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Research Article

Clinical Profile of Neonatal Sepsis With Reference to Antibiotic Resistance

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Abstract :

Introduction : Neonatal sepsis continues to be a major cause of morbidity and mortality in neonates. It is 30 per 1000 live births in India. The prevalence is more in preterm neonates.

Objectives

- **To describe the clinical and bacteriological spectrum in early onset sepsis and late onset sepsis.**
- **To describe the antibiotic resistance profile of bacteria causing early and late onset sepsis.**
- **To compare the risk factors and bacteriological spectrum in early onset and late onset sepsis.**

Setting: NICU of civil hospital Ahmedabad
Study period: June 2016 to December 2016
Design: retrospective cohort study
Methods: all neonate admitted in NICU of civil hospital Ahmedabad during the abovementioned period were assessed.
Inclusion criteria: presence of one or more of established clinical features like , (fever/hypothermia, poor feeding, poor activity, respiratory distress/apneic spells, hepatospleenomegaly, vomitting, abdominal distension, seizures, signs of either respiratory or circulatory dysfunction evidenced by tachycardia/bradycardia, capillary refill time>3 seconds,, respiratory rate>60/minute, chest indrawing and/or grunting)along with >_2 of the following laboratory criteria(total blood leukocyte count<5000 or>15000, absolute neutrophil count(ANC)<500 cells/mm^{3}or >1500 cells/mm^3,C reactive protein (CRP)>0.6microgram/ml, positive blood culture). Information assessed in a proforma. Cases were divided into early onset sepsis(EOS) (presenting in the first 72 hours) and late onset sepsis(LOS) (presenting after 72 hours). All cases were started on antibiotics and upgraded or stopped based on culture and sensitivity. Cases were followed to discharge/death.

Introduction

Neonatal sepsis is defined by generalized bacterial infection documented by a positive blood culture in the first 4 weeks of life along with clinical syndrome characterized by systemic signs of infection. It is one of the most important cause of neonatal death worldwide with prematurity and asphyxia[1]. Sepsis occurring in first 72 hours of life is defined as early onset sepsis(EOS) and that occurring after 72 hours of life is defined as late onset sepsis(LOS)[2]. Neonatal sepsis is a significant cause of morbidity and mortality among neonates. In the developing world Ecoli, klebsiella species and Staphylococcus aureus are the most common cause of EOS whereas staphylococcus aureus, streptococcus pneumonia and streptococcus pyogenes are the most commonly reported organism in LOS.[2] Although most isolates remain sensitive to new antibiotics, emergence of resistant strains cannot be excluded. The spectrum of organism causing EOS and LOS are different and they change rapidly with over time and is influenced by various external factors. The main source of EOS are from maternal flora or during delivery and that of LOS is from community or from health care associates[3] . various risk factors are described for neonatal sepsis which includes maternal risk factors like fever, Premature rupture of membrane>24hrs, chorioamnionitis. Fetal factors include prematurity, low birth weight[7.] Clinical feature of EOS are apparent within few hours of life. The signs and symptoms may be subtle. Blood culture is usually needed for bacteriological confirmation but the yield is low[4,5]. CRP and procalcitonin are also used to identify neonatal sepsis and for prognostication[6]. We have attempted to look at the pattern of neonatal sepsis in our hospital. This will help in choosing appropriate antibiotics and will also help to develop neonatal antibiotic protocols.

Methods

A retrospective cohort study was done in NICU, Department of pediatrics, civil hospital Ahmedabad was carried out. The culture and sensitivity pattern of cases of neonatal sepsis from 1st june 2016 to 31st december 2016 were collected. Neonates

with clinical features of sepsis and fulfilling the inclusion criteria were included in the study. Information regarding maternal (age, parity, prolonged rupture of membrane, predisposing factors) and neonatal(gestationl age, sex birth weight, time of onset of symptoms, antibiotic treatment) were assessed in the proforma. 250 cases of confirmed sepsis were enrolled and divided into early onset sepsis and late onset sepsis. All cases were started on antibiotics as per the departmental protocol and later upgraded or stopped based on the culture sensitivity. Cases were followed upto discharge/ death.

