African Journal of Emergency Medicine 12 (2022) 362–365

Contents lists available at ScienceDirect

African Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/afjem

ORIGINAL ARTICLE

Prevalence and presentation of neonatal sepsis at a paediatric emergency department in Johannesburg, South Africa

Tchouambou SN Clotilde, Feroza Motara, Abdullah E Laher*

Department of Emergency Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

ARTICLE INFO

Keywords:
Neonatal sepsis
Emergency centre
Perinatal HIV exposure
Preterm birth
Low birth weight
Breast feeding

ABSTRACT

Background: Despite a significant reduction in the prevalence of neonatal sepsis over the past three decades, the prevalence still remains high, especially in low- and middle-income countries. The aim of this study was to determine the prevalence and presenting features of neonatal sepsis at a paediatric emergency centre (PEC).

Methods: Medical records of all neonates presenting to an academic hospital PEC over a six-month period were analysed. Data was compared between neonates with and without sepsis. The odds ratio was calculated to determine factors associated with neonatal sepsis.

Results: Of the 210 neonates who were included, 43 (20.5%) were diagnosed with neonatal sepsis. Of these, 19 (44.2%) presented within the first 72 hours of life (early-onset neonatal sepsis) and 4 (9.3%) died prior to hospital discharge. A history of maternal employment (odds ratio (OR) 2.38, p=0.021), preterm birth (OR 3.24, p=0.019), low birth weight (<2.5kg) (OR 2.67, p=0.026), perinatal human immunodeficiency virus exposure (OR 3.35, p=0.002), not being breast fed (OR 4.36, p=0.001), and signs of lethargy (OR 14.01, p<0.001), dehydration (or 11.14, p<0.001), poor feeding (OR 7.20, p<0.001), irritability (OR 6.93, p<0.001), fever (OR 5.50, p<0.001), vomiting (OR 4.14, p<0.001) and respiratory distress (OR 4.12, p<0.001) were significantly associated with neonatal sepsis.

Conclusion: Among neonates presenting to the PEC, various clinical features on history and examination may be useful in predicting the diagnosis of neonatal sepsis. Clinicians working in the PEC must adopt a high index of suspicion when attending to neonates presenting with these features.

African relevance

- The incidence of neonatal sepsis in low- and middle-income countries is estimated at 3930 cases per 100 000 live births.
- Neonatal sepsis accounts for a third of neonatal deaths in low-income countries.
- A history of preterm birth, low birth weight, perinatal HIV exposure, not being breast fed and presentation with lethargy, dehydration, poor feeding, irritability, fever, vomiting, and respiratory distress are associated with a significantly higher likelihood of neonatal sepsis.
- EC clinicians must adopt a high index of suspicion when attending to neonates presenting with these features.

Introduction

Neonatal sepsis can be defined as a clinical syndrome that manifests with non-specific signs and symptoms that are secondary to an underlying bacterial bloodstream infection that presents within the first 28 days of life [1]. Despite a significant reduction in global neonatal mortality over the past three decades, the burden remains high, with there being 18 recorded neonatal deaths per 1000 live births reported in 2017. It is projected that between 2018 and 2030, 27.8 million children will die in their first month of life [2]. In low-income countries, neonatal sepsis has been shown to be responsible for approximately a third of neonatal deaths [3].

Between 2009 and 2018, the incidence of neonatal sepsis in low- and middle-income countries was estimated as 3930 cases per 100 000 live births [4]. In sub-Saharan Africa, it is estimated that neonatal sepsis is associated with a loss of 5.29 to 8.73 million disability- adjusted life years (DALYs), which translates to an annual economic burden of 10 to 469 billion US dollars [5]. Every year, a million neonates die from neonatal sepsis, with approximately 42% of these deaths occurring within the first seven days of life [6]. The overall mortality associated with neonatal sepsis has been estimated at 17.6% [4].

The clinical presentation of neonatal sepsis is predominantly non-specific and includes a myriad of signs and symptoms that include lethargy, dehydration, poor feeding, irritability, fever, vomiting, diarrhoea, respiratory distress, jaundice, seizures, hypothermia, and haemodynamic shock. This coupled with the low yield of true positive labora-

* Corresponding author at:
E-mail address: abdullahlaher@msn.com (A.E. Laher).

https://doi.org/10.1016/j.afjem.2022.07.013
Received 6 November 2021; Received in revised form 4 May 2022; Accepted 24 July 2022

tory culture findings renders the diagnosis of neonatal sepsis challenging [7].

