



FACTORS OF DEATH AMONG HOSPITALIZED NEONATES WITH SEPSIS IN THE FLOOD DISASTERS AREAS OF PAKISTAN

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Abstract

Background: Sepsis is the main factor in infant death and neurological impairment among neonates. One-third of all neonatal deaths in Pakistan are attributable to it. Neonates experience a high rate of mortality. Newborn mortality is decreased by identifying and preventing neonatal sepsis predictors.

Objective: The purpose of the study was to identify the factors of death among hospitalized neonates with sepsis during the period of flood disaster.

Methodology: 73 neonates were evaluated at General hospital in the southern Punjab and upper Punjab from June to September 2022. Cases were admitted babies who died from sepsis, whereas controls were those who survived. The deaths of neonates diagnosed with neonatal sepsis were picked in chronological order. The three controls listed below were chosen at random from the NICU case registration book. Information was acquired from baby records using specified checklists. Data was evaluated using SPSS 26. Death variables were examined using logistic regression.

Results: Fifteen cases and fifty-eight controls were included in this study. More than three-quarters of cases (73.4%) had an early start of sepsis. In this investigation, inadequate feeding (AOR = 2.11), respiratory distress (AOR = 1.84), estimated gestational age shorter than 34 weeks (AOR = 5.75), and convulsion (AOR = 2.12) were significantly associated with Death.

Conclusion: This study demonstrated that the causes of sepsis-related infant death were preterm, convulsion, inadequate feeding, and respiratory distress. To lower sepsis-related mortality, it's crucial to pay attention to babies who have any of the identified risks when they're septicemic.

Keywords: Neonates, Sepsis, Pakistan, Death factors, flood

Introduction

Neonatal sepsis is a bacterial infection that develops within the first 28 days of life. It could be caused by viruses or fungus in the bloodstream ¹. It encompasses septicemia, pneumonia,

meningitis, arthritis, and other conditions, but excludes superficial mucocutaneous infections such as thrush². Neonatal sepsis can develop early in the first week or late after one week. The period following birth is the most perilous for a child's survival¹. During this phase, all organ systems undergo considerable physiologic changes and learn to respond to external stimuli, making it a period of extreme vulnerability as they adapt for extrauterine survival³. Immune system immaturity, especially in premature infants, confers unique clinical, physiologic, and prognostic characteristics to infections throughout this period. Infants are more susceptible to infection due to their underdeveloped skin barriers, mucosal defense mechanisms, and blood-brain barriers. Neonatal infants are more susceptible to a wide range of illnesses, including those caused by low-virulence pathogens such as listeria, par echoviruses, and Candida³.

The definition of neonatal mortality is death before or after the seventh day of life. Sepsis is the main cause of neonatal mortality and neurological impairment, accounting for 39% of fatalities⁴. Each year, invasive infections kill over 1.4 million newborns⁵. Mortality from infections varies with region, gestational age, and body mass. It accounts for 30 to 50% of newborn deaths in developing nations⁶. Asia has the majority of the top 10 nations with the highest neonatal death rate. According to estimates, Pakistan is responsible for 298,000 newborn deaths each year, or 7% of all neonatal deaths globally⁷. According to the World Bank, Pakistan has the world's second-highest infant mortality rate. The neonatal mortality rate (NMR) is the number of neonatal fatalities per 1,000 live births in the first month. Pakistan's NMR is 40. Lesotho has a lower NMR than Pakistan, while South Sudan has a lower NMR (40). Infant mortality is increased by preterm birth, low birth weight, birth asphyxia, and birth anomalies. Malnutrition in mothers and children contributes to high neonatal mortality⁸. More than 30 million people have been affected by flooding, and 6.4 million of them require assistance from organizations. Around 130,000 pregnant women require immediate medical treatment. Despite this, over 42,000 women are anticipated to give birth during the following three months.

This current study uses multivariate logistic regression models to identify factors of sepsis-related neonatal deaths, allowing health professionals and policymakers to identify monitoring indicators and apply appropriate preventative strategies to reduce neonates' death in the flood regions of lower Punjab and upper Punjab, Pakistan.

Methods

The case control study was conducted in the District Hospital of Attock and Bahawalpur and Multan, where the cases were received during the period of the flood disaster; a total of 110 cases were registered in the hospital. In the current study 75 cases were taken in which (17cases and 58 were controls). This investigation focused on the neonatal sepsis-related infant mortality (registered as sepsis related death by attending physician). In this study, infant sepsis was identified using hematological criteria and IMNCI (Integrated Management of Neonatal and Childhood Illness) clinical symptoms. Neonatal sepsis patients who met two hematological criteria—total leukocyte count (5000 or > 12,000 cells/m³, absolute neutrophil count (1500 or > 12,000)—and one or more IMNCI clinical features—fever (> 38 °C) or hypothermia (36 °C), fast breathing (> 60 breaths per minute), severe chest indrawing, poor feeding, movement only when stimulated, convulsion, lethargic, or unconsciousness—were (improved). Neonatal patients hospitalized to the NICU with early-onset or late-onset sepsis served as the cases and controls. All newborns with sepsis (LONS or EONS) admitted to the neonatal unit during the study period were included. The study excluded neonates who were transferred to other hospitals or referred before the outcomes were evaluated, as well as those whose records or charts were inadequate at the time of data collection.

