International Journal of Contemporary Pediatrics
Gosai D et al. Int J Contemp Pediatr. 2020 Oct;7(10):2037-2040
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20204049

Original Research Article

Predictors of mortality in neonatal septicemia in a tertiary care centre

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Received: 27 July 2020
Accepted: 02 September 2020

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ABSTRACT

Background: Neonatal septicemia continues to be a major cause of mortality and morbidity in new-borns all over the world. Aim and objectives of the study were determining the risk factors for mortality in neonatal septicemia.
Methods: A retrospective observational study of the demographics, clinical features and laboratory parameters of 100 neonates admitted in NICU of a tertiary care hospital from September 2019 to March 2020.
Results: 67% of neonates delivered outside centre and 33% of neonates delivered at centre were found to have sepsis exclusively based on culture positivity. A significant association was found between very low birth rate (VLBW) (p value<0.001), prematurity (p value<0.01) and high neonatal mortality. Among the different clinical presentations of neonatal sepsis, lethargy (p value<0.02), apnea (p value<0.01) and hypothermia (p value<0.02) were found to be frequently associated with neonatal mortality. Further, C-reactive protein (CRP) positivity (p value<0.003), hyperglycaemia (p value<0.0009) and thrombocytopenia (p value<0.0009) were also associated with high neonatal mortality. Gram positive bacteria were frequently isolated from blood cultures of deceased neonates, *Coagulase negative staphylococci (CoNS)* (36.1%), being the commonest bacteria followed by *B. subtilis* (11.1%), *Klebsiella spp*. (11.1%) and *Acinetobacter spp.* (8.3%).
Conclusion: Demographic factors like VLBW, prematurity, outborn deliveries, clinical and laboratory parameters like lethargy, apnea, hypothermia, thrombocytopenia and hyperglycemia are strong predictors of mortality in neonatal.

Keywords: Morbidity, Neonatal mortality, Septicemia

INTRODUCTION

Globally, sepsis is a major cause of morbidity and mortality in neonates despite the advances in healthcare field. The estimated global burden for neonatal sepsis was 2, 202 (95% CI:1099-4,360) per 1,00,000 live births.[1,2] More than 40% of under five deaths occur in neonatal period, resulting in 3.1 million new-born deaths each year.[3] According to Global Sepsis Alliance, infections leading to sepsis are responsible for around one-fifth of world's neonatal death, and in South Asia and Sub-Saharan Africa, it was about 25% of all neonatal deaths.[4] Neonatal sepsis poses a massive public health burden in developing countries. The survivors of neonatal sepsis are prone for many neurodevelopment defects. This study analyses demographics, laboratory parameters and clinical features that define neonatal septicemia.

METHODS

The study aims at determining the risk factors for mortality in neonatal septicemia in neonatal intensive care unit of a paediatric tertiary care hospital. A retrospective observational study of the demographics, clinical features and laboratory parameters of 100 neonates admitted in NICU of a paediatric tertiary care hospital from September 2019 to March 2020. Data were collected from the integrated case registry maintained by the paediatric department. All new-born babies admitted in NICU with blood culture positive sepsis were included

in the study. Babies with blood culture positive sepsis, those who took discharge against medical advice, clinically suspected cases of neonatal sepsis whose blood cultures are negative were excluded. Out of the 100 patients (n=100), survivors (patients who got discharged) formed group A (n=64) and the deceased, formed group B (n=36). Clinical definitions for the study included the following:[4]

- Early onset sepsis (EOS)-clinical manifestation of sepsis appeared within <72 hours of life.
- Late onset sepsis (LOS)-clinical manifestation of sepsis appeared >72 hours of life.
- Thrombocytopenia-platelet count <150 × 103/µl.
- Hyperglycaemia-whole blood glucose level>125 mg/dl or plasma glucose level >145 mg/dl.
- Positive crp - levels more than 3 mg/dl.
- Leukopenia-total leucocyte count <5000/mm.[3]

Data analysis was done using SPSS software version 20.0 according to the objectives of the study with 2-tailed p<0.05 as statistically significant.

RESULTS

On analysis of data, found that 67 % of subjects born outside centre against 33% of in-born patients. Further, among the analysed demographic factors, VLBW (p value <0.001), out born births (p value<0.02) and prematurity (p value 0.01) were associated with high mortality. However, presence of EOS and LOS were not associated with increased mortality.

Among the different clinical presentations of neonatal sepsis, lethargy (p value<0.02), apnea (p value<0.01) and hypothermia (p value<0.02) were found to be frequently associated with neonatal mortality. Further, CRP positivity (p value<0.003), hyperglycaemia (p value<0.0009) and thrombocytopenia (p value<0.0009) were also associated with high neonatal mortality.

Table 1: Demographic risk factors associated with neonatal mortality.

Parameter	Discharged (n=64) (%)	Expired (n=36) (%)	Chi square	P value
EOS	30 (46.8)	23 (63.8)	2.667	0.1
LOS	34 (53.1)	13 (36.2)	0.78	0.7
VLBW	6 (9.3)	10 (27.7)	10.7	0.001
Out born	48 (75)	19 (52.7)	5.14	0.02
Preterm	14 (21)	16 (44)	5.58	0.01

Table 2: Clinical and laboratory parameters associated with neonatal mortality.

