# The Evaluation of the Newborn Patients with Diagnosis of the Culture-Proven Sepsis

Melek Büyükeren,<sup>1</sup>
 Yasemin Akın,<sup>2</sup>
 Fatma Narter,<sup>2</sup>
 Nilüfer Çelik,<sup>1</sup>
 Melek Özbenli,<sup>1</sup>
 Özben Göktaş<sup>1</sup>

<sup>1</sup>Department of Pediatrics, University of Health Sciences, Kartal Dr. Lütfi Kırdar Training and Research Hospital, İstanbul, Turkey <sup>2</sup>Division of Neonatology, Department of Pediatrics, University of Health Sciences, Kartal Dr. Lütfi Kırdar Training and Research Hospital, İstanbul, Turkey

> Submitted: 25.02.2019 Accepted: 04.12.2019

Correspondence: Melek Büyükeren, Sağlık Bilimleri Üniversitesi Kartal Dr. Lütfi Kırdar Eğitim ve Araştırma Hastanesi, Pediatri Anabilim Dalı, İstanbul, Turkey E-mail:

melekbuyukeren@hotmail.com



**Keywords:** CRP; mean platelet volume (MPV); mortality; neonatal; sepsis.



# INTRODUCTION

Neonatal sepsis is a clinical syndrome seen in the first month of life accompanied by bacteremia and systemic signs of infection where the causative pathogen is isolated from blood. Neonatal sepsis is a serious cause of mortality and morbidity in newborn units.<sup>[1]</sup> Its frequency is 16 in 1000 live births in developing countries.<sup>[2]</sup>

Isolation of pathogens (bacteria or fungi), which are active in one or more blood cultures, is the gold standard in diagnosis. In newborns, the isolation of the causative agentis is challenging, in addition to laboratory tests and examination findings, auxiliary diagnostic methods are recommended for diagnosis. Various laboratory parameters (such as Creactive protein, procalcitonin, interleukin-6) are used for the diagnosis of sepsis in newborn units.<sup>[3]</sup> In some studies, leukocyte, and platelet counts and mean platelet volume (MPV) have also been used as sepsis markers.<sup>[4-6]</sup>

# ABSTRACT

**Objective:** Neonatal sepsis continues to be an important cause of morbidity and mortality in infants despite improvements in diagnosis and treatment. This study was planned to evaluate the demographic data, causative microorganisms and acute phase reactants at the time of diagnosis of blood culture positive sepsis in our neonatal intensive care unit.

**Methods:** We evaluated our patients diagnosed with blood culture positive sepsis in the neonatal intensive care unit during three years retrospectively. In this study, 131 patients whose clinical and laboratory findings were consistent with sepsis were included.

**Results:** The most common microorganism isolated from blood cultures that were taken at the time of diagnosis was *S. aureus* (n=36, 27.5%). Nineteen of them were methicillinresistant *S. aureus. Klebsiella species* were isolated in 26 cases (19.8%) (*K. pneumoniae, K. oxytoca* and ESBL positive *Klebsiella species* in 13, 2 and 11 cases, respectively). Thrombocyte counts of our patients were statistically significantly lower on the first day of culture sampling compared to the fifth-day values (p<0.05), in contrast, CRP and mean platelet volume (MPV) values were significantly higher (p<0.05). According to our findings, on the first day of culture sampling, the CRP and mean of maximum CRP values of our patients with gram-positive sepsis were significantly lower than the values of our patients with gramnegative sepsis (p<0.05).

**Conclusion:** In this study, the most common microorganisms which cause sepsis in our neonatal intensive care unit were determined. We detected that the clinical findings and markers of sepsis differ depending on the type of the organism, whether gram-positive or gram-negative and the type of infection, whether it is nosocomial or not.

In our study, the cases diagnosed with culture-proven neonatal sepsis in a three-year period in the Neonatal Intensive Care Unit of our hospital were evaluated; We aimed to investigate both the risk factors that are important in the development of neonatal sepsis, and causative factors of sepsis, and also to find the factors that affect mortality and morbidity in neonatal sepsis and changes in acute phase reactant for the identification of gram-positive or gram-negative pathogens.

# MATERIALS AND METHODS

## Patients

For this retrospective study, the patients diagnosed as sepsis based on clinical examination findings, and laboratory results in the neonatal intensive care unit of our hospital between 2009–2012 whose causative agents were isolated in the blood culture were determined and all recorded file data were examined in detail. Among 152 patients identified as a result of this screening, data of 21 patients were not available on the 5<sup>th</sup> day and the remaining 131 newborn patients constituted our study group.

In accordance with the clinical features, sepsis was diagnosed in patients whose causative infectious agents were isolated in blood culture, and diagnosis of meningitis was made in patients whose infectious agents were isolated in CSF culture. Anamnesis, physical examination, and laboratory results of the newborns constituting the study group were noted on the pre-prepared forms.