Ethical Statement

The research topic was approved from the research committee of University of Riphah and the ethical reference number is REF-546.

Statistical Analysis

After ensuring the data were complete and consistent, we were coded and entered into SPSS version 25 for analysis. Using descriptive statistics, cases and controls were summarized. Using bivariate analysis, to examine the association between dependent and independent variables was determined. Variables associated with infant mortality due to sepsis in the bivariate model ($p = 0.25$) were included into a multivariate logistic regression model and analyzed using a backward stepwise procedure.

Results

Table 1 characteristics of the Neonatal participants and Mothers (N=73)

Variable	Neonatal Case (n=15)	Neonatal Controls (n= 58)	M(SD)
Neonatal Gender			
Boy	9 (60.0)	23 (39.6)	
Girl	6 (40.0)	35 (60.4)	
Mother Residence			
Flood affected rural area	11 (73.4)	34 (58.6)	
Urban	4 (26.6)	24 (41.4)	
Age of Neonatal			
More than 7days	7(46.6)	31(53.4)	4.32(3.89)
Less than 7days	8(53.4)	27(46.6)	
Neonatal Weight at birth			
More than 2.5kg	9(60.0)	31 (53.4)	
Less than 2.5 kg	6(40.0)	27(46.6)	
Mother Characteristics of Neonates			
Method of Delivery			
Vaginal Delivery	5 (33.3)	37 (63.7)	
Cesarean Section	10 (66.7)	21 (36.3)	
Received Antenatal care			
Yes	2 (13.4)	11 (18.9)	
No	13 (86.7)	47 (81.1)	
Birth Place			
Home	9 (60.0)	35 (60.4)	
Hospital	6 (40.0)	28 (48.6)	
Mother HIV status			
Negative	8 (53.3)	38 (65.5)	
Positive	4 (26.6)	9 (15.5)	
Don't Know	3 (20.1)	11 (19.0)	
Routine Checkup visit			
No visit	3 (20.0)	06 (10.4)	
1-3 visit	9 (60.0)	41 (70.7)	
More than 3visits	3(20.0)	11 (18.9)	

In the present investigation (table-1), data were separated into two clusters, with neonatal fatalities classified as cases and neonates who survived as controls. In the sample of cases (N = 15), there are 58 neonates in the control group. All data was collected from the Dera Ghazi Khan Neonates intensive care unit in south Punjab. The majority of hospitalized newborns were from the flood-affected rural areas. The majority of newborns was older than 7 days and weighed more than 2.5 kg at birth. Moreover, 54% of all mothers deliver vaginally, while 46% deliver via cesarean section. The majority of mothers (85%) said they did not receive prenatal care. Some women reported receiving a positive HIV diagnosis throughout their pregnancies.

Table 2 Death factors in Case and Control Neonatal (N=73)

Variables	Neonatal Case (n= 15)	Neonatal Controls (n=58)
Temperature at the axilla		
Normal	2 (13.4)	31 (53.4)
Fever	5 (33.4)	08 (13.8)
Hypothermia	8 (53.2)	19 (32.8)
Neonate rate of Respiratory and Distress		
Respiratory Distress Yes	9 (60.0)	13 (22.5)
Respiratory Distress No	6 (40.0)	45 (77.5)
Normal Breathing	6 (40.0)	37 (63.7)
Bradypnea	7 (46.6)	14 (24.1)
Tachypnea	2 (13.4)	7 (12.2)
Neonate Pulse rate at time of birth		
Normal pulse rate	8 (53.4)	43 (74.1)
Bradycardia	5 (33.4)	9 (15.5)
Tachycardia	2 (13.2)	6 (10.4)
Feeding		
Poor	9 (60.0)	19 (32.7)
Normal	6 (40.0)	39 (67.3)
APGAR Test score		
Poor	7(46.6)	17(29.3)
Normal	8 (53.4)	41 (70.7)
Jaundice at Birth		
Yes	4 (26.7)	13 (22.4)
No	11 (73.3)	45 (77.6)
Comorbidity		
Yes	7 (46.6)	47 (81.1)
No	8 (53.4)	11 (18.9)
Platelet's Normal count among neonates	7(46.6)	37 (63.7)
Neutrophil Normal level count among neonate	8(53.4)	45(77.6)
Blood glucose level among neonates	11(73.4)	47(81.1)

Table-2 depicts in this study, seven cases (46.6% of the total) and seventeen controls (29.3% of the total) of babies with first- and fifth-minute low Apgar scores were found. The majority of neonates (9 (60%) of cases and 19 (32.7%) of controls) had poor feeding among other clinical criteria. The majority of the controls (53.4%) appeared to have normal body temperature, whereas more than half of the neonates (85.3%) were hypothermic.

