Original Research Article

Clinical study of neonatal sepsis at a tertiary center NICU

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Abstract

Background: The world health organization estimated that there are approximately five million neonatal deaths per year of which 98% occur in developing countries. The number of children dying from sepsis in the world has almost doubled in the past 20 years. They also estimated that 1.6 million deaths occur globally every year due to neonatal infections and 40% of all neonatal deaths occur in developing countries. Most of the neonatal sepsis related deaths are preventable if suspected early and treated with appropriate antibiotics. The aim of the present study was to study the clinical profile of neonates clinically suspected with neonatal sepsis at our tertiary care center. **Material and Methods:** Present study was prospective, observational study conducted in neonates with suspected or diagnosed for neonatal sepsis admitted to neonatal intensive care unit during the study period. **Results:** In present study, after applying inclusion and exclusion criteria, total 134 neonates were included. Male neonates were more (58 %) as compared to female (42 %), male to female ratio was 1.4:1. 43 % neonates were pre-term (gestational age < 37 weeks) while 57 % neonates were term (gestational age > 37 weeks). 63% neonates had birth weight > 2.5 kg, rest 37 % had less than 2.5 kg birth-weight. In present study incidence of early onset sepsis (i.e within 72 hours after birth) was 56%, rest 44% had late onset sepsis (i.e after 72 hours after birth). Major perinatal factors for neonatal sepsis in present study were prolonged labor (>24 h) (22%), premature rupture of membrane (>18 h) (26%), maternal fever within 2 weeks (>38°c) (22%), foul-smelling liquor (13%), birth asphyxia (20%) and unclean or >3 sterile vaginal examinations (7%). **Conclusion:** Neonatal sepsis is a leading cause of neonatal admission, morbidity and mortality in developing countries. Bacterial spectrum, sensitivity pattern could be different in different areas, NICUs. Accordingly, the knowledge of prevailing strains and the antibiotic sensitivity patterns in the region is mandatory for each center for proper treatment.

Key Words: Neonatal sepsis; Clinical outcome; late onset; early onset

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Received Date: 02/12/2019 Revised Date: 08/01/2020 Accepted Date: 12/02/2020
DOI: https://doi.org/10.26611/10141636

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 26 December 2020

INTRODUCTION

Neonatal sepsis encompasses various systemic infections of the newborn, such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis etc. The world health organization estimated that there are approximately five million neonatal deaths per year of which 98% occur in developing countries. The number of children dying from sepsis in the world has almost doubled in the past 20 years.[1] World Health Organization has estimated that 1.6 million deaths occur globally every year due to neonatal infections and 40% of all neonatal deaths occur in developing countries.[2] The major causes of neonatal sepsis are disruption of amniotic membranes, infection upon passing through the birth canal, exposure to infected blood at delivery and trans-placental transmission of infection are some of the major causes of neonatal septicemia.[3] Neonatal conditions such as preterm, Low Birth Weight (LBW), male sex and twin gestation appear to be risk factors too.[4] Bacterial sepsis is considered to be an important cause of neonatal mortality (deaths) in the first month of life.[5] Neonatal sepsis may be classified according to the time of onset of the disease: Early Onset Sepsis (EOS) is (0-7

days) and Late-Onset Sepsis (LOS) is (8-28 days). A few papers distinguish between very early onset sepsis (within 24 hours), EOS (24 hours to seven days), and LOS (more than seven days) sepsis.[6] The distinction has clinical relevance, as EOS disease is mainly due to bacteria acquired before and during delivery, and LOS disease to bacteria acquired after delivery (nosocomial or community sources). Independent risk factors for early onset neonatal sepsis (EONS) such as clinical chorioamnionitis, repeated per vaginal examinations, male sex, birth weight<1500 grams, gestation<30 weeks and non-exposure to intrapartum antibiotic prophylaxis (IAP).[7] Most of the neonatal sepsis related deaths are preventable if suspected early and treated with appropriate antibiotics. The aim of the present study was to study the clinical profile of neonates clinically suspected with neonatal sepsis at our tertiary care center.

