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RESEARCH ARTICLES

Pathogens and Antibiogram of Blood Stream Isolates in Neonatal Sepsis: Findings from a Tertiary Care Hospital, Bangladesh

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ABSTRACT

Background: Neonatal sepsis is associated with increased mortality and morbidity, including neurodevelopmental impairment and prolonged hospital stay. The organism responsible for neonatal sepsis may vary across geographical boundaries, even from institution to institution, and with the time of illness; thus, periodic surveillance is necessary. Therefore, the present study was carried out to determine the common pathogens and their antibiotic sensitivity pattern. **Objectives:** To isolate the bacterial agents causing neonatal sepsis, determine the sensitivity pattern of the causative bacterial agents. **Methods:** This cross-sectional study was carried out in the neonatal intensive care unit of BSMMU from December 2012 to July 2013. Neonates (0-28 days) who were admitted to neonatal intensive care unit with suspected sepsis were included in this study. After admission, written informed consent from parents was obtained, emergency management was given to the baby, and then septic screening along with blood culture and antimicrobial sensitivity was done. All data were compiled, tabulated, and then analyzed by SPSS V.12 according to the study's objectives. **Results:** A total of 94 newborn babies with suspected sepsis were included in this study. Most babies (54.3%) were admitted within 24 hours after birth, 86.17% of babies were preterm, and 81.92% of babies' birth weight was <2500 gm. There was a preponderance of male babies over females comprising 53% male and 47% female. Among the suspected septic newborns, 27.66% of babies had culture-positive sepsis, and 73.41% had culture-negative sepsis. Among the culture-positive cases, 72% of babies developed late onset sepsis, and 28% developed early onset sepsis. The isolates from blood culture were Klebsiella pneumoniae in 9 (34%) cases, 6 (23%) cases were E. coli, Acinetobacter, Staphylococcus was found in 2 (8%) cases, and Pseudomonas, Enterobacter, and Citrobacter were found in 1 (4%) case. Gram-negative organisms predominated on Gram-positive bacteria. Imipenem, Ciprofloxacin, Colistin, and Netilmicin were the most sensitive antibiotics to the commonly isolated organisms. Almost all organisms were resistant to Ampicillin and Gentamicin. **Conclusion:** Klebsiella pneumoniae is the commonest organism responsible for neonatal sepsis in BSMMU. There is an overall decline in antibiotic susceptibility to commonly isolated bacterial pathogens.

KEYWORDS: Antibiotic Susceptibility; Bacterial Isolates; Neonates.

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INTRODUCTION

The World Health Organization (WHO) estimates that 4 million neonatal deaths occur worldwide every year.[1] Approximately 98% of these deaths occur in developing countries and are attributable to infections, asphyxia, and consequences of prematurity and low birth weight.[2] Overall, neonatal mortality accounts for nearly two-thirds of infant mortality and one-third of under-five childhood mortality worldwide.[3-5] Serious bacterial infections are major contributors to newborn morbidity and mortality. An estimated 20% of all children born in developing

