STUDY OF BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY OF NEONATAL SEPSIS IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Neonatal sepsis is a major cause of mortality and morbidity in newborn. The spectrum of organisms causing sepsis is different in developing countries. Data on the recent trends of organisms causing sepsis are limited. There are many factors that contribute to neonatal sepsis. The organisms responsible for early and late onset sepsis are different. This study was conducted to analyze the organisms responsible for early and late onset neonatal sepsis and to see the sensitivity of drugs. **Materials and methods:** A prospective hospital based study over the period of one year (January 2015 to December 2015) was conducted at Neonatal Intensive Care Unit (NICU) in Bangabandhu Memorial Hospital, USTC, Chittagong. **Results:** A total of 114 neonates were enrolled during the study period. Among them 98 neonates were selected considering inclusion and exclusion criteria. Blood culture was positive in 44(44.9%) neonates. The male female ratio of culture proven sepsis was 1.2:1. More than half were preterm 24(54.54%) LBW 27(61.37%). Among all of the culture-proven septic neonates, Klebsiella 22 (64.7%) were found to be the most common organism in early onset sepsis. Escherichia coli 6(60%) was common in late onset sepsis. Other organisms causing sepsis were Pseudomonas 10(22.72%) and Staphylococcus areus 2(4.54%) among all culture proven sepsis. We observed high resistance to penicillin against all organisms. Ceftazidime had good sensitivity against Pseudomonas. Quinolones and Aminoglycosides were sensitive mostly against Klebsiella, then Pseudomonas and E. coli. Imipenam showed good sensitivity against Klebsiella. **Conclusion:** Klebsiella were the most common organism in early onset sepsis. Escherichia coli was significantly more common in late onset sepsis than early onset sepsis. Resistance to penicillin and cephalosporin are increasing day by day. Our study revealed that quinolones and imipenam had good sensitivity against most of the organism in neonatal sepsis.

Key words

Bacteriological profile; Early onset sepsis; Late onset sepsis; Neonate.

Introduction

Neonatal sepsis is a clinical syndrome characterized by systemic signs of circulatory compromise caused by invasion of the blood stream by bacteria in the first four weeks of life, and is more common in developing countries compared with developed countries[1-2]. The incidence of this disease in developed countries is 1/1,000 in normal term neonates and 4/1,000 in preterm neonates. These values increase in low-weight preterm neonates[3]. In developing countries, this incidence increases to 2.2-8.6/1,000 live birth[4]. EONS can be acquired vertically from the pregnant woman before or during delivery. In this case, micro organisms present in the genital tract of the mothers are of great Importance[5]. The symptoms appear within the 72 hours of life. EONS is a serious problem among Very Low-Birth-Weight (VLBW) neonates and is associated with at least a three-fold increased risk of mortality[6]. Sepsis is one

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of the leading causes of neonatal mortality and morbidity. Bangladesh has been working hard to achieve Millennium Development Goal (MDG) on reducing child mortality. One of the component of this goal is reduction of Infant Mortality Rate (IMR).The target IMR in Bangladesh by 2015 is 32 per 1000 live birth. However the major challenge to reach the desired target is the unacceptably high neonatal deaths. Current neonatal mortality rates in our country being 24 per 1000 live births, which remain still very high in comparison to developed world[7]. It is obvious that reduction of IMR is not possible without reducing Neonatal Morality Rate (NMR).

