

“Risk Factors of Neonatal Sepsis: A Study in a Tertiary Care Paediatric Hospital, Dhaka, Bangladesh”

Dr. Ferdousi Begum¹, Dr. Salina Shaheen Parul², Dr. Md. Tazul Islam³

¹Registrar, High dependency and Isolation unit, Dhaka Shishu(children) Hospital, Dhaka, Bangladesh

²Assistant Professor, Bio-chemistry Department, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh

³Junior Consultant (Paediatrics), 250 Bedded General Hospital, Jamalpur, Bangladesh

Corresponding Author: Dr. Ferdousi Begum

Abstract: Neonatal sepsis is invasive infection, usually bacterial, occurring during the neonatal period. Signs are multiple, nonspecific, and include diminished spontaneous activity, less vigorous sucking, apnea, bradycardia, temperature instability, respiratory distress, vomiting, diarrhoea, abdominal distention, jitteriness, seizures, and jaundice. Hence based on above findings the present study was planned to evaluate the various factors and occurrence of neonatal septicemia in the children admitted to the Department of Paediatrics of Dhaka Shishu(children) Hospital, Dhaka, Bangladesh. The study was planned by enrolling 176 neonates admitted in the selected hospital. Forty (40) neonates diagnosed with the septicemia were enrolled. In the present 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 more than 80% of mothers and modes of delivery were cesarean 60% of mothers. Late Onset Sepsis was 65% of neonates and Gram positive were 25% of the neonates. 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. Improving the survival rate, better approach suggested is a risk approach with 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

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I. Introduction

Septicemia, also known as sepsis, is a life-threatening complication that can happen when bacteria from another infection enter the blood and spread throughout the 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 is 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 premature neonates. Other cases tend to be caused by gram-negative enteric bacilli (eg, *Klebsiella* spp) and certain gram-positive organisms (*Listeria monocytogenes*, enterococci [eg, *Enterococcus faecalis*, *E. faecium*], group D streptococci [eg, *Streptococcus bovis*], alpha-hemolytic streptococci, and staphylococci). Also, *S. pneumoniae*, *H. influenzae* type b, and, less commonly, *Neisseria meningitidis* have been isolated. Asymptomatic gonorrhoea 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 (eg, rubella, cytomegalovirus), protozoal (eg, *Toxoplasma gondii*), and treponemal (eg, *Treponema pallidum*) pathogens. A few bacterial pathogens (eg, *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%). It appeared that the major reason for these frightening data were that Doctors often do not take blood cultures before starting antibiotics, if blood cultures are performed and are negative, antibiotics are almost always continued, if the baby remains "sick", more and more potent broad spectrum antibiotics are used, and the belief that a raised serum C-reactive protein (CRP) is proof of sepsis, even if blood cultures are negative¹. 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 (eg, 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 misclassification and underestimation or overestimation of the incidence of sepsis²⁻⁴.

II. Objectives

General objective:

- To assess risk factors of Neonate sepsis in Bangladesh

Specific objectives:

- To assess causative microbes; responsible for Neonate sepsis in Bangladesh
- To assess drug sensitivity of positive sepsis cases in Bangladesh

III. Methodology and Materials

The 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 from January 2017 to December 2017. The 40 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"

IV. Results

The 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 from January 2017 to December 2017. Forty (40) 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%.

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Table I: Clinical Details of Mothers of neonates (n=40)

Parameters	n	%
Mother Age		
• Less than 20years	12	30
• 20 to 30years	18	45
• Above 30years	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		
1. Normal	16	40
2. Caesarean	24	60

Table II: 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 III: 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

V. Discussion

In our study, 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. There is also delay in appreciating and seeking treatment. Besides, most deliveries in these families are conducted at home under improper aseptic conditions⁵. Adequate antenatal care is crucial for a favourable outcome of pregnancy. Lack of adequate antenatal care associated with home deliveries without aseptic precautions, conducted by untrained dais are the preconditions for sepsis. Studies have reported 3 times higher mortality in babies with inadequate antenatal care compared to those with adequate antenatal care⁶. Instrument assisted deliveries had higher mortality as shown in a number of other studies due to increasing chance of infection^{7,8}. 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 studies⁹. Once again as observed in other studies neonates who had IPPV demonstrated high risk of infection and significant fatality¹⁰. 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 mortality¹¹. 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. In another study done in Indore, Madhya Pradesh *Klebsiella* was found to be the most commonly associated organism. This may be due to 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 isolated¹². Similar results were reported according to NNPD 2002-03 in which among intramural births *Klebsiella* was the most frequently associated pathogen (32.5%) followed by *Staph. aureus* (13.6%). Similar results with *Klebsiella* as the most common isolate was found in other studies^[13]. 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 pneumoniae*, 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

This was a single Centre study with small number of sample size. So, the study result might not be reflected in the whole country.

VI. Conclusion

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. Improving the survival rate, better approach suggested is a risk approach with early initiation of appropriate antibiotics and aggressive supportive care based on local sensitivity pattern and fatal risk factors.

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