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Risk Factors for Neonatal Sepsis: A Case-Control Study in a Tertiary Level Hospital of Nepal

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ABSTRACT

Introduction

Neonatal sepsis is estimated to be a major contributor to neonatal mortality and morbidity with a higher burden in LMICs. Studies have shown that neonatal sepsis is associated with the neonatal and maternal characteristics and obstetric care received. Hence, this study aims to determine the risk factors of neonatal sepsis among neonates admitted to a Neonatal Intensive Care Unit (NICU) of a tertiary level hospital in Nepal.

Methods

A hospital-based unmatched case-control study was conducted from 1st April 2020 to March 31st 2021 in the NICU, Department of Pediatrics at College of Medical Sciences & Teaching Hospital, Chitwan Nepal. A structured questionnaire was used for data collection of neonatal and maternal characteristics. Neonatal characteristics included neonates' age, sex and birthweight. Maternal characteristics included maternal age. Data were analyzed using STATA-13. Univariate and multivariate logistic regression were applied to test the association between independent variables and neonatal sepsis. Statistical tests were considered significant at a p-value < 0.05 (95% CI).

Results

A total of 210 suspected neonatal sepsis cases were compared with 70 controls. We obtained statistical significance ($p<0.05$) among age, Apgar score at 5 minutes of birth, ANC visits, resuscitation at birth and gestation age with the neonatal sepsis among neonates.

Conclusions

The results suggest the need for careful handling of neonates with routine screening for sepsis. Further, interventions encouraging to receive obstetric care should be instilled.

Keywords: neonatal sepsis; case-control; risk factor; pediatrics.

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INTRODUCTION

In 2019, globally, 2.4 million children died in the first month of life – approximately 6,700 neonatal deaths every day.[1] In 2020, neonatal mortality was highest in the South Asian region at 23 deaths per live birth after sub-Saharan Africa with the neonatal mortality rate.[2] In 2020, a child born in South Asia was nine times more likely to die in the first month than a child born in a high-income country.[3] In 2020 Nepal had a neonatal mortality rate of 16 per 1000 live births.[4]

Neonatal sepsis commonly referred to as a bloodstream infection mostly having bacterial origin occurs among newborn infants less than 28 days old.[5-7] Neonatal sepsis is identified as a risk factor for early life neurological development leading to neurodevelopment impairment and growth outcomes both early and later in life.[8-11]

In 2017, 25.7% of neonatal disorders remained the second most common cause of sepsis among children younger than five.[12] Neonatal sepsis is estimated to be a major contributor to neonatal mortality and morbidity with a higher burden in LMICs.[13] A meta-analysis reported a pooled prevalence of 29.76% in East Africa.[14] A study estimated to avert 5.29-8.73 million Disability-adjusted life-years (DALYs) annually in sub-Saharan Africa if all the neonatal sepsis cases were either successfully prevented or treated. In addition, this region also predicted an annual economic burden ranging from $10 to $469 billion.[15] Neonatal sepsis incidence in South Asia is 4 to 10 times higher than that in developed countries.[16]

In Nepal, neonatal sepsis had the highest proportion as a leading cause of death among neonates.[17] A nationwide hospital-based study from Nepal showed the incidence rate of neonatal sepsis as 7.3 per 1000 live birth per year.[18] Studies have reported a range of sepsis occurrences among neonates from 15% to 32%.[19–22] The cost for neonates admitted to NICU and with sepsis was $226.30 (172.19-291.34) as compared to those without sepsis at $174.02 (99.67-221.96). [23]

Neonatal sepsis is associated with low socioeconomic status and resource setting, neonatal age, sex of the neonates, gestation age, low birth weight, birth asphyxia, APGAR score in the first and five minutes, resuscitation at birth, antenatal care received, prolonged rupture of membrane (PROM), delivery settings and delivery mode. [24–31] In Nepal, studies showed an association of neonatal sepsis with neonates born to mothers with no antenatal checkup visits, preterm birth, delivered through cesarean section, PROM, APGAR score in the first and five minutes, and birth asphyxia. [18,32–34] Nepal aims to reduce the neonatal mortality rate to 11 per 1000 live births by 2035 and includes the management of sepsis as a major intervention to reach this target [35]. Evidence has suggested focusing on reducing the health disparities and quality service provisions providing light on associated risk factors for neonatal sepsis.[36] Studies have identified risk factors for neonatal sepsis among tertiary-level hospitals in Nepal that highlight neonatal sepsis as a public health problem.[18] However, none of the studies has reported associated risk factors for neonatal sepsis from the study site offering a similar level of care. Hence, this study was conducted to determine the risk factors of neonatal sepsis among neonates admitted to a Neonatal Intensive Care Unit (NICU) of a tertiary level hospital in Nepal.

