RESEARCH ARTICLE

Early- and Late-onset neonatal sepsis: pathogens, maternal risk factors, and the predictive value of hematological biomarkers

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ABSTRACT

Introduction: Neonatal sepsis is a major cause of morbidity and mortality, especially in low- and middle-income countries (LMICs). Preterm neonates are at higher risk due to immune immaturity, comorbidities, and prolonged NICU hospitalization. Early recognition and treatment are crucial, but no ideal biomarker exists. Mean platelet volume (MPV) and red cell distribution width (RDW) have been suggested as potential markers. This study evaluates their significance.

Objectives: To determine the incidence of early- and late-onset sepsis (EOS, LOS), analyze causative pathogens, and assess biochemical parameters (RDW, MPV, platelet count [PLT], and C-reactive protein [CRP]). The study also examines maternal conditions influencing sepsis and neonatal outcomes. A retrospective analysis was conducted on 139 NICU patients at CCU Sarajevo from January 1, 2021, to December 31, 2023. Specifically, all microorganisms were isolated from blood cultures.

Results: Neonatal sepsis incidence was 12.5%, with 25.2% classified as EOS and 74.8% as LOS. EOS occurred mostly in full-term neonates (mean birth weight 2,044g), while LOS was more common in preterms (1,830g). Escherichia coli was the main EOS pathogen, while Acinetobacter baumannii caused 19.4% of LOS cases. Thrombophilia in mothers was significantly associated with EOS. CRP was the most predictive biomarker for EOS, while MPV, CRP, and PLT were significant in LOS. RDW was not relevant. Mortality was 22.3%, higher in LOS.

Conclusion: No single biomarker reliably predicts neonatal sepsis. A combination improves diagnostic accuracy, emphasizing the need for further research.

Keywords: neonatal sepsis, biomarkers, mean platelet volume, red cell distribution width

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Introduction

Neonatal sepsis is a serious global issue. On a worldwide level, approximately 2.6 million children die during the neonatal period [1]. Neonatal sepsis is one of major causes of neonatal mortality in low- and middle-income countries (LMICs). The mortality rate is higher in preterm infants than in full term neonates [2]. Higher mortality risk includes more illness or death early in life, in the first year of life and perhaps even years later. Under the Sustainable Development Goal 3 (SDG 3), which states that, 'to reduce neonatal mortality to at least 12 per 1000 live births by 2030', it is quite impossible for LMICs to achieve without a dramatic reduction in deaths arising from infections in neonates [3].

Neonatal sepsis is classified based on culture positivity, where it can be confirmed as culture-positive sepsis or clinically/culture-negative sepsis. Another widely accepted classification differentiates hospital-acquired (nosocomial) sepsis from community-acquired sepsis [4]. It primarily effects preterm neonates especially with low birth weight. One of the important causes is an immature immune system, which consequently increases the risk of developing nosocomial infections [5]. Other risk factors for neonatal sepsis are low birth weight, prematurity, premature rupture of membranes (PROM), complications resulting in perinatal asphyxia, prolonged NICU stay, poor sanitation conditions, low socioeconomic status, malnutrition and overcrowding. The conditions, compounded by the rising figures of multidrug resistant agents, particularly Gram-negative bacteria, have made the situation grim from management of antimicrobial standpoint as well as neonatal mortality and morbidity [6].

The most commonly used classification is an early- (EOS) and late onset sepsis (LOS). EOS refers to sepsis in neonates at or before 72 hours of life (some use 7 days), and LOS is defined as sepsis occurring at or after 72 hours of life (2) EOS is caused by micro-organisms including Group B Streptococcus, Klebsiella, Listeria monocytogenes, atypical Haemophilus influenzae, and Escherichia

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coli [7]. Late-onset sepsis (LOS) is transmitted horizontally postpartum, from the ambient environment to the infant during or after hospitalization [8]. The causative agents can be the same as those in EOS, but infections caused by hospital-acquired pathogens are more common: Klebsiella, Acinetobacter baumannii, Stenotrophomonas maltophilia, etc. Additionally, infections with pathogens affecting the infant population, such as Haemophilus influenzae, Streptococcus pneumoniae, and Neisseria meningitidis, are also frequent. Conditions that mimic sepsis-like symptoms are often caused by viral agents, such as Herpes simplex virus (HSV), Cytomegalovirus (CMV), or enteroviruses [9]. Neonatal sepsis varies in signs and symptoms ranging from nonspecific or vague symptoms to hemodynamic collapse. Early symptoms may appear as feeding intolerance, irritability or lethargy. In many cases, neonatal sepsis leads to the development of respiratory distress, characterized by grunting, tachypnea, apnea, and cyanosis. Neonates also become temperature unstable, presenting with either hypothermia or hyperthermia. Circulatory signs include tachycardia, hypotension with poor perfusion, and even shock. The most common central nervous system symptoms are seizures, bulging fontanelle, irritability, and inconsolable crying [8,9].

