Neonatal sepsis: Risk factors, clinical and bacteriological profile, and antibiotic sensitivity

Anitha B Sethi[1], Vedavyasa Srigade[2], Guntur Dharmateja[3]

From [1]Professor, [2]Asssociate Professor, [3]Postgraduate, Department of Paediatrics, Niloufer Hospital, Hyderabad, Telangana, India

Correspondence to: Dr. Vedavyasa Srigade, 1-1-405/8/1, Near St. Gregorios Cathedral, Gandhinagar, Hyderabad - 500 080, Telangana, India. E-mail: vsrigade@gmail.com

Received - 27 May 2018 Initial Review - 10 June 2018 Accepted - 26 June 2018

ABSTRACT

Background: Neonatal sepsis (NS) is a cause of very high morbidity and mortality. Reviews of bacterial spectrum and antimicrobial susceptibility help to treat NS and to develop strategies to lower neonatal mortality. **Objectives:** The objectives were to study organisms causing NS, their antimicrobial susceptibility pattern, predisposing factors of NS, and the presentations of NS. **Methods:** This prospective study was done for 1 year from August 2016 to July 2017 at a tertiary care hospital, Hyderabad with C-reactive protein (CRP), aerobic blood cultures, and sensitivities in 300 neonates with clinical sepsis. Risk factors for NS and clinical features were recorded. Significances for sex, gestational age, birth weight, and age of onset of sepsis differences were assessed. **Results:** Male to female ratio was 1.65:1, 39% were preterm, 40% were <2500 g in weight, and 54% had sepsis in <72 h (early onset sepsis - EOS) ($p<0.05$). Prolonged labor and rupture of membranes, maternal fever within 2 weeks, foul-smelling liquor, birth asphyxia, and iatrogenic factors were the risk factors in decreasing order of frequency. Refusal to feed was the most common presentation. CRP showed good sensitivity and negative predictive value while 117 (39%) cases were blood culture positive. Organisms in decreasing order of frequency were *Klebsiella pneumoniae*, coagulase-negative staphylococci, enterococcus, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, Acinetobacter, *Escherichia coli*, and Group-B streptococci. Gram-negative isolates (44%) were sensitive to meropenem, amikacin, and piperacillin-tazobactam while Gram-positive isolates (56%) were sensitive to vancomycin and netilmicin and both were least sensitive to cefotaxime and ampicillin. **Conclusion:** Obstetric and neonatal care practices around birth need to be reviewed as EOS proportion in India is very high. Most of the isolates were resistant to cefotaxime and ampicillin, underscoring the need for the addition of penicillinase inhibitors. Timely review of antibiotics is necessary in view of widespread resistance. Focus on prevention of NS and the improvement of health systems to effectively manage it is very much needed in India.

Key words: *Antibiotic sensitivity, Clinical features, C-reactive protein, Neonatal sepsis, Organisms, Risk factors*

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 [1]. Estimates of neonatal sepsis (NS) burden vary by setting. Incidence of NS in India was 30/1000 live births and culture-proven sepsis was 8.5/1000 live births and 2.3% of intramural live births according to the National Neonatal Perinatal Database (NNPD) report 2002–2003 [2]. A study (2002–2005) 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 [3]. 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 [4].

The clinical manifestations range from subclinical, nonspecific to severe manifestations. The organisms differ significantly between developed and developing countries [5]. Even among developing countries, regional variation exists [6]. In EOS (Sepsis within 72 h of birth), Gram-negative organisms such as *Escherichia coli*, Klebsiella, and Enterobacters are the prime cause of sepsis in India [7,8]. Some studies mention Gram-positive organisms as the chief cause, among which *Staphylococcus aureus*, coagulase-negative staphylococci (CONS), Streptococcus virdans, and Group B Streptococci (GBS) are more common [9,10]. The organisms commonly associated with late-onset sepsis (LOS: Sepsis developing after >72 h of age) include CONS, *S. aureus*, *Klebsiella pneumoniae*, *E. coli*, Enterobacter spp., *Pseudomonas aeruginosa,* and Acinetobacter species [11]. NNPD database shows Klebsiella as the most common organism (32.5%) followed by *S. aureus* (13%) and *E. coli* (10.6%) [2].

