

Original Research Article

Combating neonatal sepsis: insights and improved outcome interventions for neonatal intensive care unit

Muhammad Ans^{1,2}, Waqas A. Aziz^{2,3}, Ejaz Ahmed⁴, Maida Noor⁴, Rehan Rustam⁴,
Muhammad A. Ali⁵, Abiha Zainab⁴, Ahsan Zafar⁴, Sameen Abbas^{4*}

¹University College of Pharmacy, University of the Punjab, Lahore, Pakistan

²Department of Public Health, Health Services Academy, Islamabad, Pakistan

³Department of Humanities and Social Sciences, Bahria University, Islamabad, Pakistan

⁴Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan

⁵Faculty of Pharmacy, Baha-Ud-Din Zakariya University, Multan, Pakistan

Received: 18 March 2025

Revised: 15 April 2025

Accepted: 18 April 2025

*Correspondence:

Dr. Sameen Abbas,

E-mail: sameenabbas@bs.qau.edu.pk

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Neonatal sepsis (NS) is a severe systemic infection caused by bacteria, viruses, or fungi disrupting the immune systems of newborns. Based on the timing of symptom onset, it is classified into early-onset (EONS) and late-onset (LONS). This study aimed to investigate the incidence, risk factors, and clinical outcomes of NS in a neonatal intensive care unit (NICU).

Methods: A cross-sectional descriptive study was conducted from December 2022 to August 2023, involving 121 patients in the NICU and outpatient departments. Data was analyzed using statistical package for the social sciences (SPSS) version 24.0.

Results: The neonatal cohort had 62 (51.2%) males and 59 (48.8%) females, with 81 (66.9%) exhibiting EONS. Significantly higher antimicrobial usage ($p < 0.01$), especially penicillin ($p < 0.01$), was noted. MANOVA showed significant associations between sepsis and neonatal factors like gestational age, age, admission type, birth weight, birth asphyxia, and resuscitation at birth ($p < 0.01$). Maternal factors like age, occupation, education, residence, parity, and mode of delivery showed significant associations ($p < 0.0001$), along with place of delivery ($p = 0.007$), UTI ($p = 0.001$), intrapartum fever ($p = 0.006$), premature rupture of membranes ($p = 0.004$), labor duration ($p = 0.001$), bleeding disorders ($p = 0.006$), and diabetes ($p = 0.006$).

Conclusions: The study concluded that neonatal and maternal factors significantly contribute to the risk of NS. Appropriate and adequate antenatal screening for early diagnosis and treatment of maternal infection during pregnancy as well as identifying high-risk pregnancy for adequate perinatal management of neonates are recommended to prevent NS-related morbidity and mortality.

Keywords: Neonatal sepsis prevalence, Neonatal antimicrobial use pattern, Neonatal sepsis risk factors, Pakistan

INTRODUCTION

Neonatal sepsis (NS) is a systemic illness that disrupts the immune system of newborns (<28 days of age) caused by bacterial, viral, or fungal bloodstream infections. It continues to be a major cause of high morbidity and mortality rates in this vulnerable population, presenting

with systemic signs of infection, circulatory shock, and multiple organ failure.¹⁻⁴ Globally, NS affects 1 to 50 out of every 1,000 live births and contributes to 3 to 30 percent of infant and child fatalities annually.⁵

NS manifests through hemodynamic, post-inflammatory, and immunosuppressive alterations that significantly

impact mortality and morbidity rates. Clinical manifestations include fever or hypothermia, respiratory issues such as shortness of breath and cyanosis, feeding problems, abdominal distension, vomiting, diarrhea, reduced urine output, lethargy, and irritability.⁶ Despite its global prevalence, there is limited data on the incidence of NS in Pakistan, with reported rates ranging from 1.13 to 3.8 per 1,000 live births.⁷

Neonatal sepsis is classified into early-onset (EONS) and late-onset (LONS) based on the timing of symptom onset. EONS occurs within the first 72 hours of life and is typically vertically transmitted, whereas LONS appears after 72 hours and is often acquired horizontally from the environment.⁸ Group B streptococcus and *Escherichia coli* are common pathogens in EONS, while coagulase-negative Staphylococci predominate in LONS. These classifications aid in standardizing NS diagnosis, reporting, and management, facilitating the identification of risk factors, appropriate antimicrobial selection, and therapeutic outcome monitoring.⁹⁻¹¹

Managing NS poses a significant challenge for healthcare providers, as early detection and treatment can substantially reduce its risks and improve outcomes.¹² In Pakistan, a country with a high neonatal mortality rate, NS remains a pressing public health issue exacerbated by inadequate healthcare resources, poor access to quality maternal and neonatal care, and suboptimal infection control practices. Moreover, variations in antimicrobial prescribing for NS treatment may influence clinical outcomes, antimicrobial resistance patterns, and treatment efficacy. A comprehensive understanding of the risk factors, early diagnosis, and effective treatment strategies are essential to improve outcomes for neonates afflicted with sepsis. So, this study aims to address the knowledge gaps surrounding NS in Pakistan by conducting a multicenter investigation into its incidence, risk factors, antibiotic prescribing patterns, and clinical outcomes in neonatal intensive care units (NICUs).