It is estimated that 20% of all neonates develop sepsis[8]. It is responsible for 30-50% of total neonatal deaths in developing countries. The reported incidence of neonatal sepsis varies from 7.1 to 38 per 1000 live birth in Asia[9]. However, it is much lower in the developed countries. For instance, it ranges from 1.5 to 3.5 per 1000 for Early Onset Sepsis (EOS) and up to 6 per 1000 live births for Late Onset Sepsis (LOS) in USA and Australia, and it comprise a total of 6–9 per 1000 for neonatal sepsis[9]. Infection can occur either in fetal life, during birth or after birth. It can be acquired either from the community or at the nursery in the hospital. There are many additional factors that predispose newborns in developing countries at a greater risk for developing neonatal sepsis compared with newborns in developed countries. These include intrinsic factors and extrinsic factors in the antenatal, intra-partum and the neonatal period[10]. Intrinsic factors in the developing world include higher rates of prematurity, intrauterine growth retardation, birth asphyxia, prematurity and prolonged rupture of membranes and maternal peripartum infections. Among the most important extrinsic factors contributing to the high risk of sepsis are the lack of antenatal care, unhygienic birth practices and birth attended by an untrained birth attendant. The absence of skilled personnel at delivery also results in a failure to identify and refer high-risk newborns to better centers and a delay in managing complications when they occur.Neonatal sepsis is broadly divided according to age of onset into 2 types, early onset sepsis (<72 hrs) and late onset sepsis (72 hrs-28 days)[11]. This classification is generally of importance for identification of predominant organisms causing infections during these phases. Early onset sepsis is acquired during fetal life, delivery or at the nursery and Group B Streptococcus, Escherichia coli or Listeria monocytogens happen to be most common organisms[8]. Late onset sepsis is most commonly caused by Coagulase-Negative Staphylococci (CONS) Staphylococcus aureus, Escherichia coli, Klebsiellaand Pseudomonas and is usually acquired in the Neonatal Intensive Care Unit (NICU) or the community[12]. But organism profile is not same in all nursery even in the same country. It varies from centre to centre with time. Moreover indiscrimination of antibiotics are used in many centres in our country which leads to antibiotic resistances. So, Periodic evaluation of organisms responsible for neonatal sepsis is essential for the appropriate management of neonates. Therefore, this study were conducted to find out the common organisms causing sepsis in neonates admitted in a tertiary level children's hospital. This result may have positive outcome in the management of neonatal sepsis.

Materials and methods

This was a prospective study of bacteriological profile of neonatal sepsis was conducted in the Neonatal Intensive Care Unit (NICU) of Bangabandhu Memorial Hospital, USTC, Chittagong over one year period (January to December 2014) Ninety eight neonates with suspected sepsis were enrolled in this study.

Inclusion criteria:

i) Babies younger than 28 days

ii) Presence of clinical features of neonatal sepsis

Exclusion criteria:

i) Age more than 28 days

ii) Cases of neonatal tetanus, RDS, congenital heart disease.

Sepsis was suspected if the mother showed evidence of chorioamnionitis, prolonged rupture of membranes (>24 h) urinary tract infection or fever and the neonate presented with one of the following signs or symptoms, fever (Temperature >38°C) hypothermia (Temperature <36°C) decreased sucking, poor sucking or not sucking, feeding intolerance, lethargy, irritability, seizure, apnea, cough, respiratory distress, abdominal distention, petechiae, purpura and bleeding.

The duration of data collection in current study is only 1 year. Therefore considering resource and time constraints, 98 clinically suspected neonatal sepsis patients were included in this study.

After admission in NICU, study cases were selected according to the inclusion criteria. A written informed consent was filled up by the attendant for permission. Data was collected by a questionnaire. After a detailed history, examination was done properly, 114 neonates with suspected sepsis were taken. Those who were admitted with respiratory distress chest X–ray had been done. After taking history, proper clinical examination and necessary investigations 18 cases were excluded. In remaining 98 patients blood samples were collected under all aseptic precaution using appropriate fan bottle. Bottles were incubated in the BacTec / Alert automated system for 5-7 days at Chevron Laboratories, Chittagong. Positive bottles were processed by preparing a smear for Gram stain and sub culturing onto sheep blood, chocolate and MacConkey agars. The sheep blood & chocolate agar was incubated in Co_2 (Candle jar) at 35 – 37^{o}c for 48 hrs, the MacConkey agar in air for at 35-37c for 48hrs. Suspected colonies were identified by serological test. Antimicrobial sensitivity was assessed by the disc diffusion methods or E-test on a Muller-Hilton agar plate according to CLSI guidelines.