Although there are multitudes of publications relating to the subject of neonatal sepsis, there is a paucity of data on the prevalence and presenting features of neonatal sepsis in the paediatric emergency centre (PEC) setting. Hence, the aim of this study was to determine the prevalence and presenting features of neonatal sepsis at a PEC in Johannesburg, South Africa.

Methods

This prospective cross-sectional study was conducted at the Charlotte Maxeke Johannesburg Academic Hospital Paediatric Emergency Department (CMJAH PED) between 01 January and 30 June 2018. The facility has approximately a thousand beds that includes 15 neonatal intensive care unit (ICU) beds and another 80 neonatal ward beds. Since the hospital is a designated tertiary care facility, it has the capability to caters for comprehensive obstetric and neonatal care.

Annually, approximately 400-500 neonates attend the PEC, all of whom are triaged into the unit for formal assessment by the on-shift EC doctor. As per the PEC unit protocol, laboratory investigations including sepsis biomarkers, blood culture, urine culture and cerebrospinal fluid analysis are conducted on all patients presenting with suspected neonatal sepsis. Furthermore, empiric antibiotics are also commenced in these patients. Neonates requiring possible admission are referred to the on-call neonatology registrar. Since there are no specific criteria dictating referral to the neonatology department, the decision is left to the discretion of the attending EC doctor.

Permission to conduct the study was granted by the hospital manager, while ethics clearance was obtained from the Human Research Ethics Committee of the University of the Witwatersrand (certificate no M160608). The study enrolled all neonates who presented during the data collection period and in whom consent for study participation was obtained.

For the purpose of this study, neonatal sepsis was defined as presentation within the first 28 days of life with either laboratory culture confirmed infection or with clinical and/or other laboratory findings that the attending specialist neonatologist attributed to the presence of neonatal sepsis and treated as such [7]. Early-onset neonatal sepsis was defined as presentation within the first 72 hours of birth, while late-onset neonatal sepsis was defined as presentation after 72 hours of birth [8]. Preterm birth was defined as birth prior to 37 completed weeks of pregnancy [9], while low birth weight was defined as a weight at birth of less than 2.5kg [10]. Neonates who initially received empiric antibiotic therapy for possible neonatal sepsis, but in whom the diagnosis was later reviewed to a non-sepsis diagnosis, were categorised as not presenting with sepsis.

Doctors and nurses employed at the PEC were briefed regarding the study protocol and were thereafter requested to inform the primary investigator of all neonates (≤28 days of age) who presented over the data collection period. The primary investigator also reviewed the PEC patient register to identify potential study subjects who were missed by the unit staff. Informed consent for study participation was obtained from the primary caregiver of the neonate. Data from hospital records were collected daily by the primary investigator over the entire duration of hospital stay and entered into a standardised data collection sheet. Where necessary, additional information relevant to the study but not found in the patient's hospital records was directly obtained from the participant, the participants laboratory records, or the primary caregiver. Collected data included demographic details (sex, maternal employment), patient referral, preterm birth status, birth weight, perinatal HIV exposure, method of delivery, method of feeding, in-hospital mortality and presenting clinical features. Subjects were followed-up until data collection was completed.

The data was thereafter entered into Microsoft® Excel® (Microsoft 365, Version 16.0.13029.20232) and exported to Stata version 16 (StataCorp Limited, Texas, United States of America) for statistical analysis. Frequency and percentage were determined for each of the variables. The chi-square test was utilized to determine if there were significant differences between neonates with and without sepsis The odds ratio (OR) and 95% confidence interval (CI) were also calculated for each variable. A p-value of less than 0.05 was regarded as significant. Study reporting conformed with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [11].

Results

A total of 221 neonates presented to the PEC during the period of data collection. Consent for study participation could not be obtained for 11 neonates, hence, a total of 210 neonates were included in the final study sample. Of these, 43 (20.5%) were diagnosed with neonatal sepsis, comprising 19 (44.2%) subjects with early-onset neonatal sepsis and 24 (55.8%) subjects with late-onset neonatal sepsis.