METHODS

A cross-sectional descriptive study was conducted from December 2022 to August 2023 in the NICU and outpatient departments of Polyclinic Federal Hospital and PIMS Hospital Islamabad. The study included neonates aged <4 weeks with a gestational age >36 weeks, including premature and low birth weight neonates. Exclusion criteria were gestational age <36 weeks, hospital stays <2 days, incomplete patient data, and neonates who expired without receiving treatment upon arrival. A total of 121 responses were collected using a non-random convenience sampling method, with the sample size calculated through the Rao-soft sample size calculator for statistical significance. The Bioethics Committee of Health Services Academy, Islamabad, approved the research proposal, and informed consent was obtained from all participants, ensuring data confidentiality.

The data was collected using a structured questionnaire consisting of the following parts.

Socio-demographic variables

The data was collected in a structured proforma that included socio-demographic variables such as neonatal gender and age, mother's age, occupation, residential area, socioeconomic status, class, and education.

Clinical characteristics

This section was related to clinical details that are risk factors associated with the neonates, which included gestational age, birth weight, admission type, duration of hospital stay, respiratory disorders, meconium aspiration, birth asphyxia, resuscitation at birth, and white blood cells (WBCs) count. The maternal risk factors included parity, mode of delivery, place of delivery, the mother with urinary tract infection (UTI) during delivery, intrapartum fever, premature rupture of the brain, duration of labor, twin pregnancy, bleeding disorders, antenatal care, diabetic, any other comorbidity, and name of other comorbidities.

Incidence of neonatal sepsis

This section was related to the incidence of NS, including the onset of EONS and LONS.

Pattern of antimicrobial use and treatment outcomes

This section was related to the pattern of antimicrobial use and treatment outcomes. It comprises the antibiotic prescribed, the name of the antibiotic prescribed to the neonate, the number of antibiotics received by the neonate, antibiotics used for other treatments, antibiotics recommended according to standards, switching of medication, and the outcome of treatment.

Statistical analysis

Data analysis was performed using statistical package for the social sciences (SPSS) version 24.0. Descriptive statistics, including frequencies and percentages, summarized demographic and clinical variables. Multivariate analysis of variance (MANOVA) and multivariate regression analysis identified factors associated with sepsis, with a p value <0.05 considered significant.

RESULTS

A total of 120 patients participated in the study with a 100% response rate. Most neonates were male (62, 51.2%) and under 8 days old (85, 71.2%). Among mothers, 66.9% were aged 20-30 years, 71.1% were housewives, 55.4% lived in urban areas, 63.6% had middle income, and 54.5% had an intermediate level of education. Statistical analysis showed significant associations for neonates <8 days old

($p=0.0001$), mothers aged 20-30 years ($p<0.01$), housewives ($p<0.0001$), urban residency ($p=0.0107$), middle-income status ($p<0.01$), and intermediate education ($p=0.001$). Neonatal gender did not show significant results ($p=0.1585$). A detailed summary is presented in Table 1.

Table 1: Baseline clinical findings among respondents under study (n=121).

Variables	Frequency (%)	P value
Neonatal gender		
Male	62 (51.2)	0.1585
Female	59 (48.8)	
Neonatal age (in days)		
<8	85 (71.2)	0.0001*
8-15	22 (18.2)	
15-28	14 (11.6)	
Mother's age (in years)		
<20	31 (25.6)	<0.01*
20-30	81 (66.9)	
>30	9 (7.4)	
Mother's occupation		
Housewives	86 (71.1)	<0.01*
Working	35 (44.6)	
Mother's residential area		
Rural	54 (44.6)	0.0107*
Urban	67 (55.4)	
Mother's socioeconomic status		
Low income	19 (15.7)	<0.01*
Middle income	77 (63.6)	
High income	25 (20.7)	
Mother's education		
Illiterate	4 (3.3)	0.001*
Matric	24 (19.8)	
Intermediate	66 (54.5)	
Graduate	27 (22.3)	