Although a blood culture is the gold standard for diagnosis, because of the time it takes to obtain it, it is important to find other markers. Sometimes, sepsis is diagnosed based on laboratory findings, which shows hypo- or hyperglycemia, hyperbilirubinemia or acidosis [7]. Complete blood count (CBC) with differential and C-reactive protein (CRP) are critically important in a serially obtained laboratory test. Thrombocytopenia in sepsis has been emphasized as one of the predictive risk factors for sepsis related mortality in neonates who have very low birth weight (VLBW) and studies have stressed its significance [10]. Elevated levels of MPV may indicate ongoing inflammation or immune activation that is part of the immune response by releasing large amounts of cytokines and inflammatory mediators. Studies also show that red cell distribution width (RDW) varies significantly in pathological conditions associated with inflammation and infection [11]. Diagnostic confirmation or evaluation of the treatment efficacy can also be done by using some other inflammatory biomarkers like, haptoglobin, procalcitonin, and cytokines. In order to obtain accurate diagnosis, it is essential to find reliable an inexpensive test, for their use in LMICs where the availability of expensive assays is limited.

The objectives of our study were to estimate the incidence of early and late neonatal sepsis, identify the causative pathogens, examine the effect of pathological conditions of mother on sepsis development, analyze biochemical parameters to assess their predictive value, and evaluate patients' outcomes.

Methods

Study Area

This study was conducted at the Neonatal Intensive Care Unit (NICU) of the Pediatric Clinic, Clinical Center University of Sarajevo (CCU Sarajevo).

Study Design and Sampling Procedure

A retrospective, descriptive analysis of medical records was performed on newborns hospitalized in the NICU from January 1, 2021, to December 31, 2023. A total of 139 neonates diagnosed with sepsis were included. Inclusion criteria were neonatal hospitalization in the NICU with a confirmed diagnosis of sepsis. Patients were categorized into early-onset sepsis (EOS) and late-onset sepsis (LOS) groups. Those without sepsis were excluded. Specifically, all microorganisms were isolated from blood cultures.

Measures

Maternal risk factors analyzed included hypertension, diabetes mellitus, thrombophilia, placental abruption, anemia, COVID-19 infection, endometriosis, Hashimoto's thyroiditis, HELLP syndrome, hydronephrosis, colpitis, IVF pregnancy, and urinary tract infections. Data collected included gestational age, sex, birth weight, type of sepsis, laboratory parameters (white blood cell count, platelet count, CRP, RDW, and MPV), blood culture results, and patient outcomes.

Data Collection

Medical records of eligible neonates were reviewed, and relevant clinical and laboratory data were extracted. Ethical approval for this study was obtained from the Ethical Committee of CCU Sarajevo.

Statistical Analysis

Data were analyzed using R 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria) and RStudio 2024.04.1 (Posit Software, PBC, Boston, Massachusetts, USA). Numerical variables are presented as means ± standard deviations or medians with interquartile ranges (Q1–Q3). The Shapiro-Wilk test, QQ-plots, and histograms assessed normality. The t-test or Wilcoxon rank sum test was used for comparing quantitative variables, while Pearson's χ^2 test or Fisher's exact test was applied for categorical variables. Diagnostic performance was evaluated using the area under the ROC curve (AUC). A p-value of <0.05 was considered statistically significant.

Ethical statement

The University of Sarajevo-Faculty of Medicine committee approved this research (Ref. No. 01-4-TK-3862/24), according to the Declaration of Helsinki.

Results

Socio-Demographic Characteristics

During the study period (2021-2023), a total of 1,112 newborns were hospitalized, of which 139 (12.5%) were diagnosed with neonatal sepsis. The distribution of sepsis cases varied over the years, with the highest occurrence in 2021 (54 cases), followed by 2023 (45 cases), and 2022 (40 cases). Among the sepsis cases, 25.2% were classified as early-onset sepsis (EOS), and 74.8% as late-onset sepsis (LOS). Female neonates had a higher distribution of sepsis cases (53.2%) compared to males (46.8%). The average birth weight was 2,044 grams (SD = 1,017 grams), with an average in the EOS group of 2,676 grams and in the LOS group of 1,830 grams (p<0.001). There was a significant difference in birth weight between EOS and LOS groups, with a higher number of low-birth-weight neonates in the LOS group. EOS neonates had a significantly longer gestation period (36.2 ± 4.3 weeks) compared to LOS neonates (32.1 ± 4.8 weeks) (p<0.001) (Table 1).

Risk Factors

Maternal conditions that were analyzed included hypertension (7.9%), diabetes mellitus (5.8%), and infections (9.4%). There were 5.0% of pregnancies resulting from in-vitro fertilization, and 4.3% of mothers had COVID-19. Thrombophilia was observed significantly more in EOS cases (11.4%) compared to LOS (1%) (p=0.014) (Table 2).

