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Original Research Article

Bacteriological Profile and Antibiotic Sensitivity Pattern in Early Onset and Late-Onset Sepsis

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Abstract

Background: Diagnosis of bloodstream infections in newborns is difficult due to a wide range of symptoms. Empirical therapy guided by a knowledge of the causative agents and their local antibiotic susceptibility profile is a crucial step in improving therapeutic results. As a result, we planned to investigate the bacteriological profile and antibiotic susceptibility pattern in neonatal sepsis. This was to compare the efficacy of a combination of ampicillin and gentamicin against 3rd generation cephalosporins for empirical antibiotic treatment of neonatal sepsis. ***Methods:*** It was a cross sectional observational study conducted over one and a half years.The period of study was from January 2019 to June 2020 in the Department of Paediatrics and Microbiology of a tertiary care Teaching hospital, Hydrabad. Blood culture samples of neonates suspected of having EOS or LOS were sent to the Microbiology department where they were inoculated into BACTEC TM Peds plus/F which was then inserted into the BD BACTEC fluorescent series instrument for incubation. Antibiotic sensitivity testing was done by disc diffusion as per CLSI guidelines. Zone sizes were measured and interpreted by BD PHOENIX AUTOMATED AST machine according to CLSI standards 2016. ***Results:*** 402 neonates were admitted to the neonatal unit of our hospital with suspected sepsis between January 2021 to June 2021. Out of which parents of 372 neonates consented to take part in the study. Out of which 196 were male and 176 were female neonates. Bacteria were isolated from 195 samples and 177 samples were negative out of listed 72 neonates. These 195 neonates were enrolled as cases in the study. Out of 195 cases, 75 cases were inborn and 120 were outborn. The blood culture isolation rate was 33.2 % and 56.5% in inborn and outborn respectively. There were 105 males and 90 females in the study. The culture positivity rate was 52.4%. Bacteria were isolated from 41 samples of suspected EOS neonates with a positivity rate of 33.8% and 154 samples of suspected LOS with a positivity rate of 34.5%. Gram-positive bacteria were isolated from the 107 cases and gram-negative bacteria were grown in 88 cases. The most common isolate was Staphylococcus aureus in 59(30.26%) followed by non- fermenters in 45(23.08%) cases. ***Conclusion:*** The prevalent pattern of causative etiological agents and their sensitivity pattern is critical because it aids in the selection of particular and effective antibiotic(s) for the index case's therapy. It also aids in the development of an institutional strategy for the selection of antibiotics for newborns admitted with suspected sepsis at the time of admission. This helps to avoid antibiotic abuse and the development of antibiotic resistance.

Keywords: Bacteraemia, Identification, Organisms, Septicaemia, EarlyOnsetSepsis, Late-Onset Sepsis.

INTRODUCTION:

Sepsis is one of the important causes of death among neonates around the world, with 3 million deaths due to neonatal sepsis each year. In underdeveloped nations like India, where 1700 cases/100000 newborns die each year from sepsis, the problem is much more concerning.[1] Septicemia is responsible for almost a quarter of all deaths worldwide, with newborn septicemia accounting for 15% of all deaths. Prompt diagnosis and correct antimicrobial agent selection are two effective techniques for reducing mortality and morbidity associated with newborn sepsis. The signs and symptoms of neonatal sepsis are ambiguous, and culture sensitivity data arrive late.[1,2]

Between the presentation of neonatal sepsis and the reporting of blood culture and sensitivity results, there is a period of time that is extremely valuable. Thus, the prevailing pattern of causative etiological agents and their sensitivity pattern is critical since it aids in the selection of particular and effective antibiotic(s) for the index case's therapy. It also aids in the development of an institutional strategy for the selection of antibiotics for newborns admitted with suspected sepsis at the time of admission. This helps to avoid antibiotic abuse and the emergence of antibiotic resistance. This also aids in the detection of antibiotic resistance. So we planned to study the bacteriological profile and antibiotic sensitivity pattern in neonatal sepsis, so empirical antibiotics treatment could be started promptly to treat neonatal sepsis and prevent any further complications.[3,4]

MATERIAL AND METHODS:

It was a cross sectional observational study conducted throughout one year from January 2019 to June 2020 in the Department of Paediatrics and Microbiology of a tertiary care Hospital in Hydrabad.

