ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 02 | February - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SUSCEPTIBILITY OF NEONATAL SEPSIS IN NEONATAL INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL IN SHIVAMOGGA, KARNATAKA.

Paediatrics

Dr Anjana H Rao	Specialist-Paediatric Dept, Shimoga Institute of Medical Science, Shivamogga
Dr Gururaju D	Senior Resident-Paediatric Dept, Shimoga Institute of Medical Science, Shivamogga
Dr Manjunath Swamy R	Associate Professor- Paediatric Dept.,Shimoga Institute of Medical Science, Shivamogga
Dr Vinayaka Hegade. P	Consultant Paediatrician – Private hospital, Shivamogga

KEYWORDS

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteraemia in the first month of life. It is one of the most common causes of neonatal mortality and morbidity globally.[1] Neonatal septicaemia continues to be a major problem for neonates in neonatal intensive care units in India also and contributes to almost 20% of neonatal mortality in India [2]

Neonatal sepsis can be classified into two major categories depending upon the age of onset of symptoms: Early-onset sepsis (<72 hrs) and late-onset sepsis (≥72 hrs-28 days). Early-onset sepsis is acquired during foetal life, delivery, or at the nursery.[3] Late onset sepsis can be either health care associated infection or community acquired.

Neonatal septicaemia can be life threatening if proper treatment is not given in time. Neonatal sepsis is often difficult to diagnose clinically as it presents with nonspecific signs and symptoms. Though various diagnostic modalities exist for neonatal sepsis including C-reactive protein, complete blood count, and micro erythrocyte sedimentation rate, yet blood culture is the gold standard [4].

Neonatal sepsis is caused by a variety of Gram-positive as well as Gram-negative bacteria, and sometimes certain fungi.[5] Early diagnosis of neonatal sepsis is very difficult because the signs and symptoms are subtle and nonspecific leading to high rate of empirical antibiotic utilization, which has further led to widespread emergence of antibiotic resistance to commonly used antibiotics.

Antibiotic sensitivity patterns vary geographically depending upon the prevalent local pathogens and common antibiotic used in neonatal unit [6]. A combination of ampicillin or third generation cephalosporins with an aminoglycoside was the commonly used empirical regimen[7]. However, with multidrug resistant bacteria on the rise, the appropriateness of this empirical therapy is being challenged in the present era. The varying microbiological pattern of septicaemia in neonates warrants the need for an ongoing review of the causative organisms in their respective units and their antimicrobial susceptibility pattern. This study was therefore undertaken to determine the common bacterial agents associated with neonatal sepsis and their antibiotic susceptibility pattern in a tertiary care hospital in Shivamogga, Karnataka.

MATERIALS AND METHODS

This was a prospective observational study carried out in the Neonatal Intensive Care Unit (NICU) of a teaching medical college hospital in Shivamogga, Karnataka, India. Neonates (0–28 days) admitted to our NICU from June 2021 to November 2021, with a diagnosis of probable sepsis were studied. The study included 198 cases of clinically suspected septicaemia in neonates.

By reviewing literature, a standardized questionnaire was prepared to collect demographic data, risk factors, clinical features of sepsis and investigations. Ethical approval was obtained from the Institutional Ethics Committee. Fully informed and voluntary signed consents were obtained from the parents or attendants. Discontinuation criteria were considered when the baby got discharged against medical advice or when the baby expired during the hospital stay.

Inclusion criteria

The indications for drawing samples for blood culture were:

1. Clinical features in the neonate (1 or more features): lethargy, apnea, tachypnea, tachycardia, hypotension, instability of temperature, poor feeding, poor perfusion, and abdominal distension, mottling[8].
2. Perinatal risk factors (1 or more features): maternal fever, prolonged rupture of the membranes for more than 24 hours, foul-smelling or meconium-stained liquor, or frequent (>3) unclean vaginal examinations, and/or having severe prematurity, or birth asphyxia necessitating active resuscitation[8].

Exclusion criteria

1) Babies with gross congenital anomalies were excluded.
2) Congenital or acquired causes of thrombocytopenia other than sepsis i.e., intrauterine growth restriction, maternal antiplatelet drug usage, auto immune thrombocytopenia, alloimmune thrombocytopenia were excluded from the study.

