J Nepal Health Res Counc 2022 Oct-Dec;20(57): 967-72

Clinical, Bacteriological Profile and Outcome of Neonatal Sepsis

Shraddha Siwakoti,[1] Rinku Sah,[1] Rupa Rajbhandari Singh,[2] Basudha Khanal[1]

[1]Department of Microbiology, B. P. Koirala Institute of Health Sciences, Dharan, Nepal, [2]Department of Paedriatics, B. P. Koirala Institute of Health Sciences, Dharan, Nepal.

ABSTRACT

Background: Sepsis is a major cause of morbidity and mortality among neonates in Nepal. This study was conducted to determine the clinical-bacteriological profile, their antibiotic susceptibility patterns, and clinical outcome of culture-positive neonatal sepsis.

Methods: This was a prospective study conducted at B.P Koirala Institute of Health Sciences from July 2018 to June 2019. Neonates with clinically diagnosed sepsis having blood culture positive were included in the study. Blood samples culture and antimicrobial susceptibility testing were performed with the standard microbiological method. Demographic, clinical information, and clinical outcomes were documented.

Results: The incidence of culture-positive sepsis was 10.3% (183/1773) of neonatal admissions. Poor feeding 85(46%) and fever 68(37%) were the common clinical features at presentation. The incidence of early-onset sepsis and late-onset sepsis were found to be 116 (63%) and 67(37%) respectively. *Staphylococcus aureus* was the common pathogen in both early-onset 61(49%) and late-onset 34(41%) sepsis. The incidence of multidrug-resistant cases was 41% (75/183) with 20% (15/75) extensively drug-resistant gram-negative bacilli, 36% (20/75) multidrug-resistant gram-negative bacilli, and 44% (33/75) Methicillin-resistant *Staphylococcus aureus* cases. In-hospital mortality rate was 12 (7%) with a higher frequency in multidrug-resistant sepsis 92% (11/12) than non- multidrug-resistant 8% (1/12). The median hospital days were longer in multidrug-resistant cases than non- multidrug-resistant [11(9-13) verses 3(2-5)].

Conclusions: The incidence of multidrug-resistant pathogens causing neonatal sepsis is high at our hospital and are associated with more in-hospital mortality and longer hospital stay. Implementation of effective preventive strategies to combat the emergence of antimicrobial resistance is immediately needed.

Keywords: Bacteriological profile; incidence; MDR; neonatal sepsis; outcome

INTRODUCTION

Sepsis is a major cause of mortality among neonates in the developing countries.[1] The Nepal demographic and health survey of 2016 have reported neonatal mortality rate to be 21/1000 live births with the infection including sepsis contributing 16% of the mortality.[2] In neonatal sepsis, clinical presentations are non-specific,[3] various diagnostic modalities exist but blood culture is the gold standard.[4] Recently, the emergence of bacterial resistance has made the treatment of neonates complicated with increased threat in Nepal.[5] It is essential to promptly start the empiric therapy to prevent the life-threatening consequences of sepsis. Thus, each region needs to recognize the common pathogens and related antimicrobial susceptibility to update the empirical treatment protocol. This study was therefore aimed at determining the incidence, clinical-bacteriological profile, their antibiotic susceptibility pattern, and clinical outcome of culture-positive sepsis of neonates admitted in the neonatal unit of BP Koirala Institute of Health Sciences (BPKIHS).

METHODS

This study was designed as prospective observational study. Neonates with clinical signs and symptoms of sepsis with a positive blood culture admitted in the neonatal unit of BPKIHS from July 2018 to June 2019 were included. Neonatal sepsis was defined as the presence of at least two clinical signs and/or two laboratory findings with a positive blood culture. Neonatal sepsis was

Correspondence: Dr Shraddha Siwakoti, Department of Microbiology, B. P. Koirala Institute of Health Sciences, Dharan, Nepal. Email: shraddha.siwakoti@bpkihs.edu, Phone: +9779842352163

categorized into two subgroups according to neonate age at the onset of symptoms: early-onset neonatal sepsis (EOS), before 72hours of life, and late-onset neonatal sepsis (LOS), beyond 72hours after birth and before 28 days. Demographic and clinical details were obtained by attending pediatrician/s. The relevant data including neonatal details, maternal details, and clinical outcomes were transferred to the study proforma designed for this study. The clinical outcome was recorded as improved, left against medical advice, referred, in-hospital mortality, and length of hospital stay (LOS).