MATERIAL AND METHODS

The study was conducted in Neonatal Intensive Care Unit (NICU), department of Neonatology, Shri Bhausaheb Hire Government Medical College. Present study was prospective, observational study conducted for six months from July 1 to December 31, 2019. Institutional ethical committee approval for present study was taken. Neonates admitted with clinical suspicion of sepsis were included in the study. A written informed consent was taken for participation in present study, from parents/guardians.

Inclusion criteria: All neonates with suspected or diagnosed for neonatal sepsis admitted to neonatal intensive care units during the study period.

Exclusion criteria:

- Neonates discharged out of the study period
- Neonates who died without taking any treatment
- Neonates with incomplete patient chart information
- Neonates with birth weight <1000 g, neonates with obvious malformations/congenital anomalies

Demographic details such as neonatal age, sex, weight, birth weight, gestational age, mode of delivery, duration of labor details were noted. Maternal conditions such as comorbid diseases, fever and urinary tract infections were noted. Clinical features of sepsis (lethargy, refusal to feed, abdominal distension, vomiting, respiratory distress, fever, hypothermia, convulsion, sclerema, apnea, and mottling) and risk factors for the sepsis (foul-smelling liquor/ meconium stained liquor, unclean vaginal examination done before delivery/>3 sterile vaginal examinations, prolonged labor, prolonged rupture of membranes, maternal pyrexia within 2 weeks of labor, and birth asphyxia) were recorded.

C-reactive protein (CRP) was done by latex agglutination test. Aerobic blood cultures were done and bacterial isolates, if identified were studied for antibiotic susceptibility by Kirby–Bauer disc diffusion method. Data were entered into an excel spreadsheet and group comparisons were done by applying t-test and $\chi 2$ (Chi-squared test). $p<0.05$ was taken as significant. Statistical analysis was done using descriptive statistics.

RESULTS

In present study, after applying inclusion and exclusion criteria, total 134 neonates were included. Male neonates were more (58 %) as compared to female (42 %), male to female ratio was 1.4:1. 43 % neonates were pre-term (gestational age < 37 weeks) while 57 % neonates were term (gestational age > 37 weeks). 63% neonates had birth weight > 2.5 kg, rest 37 % had less than 2.5 kg birth-weight. 72% neonates presented at first week of life only, 22%, 5% and 1% presented in second, third and fourth weeks respectively. In present study incidence of early onset sepsis (i.e within 72 hours after birth) was 56%, rest 44% had late onset sepsis (i.e after 72 hours after birth). Duration of labour was 6-12 hours in 64 % neonates followed by 12-24 hours in 29 % neonates, >24 hours in 4 % neonates and < 6 hours in 2 % neonates.

Table 1: Characteristics of neonates and results of blood cultures

Characteristics of neonates		No. of cases	Percentage
Gender	Male	78	58%
	Female	56	42%
Gestational age (weeks)	<37	58	43%
	>37	76	57%
	Mean (weeks)	34.96±3.67	
Birth weight (kg)	<2.5	49	37%
	>2.5	85	63%
	Mean (kgs)	2.09±0.72	
Age (weeks)	<1	96	72%
	1-2	29	22%
	2-3	7	5%
	3-4	2	1%
Duration of labor	<6 hr	3	2%

	6-12 hr	86	64%
	12-24 hr	39	29%
	>24 hr	6	4%
Onset of sepsis	Early	75	56%
	Late	59	44%
Day of life at presentation (mean)		2.15±3.15 days	
Hospital days (mean)		9.12±8.29 days	
Hospital days among survivors (mean)		11.89±9.23 days	
Hospital days among expired (mean)		6.39±4.48 days	
Blood culture	Growth	55	41%
	No growth	79	59%

When neonatal sepsis was correlated with perinatal risk factors, we noted following findings. Major perinatal factors for neonatal sepsis in present study were prolonged labor (>24 h) (22%), premature rupture of membrane (>18 h) (26%), maternal fever within 2 weeks (>38°c) (22%), foul-smelling liquor (13%), birth asphyxia (20%) and unclean or >3 sterile vaginal examinations (7%).