Blood samples were collected with all aseptic precautions for sepsis screen, culture and sensitivity studies following universal precautions. BacT/ALERT 3D blood culture system was used which as based on the colorimetric detection of growth of organisms and the antibiotic sensitivity was performed by Kirby Bauer's disc diffusion method, as recommended in the National Committee for Clinical Laboratory Standards (NCCLS) guidelines.

All positive blood cultures were considered a “gold standard” of diagnosis of neonatal sepsis[9] Intermediate susceptibility was taken as resistant. Blood culture bottles showing no growth on subculture done after incubation of 7 days were reported as negative.

The components of a sepsis screen included a total leucocyte count of <5000/cumm or >20000/cumm [10], an absolute neutrophil count (Monroe and Mouzinho charts), I :T ratio of ≥0.2, an micro erythrocyte sedimentation rate ESR> 15mm in the 1st hour, and C – reactive protein CRP ≥ 1 mg/L [1].

Operational Definitions

(1) Clinical sepsis (CS) was defined as neonates who have signs and symptoms of neonatal sepsis with or without risk factors.
(2) Culture-positive/proven sepsis (CPS) means neonates who have clinical sepsis with positive blood culture growths.
(3) A positive sepsis screen was defined as having two positive sepsis screen parameters out of five.
(4) A negative sepsis screen was defined as having negative sepsis screen parameters.

Statistical Analysis

Descriptive statistics are expressed in frequencies and percentages. Chi square test has been applied to see the association between different factors. Sensitivity, specificity, PPV, NPV etc were calculated using the SPSS version 21.

RESULTS

In this study, a total of 1345 neonates were admitted to the neonatal unit during the period of study, 815(60.6%) were inborn and 530(39.4%) were outborn.

The study included 198 neonates who satisfied the inclusion and exclusion criteria for clinical sepsis. Blood culture reports were positive in 83 cases (41.9%).

Of the 198 babies with a diagnosis of clinical sepsis, 104 (52.5%) were males, 91 (46%) were preterm babies, 133(67.2%) were inborn and 118 (59.6%) had birth weight less than 2.5 kg (low birth weight). The basic characteristics of neonates with clinical sepsis are shown in Table 1.

There were 83 culture-positive cases. Majority 50 (60.2%) were males, 42 (50.6%) were preterm babies, 55(66.2%) were inborn and 46 (55.4%) had a birth weight less than 2.5 kg (low birth weight). The basic characteristics of neonates with culture positive sepsis are shown in Table 2.

Table 1- Basic characteristics of neonates with clinical sepsis

Characteristics	Categories	Frequency (%)
Gender	Male	104 (52.5)
	Female	94 (47.5)
Gestational age	Term	107 (54)
	Preterm	91 (46)
Birth weight(kg)	<1.5	15 (7.6)
	1.5-1.9	39 (19.7)
	2-2.49	64 (32.3)
	2.5 and above	80 (40.4)
Place of delivery	Inborn	133 (67.2)
	Outborn	65 (32.8)

Table 2- Basic characteristics of neonates with culture positive sepsis

Characteristics	Categories	Frequency (%)
Gender	Male	50 (60.2)
	Female	33 (39.8)
Gestational age	Term	41(49.3)
	Preterm	42 (50.6)
Birth weight(kg)	<1.5	5 (6)
	1.5-1.9	19 (22.9)
	2-2.49	22 (26.5)
	2.5 and above	37 (44.6)
Place of delivery	Inborn	55 (66.3)
	Outborn	28 (33.7)

In this study, a total of 1345 neonates were admitted to the neonatal unit. Of the total admissions, 198 (14.7%) fulfilled the criteria for clinical sepsis. 73 neonates (36.9%) were early-onset, culture-negative sepsis (Figure 1).