Blood culture was routinely sent for all neonates admitted to NICU as per the protocol using aseptic techniques. 2ml blood is collected in 5ml disposable syringe and added to blood culture bottle . Blood culture is reported by microbiologist. CSF analysis and culture was done ony in suspected cases of meningitis and late onset sepsis. Urine analysis was performed in selected cases only.

Aims and objectives

- To describe the clinical and bacteriological spectrum in early onset sepsis and late onset sepsis.
- To describe the antibiotic resistance profile of bacteria causing early and late onset sepsis.
- To compare the risk factors and bacteriological spectrum in early onset and late onset sepsis.

Inclusion criteria

Presence of one or more of established clinical features like , (fever/hypothermia, poor feeding, poor activity, respiratory distress/apneic spells, hepatospleenomegaly, vomitting, abdominal distension, seizures, signs of either respiratory or circulatory dysfunction evidenced by tachycardia/bradycardia, capillary refill time>3 seconds,, respiratory rate>60/minute, chest indrawing and/or grunting)along with >_2 of the following laboratory criteria(total blood leukocyte count<5000 or>15000, absolute neutrophil count(ANC)<500 cells/mm^3or >1500 cells/mm^3,C reactive protein (CRP)>0.6microgram/ml, positive blood culture).

Results

There were 3678 admissions during the study period of this 375 cases were of suspected sepsis. Septic screen was positive in 220 cases(58.66%). The presumed sepsis during the same period was 220/3678(5.9%). Of these neonates 109(49.54%) had culture positive sepsis. Hence the incidence of culture positive sepsis in our study is 109/375(29.06%). Of these 47(43.11%) were eary onset sepsis and 62 (56.88%) were late onset sepsis. The total deaths were 461. Of these deaths 73 deaths had culture positivity. Male: female ratio was 1.42:1 in this study. Maternal complications were documented in 16 patients(21.91%). History of perinatal depression was evienced in 8(10.95%). Of these neonates 97(88.99%) were term neonates. 89 (81.65%) were AGA, 17(15.59%) were SGA and 3(2.75%) were LGA.

Table 1 clinical presentation of culture positive sepsis

	N	%
Respiratory distress	27	24.77%
Temperature instability	13	11.92%
Jaundice	12	11%
Poor feeding	12	11%
Seizures	6	5.5%
Abdominal distension	2	1.83%
Cyanosis	3	2.75%
Hypoglycemia	2	1.83%
Bleeding	14	12.8%

Table 2 comparison of clinical features of EOS and LOS

	EOS(N=47)	LOS(N=62)
Male:female	25:22	39:23
AGA:SGA	36:11	33:29
Preterm:term	16:29	26:36
N:LSCS	19:26	13:49
Maternal infection	7	11
PROM	5	13
Asphyxia	10	24
Respiratory distress	9	18
Poor feeding	4	8
Seizures	1	5
Temperature instability	5	8
Cyanosis	1	2
Hypoglycemia	-	2
Bleeding	3	11
CRP high	32	48
TLC<5000	11	29
ANC<1500	4	15
Platelet<1 lakh	27	51
Deaths	7	12

Table 3 bacteriological spectrum in neonatal sepsis

	EOS(n=47)	LOS(n=62)	Total
Staphylococcus	9	8	17%)
Klebsiella	16	21	37(33.94%)
Acinetobacter	3	5	8(7.33%)
Pseudomonas	6	8	14(12.84%)
E coli	9	4	13(11.92%)
Streptococci	2	-	2(1.83%)
CONS	10	11	21(19.26%)

Table 4 pattern of resistance to selected antibiotics in neonatal sepsis(%)

Antibiotics	Percentage
Ampicillin	77.7%
Amoxicillin	81.5%
Gentamycin	55.1%
Amikacin	17.4%
Cefotaxime	63.1%
Ceftriaxone	66.9%
Ciprofloxacin	40%
Ofloxacin	38.5%
Imipenem	42.3%
vancomycin	0