* $P<0.05$ is significant

Neonatal risk factors

Among the 121 neonates, 2.5% were <36 weeks, 20.7% were 37 weeks, 70.2% were 37-40 weeks, and 6.6% were >40 weeks, with a significantly higher proportion ($p<0.01$) at 37-40 weeks. At birth, 19.8% weighed <1.5 kg, 60.3% weighed 1.5-2.5 kg, and 19.8% weighed >2.5 kg, with a significantly higher proportion ($p<0.01$) at 1.5-2.5 kg. The neonates included 51.2% males and 48.8% females, with most (71.2%) being <8 days old. A significantly higher proportion (82.6%, $p<0.01$) had ICU admissions. Hospital stays varied, with 27.3% staying <3 days, 65.3% staying 3-7 days, 6.6% staying 7-14 days, and 0.8% staying >14 days, with a significantly higher number ($p<0.01$) staying 3-7 days. Respiratory disorders were present in 72.7% ($p<0.01$). Meconium aspiration occurred in 88.4% ($p<0.0001$), and birth asphyxia was seen in 83.4% ($p<0.01$). Resuscitation at birth was required for 85.1% ($p<0.01$). WBC counts showed 4.1% <5000/mm³, 71.1%

5000-12000/mm³, and 24.8% >12000/mm³, with a significantly higher number ($p<0.01$) >12000/mm³ (Table 2).

Table 2: Neonatal risk factors (n=121).

Variables	Frequency (%)	P value
Admission type		
ICU	100 (82.6)	<0.01*
OPD/ward	21 (17.4)	
Duration of hospital stay		
<3	33 (27.3)	<0.01*
3-7	79 (65.3)	
7-14	8 (6.6)	
>14	1 (0.8)	
Respiratory disorders		
Yes	88 (72.7%)	<0.01*
No	33 (27.3%)	
Meconium aspiration		
Yes	107 (88.4%)	<0.01*
No	13 (10.7%)	
Birth asphyxia		
Yes	100 (83.4)	<0.01*
No	20 (16.6)	
Resuscitation at birth		
Yes	103 (85.1)	<0.01*
No	18 (14.9)	
WBC count		
<5000	5 (4.1)	<0.01*
5000-12000	86 (71.1)	
>12000	30 (24.8)	

* $P<0.05$ is significant

Maternal risk factors

Among the 121 study participants (as shown in Table 3), 37.2% of mothers had a parity score of 1, 52.9% had a score of 2, and 9.9% had a score of ≥ 3 , with a significantly higher proportion ($p=0.0232$) having a score of 2. Delivery mode showed 65.3% through C-section, 33.1% vaginal, and 1.7% instrumental, with a significantly higher proportion ($p<0.01$) via C-section.

Most mothers (94.2%) delivered in a hospital. Urinary tract infections were reported by 33.1%, while 66.9% had none ($p<0.01$). Intrapartum fever was present in 70.2% ($p<0.01$), and 66.9% had a premature rupture of membranes ($p<0.01$). Labor duration was <12 hours for 68.6% ($p<0.01$). Single pregnancies were 84.3% ($p<0.01$). Bleeding disorders affected 80.2% ($p<0.01$). Regular antenatal check-ups were reported by 68.6% ($p<0.01$). Diabetes was present in 9.9%, with 90.1% being non-diabetic ($p<0.01$).

Other comorbidities were seen in 55.4% of mothers ($p<0.01$). Hypertension, PVL, PVB, and combined PVL and PVB showed no significant differences.

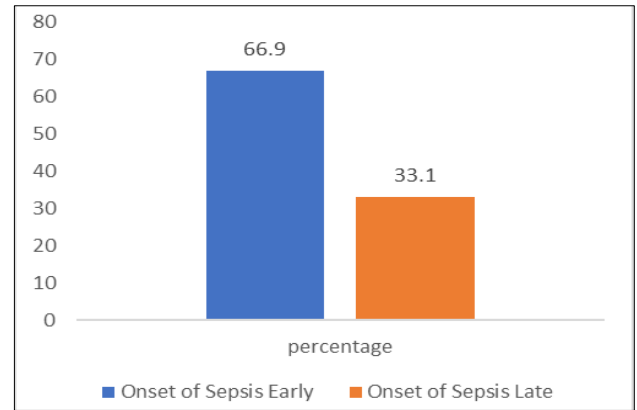
Table 3: Maternal risk factors (n=121).

