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Study on Microbiological Profile of Bacterial Infection in Newborns of Tertiary Care Neonatal Unit

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ABSTRACT

Background: Sepsis neonatorum, or neonatal sepsis, is a clinical illness brought on by the pathophysiologic consequences of a systemic or localized infection. It includes systemic illnesses such as meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections and affects babies under one month of age . Neonates are immune-compromised and resist weakly to bacterial infections.

Aim and Objectives: To study bacteriological profile of neonatal sepsis and to study the antibiotic sensitivity pattern of different bacterial pathogens isolated.

Materials and Methods: A total of 180 neonates with suspected sepsis were included in the study based on inclusion and exclusion criteria. 2-3 mL of blood was collected from each patients by the nursing personnel under aseptic precautions and inoculated immediately into 20 mL of glucose citrate broth with 0.025% of sodium polyanethol sulphonate as anticoagulant (HI media, a commercial firm). The broths were sub cultured on 5% sheep blood agar and Mac-Conkey agar after overnight incubation. A negative result was followed-up by examining the broth daily and doing a final subculture at the end of the seventh day. Positive growth was identified by Gram staining and antimicrobial susceptibility test was performed by Kirby-Bauer disk diffusion method as per NCCLS guidelines.

Discussion and Conclusion: Neonatal septicemia is an life threatening emergency and rapid treatment with antimicrobial agent is highly essential for favorable outcome. For the effective management of the cases with neonatal septicemia, the study of microbiological profile with their antibiotic sensitivity pattern always plays a significant role. In our study, the prevalence of neonatal sepsis was found to be 33.3% and the prevalence was higher in males compared to females. Among the neonates 56.7% had early onset sepsis and 43.3% had late onset sepsis. The clinical presentation was studied in all the patients, it was found that the most common clinical symptom was respiratory distress and pneumonia was more common in early onset

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sepsis. Among neonates gram negative septicemia was more common compared to gram positive septicemia. Staph aureus was most common among gram positive and pseudomonas was more common among gram negative isolates. Antibiotic susceptibility showed that the gram positive organisms were highly sensitive to vancomycin, linezolid, teicoplanin and also sensitive to amoxycillin and clindamycin and were least sensitive to penicillin and ampicillin. Antibiotic susceptibility showed that the gram negative organisms were highly sensitive to colistin, tigecycline, meropenem and imipenem, and sensitive to ampicillin and gentamycin. An antibiotic policy should be formulated in our hospital and depending upon antibiotic sensitivity pattern of the isolated pathogen, antibiotic should be used.

Key-words: gram positive, gram negative, neonatal sepsis and antibiotic susceptibility test.

INTRODUCTION:

Sepsis neonatorum, or neonatal sepsis, is a clinical illness brought on by the pathophysiologic consequences of a systemic or localized infection. It includes systemic illnesses such as meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections and affects babies under one month of age [1, 2]. Neonates are immune-compromised and resist weakly to bacterial infections. Group B streptococci, Escherichia coli, Listeria monocytogenes, staphylococcus aureus, coagulase-negative staphylococci (CoNS), Enterococci, Klebsiella spp., Enterobacter spp., Pseudomonas spp., Salmonella spp., H. influenzae, Neisseria meningitidis, and Streptococcus pneumoniae are the bacterial agents linked to neonatal sepsis [3,4,5]. Unsafe delivery methods have a major role in the transmission of newborn illnesses in poor nations. An estimated 2.5–3 million newborn morbidity and death cases occur each year worldwide [6].

Neonatal sepsis can be divided into three main subtypes: Early onset septicemia (EOS) from birth to 7 days usually <72 hours, late onset septicemia (LOS): 7 to 30 days and very late onset septicemia: 30 to 90 days. Early onset septicemia occurs either due to ascending infection following rupture of membranes or during the passage of baby through the infected birth canal or at the time of resuscitation in the labor room. Late onset sepsis (LOS) is considered to be of environmental origin, the pathogen being acquired through care giving practices in homes and hospitals.