METHODS

Setting and study design

A hospital-based unmatched Case-Control

study was conducted from1st April 2020 to 31st March 2021 in the NICU, Department of Pediatrics at College of Medical Sciences & Teaching, Chitwan, Nepal. This study was conducted among 210 case neonatal with sepsis and 70 control without neonatal sepsis. Ethical approval was obtained from Institutional Review Committee of College of Medical sciences, Bharatpur (Ref No. COMSTH-IRC/2020-041.1). Inform and written consent was obtained from respective parents before starting data collection. All the inborn and outborn cases from birth to 28 days of age were included in our study whereas we excluded those babies who have undergone recent surgical interventions and have congenital anomalies rendering them easily susceptible to infections such as; Cystic fibrosis, Down's syndrome, tracheo-esophageal atresia & others. Sepsis was diagnosed as : Newborns having fever, hypothermia, letharginess, refusal of feeding, having seizure considered as neonatal sepsis clinically & were undergoing septic screening along with chest X-ray, complete blood count, CRP, blood culture and sensitivity profile. Selected newborns suspected of having meningitis underwent lumbar puncture and some had urine culture and sensitivity profiles. Physical examination with investigations were done and obtained findings were recorded in a predesigned proforma. A detailed record of neonatal and maternal characteristics was obtained using a semi-structured questionnaire. Neonatal characteristics included neonates' age, sex, birth weight and Apgar score. Maternal characteristics included maternal age. Obstetric characteristics included Antenatal Checkup (ANC) visits, mode of delivery, resuscitation at birth, gestational age in week and prolonged ruptured of membrane (>18 hours). Data were analyzed using STATA-13. Categorical variables were reported as proportions and percentages and numerical as mean and standard deviation. Univariate and multivariate logistic regression were applied to test the association between independent variables and neonatal sepsis. Statistical tests were considered significant at a p-value < 0.05 (95% CI).

RESULTS

Neonatal characteristics

A total of 210 newborns were admitted in the NICU department at CMSTH for suspected neonatal sepsis, of which 44 cases were outborn. A total of 210 suspected neonatal sepsis cases were compared with 70 controls. The mean age of cases with neonatal sepsis was 6.5±8.2 days and 11.1± 17.1 days for controls without neonatal sepsis. The majority were male (58.6%) for cases and female (67.1%) for controls. The mean birth weight (in grams) of cases was 2752.5±513.6 and 2858.8± 636.2 for controls (Table 1).

Maternal and obstetric characteristics

Mean age of mothers of cases was 23.4±3.1 years and 23.9±4.1 years for controls. Nearly two-thirds (64.8%) and almost all (98.6%) of the mothers of cases and controls respectively went for ANC visits during their pregnancy. For Apgar score at 5 minutes, mainly cases had 7 and above score, while, most controls had score less than 7. The majority of cases (76.8%) and controls (62.9%) were born through vaginal delivery mode. A total of 18.6% of cases and 22.9% of controls were resuscitated after birth. Majority of the cases (91.4%) and controls (81.4%) were mostly born at 37 weeks and above. Around one in five cases (21.3%) and one third of controls (35.7%) had prolonged rupture of membrane (>18 hours). (Table 1)

Table 1. Characteristics of study participants.

Characteristics	Case n(%)	Control n(%)
Neonatal characteristics		
Age of neonates (days)	6.5±8.2	11.1± 17.1
Sex		
Female	87(41.4)	47(67.1)
Male	123(58.6)	23(32.9)
Birthweight (grams)		
< 2500	54(25.7)	17(24.3)
≥ 2500	156(74.3)	53(75.1)
Mean± SD	2752.5±513.6	2858.8± 636.2
Maternal characteristics		
Age of mother (years)	23.4±3.1	23.9±4.1
Obstetric characteristics		
ANC visits		
No	74(35.2)	1(1.4)
Yes	136(64.8)	69(98.6)
Apgar score at 5 minutes		
<7	36(17.1)	49(70)
7 and above	174(82.7)	21(30)
Mode of delivery		
Cesarean section	35(16.7)	26(37.1)
Vaginal delivery	161(76.8)	44(62.9)
Vacuum extraction	14(6.7)	0
Resuscitation at birth		
No	171(81.4)	54(77.1)
Yes	39(18.6)	16(22.9)
Gestation age		
<37 weeks	18(8.6)	13(18.6)
37 weeks and above	192(91.4)	57(81.4)
Prolonged rupture of membrane(>18 hours)		
No	159(75.7)	45(64.3)
Yes	51(21.3)	25(35.7)

