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The bacteriological and demographic pattern of term and late preterm neonatal sepsis in a tertiary care hospital

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Abstract
Background: Neonatal sepsis is a clinical condition defined as an infection in newborns accompanied by or caused by an infection of the blood, typically bacterial and rarely fungal. The spectrum of organisms that cause neonatal sepsis changes over time and also varies from region to region. Present study was aimed to bacteriological and demographic pattern of term and late preterm neonatal sepsis in a tertiary care hospital. **Material and Methods:** Present study was retrospective, observational study, conducted in neonates with suspected or diagnosed for neonatal sepsis admitted to neonatal intensive care units during the study period. Results: In present study, total admissions from 0 to 28 days of life in NICU during study period were 940. Out of 940 admissions 106 to be screened for sepsis. Male neonates were more (57.55 %) as compared to female (42.45 %), male to female ratio was 1.4:1. Majority of neonates were term (gestational age > 37 weeks) (51.89 %), had birth weight > 2.5 kg (55.66 %), presented at first week of life only (75.47 %) & had duration of labour as 12-24 hours (51.89 %). 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). On admission, blood samples of each neonate admitted with suspected sepsis were sent for blood culture. Growth of organisms was reported in 46 neonates (43.4 %). 27 neonates (58.7 %) from early onset sepsis had positive growth on culture. Common organisms isolated were Staph Aureus (MSSA) (17.39 %), E. Coli (15.22 %), Klebsiella Pneumonae (8.7 %). 57.55 % neonates required ventilatory support & total 14.15 % neonatal mortality was noted. **Conclusion:** Neonatal sepsis is a leading cause of neonatal admission, morbidity and mortality in developing countries.

Keywords: Neonatal sepsis, neonatal morbidity, early onset sepsis, term neonate

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Introduction

Neonatal sepsis is a clinical condition defined as an infection in newborns accompanied by or caused by an infection of the blood, typically bacterial and rarely fungal.[1] In 2018, an estimated 15% of all neonatal deaths globally were due to sepsis. [2] Studies have shown that the highest incidence of neonatal sepsis occurs in pre-term and low-birth-weight infants. However, the overall incidence of neonatal sepsis is highest in low-income countries.[2]

In neonates, sepsis is an important cause of morbidity and mortality. In developing countries, gram-negative organisms contribute to the major burden of neonatal sepsis. Risk factor for sepsis include prematurity, neonates who require prolonged intravenous access, endotracheal intubation or other invasive procedures that impair the normal protective barrier providing a portal of entry for pathogen.[3] Certain other maternal predisposing factors as prolonged

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rupture of membrane, fever, foul smelling liquor and chorioamnionitis also contribute for infection in neonates.[4]

The spectrum of organisms that cause neonatal sepsis changes over time and also varies from region to region.[5] The uncertainty regarding the clinical approach to treatment of neonatal sepsis can be minimized by periodic surveillance for bacteriological flora and susceptibility pattern so that appropriate choice of antimicrobials for empirical therapy can be outlined and re-evaluated in timely manner. the knowledge of prevalence of local isolates and their antimicrobial sensitivity pattern is of utmost necessary for prompt antimicrobial therapy of neonatal sepsis. Present study was aimed to bacteriological and demographic pattern of term and late preterm neonatal sepsis in a tertiary care hospital.

Material And Methods

Present study was retrospective, observational study, conducted in Neonatal Intensive Care Unit (NICU), department of Paediatrics, at Government medical college & hospital, Kathua, India. Study duration was of 10 months (from 1st January to 31st October 2022). Neonates admitted with clinical suspicion of sepsis were included in the study. Study approval was obtained from institutional ethical committee.

Inclusion criteria: All babies, late preterm and term babies with weight appropriate for gestation ages who were admitted during this period with evidence of sepsis.

Exclusion criteria: Babies with congenital malformations and chromosomal anomalies.

Sepsis was defined according to international sepsis definition conference as "clinical syndrome characterized by presence of both infection and systemic inflammatory response syndrome".[6] Systemic inflammatory response syndrome in case of neonates is defined as two or more of the following:

- Tachypnea (respiratory rate more than 60 bpm + grunting or retractions.
- Temperature instability < 36°C or more than 37.9°C.
- Capillary refill time more than 3 seconds.
- White blood cell count < 5000/µl or more than 34000/µl.
- CRP more than 10 mg/dl IL-6 more than 70 pg/ml.
- Procalcitonin more than 8.1 mg/dl or more than 2 SD above normal values.

