International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 29-03-2019; Accepted: 01-04-2019
www.medicalsciencejournal.com
Volume 5; Issue 6; June 2019; Page No. 09-12

Causative agents of neonatal sepsis: A study in Tertiary Care Paediatric Hospital, Dhaka, Bangladesh

Md. Kamruzzaman[1*], Md. Mosharaf Hossain[2], Mohammad Nazmul Hasan Chowdhary[3], Probir Kumar Sarkar[4], Sarabon Tahura[5]

[1] Assistant Professor, Department of Respiratory Medicine, Dhaka Shishu (Children) Hospital, Bangladesh
[2] Assistant Professor, Department of Paediatrics, Dhaka Shishu (Children) Hospital, Bangladesh
[3] Resident Medical Officer, Department of Respiratory Medicine, Dhaka Shishu (Children) Hospital, Bangladesh
[4, 5] Assistant Professor, Department of Paediatrics, Dhaka Shishu (Children) Hospital, Bangladesh

Abstract
Sepsis means the presence of bacteria (bacteremia), other infectious organisms, or toxins created by infectious organisms in the bloodstream with spread throughout the body. Neonatal sepsis is an invasive infection, usually bacterial, occurring during the neonatal period. Signs are multiple, nonspecific, and including diminished spontaneous activity, less vigorous sucking, apnea, bradycardia, temperature instability, respiratory distress, vomiting, diarrhea, abdominal distention, jitteriness, seizures, and jaundice. The aim of this study was to evaluate the causative agents of neonatal septicemia in the children admitted to the Department of Paediatrics of Dhaka Shishu (children) Hospital, Dhaka, Bangladesh during the period from January 2017 to December 2017. The study was planned by enrolling 176 neonates admitted in the selected hospital. The 50 neonates diagnosed with the septicemia were enrolled. In the study; most of the mothers were 20-30 years age group, representing 45%. Most of them were completed higher secondary education, representing 52.50%. Socio-economic classes lower representing 55% of the study participants. Regarding parity; 67.50% of the study participants were parity one (1). Only 32.50% mothers taken antenatal care more than 3 times. Predisposing factors were negative in more than 80% of mothers and most of modes of delivery were 60% of mothers. Late Onset Sepsis was 65% of babies and Gram positive were 25% of the patients. In this study, the most common bacteria found associated with neonatal sepsis in the inborn unit was Klebsiella (45%) followed by Acinetobacter 17.50%, Citrobacter 7.50% and Pseudomonas 2.50%. The data from the present study revealed that, there is need to undertake research to understand the pathogenesis of early-onset sepsis and to devise measures to prevent related morbidity and mortality. To improve the survival rate, better approach is to take early initiation of appropriate antibiotics and aggressive supportive care based on local sensitivity pattern and fatal risk factors.