We attempted this study as a concern about variable, and extended drug resistance is on the rise, and also treatment, policy decisions, rational use of antibiotics require updated

Table 1: Characteristics of neonates and results of blood cultures

Gender		Gestational age (weeks)		Birth weight (kg)		Onset of sepsis		Blood culture	
Male	Female	<37	>37	<2.5	>2.5	Early	Late	Growth	No growth
187 (62%)	113 (38%)	117 (39%)	183 (61%)	120 (40%)	180 (60%)	162 (54%)	138 (46%)	117 (39%)	183 (61%)
p=0.000		p=0.000		p=0.000		p=0.049			

Table 2: Perinatal risk factors for NS

Risk factors	n (%)
Prolonged labor (>24 h)	77 (25.7)
Premature rupture of membrane (>18 h)	75 (25)
Maternal fever within 2 weeks (>38°C)	59 (19.7)
Foul-smelling liquor	54 (18)
Birth asphyxia	46 (15.3)
Unclean or >3 sterile vaginal examinations	15 (5)

NS: Neonatal sepsis

Table 3: Clinical manifestations in NS

Clinical features	n (%)
Refusal of feed	230 (76.7)
Lethargy	199 (66.3)
Respiratory distress	120 (40)
Convulsion	114 (38)
Hypothermia	86 (28.7)
Mottling	86 (28.7)
Sclerema	82 (27.3)
Fever	66 (22)
Vomiting	57 (19)
Abdominal distension	57 (19)
Apnea	48 (16)

NS: Neonatal sepsis

knowledge of common pathogens and their drug sensitivity pattern. The primary objective was to study the bacteriological profile and determine the antimicrobial sensitivity pattern of organisms causing NS. Secondary objectives were to study the various maternal and perinatal risk factors of NS and the clinical manifestations of NS.

METHODS

This prospective observational study was conducted at Niloufer Hospital, Hyderabad, for a period of 1 year from August 2016 to July 2017. 300 neonates admitted with clinical suspicion of sepsis were included in the study. A data entry sheet was used to obtain patient details. Institutional Ethics Committee approval was obtained for the study. 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.

Babies with birth weight <1000 g, neonates with obvious malformations/congenital anomalies were excluded. 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 χ^2 (Chi-squared test). $p<0.05$ was taken as significant.

RESULTS

A total of 300 neonates were included in the study and the male to female ratio was 1.65:1. The percentage of septicemic preterm babies (39%) was higher than their proportion of 10–12% of all births. 40% had low birth weight (LBW), which was higher than their proportion of 25–30% of all births. The value of p was <0.05 (calculated by one sample t-test) for gender, gestational age, birth weight, and onset of sepsis groups. Demographic characteristics, onset of sepsis, and culture details are given in Table 1.

EOS contributed to 54% of the cases. Blood cultures were positive in 39% of the cases. Perinatal risk factors responsible for the EOS are enumerated in Table 2, which shows that a very high proportion of the babies had these risk factors making them susceptible to sepsis. There was a coexistence of more than one factor in many cases.

The presentations of the babies with sepsis are given in Table 3. Refusal to feed and lethargy were the dominant presentations. More ominous features were observed in nearly 40% of the babies.

CRP was positive in 208 babies of the total of 300, of which 114 were culture positive, and 94 were negative. In 92 babies with negative CRP, 3 were culture positive. Considering culture as the standard for diagnosis of NS, parameters for CRP derived were 97.4% sensitivity, 48.6% specificity, 54.8% positive predictive value, and 96.7% negative predictive value. Of the 39% positive blood cultures, *K. pneumoniae*, CONS, Enterococcus, and *S. aureus* were the predominant isolates as shown in Table 4. Klebsiella was relatively more common in LOS while enterococcus was more frequent in EOS.

Tables 5 and 6 give the details of the bacterial isolates' drug sensitivity patterns. As all isolates were not tested for all drugs, number of samples tested for a particular drug is mentioned in the tables along with percentage of sensitivity.

Excepting Enterococcus and Pseudomonas, all other organisms were sensitive to aminoglycosides. While cefotaxime and ampicillin had the lowest sensitivity, drugs with added penicillinases (Cefoperazone + Sulbactam and Piperacillin + Tazobactam) had better sensitivity. Levofloxacin had better

Table 4: Bacteria isolated from cases of NS

Bacteria grown	Total (%)	EOS (%)	LOS (%)	Studies with similar results
K. pneumoniae	34 (29)	24 (37)	10 (19)	[3,12,13]
CONS	26 (22)	14 (22)	12 (22)	[3,12]
Enterococcus	24 (20)	9 (14)	15 (28)	[3,12,14]
S. aureus	14 (12)	6 (9)	8 (15)	[3,13]
P. aeruginosa	8 (7)	5 (8)	3 (6)	[13]
Acinetobacter	7 (6)	5 (8)	2 (4)	[13]
E. coli	2 (2)		2 (4)	[13]
GBS	2 (2)	1 (2)	1 (2)	

