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Bacteriological Profile of Neonatal Septicaemia and Antibiotic Susceptibility Pattern of the Isolates Admitted in SCANU of a Tertiary Levels Hospital of North Bengal, Bangladesh

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Abstract

***Introduction*:** Neonatal septicemia is one of the most common causes of infection and mortality in neonates, due to which 30–50% of neonates die each year in developing nations. Various studies have suggested that bacteremia occurs in 20% of neonates, and approximately 1% die due to neonatal sepsis. It affects newborns below 1 month of age and encompasses systemic infections including meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infections. ***Objective*:** To assess the Bacteriological profile of neonatal septicaemia and antibiotic susceptibility pattern of the isolates admitted in SCANU of a tertiary levels hospital of North Bengal, Bangladesh. ***Methods*:** A prospective study was conducted including 50 suspected cases of septicemia admitted to the Special Care Neonatal Unit (SCANU) of the selected Department of Paediatrics, TMSS Medical College, Bogura Bangladesh July to December 2022. Demographic data included birth weight, gestational age, postnatal age, and treatment as well as survival outcome. Clinical and laboratory data included the number of days between birth and admission to the SCANU, admitting and discharge diagnoses, and pharmacological treatment. Data was analysed by percentages of each antibiotic used. And which organism was responsible for neonatal sepsis. ***Results*:** Total 50 cases clinically suspected neonatal sepsis were included in the study. The mean age was 8.33±7.36 days, mean birth weight was 2816.25±288.6gm, male were predominant which was 70%. Among gestational age of the Neonates having septicemia Preterm (<37) 66% and Term (37 up to 42) 36%. Out of the 50 proven sepsis cases, 36 cases (72%) were early onset and 14 cases (28%) were late onset. In this study out of 50 cases 16 cases were culture positive septicemia which was 32%. Gram negative organism were predominant with 10 isolates (62.5%) in comparison to gram-positive 6 (37.5%) isolates was the most common S. aureus (25.0%) and E. coli (12.5%) among the organism isolated. Other organisms isolated were Staphylococcus Pneumoniae (6.3%), Staphylococcus epidermidis (18.7%), Proteus (18.7%), Listeria species (6.3%), Pseudomonas (6.3%), and Enterococci (6.3%). In this study, Staphylococcus aureus was the commonest organism isolated from both EOS (20%) and LOS (33.3%) followed by Staphylococcus epidermidis (10% & 33.3%). Amoxiclave is highly sensitive to S. aureus & E. coli. In this study, vancomycin showed 25.0% sensitivity to S. aureus but for Nitrofurantoin it was only 33.3%. The Listeria species isolates here were 100% sensitive to meropenum. In our study, ciprofloxacin showed 33.3% to 100% sensitivity to different isolates. ***Conclusion*:** In the present study, high bacterial resistance among the pathogens suspected to cause neonatal septicemia is demonstrated which can be controlled by prudent use of available antibiotics. This study suggests regular monitoring of the antimicrobial sensitivity of the causative organisms in a particular setting is very important.

Keywords: Neonatal Sepsis, Antibiotics, Microorganism, Bacteriological Profile.

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INTRODUCTION

Neonatal septicemia is one of the most common causes of infection and mortality in neonates, due to which 30– 50% of neonates die each year in developing nations. Various studies have suggested that bacteremia occurs in 20% of neonates, and approximately 1% die due to neonatal sepsis [1]. It affects newborns below 1 month of age and encompasses systemic infections including meningitis, pneumonia, arthritis, osteomyelitis and urinary tract