Keywords: risk factors, neonatal sepsis, invasive infection

1. Introduction

Sepsis, also known as septicemia, is a life-threatening complication that can happen when bacteria from another infection enter the blood steam and spread throughout the whole body. Signs are multiple, nonspecific, and include diminished spontaneous activity, less vigorous sucking, apnea, bradycardia, temperature instability, respiratory distress, vomiting, diarrhea, abdominal distention, jitteriness, seizures, and jaundice. Diagnosis are clinical and based on culture results. The density of colonization determines the risk of early-onset invasive disease in neonates, which is 40 times higher with heavy colonization. Although only 1/100 of neonates colonized develop invasive disease due to GBS, > 50% of those present within the first 6 h of life. Nontypeable Haemophilus influenzae sepsis has also been identified in neonates, especially in premature neonates. Other cases tend to be caused by gram-negative enteric bacilli (eg, *Klebsiella spp*.) and certain gram-positive organisms such as Listeria monocytogenes, enterococci [e.g. *Enterococcus faecalis*, *E. faecium*], group D streptococci [e.g. *Streptococcus bovis*], alpha-hemolytic streptococci, and staphylococci. Also, *S. pneumoniae*, *H. influenzae* type b, and, less commonly, Neisseria meningitidis have been isolated. Asymptomatic gonorrhea occurs occasionally in pregnancy, so *N. gonorrhoeae* may rarely be a pathogen. Late-onset neonatal sepsis is usually acquired from the environment (See Neonatal Hospital-Acquired Infection). Staphylococci account for 30 to 60% of late-onset cases and are most frequently due to intravascular devices (particularly central vascular catheters). E. coli is also becoming increasingly recognized as a significant cause of late-onset sepsis, especially in extremely LBW infants. Isolation of Enterobacter cloacae or Cronobacter (formerly Enterobacter) sakazakii from blood or CSF may be due to contaminated feedings. Contaminated respiratory equipment is suspected in outbreaks of hospital-acquired Pseudomonas aeruginosa pneumonia or sepsis. Although universal screening and intrapartum antibiotic prophylaxis for group B streptococcus have significantly decreased the rate of early-onset disease due to this organism, the rate of late-onset GBS sepsis has remained unchanged, which is consistent with the hypothesis that late-onset disease is usually acquired from the environment. The role of anaerobes (particularly Bacteroides fragilis) in late-onset sepsis remains unclear, although deaths have been attributed to Bacteroides bacteremia. *Candida spp.* are increasingly important causes of late-onset sepsis, occurring in 12 to 18% of extremely LBW infants. Hematogenous and transplacental dissemination of maternal infection occurs in the transmission of certain viral (e.g. rubella,

cytomegalovirus), protozoal (e.g. *Toxoplasma gondii*), and treponemal (e.g. *Treponema pallidum*) pathogens. A few bacterial pathogens (e.g. *L. monocytogenes*, *Mycobacterium tuberculosis*) may reach the fetus transplacentally, but most are acquired by the ascending route in utero or as the fetus passes through the colonized birth canal. Though the intensity of maternal colonization is directly related to risk of invasive disease in the neonate, many mothers with low-density colonization give birth to infants with high-density colonization who are therefore at risk. Amniotic fluid contaminated with meconium or vernix caseosa promotes growth of group B streptococcus and *E. coli*. Hence, the few organisms in the vaginal vault are able to proliferate rapidly after PROM, possibly contributing to this paradox. Organisms usually reach the bloodstream by fetal aspiration or swallowing of contaminated amniotic fluid, leading to bacteremia. Most worrying was that, there are exceedingly high rates of resistance of Gram negative bacilli to almost all antibiotics. Resistance to aminoglycosides is about 50% for amikacin, higher for netilmicin and over 75% for gentamicin. Resistance to third generation cephalosporins is 80% plus. Bacteria are less resistant (30-46%) to piperacillin-tazobactam. Imipenem resistance is already appearing (about 20%). The currently available multisite studies on sepsis are from well-established surveillance networks in high income countries such as the USA, the UK, and Germany. Such infection surveillance networks are a rarity in low-income and middle-income countries; the few available ones have used passive surveillance (e.g. the National Neonatal Perinatal Database [NNPD] and the Asia-Pacific Neonatal Infections Study [APNIS]). Most of the other studies from low-income and middle-income countries are typically from a single site, retrospective, or have relied on routine laboratory reports. They often lack rigorous data collection and reporting methods, and run the risk of mis-classification and underestimation or overestimation of the incidence of sepsis [1-3].