NS: Neonatal sepsis, *K. pneumoniae: Klebsiella pneumoniae*, CONS: Coagulase-negative staphylococci, *S. aureus: Staphylococcus aureus, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli*, GBS: Group B streptococci

Table 5: Antibiotic sensitivity pattern of bacteria in NS

Antibiotic	Organism-wise number of samples showing sensitivity/total samples tested (% sensitivity)			
	Klebsiella	CONS	Enterococcus	*S. aureus*
Amikacin	25/34 (73.5)	20/26 (76.9)	4/20 (20)	12/14 (85.7)
Netilmicin	26/34 (76.5)	23/26 (88.5)	6/22 (27.3)	14/14 (100)
Cefoperazone sulbactam	10/34 (29.4)	4/16 (25)	-	6/12 (50)
Gentamicin	19/30 (63.3)	5/26 (19.2)	8/20 (40)	7/12 (58.3)
Cefotaxime	3/25 (12)	3/15 (20)	0/12 (0)	3/12 (25)
Ciprofloxacin	6/24 (25)	14/23 (60.8)	0/7 (0)	-
Ampicillin	4/32 (12.5)	3/15 (20)	0/11 (0)	2/13 (15.4)
Imipenem	19/29 (65.5)	-	-	-
Meropenem	23/26 (88.5)	-	-	-
Piperacillin-tazobactam	20/30 (66.7)	-	-	-
Vancomycin	-	23/26 (88.5)	23/23 (100)	13/14 (92.8)
Levofloxacin	-	13/16 (81.3)	3/15 (20)	9/12 (75)

NS: Neonatal sepsis, CONS: Coagulase-negative staphylococci, *S. aureus: Staphylococcus aureus*

Table 6: Antibiotic sensitivity pattern of bacteria in NS

Antibiotic	Organism-wise number of samples showing sensitivity/total samples tested (% sensitivity)			
	Pseudomonas	Acinetobacter	*E. coli*	GBS
Amikacin	1/6 (16.7)	4/7 (57.1)	2/2 (100)	-
Netilmicin	2/5 (40)	3/3 (100)	2/2 (100)	2/2 (100)
Cefaperazone-sulbactam	0/3 (0)	4/4 (100)	-	-
Gentamicin	2/7 (28.6)	4/7 (57.1)	2/2 (100)	2/2 (100)
Cefotaxime	-	0/4 (0)	0/2 (0)	0/2 (0)
Ciprofloxacin	-	3/6 (50)	-	2/2 (100)
Ampicillin	0/4 (0)	4/4 (100)	0/1 (0)	-
Imipenem	8/8 (100)	7/7 (100)	2/2 (100)	-
Meropenem	7/8 (87.5)	7/7 (100)	2/2 (100)	-
Piperacillin tazobactam	7/8 (87.5)	6/7 (85.7)	2/2 (100)	-
Vancomycin	-	-	-	2/2 (100)
Levofloxacin	-	-	-	2/2 (100)

NS: Neonatal sepsis, *E. coli: Escherichia coli*, GBS: Group B streptococci

sensitivity than ciprofloxacin. Some isolates were resistant to carbapenems and vancomycin also.

DISCUSSION

NS being a life-threatening condition, changes in risk factors, etiology, and growing multidrug resistance must be properly addressed at each level of care. Considering this purpose, the present study looked at the said elements of concern. We observed male-female ratio as 1.65:1 ($p<0.05$) similar to other works (1.2:1–1.8:1) [15-18]. In contrast to it, one study reported a ratio of 1:1 [19]. As immunoglobulin genes are on chromosome X, females may be relatively resistant to infections. Notably, 39% were preterm in the study while their proportion being 10–12%

Table 7: Comparison of antibiotic sensitivity of organisms among North and South Indian studies