Factors associated with neonatal sepsis

There was a significant association between the age of neonates and neonatal sepsis (p<0.001). When we compared two groups of neonates differing by 1 day of age, the odds of having neonatal sepsis is 6% lower among neonates in the older group (95%CI: 0.91-0.98). The odds of having neonatal sepsis is 96% lower among

neonates whose mothers had at least one ANC visit (p=0.002; 95%CI: 0.004-0.22). There was a significant association between Apgar score at 5 minutes and neonatal sepsis. When there is an increase in 1 unit Apgar score at 5 minutes, the odds of having neonatal sepsis is 97% lower among neonates with a high Apgar score (p<0.001; 95%CI: (0.01-0.08). The odds of having neonatal sepsis is 3.43 times higher among neonates who were resuscitated at birth than those who were not (p=0.028; 95%CI:1.14-10.33). The likelihood of having neonatal sepsis increased by 5.74 times among those who were born at 37 weeks and above as compared to those less than 37 weeks of gestation age (p=0.008; 95%CI: 1.57-21.03). (Table 2)

Table 2. Factors associated with neonatal sepsis.

Characteristics	Univariate		Multivariate	
	OR (95% CI)	p-value	aOR (95% CI)	p-value
Neonatal Characteristics				
Age of neonates (days)	0.96 (0.94-0.99)	0.006	0.94 (0.91-0.98)	0.004
Sex				
Female	ref			
Male	0.69 (0.39-1.2)	0.2	0.57 (0.25-1.3)	0.187
Birthweight (grams)	0.99 (0.99-1.0)	0.16	1 (0.99-1.0)	0.12
Maternal characteristics				
Age of mother (years)	0.95 (0.88-1.03)	0.28	0.91 (0.8-1.01)	0.077
Obstetric characteristics				
ANC visits				
No	ref			
Yes	0.02 (0.003-0.19)	<0.001	0.04 (0.004-0.22)	0.002
Apgar score at 5 minutes	0.08 (0.01-0.16)	<0.001	0.03 (0.01-0.08)	<0.001
Mode of delivery				
Cesarean section	ref			
Vaginal delivery	2.71 (1.48-4.98)	0.001	1.61 (0.68-4.99)	0.264
Vacuum extraction	1	-	1	-
Resuscitation at birth				
No	ref			
Yes	0.76 (0.39-1.48)	0.435	3.43 (1.14-10.33)	0.028
Gestation age				
<37 weeks	ref			
37 weeks and above	2.43 (1.12-5.26)	0.024	5.74 (1.57-21.03)	0.008
Prolonged rupture of membrane (>18 hours)				
No	ref			
Yes	0.57 (0.32-1.03)	0.064	0.73 (0.31-1.72)	0.477