Patients with infection detected in the first seven days were evaluated as early-onset neonatal sepsis, patients diagnosed after day 7 as late-onset neonatal sepsis, while patients diagnosed after day 30 as very late- onset neonatal sepsis.<sup>[7,8]</sup> An infection that developed within the first 72 hours after admission to the hospital was evaluated as hospital-acquired sepsis.<sup>[9]</sup>

Lumbar puncture should be performed in all infants who are clinically considered to have sepsis before initiation of the antibiotics.<sup>[10]</sup> In our follow-up, antibiotic treatment was initiated without lumbar puncture in patients who were not given consent to perform lumbar puncture by their family or patients who could not tolerate the procedure because their clinical condition was impaired.

## Laboratory examinations

Blood samples (0.5–1 ml venous blood) taken in our unit were incubated in pediatric BACTEC culture media and the media were placed in the BACTEC 9050 (Becton Dickinson, USA) blood culture device. The causative microorganism was identified among those grown in blood cultures and antibiograms were performed.

Complete blood count (leukocyte counts, hemoglobin, platelet counts, MPV) values, C-reactive protein (CRP) and immature/total neutrophil (I/T) ratio were evaluated at the time of diagnosis of sepsis. In the peripheral smear evaluation, the I/T ratio  $\geq 0.2$  was considered to be pathological.<sup>[10]</sup> Complete blood count was performed using Beckman Coulter LH 780 hematology analyzer. C-reactive protein was analyzed using an immunonefelometer (Dade Behring, MarburgGmbh, Germany). Normal CRP value was accepted as <10 mg/L.<sup>[11]</sup>

### Statistical analysis

In our study, statistical analyzes were performed using SPSS 18.0 package program. Variables with normal distribution were evaluated using independent t-test and variables without normal distribution were evaluated using the non-parametric Mann-Whitney U test. A p-value of <0.05 was considered statistically significant.

## RESULTS

This study included 131 patients whose infectious agent

was isolated in blood culture and whose clinic was compatible with sepsis. Demographic and neonatal characteristics of the patients are given in Table 1.

Considering the sepsis distribution rate, 131 (4.7%) of 2785 patients hospitalized in the neonatal intensive care unit were diagnosed with culture-proven sepsis during this study.

When the clinical findings of the patients were evaluated, decrease in sucking reflex was detected in 90%, respiratory distress in 70%, jaundice in 69%, fever in 67, vomiting in 30%, abdominal distention in 27%, restlessness in 23%, bruising in 8%, febrile seizures in 2%, and rashes in 1% of the newborns.

When the microorganisms grown in the blood culture obtained when the patients were diagnosed with sepsis; *Staphylococcus aureus* was the most frequently isolated microorganism in 36 (27.5%) patients (methicillin-resistant *S. aureus* was grown in 19 cases). *Klebsiella spp.* was isolated in 26 (19.8%) patients (*Klebsiella pneumoniae* were isolated in 13, *Klebsiella oxytoca* in 2 cases, while ESBL-positivity was detected in 11 cases) followed by *Coagulase-negative staphylococcus* (CNS) which was isolated in 24 patients (18.3%) and *E.coli* in 16 patients (ESBL positivity was detected in five (12.2%) patients. The infectious agents isolated in blood cultures according to various stages of sepsis are given in Table 2.

The mean gestational age (mean $\pm$ standard deviation; 35 $\pm$ 4 weeks) of the early-onset neonatal sepsis group was statistically significantly higher than the mean gestational age

| Table I.         Demographic and neonatal characteristics of the cases with sepsis |            |                          |  |
|--|------------|--------------------------|--|
| Characteristics  |            | n (%)                    |  |
| Gender (male/fem   | ale)       | 67/64 (51.2/48.8)        |  |
| Types of delivery  |            | 39/92 (29.8/70.2)        |  |
| (NVSD/cesarean)  |            |                          |  |
| Gestational week <sup>*</sup>  |            | 29 (23–40)               |  |
| SGA/AGA/LGA  |            | 18/108/5 (13.7/82.5/3.8) |  |
| Resuscitation  |            | 25 (19.1)                |  |
| Onset of sepsis  |            | 67/61/3 (51.2/46.6/2.2)  |  |
| (early/late/very lat   | e)         |                          |  |
| Birth weight (gr)*   |            | 980 (520–4940)           |  |
| Premature rupture  | e of       | II (8.4)                 |  |
| membranes (+)  |            |                          |  |
| Antenatal use of s   | teroid (+) | 32 (24.4)                |  |
| Mortality  |            | 32 (24.4)                |  |
| Hospital-acquired  | infection  | 67 (51.2)                |  |
| Ventilatory support  | rt         | 74 (56.5)                |  |
| Pneumonia  |            | 72 (54.9)                |  |
| Urinary tract infe   | tion       | 45 (34.3)                |  |
| Asphyxia   |            | 8 (6.1)                  |  |
| Necrotizing enter  | ocolitis   | 3 (2.2)                  |  |
| Pneumothorax   |            | 7 (5.3)                  |  |