infections [1, 2]. In developing countries, unsafe birthing practices have critical role to cause neonatal infections. World Health Organization has estimated that 1.6 million deaths occur globally every year due to neonatal infections and 40% of all neonatal deaths occur in developing countries. Globally, the neonatal morbidity and mortality cases have been estimated to 2.5–3 million, annually [3]. Neonatal mortality rate (NMR) distribution disparities can be seen based on socioeconomic, educational and geographical parameters. The major cause of mortality in neonates is neonatal sepsis in developing countries. It may be presented nonspecific clinical signs and may lead to severe consequences [4, 5]. According to Global Health Observatory data suggest, in 2016, 2.6 million neonates died. Prematurity, low birth weight, infections, asphyxia and birth trauma are main cause of neonatal death. Around one third death in neonates world widely cause by sepsis [6]. Definition of neonatal septicemia is a clinical syndrome characterized by systemic signs and symptoms of inflammatory response following the appearance or confirmation of infection during the first month of life [6, 7]. Neonatal septicemia can be divided into early onset in the first 7 days of life and late onset after the first 7 days of life. The most important risk factors for early onset septicemia related to the mother (early rupture of membrane and the long duration of time for the birth of the baby) and at the same time the risk factors for infection related to fetus are prematurity. Nosocomial infections are the most significant risk factor in late neonatal septicemia [8]. There is atypical presentation of early signs and symptoms of neonatal infection especially sepsis it lack specificity. The symptoms are like primary apnea, simple febrile disease, feeding intolerance, anemia and other non-infectious diseases, which are difficult to diagnose which is responsible for delay in treatment or may lead to overtreatment [8, 9]. Early diagnosis of neonatal septicaemia and initiation of proper antibiotic is main in treatment.

MATERIALS & METHODS

A prospective study was conducted including 50 suspected cases of septicemia admitted to the Special Care Neonatal Unit (SCANU) of the selected Department of Paediatrics, TMSS Medical College, Bogura Bangladesh July to December 2022. According to the American Academy of Pediatrician (AAP) classification, the SCANU of this hospital falls in level-II (A) neonatal care facility [10].

Inclusion and exclusion criteria: Septicemia was suspected from clinical history, if one or more of the following symptoms were present: lethargy, refusal to feeds, abdominal distension, vomiting, grunting, respiratory distress, hypothermia, hyperthermia, sclerema with or without supporting evidence of risk factors such as prematurity, low birth weight, history of prolong rupture of membrane (>18h). Neonates with extreme prematurity, respiratory distress syndrome (RDS) and gross congenital anomalies were excluded from this study.

Demographic data included birth weight, gestational age, postnatal age, and treatment as well as survival outcome. Clinical and laboratory data included the number of days between birth and admission to the SCANU, admitting and discharge diagnoses, and pharmacological treatment. The culture bottles were incubated immediately at 37°C for 5–7 days and were examined daily for growth and turbidity, hemolysis of red cells, gas bubbles and clot formation of discrete colonies. This helps in the presumptive diagnosis of positive broth culture. After incubation, subcultured from BHI broth was performed on blood agar (BA; HiMedia, M073) and MacConkey agar (MA; HiMedia, M081). The MA plates were incubated aerobically and BA plates were incubated anaerobically using BBL anaerobic jar with a GasPak™ EZ Gas Generating Container (Becton–Dickinson) at 37°C for 24h. The pure isolates obtained from subcultured plates were identified by following standard microbiological techniques which include studies of colony morphology, Gram-staining reactions and various biochemical properties (catalase and oxidase tests, slide and tube coagulase tests, SIM, MRVP, citrate, triple sugar iron, urease tests) [11-13].

Neonates were classified as having proven sepsis, probable sepsis, or other infection. We defined proven sepsis based on clinical signs, laboratory findings, and confirmation by blood culture. A positive blood culture was considered growth within 5 days on BacT/ALERT PF culture medium using minimum of 0.5 cc of blood with 2 cultures performed if possible. Patients with clinical symptoms and/or laboratory findings with no growth on culture medium were considered to have probable sepsis. Other infections were defined by clinical diagnosis. Culture-positive sepsis was categorized as early onset sepsis, defined as 0-6 days, and late onset sepsis, defined as 7 days-3 months. Only patient data from those admitted in study period included pharmacological treatment information.

All the data were entered in the worksheet of SPSS software version (21.0) and Chi square test was performed. P value was calculated and considered significant only when it was less than or equal to 0.05.

RESULTS

Table 1: Distribution of Sex (N=50)

Sex	N	%
Male	35	70%
Female	15	30%

Total 50 cases clinically suspected neonatal sepsis were included in the study. The mean age was 8.33±7.36 days, mean birth weight was 2816.25±288.6gm, male were predominant which was 70% (Table-I).