Table 1. Demographic characteristics of the patients

Variable	Overall (N=139)	Group		p-value
		EOS (N=35)	LOS (N=104)	
Birth weight (g)				<0.001[1]
Mean (±SD)	2.044 (±1.017)	2.676 (±985)	1.830 (±939)	
Median [Q1–Q3]	1.890 [1.156–2.888]	2.800 [1.955–3.455]	1.610 [1.080–2.220]	
Range (Min – Max)	540–4.240	540–4.160	600–4.240	
Unknown	1	0	1	
Birth weight caterories n (%)				<0.001[2]
ELBW (<1.000g)	22 (15.9%)	2 (5.7%)	20 (19.4%)	
VLBW (<1.500g)	32 (23.2%)	3 (8.6%)	29 (28.2%)	
LBW (<2.500g)	40 (29.0%)	9 (25.7%)	31 (30.1%)	
NBW (2.500-4.000g)	38 (27.5%)	18 (51.4%)	20 (19.4%)	
HBW (≥4.000g)	6 (4.3%)	3 (8.6%)	3 (2.9%)	
Unknown	1	0	1	
Gestation weeks				<0.001[1]
Mean (±SD)	33.1 (±5.0)	36.2 (±4.3)	32.1 (±4.8)	
Median [Q1–Q3]	33.0 [29.0–38.0]	37.0 [34.5–40.0]	31.5 [28.0–36.0]	
Range (Min – Max)	24.0–41.0	24.0–41.0	25.0–41.0	
Delivery mode n (%)				0.3[3]
C-section	78 (57.8%)	17 (50.0%)	61 (60.4%)	
Vaginal	57 (42.2%)	17 (50.0%)	40 (39.6%)	
Unknown	4	1	3	

[1]Welch T-test
[2]Fisher test
[3]Pearson χ^2 test

Table 2. Mother's diseases

Mother's diseases	Overall (N=139)	Group		p-value
		EOS (N=35)[1]	LOS (N=104)[1]	
Placenal abruption	4 (2,9%)	2 (5,7%)	2 (1,9%)	0,3[2]
Anemia	1 (0,7%)	1 (2,9%)	0 (0,0%)	0,3[2]
Anhydramnion	3 (2,2%)	0 (0,0%)	3 (2,9%)	0,6[2]
Coeliakia	1 (0,7%)	1 (2,9%)	0 (0,0%)	0,3[2]
COVID-19	6 (4,3%)	2 (5,7%)	4 (3,8%)	0,6[2]
Diabetes mellitus	8 (5,8%)	2 (5,7%)	6 (5,8%)	>0,9[2]
E. coli (vaginal smear)	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
Eclampsia	1 (0,7%)	1 (2,9%)	0 (0,0%)	0,3[2]
Endometriosis	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
Hashimoto tireoiditis	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
HELLP	2 (1,4%)	0 (0,0%)	2 (1,9%)	>0,9[2]
Hydronephrosis	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
Hypertension	11 (7,9%)	2 (5,7%)	9 (8,7%)	0,7[2]
Hyperthyreosis	1 (0,7%)	1 (2,9%)	0 (0,0%)	0,3[2]
Hypothyreosis	5 (3,6%)	0 (0,0%)	5 (4,8%)	0,3[2]
Infection	13 (9,4%)	1 (2,9%)	12 (11,5%)	0,2[2]

Mother's diseases	Overall (N=139)	Group		p-value
		EOS (N=35)[1]	LOS (N=104)[1]	
IVF	7 (5,0%)	2 (5,7%)	5 (4,8%)	>0,9[2]
Colpitis	1 (0,7%)	1 (2,9%)	0 (0,0%)	0,3[2]
Oligohydramnion	5 (3,6%)	0 (0,0%)	5 (4,8%)	0,3[2]
Placenta previa	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
Polyhidriamnion	3 (2,2%)	0 (0,0%)	3 (2,9%)	0,6[2]
Preeclampsia	4 (2,9%)	0 (0,0%)	4 (3,8%)	0,6[2]
Pulmonary thromboembolism	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
RVP	3 (2,2%)	1 (2,9%)	2 (1,9%)	>0,9[2]
Takayashi arteritis	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
Trombophyllia	5 (3,6%)	4 (11,4%)	1 (1,0%)	0,014[2]
Urinary infection	2 (1,4%)	0 (0,0%)	2 (1,9%)	>0,9[2]
Uterus bicornis	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]
Variccela in the first trimester	1 (0,7%)	0 (0,0%)	1 (1,0%)	>0,9[2]

[1]n (%)
[2]Fisher test

Causative Agents

The main pathogens in EOS included Escherichia coli, Klebsiella pneumoniae, and Enterobacter cloacae. Acinetobacter baumannii was the predominant pathogen in LOS, accounting for 19.4% of cases. Escherichia coli occurred more frequently in the EOS group (14.3%) than in the LOS group (3.8%) (p=0.045). Other pathogens, such as Candida spp. and Streptococcus agalactiae, were found exclusively in the LOS group (Figure 1).