Organism	Sensitivity highest (H) Lowest (L)	Present study	Marwah *et al*.[31] GMCH, Chandigarh	Leela *et al*.[32] Govt. Kilpauk Medical College, Chennai	Sathyamurthi *et al*.[33] Government Kilpauk Medical College, Chennai
K. Pneumoniae	H	Meropenem (88.5%)	Vancomycin and linezolid (100%)	Cefmetazole (100%), Amikacin (90.9%) Cefoperazone-sulbactam	Piperacillin tazobactam Ciprofloxacin
	L	Cefotaxime (12%)	Ceftazidime (0%)	Ampicillin (0%)	Imipenem third-generation Cephalosporins
CONS	H	Vancomycin and netilmycin (88.5%)		Vancomycin and amikacin (100%)	Vancomycin (90%)
	L	Gentamycin (19.2%)		Ampicillin (0%)	Ceftriaxone (5%)
S. aureus	H	Netilmicin (100%), vancomycin (92.8%)	aminoglycosides, vancomycin and linezolid	Vancomycin and amikacin (100%)	Vancomycin (96.15%)
	L	Cefotaxime (25%), Ampicillin (15.4%)	oxacillin	Ciprofloxacin (0%)	Cefaperazone (3.84%)
P. monas	H	Imipenem (100%), meropenem (87.5%) Piperacillin tazobactam (87.5%)		second and third-generation cephalosporins, Cefoperazone-sulbactam, Amikacin and Ciprofloxacin	Imipenem (71.42%)
	L	Ampicillin (0%)		Ampicillin, Gentamicin	Ampicillin (14.28%)
A. bacter	H	Ampicillin and meropenem (100%)	Colistin Polymyxin B	Ceftazidime (100%), Cefoperazone-sulbactam, amikacin (100%)	Imipenem (76.15%)
	L	Cefotaxime (0%)	Gentamicin Ampicillin	Ciprofloxacin (0%)	Vancomycin (4.16%)
E. coli	H	Imipenem and amikacin (100%)	Imipenem (85.7%)	Cefoperazone-sulbactam	Imipenem (75%)
	L	Cefotaxime (0%), ampicillin (0%)	Ampicillin (0%)		Gentamycin (25%)

K. pneumoniae: Klebsiella pneumoniae*, CONS: Coagulase-negative staphylococci, *S. aureus: Staphylococcus aureus, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli, A. bacter: Acinetobacter

of all births correlating with similar observations in two previous studies (32% and 39%) [19,20]. Prematurity and LBW coexist, and 40% cases were LBW which is similar to other studies [20-22].

Nearly 54% were EOS, while 46% were LOS ($p<0.05$) and a higher incidence of EOS was also observed elsewhere [4,23,24]. Conversely, some reported a higher incidence of LOS [6]. In developed countries, the proportion of EOS is in the range of 10–20% [25,26]. Perinatal risk factors have a significant impact on the incidence of EOS. There is a huge difference in the incidence of EOS in between India and developed countries, which clearly emphasizes the need for reduction of perinatal risk factors for sepsis in India. PROM (25 %) and prolonged labor (25.7%) were the major perinatal risk factors, which were similar to two studies [19,21]. There was the coexistence of more than one factor in several cases. Refusal to feed (76.7%) was the most common mode of presentation as seen in other studies (75–92%). Rests of the clinical features were also similar in frequencies to other works [12,19,20]. CRP was positive in 69.3% of the clinical sepsis cases. CRP had good sensitivity and negative predictive value than specificity and positive predictive value when culture is taken as standard similar to previous observations [27,28]. This implies when CRP is negative, culture is negative most of the times, but CRP positivity does not denote culture positivity.

The culture positivity rate (39%) depends on a multitude of factors. Studies showed culture positivity rates in the same range (28.6–47.5%) [2,29,30]. Klebsiella was the most frequently isolated organism in this study, whereas *E. coli* was the most common organism in the past [8,15]. GBS which is one of the most common isolates in West was not grown in significant numbers in any Indian study. Enterococcus has emerged as a major pathogen which is associated with LOS in preterms and nosocomial infections. The frequencies of bacterial isolates are comparable to studies in India and abroad, references of which are included in Table 4.

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. A comparison of antibiotic sensitivity of organisms among North and South Indian studies is presented in Table 7, which illustrates the differences

from center to center and differences at the same center, and also gives an idea of sensitivities across India.

GBS showed 100% sensitivity to gentamicin and vancomycin while no sensitivity to cefotaxime.

A population-based study of NS in 223 villages of Odisha state recorded a very high level of resistance to penicillin and ampicillin, moderate resistance to cephalosporins, and extremely low resistance to gentamicin, amikacin, and 2nd generation cephalosporins. No resistance was seen to imipenem or vancomycin; although 27% of the *S. aureus* isolates were intermediate sensitive to vancomycin. High numbers of the Gram-negative organisms were extended-spectrum beta-lactamase producers and harbored multidrug resistance. Removal of an antibiotic from the therapeutic regimen may lead to a reversal of microbial resistance resulting in susceptible phenotypes [3]. Amikacin, the most widely used semisynthetic aminoglycoside, is refractory to most aminoglycoside modifying enzymes except acetylation by the aminoglycoside 6'-N-acetyltransferase Type Ib [AAC(6')-Ib] [34].

