n=28)	76.56(n=49)	-
Cotrimoxazole	44.32(n=23)	46.88(n=30)	50(n=20)
ESBL (Resistant to Ceftazidime but sensitive to Ceftazidime-clavulanic acid)	-	**17.19(ESBL)(n=11)**	-

Table 3: Sensitivity of Gram-Positive Isolates (In%)

Drugs	**Staph aureus(n=59)**	**CONS (n=105)**	**Enterococcus spp.(n=6)**
Ampicillin	-	-	0(n=0)
Penicillin	10.16 (n=6)	4.76(n=5)	0(n=0)
Rifampicin	83.05(n=59)	80(n=84)	0(n=0)
Linezolid	100(n=59)	100(n=105)	100(n=6)
Vancomycin	100(n=59)	100(n=105)	83.33(n=5)
Chloramphenicol	100(n=59)	100(n=105)	66.66(n=4)
Gentamycin	67.78(n=40)	42.86(n=45)	-
Ciprofloxacin	25.42(n=15)	28.57(n-30)	-
Levofloxacin	**-**	-	-
Erythromycin	45.76(n=27)	33.33(n=35)	0(n=0)
Clindamycin	45.76(n=27)	33.33(n=35)	-
Tetracycline	50.84(n=30)	66.67(n=70)	-
Cotrimoxazole	38.98(n=23)	50.48(n=53)	-
Cefoxitin	67.78(n=40)	61.90(n=65)	-
High level Gentamycin	**-**	-	50(n=3)
High level Streptomycin	**-**	-	50(n=3)
MRSA / MRS / VRE	**32.20 (MRSA) (n=19)**	**38.09 (MRS) (n=40)**	**16.67 (VRE) (n=1)**

Karthikeyan et al[20] were different from this study were in which Staphylococcus aureus was the predominant pathogen (61.5%) followed by Klebsiella (21.9%) and E. coli (13.5%). The results of antibiotic sensitivity revealed that gram-negative organisms were sensitive to Meropenem, Piperacillin-tazobactam, Cefepime, Ceftazidime. In isolates of Staphylococcus aureus MRSA prevalence was 32.20% in this study which was sensitive to vancomycin and linezolid. Studies conducted by Mathur et al, K hatua et al, and Tallur et al[15,20,21] also had similar observations. Vancomycin still remains the most sensitive drug for Staphylococcus aureus. Similar results were also reported in studies conducted by Mathur et al, K hatua et al, and Tallur et al.[15,20,21] Presently there is increasing incidence of Acinetobacter spp. infections in tertiary neonatal units of India.[22] In our study Acinetobacter spp. contributed 12.27% of the positive growth.

6. Conclusion

High mortality in neonatal sepsis in modern intensive care era is due to emergence of multi drug resistance organisms. Early isolation of organism and antibiogram guided treatment can help in prior establishment of empirical therapy and thus enhancing survival of affected neonates. Multi-drug resistant organisms are emerging in neonatal septicemia. Strict antibiotic stewardship should be practiced to avoid the upcoming treatment difficulties.

7. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

8. Source of Funding

None.

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Cite this article: Bhattacharya A, Mistry M, Parmar TK. Neonatal septicemia and current scenario of antibiotic sensitivity pattern – A study of blood culture isolates in a tertiary care hospital, Rajkot. *IP Int J Med Microbiol Trop Dis* 2021;7(4):222-226.