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Evaluation of factors responsible for the neonatal sepsis in Darbhanga, Bihar

Dr. Krishan Kumar Jha[1], Dr. Nagendra Prasad Gupta[2*]

[1] Associate Professor, Department of Paediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India

[2] Professor, Department of Paediatrics, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India

[*] Corresponding Author: Dr. Nagendra Prasad Gupta

Abstract

Systemic infection in the newborn is the commonest cause of neonatal mortality. Data from National Neonatal Perinatal Database 2000 suggests that Klebsiella pneumoniae and Staphylococcus aureus are the commonest causes of neonatal sepsis in India. Two forms of clinical presentations have been identified. Early onset sepsis, probably related to perinatal risk factors, usually presents with respiratory distress and pneumonia within 72 hours of age. Late onset sepsis, related to hospital acquired infections, usually presents with septicemia and pneumonia after 72 hours of age. Hence the present study was planned to evaluate the factors responsible for the neonatal sepsis in the darbhanga, bihar region.

The present study was planned in the Department of Paediatrics, Darbhanga Medical College and Hospital. Out of the Total 350 neonates admitted to the Hospital 30 cases were found positive for the septicemia were enrolled in the present study. Case records of newborns admitted to the Neonatal Intensive Care Unit of our tertiary care hospital during this period were obtained from the medical records section. Details of newborns with the final diagnosis of sepsis were reviewed. Neonates fulfilling the criteria for community- and hospital-acquired infections with positive blood culture were included in the study.

The study also emphasizes the need for preventive measures such as early and exclusive breastfeeding, promoting hospital deliveries to reduce the number of community-acquired infections. The present study showed an alarming increase in the prevalence of strains resistant to the commonly used antibiotics. Therefore, a great caution is required in the selection of suitable antibiotic therapy. Early diagnosis with a reasonable degree of accuracy will help the clinician to decide on the usage of proper antibiotic which will help in reducing the morbidity and mortality.

Keywords: newborns, sepsis, septicemia, early on set, late on set, Bihar, etc

Introduction

Neonatal sepsis is a type of neonatal infection and specifically refers to the presence in a newborn baby of a bacterial blood stream infection (BSI) (such as meningitis, pneumonia, pyelonephritis, or gastroenteritis) in the setting of fever. Older textbooks may refer to neonatal sepsis as "sepsis neonatorum". Criteria with regards to hemodynamic compromise or respiratory failure are not useful clinically because these symptoms often do not arise in neonates until death is imminent and unpreventable. Neonatal sepsis is divided into two categories: early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS refers to sepsis presenting in the first 7 days of life (although some refer to EOS as within the first 72 hours of life), with LOS referring to presentation of sepsis after 7 days (or 72 hours, depending on the system used). Neonatal sepsis is the single most common cause of neonatal death in hospital as well as community in developing country.

It is difficult to clinically exclude sepsis in newborns less than 90 days old that have fever (defined as a temperature > 38 °C (100.4 °F). Except in the case of obvious acute viral bronchiolitis, the current practice in newborns less than 30 days old is to perform a complete workup including complete blood count with differential, blood culture, urinalysis, urine culture, and cerebrospinal fluid (CSF) studies and CSF culture, admit the newborn to the hospital, and treat empirically for serious bacterial infection for at least 48 hours until cultures are demonstrated to show no growth. Attempts have been made to see whether it is possible to risk stratify newborns in order to decide if a newborn can be safely monitored at home without treatment despite having a fever. One such attempt is the Rochester criteria [1].

Early-onset neonatal sepsis usually results from organisms acquired intrapartum. Most infants have symptoms within 6 h of birth. Most cases are caused by Group B streptococcus (GBS) and gram-negative enteric organisms (predominantly Escherichia coli). Vaginal or rectal cultures of women at term may show GBS colonization rates of up to 35%. At least 35% of their infants also become colonized. The density of infant colonization determines the risk of early-onset invasive disease, which is 40 times higher with heavy colonization. Although only 1/100 of infants 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 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 [2].

Septicemia in neonates is one of the four leading causes of neonatal mortality in India [3]. The incidence of neonatal sepsis according to the data from the National Neonatal-Perinatal Database (2002–2003) is 30/1000 live birth [4]. Neonatal sepsis may be early onset or late onset depending on the time of onset. Early-onset sepsis is considered to be acquired from the maternal genital tract whereas late-onset sepsis (LOS) is considered to originate from health-care setting or from the community. There is a lack of etiological data on neonatal sepsis acquired in the community, due to insufficient laboratory facilities in rural areas and potentially low levels of care seeking, resulting in much-unreported morbidity and mortality [5]. In developing nations, the likelihood of these infections is increased due to unsafe delivery practices, lack of early, and exclusive breastfeeding. The national nosocomial infection surveillance system reports a rate of 14.15 nosocomial infection per 1000 patients [6].