EOS is caused by organisms prevalent in the genital tract or in the labor room and operation theater. In the west, early onset infections are mostly caused by Group B Streptococcus (GBS) and E. coli while in developing countries most cases are due to Gram negative organisms especially E. coli, Klebsiella and Enterobacter sp. About two-third cases of late onset septicemia are caused by Gram negative bacilli Klebsiella pneumonia, Enterobacter, E. coli, Pseudomonas aeruginosa, Proteus, Citrobacter while the rest are contributed by Gram positive organisms including coagulase negative Staphylococcus (CONS). Neonatal sepsis presents with nonspecific and subtle features, which often overlap with common non-infectious conditions. Alteration in feeding pattern is one of the most common findings manifesting as lethargy/poor activity, refusal to suck or unresponsiveness in a neonate who feed well before. EOS manifests commonly with respiratory symptoms and less frequently as septicemia or meningitis. LOS presents as generalized septicemia or may be localized to one organ systems.

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One of the most important differential diagnosis for EOS is perinatal asphyxia. Other common sepsis mimickers are hypoglycemia, temperature instability, respiratory distress syndrome and meconium aspiration syndrome. It can be diagnosed by:

1) Blood culture Isolation of the pathogen remains the gold standard method for the diagnosis of neonatal septicemia and should be done in all cases of suspected neonatal sepsis[7].
2) Sepsis Screen: It is considered positive when two or more of the following parameters exceed their cutoffs: TLC, ANC, I:T Ratio, CRP and Micro ESR
3) Lumbar puncture (LP)[8]: Indications for lumbar puncture are:
    a. In EOS: symptomatic infants and positive blood culture patients
    b. In all LOS cases

4) Other investigations:
    a. Culture of other sterile body fluids like urine, peritoneal/pleural/synovial tap
    b. Biomarkers- Procalcitonin, Interleukin-6
    c. Radiology: Chest X ray, abdominal X ray or cranial USG/CT

The rational use of antimicrobial agents in neonatal sepsis is governed by the knowledge of the prevalent bacterial flora of a particular newborn nursery and their sensitivity pattern against available antibiotics. Thus, a single empiric regimen cannot be universal. The spectrum of organisms that cause neonatal sepsis changes over times and varies from region to region. Periodic evaluation of organisms responsible for neonatal sepsis is essential for the appropriate management of neonates.

Therefore, this study was undertaken to determine the microbiological profile of bacterial infection in newborns and their antibiotic sensitivity pattern in a tertiary care neonatal unit, PIMS Lucknow

AIM AND OBJECTIVES:

1. To study bacteriological profile of neonatal sepsis.
2. To study the antibiotic sensitivity pattern of different bacterial pathogens isolated.

MATERIALS AND METHODS:

Study setting

The present study was conducted in the department of paediatrics, at Prasad Institute of Medical Sciences, Lucknow for the duration of one year.

Study design: Prospective hospital based study.
Sample size: 180 suspected cases of neonatal sepsis.
Study subjects: All neonates admitted in NICU fulfilling the inclusion criteria were enrolled in the study.
Inclusion Criteria:

a. age less than 28 years.
b. Duration of stay in hospital beyond 48 hours of admission.
c. Neonates with suspected neonatal sepsis.

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Exclusion Criteria:

a. Administration of antibiotics prior to admission.

b. Neonates with birth asphyxia and aspiration syndrome.

c. Neonates with congenital anomalies and inborn errors of metabolism.

Investigations

a. Blood for sepsis screen: total leukocyte counts (TLC), absolute neutrophil count, immature to total neutrophil ratio, c-reactive protein and micro-ESR

b. Blood for culture and sensitivity.

c. Serum electrolytes.

d. Serum Bilirubin- Total/Direct/Indirect.

e. Random blood sugar.

2-3 mL of blood was collected from each patients by the nursing personnel under aseptic precautions and inoculated immediately into 20 mL of glucose citrate broth with 0.025% of sodium polyanethol sulphonate as anticoagulant (HI media, a commercial firm). The broths were sub cultured on 5% sheep blood agar and Mac-Conkey agar after overnight incubation. A negative result was followed-up by examining the broth daily and doing a final subculture at the end of the seventh day. Positive growth was identified by Gram staining and antimicrobial susceptibility test was performed by Kirby-Bauer disk diffusion method as per NCCLS guidelines. The antibiotic discs to be used are Ampicillin (10 mg), Amoxiclav (20/10 mg), penicillin (10 units), Vancomycin (30 mg), Cephalexin (30 mg), Ceftazidime (30 mg), Ceftriaxone (30 mg), Gentamycin (10 mg), Tobramycin (10 mg), Amikacin (30 mg), Netilmicin (30 mg), Ciprofloxacin (5 mg), Chloramphenicol (30 mg), Tetracycline (30 mg), Trimethoprim/Sulfamethoxazole (1.25/23.75) and cefoperazone/sulbactam (75/30 mg). **Statistical analysis:** The data was analysed using SPSS Windows Version 16 and online GraphPad software.