- **Inclusion criteria**
  - All the neonates were admitted with suspected sepsis.
  - Patients who consented to the study of their neonates.
- **Exclusion criteria**
  - Parents not willing to enroll their neonates in the study.
  - Neonates admitted to the other hospital before the admission our hospital

All the newborns who were admitted to the newborn unit of the Department of Paediatrics with suspected sepsis and meeting the criteria for enrolment were enrolled in the study. Blood culture samples were taken observing standard precautions and procedures from all enrolled cases. The sample was sent to the Microbiology department where they were inoculated into BACTEC TM Peds plus/F which was then inoculated into the BD BACTEC fluorescent series instrument for incubation. Each bottle contained a sensor that detects the increase in CO2 produced by the growth of microorganisms. The bottle sensor monitors every 10 minutes for an increase in its fluorescence, which was proportional to the amount of CO2 present. A positive reading indicates the presumptive presence of viable microorganisms in the bottle. A positive bottle was sub-cultured on blood agar and MacConkey agar plates. Following the subculture on solid media from each positive bottle a smear was prepared for gram staining from that blood culture bottle. The Gram-stained smear was examined for the presence of microorganisms and a presumptive report conveyed to departments of Paediatrics.

The Blood agar and Mac Conkey agar plates were incubated aerobically at 37ºc for 24 to 48 hrs and then observed for the growth of bacteria. All bacterial isolates were identified using standard biochemical identification methods which included catalase, oxidase, coagulase, bile solubility, Sugar fermentation, indole, methyl red, citrate utilization, urease, and nitrate reduction test for identification to the genus or species level. The antibiotic sensitivity testing was done by disc diffusion as per CLSI guidelines. 23 Zone sizes were measured and interpreted by BD PHOENIX AUTOMATED AST machine according to CLSI standards. The data was analyzed for the blood culture positivity rate, bacteriological profile, and sensitivity pattern in early and late-onset sepsis.

Statistical Analysis: The data collected will be entered into a spreadsheet. The data will be checked for any missing values and completed. Analysis in terms of demographic variables, positivity in the processed samples, type of species prevalent.

RESULTS:

402 neonates were admitted to the neonatal unit of our hospital with suspected sepsis between January 2019 to June 2020. Out of which parents of 372 neonates consented to take part in the study. Out of which 196 were male and 176 were female neonates. 80 neonates were < 3days of age and were listed as suspected early-onset sepsis (EOS) and 292 neonates were>3 days and were listed as suspected late-onset sepsis (LOS). Out of these 151 newborns were inborn i.e. who were delivered in our hospital and were suspected of sepsis while 221 newborns were outborn i.e. who were referred from other hospitals with clinical suspicion of sepsis. (Table-1)

Table-1: Socio-demiographic profiles of all the neonates were admitted with suspected sepsis.

	Age		Sex		Place of delivery		Gram staining	
	EOS	LOS	Male	Female	Inborn	Out born	Positive	Negative
Suspected	80	292	196	176	151	221	NA	NA
Confirmed	41	154	105	90	75	120	107	88

Bacteria were isolated from 195 samples and 177 samples were negative out of listed 372 neonates. These 195 neonates were enrolled as cases in the study. Out of 195 cases, 75 cases were inborn and 120 were outborn. The blood culture isolation rate was 33.2 % and 56.5% in inborn and outborn respectively. There were 105 males and 90 females in the study. The culture positivity rate was 52.4%. Bacteria were isolated from 41 samples of suspected EOS neonates with a positivity rate of 33.8% and 154 samples of suspected LOS with a positivity rate of 34.5%. Gram-positive bacteria were isolated from the 107 cases and gram-negative bacteria were grown in 88 cases. The most common isolate was Staphylococcus aureus in 59(30.26%) followed by non- fermenters in 45 (23.08%) cases. Details of various isolates among 195 cases have been given in Table 2.

Table 2: Distribution of bacterial isolates from blood culture

Bacteria	Number	Percentage
Staphylococcus aureus	59	30.26
Non fermenters	45	23.08
Coagulase negative Staphylococcus	38	19.49
Klebsiella	19	9.74
Enterobactor	15	7.69
E. coli	7	3.59
Citrobacter	6	3.08
Pseudomonas	5	2.56
Diphtheroids	4	2.05
Proteus mirabilis	2	1.03
Enterococcus	1	0.51
Total	195	100

