Microbiological profile and sensitivity pattern in neonatal sepsis in a tertiary care Centre in Western UP

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Abstract

Objective: To determine the Microbiological Profile and Sensitivity Pattern in Neonatal Sepsis in the Nursery of a Tertiary Care Centre in Western UP.

Method: A prospective observational study was conducted in the Department of Pediatrics, Subharti Medical College, Meerut, over one year (October 2015 - October 2016) on 240 patients, after clearance from the ethical Committee. All babies admitted in NICU or Nursery with risk factors or clinical features of neonatal sepsis or those evaluated for sepsis during their admission period, were included in the study, after taking written consent from parents. A detailed history and thorough examination was done of all babies enrolled and sepsis screen was sent.

Results: On analyzing the results of the sepsis screen of all the enrolled patients it was found that, out of all sepsis positive cases, 28% had a gram positive infection while 72% had a gram negative infection. In all patients having Gram positive sepsis, 41% had an Enterococcus infection, while in those having Gram negative sepsis 42% had Klebsiella infection.

It was observed that $\geq$50% Gram positive organisms were sensitive to Piperacillin + Tazobactum, Imipenem, Amikacin and Vancomycin. While $\geq$50% Gram negative organisms were sensitive to Piperacillin + Tazobactum and Imipenem.

Conclusion: It can thus be concluded from the data that an empirical antibiotic therapy of Piperacillin + Tazobactum and Amikacin would be most efficacious in our set up as first line antibiotics rather than the combination of Cefotaxime and Amikacin which were being used up till now.

Introduction

Globally, sepsis is still one of the major causes of morbidity and mortality in neonates, in spite of recent advances, in health care units. More than 40% of under-five deaths globally occur in the neonatal period, resulting in 3.1 million newborn deaths each year.(1) Sepsis is the most common cause of neonatal mortality world over. It is more common in developing countries compared with developed countries. Studies have recorded an incidence of neonatal sepsis between 11 - 24.5/1000 live births in some Asian countries.(2) The Infant Mortality Rate in India is 40.5/1000 live births as per the 2016 CIA World Fact book. In India too, sepsis continues to be a major cause of neonatal mortality. As per National Neonatal Perinatal Database 2002-2003, the incidence of neonatal sepsis in India was 30/1000 live birth.(3) Some other population-based studies have reported clinical sepsis rates ranging from 49 to 170/1000 live births in rural India.(4) Incidence has not changed much over the past decade, and the fatality due to sepsis is between 30 - 65%.(5)

Early empirical antibiotic treatment of neonates suspected of having septicemia is the standard practice. The spectrum of organisms that cause neonatal septicemia varies in different countries, and sometimes changes from one centre to another within the same country. The pathogens most often implicated in neonatal sepsis in developing countries differ from those seen in developed countries. Hence, the need of this study: to define first line empirical antibiotic therapy at our centre.

Neonatal sepsis is usually caused by a variety of Gram-positive as well as Gram-negative bacteria, and sometimes yeasts. Overall, Gram-negative organisms are more common and are mainly represented by Klebsiella, Escherichia coli, Pseudomonas, and Salmonella. Of the Gram-positive organisms, Staphylococcus aureus, Coagulase negative staphylococci (CONS), Streptococcus pneumoniae, and S. pyogenes are most commonly isolated.(6) Early diagnosis and appropriate therapy of septicemia is of utmost importance to prevent morbidity and mortality.

Materials and Methods

This study was conducted in the NICU and Nursery of the Department of Pediatrics, in collaboration with the Department of Microbiology in Subharti Medical College, Meerut. This is a tertiary care, referral hospital in Western UP.

This prospective observational study was conducted over one year, from October 2015 to October 2016 on 240 babies (presuming the prevalence of sepsis in the neonatal ward to be 25%, and assuming a confidence interval of 6.29%, with confidence level of 95%, a sample size of 270 was calculated), after taking ethical clearance from the institutional ethical committee. All babies admitted in NICU or Nursery in the Department of Pediatrics with risk factors or clinical features of neonatal sepsis or babies who required evaluation for sepsis during the period of stay in the Nursery were include in the study. Neonates with gross congenital malformations, severe cardiac abnormalities,

history of perinatal asphyxia, severe intracranial hemorrhage or respiratory distress syndrome and neonates taken away against medical advice (LAMA) before being investigated or where the parents were not willing to enroll their babies in the study, were excluded from the study

After taking a written consent from all potentially eligible parents a detailed history and physical examination was performed and recorded. Patients were investigated and treatment was initiated. Cases were followed up till they were discharged, expired or left against medical advice.

