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CULTURE AND SENSITIVITY PATTERNS OF SEPSIS IN NEWBORNS

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Abstract

Introduction

As neonatal sepsis is associated with many complications and high mortality, proper policy regarding antimicrobial strategy is of very much importance and should be individualized according to predominant organisms and their sensitivity patterns of individual NICU of the corresponding institute.

Objectives

To determine the frequency of micro-organisms causing sepsis in neonates requiring ventilator support and to determine the sensitivity patterns of those micro-organisms.

Methodology

A total of 130 neonates with sepsis after 48 hours of having ventilation were included. Patients with congenital CNS anomaly, like hydrocephalus, meningomyelocele, renal anomalies and congenital anomalies like gastroschisis, omphalocele were excluded. Those meeting the exclusion criteria were excluded and rest were evaluated for inclusion by sending blood culture, urine culture and CSF culture. Antibiotic susceptibility of organisms was tested by Disc diffusion method. In it the organisms were grown on agar plate and exposed to antibiotic disc.

Results

In this study, I have found the E. coli as the most common organism and found in 16.92% cases, followed by Pseudomonas aeruginosa 8.46%, Staphylococcus aureus 10.0%, Kleibsella in 11.54% and Staphylococcus epidermidis in 3.08%.

Conclusion

This study has shown that the E. coli as the most common organism followed by Pseudomonas aeruginosa, Staphylococcus aureus, Kleibsella and Staphylococcus epidermidis in neonatal sepsis

INTRODUCTION

Neonatal sepsis (NS) is a serious problem that presents a management challenge to neonatologists and other caregivers around the world. Neonates are at the greatest risk for bacterial sepsis, with the prevalence at 1 to 10 per 1000 live births around the world.[1, 2] In Africa, south Asia and Latin America; the case fatality risk associated with neonatal sepsis is 9.8%.[3] A study conducted in tertiary care hospital of Pakistan shows that sepsis causes about 26% of

neonatal deaths.[4] Despite being highly preventable, sepsis causes 10% of maternal and 26% of neonatal death.[5] Over the past 2 decades, sepsis has caused increased mortality by approximately 13.7% every year.[6] Sepsis carries the greatest burden on developing countries; sepsis related mortality rate was estimated as high as 50% for untreated infants. Thus, this formed a major cause of infant fatality during the 1st month of life. According to the international pediatric sepsis consensus conference of 2005, neonatal sepsis is defined as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate. Infection could be of viral, bacterial, fungal or rickettsial origin.[7-9] In one study held in 2016, 15 (31.3%) neonates were found to be culture positive. Klebsiella species was most common (33.3%) organism isolated, followed by Pseudomonas aeruginosa (20%).10 Most common antibiotic found to be sensitive was Meropenem (86.67%), followed by Colistin and Tigecycline (80% each).[10] Depending on the onset age of the disease, neonatal sepsis is divided into early neonatal sepsis or late onset sepsis. Early neonatal sepsis is acquired before and during delivery. Late onset sepsis is acquired after delivery. There is little consensus as to what age limits applies with early onset before and late onset after the 1st week of life.[8] Neonates with bacterial sepsis present with either nonspecific signs and symptoms or focal signs of infection including tachycardia or bradycardia, respiratory distress or apnea, cyanosis, temperature instability, irritability, lethargy, seizures, feeding intolerance, petechiae, purpura and bleeding.[8] Complications of sepsis include the respiratory failure, cardiac failure, cerebral edema, liver dysfunction, renal failure, adrenal hemorrhage, bone marrow dysfunction and DIC.[8] Recent advances in diagnosing and managing sepsis, can reduce its complications, and mortality, and improve its outcome, especially in preterm infants.[9] Bacterial resistance to commonly used antibiotics and increased use of invasive procedures has led to a rise in the incidence of sepsis in recent years. And this may be because of widespread use of common antibiotics.[10] Due to poor response to initial empirically started antibiotics, up gradation of the antibacterial regimen is often indicated after results of blood culture.[10]