DISCUSSION

This research among 210 and 70 control showed that the mean age of cases with neonatal sepsis was 6.5±8.2 days and 11.1± 17.1 days for controls without neonatal sepsis. The majority were male (58.6%) for cases while female (67.1%) for controls. The mean birth weight (in grams) of cases was 2752.5±513.6 and 2858.8± 636.2 for controls. Mean age of mothers of cases was 23.4±3.1 years and 23.9±4.1 years for controls. Nearly two-thirds (64.8%) and almost all (98.6%) of the mothers of cases and controls respectively went for ANC visits during their pregnancy. Finding showed that neonatal characteristics such as age and Apgar score at 5 minutes significantly associated with the sepsis status of the neonates. Similarly, among maternal and obstetric characteristics the study showed a significant association between the ANC visits, resuscitation status at birth and gestation age and neonatal sepsis. The likelihood of developing neonatal sepsis decreased among older neonates. A retrospective case-control study obtained similar relationship among age and sepsis occurrence.[28] Early neonatal sepsis is linked with immune response of neonates.[37] Our study showed odds of having neonatal sepsis decreased with the increasing Apgar score at 5 minutes. This finding is in line with the studies determining lower Apgar score at birth as a risk factor for neonatal sepsis.[30,32] Another case-control study reported an association among neonates with low Apgar scores at birth.[34,38]Neonates with low Apgar scores are more prone to infection as they are more likely to be administered emergency support making them susceptible to microorganisms. Studies conducted in similar low-resource settings reported the male sex of neonates as one of the risk factors for developing sepsis.[26] Nevertheless, there was no significant association between the sex of the neonate and sepsis. Studies have shown birth weight is associated with neonatal sepsis.[28] However, we did not obtain an impact of birthweight on the occurrence of neonatal sepsis. The odds of having neonatal sepsis among neonates were lower whose mothers had at least one ANC visit than for those who did not have any ANC visits. A study carried out in Nepal also reported that neonates were at higher risk of developing sepsis if their mothers did not receive any ANC during pregnancy.[18] Neonates provided with resuscitation at birth were three times more likely to have neonatal sepsis as compared to those with no resuscitation. While most studies showed that neonates born <37 weeks gestation age are more likely to develop neonatal sepsis, however, in this study, neonates born at 37 weeks and above were five times at higher risk.[26]

Studies show a strong relationship between the mother's ages with the occurrence of neonatal outcomes such as neonatal sepsis.[39] In contrast, our study did not obtain a significant association between maternal age and neonatal sepsis. No significant association was found between mode of delivery and neonatal sepsis which is in line with the study conducted in Ethiopia.[30] Studies show that odds of neonatal sepsis increased with the prolonged rupture of membrane for more than 18 hours.[30,40] However, we did not obtain any significant association for prolonged rupture of membrane. Our study is one of the first few studies exploring the risk factors using a case-control study design. However, this study has a few limitations. First, the study was single-centered and enrolled only admitted cases of neonatal sepsis in the study. This might have limited the generalizability of the findings to the general population. The number of cases in the study was thrice the number of controls which might have reduced the statistical power of the study. However, this may not have necessarily caused selection bias as the controls were those who were admitted to the hospital and did not have neonatal sepsis.

CONCLUSIONS

This study concluded that age and sex of neonates, Apgar scores at 5 minutes of birth, ANC visits, resuscitation at birth, and gestation age were significantly associated with neonatal sepsis. Findings suggest the need for careful handling of neonates with routine screening for sepsis. Further, interventions encouraging to receive obstetric care should be instilled. This study will stimulate future researcher to conduct matched case control study, which will be benefitting the policy makers in crafting preventive strategies.

REFERENCES

1. World Health Organization. Newborns: improving survival and well-being. 2020 [cited 14 Jun 2022]. Available: https://www.who.int/news-room/fact-sheets/detail/newborns-reducing-mortality
2. World Health Organization. Newborn Mortality. [cited 28 Jun 2022]. Available: https://www.who.int/news-room/fact-sheets/detail/levels-and-trends-in-child-mortality-report-2021
3. Neonatal mortality. In: UNICEF DATA [Internet]. [cited 16 Jul 2022]. Available: https://data.unicef.org/topic/child-survival/neonatal-mortality/
4. Department of Health Services, Ministry of Health and Population, Government of Nepal. Annual Report- 2076/77 (2019/20). 2021. Available: https://dohs.gov.np/wp-content/uploads/2021/07/DoHS-Annual-Report-FY-2076-77-for-website.pdf
5. Sands K, Carvalho MJ, Portal E, Thomson K, Dyer C, Akpulu C, et al. Characterization of antimicrobial-resistant Gram-negative bacteria that cause neonatal sepsis in seven low- and middle-income countries. Nature microbiology. 2021;6: 512–523.
6. Okomo U, Akpalu ENK, Le Doare K, Roca A, Cousens S, Jarde A, et al. Aetiology of invasive bacterial infection and antimicrobial resistance in neonates in sub-Saharan Africa: a systematic review and meta-analysis in line with the STROBE-NI reporting guidelines. The Lancet Infectious Diseases. 2019;19: 1219–1234. doi:10.1016/S1473-3099(19)30414-1
7. Singh M, Alsaleem M, Gray CP. Neonatal Sepsis. StatPearls. Treasure Island (FL): StatPearls Publishing; 2022. Available: http://www.ncbi.nlm.nih.gov/books/NBK531478/
8. Ferreira RC, Mello RR, Silva KS. Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight. J Pediatr (Rio J). 2014;90: 293–299. doi:10.1016/j.jped.2013.09.006
9. Stoll BJ, Hansen NI, Adams-Chapman I, Fanaroff AA, Hintz SR, Vohr B, et al. Neurodevelopmental and growth impairment among extremely low-birth-weight infants with neonatal infection. JAMA. 2004;292: 2357–2365. doi:10.1001/jama.292.19.2357
10. Mukhopadhyay S, Puopolo KM, Hansen NI, Lorch SA, DeMauro SB, Greenberg RG, et al. Impact of Early-Onset Sepsis and Antibiotic Use on Death or Survival with Neurodevelopmental Impairment at 2 Years of Age among Extremely Preterm Infants. The