Table 2: Perinatal risk factors for Neonatal sepsis

Risk factors	n (%)
Prolonged labor (>24 h)	29 (22%)
Premature rupture of membrane (>18 h)	35 (26%)
Maternal fever within 2 weeks (>38°C)	29 (22%)
Foul-smelling liquor	18 (13%)
Birth asphyxia	27 (20%)
Unclean or >3 sterile vaginal examinations	10 (7%)

Blood samples were sent for blood cultute in each neonate admitted with suspected sepsis. Growth of organisms was reported in 55 neonates (41 %), rest 79 (59 %) samples were sterile. Out of 55 samples with positive growth 69% had of early onset sepsis, rest 31% had late onset sepsis, statistical difference was significant. Klebsiella pneumoniae (60%), coagulase negative staphylococci (CONS) (13%), Acinetobacter spp. (7%), Escherichia coli (5%), Enterobacter spp. (5%), Streptococcus pneumoniae (4%), Pseudomonas stutzeri (4%) and Group B Streptococcus (2%) were isolated from blood samples. Klebsiella pneumoniae (60%) was most common organism noted, 49 % in early onset sepsis and 11% in late onset sepsis, statistical difference was significant. In present study, 63 % neonates required ventilatory support and total 15 % neonatal mortality was noted.

Table 3: Distribution of isolated organisms

Organism	Early-onset sepsis		Late-onset sepsis		Total	P value
	No. of isolates	(%)	No. of isolates	(%)		
Klebsiella pneumoniae	27	49%	6	11%	33 (60%)	Significant
coagulase negative staphylococci (CONS)	3	5%	4	7%	7 (13%)	Not Significant
Acinetobacter spp.	2	4%	2	4%	4 (7%)	Not Significant
Escherichia coli	1	2%	2	4%	3 (5%)	Not Significant
Enterobacter spp.	2	4%	1	2%	3 (5%)	Not Significant
Streptococcus pneumoniae	2	4%	0	0%	2 (4%)	--
Pseudomonas stutzeri	1	2%	1	2%	2 (4%)	--
Group B Streptococcus	0	0%	1	2%	1 (2%)	Not Significant
Total	**38**	**69%**	**17**	**31%**	**55**	**Significant**

DISCUSSION

According to a report , about 0.76 million neonatal deaths occur in India, the highest for any country in the world.[8] Although the neonatal mortality rate (NMR) has declined in the last 2 decades, the early NMR has been the slowest to decline.[9] The three major causes of neonatal deaths are preterm birth complications, infections, and intrapartum related complications; together, they contribute to nearly 90% of total neonatal deaths.[10] Neonatal sepsis is the third most common cause of deaths among neonates, accounting for 225 000 deaths globally every year.[11] South Asia and sub-Saharan Africa have the highest burden of neonatal sepsis in the world. Of the total sepsis related neonatal deaths in 2013, 38.9% occurred in South Asia. Poverty, low coverage of effective interventions, including facility births, and gross inequities in delivery of healthcare