Variables	Frequency (%)	P value
Parity		
1	45 (37.2)	0.0232*
2	64 (52.9)	
≥3	12 (9.9)	
Mode of delivery		
Instrumental	2 (1.7)	<0.01*
Vaginal	40 (33.1)	
C-section	79 (65.3)	
Place of delivery		
Home	7 (5.8)	<0.01*
Hospital	114 (94.2)	
Mother with UTI		
Yes	40 (33.1)	<0.01*
No	81 (66.9)	
Intrapartum fever		
Yes	85 (70.2)	<0.01*
No	36 (29.8)	
Premature rupture of membrane		
Yes	81 (66.9)	<0.01*
No	40 (33.1)	
Duration of labor		
<12	83 (68.6)	<0.01*
12-24	37 (30.6)	
>24	1 (0.8)	
Twin pregnancy		
Yes	19 (15.7)	<0.01*
No	102 (84.3)	
Bleeding disorders		
Yes	97 (80.2)	<0.01*
No	24 (19.8)	
Antenatal check-ups		
Regular	83 (68.6)	<0.01*
Irregular	38 (31.4)	
Diabetes		
Yes	12 (9.9)	<0.01*
No	109 (90.1)	
Any other comorbidity		
Yes	67 (55.4)	<0.01*
No	54 (44.6)	
Any other comorbidity		
Hypertension	7 (5.8)	0.1388
PVL	32 (26.4)	
PVB	18 (14.9)	
PVL and PVB	10 (8.3)	

*P<0.05 is significant

Incidence of neonatal sepsis

Among the study population, 81 (66.9%) NS patients had EONS, and 40 (33.1%) had LONS. Significantly (p<0.0001), more NS patients had EONS (Figure 1).


Figure 1: Incidence of NS (onset of sepsis).

Pattern of antimicrobial use and treatment outcomes

All respondents used antibiotics. The most commonly prescribed were penicillins (95%), followed by cephalosporins (91.6%), fluoroquinolones (83.3%), and glycopeptides (37.5%), with penicillins being significantly higher (p<0.01). Only 0.8% used one antibiotic, 23.1% used two, 48.8% used three, and 27.3% used more than three, with three antibiotics being significantly higher (p=0.005). Among the study population, 25.6% used antibiotics for other treatments, while 73.6% did not (p<0.0001). Additionally, 14.9% switched medications, whereas 85.1% did not (p<0.01). Most patients (80.2%) recovered, 14.9% were discharged, and 5% died, with recovery being significantly higher (p<0.01) (Table 4).

Multivariate analysis of variance for factors associated with NS

MANOVA results (Table 5) showed that neonatal risk factors significantly associated with NS were age, gestational age, birth weight, ICU admission, birth asphyxia, and resuscitation at birth (all p<0.0001). Respiratory disorders (p=0.108) and meconium aspiration (p=0.230) were insignificant. Among maternal risk factors, maternal age, occupation, residence, education, parity, mode of delivery, place of delivery (p=0.007), UTI (p=0.001), intrapartum fever (p=0.006), premature rupture of membranes (p=0.004), duration of labor (p=0.001), bleeding disorders (p=0.006), and diabetes (p=0.006) were significantly associated with NS, while twin pregnancy and antenatal check-ups were not.

Multivariate linear regression analysis for factors associated with NS

Multivariate linear regression analysis identified significant contributors to NS. Among neonatal risk factors, age (p<0.0001) and birth asphyxia (p=0.005) were significantly associated with NS, while gestational age, birth weight, ICU admission, respiratory disorders, meconium aspiration, and resuscitation at birth were not. Among maternal risk factors, age (p<0.0001), occupation

($p=0.006$), residence ($p=0.003$), parity ($p<0.0001$), mode of delivery ($p=0.004$), premature rupture of membranes ($p=0.001$), and diabetes ($p=0.002$) were significantly associated with NS. Maternal education, place of delivery,

UTI, intrapartum fever ($p=0.054$), duration of labor, twin pregnancy, bleeding disorders, and antenatal checkups were not significantly associated with NS. Details are presented in Table 6.

Table 4: Pattern of antimicrobial use and treatment outcomes (n=121).

Variables	Categories	Frequency (%)	P value
Penicillins	114	95	<0.01*
Cephalosporins	110	91.6	<0.01*
Fluoroquinolones	100	83.3	<0.01*
Glycopeptides	45	37.5	0.01*
Number of antibiotics prescribed	1	1 (0.8)	0.005*
	2	28 (23.1)	
	3	59 (48.8)	
	>3	33 (27.3)	
Antibiotics used for other treatments	Yes	31 (25.6)	<0.01*
	No	89 (73.6)	
Switching of medication	Yes	18 (14.9)	<0.01*
	No	103 (85.1)	
Clinical outcome	Recovered	97 (80.2)	<0.01*
	Discharged	18 (14.9)	
	Death	6 (5)	

* $P<0.05$ is significant

Table 5: Multivariate analysis of variance for factors associated with neonates and mothers.