Sepsis is defined as one or more systemic inflammatory response syndrome criteria with signs of infection.[7] Only first episode of sepsis in a patient was included. Sepsis evaluation was based on clinical signs and symptoms and rapid screening tests for sepsis, blood culture, urine microscopy and culture and CRP. Lumbar puncture for cerebrospinal fluid (CSF) analysis and culture, stool culture and chest radiographs, were obtained at the discretion of the attending pediatrician.

In case of CONS sepsis repeat blood culture was taken to rule out contamination. Blood for culture (1ml of blood) and complete blood counts was obtained by means of venipuncture. Blood cultures were monitored by an automated system (Bac T/ALERT 3D). The WBC count with differential and the platelet count were quantified using automated laboratory equipment (Sysmex KX-21). Urine was obtained by urethral catheterization using a sterile technique. A careful urinalysis, on a fresh urine sample, can identify children with a high likelihood of UTI to enable presumptive treatment while awaiting results of urine culture, the WBC in the urine were quantified by standard microscopic examination and expressed as WBC >5 leukocytes/high power field in a centrifuged sample or >10 leukocytes / mm3 in an uncentrifuged sample.

Urinary tract infection was defined as growth of single known pathogen on urine culture with ≥100,000 cfu/mL of urine obtained by urethral catheterization. Urosepsis was taken as UTI with signs of SIRS. The urine, CSF, and stool cultures were monitored using standard laboratory techniques. Normal CSF in neonates was defined as, cells up to 8(0- 30)/mm3,

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proteins 90(20-170)mg/dl, polymorphonuclear cells up to 60% of TLC, CSF glucose content 52(34-119)mg/dl and values beyond it were always taken abnormal in all patients.
Early-onset neonatal sepsis (EONS) occurs within first 72 hr of life, while the late-onset neonatal sepsis (LONS) was taken beyond 72hr of life. Mortality was defined as death before discharge. Infants discharged to home were considered survivors.
For statistical analysis data was expressed as mean ±SD. Analysis was done by using student t-test for parametric data. Proportions were compared using X2 test of significance. Values were considered significant if $p< 0.05$. The data was analysed using SPSS package.

Results

In present study, total admissions from 0 to 28 days of life in NICU during study period were 940. Out of 940 admissions 106 to be screened for sepsis. Male neonates were more (57.55 %) as compared to female (42.45 %), male to female ratio was 1.4:1. Majority of neonates were term (gestational age > 37 weeks) (51.89 %), had birth weight > 2.5 kg (55.66 %), presented at first week of life only (75.47 %) & had duration of labour as 12-24 hours (51.89 %).

Table 1: General characteristics

Characteristics of neonates	No. of patients	Percentage
Gender		
Male	61	57.55
Female	45	42.45
Gestational age (weeks)		
<37	51	48.11
>37	55	51.89
Mean (weeks)	35.62 ± 3.67	
Birth weight		
<2.5	47	44.34
>2.5	59	55.66
Mean (kgs)	2.19 ± 0.72	
Age (weeks)		
<1	80	75.47
1-2	15	14.15
2-3	8	7.55
3-4	3	2.83
Duration of labor		
<6 hr	1	0.94
6-12 hr	41	38.68
12-24 hr	55	51.89
>24 hr	9	8.49

Neonatal sepsis is grouped into two subtypes depending on onset of infection onset before 72 hours of life (Early onset Sepsis) or after 72 hours (Late onset Sepsis). 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). On admission, blood samples of each neonate admitted with suspected sepsis were sent for blood culture. Growth of organisms was reported in 46 neonates (43.4 %).
When neonatal sepsis was correlated with perinatal risk factors, major factors were Birth asphyxia (25.47 %), Unclean or >3 sterile vaginal examinations (19.81 %), Premature rupture

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of membrane (>18 h) (17.92 %), Foul-smelling liquor (14.15 %), Maternal fever within 2 weeks (>38°C) (10.38 %) & Prolonged labor (>24 h) (8.49 %).