Journal of Pediatrics. 2020;221: 39-46.e5. doi:10.1016/j.jpeds.2020.02.038

11. Sewell E, Roberts J, Mukhopadhyay S. Association of Infection in Neonates and Long-Term Neurodevelopmental Outcome. Clinics in Perinatology. 2021;48: 251–261. doi:10.1016/j.clp.2021.03.001
12. 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: 200–211. doi:10.1016/S0140-6736(19)32989-7
13. Fleischmann C, Reichert F, Cassini A, Horner R, Harder T, Markwart R, et al. Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. Archives of Disease in Childhood. 2021;106: 745–752. doi:10.1136/archdischild-2020-320217
14. Abate BB, Kasie AM, Reta MA, Kassaw MW. Neonatal sepsis and its associated factors in East Africa: a systematic review and meta-analysis. Int J Public Health. 2020;65: 1623–1633. doi:10.1007/s00038-020-01489-x
15. Ranjeva SL, Warf BC, Schiff SJ. Economic burden of neonatal sepsis in sub-Saharan Africa. BMJ Global Health. 2018;3: e000347. doi:10.1136/bmjgh-2017-000347
16. Chaurasia S, Sivanandan S, Agarwal R, Ellis S, Sharland M, Sankar MJ. Neonatal sepsis in South Asia: huge burden and spiralling antimicrobial resistance. bmj. 2019;364.
17. Erchick DJ, Lackner JB, Mullany LC, Bhandari NN, Shedain PR, Khanal S, et al. Causes and age of neonatal death and associations with maternal and newborn care characteristics in Nepal: a verbal autopsy study. Archives of Public Health. 2022;80: 26. doi:10.1186/s13690-021-00771-5
18. Budhathoki SS, Sunny AK, Paudel PG, Thapa J, Basnet LB, Karki S, et al. Epidemiology of neonatal infections in hospitals of Nepal: evidence from a large-scale study. Archives of Public Health. 2020;78: 1–8.
19. Pokhrel B, Koirala T, 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. doi:10.1186/s12887-018-1176-x
20. Yadav NS, Sharma S, Chaudhary DK, Panthi P, Pokhrel P, Shrestha A, et al. Bacteriological profile of neonatal sepsis and antibiotic susceptibility pattern of isolates admitted at Kanti Children's Hospital, Kathmandu, Nepal. BMC Research Notes. 2018;11: 301. doi:10.1186/s13104-018-3394-6
21. Manandhar S, Amatya P, Ansari I, Joshi N, Maharjan N, Dongol S, et al. Risk factors for the development of neonatal sepsis in a neonatal intensive care unit of a tertiary care hospital of Nepal. BMC Infectious Diseases. 2021;21: 546. doi:10.1186/s12879-021-06261-x
22. Chapagain RH, Acharya R, Shrestha N, Giri BR, Bagale BB, Kayastha M. Bacteriological Profile of Neonatal Sepsis in Neonatal Intermediate Care Unit of Central Paediatric Referral Hospital in Nepal. J Nepal Health Res Counc. 2015;13: 205–208.
23. Sharma S, Chapagain RH, Pathak OK,

Gupta A, Rai KR, Karn S, et al. The economic burden of neonatal intensive care unit admission at a community hospital of central Nepal. Journal of Nepal Paediatric Society. 2020;40: 41–47.

24. Bohanon FJ, Lopez ON, Adhikari D, Mehta HB, Rojas-Khalil Y, Bowen-Jallow KA, et al. Race, income, and insurance status affect neonatal sepsis mortality and healthcare resource utilization. The Pediatric infectious disease journal. 2018;37: e178.