RESULTS:

Table 1: Distribution of total cases

	Variable	Number	Percentage
Sex	Male	112	62.2
	Female	68	37.8
Type of Septicemia	EOS	119	66.1
	LOS	61	33.9
Type of isolates	Sterile	120	66.7
	Gram positive	23	12.8
	Gram negative	32	17.8
	Candida	5	2.7

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Table 2: Clinical presentation of study subjects		
Variable	**Number**	**Percentage**
Respiratory distress	135	75
Seizure	69	38.3
Refusal to feed	68	37.8
Lethargy	65	36.1
Temperature instability	45	25

Table 3: Distribution of culture isolates from neonatal septicemia positive cases			
Organism	**EOS (n=34) Number (%)**	**LOS (n=26) Number (%)**	**Total (n=60) Number (%)**
Gram positive			
Staph aureus	10 (29)	4 (15.4)	14 (23)
CONS	3 (9)	4 (15.4)	7 (12)
Enterococcus	1 (3)	0	1 (1)
Streptococcus	1 (3)	1 (3.8)	1 (3)
Gram Negative			
Pseudomonas	7 (21)	4 (15.4)	11 (18)
Acinetobacter	3 (9)	4 (15.4)	7 (11)
Ecoli	4 (12)	0	4 (7)
Klebsiella	2 (6)	1 (3.8)	3 (5)
Citrobacter	1 (3)	3 (11.5)	4 (7)
Burholderia	1 (3)	1 (3.8)	2 (3)
Enterobacter	0	1 (3.8)	1 (2)
Yeast			
Candida spp	2 (6)	3 (11.5)	5 (8)

Table 4: Sensitivity to Gram Positive Cocci

Organisms	Penicillin	Ampicillin	Amoxiclav	Cefoxitin	Erythromycin	Clindamycin	Co-trimoxazole	Gentamicin	Gentamicin (high level)	Ciprofloxacin	Vancomycin	Teicoplanin	Tetracycline	Doxycycline	Linezolid	Chloramphenicol
Staphylococcus aureus	9	36	52	42	25	58	24	40	..	33	100	100	75	78	100	19
Coagulase Negative Staphylococcus	0	28	60	40	8	56	20	32	..	32	100	100	72	72	100	80
Enterococcus sup.	..	20	..	..	0	..	0	..	15	25	50	50	75	75	100	50
Streptococcus pneumonia	30	..	..	..	75	100	75	100	..	75	100	100	100	100	100	100

Table 5: Sensitivity to Gram Negative Cocci

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Organisms	Ampicillin	Amoxicillin clavulanic	Cefoxitin	Ceftriaxone	Cefoperazone -sulbactam	Ceftazidime	Ceftazidime–clavulanic Acid	Clotrimaxazole	Gentamicin	Amikacin	Ciprofloxacin	Piperacillin - tazobactam	Ertapenem	Imipenem	Meropenem	Colistin	Tigecycline
Acinetobacter spp.	6	15	20	34	62	35	45	50	18	25	50	53	0	53	53	80	75
Citrobacter spp.	0	10	10	22	27	22	27	27	22	27	27	27	22	50	50	100	72
Enterobacter spp.	0	20	10	20	40	20	20	0	20	20	20	20	40	60	60	100	80
Escherschia coli	11	25	20	33	66	22	55	55	44	66	66	66	55	70	70	100	77
Klebsiella pneumoniac	7	15	20	21	28	21	21	28	21	50	50	35	57	50	50	100	92
Pseudomonas aeruginosa	0	0	0	0	58	75	78	50	15	33	77	77	0	60	60	70	0

Table 6: Correlation of mortality with blood culture sensitivity

Blood culture	Mortality (n=36) No (%)	Survival (n=144) No (%)	Total (n=180) No (%)
Positive	22 (36.7%)	38(63.3)	63(33.3)
Negative	14 (11.7%)	106(88.3%)	120(66.7)

DISCUSSION:

The present study was conducted in the department of paediatrics NICU of our tertiary care hospital. During the study period a total of 180 suspected cases of neonatal sepsis were included, as per the inclusion and exclusion criteria. The present study aimed to assess the micobiological profile of bacterial infection in neonates and their antibiotic sensitivity pattern at tertiary care neonatal unit.