Variables	MANOVA		
	R ²	Adjusted R ²	P value
Neonatal factors			
Neonatal age	0.678	0.632	<0.0001*
Gestational age	0.106	0.098	<0.0001*
Birth weight	0.115	0.107	<0.0001*
Admission Type	0.059	0.051	<0.0001*
Respiratory disorders	0.059	0.051	0.108
Meconium aspiration	0.013	0.004	0.230
Birth asphyxia	0.669	0.666	<0.0001*
Resuscitation at birth	0.188	0.181	<0.0001*
Maternal factors			
Maternal age	0.248	0.242	<0.0001*
Maternal occupation	0.181	0.173	<0.0001*
Maternal residence	0.584	0.581	<0.0001*
Mother's education	0.059	0.051	<0.0001*
Parity	0.360	0.354	<0.0001*
Mode of delivery	0.289	0.282	<0.0001*
Place of delivery	0.064	0.055	0.007*
UTI	0.089	0.081	0.001*
Intrapartum fever	0.066	0.058	0.006*
Premature rupture of membrane	0.072	0.063	0.004*
Duration of labor	0.095	0.087	0.001*
Twin pregnancy	0.019	0.010	0.145
Bleeding disorders	0.000	-0.009	0.006*
Antenatal check-ups	0.000	-0.009	0.950
Diabetes	0.004	-0.005	0.006*

* $P<0.05$ is significant

Table 6: Multiple regression for factors associated with NS.

Variables	Multiple regression (95% CI)			
	B	LL	UL	P value
Neonatal factors				
Neonatal age	-0.232	-0.153	-0.065	<0.0001*
Gestational age	0.004	-0.053	0.059	0.918
Birth weight	-0.067	-0.172	-0.050	0.275
Admission type	0.001	-0.067	0.063	0.954
Respiratory disorders	0.020	-0.064	0.104	0.638
Meconium aspiration	-0.018	-0.119	0.066	0.572
Birth asphyxia	-0.184	-0.291	-0.053	0.005*
Resuscitation at birth	-0.014	-0.089	0.063	0.731
Maternal factors				
Maternal age	-0.381	-0.362	-0.161	<0.0001*
Maternal occupation	0.193	0.057	0.328	0.006*
Maternal residence	0.156	0.051	0.239	0.003*
Mother's education	-0.003	-0.116	0.112	0.970
Parity	0.629	0.313	0.618	<0.0001*
Mode of delivery	0.224	-0.185	-0.037	0.004*
Place of delivery	0.049	-0.108	0.387	0.264
UTI	-0.014	-0.352	0.324	0.935
Intrapartum fever	-0.060	-0.142	0.001	0.05*
Premature rupture of membrane	-0.227	-0.354	-0.096	0.001*
Duration of labor	-0.129	-0.478	0.229	0.485
Twin pregnancy	-0.020	-0.104	0.0054	0.532
Bleeding disorders	-0.057	-0.278	0.024	0.098
Antenatal check-ups	0.013	-0.069	0.096	0.747
Diabetes	0.309	0.122	0.497	0.002*

*P<0.05 is significant

DISCUSSION

NS continues to be a substantial cause of both disease and death among neonates. The study aimed to determine the NS incidence together with risk factors, and clinical outcomes in the NICU. In this study, the incidence of EONS 66.9% was significantly higher than LONS. The data is consistent with studies done in Egypt and Ethiopia, which discovered that there was a greater incidence of EONS in NICUs, at 65%, 40.5%, and 31.8%, respectively.¹³⁻¹⁵ Studies showing a greater incidence of LONS than EONS were found to be more common in hospitals in Indonesia (26.6%), India (20.9%), and Wolaita Sodo Town (26.9%), respectively.¹⁶⁻¹⁸ Different sociodemographic features likely contribute to inequality, with people in advanced nations being more aware and knowledgeable. In Pakistan, lack of awareness and the cost of newborn care are primary issues. Additionally, varying diagnostic standards for EONS play a role; while advanced countries use culture-positive results, this study relied on clinical indications, potentially overestimating EONS. Other factors include a lack of standardized infection screening guidelines for asymptomatic pregnant women and substandard antenatal care, resulting in inadequate time for mothers to receive necessary antibiotic treatment before or during birth.