Table 5 resistance of various causative bacteria to antibiotics

	ampicillin	amoxicillin	cefotaxime	ceftriaxone	gentmycin	amikacin	ciprofloxacin	ofloxacin	imipenem	vancomycin
Staphylococcus	77.1%	77.1%	80%	74.3%	-	-	30.4%	74.2%	74.2%	-
Klebsiella	92.3%	100%	14.6%	14.6%	48.9%	26.6%	26.37%	7.6%	7.6%	-
Acinetobacter	98.1%	98.1%	82.36%	98%	66.6%	46.6%	70.5%	52.9%	52.9%	-
Pseudomonas	77.1%	92.3%	80%	14.6%	-	-	30.4%	20%	20%	-
Ecoli	73.3%	76.6%	30.76%	40%	60%	3.3%	40.33%	20%	20%	-
Streptococci	14.28%	20.8%	20%	40%	-	-	20.8%	13.5%	13.5%	-

Discussion

Neonatal sepsis is a clinical syndrome of bacteremia with features of systemic signs and symptoms of infection in the first 4 weeks of life. This is a very vulnerable period. As per national neonatal perinatal data 2002-2003, the incidence if neonatal sepsis in India was 30/1000 live birth.[4] many studies have reported clinical sepsis rates ranging from 49 to 170/1000 live births in rural india[5]. This study was done in tertiary care of teaching hospital level 2 NICU which admitted neonates born outside and inside the hospital. The presumed sepsis during the study period was 5.9%. of these 109(29.06%) had culture positive sepsis. A study from Vellore have reported sepsis in 9.8 per 1000 live births and 4.4% of all nursery admissions[7]. A study from Andhra Pradesh comparing the incidence and mortality rates of neonatal sepsis between two different time periods(June 2003-may2004) and (June 2013-May 2014) of a decade apart found that the overall incidence of sepsis has remained the same (6.04% and 6.03%) but the incidence of EOS decreased from 3.08% to 2.57% and LOS increased from 2.96% to 3.44% of the total pediatric admissions[6]. In the similar study from North India[8,9] estimated the increase in incidence of LOS from 12 to 16.5 per 1000 live births. In this study 64 were males (58.71%). In Vellore study 85 were male infants (68.3%)[7]. In a study from Nepal, 61.4% were males and 38.6% were females. Similar higher rates of septicemia in male was also reported by Karambin and Zarkesh from Iran[11]. And Al-Shamahy et al from Yemen[12].

In this study, among the outborn neonates 53.2% were delivered at government hospitals, 32.5% in private hospital. 64(68.8%) were delivered by cesarean section while 32(29.35%) were delivered vaginally. In a study from Egypt, 69.7% were delivered by cesarean section whereas 30.3% were delivered normally. History of perinatal depression was found in 34(31.19%) neonates. Only 10 neonates were given antibiotics before referral. Of these 65(59.63%) were term neonates. 69(63.3%) were appropriate for gestational age and 40(36.69%) were small for gestational age. In our study 44(40.3%) were preterms whereas in study rom Vellore it was 9.8%. in our study 109 were culture positive sepsis. Of 109 culture positive cases 47 (43.11%)were of EOS while 62(56.88%) were of LOS The prevalance rate being 11.3% of culture positive sepsis. Emam El-din reported 140(40.7%) cases of culture positive sepsis: 49 of EOS and 91 of LOS. There was a significant difference in the positivity rate between EOS and LOS groups (p value<0.05)[13]. The result indicated that the incidence of EOS was more common than LOS.[10,14,15,16,17,18]. Gram positive and gram negative bacteria were isolated in different cases. Gram negative bacteria were

common than gram positive bacteria. Klebsiella was the most common pathogen found in our study. Klebsiella was found in both EOS and LOS, but mainly in LOS as compared to EOS. The 2nd most common organism was CONS. Among the gram positive bacteria staphylococcus accounted for 15.53% of neonatal sepsis. Pseudomonas was isolated in 12.8% of the patients while acinetobacter was isolated in 7.5%. streptococci was isolated in 1.835 of the cases and all were isolated in EOS. Awoniyi et al have described that streptococci species causes neonatal sepsis only in 5% of cases mainly found in EOS which was consistent with our study. Shaw et al[19] have found streptococci in 10.72% of cases mainly in EOS. These similar findings were described in a study by Multan Afteb et al.[22]