Table 3 Logistic Regression analysis to predict sepsis related factors of death among the neonates (N=73)

Predictors	Adjusted Odd Ratio	95% Confidence Interval	Sig-Value
Inadequate Feeding	2.11	0.52 7.24	0.000
Respiratory distress	1.84	1.43 4.73	0.06
Estimated gestational age shorter than 34 weeks	5.75	3.25 10.82	0.001
Convulsion	2.12	2.34 9.52	0.03

Logistic analysis (table-3) found that infants with a history of poor feeding had nearly twice the risk of sepsis-related death (AOR = 2.11; CI 0.52, 7.24). This study found that newborns with respiratory distress had a 1.8-fold increased risk of dying from sepsis (AOR = 1.84; CI 1.50, 4.73). The chances of sepsis-related death were two times higher in newborns with a history of convulsions (AOR = 2.12; CI (2.34, 9.52)). This study also revealed that preterm infants, those born before 34 weeks of gestation, were at higher risk for neonatal mortality owing to sepsis. Preterm

newborns (those born before 34 complete weeks of gestation) were 5 times more likely to experience neonatal death (AOR = 5.75; CI (3.25, 10.82)).

Discussion

In order to find out causes neonates to die from sepsis, this study looked at as many risk factors as possible. By using logistic regression analysis, it was found that convulsions, an estimated gestational age of less than 37 weeks (prematurity), poor feeding, a history of respiratory distress, and an estimated gestational age of less than 37 weeks are all risk factors for death in neonates with sepsis. According to this study, sepsis related death and respiratory distress have the association as there was a threefold increased risk of sepsis related death in neonates who were in respiratory distress. This conclusion is supported by earlier investigations conducted in Nigeria⁹ and Iraq¹⁰. This might be as a result of surfactant deficiency, which raises neonatal death in neonates with respiratory distress by preventing air sacs from collapsing.

A history of poor feeding was reported by 60% of participants in this study, quadrupling the risk of sepsis-related death. This finding is consistent with a prior study from Thailand¹¹ that discovered patients with clinical signs of inadequate feeding have an eight-fold higher risk of newborn death. A study from India¹² claims breastfeeding protects infants with septicemia. Poor calorie intake or inadequate infant feeding might result in hypoglycemia. By inhibiting gluconeogenesis and increasing glucose demands, endotoxemia and sepsis cause hypoglycemia. Breast milk contains vitamin A and antibodies that fight infections¹³. The risk of death may be higher for this particular group of infants. Compared to later-born neonates, prematurity (gestational age of fewer than 37 weeks) increases the risk of sepsis-related infant death by 4.6. Studies carried out in developing countries all support this result¹⁴. Due to humoral and cellular immunological deficiencies, premature newborns are susceptible to the effects of septicemia.

According to this study, newborns with a history of convulsions had a threefold increased risk of sepsis related Death compared to infants without such a history. This outcome is in line with earlier studies linking this factor to poor neonatal prognosis and death¹⁵. Neonatal convulsions worsen structural brain abnormalities such as intra cerebral, subarachnoid, and intra ventricular hemorrhage and infarctions, which affects the infant's hemodynamic and physiological stability. Potentially, acute newborn encephalopathy could lead to an increase in Death.

This study has limitations due to its retrospective review of test results and neonatal data. As a result, data collection was restricted to previously acquired information, meaning that some of the relevant variables under examination may be lacking data. In addition, this study lacks information on microorganisms, including culture results, drug resistance, and sensitivity patterns. In addition, because the study only included neonates who were admitted to a single hospital and did not include those who were transferred to other hospitals, the results may not be applicable to the total sepsis patient community.

Conclusion

In septicemic neonates admitted to NICUs, respiratory distress, poor feeding, premature birth, and convulsions were connected to sepsis-related neonatal mortality. Infants born prematurely must have the appropriate treatment supports, antibiotics, and close observation for indicators of sepsis. Identifying and treating respiratory distress, poor feeding, and convulsions in neonates as soon as possible reduces mortality caused by sepsis. In order to prevent hypoglycemia, newborns with sepsis and a history of malnutrition should have their blood sugar monitored often. NICUs should be supplied with the proper breathing equipment to help newborns requiring respiratory support, routine neonatal sepsis screening should be instituted, and primary care organizations should increase their support for maternal education.