In the present study, Netilmicin and amikacin showed good sensitivity to most of the isolates except enterococcus and pseudomonas. Imipenem, meropenem, and piperacillin-tazobactam showed good sensitivity to Gram-negative organisms. Gram-positive organisms were sensitive to vancomycin. Most of the bacterial isolates were resistant to cefotaxime and ampicillin. Limitations of the study are not using fungal and anaerobic organisms' culture methods, not testing antibiotic sensitivity of isolates with a similar set of antibiotics, and all the bacterial isolates were not tested by a given antibiotic.

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 [35,36].

CONCLUSIONS

This study revealed variation in antibiotic susceptibility pattern among bacterial isolates and also showed that third-generation cephalosporins and penicillins are no more effective in treating NS. Addition of penicillinase inhibitors to them is advocated. Aminoglycosides, as first-line antibiotics are still effective. Review of antibiotics every 48–72 h, in view of high drug resistance, is critical. Recognizing NS as a seriously concerning public health problem and implementing measures aimed at changes in health systems and personnel are imperative to reduce neonatal mortality.

REFERENCES

1. Oza S, Lawn JE, Hogan DR, Mathers C, Cousens SN. Neonatal cause-of-death estimates for the early and late neonatal periods for 194 countries: 2000-2013. Bull World Health Organ 2015;93:19-28.
2. National Neonatal Perinatal Database. NNPD report 2002-03. Available from: http://www.newbornwhoccorg/pdf/nnpd_report_2002-03 PDF.[Last accessed on 2018 July 15].
3. Panigrahi P, Chandel DS, Hansen NI, Sharma N, Kandefer S, Parida S, *et al.* Neonatal sepsis in rural India: Timing, microbiology and antibiotic resistance in a population-based prospective study in the community setting. J Perinatol 2017;37:911-21.
4. Investigators of the Delhi Neonatal Infection Study (DeNIS) collaboration. Characterisation and antimicrobial resistance of sepsis pathogens in neonates born in tertiary care centres in Delhi, India: A cohort study. Lancet Glob Health 2016;4:e752-60.
5. Sanghvi KP, Tudehope DI. Neonatal bacterial sepsis in a neonatal intensive care unit: A 5 year analysis. J Paediatr Child Health 1996;32:333-8.
6. Kuruvilla KA, Pillai S, Jesudason M, Jana AK. Bacterial profile of sepsis in a neonatal unit in South India. Indian Pediatr 1998;35:851-8.
7. Bhakoo ON, Agarwal KC, Narang A, Bhattacharjee S. Prognosis and treatment of neonatal septicemia-a clinico-bacteriological study of 100 cases. Indian Pediatr 1974;11:519-28.
8. Guha DK, Jaspal D, Das K, Guha AR, Khatri RL, Srikumar R. Outcome of neonatal septicemia–a clinical and bacteriological profile. Indian Pediatr 1978;15:423-7.
9. Ako-Nai AK. Bacteriology of neonatal septicemia in Nigeria. J Trop Pediatr 1999;43:146-51.
10. Sinha N. Deb A, Mukherjee AK. Septicemia in neonates and early infancy. J Indian Pediatr 1978;15:747-9.
11. 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.
12. Rana U, Purani C, Patel P, Gupta K. Clinico-bacteriological profile of neonatal sepsis in a tertiary care hospital. ARC J Pediatr 2016;2:1-8.
13. Zaidi AK, Thaver D, Ali SA, Khan TA. Pathogens associated with sepsis in newborns and young infants in developing countries. Pediatr Infect Dis J 2009;28:S10-8.
14. Shailaja VV, Reddy AK, Rangaiahgari A, Alimelu M, Sadanand LN. Increased isolation of *Enterococcus faecium* from neonates with sepsis: An attempt to investigate the suspected outbreak. Int J Infect Dis 2016;45:341-2.
15. Gluck L, Wood H F, Fousek MD. Septicemia of newborn. PCNA 1966;13:1131-47.
16. Shaw CK, Shaw P, Thapalial A. Neonatal sepsis bacterial isolates and antibiotic susceptibility patterns at a NICU in a tertiary care hospital in Western Nepal: A retrospective analysis. Kathmandu Univ Med J (KUMJ) 2007;5:153-60.
17. Somu N, Shetty MV, Moses LG, Subramaniam L, Raju VB. A critical analysis of septicemia in infancy. Indian pediatr 1976;13:443-6.
18. Bhale CP, Kale AV, Kale SS, Mahajan M, Mulay SS. Utility of sepsis screen in the early diagnosis of neonatal sepsis. Indian J Neonatal Med Res 2016;4:IO01-7.
19. Raghavan M, Mondal GP, Bhat BV, Srinvias S. Periantal risk factors in neonatal infections. Indian J Pediatr 1992;59:335-40
20. Tallur SS, Kasturi AV, Nadgir SD, Krishna BV. Clinico-bacteriological study of neonatal septicemia in Hubli. Indian J Pediatr 2000;67:169-74.
21. Fareedul H, Shamshad K,Prakash S. Clinical profile and risk factors in neonatal sepsis. IOSR J Dent Med Sci 2014;13:44-7.
22. Mehrotra N, Kumar A, Chansoria M, Kaul K. Neonatal sepsis: Correlation of maternal and neonatal factors to positive bacterial cultures. Indian Pediatr 1985;22:275-80.
23. Premalatha DE, Koppad M, Halesh LH, Siddesh KC, Prakash N. The bacterial profile and antibiogram of neonatal septicaemia in a tertiary care hospital. Int J Recent Trends Sci Technol 2014;10:451-5.
24. Chacko B, Sohi I. Early onset neonatal sepsis. Indian J Pediatr 2005;72:23-6.
25. Gkentzi D, Kortsalioudaki C, Cailes BC, Zaoutis T, Kopsidas J, Tsolia M, *et al.* Epidemiology of infections and antimicrobial use in Greek neonatal units. Arch Dis Child Fetal Neonatal Ed 2018: pii: fetalneonatal-2018-315024.
26. Cailes B, Kortsalioudaki C, Buttery J, Pattnayak S, Greenough A, Matthes J, *et al*. Epidemiology of UK Neonatal Infections: The Neon in Infection Surveillance Network. Archives of Disease in Childhood-Fetal and