Parameters	Discharged (n=64) (%)	Expired (n=36) (%)	Chi square	P value
Lethargy	21 (32.8)	35 (97.2)	39.6	0.02
Apnea	14 (21.9)	16 (44.4)	5.58	0.01
Hypothermia	48 (75)	19 (52.7)	5.14	0.02
Jaundice	25 (39.06)	8 (22.2)	2.95	0.08
Hyperglycaemia	3 (4.6)	10 (27.7)	10.86	0.0009
Leukopenia	50 (78.125)	20 (55.55)	5.588	0.018
Thrombocytopenia	10 (15.6)	21 (58.3)	19.64	0.00009
CRP positivity	27 (42.1)	26 (72.3)	8.34	0.003

Table 3: Blood culture isolates obtained from septicemic neonates.

Organisms	Expired (n=36) (%)	Discharged (n=64) (%)	Chi square	P value
Gram negative				
Burkholderia	3 (8.3)	1 (1.5)	2.87	0.09
Klebsiella	4 (11.1)	3 (4.6)	1.46	0.22
Stenotrophomonas	1 (2.7)	3 (4.6)	0.14	0.79
E. coli	2 (5.5)	1 (1.5)	1.75	0.18
Enterobacter	1 (2.7)	1 (1.5)	0.03	0.85
Acinetobacter	3 (8.3)	6 (9.3)	0.38	0.53
Pseudomonas	1 (2.7)	1 (1.5)	0.03	0.85
Sphingomonas	1 (2.7)	3 (4.6)	0.14	0.79
Gram positive				
S. aureus	1 (2.7)	3 (4.6)	0.14	0.79

Continued.

Organisms	Expired (n=36) (%)	Discharged (n=64) (%)	Chi square	P value
CoNS	13 (36.1)	29 (45.31)	0.03	0.85
Streptococcus spp.	1 (2.7)	1 (1.5)	0.03	0.85
B. subtilis	4 (11.1)	13 (20.3)	0.004	0.94
Candida	1 (2.7)	1 (1.5)	0.03	0.85

Gram positive bacteria were frequently isolated from blood cultures of deceased neonates, *CoNS* (36.1%), being the commonest bacteria followed by *B. subtilis* (11.1%), *Klebsiella* spp. (11.1%) and *Acinetobacter* spp. (8.3%).

DISCUSSION

A plethora of agents like maternal, fetal and environmental factors contribute to sepsis in neonates. Some of the maternal factors involved are premature rupture of membranes, maternal fever 2 weeks prior to delivery, foul smelling amniotic fluid, urinary tract infection in mother and instrumental delivery. contributing fetal factors are low birth weight, birth asphyxia, prematurity, low Apgar score and male sex.[7] Neonatal mortality rate as per study was 36%. Similar high mortality rates were reported by Meshram et al (38.24%), Jumah et al and Bhutta et al (44.27%).[6,7,9]

The mortality in EOS group was 63.8% compared to LOS group (34.7%) which underscores the fact that factors like maternal genito-urinary tract infections have a direct implication on incidence of neonatal sepsis. Similar results were reported by Meshram et al, Jumah et al and Tareen et al.[5-7] However, few studies report higher mortality rate due to LOS as well.[16,18,20] Higher rates in LOS group was ascribed to invasive diagnostic procedures, prolonged hospitalisation and prolonged antibiotic use.[4,7]

In study, prematurity (<37 weeks) was associated with a higher mortality (54%) in concordance with many other studies done at different centres.[5,14,15] Further, clinical features like hypothermia, apnea and lethargy were significantly associated with mortality in neonatal sepsis. Similar observations were recorded by Jajoo M et al, Bhutta et al, Jumah et al and many others.[7-10,12,13] Similarly, associate higher mortality rates in patients with thrombocytopenia, CRP positivity, leucopoenia and hyperglycaemia. Although non-specific for neonatal sepsis, CRP has the highest sensitivity, specificity and high negative and high positive predictive values.[18] Few studies have documented the association between thrombocytopenia and gram-negative septicemia.[7,21,22] The underlying mechanism was found to be a combination of diffuse endothelial injury, bacterial/fungal toxins, increased platelet activation and DIC.[22]

In study, *CoNS* (36.1%) was the most common bacteria isolated from expired septic neonates. However, Tareen et al reported *E. coli* (18%) as commonest isolate, followed by *Klebsiella* (15.9%) and *Enterobacter* (15.9%).[5]