countries, or 30 million annually, develop an infection during the neonatal period and infectious diseases deaths.[1,6] It is considered one of the most common reasons for admission to a neonatal unit in developing countries.[7] Neonatal sepsis is a clinical syndrome characterized by systemic signs and symptoms of infection with accompanying bacteremia in the first month of life.8 Sepsis occurring in the first 72 hours of life is defined as early-onset sepsis (EOS), and that was occurring beyond 72 hours as of late-onset sepsis (LOS).[9,10] There is a difference in the causative organisms for neonatal sepsis between developed and developing countries.[10-17] Within developing countries, there are regional variations in the spectrum of organisms causing neonatal sepsis. In the United States, the National Institute of Child Health and Development (NICHD) reported that common pathogens causing EOS are group B Streptococcus (GBS) and Escherichia coli. GBS remaining the most frequent pathogen in term infants, E. coli the most significant in preterm infants with EOS.10 Similarly, a study from the United Kingdom has reported GBS to be the most frequent pathogen (31%) followed by coagulase-negative Staphylococcus (CoNS), non-pyogenic Streptococci and E. coli.11 In the developed countries, Gram-positive organisms account for about 70% of all LOS. The common pathogens causing LOS in very low birth weight (VLBW) infants include CoNS, followed by Staphylococcus aureus, Enterococcus spp., and GBS.[11-13] About 18-20% of late-onset sepsis is caused by Gram-negative organisms, especially Enterobacteriaceae spp. and E. coli. Fungi, especially Candida species cause about 12% of late-onset sepsis.[13] In the developing world, E. coli, Klebsiella species, and S. aureus are the most common pathogens of EOS, whereas S. aureus, Streptococcus pneumoniae, and Streptococcus pyogenes are the most commonly reported organisms in LOS.[14-16] According to India's National Neonatal Perinatal Database, Klebsiella pneumoniae, Staphylococcus aureus, and E. coli are the three most common organisms causing neonatal sepsis both in hospital and community.[16] Moreover, the causative organisms of EOS and LOS sepsis are similar, especially in the hospital setting in developing countries.[17] The two studies done at Dhaka Shishu Hospital showed Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa as the common neonatal septicemia and meningitis organisms.[18,19] A retrospective study on BSMMU from 2007 to 2009 showed that the organisms that cause neonatal sepsis include the following: Klebsiella, E Coli, Pseudomonas, Acinetobacter, Enterobacter.[20] The majority of cases of EOS result from vertical transmission of bacteria from the mother to the neonate during the intrapartum period. LOS is due to the horizontal transmission of pathogens from the environment or the hands of the caregiver. Several prepartum and intrapartum obstetric complications are associated with an increased incidence of neonatal sepsis. Examples are Premature onset of labour (<37 weeks of gestation), premature or prolonged rupture of membrane (>24 hours), prolonged labour or excessive manipulation during labour, intrapartum maternal fever.[21,22] Preterm and low birth weight babies are particularly high risk of infection.[21] The clinical manifestations of sepsis vary from being specific to subtle. Subtle and nonspecific symptoms and signs of sepsis may delay recognition, and treatment may change the prognosis.18 The common features were found to have reluctant to feed, lethargy, feeding intolerance, temperature instability, apnoeas, jaundice, respiratory distress, etc.[20] Antibiotics should be given to most of the neonates suspected of infection. In this study, an attempt has been made to know the pattern of organism isolates and the antimicrobial sensitivity pattern in neonatal sepsis.

MATERIALS AND METHODS

A cross-sectional study was done in the NICU of BSMMU over 8 months from December 2012 to July 2013. All neonates (0-28 days) admitted to NICU with suspected sepsis were included in the study. Neonates with a diagnosis other than sepsis were excluded from the study. After admission to NICU, written informed consent was taken from guardians. All data were recorded in a specially designed questionnaire form. All babies were followed up till discharge or death. The entire clinical events that occurred during the hospital stay were noted. Gestational age was determined from the mother's history of last menstrual period (LMP), early fetal ultrasound examination in the first trimester, or the New Ballard Scoring system within 72 hours after birth. Weight was measured using a digital weighing scale. The temperature was recorded by using a clinical thermometer for three minutes. After giving emergency management, septic screening was sent. Blood culture samples were collected aseptically by applying Povidone-iodine and 70% alcohol at the venipuncture site.

The attending nurse drew 2 ml of venous blood from the peripheral vein, and then the blood was then inoculated into a blood culture bottle containing Tryptone Soy Broth (TSB). The specimens were transported immediately to the microbiological laboratory and were incubated for 12-24 hours at 37°C and checked for bacterial growth evidence. For positive broth cultures, subcultures were made on solid media (blood agar and McConkey agar) and were incubated at 37°C for 24 to 48 hours. The grown bacteria were identified by colony morphology, Gram stain, and biochemical tests. Antimicrobial sensitivity testing was performed for all blood culture isolates according to the criteria of the National Committee for Clinical Laboratory Standards by disk diffusion method. Collected data were checked and corrected. Editing and coding were done, and then data was entered into the computer. Data analysis was done by employing Statistical Package for Social Science (SPSS), version- 12.0.