The estimation of the sample size (N) was based on 20% prevalence(P) of culture-positive neonatal sepsis of clinically suspected neonatal septicemia reported in a previous study from BPKIHS[6] using Fischer's formula with a maximum error of 5% (d) within a standard normal deviation of 1.96 for 95% confidence interval (CI). Therefore, the sample size was 246 neonates. Using a finite population correction factor, the final sample size was 167. Our study included 183 neonates with all the admitted culture-positive cases within a year study period.

One milliliter of venous blood sample was aseptically collected from each neonate with signs of sepsis and inoculated into pediatric brain heart infusion (BHI) broth. Blood culture bottles were incubated at 37°C for 24 h in aerobic condition after which aliquots were sub-cultured on solid agar plates; Sheep blood and MacConkey agars for up to 96 h before being regarded as no growth. Colonies on solid agar plates were identified by following standard microbiological techniques which include studies of colony morphology, gram-staining reactions, and various biochemical properties (catalase, slide and tube coagulase tests, oxidase tests, SIM, citrate, triple sugar iron, urease tests)[7] Antibiotic susceptibility test of isolates was performed by modified Kirby-Bauer disk diffusion method according to guidelines of Clinical and Laboratory Standards Institute (CLSI).[8] Quality control for culture plates and antibiotic susceptibility was performed using *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* 25923.

The bacterial isolates were identified as multidrug-resistant (MDR) or extensively drug-resistant (XDR) as per the definitions proposed by international experts of the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC)[9] MDR was defined as non-susceptibility to at least one agent in three or more antimicrobial categories, XDR was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e. bacterial isolates remain susceptible to only one or two categories). Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected using a 30 µg cefoxitin disc on Mueller–Hinton agar.

Ethical clearance was obtained from Institutional review board of BPKIHS Dharan. Informed written consent was obtained from the parents of each patient.

Data were entered in the MS Excel 2007 and analyzed with STATA version 14 (Stata corporation, college station, TX, USA). Incidence rates of infection were calculated by dividing the number of infections occurring during the time of exposure by the total of exposure time. Data are reported as number (percentage) and median (interquartile range). Fisher's exact test was used to infer any differences between the categorical variables and p-value of less than 0.05 was considered statistically significant.

RESULTS

Among 1773 neonates admitted in the neonatal division, 885 neonates were diagnosed with clinically suspected septicaemia and 183 neonates had culture-positive sepsis. The incidence of culture-positive sepsis was 10.3% or 103 per 1000 neonatal admissions. In terms of clinically suspected septicaemia, the incidence of culture-positive sepsis was 20.6%. Among the 183 cases of culture-positive neonatal sepsis, the incidence of EOS and LOS were found to be 116 (63%) and 67(37%) respectively. Approximately more than half of enrolled neonates 100 (55%) were low birth weight (less than 2500 g), and preterm 94(51%). A third of included neonates 59 (32%) in this study were born by caesarean section (Table 1). Poor feeding 85(46%), fever 68 (37%), and jaundice 49(27%) were the major clinical features associated with both the groups (Table 2). Of the total 207 isolates, there were 108(52%) gram-positive and 99 (48%) gram-negative bacteria. Polymicrobial infection was present in 23(13%) cases.

Table 1. Risk factors and clinical outcome among enrolled neonates with sepsis.

Variables	Total (n=183) n (%)	Early-onset (n=116) n(%)	Late-onset (n=67) n(%)	p value
Gender				
Male	125(68%)	79(68%)	46(69%)	1.00
Female	58(32%)	37(32%)	21(31%)	
Gestational age at birth:				

Preterm (<37 weeks)	94(51%)	42(36%)	52(78%)	<0.0001
Term (>37 weeks)	89(49%)	74(64%)	15(22%)	
Birth weight(g) <2500	100(55%)	59(51%)	41(61%)	0.2178
APGAR score < 6 at 5 min	12(7%)	12(10%)	0(0%)	0.0043
Birth asphyxia	23(13%)	15(13%)	8(12%)	1.0000
Meconium aspiration syndrome	9(5%)	9(8%)	0(0%)	0.0274
Mode of delivery				
Vaginal	124(68%)	85(73%)	46(69%)	0.5023
Caesarean section	59(32%)	31(27%)	21(31%)	
Maternal fever (7d before delivery)	20(11%)	19(16%)	1(1%)	0.0011
PROM > 12 h	56(31%)	48(41%)	8(12%)	<0.0001
Twin pregnancy	4(4%)	2(2%)	2(3%)	0.6244
Clinical Outcome				
Improved	141(76%)	91(78%)	50(75%)	0.5868
In-hospital mortality	12(7%)	7(6%)	5(8%)	0.7610
Left against medical advice	27(15%)	16(14%)	11(16%)	0.6682
Referred	3(2%)	2(2%)	1(1%)	1.0000
Median length of stay (IQR)	6(3-10)	4(3-8)	9(6-13)	0.0162

Table 2. Clinical presentations of neonatal sepsis.