contribute to this situation.[12] Sepsis is a major cause of neonatal morbidity and mortality. In 2013, sepsis accounted for 15.6% of 2.8 million neonatal deaths and 47.6% of late neonatal deaths. Early onset sepsis is thought to be caused by pathogens vertically transmitted from mothers while late onset sepsis is attributed to pathogens acquired horizontally from the environment or care givers, or both. About 62% of the infections in South Asia occur in the first 72 hours of life, roughly translating into an incidence of 9.8 per 1000 live births.[13] In present study incidence of early onset sepsis was 56%, rest 44% had late onset sepsis. Early-onset neonatal sepsis is acquired transplacentally or as an ascending infection from cervix or during passage of the baby through a colonized birth canal. Late-onset neonatal sepsis is usually acquired from the care-giving environment and coagulase-negative staphylococci (CONS), Staphylococcus aureus, Escherichia coli and Klebsiella species are the common agents involved.[14] In present study, klebsiella pneumoniae (60%) was most common organism noted, 49 % in early onset sepsis and 11% in late onset sepsis. Although Group B Streptococcus was considered as an important agent associated with early onset sepsis, the recent studies are showing a decreasing trend in the incidence of this pathogen.[15] Growth of organisms was reported in 55 neonates (41 %), rest 79 (59 %) samples were sterile. Because of the difficulty in obtaining an adequate volume of blood in preterm neonates and the low levels of bacteraemia, blood cultures tend to be sterile in many neonates. The culture positive versus culture negative sepsis ratio ranges from 1:6 to 1:16 in high income countries.[16] The ratio is likely to be more skewed towards culture negative sepsis in South Asia, given the poor microbiological laboratory support in most units. The ANISA study showed that many neonates with negative blood cultures had viral infections.[17] The low case fatality in neonates with culture negative sepsis (only one fifth of that of culture positive sepsis) in the multisite study from Delhi[18] also suggests that many of these neonates either had viral infections or did not have sepsis at all. More reliable and accurate point-of-care diagnostic method(s) are needed to rule out sepsis, thereby preventing indiscriminate use of antibiotics in neonatal intensive care units. [17] A study from rural Orissa reports the incidence of culture-confirmed neonatal (0–28 days of life) sepsis as 4.6/1000 live births, 5.5% mortality for clinical NS, and 10.3% mortality for culture-proven NS.[19] Investigators of the Delhi Neonatal Infection Study (DeNIS) collaboration found that, in the 13530 neonates who were enrolled of 88636 live births from 2011 to 2014, the incidence of total sepsis was 14.3% and of culture-positive sepsis was 6.2% of which 83% were early onset sepsis (EOS). The population attributable risks of mortality were 8.6% in culture-negative sepsis, 15.7% in culture-positive sepsis by multidrug-resistant organisms, and 12.0% in culture-positive sepsis by non-multidrug-resistant organisms.[18] CRP had good sensitivity and negative predictive value than specificity and positive predictive value when culture is taken as standard similar to previous observations.[20] A study published by Jajoo M[21], studied the incidence of sepsis in outborn Nicu, had an overall sepsis rate of 18/1000 neonates admitted. *Klebsiella pneumonie* (36%), *Staphylococcus aureus* (21%), and *Escherichia coli* (14%) were the most common organisms.[21] In Zakariya BPs[22] study, incidence of culture proven sepsis was 41.6% (50 of 120).12 *Klebsiella pneumoniae* was isolated from 66% of culture positive cases followed by Coagulase-negative *staphylococci* in 12% of cases. Our findings are similar to previous study. In developing nations, the likelihood of these infections is increased due to unsafe delivery practices, lack of early, and exclusive breastfeeding.[23] The risk of nosocomial infections is predominantly affected by prematurity, invasive procedures, and duration of stay in the hospital. These infections are a significant hazard in health-care facilities, causing increased morbidity and mortality in newborns. Factors in the postnatal period associated with an increased risk of sepsis or septic shock include male gender, birth weight <1000 grams, hypogammaglobulinemia, intravenous alimentation, central venous catheters, use of steroids or drugs that decrease gastric acid acidity, and prolonged duration of mechanical ventilation. The development of severe necrotizing enterocolitis (NEC) is also associated with severe sepsis, shock, multi-organ system failure and death.[24] The overall improvement in the neonatal survival due to newer drugs, better neonatal care and advanced life support facilities has led to a change in the spectrum of agents causing neonatal sepsis in developed countries.

CONCLUSION

Neonatal sepsis is a leading cause of neonatal admission, morbidity and mortality in developing countries. Bacterial spectrum, sensitivity pattern could be different in different areas, NICUs. Accordingly, the knowledge of prevailing strains and the antibiotic sensitivity patterns in the region is mandatory for each center for proper treatment. Most of the neonatal sepsis related deaths are preventable if suspected early and treated with appropriate antibiotics.

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Source of Support: None Declared
Conflict of Interest: None Declared