Table 2: Gestational age (Weeks) (N=50)

Variable	N	%
Preterm (<37)	32	66%
Term (37 up to 42)	18	36%

Table-2 shows that Gestational Age of the Neonates having septicemia Preterm (<37) 66% and Term (37 up to 42) 36%. In addition, 70% of neonates were born weighing between 2.00 and 3.50 kg, 1% were born above 4.0 kg, and 29% weighed between 1.00-1.5 kg.

Table 3: Mode of delivery (N=50)

Variables	N	%
Normal	12	24%
Caesarean section	38	76%

Table-3 shows that, mode of delivery normal cases 24% and CS 76%.

Table 4: Onset of proven sepsis cases (N=50)

Variables	N	%
Early	36	72%
Late	14	28%

Out of the 50 proven sepsis cases, 36 cases (72%) were early onset and 14 cases (28%) were late onset.

Table 5: Blood culture findings (N=50)

Blood culture	N	%
Culture positive	16	32%
Culture negative	34	68%

In this study out of 50 cases 16 cases were culture positive septicemia which was 32% (Table-5).

Table 6: Pattern of organisms isolated from blood cultures (n=15)

Organisms	EOS		LOS		Total	
	No.	(%)	No.	(%)	No.	(%)
Staphylococcus aureus	2	20.0	2	33.3	4	25.0
Staphylococcus Pneumoniae	1	10.0	0		1	6.3
Staphylococcus epidermidis	1	10.0	2	33.3	3	18.7
Proteus	2	20.0	1	16.7	3	18.7
Escherichia Coli	1	10.0	1	16.7	2	12.5
Listeria species.	1	10.0	0		1	6.3
Pseudomonas	1	10.0	0		1	6.3
Enterococci	1	10.0	0		1	6.3
Total	**10**	**62.5**	**6**	**37.5**	**16**	**100.0**

Blood cultures EOS were predominant with 10 isolates (62.5%) in comparison to LOS 6 (37.5%) isolates were the most common S. aureus (25.0%) and E. coli (12.5%) among the organism isolated. Other organisms isolated were Staphylococcus Pneumoniae (6.3%), Staphylococcus epidermidis (18.7%), Proteus (18.7%), Listeria species (6.3%), Pseudomonas (6.3%), and Enterococci (6.3%). In this study, Staphylococcus aureus was the commonest organism isolated from both

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EOS (20%) and LOS (33.3%) followed by Staphylococcus epidermidis (10% & 33.3%) (Table-6).

Table 7: Sensitivity pattern of organisms isolated on blood culture of septicaemic neonates (N=15)

Percentage of cases								
Antibiotics	**Staphylococcus aureus (n=4)**	**Staphylococcus Pneumoniae (n=1)**	**Staphylococcus epidermidis (n=3)**	**Proteus (n=3)**	**Escherichia Coli (n=2)**	**Listeria species (n=1)**	**Pseudomonas (n=1)**	**Enterococci (n=1)**
Amoxiclave	100.0	0	100.0	0	100.0	100	100	100
Amikacin	100.0	100.0	66.7	66.7	100.0	100	100	100
Gentamicin	100.0	100.0	0	66.7	100.0	0	0	100
Co-Trimoxazole	75.0	0	33.3	33.3	50.0	0	0	100
Meropenum	100.0	0	0	66.7	100.0	100	100	100
Linezolid	75.0	100.0	66.7	33.3	50.0	100	0	100
Flucloxacillin	25.0	0	0	0	0	0	0	0
Ceftriaxone	25.0	0	0	33.3	50.0	0	0	0
Ceftrazidime	0	0	0	0	50.0	0	0	0
Cefipime	50.0	0	0	0	0	0	0	0
Cefuroxime	50.0	0	0	33.3	50.0	0	0	0
Ciprofloxacin	100.0	0	33.3	33.3	100.0	100	100	0
Levofloxacin	100.0	0	33.3	33.3	100.0	100	0	0
Piperacillin+ Tazobactum	100.0	0	66.7	33.3	50.0	100	100	100
Azithromycin/ Clarithromycin	0	0	0	33.3	0	100	0	0
Colistin	0	0	0	33.3	0	0	0	0
Nitrofurantoin	0	0	33.3	0	50.0	100	0	0
Vancomycin	25.0	100.0	66.7	33.3	50.0	100	100	0