Blood, urine, and CSF samples were collected for laboratory microscopy, sensitivity, and culture analysis in a total of 94 (44.8%) subjects. Of these, culture confirmed sepsis was present in 9 (9.6%) neonates, while the diagnosis of neonatal sepsis was based on clinical and/or other laboratory findings in 34 (36.2%) subjects. All 43 subjects with a diagnosis of neonatal sepsis received empiric antibiotic therapy in the PEC and were admitted. Among the 167 (79.5%) subjects without neonatal sepsis, 51 (30.5%) received empiric antibiotic therapy in the PEC and 25 (15.0%) required hospital admission.

Table 1 compares data pertaining to patient demographics, clinical history findings and in-hospital mortality between neonates who presented with and without sepsis. Of note, maternal employment (OR 2.38, p =0.021) and low birth weight (<2.5kg) (OR 2.67, p=0.026) was associated with a greater than two times higher likelihood of neonatal sepsis, while premature birth (OR 3.24, p =0.019) and perinatal HIV exposure (OR 3.35, p=0.002) was associated with a greater than three times higher likelihood of neonatal sepsis, and formulae feeding (OR 4.36, p =0.001) and in-hospital mortality (OR 4.18, p =0.049) was associated with a greater than four times higher likelihood of neonatal sepsis. There were no significant differences with regards to sex, self-referral to hospital, and the method of delivery.

Table 2 compares clinical features between neonates who presented with and without sepsis. Of note, lethargy (OR 14.01, p < 0.001), dehydration (OR 11.14, p <0.001), poor feeding (OR 7.20, p <0.001), irritability (OR 6.93, p <0.001), fever (OR 5.50, p <0.001), vomiting (OR 4.14, p <0.001) and respiratory distress (OR 4.12, p <0.001) were associated with a significantly higher likelihood of neonatal sepsis, while jaundice was associated with a significantly lower likelihood of neonatal sepsis (OR 0.37, p =0.012).

Discussion

To our knowledge, this is the first study to describe the prevalence and characteristics of patients presenting with neonatal sepsis to a PEC setting in Southern Africa. In this study, neonatal sepsis was diagnosed in approximately one-fifth (20.5%) of all neonates presenting to the CMJAH PED. Comparatively, a systematic review and meta-analysis which comprised of 14 683 neonates across 22 studies that were conducted in Iran, reported that the pooled national prevalence of neonatal sepsis in Iran was 15.98%, with there being a slightly higher prevalence in males [12]. In another study that was conducted at a tertiary level hospital in North West Nigeria, the reported prevalence of neonatal sepsis was much higher at 37.6% [13].

In our study, among subjects diagnosed with neonatal sepsis, 44.2% presented with early-onset neonatal sepsis. Comparatively, a systematic review and metanalysis of 18 studies that were conducted in Ethiopia, reported a much higher prevalence of early onset-neonatal sepsis of 75.4% [14]. The study conducted in North West Nigeria also reported a high prevalence of early onset-neonatal sepsis of 78.2% [13]. A likely

Table 1
Comparison of demographic data, clinical history findings and in-hospital mortality between neonates presenting with and without sepsis.

Variable	Neonatal sepsis		OR (95% CI)	P-Value
	Yes(n=43)	No(n=167)		
Sex				
Male	24 (55.8)	74 (44.3)	1.00 (reference)	0.179
Female	19 (44.2)	93 (55.7)	1.59 (0.81-3.12)	
Maternal employment	31 (72.1)	87 (52.1)	2.38 (1.14-4.94)	**0.021**
Self-referral	12 (27.9)	34 (20.3)	1.54 (0.72-3.31	0.271
Preterm birth	8 (18.6)	11 (6.6)	3.24 (1.21-8.65)	**0.019**
Low birth weight (<2.5kg)	10 (23.2)	17 (10.2)	2.67 (1.12-6.36)	**0.026**
HIV-exposed	15 (34.9)	23 (13.8)	3.35 (1.56-7.23)	**0.002**
Method of birth delivery				
Vaginal delivery	34 (79.1)	123 (73.7)	1.00 (reference)	0.467
Caesarean section	9 (20.9)	44 (26.3)	1.35 (0.60-3.04)	
Feeding				
Formulae feeds	21 (48.8)	30 (18.0)	1.00 (reference)	**0.001**
Breast fed	22 (51.2)	137 (82.0)	4.36 (2.12-8.93)	
In-hospital mortality	4 (9.3)	4 (2.4)	4.18 (1.00-17.45)	**0.049**

OR – odds ratio; CI – confidence interval; EC – emergency centre.