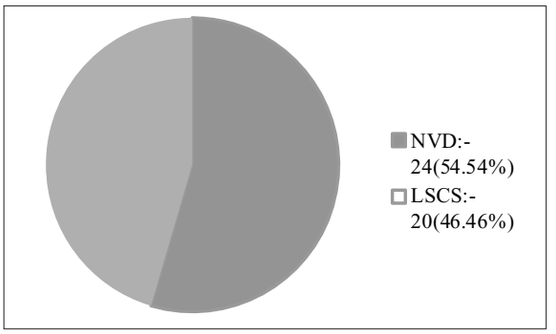
Results

Table I : Distribution of isolated organisms (n=44)

Organisms	Number	Percentage (%)
Klebsiella	24	54.54
Pseudomonas	10	22.72
E.coli	08	18.18
Staph areus	02	4.54
Total	44	100

Table II : Comparison of common isolated organisms by type of onset of sepsis (n=44)

Organisms	EOS sepsis no (%)	LOS sepsis no (%)	Total cases (n)
Klebsiella	22 (64.7%)	2 (20%)	24
Pseudomonas	8 (23.53%)	2 (20%)	10
E.coli	2 (5.88%)	6 (60%)	08
Staph areus	2 (5.88%)		02
Total	34 (100%)	10 (60%)	44



Pie Chart : Influence the mode of delivery on development of neonatal sepsis (n=44) NVD: 24 (54.54%), LSCS: 20 (45.45%)

Table III : Association of risk factors with development of sepsis

Risk factors	Total positive cases(n=44)		In EONS (n= 34)		In LONS (n= 10)	
	No.	(%)	No.	(%)	No.	(%)
LBW	27	61.37	18	66.67	9	33.33
Preterm	24	54.54	16	66.67	8	33.33
PNA	19	43.2	10	52.63	9	47.37
PROM	12	27.27	8	66.67	4	33.33
Chorioamnionitis	5	11.36	4	80	1	20
UTI	3	6.82	2	66.67	1	33.33
Umbilical sepsis	8	18.18	4	50	4	50

Table IV : Sensitivity pattern of main organisms isolated in the study

	Klebsiella (n=24)	Pseudomonas (n=10)	Ecoli (n= 8)	Staph areus (n= 2)
Penicillin	0	0	0	0
Ampicillin	0	0	0	0
Doxycycline	02			
Imipenam	16		06	02
Meropenam	04			02
Cefotaxim	03	03		
Ceftazidime		08		
Ceftriaxone	01	01		
Gentamycin	10	02		
Amikacin	08		04	04
Ciprofloxacin	16	10	06	02
Levofloxacin	12	08	06	
Azithromycin	18	02	02	
Cotrimoxazole	12	08		
Chloramphenicol	08		02	
Nitrofurantoin	02			
Nalidaxic acid	06			

During the study period there were 591 neonates admitted in the NICU. Total 114 neonates were taken in the study. Among them blood cultures were done in 98 cases as a part of septic screening in suspected neonatal sepsis. 16 neonate were excluded following exclusion criteria. The total number of culture positive cases was found to be 44 with the culture positivity rate was 44.9%. Among the culture positive cases there were 24 (54.54%) males and 20 (45.45%) female neonates with the male to female ratio of 1.2:1. No of inborn patient were 11 (25%) and outborn patient were 33 (75%). EOS constituted majority 34 (77.27%) and LOS were 10 (22.73%) of culture-proven cases in our study. Klebsiella constituted the majority of the isolated organisms followed by Pseudomonas, then E coli, Staph aureus (Table I). As shown in Table II, Klebsiella were responsible in 22 (64.7%) neonate of the cases in early onset sepsis. Pseudomanas made 8 (23.53%) of the cases followed by E coli 2 (5.88%) in early onset sepsis. E. coli 6 (60%) was more common in late onset sepsis. 54.54% of cases were born by NVD and 45.45% were delivered by LSCS. The common risk factors were LBW neonates 27(61.37%) preterm 24 (54.54%) PNA 19 (43.2%) premature ruptured membranes 12 (27.27%). PROM and chorioamnionitis were more common in EOS than LOS. We observed high resistance to penicillin, gentamycin but good sensitivity to amikacin, imipenam, ciprofloxacin and levofloxacin. High cephalosporin resistance was noticed in this study. We observed high resistance to penicillin against all organisms. Ceftazidime had good sensitivity against Pseudomonas, drugs of aminoglycosides and quinolones groups were sensitive mostly against Klebsiella, then Pseudomonas and E. coli. Imipenam showed good sensitivity against Klebsiella.