Clinical features	Total (n=183)	Early-onset (n=116)	Late-onset (n=67)	p value
Refusal to feed	85(46%)	60(52%)	25(37%)	0.0663
Fever	68(37%)	37(32%)	31(46%)	0.0583
Jaundice	49(27%)	29(25%)	20(30%)	0.4923
Respiratory distress	45(25%)	27(23%)	18(27%)	0.5972
seizures	35(19%)	19(16%)	16(245)	0.2439
Lethargy	27(15%)	17(15%)	10(15%)	1.0000
Hypothermia	16(9%)	13(11%)	3(4%)	0.1745
Abdominal distention	5(3%)	0(0%)	5(7%)	0.0060

Staphylococcus aureus 95(46%) was the commonly isolated organism with 35% MRSA followed by *Acinetobacter* spp 49(24%) with 41% MDR and *Klebsiella pneumoniae* 14(7%) with 71% MDR strains (Table 3). *S. aureus* was the most common pathogen in both EOS 61(49%) and LOS 34(41%) with 28% and 47% MRSA respectively. Among gram-positive pathogens, all the isolates of *S. aureus* were susceptible to vancomycin but (1/13, 7%) of enterococcus isolate was resistant. A high degree of antimicrobial resistance was noted among the majority of gram-negative pathogens to commonly used antibiotics and also to reserve antibiotics such as extended-spectrum cephalosporins and carbapenems. Imipenem resistance was noted in (10/49, 20%) *Acinetobacter* spp, (3/14, 21%) *K. pneumoniae*, (2/12, 17%) *Pseudomonas aeruginosa* and (1/10, 10%) *Escherichia coli*. Tigecycline resistance was detected in (1/14, 7%) *K. pneumoniae* (Table 4).

Table 3. Distribution of isolates based on sepsis onset.

Bacterial Isolates	Total (n=207)		Early-onset (n=124)		Late-onset (n=83)	
	Isolate n(%)	Multi-drug resistant	Isolate n(%)	Multi-drug resistant	Isolate n(%)	Multi-drug resistant
Gram-positive Organisms	108(52%)	35(32%)	68(55%)	19(30%)	40(48%)	16(40%)
Staphylococcus aureus	95(46%)	33(35%)	61(49%)	17(28%)	34(41%)	16(47%)
Enterococcus faecalis	13(6%)	2(15%)	7(6%)	2(29%)	6(7%)	0(0%)
Gram-negative Organisms	99(48%)	37(37%)	56(45%)	17(30%)	43(52%)	23(53%)
Acinetobacter spp	49(24%)	20(41%)	28(23%)	8(29%)	21(25%)	12(57%)
Pseudomonas aeruginosa	12(6%)	2(17%)	9(7%)	2(22%)	5(6%)	2(40%)
Klebsiella pneumoniae	14(7%)	10(71%)	8(6%)	4(50%)	6(7%)	6(100%)
Escherichia coli	10(5%)	2(20%)	7(6%)	1(14%)	3(4%)	1(33%)
Enterobacter aerogenes	5(2%)	3(60%)	4(3%)	2(50%)	1(1%)	1(100%)
Citrobacter freundii	5(2%0	0(0%)	0(0%)	0(0%)	5(6%)	0(0%)
Flavobacterium spp	1(0.5%)	0(0%)	0(0%)	0(0%)	1(1%)	0(0%)
Proteus mirabilis	1(0.5%)	1(100%)	0(0%)	0(0%)	1(1%)	1(100%)

Table 4. Resistant rates of common isolates causing neonatal sepsis.