All neonates evaluated for sepsis had a blood culture (in automated BacT/ALERT 3D pediatric blood culture bottle - bio Meriux) and a sepsis screen done. Antimicrobial susceptibility testing was performed against relevant antibiotics and the data analyzed (using Statistical Package for Social Sciences, version 23 - SPSS Inc., Chicago, IL).

Results

A total of 306 neonates were enrolled in the study of which 66 were excluded, as they did not meet the inclusion criteria. Results of 240 patients were analyzed. Baseline characteristics of the study population are given in Table-1.

In our study we found that positive blood culture was seen in 138 (57.50%) cases. However 102 (42.50%) neonates clinically suspected of having sepsis had a negative blood culture. Of all babies having culture positive sepsis, 28% cases had a gram positive infection while 72% had a gram negative infection. Out of all patients having Gram positive sepsis, Enterococci (41.03%) was the predominant organism isolated followed by Staphylococcus aureus (25.64%), Coagulase Negative Staphylococcus (20.51%) and Group B Streptococcus (12.82%). In those having Gram negative sepsis, Klebsiella pneumoniae (42.42%) was the predominant isolate followed by Enterobacter (21.21%), Escherichia coli (17.17%), Pseudomonas (12.12%) and Proteus (7.07 %). On further analyzing the sensitivity pattern it was observed that $\geq$50% patients having Gram positive infection were sensitive to Piperacillin Tazobactum, Imipenem, Amikacin and Vancomycin. While $\geq$50% patients with Gram negative infection were sensitive to Piperacillin + Tazobactum and Imipenem (Table- 2, 3).

Table 1: Base line characteristics

Characteristics		Number	%
Age	0-72 hrs	98	41
	72 hrs-28 days	142	59
Gender	M:F	152:88	63:47
Socio-economic status	Middle	168	70
Gestation	Term	66	28
	Preterm	174	72
Birth weight	>2.5 kg	77	32
	LBW	114	48
	VLBW	31	13
	ELBW	8	3
	Not known	10	4
Mode of delivery	Vaginal	150	63
	Caesarian section	90	37
Place of delivery	Home	73	30
	Hospital (Inborn)	62	26
	Hospital (Outborn)	105	44

Table 2: Sensitivity pattern of Gram Positive Organisms isolated N=39 (%)

Antibiotics	Enterococci N=16 (%)	Staph. aureus N=10 (%)	Coagulase negative staph N=8 (%)	Group B Streptococcus N=5 (%)
Vancomycin	16 (100.0)	10 (100.0)	8 (100.0)	5 (100.0)
Amikacin	14 (87.5)	10 (100.0)	5 (62.5)	3 (60.0)
Imipenem	13 (81.3)	6 (60.0)	4 (50.0)	2 (40.0)
Piperacillin +Tazobactum	9 (56.3)	5 (50.0)	3 (37.5)	4 (80.0)
Ceftriaxone	5 (31.3)	3 (30.0)	2 (25.0)	1 (20.0)
Cefoperazone+ Sulbactum	3 (18.8)	4 (40.0)	1 (12.5)	0 (0.0)
Gentamicin	2 (12.5)	1 (10.0)	1 (12.5)	0 (0.0)
Ceftazidime	1 (6.3)	1 (10.0)	1 (12.5)	1 (20.0)
Ampicillin	1 (6.3)	1 (10.0)	1 (12.5)	0 (0.0)

Table 3: Sensitivity pattern of Gram Negative Organisms isolated N=99 (%)

Antibiotics	Klebsiella pneumoniae N=42 (%)	Enterobacter N=21 (%)	Escherichia coli N=17 (%)	Pseudomonas N=12 (%)	Proteus N=7 (%)
Imipenem	39 (92.3)	16 (76.2)	11 (64.7)	10 (83.3)	6 (85.7)
Piperacillin + Tazobactum	26 (61.90)	11 (52.4)	9 (52.9)	8 (66.7)	4 (57.1)
Cefoperazone+ Sulbactum	21 (50.0)	9 (42.9)	8 (47.1)	7 (58.3)	5 (71.4)
Ceftazidime	19 (45.23)	8 (38.1)	7 (41.2)	6 (50.0)	3 (42.9)
Ceftriaxone	17 (40.47)	7 (33.3)	5 (29.4)	4 (33.3)	2 (28.6)
Amikacin	16 (38.09)	6 (28.6)	4 (23.5)	3 (25.0)	1 (14.3)
Gentamicin	4 (4.0)	5 (23.8)	3 (17.6)	1 (8.3)	1 (14.3)
Ampicillin	2 (2.0)	2 (9.5)	1 (5.9)	1 (8.3)	1 (14.3)