Table 2: Sepsis related parameters

Characteristics	No. of patients	Percentage
Onset of sepsis		
Early	51	48.11
Late	56	52.83
Blood culture		
Growth	46	43.4
No growth	60	56.6
Perinatal risk factors		0
Birth asphyxia	27	25.47
Unclean or >3 sterile vaginal examinations	21	19.81
Premature rupture of membrane (>18 h)	19	17.92
Foul-smelling liquor	15	14.15
Maternal fever within 2 weeks (>38°C)	11	10.38
Prolonged labor (>24 h)	9	8.49

In present study, 27 neonates (58.7 %) from early onset sepsis had positive growth on culture. Common organisms isolated were Staph Aureus (MSSA) (17.39 %), E. Coli (15.22 %), Klebsiella Pneumonae (8.7 %), Pseudomonas Species 4 (8.7 %), MRSA 1 (2.17 %), Coagulase negative staphylococci (2.17 %), Acinetobacter Baumanni (2.17 %) & Enterococcus faecalis (2.17 %). While, 19 neonates (41.3 %) from early onset sepsis had positive growth on culture. Common organisms isolated were Staph Aureus (MSSA) (10.87 %), E. Coli (6.52 %), Klebsiella Pneumonae (4.35 %), Pseudomonas Species 4 (4.35 %), MRSA (4.35 %), Coagulase negative staphylococci (4.35 %), *Streptococcus Pyogenes*(4.35 %), Acinetobacter Baumanni (2.17 %) & Enterococcus faecalis (2.17 %).

Table 3: Bacteriological profile

Organisms	Type of sepsis		Total
	Early-onset sepsis	Late-onset sepsis	
Staph Aureus(MSSA)	8 (17.39 %)	5 (10.87 %)	13 (28.26 %)
E. Coli	7 (15.22 %)	3 (6.52 %)	10 (21.74 %)
Klebsiella Pneumonae	4 (8.7 %)	2 (4.35 %)	6 (21.04 %)
Pseudomonas Species	4 (8.7 %)	2 (4.35 %)	6 (21.04 %)
MRSA	1 (2.17 %)	2 (4.35 %)	3 (6.52 %)
Coagulase negative staphylococci	1 (2.17 %)	2 (4.35 %)	3 (6.52 %)
Streptococcus Pyogenes	0	2 (4.35 %)	2 (4.35 %)
Acinetobacter Baumanni	1 (2.17 %)	1 (2.17 %)	2 (4.35 %)
Enterococcus faecalis	1 (2.17 %)	0	1 (2.17 %)
Total	27 (58.7 %)	19 (41.3 %)	46

In present study, 57.55 % neonates required ventilatory support & total 14.15 % neonatal mortality was noted.

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Discussion

Neonates are immune compromised and defend weakly to bacterial infections. The clinical presentations of neonatal sepsis are nonspecific. This includes symptoms like fever, respiratory distress, lethargy/irritability, convulsions, bulging fontanels, refusal to feed, jaundice, bleeding, abdominal distension, and temperature dysregulation.[8]

The three most common causes of sepsis-related deaths among children were infections related to neonatal disorders (for example, preterm birth, encephalopathy, haemolytic disease), lower respiratory infections and diarrhoeal diseases.[9] Lower birth weight and gestational age were associated with an increased sepsis incidence, resulting in the highest incidence of early-onset neonatal sepsis in very low birthweight infants and preterm neonates. Male neonates, outborn admissions, need for artificial ventilation, gestational age <37 weeks and premature rupture of membranes are risk factors for sepsis among neonates in India.[10]

The bacterial agents associated with neonatal sepsis are Group B Streptococci, Escherichia coli, Listeria monocytogenes, coagulase-negative Staphylococci (CoNS), Staphylococcus aureus, Enterococci, Klebsiella spp., Enterobacter spp., Pseudomonas spp., Salmonella spp., H. influenzae, Neisseria meningitidis, and Streptococcus pneumoniae.[11,12]

With approximately 21 million pregnant women colonized with Group B Streptococcus worldwide (estimation based on a global colonization of 18% of pregnant women), this pathogen represents the leading cause of neonatal sepsis, although E. coli has also recently emerged as a major threat. Together, they account for approximately 70% of cases of all early onset sepsis.[13,14]

Pavan Kumar DV et al.,[15] studied 107 babies with a diagnosis of probable sepsis, 28 (26.2%) had shown bacteria in culture. The majority (94.4%) were of early‐onset sepsis. The predominant organisms were Staphylococcus aureus (10/28) and Klebsiella (6/28). 100% of Gram‐negative bacilli and 90% of Staphylococcus were resistant to Ampicillin. Gentamicin resistance among Gram‐negative bacilli and Staphylococcus was 52.9% and 20%, respectively, while third‐generation cephalosporin resistance was 31.2% and 20%, respectively. Among the neonates diagnosed as probable sepsis, idiopathic prematurity (P = 0.007) was found to have a statistically significant association with culture‐positive sepsis.