Antibiotics	*S. aureus* (n=97)	*E. faecalis* (n=13)	*A. spp* (n=49)	*K. pneumoniae* (n=14)	*P. aeruginosa* (n=12)	*E. coli* (n=10)
AMC	45(46%)	-	-	-	-	-
Ampicillin	-	4(31%)	-	-	-	100%
Penicillin	84(87%)	4(31%)	-	-	-	-
Piperacillin-tazobactam	-	-	17(35%)	7(50%)	0%	0%
Cefalexin	33(34%)	-	-	-	-	-
Ceftriaxone	35(36%)	-	30(61%	10(71%)	5(42%)	6(60%)
Imipenem	-	-	10(20%)	3(21%)	2(17%)	1(10%)
Amikacin	18(19%)	3(23%)	19(39%)	3(21%)	4(33%)	4(40%)
Gentamicin	23(24%)	-	22(45%)	5(36%)	5(42%)	5(50%)
High-level gentamicin	-	3(23%)	-	-	-	-
Ciprofloxacin	27(28%)	3(23%)	21(43%)	7(50%)	3(25%)	2(20%)
Ofloxacin	25(26%)	3(23%)	15(31%)	7(50%)	3(25%)	2(20%)
Chloram-phenicol	-	-	20(41%)	2(14%)	2(17%)	0(0%)
Cotrimoxazole	29(30%)	-	20(41%)	2(14%)	3(25%)	4(40%)
Tigecycline	-	-	0(0%)	1(7%)	-	0(0%)
Vancomycin	0(0%)	1(8%)	-	-	-	-
Linezolid	0(0%)	0(0%)	-	-	-	-

Table 5. Multi-drug resistant cases concerning sepsis onset, mortality and hospital days.

	Total(n=183)		Early-onset (n=116)		Late-onset (n=67)	
	Mortality	Median LOS (IQR)	Mortality	Median LOS (IQR)	Mortality	Median LOS (IQR)
Total MDR	11/75(15%)	11(9-13)	6/36(17%)	10(8-12)	5/39(13%)	12(9-15)
XDR-GNB	5/15(33%)	13(11-17)	2/6(33%)	15(11-19)	3/9(33%)	13(11-17)
MDR-GNB	2/20(10%)	9(7-12)	1/13(8%)	9(8-12)	1/14(7%)	9(6-13)
MRSA	4/33(12%)	12(9-13)	3/17(18%)	9(8-12)	1/16(6%)	13(10-16)
Non-MDR	1/108(1%)	3(2-5)	1/80(1%)	4.0±3.0	-	4.8 ± 2.5
Total	12/183(7%)	6(3-10)	7/116(6%)	4(3-8)	5/67(7%)	9(6-13)

MDR: multidrug-resistant, XDR-GNB: extensively-drug resistant gram-negative bacilli, MDR-GNB: multidrug-resistant gram-negative bacilli, MRSA: methicillin-resistant Staph aureus, non-MDR: non-multidrug-resistant, LOS: length of stay, IQR: interquartile range

With respect to the clinical outcome, 141 (76%) neonates were discharged after improvement, 27 (15%) left against medical advice, 3(2%) neonate was referred to higher center and there were 12 (7%) in-hospital mortality. The incidence of MDR cases was (75/183, 41%) with (15/75, 20%) XDR-GNB, (20/75, 36%) MDR-GNB, and (33/75, 44%) MRSA cases. Neonatal sepsis caused by these MDR pathogens were associated with a poorer outcome than non-MDR cases. In-hospital mortality was higher in cases with MDR sepsis (11/12, 92%) than non-MDR (1/12, 8%). Also, the median hospital days with MDR cases was longer than non-MDR [11(9-13) verses 3(2-5)] Table 5.

DISCUSSION

In our study, culture-positive neonatal sepsis was found to be 10.3% of total admissions. A previous study conducted in the same hospital during 2014 showed 16.4%.[10] This slightly decrease incidence rate in the present study is attributed to implementation of infection control measures. Our finding is lesser than reports from other studies in Nepal of 19.5%[6] and 20.7%[11] which were also hospital based and crossectional studies. This variation

may be due to differences in the sample size. Majority of the neonates from this study presented with refusal to feed and fever like the previous study done from this institution.[11] In contrast to this, other studies from Nepal reported respiratory distress as the commonest feature.[11] This variance in clinical presentations mirrors its nonspecific nature highlighting the need to identify early clinical manifestations to minimize the rate of under and misdiagnosis.