Methodology:

Descriptive, cross-sectional study. Neonatal intensive care unit, of PAEC GENERAL Hospital.20th December 2019 to 19th June 2020.Calculated by using WHO calculator [10] Confidence interval 95% Anticipated population proportion 31.3% Absolute precision required 8% Minimum sample size 130. Non-probability, consecutive sampling. Newborn aged less than 4 weeks Newborn fulfilling the operational definition of sepsis. Patient who didn't receive antibiotic in past. Patient with no recent surgery. Newborn after 48 hours of having ventilation.

Major congenital CNS anomaly, like hydrocephalus, meningomyelocele. Congenital renal anomalies or urinary tract malformations. Other congenital anomalies like gastroschisis, omphalocele. Referred from any other neonatal care unit.

Study had been approved by ethical committee of the hospital. All children under 1 month of age, admitted in NICU of PAEC GENERAL Hospital were evaluated for enrolment in study by taking complete history to look for evidence of sepsis like hypothermia, hyperthermia, tachypnea, hypotension, seizures, inability to feed and lethargy. Those meeting the exclusion criteria were excluded and rest were evaluated for inclusion by sending blood culture, urine culture and CSF culture. Informed consent was taken from parent/guardians. Personal data, name, age, sex, fathers name, hospital number was entered in individual performa by me in isolation. 5ml of clean urine sample was collected in a sterile container and processed within one hour of collection using standard methods. A sterile 3mm platinum wire calibrated loop was used which delivered 0.01ml of urine. This loopful urine sample was inoculated on CLED medium, blood agar and MacConkey agar, and incubated aerobically at 370C overnight and read to assess the growth of significant bacteria. Bacterial

identification was based on standard culture and biochemical characteristics of isolates.

The volume of the blood, drawn from infants was based on child's age and was not exceeded 1% of the patients total blood volume. Strict aseptic measures were used before taking sample. Tincture of iodine or chloride peroxide was applied before sample collection. Aerobic and anaerobic culture bottles was taken. Aerobic bottles were filled 1st. Specimen was kept at room temperature. Commonly used media are Trypticase Soya broth and Brain Heart Infusion (BHI) broths. The bottles are incubated at 370C aerobically and examined daily for visible turbidity. Bacterial identification was based on standard culture and biochemical characteristics of the isolates.14 CSF was obtained by lumber puncture, collected in a culture bottle and was kept at 370C in an incubator. Culture media used for CSF are blood agar, chocolate agar and McConkey agar plates and inoculated into a thioglycollate broth tube. Plates were incubated in carbon dioxide at 350C, and broth tubes were incubated in room air at 350C. L.J medium was used if Tuberculous Meningitis is the suspicion. Culture plates were read manually daily, generally in the morning hours.15 If growth is present, bacterial identification was done based on standard culture and biochemical characteristics of the organism.

Antibiotic susceptibility of organisms was tested by Disc diffusion method. In it the organisms were grown on agar plate and exposed to antibiotic disc. The zone of growth inhibition around each antibiotic disc was measured. The diameter of the zone was related to the susceptibility of the isolate and to the diffusion rate of the drug through the agar medium. The zone diameter of each drug was interpreted using the criteria published by CLSI.13

All data was entered in SPSS version-20 for analysis. Mean and SD was calculated for age and duration of ventilation. Qualitative variables like gender, microorganism, sensitivity, resistance were measured in terms of frequency and percentages and were presented through tables and charts Effect modifiers like early onset or late onset sepsis, duration of ventilation, antibiotic use, maternal infection, and mode of delivery were controlled by stratification and post stratification chi-square test was applied. P value less than 0.05 was significant.