In study by Dalal P et al., [16] incidence of neonatal sepsis was 11.62 per 1,000 live births. Three hundred fifty- six microbes were isolated, out of which 50% presented as early onset sepsis and remaining as late onset sepsis. Pseudomonas aeruginosa was the most common organism encountered in both early (43.82%) and late onset sepsis (51.35%). Gram negative bacilli were sensitive to carbapenems (92%) followed by piperacillin-tazobactam (90%) whereas linezolid (90%) was most sensitive antimicrobial for gram positive cocci.

Saha AK et al., [17] studied 7180 admitted neonates, 433 (6.03%) were blood culture positive with early onset sepsis (EOS) in 50.1% of cases. Gram negative bacteria was the causative organism in 371 (85.7%) babies with klebsiella being the commonest pathogen (43.6%). The pathogen mix of early onset and late onset sepsis was similar and 90% of gram negative isolates were resistant to penicillin group. Multi drug resistance (MDR) was found in 51.2% of the gram negative organisms. EOS (Odds ratio 1.99; 95% confidence interval, 1.29-3.05) and MDR (Odds ratio 2.07; 95% confidence interval, 1.77-4.12) were independently associated with neonatal death due to sepsis.

Thakur S et al.,[18] did blood cultures for 450 neonates and 42% were culture positive. Early onset sepsis were 92 (49%) and 96 (51%) were late onset sepsis. Gram‐positive isolates were 60% and 40% were Gram‐negative. Staphylococcus aureus (40%), coagulase negative Staphylococcus species (16%), non‐fermenter group of organisms (NFGOs) (15%), and Klebsiella pneumoniae (10%) were the main isolates. Nasal cannula 101 (54%), birth asphyxia 91 (48%), and prematurity 73 (38%) were the prominent risk factors associated with septicemia. Gram‐positive organisms were highly resistant to penicillin (87%) whereas

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Gram‐ negative isolates showed high resistance to third generation cephalosporins (53–89%) and aminoglycosides (50–67%). The S. aureus isolates were methicillin‐ resistant in 41% whereas extended spectrum beta lactamase production was seen in 48% Gram‐ negative isolates.

Zakariya BP et al.,[11] noted that out of the 120 clinically suspected and positive screening test cases of neonatal sepsis, 41.6% (50 of 120) were culture-proven cases of neonatal sepsis. Klebsiella pneumoniae was isolated from 66% of culture positive cases followed by Coagulase-negative staphylococci in 12% of cases. Klebsiella pneumoniae was resistant to most of the antibiotics tested except amikacin and meropenem. Of the total 33 Klebsiella pneumoniae isolates, 16 (32.0%) were ESBL producers. The prevalence of ESBL producing Klebsiella pneumoniae during two month outbreak and rest of the study period was 83.3% (15 of 18) and 20% (3 of 15) respectively (P value 0.0010).

Robust infection control practices in nursery and labor room, minimally invasive procedures, and restricting the use of aminoglycosides and quinolones as first‐ line antibiotics and carbapenems as second‐ line antibiotics are practical options to minimize mortality from sepsis.[19] Judicious use of antibiotic is important to prevent the microbial resistance. The need for antibiotic therapy should be decided by the clinician based on the culture results, maternal and intrapartum risk factors, CSF cultures, Complete blood cell count and differentials, CRP trends, radio graphs and Clinical progress.

Conclusion

Neonatal sepsis is a leading cause of neonatal admission, morbidity and mortality in developing countries. Most of the neonatal sepsis related deaths are preventable if suspected early and treated with appropriate antibiotics. Also, there is need for large sample research to understand the pathogenesis of neonatal sepsis and to devise measures to prevent related morbidity and mortality.