In context of clinically suspected septicaemia, this study found the incidence of culture positive neonatal sepsis to be 20.6%. Some studies from Nepal have shown similar bacterial isolation rate of 20%[12] and 20.3%[13] whereas some studies have reported lower rate of 12.6%[14] and 10.8%[15] The growth positivity rate differs depending upon the cultural techniques and duration of the study period. Majority of the sepsis episodes occurred at an early age within 72 hrs of life which is consistent with other reports from Nepal and India.[11,14,16]

Gram-positive organisms were isolated commonly both in EOS and LOS corroborating findings by studies from Nepal[12,14,17] and India[18] Our study finding included the classic LOS nosocomial pathogens including *Acinetobacter* spp, *P. aeruginosa*, and *K. pneumoniae* as the predominant bacterial isolates causing EOS. These EOS pathogens were in contrast with the traditional common EOS pathogens acquired from the mother comprising *E coli, Group B streptococci (*GBS*), Listeria monocytogenes, and Enterococcus* spp. This changing trend could be due to early horizontal transmission of nosocomial pathogens from delivery rooms and NICU [19] or vertical transmission from the maternal genital tract colonized with these pathogens after unhygienic personal and obstetric practices.[20,21] GBS, a predominant EOS pathogen in the west[22] was not isolated in our study consistent with other reports from Nepal[11,14,23] and may be related to the low rate of GBS colonization in Nepalese pregnant women.

The present study revealed high rate of organisms exhibiting resistance to many of the antibiotics comparable to recent reports from Nepal.[11,14] We found *S. aureus* to be 35% resistant to methicillin similar to 36.3% reported by Sangita et al.[15] from another region of Nepal. Vancomycin, a glycopeptide antibiotic, is a drug of choice for MRSA infections. Vancomycin-resistant *S. aureus* was not reported in our study and similarly from other studies from Nepal [11,24] But the rational use of vancomycin should be done in Nepal for delaying the emergence of vancomycin-resistant strains. Common GNB isolates *Acinetobacter* spp, *P. aeruginosa*, and *K. pneumoniae* showed a high rate of resistance to commonly used antibiotics fluoroquinolones, aminoglycosides, and extended-spectrum cephalosporins. A similar pattern of antibiotic resistance has been noted from central Nepal.[23] Higher spectrum antibiotics carbapenem and tigecycline are the reserve drug for the treatment of drug-resistant cases. Resistance rates of carbapenem among all the common GNB isolates and tigecycline to *K. pneumoniae* from this study revealed an alarming situation of antimicrobial resistance. Studies from central Nepal[11] and India[16] also have reported similar resistance patterns of carbapenem and tigecycline among the common GNB isolates. These situations have created difficulty in choosing antibiotics for treating resistant neonatal sepsis and thus, increasing mortality and morbidity. This study reported 7% in-hospital mortality rate which is lower than another[11] hospital-based study from central Nepal with 15% mortality. Probably, this may be due to the high incidence of MDR neonatal sepsis (73%) in their study than our finding of 41%.

Our study had few limitations. This was a single-centered study enrolling a small study population with a limited yield of some pathogens. Further, multi-center studies from different parts of Nepal are needed to corroborate our findings.

CONCLUSIONS

The incidence of culture-positive neonatal sepsis was 10.3% or 103 per 1000 neonatal admissions. *S. aureus* and *Acinetobacter* spp were the common pathogen in both EOS and LOS. The isolates showed high resistance to commonly used antibiotics with significant proportion of MDR. The clinical outcomes in-hospital mortality rate and mean HD were 7% and 1.6±4.0 respectively with both outcomes higher in MDR cases. Implementation of effective preventive strategies to combat the emergence of antimicrobial resistance is immediately needed.

CONFLICT OF INTEREST

The authors declare no conflict of interest

REFERENCES

1. Edmond K, Zaidi A. New approaches to preventing, diagnosing \\and treating neonatal sepsis. PLOS Med 2010;7 (3): e1000213.[Article]

2. United Nations Inter-agency Group for Child Mortality Estimation (UNIGME). Levels and trends in child mortality report 2017. New York: United Nations Children's Fund; 2017.36p. https://www.unicef.org/publications/files/Child_Mortality_Report_2017.pdf. Accessed 1Dec 2017.

3. Ministry of Health, Nepal; New ERA; ICF. Nepal

demographic and health survey 2016. Kathmandu, Nepal: Ministry of Health, Nepal; 2017 Nov. 411p.Available from: https://www.dhsprogram.com/pubs/pdf/FR336/FR336.pdf.Accessed 1 Dec 2017.