Results:

Mean age of neonates was 3.43 ± 1.33 days. Mean duration of ventilation was 5.44 ± 2.26 days (Table II). Distribution of patients according to mode of delivery and sepsis is shown in Table II & III respectively. Distribution of patients according to antibiotic use and maternal infection is shown in Table IV & V respectively. In this study, I have found the E. coli as the most common organism and found in 16.92% cases, followed by Pseudomonas aeruginosa 8.46%, Staphylococcus aureus 10.0%, Kleibsella in 11.54% and Staphylococcus epidermidis in 3.08%. (Table VI). Antibiotic susceptibility pattern of various pathogens is shown in table VII. Stratification of micro-organisms with respect to duration of ventilation and mode of delivery is shown in Table VIII & IX respectively. Stratification of micro-organisms with respect sepsis, antibiotic use and maternal infection is shown in Table X, XI & XII respectively.

Table-I: Distribution of patients according to duration of ventilation (n=130).

Age (in days)	No. of Patients	%age
≤5	95	73.08
>5	35	26.92
Total	130	100.0

- **Mean ± SD = 5.44 ± 2.26 days**

Table-II: Distribution of patients according to mode of delivery (n=130).

Mode of delivery	No. of Patients	%age
SVD	61	46.92
Cesarean section	69	53.08
Total	130	100.0

Table-III: Distribution of patients according to sepsis (n=130).

Sepsis	No. of Patients	%age
Early	58	44.62
Late	72	55.38
Total	130	100.0

Table-IV: Distribution of patients according to antibiotic use (n=130).

Antibiotic use	No. of Patients	%age
Yes	94	72.31
No	36	27.69
Total	130	100.0

Table-V: Distribution of patients according to maternal infection (n=130).

Maternal infection	No. of Patients	%age
Yes	56	43.08
No	74	56.92
Total	130	100.0

Table VI: Frequency of micro-organisms causing sepsis in neonates requiring ventilator support

micro-organisms	Frequency	Percentage
Escherichia Coli	22	16.92
Kleibsella	11	8.46
Staphylococcus aureus	13	10.0
Pseudomonas aeruginosa	15	11.54
Staphylococcus epidermidis	04	3.08
No organism	65	50.0

Table VII: Antibiotic susceptibility pattern of various pathogens

Antibiotic	Sensitive	Resistant
Ampicillin	34.74%	65.26%
Amoxacillin-clavulanate	27.37%	72.63%
Trimethoprin-sulfamethoxazole	40.0%	60.0%
Ceftriaxone	54.74%	45.26%
Cefipime	49.47%	50.53%
Ciprofloxacin	35.79%	64.21%
Imipenem	89.47%	10.53%
Meropenem	93.68%	6.32%
Cefoperazone-sulbactam	78.95%	21.05%
Pipercallin-tazobactam	72.63%	27.37%
Gentamicin	27.37%	72.63%
Polymyxin B(300ug)	92.63%	7.37%

Table VIII: Stratification of micro-organisms with respect to duration.

		≤5 days (n=95)	>5 days (n=35)	P-value
Escherichia Coli	Yes	14	08	0.273
	No	81	27	
Kleibsella	Yes	05	06	0.033
	No	89	29	
Staphylococcus aureus	Yes	11	02	0.323
	No	84	33	
Pseudomonas aeruginosa	Yes	09	06	0.225
	No	86	29	
Staphylococcus epidermidis	Yes	04	00	0.218
	No	91	35	

Table IX: Stratification of micro-organisms with respect to mode of delivery.

		SVD (n=61)	CS (n=69)	P-value
Escherichia Coli	Yes	14	08	0.085

	No	47	61	
Kleibsella	Yes	00	11	0.001
	No	61	58	
Staphylococcus aureus	Yes	10	03	0.022
	No	51	66	
Pseudomonas aeruginosa	Yes	10	05	0.103
	No	51	64	
Staphylococcus epidermidis	Yes	03	01	0.253
	No	58	68	

Table X: Stratification of micro-organisms with respect to sepsis.