25. Milton R, Gillespie D, Dyer C, Taiyari K, Carvalho MJ, Thomson K, et al. Neonatal sepsis and mortality in low-income and middle-income countries from a facility-based birth cohort: an international multisite prospective observational study. The Lancet Global Health. 2022;10: e661–e672.

26. Murthy S, Godinho MA, Guddattu V, Lewis LES, Nair NS. Risk factors of neonatal sepsis in India: A systematic review and meta-analysis. PloS one. 2019;14: e0215683.

27. Adatara P, Afaya A, Salia SM, Afaya RA, Konlan KD, Agyabeng-Fandoh E, et al. Risk factors associated with neonatal sepsis: a case study at a specialist hospital in Ghana. The Scientific World Journal. 2019;2019.

28. Adatara P, Afaya A, Salia SM, Afaya RA, Kuug AK, Agbinku E, et al. Risk Factors for Neonatal Sepsis: A Retrospective Case-Control Study among Neonates Who Were Delivered by Caesarean Section at the Trauma and Specialist Hospital, Winneba, Ghana. BioMed Research International. 2018;2018: e6153501. doi:10.1155/2018/6153501

29. Agnche Z, Yenus Yeshita H, Abdela Gonete K. Neonatal Sepsis and Its Associated Factors Among Neonates Admitted to Neonatal Intensive Care Units in Primary Hospitals in Central Gondar Zone, Northwest Ethiopia, 2019. Infect Drug Resist. 2020;13: 3957–3967. doi:10.2147/IDR.S276678

30. Gebremedhin D, Berhe H, Gebrekirstos K. Risk Factors for Neonatal Sepsis in Public Hospitals of Mekelle City, North Ethiopia, 2015: Unmatched Case Control Study. PLOS ONE. 2016;11: e0154798. doi:10.1371/journal.pone.0154798

31. Masanja PP, Kibusi SM, Mkhoi ML. Predictors of Early Onset Neonatal Sepsis among Neonates in Dodoma, Tanzania: A Case Control Study. Journal of Tropical Pediatrics. 2020;66: 257–266. doi:10.1093/tropej/fmz062

32. Thapa B, Thapa A, Aryal DR, Thapa K, Pun A, Khanal S, et al. Neonatal sepsis as a major cause of morbidity in a tertiary center in Kathmandu. JNMA J Nepal Med Assoc. 2013;52: 549–556.

33. Paudel L, Kalakheti B, Sharma K. Prevalence and outcome of preterm neonates admitted to neonatal unit of a tertiary care center in Western Nepal. Journal of Lumbini Medical College. 2018;6: 87–91.

34. Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. Kathmandu Univ Med J (KUMJ). 2006;4: 187–191.

35. Ministry of Health, Government of Nepal. Nepal's every newborn action plan. 2016. Available: https://www.healthynewbornnetwork.org/hnn-content/uploads/

NENAP-final-low-resolution.pdf#:~:text=Nepal%E2%80%99s%20Every%20Newborn%20Action%20Plan%20proposes%20cost-effective%20maternal,11%20stillbirths%20per%201000%20total%20births%20by%202035.

36. Kc A, Jha AK, Shrestha MP, Zhou H, Gurung A, Thapa J, et al. Trends for Neonatal Deaths in Nepal (2001–2016) to Project Progress Towards the SDG Target in 2030, and Risk Factor Analyses to Focus Action. Matern Child Health J. 2020;24: 5–14. doi:10.1007/s10995-019-02826-0

37. 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. Pediatrics & Neonatology. 2016;57: 265–273. doi:10.1016/j.pedneo.2015.09.007

38. Bhutta ZA, Yusuf K. Early-Onset Neonatal Sepsis in Pakistan: A Case Control Study of Risk Factors in a Birth Cohort. Am J Perinatol. 1997;14: 577–581. doi:10.1055/s-2007-994338

39. SOMAN M, GREEN B, DALING J. RISK FACTORS FOR EARLY NEONATAL SEPSIS. American Journal of Epidemiology. 1985;121: 712–719. doi:10.1093/aje/121.5.712

40. Gebrehiwot A, Lakew W, Moges F, Moges B, Anagaw B, Unakal C, et al. Predictors of positive blood culture and death among neonates with suspected neonatal sepsis in Gondar University Hospital, Northwest Ethiopia. European Journal of Experimental Biology. 2012;2: 2212–2218.

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