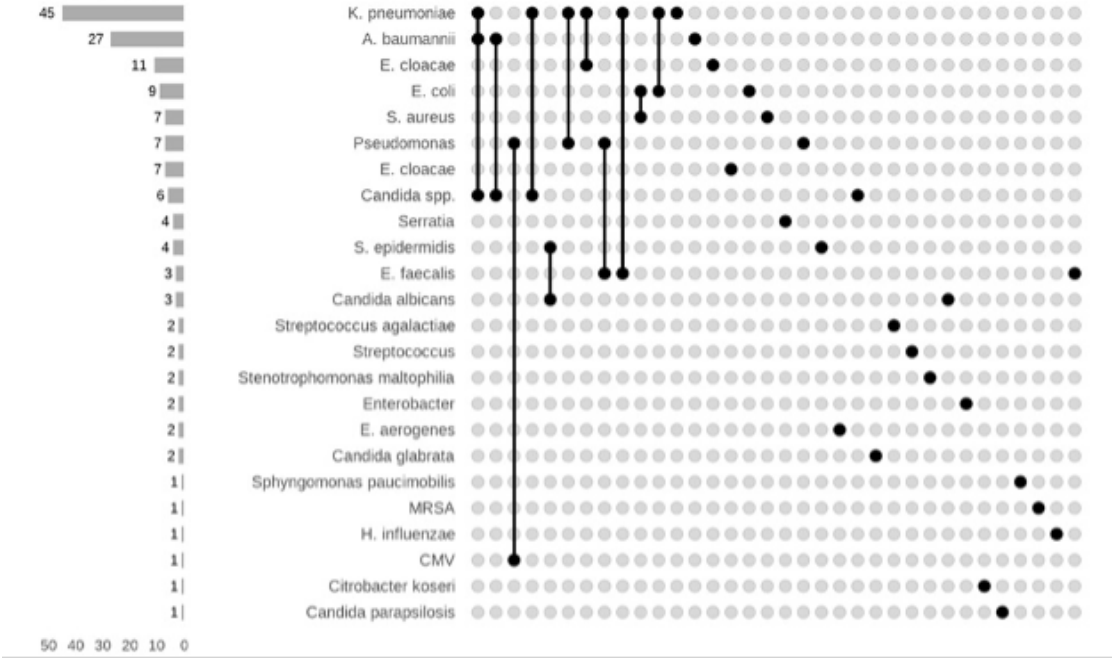

Figure 1: Causative agents of neonatal sepsis

Diagnostic Parameters

For EOS, C-reactive protein (CRP) was the most significant predictive factor for sepsis (OR=1.06, p<0.001). Leukocyte count was negatively associated with EOS (OR=0.93, p<0.056). MPV, RDW, and platelet count showed no significant associations. For LOS, significant changes were recorded in CRP, mean platelet volume (MPV), and platelet count (PLT). MPV increased significantly (p<0.001), and CRP rose from 8.7 ± 12.0 mg/L to 72.9 ± 66.5 mg/L (p<0.001), while platelet count decreased significantly from 247.0 ± 105.9 x10^9/L to 167.9 ± 136.9 x10^9/L (p<0.001) (Figure 2-3).

Outcomes

A total of 31 (22.3%) fatal outcomes were recorded, with 6 cases of EOS and 25 of LOS. This difference was not statistically significant (p=0.4)

Discussion

Sepsis, one of the leading causes of neonatal morbidity and mortality, accounts for one-third of neonatal deaths globally [12]. However, the incidence of neonatal sepsis and mortality are unequally distributed. In high income countries (HIC), neonatal sepsis accounts from 1 to 5 cases per 1,000 live births but is reported to be 3 or 20 times higher