2. Objectives

General objective

- To find out the causative microbes responsible for neonatal sepsis in Bangladesh

Specific objectives

- To evaluate the risk factors of neonate sepsis in Bangladesh
- To assess drug sensitivity of positive sepsis cases in Bangladesh

3. Materials and Methods

It was a cross sectional study which was planned by enrolling the 176 neonates admitted in Neonatal unit of Department of Paediatrics, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh during the period from January 2017 to December 2017. The 50 neonates diagnosed with the septicemia were enrolled in the present study. Neonatal septicemia was diagnosed as per the clinical criteria. Blood sample (0.5 to 2 ml) was collected with all aseptic precaution and was inoculated into blood culture bottle. The blood and broth were mixed gently and bottles were transported to laboratory for incubation in BacT/Alert 3D system and further processing was done as per manufacturer's guideline. Those blood culture bottles which were indicated positive, query positive and query negative by Bact/ Alert 3D system were sub cultured on Sheep blood agar and MacConkey agar. The blood agar and MacConkey's medium were incubated at 35 ± 20˚ Celsius for 18 - 24 hours in aerobic atmosphere. Various organisms were identified on the basis of colony morphology and standard biochemical tests. Those blood culture bottles which were indicated as negative by 5 days (as per setting of Bact / Alert 3D system) were reported as "no growth".

4. Results

The cross sectional study was planned by enrolling the 176 neonates admitted in Neonatal unit of Department of Paediatrics, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh during the period from January 2017 to December 2017. Fifty (50) neonates diagnosed with the septicemia were enrolled in the present study. Neonatal septicemia was diagnosed as per the clinical criteria. Blood sample (0.5 to 2 ml) was collected with all aseptic precaution and was inoculated into blood culture bottle. In our study, most of the mothers were 20-30 years group, representing 45%. Most of them were completed higher secondary education, representing 52.50%. Socio-economic classes lower representing 55% of the study participants. Regarding parity; 67.50% of the study participants were parity one (1). Only 32.50% mothers taken antenatal care more than 3 times. Predisposing factors were negative more than 80% 0f mothers and most of modes of delivery were 60% of mothers. Late Onset Sepsis was 65% of babies and Gram positive were 25% of the patients. In this study, the most common bacteria found associated with neonatal sepsis in the inborn unit was Klebsiella (45%) followed by Acinetobacter 17.50%, Citrobacter 7.50% and Pseudomonas 2.50%.

Table 1: Economic status and educational status of the parents of study participants (n=50)

Socio-demographic characteristics		
Economic Class		
	n	%
Insufficient	8	16
Slightly Sufficient	35	71
Sufficient	5	10
Sufficient and Save	2	3
Educational Status		
Illiterate	17	33
Literate	27	56
Educated	4	9
Highly Educated	1	2

Table 2: Clinical Details of Mothers of neonates (n=50)

Parameters	n	%
Mother Age		
Less than 20 years	12	30
21 to 30 years	18	45
Above 30 years	10	25
Literacy		
Primary education	8	20
Higher secondary	21	52.50
Graduate	10	25
Post graduate	1	2.50
Economic Status		
Lower	22	55
Middle	15	37.50
Higher	3	7.50
Parity of Mother		
1	27	67.50
2	10	25
More than 2	3	7.50
Antenatal Care		
Less than 3	27	67.50
More than 3	13	32.50
Predisposing Factors		
Positive	8	20
Negative	32	80
Mode of Delivery		
Normal	16	40
Caesarean	24	60

Table 3: Type & Causative Microbes of patients (n=40)

Parameters	No. of Cases	%
Type of Sepsis		
Early Onset Sepsis	14	35
Late Onset Sepsis	26	65
Causative Bacteria		
Gram Positive	10	25
Gram Negative	30	75

Table 4: Positive Cases and Drug Sensitivity of the organisms (n=40)

Organisms	Blood culture positive Cases	%
Gram-positive		
Staphylococcus aureus	5	12.50
Methicillin-resistant Staphylococcus aureus	3	7.50
Staphylococcus epidermidis	3	7.50
Total Cases	11 cases	27.50
Gram-negative		
Klebsiella pneumoniae	18	45
Acinetobacter	7	17.50
Citrobacter	3	7.50
Pseudomonas	1	2.50
Total Cases	29 cases	72.50