Neonatal age was significantly associated with NS. This outcome is consistent with studies conducted in Ethiopia and Ghana that showed neonatal age had a significant association with NS.^{13,19} Gestational age was significantly associated with NS. This outcome is comparable to the studies that revealed NS was significantly linked with the gestational age of neonates.^{13,20,21} Neonates with a birth weight of less than 2.5 kg were more likely to develop NS infection compared to normal babies. This finding is consistent with the study that showed neonates with a birth weight of <2.5 kg were 1.42 times more expected to get NS infection.²² Birth asphyxia was significantly associated with NS. This data is comparable with a study that showed an association between birth asphyxia and NS.¹³ According to certain reports, NS and birth asphyxia together can cause more serious clinical consequences in newborns. According to a study, neonates with birth asphyxia plus NS died at a greater rate than those with NS alone.²³ Furthermore, retrospective cohort research revealed that morbidity was higher and hospital admissions were longer in neonates with EONS and a history of birth asphyxia.²⁴

The present study showed that resuscitation at birth was associated with NS. The result of the current study is similar to a study regarding the association of resuscitation at birth with NS.¹⁹ There is evidence that NS risk factors

for patients with weakened immune systems, including hospitalized patients, newborns, and the elderly, include resuscitation of neonates.^{25,26} The newborn might be predisposed to a larger risk of developing NS due to poor practices and noncompliance with recommendations by healthcare professionals during resuscitation, and this might stay the same with the results of the current study.

Maternal age was associated with NS. This outcome is comparable with the study that showed maternal age of 15-20, as well as 21-30, has higher odds of obtaining NS than neonates of mothers who were greater than 31 years of age.²⁷ This finding is also consistent with the study carried out in Ghana, which showed maternal age as a significant factor.²⁶ A strong association was found among mothers who were full-time housewives and NS. This result was similar to the community cohort study conducted in Uganda in which most mothers were whole-time housewives and were significantly associated with NS.²⁸ The higher rate of NS among neonates could be due to most of the population using private or public healthcare facilities, which often have higher costs and fewer resources. Many mothers work full-time as housewives and are financially dependent on their husbands for transportation, medical expenses, and family care. This financial dependence may influence their decisions on where to give birth and affect their well-being during pregnancy, delivery, and postpartum, leading to higher NS rates among neonates whose mothers lacked financial support from their fathers.

Maternal higher urban residence was significantly associated with NS. This result is similar to the report that depicted that neonates who were from urban residences were two and a half times more likely to develop NS than neonates from rural residences.²⁸ This might be because most of the neonates from cities were born at health facilities, and they might get nosocomial infections. Another thing is that few of the neonates were living in urban slum areas where cleanliness and sanitation, maternal and neonate health facilities are very low. Maternal socio-economic status, that is, middle income, was significantly associated with NS. This outcome is not comparable with the study, which showed maternal social and economic factors associated with poor outcomes of NS comprised low-income level.²⁹ The income difference might be due to the influence of factors like regional economic disparities, varying levels of healthcare utilization, differences in healthcare infrastructure, access to prenatal care, and social support networks, all of which could impact the health outcomes of NS within different socioeconomic groups.

Parity was significantly associated with NS. The current project aligns with the study conducted in Ghana, which showed parity as a significant maternal risk factor in NS.¹⁹ This conclusion is also comparable with another study, which showed a significant link of parity with the occurrence of NS.²⁶ The maternal risk factor mode of delivery, that is, C-section, showed an association with

NS. This data is comparable with the study, which revealed a significant link between the mode of delivery and NS.¹⁹ Infants delivered by C-section often have longer hospital stays and delayed breastfeeding, missing out on colostrum's immunity-building properties and protection against harmful pathogens.³⁰ The current study's conclusions contradict those of Siakwa et al, who discovered that the mode of delivery is not significantly associated with NS.²⁶

The place of birth, which is more in hospitals in the current study, was found to be statistically significant with NS. This outcome is inconsistent with the study that showed neonates delivered at the hospitals were 3 times less likely to get NS delivered at hospitals.³¹ Hospital deliveries might have a higher NS risk due to hospital-acquired infections, extended stays, invasive procedures, immature immune systems, and antibiotic use, despite medical care benefits. The UTI risk factor for NS aligns with an Ethiopian study showing higher NS risk in neonates born to mothers with antenatal UTIs.³² Premature rupture of the membrane was associated with NS, consistent with other studies showing higher NS risk. Long labor duration also showed an NS association, aligning with an Ethiopian study indicating labor >12 hours increases NS risk, likely due to extended delivery periods in primiparous women.³³ Bleeding disorders were associated with NS, which is consistent with the study demonstrating a positive association.¹⁹ Diabetes among mothers increases the risk of NS. The result is similar to the finding that depicted that women with gestational diabetes demonstrate an enhanced risk of NS by inflammation as well as autophagy in the placenta.³³

However, it is possible that not all the crucial information was properly documented or was not readily available. Patient charts were not provided for certain serious cases, making data collecting impossible. Most patient charts lacked information on complications and previous medication treatments.