Systemic infection in the newborn is the commonest cause of neonatal mortality. Data from National Neonatal Perinatal Database 2000 suggests that Klebsiella pneumoniae and Staphylococcus aureus are the commonest causes of neonatal sepsis in India. Two forms of clinical presentations have been identified. Early onset sepsis, probably related to perinatal risk factors, usually presents with respiratory distress and pneumonia within 72 hours of age. Late onset sepsis, related to hospital acquired infections, usually presents with septicemia and pneumonia after 72 hours of age. Hence the present study was planned to evaluate the factors responsible for the neonatal sepsis in the darbhanga, bihar region.

Methodology

The present study was planned in the Department of Paediatrics, Darbhanga Medical College and Hospital. Out of the Total 350 neonates admitted to the Hospital 30 cases were found positive for the septicemia were enrolled in the present study. Case records of newborns admitted to the Neonatal Intensive Care Unit of our tertiary care hospital during this period were obtained from the medical records section. Details of newborns with the final diagnosis of sepsis were reviewed. Neonates fulfilling the criteria for community- and hospital-acquired infections with positive blood culture were included in the study.

Neonatal septicemia was diagnosed as per the clinical criteria given by Vergnano *et al* [6]. Blood sample (0.5 to 2 ml) was collected with all aseptic precaution and was inoculated into blood culture bottle BactT/Alert® PF (BIOMERIEUX, INC. Durhams, NC 27704) containing 20 ml of broth.

Nosocomial infection was defined as any infection causing illness that was not present at the time of admission and occurred after 48 h of hospitalization. Details of study participants were obtained from case records including birth weight, gestational age, place and mode of delivery, breastfeeding pattern (prelacteal feeds, diluted animal milk, and bottle feeding), invasive procedures, duration of stay in the hospital, and other relevant information. Culture reports with their antibiotic sensitivity pattern were also noted from the records. Antibiotic sensitivity testing was performed by modified Kirby-Bauer disc diffusion method as per CLSI recommendations.

All the cases were informed consents. The aim and the objective of the present study were conveyed to parents of the neonates. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study:

Inclusion Criteria

Premature rupture of membranes (PROM) > 12 hours; More than 3 vaginal examinations after rupture of membranes; Intrapartum fever (>38^0C); Foul-smelling liquor; Meconium stained liquor; Maternal UTI within 2 weeks prior to delivery; Prolonged and difficult delivery with instrumentation.

Exclusion Criteria

New born babies with gestational age < 28 weeks; Neonates with birth weight less than <1000 gm; Neonates with lethal congenital anomalies; Still born and fetal deaths; Post-dated neonates.

Results & Discussion

Sepsis is commonest cause of neonatal mortality and is probably responsible for 30% - 50% of the neonatal death each year in developing countries. It is estimated that 20% to 30% of neonates develop sepsis and approximately 1% die of sepsis related causes. Sepsis related mortality is largely preventable with rational anti-microbial therapy and aggressive supportive care. In 2006, the World Health Organization (WHO) reported that out of the 130 million live births every year, 4 million die within the first four weeks of life. Of these deaths, 99% occur in developing countries (Approximately half following difficult deliveries at home) against 1% in developed countries [7].

Table 1: Clinical Details of Mother

Parameters	No. of Cases
Mother Age:	
Less than 20 years	8
20 to 30 years	15
Above 30 years	7
Literacy:	
Literate	12
Illiterate	18
Economic Status:	
Lower	11
Middle	13
Higher	6
Parity of Mother:	
1	17
2	8
More than 2	5
Antenatal Care:	
Less than 3	22
More than 3	8
Predisposing Factors:	
Positive	11
Negative	19
Mode of Delivery:	
Normal	13
Caesarean	17

Table 2: Type & Causative Microbes

Parameters	**No. of Cases**
Type of Sepsis	
Early Onset Sepsis	18
Late Onset Sepsis	32
Causative Bacteria	
Gram Positive	15
Gram Negative	15