Discussion

Positive blood culture for aerobic organisms in neonates were seen to vary from 25% to 60%. In our study out of 240 cases of neonatal sepsis 57.50% (138) were culture positive. Among the culture positive cases majority were gram negative, 78.33% (188 cases), followed by gram positive cases, 16.252% (39 cases). Jonnala RNR et al[7] observed that 57.1% cases (48) were culture positive. Among the culture positive cases majority were gram negative (37 cases – 77.08%) followed by gram positive (8 cases – 16.66%) and fungi (3 cases – 6.2%) which is comparable to our study.

Positive blood culture values in our study were similar to the studies by Sharma et al[8], Jain et al[9], Y R Khinchi et al[10] (52.3%) and Amru R[11](62%).

Gram-negative and Gram-positive septicemia was encountered in 78.33% and 16.25% of the culture-positive cases in our study, which is comparable to a study conducted by Agnihotri et al,[12] which reported that Gram-negative and Gram-positive organisms were responsible for 59% and 41% of the septicemia cases, respectively. The isolation rate of bacteria in our study is also comparable to the rates reported by A S M Nawshad et al[13] (Gram negative 73%, gram positive 27%). Studies by other researchers like Manucha et al,[14] Simiyu et al,[15] Anwer et al,[16] Milledge et al,[17] Kapoor et al18 and Movahedian et al,[19] also showed that gram negative bacteria were responsible in most cases of neonatal sepsis.

The pathogens most often encountered in neonatal sepsis in developing countries differ from those seen in developed countries. In our study, of all patients having Gram positive sepsis 41% had an Enterococcus infection, while in those having Gram negative sepsis 42% had Klebsiella infection. The report of the National Neonatal Perinatal database showed Klebsiella as the predominant (29%) pathogen.[20] Similar findings have been reported in previous studies by Zakariya et al[21] (66%) and Afroza et al[22] (64%).

In the studies undertaken in other developing countries Gram negative organisms were common and Klebsiella and Enterobacter were the most frequently occurring organisms.[18,19] In the developed countries Gram positive cocci are the most common bacterial isolates. Group B Streptococci was reported as the most common pathogen in term infants in United States by National Institute of Child Health Development.

In our study most of the Gram Negative Organisms were sensitive to Imipenem followed in decreasing order by Piperacillin + Tazobactum, Cefoperazone + Sulbactum, Ceftazidime, Ceftriaxone and Amikacin. Most of the Gram Positive Organisms were sensitive to Vancomycin followed by Amikacin, Imipenem, Piperacillin + Tazobactum, Ceftriaxone and Cefoperazone + Sulbactum. In a study from Sydney Neonatal Infection Surveillance, they have mentioned that all Gram Negative Bacteria were susceptible to Gentamicin and Third Generation Cephalosporin (Levine et al).[23] Waheed et al[24] found Cefotaxime as the most efficacious drug with 80% sensitivity to Klebsiella, 70% to Staphylococcus aureus and 65% to Escherichia coli. Sensitivity of Imipenem was high against Klebsiella (53%) but low against other organisms. Anwer et al[16] found Amikacin to be the most effective antibacterial with an efficacy of about 90-100%, then Cefotaxime with a sensitivity of 84-89%. Ampicillin had the least sensitivity i.e. less than 20%. Mokuolu et al[25] found that 94% of the organisms were sensitive to Azithromycin followed by Streptomycin (77.8%), Gentamicin (73.3%) and Ampicillin + Sulbactum (69.2%). The common pathogens in this study were Staphylococcus aureus, Coagulase negative staphylococcus albus, Klebsiella sp and unclassified Choliforms.

Ellabib et al[26] found Enterobacteriaceae to be most common (Serratia, Klebsiella and Enterobacter sp) followed by Coagulase negative and positive staphylococci. Low resistance was found to Imipenem, Ciprofloxacin and Piperacillin + Tazobactum, while all Staphylococci were sensitive to Vancomycin. Shresta et al[27] found highest resistance to Ampicillin (91.94%) and least to Chloramphenicol (94.84%). None of the isolates in this study were resistant to Vancomycin and Tecoplanin.

Conclusion

We can thus conclude from our data that an empirical antibiotic therapy of Piperacillin + Tazobactum and Amikacin would be most efficacious in our set up as first line antibiotics.

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