Table 2
Comparison of clinical features between neonates presenting with and without sepsis.

Variable	Neonatal sepsis		OR (95% CI)	P-Value
	Yes(n=43)	No(n=167)		
Lethargy	11 (25.6)	4 (2.4)	14.01 (4.19-46.76)	**<0.001**
Dehydration	11 (25.6)	5 (2.9)	11.14 (3.62-34.24)	**<0.001**
Poor feeding	20 (46.5)	18 (10.8)	7.20 (3.32-15.60)	**<0.001**
Irritability	10 (23.2)	7 (4.1)	6.93 (2.46-19.52)	**<0.001**
Fever	19 (44.2)	21 (12.6)	5.50 (2.58-11.72)	**<0.001**
Vomiting	20 (46.5)	29 (17.4)	4.14 (2.01-8.51)	**<0.001**
Respiratory distress	16 (37.2)	21 (12.6)	4.12 (1.91-8.89)	**<0.001**
Jaundice	10 (23.2)	75 (44.9)	0.37 (0.17-0.80)	**0.012**
Seizures	2 (4.6)	0	20.18 (0.95-428.42)	0.054
Hypothermia	3 (6.9)	3 (1.8)	4.1 (0.80-21.08)	0.091
Shock	1 (2.3)	1 (0.6)	3.95 (0.24-64.51)	0.335
Rash	7 (12.3)	12 (7.2)	2.51 (0.92-6.83)	0.071
Cough	12 (27.9)	30 (17.9)	1.77 (0.81-3.84)	0.149
Diarrhoea	6 (13.9)	17 (10.2)	1.43 (0.53-3.88)	0.482

reason for the higher reported prevalence in these two studies is that both studies defined early-onset neonatal sepsis as onset of sepsis within the first seven days of life, whereas we defined it as onset within the first three days of life. In stark contrast to our study findings, an earlier study conducted between 2001 and 2003 at the neonatal unit of the same hospital as this study, reported that only five of 96 (5.2%) neonates presented with early-onset sepsis. The study however only enrolled neonates with laboratory culture positive sepsis [15].

A study conducted in Southern Ethiopia reported that the likelihood of neonatal sepsis was 2.76 times higher in neonates who were born to mothers with lower income compared to those who were born to mothers with higher income [16]. Another study reported that every year approximately one millions neonates die from infections in low income households in Pakistan [17]. In contrast, in our study, the likelihood of developing neonatal sepsis was 2.38 times higher in neonates whose mothers were employed in comparison to neonates whose mothers were unemployed. Although we did not determine total household income and reasons for this rather surprising finding, a probable explanation may be that total household income may have been low, so these mothers were forced to seek employment and hence may not have been able to take adequate care of their baby. This finding should be further investigated in future studies.

A systematic review and metanalysis which comprised of eight studies that were all conducted in Ethiopia, reported that compared to normal birthweight neonates, those with a low birth weight (<2.5kg) were 1.42 times more likely to develop sepsis [18]. Comparatively, in our study, a low birth weight (<2.5kg) was associated with a 2.67 times higher likelihood of developing neonatal sepsis.

In our study, the prevalence of neonatal sepsis was significantly higher among neonates with a history of perinatal HIV exposure. Similarly, other studies also reported a higher incidence of sepsis among HIV exposed but uninfected infants who were <3 months old [19–22]. Group B streptococcus was the causative organism in most of these studies. In comparison to breastfed neonates, the likelihood of presentation with neonatal sepsis was 4.36 times higher among formulae fed neonates in our study. A study conducted in Bangladesh reported that compared to neonates in whom breastfeeding was initiated within an hour of birth, those in whom there was a >48-hour delay in initiating breastfeeding and those who were not breastfed, had a 4.13- and 4.7-times higher likelihood of developing severe illness in the first seven days of life, respectively [23]. Another study showed that even among partially breastfed neonates, the likelihood of neonatal sepsis was 18 times lower [24].