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References

1. Dessu S, Habte A, Melis T, Gebremedhin M. Survival status and predictors of mortality among newborns admitted with neonatal sepsis at public hospitals in Ethiopia. International Journal of Pediatrics. (2020) 2020:10.
2. Global report on the epidemiology and burden of sepsis: current evidence, identifying gaps and future directions. Geneva: World Health Organization; 2020
3. Cortese F, Scicchitano P, Gesualdo M, Filaninno A, De Giorgi E, Schettini F, et al. Early and late infections in newborns: where do we stand? A review. Pediat & Neonat. 2016;57(4):265-73.
4. Kuppala VS, Meinzen-Derr J, Morrow AL, Schibler KR. Prolonged initial empirical antibiotic treatment is associated with adverse outcomes in premature infants. J Pediatr. 2011;159(5):720-25.
5. S. Chaurasia, M. J. Sankar, R. Agarwal et al., "Characterization and antimicrobial resistance of sepsis pathogens in neonates born in tertiary care centers in Delhi, India: a cohort study," The Lancet Global Health, vol. 4, no. 10, pp. e752–e760, 2016.
6. Levy MM, Mitchell P, Marshall Je et al. 2001' SCCM/ESICM/ACCP/SIS. International sepsis definition conference.Critical. Care Med. 2003; 31: 1250-1256.
7. MA Bhat, JI Bhat, MS Kawoosa. Organism specific platelet response and factors affecting survival in thrombocytopenic very low birth weight babies with sepsis. Journal of Perinatology (2009).

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 02, 2023

8. B. J. S. A. Stoll, "Infections of the neonatal infant," in Nelson Textbook of Pediatrics, pp. 909–925, Elsevier, Philadelphia, 20th edition, 2015.
9. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200-11.
10. Murthy S, Godinho MA, Guddattu V, Lewis LES, Nair NS (2019) Risk factors of neonatal sepsis in India: A systematic review and metaanalysis. PLoS ONE 14(4): e0215683.
11. Zakariya BP, Bhat V, Harish BN, Arun Babu T, Joseph NM. Neonatal sepsis in a tertiary care hospital in South India: bacteriological profile and antibiotic sensitivity pattern. Indian J Pediatr. 2011;78:413–7.
12. Camacho-Gonzalez A, Spearman PW, Stoll BJ. Neonatal infectious diseases: evaluation of neonatal sepsis. Pediatr Clin N Am. 2013;60:367–89.
13. Lawn JE, Bianchi-Jassir F, Russell NJ, Kohli-Lynch M, Tann CJ, Hall J, et al. Group B streptococcal disease worldwide for pregnant women, stillbirths, and children: why, what, and how to undertake estimates? Clin Infect Dis. 2017;65 (Suppl 2):S89-S99.
14. Stoll BJ, Hansen NI, Sanchez PJ, Faix RG, Poindexter BB, Van Meurs KP, et al. Early onset neonatal sepsis: the burden of group B Streptococcal and E. coli disease continues. Pediatrics. 2011;127(5):817-26.
15. Pavan Kumar DV, Mohan J, Rakesh PS, Prasad J, Joseph L. Bacteriological profile of neonatal sepsis in a secondary care hospital in rural Tamil Nadu, Southern India. J Family Med Prim Care 2017;6:735-8.
16. Dalal P, Gathwala G, Gupta M, Singh J. Bacteriological profile and antimicrobial sensitivity pattern in neonatal sepsis: a study from North India. Int J Res Med Sci 2017;5:1541-5.
17. Saha AK, Tiwari AK, Chattopadhyay P, Mukherjee S, Saha B. Changing Pattern Of Bacteriological Profile, Antimicrobial Resistance And Mortality In Neonatal Sepsis In A Developing Country: A Retrospective Study. Nepal Paediatr Soc. 2021;41(3):358-366.
18. Thakur S, Thakur K, Sood A, Chaudhary S. Bacteriological profile and antibiotic sensitivity pattern of neonatal septicaemia in a rural tertiary care hospital in North India. Indian J Med Microbiol 2016;34:67-71.
19. Sivanandan S, Soraisham AS, Swarnam K. Choice and duration of antimicrobial therapy for neonatal sepsis and meningitis. Int J Pediatr. 2011;11(1): 12-18.