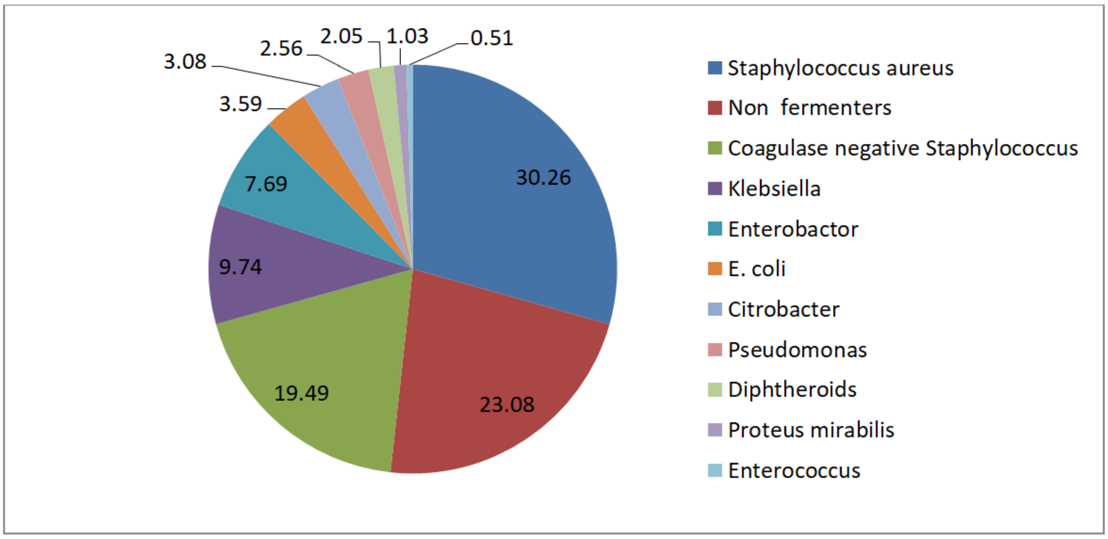

Figure-1: Distribution of bacterial isolates from blood culture

On sensitivity patterns, most of the isolates were sensitive to ampicillin and gentamicin combination and a little less proportion was sensitive to third-generation cephalosporins. Other antibiotics showed sensitivity as imipenem, meropenem, vancomycin, and linezolid as expected from 2 nd line drugs.(Table-3a-g)

As per our data analysis sensitivity of ampicillin alone in *S.aureus* isolates was 64.4%and of gentamicin was 45.8%. The sensitivity of ampicillin alone in CONS isolates was 55.3%and of gentamicin was 57.9%respectively. Sensitivity of ampicillin alone in *Citrobacte*r isolates was 50%and of gentamicin was 66.67 %respectively. Sensitivity of ampicillin alone in *E.Coli* isolates was 42.9 %and of gentamicin was 57.1% respectively. Sensitivity of ampicillin alone in *Klebsiella* isolates was 21.1%and of gentamicin was 36.8% respective. Sensitivity of ampicillin alone in Non-fermenters isolates was 44% and of gentamicin was 42.2%respectively. The third-generation antibiotics like cefotaxime, ceftazidime, ceftriaxone were not that effective. Hence our study concludes that ampicillin and gentamicin combination given together showed a better gram-positive and gram-negative cover as compared to cephalosporins given alone (Table-3a-g).

Table-3a: Showing Antibiotic Sensitivity Pattern of Staphylococcus Aureus Isolates

Sensitivity	Amika	Amoxiclav	Ampisal	Ampicillin	Aztreon	Cipro	Clinda	Cotri	Eryth	Genta	Levo	Lino	Netli	Tobra	Vanco
Sensitive	21	32	54	38	13	26	8	23	29	27	25	12	10	10	12
Resistant	38	27	5	21	0	33	5	36	30	32	34	1	3	3	1
Total	59	59	59	59	13	59	13	59	59	59	59	13	13	13	13

Table-3b: Showing Antibiotic Sensitivity Pattern of Coagulase-Negative Staphylococci

	Amika	Amoxiclav	Ampisal	Ampicill	Azithromy	Aztreon	Ceftazidime	Cipro	Clinda	Cotri	Eryth	Genta	Levo	Lino	Piper	Tetra	Tige	Vanco
Sensitive	16	18	19	21	7	19	13	17	19	21	6	22	16	19	12	18	14	19
Resistant	11	20	5	17	10	0	25	21	5	17	22	16	22	0	8	20	5	0
Total	27	38	24	38	17	19	38	38	24	38	28	38	38	19	20	38	19	19

Table-3c: Showing Antibiotic Sensitivity Pattern of Citrobacter

	Ampicillin	**Ciprofloxacin**	**Cotrimoxazole**	**Erythromycin**	**Gentamicin**	**Lincomycin**	**Vancomycin**
Sensitive	3	3	2	1	4	6	5
Resistant	3	3	4	5	2	0	1
Total	6	5	6	6	6	6	6