In our study, a positive septic screen had a sensitivity of 59.04%, specificity of 58.26%, positive predictive value of 50.5%, and negative predictive value of 66.34%, positive likelihood ratio of 1.41, negative likelihood ratio of 0.7 with blood culture being considered the gold standard to detect neonatal sepsis. (Table 3)

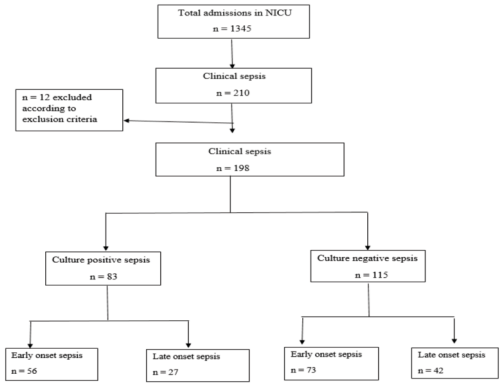

Figure 1- Flow algorithm of neonatal sepsis cases

Table 3- Validity of Sepsis screens

Screen positivity in relation to Blood C/s	Value	95%CI
Sensitivity	59.04%	47.69% to 69.72%
Specificity	58.26%	48.70% to 67.39%
Positive likelihood ratio	1.41	1.07 to 1.87
Negative likelihood ratio	0.70	0.52 to 0.95
Positive predictive value	50.52%	43.54% to 57.47%
Negative predictive value	66.34%	59.32% to 72.70%
Accuracy	58.59%	51.39% to 65.52%

Blood cultures were done for 198 neonates. 83 organisms were isolated. Blood Culture positivity rate in our study was 41.9%. Overall, 48 (58%) cultures were positive for gram-negative organisms and 35(42%) cultures were positive for gram positive organisms.

Among the total isolates, Klebsiella species, CONS, Staphylococcus aureus and Enterobacter were the most common (Table 4). Klebsiella pneumoniae was found to be the predominant pathogen followed by CONS and Staphylococcus aureus accounting for 19.2%, 16.9% and 15.7% cases respectively.

Blood culture positivity rate in EOS and LOS was 67.5% and 32.5% respectively. CONS and Klebsiella were the most predominant organisms in EOS whereas Klebsiella and Enterobacter were the commonly isolated organisms in LOS. The etiological agents of early-onset and late-onset neonatal sepsis are shown in Table 4.

Culture positive sepsis was seen in 55 inborn babies and 28 outborn babies. The most common organisms isolated among inborn babies was CONS, Staphylococcus aureus and Klebsiella whereas among outborn babies the predominant pathogens were Klebsiella, Enterobacter and Staphylococcus aureus. The etiological agents of sepsis in inborn and outborn neonates are compared in Table 5.

Table 4- Pattern of microorganisms isolated from blood culture.

Organisms isolated	Frequency	EOS (n=56)	LOS (n=27)
KLEBSIELLA	16 (19.2)	10	6
CONS	14(16.9)	12	2
STAPHYLOCOCCUS AUREUS	13 (15.7)	8	5
ENTEROBACTER	12 (14.4)	6	6
CITROBACTER	8 (9.6)	5	3
GRAM NEGATIVE NONFERMENTER	6 (7.2)	5	1
STREPTOCOCCUS	5 (6)	4	1
ENTEROCOCCUS	4 (4.8)	3	1
E COLI	3 (3.6)	3	0
PSEUDOMONAS AEROGINOSA	1 (1.2)	0	1
ACINETOBACTER	1(1.2)	0	1
TOTAL	83 (100)	56	27

Table 5- Etiological agents of sepsis among inborn and outborn babies

Organisms isolated	Frequency (Percent)	Inborn (n=55)	Outborn (n=28)
KLEBSIELLA	16 (19.2)	7	9
CONS	14(16.9)	11	3
STAPHYLOCOCCUS AUREUS	13 (15.7)	9	4
ENTEROBACTER	12 (14.4)	5	7
CITROBACTER	8 (9.6)	5	3
GRAM NEGATIVE NONFERMENTER	6 (7.2)	6	0
STREPTOCOCCUS	5 (6)	5	0
ENTEROCOCCUS	4 (4.8)	3	1
E COLI	3 (3.6)	3	0
PSEUDOMONAS AEROGINOSA	1 (1.2)	0	1
ACINETOBACTER	1(1.2)	1	0
TOTAL	83 (100)	55	28

Among cultures with gram-positive species, Coagulase-negative

Staphylococci (CONS) (n= 14) predominated. CONS showed high resistance to Penicillin (93%), Fluoroquinolones (71%) and Clindamycin (36%) but good susceptibility to Vancomycin (100%) and Linezolid (93%) as shown in Table 6. Vancomycin resistance was noted in one Streptococcus species, whereas Linezolid resistance was noted in CONS (n=1/14, 7%), and Enterococcus species (n=1/4, 25 %).