Discussion

In this study, prevalence of documented neonatal sepsis with positive culture was 44.9%. This study has shown male female ratio of 1.2:1, which is similar to the findings by Jain NK et al (2:1) and by Jia-horng Jiang et al (1.4:1)[13-14]. Probably, this could be because of the priority given to male babies for medical care in our society. Among the culture positive cases no of inborn patients were 11 (25%) and outborn patients were 33 (75%). This may be due to presence lack of antenatal care, unhygienic birth practices and birth attended by an untrained birth attendant. The absence of skilled personnel at delivery also results in a failure to identify and refer high-risk newborns to better centers and a delay in managing complications when they occur. In the present study, 77.27 % and 22.73% neonates presented with early onset sepsis and late onset sepsis respectively, which is in agreement with the reports from other developing countries eg. in Iran (77.5% vs 22.5%) and in a study of Bangladesh (70.7% vs 29.3%) but in contrast with reports from Bangladesh (40% vs 60%) Pakistan (42% vs 58%) and Libya (31 vs 69%) where late onset sepsis is more common[15-19]. The possible explanation for a higher frequency of EOS in this study might be the more referral of preterm labors to our center. Klebsiella pneumoniae (54.54%) was the predominant organism for neonatal sepsis. Pseudomanas (22.72%) was the second most common organism isolated in this study. Klebsiella pneumoniae is emerging as a common bacteria in hospital settings[17,20,21]. But the pattern of isolated organisms in our study slightly differs from the findings in a study in Iran and India where Pseudomonas aeruginosa was the most common cause of neonatal sepsis followed by Klebsiella pneumoniae and Escherichia coli (E. coli)[15,22]. In similar studies from Bangladesh, Nepal and Pakistan, E. coli was the leading cause of neonatal sepsis followed by Klebsiella pneumoniae[17,22.] In other studies gram positive bacteria such as S. aureus and Group B Streptococcus (GBS) were found to be the most common isolates in neonatal septicemia[23]. The main risk factors associated with LONS areprematurity, central venous catheterization (Duration > 10 days) nasalcanula, gastrointestinal tract pathology, exposure to antibiotics, and prolonged hospitalization[24,25]. Didier et al found three major types of Late Onset Neonatal Infections (LONI). E. coli-induced urinary tract infection, CONS septicemia affecting preterm infants and severe GBS infections[26]. This study showed predominance of Staph aureusin early onset sepsis as compared to late onset sepsis. Similar finding was also reported from India[22]. Coagulase Negativestaphylococcus (CONS) seemed to be more common in LOS sepsis than staphylococcus aureus[14,27,28]. However, a study conducted in eastern part of Nepal showed that both CONS and Staph aureus were the commonest organisms causing both EOS and LOS[29].

Conclusion

In this study most of the organisms were sensitive toimipenam,ciprofloxacin, levofloxacin and azithromycin. As ciprofloxacin and levofloxacin found to be most sensitive as well as cost effective, these two drugs may be incorporatedin first line therapy in neonatal sepsis. But as our study population was small, further study will be helpful to include these drugs as a first line therapy.

Disclosure

All authors declare no competing interest.

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