CONCLUSION

Investigations of neonatal demographics found that VLBW, prematurity and out-born deliveries are strongly associated with neonatal mortality. Laboratory risk indicators include hyperglycaemia and thrombocytopenia, which are significantly associated, while CRP positivity has also shown some correlation with neonatal mortality. Further, clinical presentations like lethargy, apnea and hypothermia should raise an early suspicion of sepsis. Gram-positive bacteria are frequently isolated from expired septicemic infants with *CoNS*, being the most common isolate. Early detection and management of these risk factors (demographic factors-like VLBW, prematurity; clinical presentation-lethargy, apnea, hypothermia; laboratory parameters-thrombocytopenia, hyperglycaemia, CRP positivity) would go a long way in preventing severe and life-threatening complications and death in neonatal septicemia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Neonatal mortality-UNICEF DATA. Available from: https://data.unicef.org/topic/child-survival/neonatal-mortality/. Accessed on 25 July 2020.
2. Struzek CF, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N.The global burden of paediatric and neonatal sepsis: a systematic review. Lancet Respir Med. 2018;6(3):223-30.
3. GSA and WHO. World sepsis day 2017-preventable maternal and neonatal sepsis a critical priority for WHO and Global Sepsis Alliance.; 2017
4. Agarwal R, Deorari A, Paul V, Sankar MJ, Sachdeva A. Sepsis in Newborn: AIIMS Protocols in Neonatalogy, edi 3rd, Noble Vision, New Delhi (India). 2019;305-15.
5. Tareen Z, Jirapradittha J, Sirivichayakul C, Chokejindachai W, Rafiqi N. Factors associated with mortality outcomes in neonatal septicaemia in Srinagarind Hospital, Thailand. Neonat Pediatr Med. 2017;3(2):1-5.
6. Meshram RM, Gajimvar VS, Bhongade SD. Predictors of mortality in out borns with neonatal

sepsis: A prospective observational study. Niger Postgrad Med J. 2019;26(4):216-22.
7. Jumah DS, Hassan MK, Duha SS. Predictors of mortality outcome in neonatal sepsis. Med J Basrah Uni. 2007;25(1):11-8.
8. Jajoo M, Kapoor K, Garg LK, Manchanda V, Mittal SK. To study the incidence and risk factors of early onset sepsis in an out born neonatal intensive care unit of India. J Clin Neonatol. 2015;4:91-5.
9. Bhutta ZA, Yusuf K. Neonatal sepsis in Karachi: Factors determining outcome and mortality. J Trop Pediatr. 1997;43:65-70.
10. Bharad RV, Singh CS, Singh LR. Risk factors and immediate outcome of early onset neonatal sepsis. J Med Sci Res. 2017;5:21050-6.
11. Sharma R, Soni TN, Rathore R, Rajput JS. A prospective study of risk factors of mortality in neonatal sepsis patients. Int J Med Res. 2018;3:72-4.
12. Oglunesi TA, Ogunfowora OB. Predictors of mortality in neonatal septicaemia in an underresourced setting. J Natl Med Assoc. 2010;102:915-21.
13. Trotman H, Bell Y, Thame M, Nicholson AM, Barton M. Predictors of poor outcome in neonates with bacterial sepsis admitted to the university hospital of West Indies. West Indian Med J. 2006;55:80-4.
14. Liang LD, Kotadia N, English L, Kissoon N, Ansermino JM, Kabakyenga J et al. Predictors of mortality in neonates and infants hospitalised with sepsis or serious infections in developing countries: A systematic review. Front Pediatr. 2018;6;277.
15. Kardana IM. Incidence and factors associated with mortality of neonatal sepsis. Pediatr Indones. 2011;51:144-8.
16. Radhy H. Neonatal sepsis causative agents and outcome. Thesis submitted to the Iraqi commission for medical specialisation. 2001;1-36.
17. Ahmed A, Ahmad I, Ahmad S, Iqbal J, Din WN, Bashir Y et al. Hematological and biochemical predictors of mortality in neonatal sepsis. Natl J Med Res. 2015;5:169-73.
18. Dawadu A, Al- Umran K, Twum Danso K. A case control study of Neonatal sepsis: Experience from Saudi Arabia. J Tropical paediatrics. 1997;(43):84-8.
19. Ahmed Z, Ghafoor T, Waqar T, Ali S, Aziz S, Mahmud S. Diagnostic value of C- reactive protein and hematological parameters in neonatal sepsis. J Coll Physician Surg pak. 2005;15(3):152-6.
20. Stoll B, Hansen N, Fanaroff A, Wright LL, Carlo WA, Ehrenkranz RA et alLate onset sepsis in very low birth weight neonates: the Experience of the NICHD Neonatal Research Network. Pediatrics. 2002 Aug;110(2 Pt 1):285-91.
21. Shyamala KV, Subbalekshmi NK, Raghuverra K. Role of platelet count and CRP level in Gram negative versus Gram positive bacterial sepsis in low birth weight neonates. Chinese clinical medicine J. 2010;(5):474-9.
22. Guida JD, Kunig AM, Leef KH, Mckenzie SE, Paul DA. Platelet count and sepsis in very low birth weight neonates: Is there an organism specific response? Pediatrics. 2003;111(6 Pt 1):1411-5.

Cite this article as: Gosai D, Shah BH, Jyothi S. Predictors of mortality in neonatal Septicemia in a tertiary care centre. Int J Contemp Pediatr 2020;7:2037-40.