Table 6- Antibiotic resistance in gram positive organisms

	CoNS (%)	Enterococci (%)	Staphylococcus aureus (%)	Streptococcus (%)
Penicillin	93	75	92.3	100
Vancomycin	0	0	0	20
Linezolid	7	25	0	0
Clindamycin	36	25	23	80
Fluoroquinolones	71	50	62	40
Gentamicin	-	25	-	20

Klebsiella which was the most common gram negative organism in our study showed high resistance to commonly used antibiotics such as; Ampicillin (81%), Cefotaxime (81%), Piptaz (56 %) . However, they showed good susceptibility to Carbapenems (68.8%), Ciprofloxacin (87.5%), and Gentamicin (69%).

Most of the gram-negative isolates were sensitive to amikacin, meropenem, imipenem, ciprofloxacin and piperacillin tazobactam. Overall sensitivity of amikacin, piperacillin tazobactam and ciprofloxacin to all common gram-negative organisms was 64.3 %, 59.4 % and 66.7 %, respectively. The analysis of drug resistance pattern showed that, among Gram-negative isolates, maximum numbers (87%) were resistant to ampicillin and lowest to imipenem (3%). Prevalence of multidrug-resistant strain was 38.6%.

DISCUSSION

For effectual management of neonatal sepsis cases, study of bacteriological profile along with the antimicrobial sensitivity pattern plays a noteworthy role.[11,12] Blood culture is the gold standard investigation in cases of suspected neonatal sepsis. Improving systems to detect bacterial growth have resulted in increased rates of positive cultures.

There has been a wide variation in the culture-positivity rate for aerobic organisms in neonates in India; ranging from 16% to 54% [13]. In this study, blood culture-positivity rate was 41.9%. Murty *et al*.[14] in 2007 reported a higher isolation rate of 52.6% . A recent study by Rajendraprasad *et al*.[15]reported 47.5% isolation rate. The variation in culture positivity rate of neonatal septicemia might be due to differences in sample size, infection with viral, fungal pathogens or anaerobes, and effective control in spread of nosocomial infection.

Majority 50 (60.2%) were males, 42 (50.6%) were preterm babies, 55(66.2%) were inborn and 46 (55.4%) had a birth weight less than 2.5 kg (low birth weight).

There were 83 culture-positive cases. Slight male predominance 60.2% was noted which was similar to other regional studies [16-18]. This sex difference may be due to a gene located on the X chromosome which is involved with the function of the thymus or with synthesis of immunoglobulins in the male infants thus leading to less immunological protection compared to females[19]. In our study, there was a slightly higher difference noted in the incidence of culture positive sepsis in preterm babies (50.6%) and low birth weight babies. (55.4%) which was however not statistically significant. A recent study which was done in India had showed preterms had a slightly higher incidence of culture positive sepsis.[20] It is known that low birth weight neonates usually have low IgG levels which make them more prone to infections.[21]

Overall, in our study 48 (58%) cultures were positive for gram-negative organisms, which was similar to studies by Verma et al., Dalal et al., and Shrestha et al. [20, 22, 23].

Klebsiella pneumoniae was found to be the predominant pathogen in our study followed by CONS and Staphylococcus aureus accounting for 19.2%, 16.9% and 15.7% cases respectively. The report of the National Neonatal-Perinatal database showed Klebsiella as the most predominant (29%) pathogen.[8]which corelates with our study. The causative agents of neonatal septicemia have changed over time and may vary from place to place. Shrestha et al. 2008 [24] isolated E. coli as the most predominant organism while Kumaravel et al. 2016 [25] isolated K. pneumoniae. This variation could be due to differences in the study population, study setting, antibiotic protocols and adherence to hand hygiene and other aseptic techniques.

We noted culture-positive EOS (67.5%) was higher than LOS (32.5%). Higher prevalence of EOS in NICU was also reported by other studies like Assudani *et al.* 2017 [26] and Hafsa *et al.* 2011 [27]. A possible explanation for lower incidence of late onset sepsis could be due to better understanding of the importance of cleanliness, hygiene, and using aseptic techniques by medical staffs.