CONCLUSION

In this study, the incidence of EONS was higher in neonates, with maternal and neonatal factors strongly linked to the risk of developing NS. Significant neonatal risk factors included age, gestational age, birth weight, birth asphyxia, respiratory disorders, meconium aspiration, and admission type. Maternal risk factors such as age, occupation, residence, socioeconomic status, education, parity, mode and place of delivery, UTI during delivery, intrapartum fever, premature rupture of membranes, labor duration, bleeding disorders, and diabetes were also prevalent. Penicillins and cephalosporins were the most commonly prescribed antibiotics for NS patients. The study concluded that promoting maternal antenatal care, reducing prevalent risk factors, and adhering to BNF and WHO guidelines for empirical NS regimens, including sensitivity testing, is essential to lower the risk of NS.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sankar MJ, Natarajan CK, Das RR, Agarwal R, Chandrasekaran A, Paul VK. When do newborns die? A systematic review of timing of overall and cause-specific neonatal deaths in developing countries. *J Perinatol.* 2016;36(1):S1-S11.
2. 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;22:364.
3. Sands K, Spiller OB, Thomson K, Portal EA, Iregbu KC, Walsh TR. Early-onset neonatal sepsis in low- and middle-income countries: current challenges and future opportunities. *Infect Drug Resistance.* 2022;1:933-46.
4. Thomson K, Moffat M, Arisa O, Jesurasa A, Richmond C, Odeniyi A, et al. Socioeconomic inequalities and adverse pregnancy outcomes in the UK and Republic of Ireland: a systematic review and meta-analysis. *BMJ Open.* 2021;11(3):e042753.
5. McGovern M, Giannoni E, Kuester H, Turner MA, van Den Hoogen A, Bliss JM, et al. Challenges in developing a consensus definition of neonatal sepsis. *Pediatr Res.* 2020;88(1):14-26.
6. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. *The Lancet.* 2017;390(10104):1770-80.
7. Ahmed A, Zahid I, Ladiwala ZF, Sheikh R, Memon AS. Breast self-examination awareness and practices in young women in developing countries: A survey of female students in Karachi, Pakistan. *J Educ Health Promotion.* 2018;7(1):90.
8. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. *Clin Microbiol Rev.* 2014;27(1):21-47.
9. Popescu CR, Cavanagh MM, Tembo B, Chiume M, Lufesi N, Goldfarb DM, et al. Neonatal sepsis in low-income countries: epidemiology, diagnosis and prevention. *Exp Rev Anti-infective Ther.* 2020;18(5):443-52.
10. Eichberger J, Resch E, Resch B. Diagnosis of neonatal sepsis: the role of inflammatory markers. *Front Pediatr.* 2022;10:840288.
11. Ray D, Alpini G, Glaser S. Probiotic Bifidobacterium species: potential beneficial effects in diarrheal disorders. Focus on "Probiotic Bifidobacterium species stimulate human SLC26A3 gene function and expression in intestinal epithelial cells". *Am J Physiol Cell Physiol.* 2014;307(12):C1081-3.
12. Afsharpaiman S, Torkaman M, Saburi A, Farzaampur A, Amirsalari S, Kavehmanesh Z. Trends in incidence of neonatal sepsis and antibiotic susceptibility of causative agents in two neonatal intensive care units in Tehran, IR Iran. *J Clin Neonatol.* 2012;1(3):124-30.
13. 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. *Int J Pediatr.* 2018;2018(1):7801272.
14. Medhat H, Khashana A. Incidence of neonatal infection in South Sinai, Egypt. *Int J Infect.* 2017;4(1).
15. Serbesa ML, Iffa MT, Geleto M. Factors associated with malnutrition among pregnant women and lactating mothers in Mieso Health Center, Ethiopia. *Eur J Midwifery.* 2019;3.
16. Mersha AG, Abegaz TM, Seid MA. Maternal and perinatal outcomes of hypertensive disorders of pregnancy in Ethiopia: systematic review and meta-analysis. *BMC Pregnancy Childbirth.* 2019;19:1-2.
17. Salsabila K, Toha NMA, Rundjan L, Pattanittum P, Sirikarn P, Rohsiswatmo R, et al. Early-onset neonatal sepsis and antibiotic use in Indonesia: a descriptive, cross-sectional study. *BMC Public Health.* 2022;22(1):992.
18. Swarnkar K, Swarnkar M. A study of early onset neonatal sepsis with special reference to sepsis screening parameters in a tertiary care centre of rural India. *Int J Infect Dis.* 2012;10(1):1-8.
19. 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. *Sci World J.* 2019;2019:9369051.
20. Demisse AG, Alemu F, Gizaw MA, Tigabu Z. Patterns of admission and factors associated with neonatal mortality among neonates admitted to the neonatal intensive care unit of University of Gondar Hospital, Northwest Ethiopia. *Pediatr Health Med Ther.* 2017;12:57-64.
21. Woldu KL, Arya B, Bacha EA, Williams IA. Impact of neonatal versus nonneonatal total repair of tetralogy of Fallot on growth in the first year of life. *Ann Thoracic Surg.* 2014;98(4):1399-404.
22. Belachew A, Tewabe T, Dessie G. Neonatal mortality and its association with antenatal care visits among live births in Ethiopia: a systematic review and meta-analysis. *J Maternal-Fetal Neonat Med.* 2022;35(2):348-55.
23. Georges Pius KM, Aurore Albane E, Marie-Paul B, Komba D, Ngando VK, Eteme A. Neonatal sepsis: highlights and controversies. *J Pediatr Neonatal.* 2022;4(1):1-5.
24. Hsu JF, Chang YF, Cheng HJ, Yang C, Lin CY, Chu SM, et al. Machine Learning Approaches to Predict In-Hospital Mortality among Neonates with Clinically Suspected Sepsis in the Neonatal Intensive Care Unit. *J Pers Med.* 2021;11(8):695.
25. Leal YA, Álvarez-Nemegyei J, Velázquez JR, Rosado-Quiab U, Diego-Rodríguez N, Paz-Baeza E, et al. Risk factors and prognosis for neonatal sepsis in southeastern Mexico: analysis of a four-year