Table-3d: Showing Antibiotic Sensitivity Pattern of E.Coli

Sensitivity	Amika	Amoxiclav	Ampisal	Ampicill	Imip	Aztreon	Cefopodo	CFZ/CLV	Ceftri	CFZ	Cipro	cefepime	Cotri	Doxy	Colis	Genta	Piper+Taz
Sensitive	3	2	5	3	3	3	3	2	4	3	2	3	2	2	3	4	4
Resistant	4	5	2	4	0	0	0	1	3	4	5	4	5	5	0	3	3
Total	7	7	7	7	3	3	3	3	7	7	7	7	7	7	3	7	7

Table-3e: Showing Antibiotic Sensitivity Pattern of Klebsiella

Sensitivity	Amika	Ampisal	Ampicill	Imip	Aztreon	Cefopodo	CFZ/CLV	Ceftri	CFZ	Cipro	Cefepime	Cotri	Colis	Genta	Mero	PB	Piper+Taz

Sensitive	4	6	4	3	3	3	5	4	4	3	3	1	10	7	7	4	3
Resistant	15	13	15	7	7	16	14	15	15	16	16	18	0	12	3	6	7
Total	19	19	19	10	10	19	19	19	19	19	19	19	10	19	10	10	10

Table-3f: Showing Antibiotic Sensitivity Pattern of Enterobacter Spp

Sensitivity	Amika	Ampicllin	Ampisal	Imp	Aztreon	Cefopodo	Ceftri	CFZ	Cipro	Cotri	Colis	Genta	Mero	PB	Piper+Taz
Sensitive	5	6	6	7	5	4	7	5	5	5	8	5	6	7	7
Resistant	10	9	4	3	3	5	8	10	10	10	0	10	3	3	8
Total	15	15	10	10	8	9	15	15	15	15	8	15	9	10	15

Table-3g: Showing Antibiotic Sensitivity Pattern of Non Fermenters

Sensitivity	Amika	Ampicillin	Imip	Aztreon	Cefopodo	Ceftri	CFZ	Cipro	cefepime	Genta	Piper+Taz
Sensitive	14	20	10	9	6	20	16	15	17	19	21
Resistant	31	25	3	4	7	25	29	30	28	26	24
Total	45	45	13	13	13	45	45	45	45	45	45

DISCUSSION:

In comparison to bacteriological culture and sensitivity of blood samples, clinical signs and symptoms in neonates have poor specificity. Staph. aureus, Non-fermentors, CONS, Klebsiella, and E.Coli were the most common isolates in our analyses, and the results are consistent with those of the previous topic. It also makes the essential point that infections caused by these agents pose a greater threat to child survival in developing nations, and that this is something that should be treated seriously.The findings of our study suggest that empirical therapy with ampicillin and gentamycin may be started as soon as possible to minimize morbidity and mortality in both EOS and LOS.[4,5]

In a study carried out on neonatal sepsis in India by Joshi et al in Pune.[3,5] It was reported that out of 100 cases of neonatal sepsis 25% of cases were blood culture positive. Among them, gram-negative bacteria constituted the most common isolates which included *P. aeruginosa* (38.3%),*K pneumoniae* (30.4%), *E.coli* (15.5%) and Acinetobacterspp (7.8%). *Acinetobacte*r and *Citrobacter* sepsis have been reported previously among newborns from Southeast Asia by ZA Bhutta in a study done in Karachi. Case death rates of 42-61% were reported among neonates with Citrobacter and Acinetobacter sepsis.[4] In a study done by Brook I in Washington it was reported that important causative agents causing bacteremia and meningitis in children under the age of one-month-old were Group B *Streptococcus, E.coli, Listeria monocytogenes, S. pneumonia, Haemophilus influenzae, S. aureus, Neisseria meningitides, and Salmonella* species.[5,6]

CONCLUSIONS:

Neonatal septicemia is a leading cause of death in newborns. The most essential factors in reducing infant fatalities are prompt and accurate clinical diagnosis, as well as initiation of empirical treatment. In comparison to bacteriological culture and sensitivity of blood samples, clinical signs and symptoms in neonates have poor specificity. Staph. aureus, Non-fermentors, CONS, Klebsiella, and E.Coli were the most common isolates in our analyses, and the results are consistent with those of the previous topic. Infections caused by these agents pose a greater threat to child survival in developing nations. Our data shows that empirical therapy with ampicillin and gentamicin should be begun as soon as possible in both EOS and LOS to reduce morbidity and death. As a result, when compared to cephalosporins given alone or in combination for empirical therapy in suspected instances of septicaemia, ampicillin and gentamicin given together demonstrated a better gram-positive and gram-negative cover.

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