Our study revealed that most of the commonly used antibiotics had high resistance of bacteria. Bacteria were highly resistant to ampicillin and amoxicillin. Overall resistance rate being 77.7% and 81.5% respectively. Staphylococcus, Klebsiella, Acinetobacter, Ecoli showed 77%, 98.1%, 92.3%, 73.3% resistance to these antibiotics respectively. Waseem et al[21] described high resistance of these bacteria against ampicillin. Awoniyi et al[23] also have found these bacteria high resistant to ampicillin. Both ampicillin and amoxycillin have been found having comparitively less resistance to streptococci i.e., resistance in 14.28% and 20.8% respectively. Waseem et al[21] found streptococci 100% sensitive to ampicillin.

Both gram positive and gram negative bacteria have been found resistant against 3rd generation cephalosporins. Cefotaxime and ceftriaxone had high resistance . many other studies have also described the emerging pattern of resistance against cefotaxime and ceftriaxone. Waseem et al[21] found that this may be due to changing pattern of resistance due to indiscriminate use of antibiotics.

Aminoglycosides show variable pattern of resistance against different bacteria. Waseem et al[21] described that gentamycin had resistance in 82.4%, 75% and 80% of these bacteria respectively. E coli, Acinetobacter and Klebsiella were resistant to amikacin.

Quinolones are not frequently used for neonatal sepsis. Resistance is emerging against them because of indiscriminate use of antibiotics, but still resistance to quinolones is low compared to commonly used antibiotics. Our study showed that ciprofloxacin had resistance in 40% cases and ofloxacin had resistance in 38.5%.

Imipenem is widely used nowadays and has high sensitivity against both gram positive and gram negative bacteria. Shaw et al[19] have found 100% sensitivity of imipenem against Staph aureus, Acinetobacter, E coli, Klebsiella, Streptococci species. The present study showed that imipenem sensitivity rate was 57.1%% of which sensitivity against individual bacteria discussed above was 25.8%, 47.1%, 92.35%, 80%, 86.5%. Waseem et al[21] also have found imipenem 100% effective against above mentioned bacteria. In our study high resistance rate may be due to resistant strains of bacteria due to improper use of antibiotics.

Vancomycin is having excellent coverage against staphylococci[19,20]. The present study also shows 100% sensitivity of staphylococci to vancomycin .

Conclusion

The incidence of culture positive sepsis is 49.54%. of these 43.11% was EOS and 56.88% was LOS. Staphylococcus and Klebsiella are the most common organisms causing neonatal sepsis. Both gram positive and gram negative bacteria have developed resistance to commonly used antibiotics like ampicillin, amoxycillin, cefotaxime, ceftriaxone and gentamycin. Less commonly used antibiotics like amikacin and vancomycin are relatively more effective.

References

1. J. O. Klein, "Bacteriology of neonatal sepsis," Pediatric Infectious Disease Journal, vol. 9, no. 10, pp. 777–778, 1990. View at Google Scholar · View at Scopus

2. Lawn JE, Wilczynska-Ketende K, Cousens SN. Estimating the causes of 4 million neonatal deaths in the year 2000. Int J Epidemiol 2006;35:706-18.

3. .Bizzarro M. J., Dembry L.-M., Baltimore R. S., Gallagher P. G. Changing patterns in neonatal *Escherichia coli* sepsis and ampi-cillin resistance in the era of intrapartum antibiotic prophylaxis. *Pediatrics*. 2008; 121(4):689–696. doi: 10.1542/peds.2007-2171. [PubMed] [Cross Ref]

4. National Neonatology Forum NNPD Network. National Neonatal-Perinatal Database: Report for 2002-2003. New Delhi: National Neonatology Forum NNPD Network; 2005

5. Shrestha S., Adhikari N., Rai B. K., Shreepaili A. Antibiotic resistance pattern of bacterial isolates in neonatal care unit. *Journal of the Nepal Medical Association*. 2010;50(4):277–281. [PubMed]

6. Bangi VA, Devi S S. Neonatal sepsis: A risk approach. J NTR Univ Health Sci 2014;3:254-8

7. Kurien Anil Kuruvilla, Swati Pillai, Mary Jesudason* and Atanu Kumar Jana Bacterial Profile of Sepsis in a Neonatal Unit in South India: Indian Pediatrics 1998; 35:851-858

8. Mathur NB, Singh A, Sharma VK, Satyanarayana L. Evaluation of risk factors for fatal neonatal sepsis. Indian Pediatr 1996;33:817-22.