RESULTS

Table-1: Demographic characteristics of the newborns.

Variable	Frequency	Percentage (%)
Male	50	53.00%
Female	44	47.00%
Normal birth weight	17	18.08%
Low birth weight	36	38.29%
Very low birth weight	39	41.51%
Extreme low birth weight	2	2.02%
Term	13	33.00%
Preterm	81	22.06%
Inborn	56	59.57%
Out Born	38	40.43%

Table-2: Pattern of Bacterial Pathogens isolated from blood culture.

Variable	Frequency	Percentage (%)
Late onset sepsis	18	72.00%
Early onset sepsis	8	28.00%
Culture negative sepsis	68	72.34%
Culture positive sepsis	26	27.66%
Gram negative organism	24	92.00%
Gram positive organism	2	8.00%

In this study, 94 neonates were included as suspected of neonatal sepsis. Blood culture and their sensitivity pattern were observed. Among them, 39 (41.51%) babies were very low birth weight, 36 (38.29%) babies were in the low birthweight group, 17 (18.08%) babies were in the normal birth weight group and 2 (2.02%) babies had extremely low birth weight. According to the sex, 50 (53%) neonates were male, and the rest were female. Eighty-one (86.17%) babies were preterm, and the rest were term. Of 94 neonates, 56 (59.57%) babies were inborn, and 38 (40.43%) babies were outborn. (Table-1)

About 26 (27.66%) babies had culture-positive sepsis, and 68 (72.34%) babies had culture-negative sepsis. Eighteen (72%) babies developed late-onset sepsis, and 8 (28%) babies developed early-onset sepsis. Gram-negative bacteria were found in 24 (92%) cases, and Gram-positive bacteria were found in 2 (8%) cases. (Table-2)

Table-3: Distribution of organisms in blood culture (n=26)

Organism	Number (%)
Klebsiella pneumoniae	9 (34%)
E. coli	6 (23%)
Acinetobacter	6 (23%)
Staphylococcus	2 (8%)
Pseudomonas	1 (4%)
Enterobacter	1 (4%)
Citrobacter	1 (4%)

This (table 3) shows the pattern of organisms in blood culture. Klebsiella pneumoniae was found in 9 (34%) cases, Acinetobacter was found in 6 (23%) cases, E Coli was found in 6 (23%), Staphylococcus was found in 2 (8%) cases, and Pseudomonas, Enterobacter, and Citrobacter were found in 1 (4%) cases.

Table-4: Antimicrobial sensitivity pattern of isolated organisms.

Organism No (%)	Antibiotics no (%)											
	AM	GM	AMK	NM	CP	CFD	CTX	NA	COL	PI	IMI	VAN
Klebsiella N=9 (34)	0	0	3 (33)	3 (33)	6 (66)	0	0	2 (2)	5 (55)	3 (33)	8 (88)	NT
Ecoli N=6 (23)	0	1 (16.6)	3 (50)	3 (50)	4 (66.7)	1 (16.6)	1 (16.6)	1 (16.6)	5 (55)	3 (33)	8 (88)	NT
Acinetobacter N=6 (23)	0	0	0	2 (33.3)	3 (50)	0	0	1 (16.6)	2 (33.3)	3 (50)	4 (66.7)	
Staph aureus N=2 (8)	0	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	NT	0	0	1 (50)
Pseudomonas n=1 (4)	0	0	1 (100)	1 (100)	0	0	NT	NT	1 (100)	1 (100)	0	NT
Enterobacter n=1 (4)	0	0	0	0	1 (100)	0	0	NT	1 (100)	1 (100)	1 (100)	NT
Citrobacter N=1 (4)	0	0	0	0	1 (100)	0	0	1 (100)	1 (100)	1 (100)	1 (100)	NT
Total n=26 (100)	0	2 (7.6)	8 (30.7)	10 (38.5)	16 (61.5)	2 (7.6)	2 (7.6)	6 (23)	10 (38.5)	7 (26.9)	19 (73)	1 (3.8)

AM: ampicillin, GM: gentamicin, AMK: Amikacin, NM: netilmicin, CFD: ceftazidime, CTX: cefotaxime, NA-nalidixic acid, IMI: Imipenem, PI: piperacillin, COL: Colistin sulphate
CP: ciprofloxacin, NT: not detected.