CONS, Klebsiella and Staphylococcus aureus were the most predominant organisms in EOS whereas Klebsiella, Enterobacter and Staphylococcus aureus were the commonly isolated organisms in LOS. In our study, Klebsiella was commonly isolated both in EOS and LOS. Staphylococcus aureus was one of the most common organisms both in EOS and LOS which was similar to the study data obtained from National Neonatal Perinatal Database.[8] CONS was the commonest gram positive organism in EOS in our study. Zakariya et al. in South India also reported CONS to be commonest gram-positive organism and the second most common organism in EONS [11]. Different studies have recommended that two positive blood cultures are required to confirm CoNS as pathogenic organism[13,28]. Huang et al. reported that there was no significant difference between the infants with CoNS isolated from a paired or a single blood culture[29]

Our sepsis screens had a sensitivity of 59.04% which could identify the true sepsis cases early for treatment.. A high negative predictive value (66.34%) meant that a negative sepsis screen had a high probability of ruling out sepsis. This was however low in comparison to studies by Zaka-ur-Rab et al. [30]

In the present study, antibiotic resistance among the gram-positive and gram-negative bacteria was quite high amongst the earlier recommended first line drugs like ampicillin and cephalosporins (84.3% and 72.3% respectively). This may be due to the easy availability and widespread use of broad-spectrum antibiotics in the presumptive treatment of infections and lack of blood culture facilities in rural areas which leads to increased resistance.

Gram positive isolates showed high resistance to Ampicillin ranging from 75% to 100%, but good susceptibility to Vancomycin (97%) and Linezolid (94%). Vancomycin remains the drug of choice for gram positive organisms in our set up. Singh et al. 2016[31] had also demonstrated high sensitivity rates(100%) of Vancomycin towards gram-positive isolates in their study. Due consideration needs to be given to antistaphylococcal antibiotics in view of its high prevalence in both early-onset and late-onset neonatal sepsis. Recently resistance to this drug has also been reported.

The analysis of drug resistance pattern in our study showed that, among Gram-negative isolates, maximum numbers (87%) were resistant to ampicillin and lowest to imipenem (3%). Increasing rates of resistance was noted for ampicillin and cephalosporins in our study. Various studies like Nepal et al. 2013 and Ansari et al. 2015 have shown similar antibiotic resistance trend in the past.[32] In another study which was done by Rajlakshmi et al.[33] 100% resistance (60/60) was noted for ampicillin, cefotaxime, and gentamicin and emerging resistance was noted for Carbapenems unlike our study.

Klebsiella which was the most common gram-negative organism in our study showed high resistance to commonly used antibiotics such as; Ampicillin (81%), Cefotaxime (81%). However, they showed good susceptibility to Carbapenems (68.8%), Ciprofloxacin (87.5%), and Gentamicin (69%). In a study by Viswanathan et al ,[28] high resistance rates were noted among the commonly used first- and second-line antibiotics like ampicillin (98.5%), gentamicin (84.4%), amikacin (65.6%) and cefotaxime (81.3%). Fortunately, in our study, Klebsiella sp and other gram-negative isolates were found to be sensitive to the aminoglycoside and ciprofloxacin group of antibiotics. Hence they are used as our first line antibiotics. This has been corroborated by many other workers.[15,34].

CONCLUSION

Klebsiella, CONS and Staphylococcus were the predominant

organisms in our study which were resistant to Ampicillin and Cephalosporins. Antibiotic combination of amikacin with piperacillin-tazobactam or amikacin with ciprofloxacin had better sensitivity against all common gram-negative organisms. Gram positive organisms showed high susceptibility to Vancomycin and Linezolid. Due consideration needs to be given to antistaphylococcal antibiotics in our unit in view of its high prevalence in both early-onset and late-onset neonatal sepsis. The rising trend of multidrug-resistant organisms and suspected nosocomial infections requires comprehensive and systematic infection control measures. The choice of antibiotics for empirical therapy should therefore be guided by routine antimicrobial surveillance for treatment of neonatal sepsis which may contribute to improved survival in culture positive neonates.

Conflicts Of Interest

None

Acknowledgements

Authors would like to express their sincere gratitude to the Department of Microbiology, SIMS, Shivamogga. We would like to thank Mrs Revathy for helping us with the statistical analysis.