Neonatal Edition Published Online First; 2017.
27. Sakha K, Husienni MB. Correlation between procalcitonin and C-reactive protein in neonatal sepsis. Pak J Biol Sci 2008;11:1785-90.
28. Borna H, Borna S. Value of laboratory tests and C-reactive protein in the detection of neonatal sepsis. Internet J Pediatr Neonatol 2005;5:60-8.
29. Roy I, Jain A, Kumar M, Agarwal SK. Bacteriology of neonatal septicaemia in a tertiary care hospital of northern India. Indian J Med Microbiol 2002;20:156-9.
30. Kumhar GD, Ramachandran VG, Gupta P. Bacteriological analysis of blood culture isolates from neonates in a tertiary care hospital in India. J Health Popul Nutr 2002;20:343-7.
31. Marwah P, Chawla D, Chander J, Guglani V, Marwah A. Bacteriological profile of neonatal sepsis in a tertiary-care hospital of Northern India. Indian Pediatr 2015;52:158-9.
32. Leela KV, Babu RN, Sugunya, Prasad VM, Deepa RR. Study of bacterial profile in neonatal sepsis and their antibiotic sensitivity pattern in a tertiary care hospital. Int J Curr Microbiol Appl Sci 2016;5:511-21.
33. Sathyamurthi B, Leela KV, Narayanababu R, Padmanaban S, Sreedevi S, Sujatha, *et al*. Clinical and bacteriological profile of neonatal sepsis in a tertiary care hospital. Int J Sci Study 2016;4:57-60.
34. Ramirez MS, Tolmasky ME. Amikacin: Uses, resistance, and prospects for inhibition. Molecules 2017;22: pii: E2267.
35. Candel FJ, Sa MB, Belda S, Bou G, Pozo JL, Estrada O, *et al*. Current Aspects in Sepsis Approach. Turning Things Around. Revista Española de Quimioterapia Advance Access Published; 2018.
36. Singhal N, Kumar M, Kanaujia PK, Virdi JS. MALDI-TOF mass spectrometry: An emerging technology for microbial identification and diagnosis. Front Microbiol 2015;6:791.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Sethi AB, Srigade V, Dharmateja G. Neonatal sepsis: Risk factors, clinical and bacteriological profile, and antibiotic sensitivity. Indian J Child Health. 2018; 5(6):432-437.

Doi: 10.32677/IJCH.2018.v05.i06.009