		Early (n=58)	Late (n=72)	P-value
Escherichia Coli	Yes	09	13	0.701
	No	49	59	
Kleibsella	Yes	04	07	0.565
	No	54	65	
Staphylococcus aureus	Yes	06	07	0.906
	No	52	65	
Pseudomonas aeruginosa	Yes	05	10	0.350
	No	53	62	
Staphylococcus epidermidis	Yes	03	01	0.214

	No	55	71	

Table XI: Stratification of micro-organisms with respect to antibiotic use.

		Yes (n=94)	No (n=36)	P-value
Escherichia Coli	Yes	17	05	0.568
	No	77	31	
Kleibsella	Yes	08	03	0.974
	No	86	33	
Staphylococcus aureus	Yes	08	05	0.360
	No	86	31	
Pseudomonas aeruginosa	Yes	12	03	0.479
	No	82	33	
Staphylococcus epidermidis	Yes	02	02	0.311
	No	92	34	

Table XII: Stratification of micro-organisms with respect to maternal infection.

		Yes (n=56)	No (n=74)	P-value
Escherichia Coli	Yes	08	14	0.485
	No	48	60	
Kleibsella	Yes	06	05	0.422
	No	50	69	
Staphylococcus aureus	Yes	05	08	0.723
	No	51	66	

Pseudomonas aeruginosa	Yes	08	07	0.394
	No	48	67	
Staphylococcus epidermidis	Yes	00	04	0.077
	No	56	70	

Discussion:

Neonatal sepsis is a clinical syndrome (sepsis neonatorum) resulting from the pathophysiologic effects of local or systemic infection. It affects newborns below 1 month of age and encompasses systemic infections including meningitis, pneumonia, arthritis; osteomyelitis and urinary tract infections.[11-12] Neonates are immune-compromised and defend weakly to bacterial infections. The bacterial agents associated with neonatal sepsis are Group B Streptococci, Escherichia coli, Listeria monocytogenes, coagulase-negative Staphylococci (CoNS), Staphylococcus aureus, Enterococci, Klebsiella spp., Enterobacter spp., Pseudomonas spp., Salmonella spp., H. influenzae, Neisseria meningitidis, and Streptococcus pneumoniae.[13-15]

In developing countries, unsafe birthing practices have critical role to cause neonatal infections. Globally, the neonatal morbidity and mortality cases have been estimated to 2.5–3 million, annually.[16] Neonatal mortality rate (NMR) distribution disparities can be seen based on socioeconomic, educational and geographical parameters. In Nepal, neonatal mortality has been found due to septicemia and emergence of drug resistant bacteria. According to Nepal Demographic and Health Survey (2011), 85% of total death is accounted to neonatal sepsis which is higher than previous surveys, 70% in 2006 and 69% in 2001.[17] NMR is higher in rural areas (34 deaths per 1000 live births) than in urban areas (23 deaths per 1000 live births). Currently, emergence of multidrug resistant bacteria imposes challenges in treatment of neonatal sepsis.[18-19] I have conducted this study to determine the frequency of micro-organisms causing sepsis in neonates requiring ventilator support and to determine the sensitivity patterns of those micro-organisms. In my study, I have found the E. coli as the most common organism and found in 16.92% cases, followed by Pseudomonas aeruginosa 8.46%, Staphylococcus aureus 10.0%, Kleibsella in 11.54% and Staphylococcus epidermidis in 3.08%. In one study held in 2016, 15 (31.3%) neonates were found to be culture positive. Klebsiella species was most common (33.3%) organism isolated, followed by Pseudomonas aeruginosa (20%). Kari et al found that Group B streptococcus (GBS) is the most common etiological agent, while Escherichia Coli (E. coli) is the most common cause of mortality [20].

Conclusion:

This study has shown that E. Coli as the most common organism followed by Pseudomonas aeruginosa, Staphylococcus aureus, Kleibsella and Staphylococcus epidermidis in neonatal sepsis. So, we recommend that early identification and management of these etiological agents should be done in order to decrease morbidity and mortality.

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