The antimicrobial susceptibility pattern of the isolates (Table-7) revealed that amoxiclave the commonly used antibiotic in our NICU & SCANU is 100% is highly sensitive to S. aureus & E. coli, the main causative pathogen; but 100% sensitive to amikacin & piperacillin+ tazobactum. Gentamicin was less sensitive to Staphylococcus aureus (100.0%), Staphylococcus pneumoniae (100.0%) & Escherichia Coli (100.0%). Whereas, amikacin was highly sensitive to Staphylococcus aureus (100.0%) and Staphylococcus pneumoniae (100.0%) in our study. In this study, vancomycin showed 25.0% sensitivity to S. aureus but for Nitrofurantoin it was only 33.3%. The Listeria species isolates here were 100% sensitive to eropenum. In our study, ciprofloxacin showed 33.3% to 100% sensitivity to different isolates. During our study, the sensitivity dics for all the antibiotics were not available always.

DISCUSSION

Neonatal infection by systemic infections is around 1.6 million every year, mostly in middle- and low-income countries [14]. Research studies in South-east Asian reported high resistance to antibiotics used commonly for empirical treatment of neonatal sepsis [15]. Most of the studies stated that widespread use of third-generation cephalosporins and lack of reliance on blood culture reports could be a major cause for this resistance. This study was planned to evaluate causative organisms of neonatal sepsis and their antibiotic sensitivity pattern in a setting with third-generation cephalosporin use because now a day in clinical practices negligible amount of third generation cephalosporin are use. Neonatal bacterial sepsis is a major cause of death in developing countries like Bangladesh. The emergence of antibiotics resistant bacteria and its dissemination is exacerbated by inappropriate antimicrobial consumption and precarious living condition. The most common organisms associated with neonatal sepsis vary with time of infections and geographical location [16]. Therefore, information on bacteriological profile of neonatal sepsis and effective antimicrobials for its treatment are important to combat with neonatal morbidity and mortality issues. Most of these referred cases had the history of antibiotics therapy prior to referral. Total 50 cases clinically suspected neonatal sepsis were included in the study. The mean age was 8.33±7.36 days, mean birth weight was 2816.25±288.6gm, male were predominant which was 70%. The finding of prevalence of positive blood culture in relation to different neonatal risk factors can be useful to determine the preventive measures for neonatal sepsis. The higher rate of growth positivity was observed in male compared to female neonates. These finding is in agreement with previous studies [14-16]. The prevalence of positive blood culture was found to be higher in 3 or above 3 days of age (late onset of sepsis) compared to below 3 days of age (early onset of sepsis). Most of the previous studies have shown similar pattern of high prevalence of neonatal sepsis in late onset of sepsis [9, 17]. Prolonged use of invasive ventilator and catheter, failure of early breast feeding, longer use of parenteral nutrition, hospitalization, surgery, cardiovascular diseases, and respiratory infections lead to late onset of sepsis among neonates [18, 19]. Positive blood culture was observed