4. Kanodia P,Yadav SK, Bhatta NK, Singh RR. Disease profile and outcome of newborn admitted to neonatology unit of BPKIHS. JCMS Nepal. 2015; 11(3):20-24.[Article]

5. Shalini Tripathi S, Malik GK: Neonatal Sepsis: past, present and future; a review article. Inter J Med Up 2010, 5(2):45–54.[Article]

6. 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. [Article]

7. Shrestha RK, Rai SK, Khanal LK, Mandal PK. Bacteriological study of neonatal sepsis and antibiotic susceptibility pattern in Kathmandu, Nepal. Nepal Med Coll J. 2013; 15:7-3.[Article]

8. Winn W, Allen S, Janda W, Koneman E, Woods G. Koneman's color atlas and textbook of diagnostic microbiology. Baltimore: Lippincott Williams &Wilkins; 2006.

9. CLSI. Clinical and laboratory standards institute. Document No M100S. Performance Standards for Antimicrobial Susceptibility Testing. 26th ed. Wayne: CLSI; 2016.

10. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG,et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012; 18(3):268–81. 21793988.[Article]

11. Shrestha S; Adhikari N; Shakya D; Manandhar L, Chand A. Bacteriological profile of neonatal blood cultures at Patan hospital. J Nepal Paediatr Soc. 2007 26(1):1–4. Available from: https://www.popline.org/node/198598.Accessed 5 Dec 2017.

12. Pokhrel B, KoiralaT, Shah G, Joshi S, Baral P. Bacteriological profile and antibiotic susceptibility of neonatal sepsis in neonatal intensive care unit of a tertiary hospital in Nepal. BMC Pediatr. 2018; 18: 208.[Article]

13. Shrestha P et al. Clinical and Bacteriological Profiles of Blood Culture Positive Sepsis in Newborns. J. Nepal Paediatr. Soc.2009 Jan; 27(2). [Article]

14. Khanal R, Manandhar S, Acharya GP. Bacteriological Profile of Neonatal Sepsis in a Tertiary Level Hospital of Nepal. J Nepal Paediatr Soc 2014; 34(3):175-180.[Article]

15. Ansari S, Nepal HP, Gautam R, Shrestha S, Neopane P, Chapagain ML. Neonatal Septicemia in Nepal: Early-Onset versus Late-Onset. International Journal of Pediatrics. vol. 2015, Article ID 379806, 2015.[Article]

16. Thapa S, Sapkota LB. Changing Trend of Neonatal Septicemia and Antibiotic Susceptibility Pattern of Isolates in Nepal. Int J Pediatr. 2019; 2019: 3784529. [Article]

17. 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 Oct; 4(10):e752-60.[Article]

18. Khanal, D. B., Shariff, M., & Deb, M. (2004). Neonatal Septicaemia: A Hospital Based Study in Eastern Nepal. Journal of Nepal Medical Association, 43(155).[Article]

19. Dutta P, Sarkar S, Ghosh MN, Gupta MS. Clinico-Bacteriological Study of Neonatal Septicaemia with Special Reference to Antibiotic Resistance Pattern in Sick Newborns Admitted in a Tertiary Care Hospital, Kolkata. International Journal of Research and Review 2020; 7: 2.[Download PDF]

20. Viswanathan R, Singh AK, Basu S, Chatterjee S, Sardar S, Isaacs D.Multi-drug resistant gram negative bacilli causing early neonatal sepsis in India. Arch Dis Child Fetal Neonatal Ed 2012; 97: F182–87.[Article]

21. Roy S, Viswanathan R, Singh A, Das P, Basu S. Gut colonization by multidrug-resistant and carbapenem-resistant Acinetobacter baumannii in neonates. Eur J Clin Microbiol Infect Dis 2010; 29: 1495–500.[Article]

22. Kamath S, Mallaya S, Shenoy S. Nosocomial infections in neonatal intensive care units: profile, risk factor assessment and antibiogram. Indian J Pediatr 2010; 77: 37–39. [Article]

23. Diancourt L, Passet V, Nemec A, Dijkshoorn L, Brisse S.The population structure of Acinetobacter baumannii: expanding multiresistant clones from an ancestral susceptible genetic pool.PLoS One 2010; 5: e10034. [Article]

24. Yadav NS, Sharma S, Chaudhary DK, Panthi P, Pokhrel P, Shrestha A, Mandal PK. Bacteriological profile of neonatal sepsis and antibiotic susceptibility pattern of isolates admitted at Kanti Children's Hospital, Kathmandu, Nepal. BMC Res Notes. 2018 May 15; 11(1):301.[Article]

25. Shrestha S, Shrestha NC, Dongol Singh S, Shrestha RPB, Kayestha S, Shrestha M et.al. Bacterial Isolates and its Antibiotic Susceptibility Pattern in NICU. Kathmandu Univ Med J 2013; 41(1):66-70.[Article]