5. Discussion

In this study, the most common bacteria found associated with neonatal sepsis in the inborn unit was Klebsiella (45%) followed by Acinetobacter 17.50%, Citrobacter 7.50% and Pseudomonas 2.50%. Here, maternal risk factors significantly associated with fatal outcome were: Illiteracy, poor socioeconomic status, inadequate antenatal care, premature rupture of membranes, assisted vaginal delivery. Babies of poor, illiterate mother have a higher incidence of sepsis because they are usually of low birth weight, delivered premature thus diminishing their immunity and predisposing them to infection. Sepsis is one of the factors of high mortality in ICUs in critically ill patients. In a study it was found that, annual mortality from this condition is estimated at 30 to 50 deaths per 100,000 population [4]. There is also delay in appreciating and seeking treatment. Besides, most deliveries in these families are conducted at home under improper aseptic conditions [5]. Instrument assisted deliveries had higher mortality as shown in a number of other studies due to increasing chance of infection [6, 7]. Neonatal risk factors significantly associated with higher mortality were gestational age, gender, birth weight, IPPV, time of onset of symptoms, delay in starting treatment and presence of complications. Gestational age and neonatal mortality were inversely related. Preterm babies need NICU admission and are subjected to invasive procedures and mechanical ventilation which increases the risk of infection. Increased incidences of sepsis and its mortality were noticed among male infants in our study as reported by authors of other studies [8]. Once again as observed in other studies neonates who had IPPV demonstrated high risk of infection and significant fatality [9]. The time gap of >12 h from the onset of symptoms and starting of treatment and consequent complications like DIC/multi organ dysfunction syndrome leads to higher mortality [10]. According to a report published by ICMR on newborn health two thirds of isolates were Gram-negative including Acinetobacter spp. (21.9%), Klebsiella spp. (16.6%), and Escherichia coli (13.7%) in inborn cohort. A study done in SP medical college, Bikaner also showed Klebsiella as the most common (48.21%) micro-organism associated with sepsis in inborn unit. A study was done in Madhya Pradesh, india and Klebsiella was found to be the most commonly associated organism. This may be due colonisation of different bacteria in different set ups. Similarly, in a study done in 2007 in Burdwan MCH Klebsiella (34.48%) was the most common organism isolated [11]. It can be concluded that though we are on the track of minimizing morbidities and mortalities but still there is a long way to go, still we have a higher prevalence of neonatal sepsis even in inborn units and most common associated bacteria is Klebsiella pneumonae, and most common indication for admission was respiratory distress which further led to neonatal sepsis. Among the patients with sepsis maximum patients were males and maximum patients belonged to urban areas and were successful in availing the government facilities for transportation up to the health facility. Neonates with sepsis were mainly preterm term and with low birth weight. Most of the neonates who had sepsis were admitted on the first day of their birth and maximum duration of stay of most of the neonates was 7 days and most of them were treated and discharged successfully.

Limitations of the study

The present study conducted in a single center with small a sample size, which might not reflect the scenarios the whole country.

6. Conclusion

History of maternal infection, PROM or leaking membrane, prolonged labor, unhealthy umbilical stump, repeated or unsterile vaginal examination are found to be associated risk factors with raised CRP in neonatal sepsis. In neonatal care unit of tertiary level hospitals like ours, there is massive

patient load and huge economic strain of the family of the patient. Here we usually apply empirical and prolonged use of antibiotic in suspected sepsis in fear of missing life threatening infections.

7. Recommendations

Multicenter study with large sample size should be carried out to determine related microbes and associated risk factors of neonate sepsis. A national guideline should be adopted on the basis of clinical data, Policy should be taken to improve community based obstetric care to reduce the incidence of neonatal Sepsis. Huge patient load may be reduced in tertiary care hospitals by establishing a new effective policy for reducing the burden of sepsis from our country as well as from the globe.

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