In our study, presentation with lethargy (OR 14.01), dehydration (OR 11.14), poor feeding (OR 7.20), irritability (OR 6.93), fever (OR 5.50), vomiting (OR 4.24) and respiratory distress (OR 4.12) were associated with a significantly higher likelihood of neonatal sepsis. Comparatively, a study that investigated the predictors of neonatal sepsis in four developing countries reported that a bulging fontanel (OR 10.0), poor feeding (OR 5.1), a history of convulsions (OR 4.2), hypothermia (OR 3.7), fever (OR 3.6) and a decrease in the level of consciousness (OR 3.0) were significantly associated with a higher likelihood of neonatal sepsis [25].

There are some limitations to this study. Firstly, this was a single centre study, hence, our findings may differ to that of other facilities where triage criteria and management protocols may vary. Secondly, due to the low yield associated with obtaining a positive laboratory cultures in neonates with sepsis, it is possible that the true prevalence of neonatal sepsis may have been under- or over-reported, thereby influencing our study findings. However, this limitation is applicable to all studies that relate to neonatal sepsis. Thirdly, due to the relatively small sample size, our data was not amenable to multivariate analysis. Hence, we were unable to determine which of the studied variables were independent predictors of neonatal sepsis. Nevertheless, it is hoped that findings of this study will encourage others to conduct similar but larger scale studies that will aim to determine the independent predictors of neonatal sepsis in lower-income settings.

Conclusion

The prevalence of neonatal sepsis among neonates presenting to the CMJAH PED over the study period was 20.5%. A history of maternal

employment, preterm birth, low birth weight, perinatal HIV exposure, not being breast fed, poor feeding and signs of lethargy, dehydration, irritability, fever, vomiting, and respiratory distress were significantly associated with a diagnosis of neonatal sepsis. Due to the non-specific presentation of neonatal sepsis and the consequences associated with missing the diagnosis, clinicians working in the PEC must adopt a high index of suspicion when attending to neonates presenting with these features.

Dissemination of results

Results from this study were shared with emergency centre staff at the study site.

Author contributions

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: TC contributed 40%; AL 35%; and FM contributed 25%. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of Competing Interest

The authors declared no conflict of interest.

Acknowledgements

The authors would like to thank the staff at the Charlotte Maxeke Johannesburg Academic Hospital Paediatric Emergency Department for their assistance with identifying potential study participants.

Funding

None.