References

1. Iroh Tam PY, Bendel CM. Diagnostics for neonatal sepsis: current approaches and future directions. *Pediatric Research*. 2017;82(4):574-583. doi:10.1038/pr.2017.134

2. Ahmed M, Yasrab M, Khushdil A, Qamar K, Ahmed Z. NEONATAL SEPSIS IN A TERTIARY CARE HOSPITAL: BACTERIOLOGICAL PROFILE AND ITS ANTIBIOTIC SENSITIVITY. *Pakistan Armed Forces Medical Journal (PAFMJ)*. 2018;68(6):1654-1658. Accessed October 12, 2022. <https://www.pafmj.org/index.php/PAFMJ/article/view/2566>
3. Vergnano S, Buttery J, Cailes B, et al. Neonatal infections: Case definition and guidelines for data collection, analysis, and presentation of immunisation safety data. *Vaccine*. 2016;34(49):6038-6046. doi:10.1016/j.vaccine.2016.03.046
4. Yadeta D, Semeredin N, Mekonnen GE. Prevalence and Predictors of Atrial Fibrillation and its Embolic Complications in Patients with Rheumatic Heart Disease at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. *Ethiopian Journal of Health Development*. 2019;33(1). doi:10.4314/ejhd.v33i1
5. Fleischmann C, Reichert F, Cassini A, et al. Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. *Archives of Disease in Childhood*. Published online January 22, 2021. doi:10.1136/archdischild-2020-320217
6. Getabelew A, Aman M, Fantaye E, Yeheyis T. Prevalence of Neonatal Sepsis and Associated Factors among Neonates in Neonatal Intensive Care Unit at Selected Governmental Hospitals in Shashemene Town, Oromia Regional State, Ethiopia, 2017. *International Journal of Pediatrics*. 2018;2018:1-7. doi:10.1155/2018/7801272
7. Malik FR, Amer K, Ullah M, Muhammad AS. Why our neonates are dying? Pattern and outcome of admissions to neonatal units of tertiary care hospitals in Peshawar from January, 2009 to December, 2011. *JPMA The Journal of the Pakistan Medical Association*. 2016;66(1):40-44. Accessed October 12, 2022. <https://pubmed.ncbi.nlm.nih.gov/26712179/>
8. Mirza Z. Pregnancy, before the flood. DAWN.COM. Published October 7, 2022. Accessed October 12, 2022. <https://www.dawn.com/news/1713900>
9. Arowosegbe AO, Ojo DA, Dedeke IO, Shittu OB, Akingbade OA. Neonatal sepsis in a Nigerian Tertiary Hospital: Clinical features, clinical outcome, aetiology and antibiotic susceptibility pattern. *Southern African Journal of Infectious Diseases*. 2017;32(4):127-131. doi:10.1080/23120053.2017.1335962
10. Atrushi AM. THE PROFILE OF NEONATAL SEPSIS IN DUHOK CITY AND PREDICTORS OF MORTALITY: A PROSPECTIVE CASE SERIES STUDY. *Duhok Medical Journal*. 2018;12(2):10-20. Accessed October 25, 2022. <https://dmj.uod.ac/index.php/dmj/article/view/53>
11. Tareen Z, Jirapradittha J, Sirivichayakul C, Chokejindachai W. Factors Associated with Mortality Outcomes in Neonatal Septicemia in Srinagarind Hospital, Thailand. *Neonatal and Pediatric Medicine*. 2017;03(02). doi:10.4172/2572-4983.1000131
12. Bandyopadhyay T, Kumar A, Saili A, Randhawa VS. Distribution, antimicrobial resistance and predictors of mortality in neonatal sepsis. *Journal of Neonatal-Perinatal Medicine*. 2018;11(2):145-153. doi:10.3233/npm-1765
13. Yeshaneh A, Tadele B, Dessalew B, et al. Incidence and predictors of mortality among neonates referred to comprehensive and specialized hospitals in Amhara regional state, North Ethiopia: a prospective follow-up study. *Italian Journal of Pediatrics*. 2021;47(1). doi:10.1186/s13052-021-01139-9
14. Liang L, Kotadia N, English L, et al. Predictors of Mortality in Neonates and Infants Hospitalized With Sepsis or Serious Infections in Developing Countries: A Systematic Review. *Frontiers in Pediatrics*. 2018;6. doi:10.3389/fped.2018.00277
15. Orsido TT, Asseffa NA, Berheto TM. Predictors of Neonatal mortality in Neonatal intensive care unit at referral Hospital in Southern Ethiopia: a retrospective cohort study. *BMC Pregnancy and Childbirth*. 2019;19(1). doi:10.1186/s12884-019-2227-5