REFERENCES-

1) R. D. Agarwal, Ashok, and V. K. Vinod, "Neonatal sepsis," in AIIMS Protocols in Neonatology, pp. 163–173, New Delhi CBS Publishers and Distributors, 2015.
2) Sankar MJ, Neogi SB, Sharma J, Chauhan M, Srivastava R, Prabhakar PK, et al... State of newborn health in India. J Perinatol. 2016;36(s3):S3.
3) Puopolo KM. Bacterial and fungal infection. In: Cloherty JP, Eichenwald EC, Stark AR, editors. Manual of neonatal care, 6th ed. Philadelphia: Lippincott William and Wilkins; 2008. p. 274-300.
4) S. Rahman, A. Hameed, and M. T. Roghani, "Multidrug resistant neonatal sepsis in Peshawar, Pakistan," Archives of Disease in Childhood, vol. 87, no. 1, pp. 52–54.
5) Gomaa HHA, Udo EE, Rajaram U. Neonatal septicemia in Al-Jahra hospital, Kuwait: Etiologic agents and antibiotic sensitivity patterns. Med Princ Pract 2001;10:145-50.
6) D. E. Premlatha et al., "The bacteriological profile and antibiogram of neonatal septicemia in a tertiary care hospital," International Journal of Science, Technology and Society, vol. 10, no. 3, pp. 451–455, 2014
7) Kaistha N, Mehta M, Singla N, Garg R, Chander J. Neonatal septicemia isolates and resistance patterns in a tertiary care hospital of North India. J Infect Dev Ctries. 2009;4:55–7.
8) National Neonatal Perinatal Database. Report for the year 2002-03. Available at: http://www.newbornwhocc.org/pdf/nnpd_report_2002- 03.
9) J. L. Wynn, H. R. Wong, T. P. Shanley, M. J. Bizzarro, L. Saiman, and R. A. Polin, "Time for a neonatal– specific consensus definition for sepsis," Pediatric Critical Care Medicine, vol. 15, no. 6, pp. 523–528, 2014.
10) R. L. Rodwell, A. L. Leslie, and D. I. Tudehope, "Early diagnosis of neonatal sepsis using a hematologic scoring system," The Journal of Pediatrics, vol. 112, no. 5, pp. 761–767, 1988.
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). Dutta S, Reddy R, Sheikh S, Kalra J, Ray P, Narang A. Intrapartum antibiotics and risk factors for early onset sepsis. Arch Dis Child Fetal Neonatal Ed 2010;95:F99-103.
13) Y. R. Bhat, L. E. Lewis, and K. E. Vandana, "Bacterial isolates of early-onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: an audit from a center in India," Italian Journal of Pediatrics, vol. 37, no. 32, 2011.
14) Murty DS, Gyaneshwari M. Blood cultures in pediatric patients: A study of clinical impact. Indian J Med Microbiol 2007;25:220-4.
15) Rajendraprasad BP, Basavaraj KN, Antony B. Bacterial spectrum of neonatal septicemia with their antibiogram with reference to various predisposing factors in a tertiary care hospital in Southern India. Ann Trop Med Public Health 2013;6:96-9.
16) V. A. B. Bangi and S. S. Devi, "Neonatal sepsis: a risk approach," Journal of Dr. NTR University of Health Sciences, vol. 3, no. 4, pp. 254–258, 2014.
17) K. Swarnkar and M. Swarnkar, "A study of early onset neonatal sepsis with special reference to sepsis screening parameters in a tertiary care centre of rural India," The Internet Journal of Infectious Diseases, vol. 10, no. 1, pp. 36–42, 2012.
18) R. K. Shrestha, S. K. Rai, L. K. Khanal, and P. K. Manda, "Bacteriological study of neonatal sepsis and antibiotic susceptibility pattern of isolates in Kathmandu, Nepal," Nepal Medical College Journal, vol. 15, no. 1, pp. 71–73, 2013.
19) J. O. Klein and S. M. Marcy, "Bacterial sepsis and meningitis," in Infectious diseases of the fetus and newborn, J. S. Remington and J. O. Klein, Eds., vol. 4, pp. 835–890, W.B. Saunders, Philadelphia, USA, 2001.