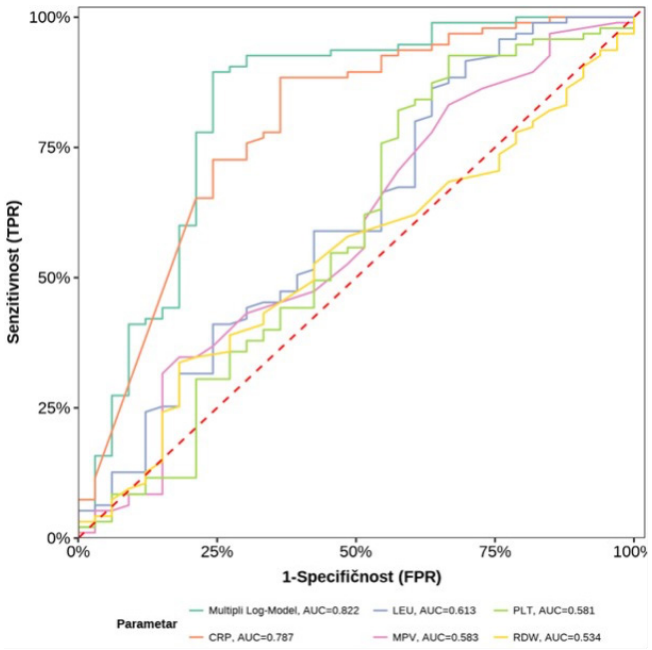

Figure 2: ROC curve for diagnostic parameters in EOS

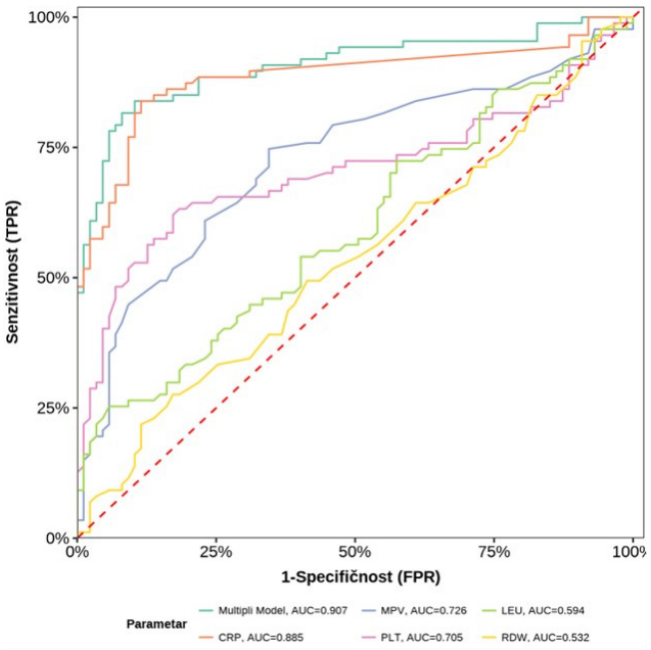

Figure 3: ROC curve for diagnostic parameters in LOS

in low- and middle-income countries (LMIC) [13].

During the study period, we found 12.5% patients with confirmed neonatal sepsis. In a cross-sectional study by Khadka et al [14], a high rate of neonatal sepsis was reported: of 171 participants, 18.7% had confirmed sepsis by blood culture. There are studies of very high sepsis prevalence up to 59% as reported by authors from Ghana [15]. Our study had encompassed three years, with the highest number of cases recorded in 2021. We assume the association with the COVID-19 pandemic and the reduced ability to prevent and screen pregnancies and expectant mothers. Besides, the ratio of early and late sepsis was significantly different over the years (χ^2=8.76; p=0.013), with the number of late neonatal sepsis cases being significantly higher in 2023 (p<0.001) and 2022(p=0.002) compared to 2021. Study from Saudi [16] reports EOS during 2019 in 6/49 (12.2%) while in 2020 22/62 (35.5%), and LOS during 2019 in 43/49 (87.7%) and in 2020 40/62 (64.5%).

The average birth weight in our study was 2,044 grams, with a standard deviation of 1,017 grams. The median birth weight was 1,890 grams, with an interquartile range from 1,156 to 2,888 grams. The lowest recorded birth weight was 540 grams, and the highest 4,240 grams. The average birth weight in the group of neonates with early sepsis was 2,676 grams, while in the group with late sepsis, it was 1,830 grams. This difference was statistically significant (p<0.001). In examining differences in the structure between groups based on the category of neonatal birth weight, a statistically significant difference was recorded (p<0.001), with a significantly higher number of low-birth-weight neonates in the group with late sepsis compared to the early sepsis group. In the evaluation of differences in the average duration of pregnancy (gestational weeks), neonates with early neonatal sepsis had a significantly longer gestation period (36.2 ± 4.3 weeks) compared to neonates with late sepsis, where the duration of pregnancy was 32.1 ± 4.8 weeks (p<0.001). In multicentric USA study [17] most infants with E coli were preterm (68 of 86 [79.1%]) with median GA of 28 (IQR, 25-33) weeks and median birth weight of 1230 (IQR, 800-2090) g. Most GBS infections were in term infants (54 of 71 [76.1%]) with median GA of 39 (IQR, 37-40) weeks and birth weight of 3199 (IQR, 2550-3440) g.

There was no difference in EOS and LOS according to mode of delivery. The maternal histories showed heterogeneous pathology; however, the differences between groups were not significant at the univariate analysis level, except for thrombophilia which was more commonly seen in EOS (p=0.014). The most frequent maternal morbidities were infection (9.4%), hypertension (7.9%), and diabetes mellitus (5.8%). Our results are consistent with studies by Rud KE et al. (14). In the study by Akalu TY et al. [18], the proportion of women with pregnancy-induced hypertension showed that 19.5% of neonates had sepsis compared to the control group, where there were 10.4%. In our study six mothers had COVID-19 infection prior to birth. As noted by Cavoretto P et al. [19] COVID infection impacts severe neonatal morbidity index.

In our study Klebsiella pneumoniae is the most common pathogen overall (32.4%)without significancy, with a slightly higher frequency in the LOS group, but without significant difference. Others report E. coli and Streptococcus agalactiae as the most common neonatal sepsis pathogens [1]. Gram-negative bacilli, including the Klebsiella,

Pseudomonas, and Escherichia coli, dominate in the digestive system of preterm infants and are capable of migrating from the intestines to cause sepsis [20]. The translocation of bacteria from the intestines of neonates is partly assisted by selective deficiencies in the defensive mechanisms of the intestinal barrier, including reduced production of protective factors like mucus, antimicrobial peptides, and IgA. As shown by our study, the frequency of Acinetobacter baumannii in general was 19.4%, significantly more common in LOS (p=0.004). Escherichia coli was more common in EOS patients p=0.045. Serratia was also important in EOS (p=0.049). According to the study by Khadka P et al. [21] the most common causes of sepsis were Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli, GPB, CoNS and Staphylococcus aureus.