References

[1] Edmond K, Zaidi A. New approaches to preventing, diagnosing, and treating neonatal sepsis. PLoS Med 2010;7:e1000213. doi:10.1371/journal.pmed.1000213.
[2] Hug L, Alexander M, You D, Alkema L. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. Lancet Glob Heal 2019;7:e710–20. doi:10.1016/S2214-109X(19)30163-9.
[3] Garces AL, McClure EM, Pérez W, Hambidge KM, Krebs NF, Figueroa L, et al. The Global Network Neonatal Cause of Death algorithm for low-resource settings. Acta Paediatr 2017;106:904–11. doi:10.1111/apa.13805.
[4] 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. Arch Dis Child 2021;106:745–52. doi:10.1136/archdischild-2020-320217.
[5] Ranjeva SL, Warf BC, Schiff SJ. Economic burden of neonatal sepsis in sub-Saharan Africa. BMJ Glob Heal 2018;3:e000347. doi:10.1136/bmjgh-2017-000347.
[6] Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? Lancet 2005;365:891–900. doi:10.1016/S0140-6736(05)71048-5.
[7] Coetzee M, Mbowane N, De Witt T. Neonatal sepsis: Highlighting the principles of diagnosis and management. South African J Child Heal 2017;11:99. doi:10.7196/SAJCH.2017.v11i2.1244.
[8] Fuchs A, Bielicki J, Mathur S, Sharland M, Van Den Anker JN. Antibiotic Use for Sepsis in Neonates and Children: 2016 Evidence Update 2016. https://www.who.int/selection_medicines/committees/expert/21/applications/s6_paed_antibiotics_appendix4_sepsis.pdf (accessed October 18, 2021).
[9] Preterm birth 2018. https://www.who.int/news-room/fact-sheets/detail/preterm-birth (accessed October 16, 2021).
[10] Low Birthweight: Country, regional and global estimates 2004. https://apps.who.int/iris/bitstream/handle/10665/43184/9280638327.pdf;sequence=1 (accessed October 18, 2021).
[11] von Elm E, DG Altman, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007;335:806–8. doi:10.1136/bmj.39335.541782.AD.
[12] Akbarian-Rad Z, Riahi SM, Abdollahi A, Sabbagh P, Ebrahimpour S, Javanian M, et al. Neonatal sepsis in Iran: A systematic review and meta-analysis on national prevalence and causative pathogens. PLoS One 2020;15:e0227570. doi:10.1371/journal.pone.0227570.
[13] Olorukooba A, Ifusemu W, Ibrahim M, Jibril M, Amadu L, Lawal B. Prevalence and factors associated with neonatal sepsis in a tertiary hospital, North West Nigeria. Niger Med J 2020;61:60. doi:10.4103/nmj.NMJ_31_19.
[14] Assemie MA, Alene M, Yismaw L, Ketema DB, Lamore Y, Petrucka P, et al. Prevalence of Neonatal Sepsis in Ethiopia: A Systematic Review and Meta-Analysis. Int J Pediatr 2020;2020:1–9. doi:10.1155/2020/6468492.
[15] Motara F, Ballot D, Perovic O. Epidemiology of neonatal sepsis at Johannesburg Hospital. South African J Epidemiol Infect 2005;20:90–3.
[16] Alemayehu A, Alemayehu M, Arba A, Abebe H, Goa A, Paulos K, et al. Predictors of neonatal sepsis in hospitals at Wolaita Sodo Town, Southern Ethiopia: institution-based unmatched case-control study, 2019. Int J Pediatr 2020;2020:1–10. doi:10.1155/2020/3709672.
[17] Zaidi AKM, Thaver D, Ali SA, Khan TA. Pathogens Associated with sepsis in newborns and young infants in developing countries. Pediatr Infect Dis J 2009;28:S10–18. doi:10.1097/INF.0b013e3181958769.
[18] Belachew A, Tewabe T. Neonatal sepsis and its association with birth weight and gestational age among admitted neonates in Ethiopia: systematic review and meta-analysis. BMC Pediatr 2020;20:55. doi:10.1186/s12887-020-1949-x.
[19] Adler C, Haelterman E, Barlow P, Marchant A, Levy J, Goetghebuer T. Severe infections in HIV-exposed uninfected infants born in a european country. PLoS One 2015;10:e0135375. doi:10.1371/journal.pone.0135375.
[20] Dangor Z, Lala SG, Cutland CL, Koen A, Jose L, Nakwa F, et al. Burden of invasive group B streptococcus disease and early neurological sequelae in south african infants. PLoS One 2015;10:e0123014. doi:10.1371/journal.pone.0123014.
[21] Epalza C, Goetghebuer T, Hainaut M, Prayez F, Barlow P, Dediste A, et al. High incidence of invasive group B streptococcal infections in HIV-exposed uninfected infants. Pediatrics 2010;126:e631–8. doi:10.1542/peds.2010-0183.
[22] Cutland CL, Schrag SJ, Thigpen MC, Velaphi SC, Wadula J, Adrian PV, et al. Increased risk for group B streptococcus sepsis in young infants exposed to HIV, Soweto, South Africa, 2004–20081. Emerg Infect Dis 2015;21:638–45. doi:10.3201/eid2104.141562.
[23] Raihana S, Dibley MJ, Rahman MM, Tahsina T, Siddique MAB, Rahman QS, et al. Early initiation of breastfeeding and severe illness in the early newborn period: An observational study in rural Bangladesh. PLOS Med 2019;16:e1002904. doi:10.1371/journal.pmed.1002904.
[24] Ashraf RN, Jalil F, Zaman S, Karlberg J, Khan SR, Lindblad BS, et al. Breast feeding and protection against neonatal sepsis in a high risk population. Arch Dis Child 1991;66:488–90. doi:10.1136/adc.66.4.488.
[25] Weber MW, Carlin JB, Gatchalian S, Lehmann D, Muhe L, Mulholland EK, et al. Predictors of neonatal sepsis in developing countries. Pediatr Infect Dis J 2003;22:711–17. doi:10.1097/01.inf.0000078163.80807.88.