- historic cohort follow-up. *BMC Pregnancy Childbirth.* 2012;12:48.
26. Siakwa M, Kpikpitse D, Mupepi SC, Semuatu M. Neonatal sepsis in rural Ghana: A case control study of risk factors in a birth cohort. *Peer Reviewed Articles.* 2014;43.
27. Alemayehu M, Gebrehiwot TG, Medhanyie AA, Desta A, Alemu T, Abrha A, et al. Utilization and factors associated with antenatal, delivery and postnatal Care Services in Tigray Region, Ethiopia: a community-based cross-sectional study. *BMC Pregnancy Childbirth.* 2020;20(1):334.
28. Kayom VO, Mugalu J, Kakuru A, Kiguli S, Karamagi C. Burden and factors associated with clinical neonatal sepsis in urban Uganda: a community cohort study. *BMC Pediatr.* 2018;18:1-8.
29. Osman MO, Nour TY, Ibrahim AM, Aden MA, Nur AM, Roble AK, et al. Epidemiology of neonatal near miss in Ethiopia: A systematic review and meta-analysis. *Int J Afr Nurs Sci.* 2022;17:100422.
30. Jepkosgei K, Ongeso A, Omuga B. Perceived Demographic and Socio-Economic Factors Contributing to Poor Outcome of Neonatal Sepsis at Paediatric Unit Kenyatta National Hospital. *East Afr J Health Sci.* 2021;4(1):16-23.
31. Auger N, Soullane S, Luu TM, Lee GE, Wei SQ, Quach C. Association of cesarean delivery with childhood hospitalization for infections before 13 years of age. *J Pediatr.* 2021;231:178-84.
32. 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 Resistance.* 2020;3:3957-67.
33. Bayih WA, Tezera TG, Alemu AY, Belay DM, Hailemeskel HS, Ayalew MY. Prevalence and determinants of asphyxia neonatorum among live births at Debre Tabor General Hospital, North Central Ethiopia: a cross-sectional study. *Afr Health Sci.* 2021;21(1):385-96.

Cite this article as: Ans M, Aziz WA, Ahmed E, Noor M, Rustam R, Ali MA, et al. Combating neonatal sepsis: insights and improved outcome interventions for neonatal intensive care unit. *Int J Sci Rep* 2025;11(6):213-21.