The above table shows the antimicrobial sensitivity pattern of isolated organisms. Nineteen (73%) organisms were susceptible to Imipenem, 16 (61.5%) organisms were susceptible to ciprofloxacin, 10 (38.5%) organisms were susceptible to Netilmicin and Colistin, 8 (30.7 %) organisms were susceptible to Amikacin, 7 (26.9%) organisms were susceptible to piperacillin-tazobactum 6 (23%) organisms were susceptible to Nalidixic acid, 2 (7.6%) organisms were susceptible to Gentamicin, Ceftazidime, and Cefotaxime (Table-4).

DISCUSSION

This study was done to determine the bacteria responsible for neonatal sepsis and their sensitivity pattern. Among them, 39 (41.51%) babies had very low birth weight, 36

(38.29%) babies had low birth weight, and 2 (2.02%) babies had extremely low birth weight. Our findings correlate with other studies.[25,26] In this study, 25 (26.59%) babies had culture-proven sepsis, and 69 (73.41%) babies had clinical sepsis. Among them, 18 (72%) babies developed late-onset sepsis, and 8 (28%) babies developed early-onset sepsis. Though early-onset neonatal sepsis is more common[27] late-onset neonatal sepsis is more common in the present study, which is consistent with another study in Bangladesh[16], which showed 45% of babies developed late-onset neonatal sepsis and 26 % of babies developed early-onset sepsis. Probably this discrepancy is since mortality in early-onset sepsis is relatively high28, and some neonates might have died before reaching the hospital. In this study, Gram-negative bacteria were found in 24 (92%) cases, and Gram-positive bacteria were found in 2 (8%) cases. Increased prevalence of Gram-negative bacteria, as found in this study, has been reported from other studies in India [27,28] and previous studies in our country.[18,19,29] Guida et al.[30] showed that Gram-positive bacteria were found in 76% cases, Gram-negative bacteria were found in 16% cases, and fungi were found in 8% cases. Manzoni et al.[31] found that Gram-negative bacteria were found in 48.2% cases, fungi were found in 25.8% cases, and Gram-positive bacteria were found in 18.8% cases. Klebsiella is emerging as common bacteria in hospital settings13, 17, and it was the predominant Gram-negative organism in the present study. In this study, Klebsiella pneumoniae was found in 9 (34%) cases, E. coli and Acinetobacter was found in 6 (23%) cases, Staphylococcus was found in 2 (8%) cases, and Pseudomonas, Enterobacter, and Citrobacter were found in 1 (4%) cases. Mannan et al.[32] and Hossain et al.[28] found that Klebsiella, Acinetobacter, Escherichia coli, and Pseudomonas were the predominant Gram-negative organisms. Hossain et al.[28] showed in their study that the majority of the Gram-positive organisms were coagulase-negative staphylococci and Staphylococcus aureus. But in this study, only 2 (8%) Staphylococcus cases were isolated. Group B streptococcus was not isolated in this study, unlike western, developed countries where it is the major agent of neonatal septicaemia.[33] The insignificance of group B streptococcus as a pathogen in many developing countries is supported by many other studies.[34,35] The low incidence of GBS sepsis in developing countries could be attributable to the low prevalence of GBS colonization rates in pregnant women or possibly to the presence of strains with low virulence.[36] The predominance of Klebsiella in the present study accords with several reports in other developing countries.[37,38] Earlier studies showed the prevalence of E. Coli, followed by Klebsiella and pseudomonas sp. and Acinetobacter.[19,39] This contrasts with some other studies [40-42] where Staphylococcus Aureus was mainly implicated. These differences could be attributed to geographic location and the time of onset of illness. In addition, one organism or a group of organisms may over time replace another as the leading cause of neonatal sepsis in a particular region.[40, 43, 44] Various types of antibiotics were used against the isolated organism. In the case of gram-negative bacteria, Ampicillin, Gentamicin, Amikacin, Netilmicin, Ceftazidime, Cefotaxime, Ciprofloxacin, Imipenem, Piperacillin, Colistin, and Nalidixic acid were used. In the case of Gram-positive bacteria, Ampicillin, Gentamicin, Amikacin, Netilmicin, Ceftazidime, Cefotaxime, Ciprofloxacin, Imipenem, Piperacillin, Nalidixic acid, and Vancomycin were used. Nineteen (73%) organisms were susceptible to Imipenem, 16 (61.5%) organisms were susceptible to Ciprofloxacin, 10 (38.5%) organisms were susceptible to Netilmicin and Colistin, 8 (30.7%) organisms were susceptible to Amikacin, 7 (26.9 %) organisms were susceptible to Piperacillin-tazobactum, 6 (23%) organisms were susceptible to Nalidixic acid, 2 (7.6%) organisms were susceptible to Gentamicin, Ceftazidime, and Cefotaxime. No organisms were susceptible to Ampicillin. Most organisms were susceptible to Imipenem, Ciprofloxacin, Netilmicin, and Colistin. These findings consisted of other studies.[45] An alarming finding in this study is that a high proportion of the organisms are resistant to all commonly used antibiotics. Imipenem and Netimicin are found to be most effective against the majority of the organisms. Gentamicin and third-generation cephalosporins and Ciprofloxacin, which previously had good sensitivity, also are becoming resistant. This observation shows that the problem of antibiotic resistance is a serious threat for treating serious bacterial infections in neonates to control antibiotic resistance. The practice of prudent or judicious use of antibiotics is very important. This change in the sensitivity pattern of antimicrobials could be attributable to the fact that microorganisms tend to become resistant to commonly used antibiotics while remaining sensitive to the rarely used ones. In addition, antimicrobial sensitivity may differ in studies and at different times. This could be due to the emergence of resistant strains due to indiscriminate use of antibiotics for both prophylaxis and treatment of sick neonates.