high (30%) in low birth weight neonates. The low birth weight is strong neonatal risk factor that leads to cause neonatal sepsis [14]. This study showed highest infection among preterm neonates compared to term neonates. The most predisposing factors of infection in neonates are premature birth and low birth weight. Preterm neonates have 3 to tenfold higher incidence of infections than full term normal birth weight infants [19]. The neonates delivered by caesarean section showed the highest positive blood culture compared to normal deliver. Studies have revealed increased risk of neonatal death delivered by caesarean compared to vaginal delivery [20]. Blood cultures EOS were predominant with 10 isolates (62.5%) in comparison to LOS 6 (37.5%) isolates were the most common S. aureus (25.0%) and E. coli (12.5%) among the organism isolated. Other organisms isolated were Staphylococcus Pneumoniae (6.3%), Staphylococcus epidermidis (18.7%), Proteus (18.7%), Listeria species (6.3%), Pseudomonas (6.3%), and Enterococci (6.3%). In this study, Staphylococcus aureus was the commonest organism isolated from both EOS (20%) and LOS (33.3%) followed by Staphylococcus epidermidis (10% & 33.3%). These bacterial strains are predominant causative agents which have been identified by several studies [8, 9, 11, 13, 15]. This study has shown the frequency of isolation of Gram-negative bacteria was higher compared to Gram-positive bacteria. The causative organism varies due to geographical area. Neonates have high chance to acquire large proportion of vaginal Gram-negative bacteria [8]. Among the Gram-positive isolates, S. aureus is predominant hospital acquired organism. Furthermore, S. aureus has greater chance of transmission from health care workers and relatives to neonates [21]. Among Gram-negative isolates, K. pneumoniae accounts the highest which causes infection in neonates. This finding was similar with previous studies conducted among neonates [22, 23]. The antimicrobial susceptibility pattern of the isolates revealed that amoxiclave the commonly used antibiotic in our NICU & SCANU is 100% is highly sensitive to S. aureus & E. coli, the main causative pathogen; but 100% sensitive to amikacin & piperacillin+ tazobactum. Gentamicin was less sensitive to Staphylococcus aureus (100.0%), Staphylococcus pneumoniae (100.0%) & Escherichia Coli (100.0%). Whereas, amikacin was highly sensitive to Staphylococcus aureus (100.0%) and Staphylococcus Pneumoniae (100.0%) in our study. In this study, vancomycin showed 25.0% sensitivity to S. aureus but for Nitrofurantoin it was only 33.3%. The Listeria species isolates here were 100% sensitive to meropenum. In our study, ciprofloxacin showed 33.3% to 100% sensitivity to different isolates. During our study, the sensitivity dics for all the antibiotics were not available always. Antimicrobial sensitivity pattern differs in different places, in different studies, as well as at different time in the same hospital. Indiscriminate use of antibiotics leads to emergence of resistant strains of pathogens. High resistance observed in this study may be primarily due to excessive and irrational use of these antibiotics at primary health facilities from where neonates are referred to our tertiary centers. We also do not adopt antibiotic regimen timely based on antibiogram in our NICU, SCANU and nurseries. Neonatal infection by systemic infections is around 1.6 million every year, mostly in middle- and low-income countries [15]. Research studies in South-east Asian reported high resistance to antibiotics used commonly for empirical treatment of neonatal sepsis [16]. Most of the studies stated that widespread use of third-generation cephalosporins and lack of reliance on blood culture reports could be a major cause for this resistance. The antibiotic sensitivity test of bacterial strains isolated from this study provides insight for selection of appropriate drugs for further control of neonatal mortality rate. Ampicillin and amoxycillin which have been revealed as ineffective drugs might be due to emergence of antimicrobial genes in bacteria and inappropriate use of antibiotics prior to hospitalization of neonatal cases [8, 13]. In overall, neonatal septicemia is a life threatening emergency and its rapid treatment with antibiotics is essential. The knowledge of the etiological organisms of neonatal sepsis and their antibiotic susceptibility profile is necessary for effective therapeutic intervention. It is therefore important to note that commencement of empirical antibiotic therapy is of essence while awaiting blood culture result. The initial empiric antibiotic use must therefore be a combination of drugs to cover for the prevalent bacterial organisms in that locality. There is still a lack of data on the incidence of neonatal sepsis in different age groups in various regions of developing countries. The current study highlights the importance of primary care physicians in counseling and providing the basic antenatal care which can reduce low-birth-weight and pre-term births and identifying the risk factors in neonates which may lead to neonatal sepsis and timely referral of such neonates to higher centers for treatment. Primary care physicians play a key role in preventing antibiotic resistance and using antibiotics judiciously.

CONCLUSION

In the present study, high bacterial resistance among the pathogens suspected to cause neonatal septicemia is demonstrated which can be controlled by prudent use of available antibiotics. This study suggests regular monitoring of the antimicrobial sensitivity of the causative organisms in a particular setting is very important. The judicial use or limited use of the antibiotics can decrease the resistance pattern in the bacteria. As in our setup third-generation cephalosporin is still sensitive. Proper antibiotic guidelines and its effective implementation could be milestone for revolution in the field of antibiotic resistance control. The epidemiology of neonatal sepsis, causative risk factors and antibiotic resistance pattern of pathogens may be used to develop guidelines for management of neonatal sepsis.

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