Table 3: Positive cases and drug sensitivity

Organisms	**Blood culture positive Cases**
Gram-positive	
Staphylococcus aureus	4
Methicillin-resistant Staphylococcus aureus	2
Staphylococcus epidermidis	2
Total Cases	8 cases
Gram-negative	
Klebsiella pneumonae	11
Acinetobacter	3
Citrobacter	4
Pseudomonas	4
Total Cases	22 cases

Most commonly isolated organisms in community-acquired infections were S. aureus, Klebsiella species, and Escherichia. These results are similar to a previous review, where the order of prevalence was S. aureus, E. coli, and Klebsiella species [8]. A recent study of hospital-acquired neonatal sepsis in developing countries showed a predominance of Gram-negative organisms with Klebsiella species being most commonly isolated, followed by S. aureus and then E. coli [9]. This is similar to our findings, which further suggest potential similarities in major pathogens between community- and hospital-acquired neonatal sepsis in developing countries.

In developing countries, pathogens isolated are different from those seen in developed nations. In our study, Klebsiella species were the most common isolated organisms in both early and LOS. This is similar to the findings reported in earlier studies and those reported in the National Neonatal Perinatal Database [10-11]. In contrast, a study from Sikkim found Pseudomonas and Enterobacter species to be the predominant pathogens among Gram-negative organisms [12]. Among the Gram-positive organisms, S. aureus was the most common isolated organism. Group B streptococcus, which is common in the west, is infrequent in India [13] and was not isolated at our center in any case.

Various factors were found to be associated with neonatal sepsis. The presence of these risk factors warrants an early diagnosis and treatment to save the life of the newborn. Low birth weight and prematurity were mainly associated with neonatal sepsis [14]. Betty *et al* reported that nearly 80% of preterm babies in their study group developed sepsis. Other determinants were febrile illness in mother 2 weeks prior to delivery, foul smelling liquor, meconium staining of liquor, prolonged rupture of membranes or prolonged labour, multiple vaginal examinations etc [15]. Tallur *et al* and Raghvan *et al.* evaluated neonates and found that birth asphyxia is a potent risk factor for neonatal sepsis [16-17]. Tallur *et al* also reported that male babies are much prone to neonatal sepsis than females [18]. Raghvan *et al* studied the maternal risk factor association with neonatal sepsis and came to conclusion that foul smelling liquor, meconium staining and prolonged labour are significantly assosciated with neonatal sepsis [19].

Blood Culture still remain the gold standard for confirming the diagnosis of neonatal sepsis. The success of isolating a bacteria from a blood sample depends on the volume of blood culture, timing and frequency of culture, duration and dilution of culture media and the choice of the culture system [19]. Schelonka *et al* found that if organisms are present at densities of < 4 CFU, blood volume of 0.5 ml or less had a significantly diminished chance of detecting

bacteremia [20].

It is difficult to comment on the clinical significance of low virulence isolates such as coagulase-negative staphylococcus, enterococci, and non-fermenting Gram-negative bacilli. However, in the clinical setting of sepsis, especially in small preterm neonates, it would not be wise to dismiss these isolates as contaminants. Babies with such isolates were treated for sepsis according to protocol, and we have reported these isolates in our study.

A survey of the studies reveals varying predominance of microbes at different times and places and even within the same setup. Hence, in any NICU, it is very essential to have periodic survey to define the organisms and their sensitivity pattern. Antibiotic sensitivity pattern varied among studies probably due to the antibiotic usage differences. Drugs used for sensitivity testing were also not the same in all the studies.

Using the combination of biomarkers to shorten the response times in diagnosis and treatment is of immense value as the presentation of NS is ambiguous and there may be a delay in its detection. Modern molecular methods on the direct sample or the identification by MALDI-TOF on positive blood culture help in optimizing the antibiotic treatment and facilitating stewardship programs. Establishing a sepsis code to decrease the time to achieve diagnosis and to treat, and to improve organization, unify criteria, promote teamwork and also commitment from health administration can reduce morbidity and mortality due to NS by great degree [20-21].

Conclusion

The study also emphasizes the need for preventive measures such as early and exclusive breastfeeding, promoting hospital deliveries to reduce the number of community-acquired infections. The present study showed an alarming increase in the prevalence of strains resistant to the commonly used antibiotics. Therefore, a great caution is required in the selection of suitable antibiotic therapy. Early diagnosis with a reasonable degree of accuracy will help the clinician to decide on the usage of proper antibiotic which will help in reducing the morbidity and mortality.

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