Respecting the blood culture as a gold standard for confirmation of neonatal sepsis, researchers continuously seek for a fast, cheap, and reliable biomarker. Numerous are known so far including, acute-phase reactants, hematological indices, and inflammatory cytokines. The most commonly used is C reactive protein (CRP) [22], But, in the face of an inflammatory response, CRP is delayed in hepatic synthesis and the CRP levels actually rose in response to a number of noninfectious stimuli including meconium aspiration, fetal distress, and maternal fever in delivery [22]. Regarding this, it is found that CRP has low sensitively and a high rate of false positive results in neonatal sepsis diagnosis. In our study CRP levels were significantly elevated in early sepsis with mean (± SD) value of 40 (± 48) mg /L. In EOS it had significance of p<0.001 and odds ratio 1.06. Aids in diagnosing neonatal sepsis include the absolute neutrophil count (ANC), white blood cell count (WBC), neutrophil-to-lymphocyte ratio (NLR) and immature-to-total neutrophil ratio (IT ratio). In this study, the value of leukocytes was negatively associated with early sepsis, with a statistical significance of p<0.056. In sepsis, it is common to have decreased central production of platelets and increased peripheral consumption. A striking platelet count reduction from previous value of 247.0 ± 105.9 x10^9/L to 167.9 ± 136.9 x10^9/L during LOS was also showed in our study (p<0.001). Thrombocytopenia is often present in sepsis along with dysregulated bodily responses, and thrombocytopenia outcome (i.e. resulting in death) is related to thrombocytopenia persistence with platelet count normal or lower than the reference limit [23]. Early platelet drop detection and assessment is important, therefore for prompt and adequate intervention in early sepsis. We noticed significant changes in the mean platelet volume (MPV) and platelet count (PLT) in LOS. MPV significantly increased (p<0.001) from 8.6 ± 1.3 fL at birth to 10.0 ± 2.2 fL during sepsis. Platelet count significantly decreased from 247.0 ± 105.9 x10^9/L to 167.9 ± 136.9 x10^9/L (p<0.001). Platelet indices are already known to be predictive and prognostic biomarkers in neonatal sepsis [24]. In neonates born at <32 weeks of gestation, an MPV ≥10.2 fL has been found to correlate with mortality by Go et al. [25] MPV measured on day 3 can be used as a surrogate marker for predicting effects of early sepsis, including mortality, in preterm infants: Hebatallah et al. [26]. Sepsis is known to cause heterogeneous changes in erythrocyte lowering of red cell distribution width (RDW), yet its clinical and experimental merit as a diagnostic is not resolved [27]. The diagnostic application of RDW in sepsis was studied by Basu S. et al. In the study population, RDW was higher in cases confirmed sepsis with the median IQRs of 18, (16.9 – 20) and p values of <0.001. Consistent with Hu et al. [28], who reported neonatal sepsis diagnostic threshold of 18.9–19.9%, this finding is also in agreement. We found that mean RDW values of (17.5 ± 1.6%) at birth and (17.7 ± 1.7%) at the time of sepsis did not significantly change (p = 0.151). There are also authors that conclude that RDW is not a good diagnostic value of sepsis due to only modest value in predicting positive blood culture in patients with suspected sepsis and more sensitive in predicting mortality in neonatal sepsis [29]. Analyzing the ROC curves, we conclude that there is no single reliable biochemical parameter. Only in combination they provide sensitivity and specificity greater than 80%.

A total mortality rate of 22.3 % was recorded and late sepsis experience was associated with slightly higher mortality. In Milton R et al. [30] study of 30,557 neonates, mortality due to sepsis was 0.83 (0.37 – 2.00) per 1,000 live births.

Several limitations of this study are worth noting: its retrospective data collection method; relatively small sample size; a short follow-up period for neonates with sepsis and singe center study. The basis of the conclusions would be strengthened by multicenter, prospective follow up studies with longer follow up periods.

Conclusion

During the study period neonatal sepsis was confirmed in 12.5% patients. Overall, a 22.3% mortality rate was observed, with higher mortality in the LOS group. Statistically significant difference was observed in the ratio of LOS to EOS (favoring LOS) over the years (χ^2=8.76; p=0.013). In the EOS group, the predominant cause was Escherichia coli, and in the LOS group, Acinetobacter baumannii was the most common causative agent. In cases of EOS, the most significant predictive factor was the CRP value while significant changes in the LOS group were observed in CRP, MPV and PLT. We found no significance of RDW in neonatal sepsis. In general, there is no single reliable biochemical parameter. Only in combination they provide satisfactory sensitivity and specificity. Further research is needed to identify the markers for early diagnosis of neonatal sepsis.

Authors' contributions

ES (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Validation; Visualization; Writing – original draft;

Writing – review & editing)
ST (Conceptualization; Formal analysis; Investigation; Methodology; Supervision; Writing – original draft; Writing – review & editing)

Conflict of interest
No conflict.