9. Sundaram V, Kumar P, Dutta S, Mukhopadhyay K, Ray P, Gautam V, et al. Blood culture confirmed bacterial sepsis in neonates in a North Indian tertiary care center: Changes over the last decade. Jpn J Infect Dis 2009;62:46-50.

10. Shamshul Ansari, Hari Prasad Nepal, Rajendra Gautam, Sony Shrestha, Puja Neopane, and Moti Lal Chapagain International Journal of Pediatrics Neonatal Septicemia in Nepal: Early-Onset versus Late-Onset Volume 2015 (2015), Article ID 379806 http://dx.doi.org/10.1155/2015/379806

11. M.-M. Karambin and M. Zarkesh, "Entrobacter, the most common pathogen of neonatal septicemia in Rasht, Iran," Iranian Journal of Pediatrics, vol. 21, no. 1, pp. 83–87, 2011. View at Google Scholar · View at Scopus

12. H. A. Al-Shamahy, A. A. Sabrah, A. B. Al-Robasi, and S. M. Naser, "Types of bacteria associated with neonatal sepsis in Al-Thawra University Hospital, Sana'a, Yemen, and their antimicrobial profile," Sultan Qaboos University Medical Journal, vol. 12, no. 1, pp. 48–54, 2012. View at Google Scholar · View at Scopus

13. Eman M. RabieShehab El-Din, 1 Moha-med M. Adel El-Sokkary, 2 , * Mohamed Reda Bassiouny, 3 and Ramadan Hassan. Epidemiology of Neonatal Sepsis and Implicated Pathogens: A Study from Egypt.Biomed Res Int. 2015; .

14. AH. Movahedian, R. Moniri, and Z. Mosayebi, "Bacterial culture of neonatal sepsis," Iranian Journal of Public Health, vol. 35, no. 4, pp. 84–89, 2006. View at Google Scholar · View at Scopus

15. S. Gheibi, Z. Fakoor, M. Karamyyar et al., "Coagulase-negative Staphylococcus; the most common cause of neonatal septice-mia in Urmia, Iran," Iranian Journal of Pediatrics, vol 18, no 3, pp 237–243, 2008. View at Google Scholar · View at Scopus

16. H. S. Naher and A. B. Khamael, "Neonatal sepsis; the bacterial causes and the risk factors," International Research Journal of Medical Sciences, vol. 1, no. 6, pp. 19–22, 2013. View at Google Scholar

17. H. Movahedian, R. Moniri, and Z. Mosayebi, "Bacterial culture of neonatal sepsis," Iranian Journal of Public Health, vol. 35, no. 4, pp. 84–89, 2006. View at Google Scholar · View at Scopus

18. S. Gheibi, Z. Fakoor, M. Karamyyar et al., "Coagulase-negative Staphylococcus; the most common cause of neonatal septicemia in Urmia, Iran," Iranian Journal of Pediatrics, vol. 18, no. 3, pp. 237–243, 2008.View at Google Scholar · View at Scopus

19. Shaw CK, Shaw P, Thapalial A. Neonatal sepsis bacterial isolates antibiotics susceptibility patterns at a NICU in a tertiary care hospital in western Nepal: A retrospective analysis. Kathmandu Uni Med J 2007;5(2):153–60.

20 Aftab R, Iqbal I. Bacteriological agents of neonatal sepsis in NICU at Nishtar Hospital, Multan. J Coll Physicians Surg Pak

21. Waseem R, Khan M, Izhar TS. Neonatal sepsis. Professional Med J 2005;12:451–6.

22 Aftab R, Iqbal I. Bacteriological agents of neonatal sepsis in NICU at Nishtar Hospital, Multan. J Coll Physicians Surg Pak

23. Awoniyi DO, Udo SJ, Oguntibeju. An epidemiological survey of neonatal sepsis in a hospital in western Nigeria. Afr J Microbiol 2009;3:385–9.