20) P. Verma, P. K. Berwal, N. Nagaraj, S. Swami, P. Jivaji, and S. Narayan, "Neonatal sepsis: epidemiology, clinical spectrum, recent antimicrobial agents and their antibiotic susceptibility pattern," International Journal of Contemporary Pediatrics, vol. 2, no. 3, pp. 176–180, 2015.
21) B. J. Stoll, "The global impact of neonatal infection," Clinics in Perinatology, vol. 24, no. 1, pp. 1–21, 1997.
22) P. Dalal, G. Gathwala, M. Gupta, and J. Singh, "Bacteriological profile and antimicrobial sensitivity pattern in neonatal sepsis: a study from North India," International Journal of Research in Medical Sciences, vol. 5, no. 4, pp. 1541–1545, 2017.
23) S. Shrestha, N. C. Shrestha, S. D. Singh et al., "Bacterial isolates and its antibiotic susceptibility pattern in NICU," Kathmandu University Medical Journal, vol. 11, no. 41, pp. 66–70, 2014
24) S. Shrestha, N. Adhikari, D. Shakya, L. Manandhar, A. Chand, and S. Shah, "Bacteriological prof le of neonatal blood cultures at Patan hospital," Journal of Nepal Paediatric Society, vol. 26, pp. 9–12, 2008.
25) K. S. Kumaravel and B. Rameshbabu, "A study of the bacteriological profile and antibiotic sensitivity in neonatal septicemia," International Journal of Contemporary Medical Research, vol. 3, no. 6, pp. 1830-1831, 2016.
26) H. J. Assudani, J. K. Gusani, S. J. Mehta, H. H. Agravat, and K. Kothari, "Bacteriological profles of septicaemia in neonates at tertiary care hospital, Gujarat, India," Journal of Research in Medical and Dental Science, vol. 3, no. 2, pp. 148–151, 2017.
27) A. Hafsa, M. Fakruddin, M. A. Hakim, and J. D. Sharma, "Neonatal bacteremia in a neonatal intensive care unit: analysis of causative organisms and antimicrobial susceptibility," Bangladesh Journal of Medical Science, vol. 10, no. 3, pp. 187–194, 2011.
28) Viswanathan R, Singh AK, Mukherjee S, Mukherjee R, Das P, Basu S. Aetiology and antimicrobial resistance of neonatal sepsis at a tertiary care centre in eastern India: A 3 year study. Indian J Pediatr. 2011;78:409–12.
29) Huang YC, Wang YH, Chou YH, Lien RI. Significance of coagulase-negative staphylococci isolated from a single blood culture from neonates in intensive care. Ann Trop Paediatr. 2006;26:311–8.
30) Z. Zaka-ur-Rab, M. Kar, V. Gupta, B. P. Kalra, and K. Akhtar, "Evaluation of laboratory markers of sepsis screen in the diagnosis of early onset neonatal septicemia," International Journal of Contemporary Pediatrics, vol. 3, no. 4, pp. 1144–1149, 2016.
31) H. K. Singh, P. Sharja, and K. Onkar, "Bacteriological profile of neonatal sepsis in neonatal intensive care unit (NICU) in a tertiary care hospital: prevalent bugs and their susceptibility patterns," European Journal of Pharmaceutical and Medical Research, vol. 3, no. 3, pp. 241–245, 2016, http://www.ejpmr .com/admin/assets/article issue/1457056566.pdf.
32) N. Gyawali and R. K. Sanjana, "Bacteriological profile and antibiogram of neonatal septicemia," e Indian Journal of Pediatrics, vol. 80, no. 5, pp. 371–374, 2013
33) Viswanathan, Rajlakshmi and Singh, Arun and Ghosh, Chiranjib and Dasgupta, Sudipta and Mukherjee, Suchandra and Basu, Sulagna. (2012). Profile of Neonatal Septicaemia at a District-level Sick Newborn Care Unit. Journal of health, population, and nutrition. 30. 41-8. 10.3329/jhpn.v30i1.11274.
34) Mane AK, Nagdeo NV, Thombare VR. Study of neonatal septicemia in a tertiary care hospital in rural Nagpur. Journal of Recent Advances In Applied Sciences J Recent Adv Appl Sci 2010;25:19-24.