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References
1. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet. 2017;390(10104):1770–80. doi: 10.1016/S0140-6736(17)31002-4
2. Karnati S, Kollikonda S, Abu-Shaweesh J. Late preterm infants – Changing trends and continuing challenges. Int J Pediatr Adolesc Med. 2020 Mar;7(1):36–44
3. WHO Sustainable Development Goals—the goals within a goal: health targets for SDG 3.
4. https://www.who.int/sdg/targets/en/ [Ref list]
5. Edwards MS, Baker CJ. Bacterial infections in the neonate. In: Long SS, Pickering LK, Prober CG,
6. editors. Principles and Practice of Pediatric Infectious Disease. 4th ed. Philadephia: Elsevier
7. Saunders; 2012. p. 538–44
8. Hayes R, Hartnett J, Semova G, Murray C, Murphy K, Carroll L, Plapp H, Hession L, O'Toole J,
9. McCollum D, Roche E, Jenkins E, Mockler D, Hurley T, McGovern M, Allen J, Meehan J, Plötz FB, Strunk T, de Boode WP, Polin R, Wynn JL, Degtyareva M, Küster H, Janota J, Giannoni E,Schlapbach LJ, Keij FM, Reiss IKM, Bliss J, Koenig JM, Turner MA, Gale C, Molloy EJ; Infection,Inflammation, Immunology and Immunisation (I4) section of the European Society for PaediatricResearch (ESPR). Neonatal sepsis definitions from randomised clinical trials. Pediatr Res. 2023Apr;93(5):1141-1148. doi: 10.1038/s41390-021-01749-3. Epub 2021 Nov 6. PMID: 34743180;PMCID: PMC10132965
10. Murthy S, Godinho MA, Guddattu V, Lewis LES, Sreekumaran Nair N. Risk factors of neonatal sepsis in India: a systematic review and meta-analysis. PLoS One. 2019;14:1–26.
11. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. Clin Microbiol Rev. 2014 Jan;27(1):21-47. doi: 10.1128/CMR.00031-13. PMID: 24396135; PMCID:PMC3910904
12. Fleischmann C., Reichert F., Cassini A., et al. Global incidence and mortality of neonatal sepsis: a
13. systematic review and meta-analysis. Archives of Disease in Childhood . 2021;106(8):745–752.
14. doi: 10.1136/archdischild-2020-320217
15. Ostrander B, Bale JF. Congenital and perinatal infections. Handb Clin Neurol. 2019;162:133-153.
16. doi: 10.1016/B978-0-444-64029-1.00006-0. PMID: 31324308.
17. Levit O, Bhandari V, Li FY, Shabanova V, Gallagher PG, Bizzarro MJ. Clinical and laboratory
18. factors that predict death in very low birth weight infants presenting with late-onset sepsis. Pediatr Infect Dis J. 2014;33(2):143–6. Doi
19. Wynn JL. Defining neonatal sepsis. Curr Opin Pediatr. 2016 Apr;28(2):135-40
20. Fleischmann C., Reichert F., Cassini A., et al. Global incidence and mortality of neonatal sepsis: a
21. systematic review and meta-analysis. Archives of Disease in Childhood . 2021;106(8):745–752.
22. doi: 10.1136/archdischild-2020-320217
23. Zaidi A. K. M., Huskins W. C., Thaver D., Bhutta Z. A., Abbas Z., Goldmann D. A. Hospitalacquired
24. neonatal infections in developing countries. The Lancet . 2005;365(9465):1175–1188. doi:
25. 10.1016/S0140-6736(05)71881-X.; Manandhar S., Amatya P., Ansari I., et al. Risk factors for the
26. development of neonatal sepsis in a neonatal intensive care unit of a tertiary care hospital of
27. Nepal. BMC Infectious Diseases . 2021;21(1):p. 546. doi: 10.1186/s12879-021-06261-x)
28. KE Rudd, SC Johnson, KM Agesa, et al. Global, regional, and national sepsis incidence and
29. mortality, 1990–2017: analysis for the Global Burden of Disease StudyLancet, 395 (2020), pp.
30. 200-211
31. Craymah JP, Tuoyire DA, Adjei-Ofori P, Ekor OE, Ninson PA, Ewusi MHKA. Neonatal sepsis in a tertiary health facility in Cape Coast, Ghana. PLoS One. 2024 May 8;19(5):e0302533. doi: 10.1371/journal.pone.0302533. PMID: 38718061; PMCID: PMC11078352
32. Mahmoud AM, Alpakistany TA, Ismail KA, Hawash YA, Jaafar N, Mohamed MM, Sami R, Khalifa OM. Effect of COVID-19 Pandemic on Neonatal Sepsis. Clin Lab. 2022 May 1;68(5). doi: 10.7754/Clin.Lab.2021.210711. PMID: 35536063)
33. Stoll BJ, Puopolo KM, Hansen NI, Sánchez PJ, Bell EF, Carlo WA, Cotten CM, D'Angio CT, Kazzi SNJ, Poindexter BB, Van Meurs KP, Hale EC, Collins MV, Das A, Baker CJ, Wyckoff MH, Yoder BA, Watterberg KL, Walsh MC, Devaskar U, Laptook AR, Sokol GM, Schrag SJ, Higgins RD; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Early-Onset Neonatal Sepsis 2015 to 2017, the Rise of Escherichia coli, and the Need for Novel Prevention Strategies. JAMA Pediatr. 2020 Jul 1;174(7):e200593. doi: 10.1001/jamapediatrics.2020.0593. Epub 2020 Jul 6. Erratum in: JAMA Pediatr. 2021 Feb 1;175(2):212. doi: 10.1001/jamapediatrics.2020.6111. PMID: 32364598; PMCID: PMC7199167
34. Akalu TY, Gebremichael B, Desta KW, Aynalem YA, Shiferaw WS, Alamneh YM. Predictors of
35. neonatal sepsis in public referral hospitals, Northwest Ethiopia: A case control study. PLoS One.
36. 2020 Jun 24;15(6):e0234472. doi: 10.1371/journal.pone.0234472. PMID: 32579580; PMCID:
37. Cavoretto P, Candiani M, Giorgione V, Inversetti A, Abu-Saba MM, Tiberio F, Sigismondi C, Farina PMC7314009
38. S. Basu. Neonatal sepsis: the gut connection. Eur. J. Clin. Microbiol. Infect. Dis., 34 (2015), pp.
39. 215-222, 10.1007/s10096-014-2232-6; M.A. Carl, I.M. Ndao, A.C. Springman, S.D. Manning, J.R.
40. Johnson, B.D. Johnston, C.A.D. Burnham, E.S. Weinstock, G.M. Weinstock, T.N. Wylie, et al.
41. Sepsis from the gut: the enteric habitat of bacteria that cause late-onset neonatal bloodstream
42. infections. Clin. Infect. Dis., 58 (2014), pp. 1211-1218, 10.1093/cid/ciu08423.
43. Khadka P, Maharjan, Govinda, Chapagain, Ganesh, JanukaThapaliya, , Paudyal, Prakash,
44. Economic and Diagnostic Biomarker Tests of Neonatal Sepsis: A Prospective Study from a
45. Tertiary Care Hospital in a Low-Income Country, BioMed Research International, 2022, 5166380,
46. 9 pages, 2022. https://doi.org/10.1155/2022/5166380
47. Friedman N, Yochpaz S, Zirkin S, Herzlich J, Marom R. C-reactive protein and the neonatal
48. earlyonset sepsis calculator for the diagnosis of neonatal sepsis). Eur J Clin Microbiol Infect Dis.
49. 2021;40(6):1227–1234. doi: 10.1007/s10096-021-04156-y
50. Schupp T, Weidner K, Rusnak J, et al. Diagnostic and prognostic role of platelets in patients with
51. sepsis and septic shock. Platelets. 2023;34(1):2131753. doi: 10.1080/09537104.2022.2131753
52. Dundar B., Dincgez Cakmak B., Ozgen G., Tasgoz F. N., Guclu T., and Ocakoglu G., Platelet indices
53. in preterm premature rupture of membranes and their relation with adverse neonatal outcomes, The Journal of Obstetrics and Gynaecology Research. (2018) 44, no. 1, 67–73,
54. https://doi.org/10.1111/jog.13484, 2-s2.0-85040982950.
55. Go H, Ohto H, Nollet KE, Takano S, Kashiwabara N, Chishiki M, et al. Using platelet parameters to
56. anticipate morbidity and mortality among preterm neonates: a retrospective study. Front
57. Pediatr. 2020 Mar 13;8:90. 10.3389/fped.2020.00090.
58. Hebatallah AS, Nesma S. Mean platelet volume in preterm: a predictor of early onset neonatal
59. sepsis. J Matern Fetal Neonatal Med. 2020;33(2):206–11. 10.1080/14767058.2018.1488161.