Out of the total 180 cases studied, 112 were males and 68 were females accounting for 62.2% and 37.8% respectively. 119 patients had early onset septicaemia and 61 had late onset septicaemia, 23 patients had gram positive isolates, 32 had gram negative isolates and 5 had candida isolates as represented in Table 1. The clinical presentation of the study subjects, revealed 135 patients had respiratory distress, 69 had seizures, 68 had refusal to feed, 65 had lethargy and 45 had temperature instability as presented in Table 2.

Table 3 represents the distribution of culture isolates from neonatal septicemia positive cases. It is seen that the gram positive isolates, gram negative isolates and candida were seen in 15, 18 and 2 patients in early onset sepsis and 9, 14 and 3 patients in late onset sepsis group respectively. Out of 15 gram positive EOS cases, staph aureus was detected in 10, CONS in 3, Enterococcus in 1 and Streptococcus in 1 patient. Similarly, out of 9 LOS cases, staph aureus was detected in 4, CONS in 4, and Streptococcus in 1 patient. Gram negative isolates were seen in 18 patients in early onset sepsis and in 14 patients in late onset sepsis group. Out of 18 EOS cases, pseudomonas was detected in 7, Acinetobacter in 3, Ecoli in 4, klebsiella in 2, Citrobacter in 1, burholderia in 1 patient. Similarly, in LOS group pseudomonas was detected in 4, Acinetobacter in 4, Ecoli in none, klebsiella in 1, Citrobacter in 1, burholderia in 1 and Enterobacter in 1 patient. Candida was detected in 2 patients in EOS group and 3 patients in LOS group. Among neonates gram negative septicemia was more common compared to gram positive septicemia. Staph aureus was most common among gram positive and pseudomonas was more common among gram negative isolates. Antibiotic susceptibility showed that the gram positive organisms were highly sensitive to vancomycin, linezolid, teicoplanin and also

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sensitive to amoxycillin and clindamycin and were least sensitive to penicillin and ampicillin. Antibiotic susceptibility showed that the gram negative organisms were highly sensitive to colistin, tigecycline, meropenem and imipenem, and sensitive to ampicillin and gentamycin. An antibiotic policy should be formulated in our hospital and depending upon antibiotic sensitivity pattern of the isolated pathogen, antibiotic should be used, as presented in Table 4 & 5. In our study the mortality was 36.7% in culture positive cases while mortality was 11.7% in culture negative cases, the difference was statistically highly significant and the association of mortality with culture positivity was statistically significant as presented in Table 6. The findings of our study were similar to the studies conducted by other authors [7-12].

CONCLUSION:

Neonatal septicemia is an life threatening emergency and rapid treatment with antimicrobial agent is highly essential for favorable outcome. For the effective management of the cases with neonatal septicemia, the study of microbiological profile with their antibiotic sensitivity pattern always plays a significant role. In our study, the prevalence of neonatal sepsis was found to be 33.3% and the prevalence was higher in males compared to females. Among the neonates 56.7% had early onset sepsis and 43.3% had late onset sepsis. The clinical presentation was studied in all the patients, it was found that the most common clinical symptom was respiratory distress and pneumonia was more common in early onset sepsis. Among neonates gram negative septicemia was more common compared to gram positive septicemia. Staph aureus was most common among gram positive and pseudomonas was more common among gram negative isolates. Antibiotic susceptibility showed that the gram positive organisms were highly sensitive to vancomycin, linezolid, teicoplanin and also sensitive to amoxycillin and clindamycin and were least sensitive to penicillin and ampicillin. Antibiotic susceptibility showed that the gram negative organisms were highly sensitive to colistin, tigecycline, meropenem and imipenem, and sensitive to ampicillin and gentamycin. An antibiotic policy should be formulated in our hospital and depending upon antibiotic sensitivity pattern of the isolated pathogen, antibiotic should be used. In our study the mortality was 36.7% in culture positive cases while mortality was 11.7% in culture negative cases, the difference was statistically highly significant and the association of mortality with culture positivity was statistically significant.

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