CONCLUSION

Neonatal sepsis is a life-threatening emergency, and thus any delay in treatment may cause death. The knowledge of the etiological organisms and their antimicrobial sensitivity profile is necessary for effective therapeutic intervention in neonatal sepsis. It is therefore important to note that commencement of antibiotic therapy empirically is of essence while awaiting blood culture results. Therefore, the initial empiric antibiotic therapy must be a combination of drugs to cover for the prevalent bacterial organisms in that locality. Therefore, the varying microbiological pattern of neonatal sepsis warrants the need for periodic review of neonatal sepsis as the knowledge of the pathogens and their antibiotic susceptibility would be a useful guide in the antibiotic therapy of such neonates with sepsis.

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AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors.

Indeed, all the authors have actively participated in the redaction, the revision of the manuscript, and provided approval for this final revised version.

Limitations

Limitations of our study include that this is not a multicentered study and organisms were not categorized as early, and late-onset sepsis and only bacterial agents were isolated, fungal infection has not been addressed. However, it is an important cause of neonatal sepsis. The sample size was small, and the duration of the study was short.

Recommendations

Based on the present study, it is probably unnecessary to commence Ampicillin and Gentamicin previously recommended as empiric antibiotics in treating neonates with suspected sepsis due to their extremely low sensitivities. It is thus pertinent to note that the current antibiotic policy of commencing a baby with suspected sepsis on Ampicillin and Gentamicin needs re-evaluation. Furthermore, steps need to be taken to prevent or control the emergence of resistant strains. Therefore, laws should be enforced to discourage the indiscriminate use of antibiotics seen commonly in our country and discourage inadequate doses that are also believed to contribute to the increasing emergence of resistant strains.

COMPETING INTERESTS

The authors declare no competing interests with this case.

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