60. Bateman R. M., Sharpe M. D., Singer M., and Ellis C. G., The effect of sepsis on the erythrocyte,
61. International Journal of Molecular Sciences. (2017) 18, no. 9,
62. https://doi.org/10.3390/ijms18091932, 2-s2.0-85029180803, 28885563].
63. Hu Z., Lippi G., and Montagnana M., Diagnostic and prognostic value of red blood cell
64. distribution width in sepsis: a narrative review, Clinical Biochemistry. (2020) 77, 1–6,
65. https://doi.org/10.1016/j.clinbiochem.2020.01
66. Ellahony DM, El-Mekkawy MS, Farag MM. A Study of Red Cell Distribution Width in Neonatal Sepsis. Pediatr Emerg Care. 2020;36(8):378–383. doi: 10.1097/PEC.0000000000001319
67. Milton R, Gillespie D, Dyer C, Taiyari K, Carvalho MJ, Thomson K, Sands K, Portal EAR, Hood K, Ferreira A, Hender T, Kirby N, Mathias J, Nieto M, Watkins WJ, Bekele D, Abayneh M, Solomon S, Basu S, Nandy RK, Saha B, Iregbu K, Modibbo FZ, Uwaezuoke S, Zahra R, Shirazi H, Najeeb SU, Mazarati JB, Rucogoza A, Gaju L, Mehtar S, Bulabula ANH, Whitelaw AC, Walsh TR; BARNARDS Group; Chan GJ. Neonatal sepsis and mortality in low-income and middle-income countries from a facility-based birth cohort: an international multisite prospective observational study. Lancet Glob Health. 2022 May;10(5):e661-e672. doi: 10.1016/S2214-109X(22)00043-2. PMID: 35427523; PMCID: PMC9023753