\*Median (minimum-maximum). NVSD: Normal vaginal spontaneous delivery; SGA: Small for gestational age; AGA: Appropriate for gestational age; LGA: Large for gestational age.  $(32\pm5 \text{ weeks})$  of the late-onset sepsis groups (p=0.037). The mean birth weights (2280±953 g) of the early-onset neonatal sepsis group were statistically significantly higher than the birth weights (1664±881 g) of the late-onset sepsis group (p=0.006). Comparison was not appropriate since there were only three patients in the very late -onset sepsis group.

The most frequently grown microorganism in the blood culture in patients with hospital-acquired sepsis was CNS (16 patients 23.9%), while in the non-hospital-associated infections most frequently S. aureus (23 patients 35.9%) was detected.

The neonatal characteristics and blood parameters of the patients with and without hospital-acquired infections at the time of diagnosis of sepsis are given in Table 3. In infants with nosocomial infection, CRP, I/T ratio was found to be statistically significantly higher (p=0.025, p=0.0001, respectively), while any statistically significant difference was not observed as for mean leukocyte counts (p=0.480).

Lumbar puncture was performed in 50 (38.2%) patients

Microorganisms isolated relative to the onset time of the sepsis

Table 2.

who were diagnosed with sepsis. Same agents of infection were isolated from blood, and CSF cultures of patients with diagnosis of sepsis accompanied by the diagnosis of meningitis. Microorganisms reproduced in CSF culture were identified as CNS, *Klebsiella pneumoniae, Serratia marcences*, MRSA, and ESBL (+) *E.coli.* 

Twelve (17.9%) patients with early -onset, 19 (31.1%) with late-onset and one patient (33.3%) with very late- onset neonatal sepsis died during follow-up. In our study, sepsis –related mortality rate was 24.4 percent. Any statistically significant difference was not observed between distributions of days of diagnosis of sepsis in terms of mortality of patients with sepsis (p=0.206).

The mean I/T ratios, the need for resuscitation and ventilation were statistically significantly higher in the deceased group compared to other patients (p=0.016; p=0.002; and p=0.0001, respectively). There was no statistically significant difference in average CRP values (p=0.180) (Table 4).

Blood cell, and platelet counts, MPV and CRP values of the patients with sepsis on the first and fifth days were

| Pathogen                               | Early-onset sepsis,<br>n=67, n (%) | Late-onset sepsis,<br>n=61, n (%) | Very late-onset sepsis,<br>n=3, n (%) | Total<br>n=131, n (%) |
|--|------------------------------------|-----------------------------------|---------------------------------------|-----------------------|
| Staphylococcus aureus                  | 21 (31.3)                          | 15 (24.6)                         | -                                     | 36 (27.5)             |
| Klebsiella spp                         | 12(17.9)                           | 14(23.0)                          | -                                     | 26 (19.8)             |
| Coagulase-negative staphylococcus      | 8(11.9)                            | 14 (23.0)                         | 2 (66.7)                              | 24 (18.3)             |
| E.coli                                 | 13 (19.4)                          | 3 (4.9)                           | -                                     | 16 (12.2)             |
| Enterococcus spp                       | 6 (9.0)                            | 6 (9.9)                           | -                                     | 12 (9.2)              |
| Alfa hemolytic strep.                  | 4 (6.0)                            | l (l.6)                           | -                                     | 5 (3.8)               |
| Citrobacter spp.                       | _                                  | 2 (3.3)                           | -                                     | 2 (1.5)               |
| Candida                                | _                                  | 2 (3.3)                           | -                                     | 2 (1.5)               |
| Nonfermentative gram- negative bacilli | l (l.5)                            | l (l.6)                           | -                                     | 2 (1.5)               |
| Serratia marcencens                    | 2 (3.0)                            | _                                 | -                                     | 2 (1.5)               |
| Diphtheroid bacilli                    | _                                  | l (l.6)                           | -                                     | l (0.8)               |
| Stenotrophomonas maltophilia           | _                                  | _                                 | l (33.3)                              | I (0.8)               |
| Pseudomonas spp                        | _                                  | l (l.6)                           | _                                     | I (0.8)               |
| Acinetobacter baumanii                 | -                                  | 1 (1.6)                           | -                                     | I (0.8)               |

Table 3. Characteristic features and blood values of patients with (HKE +)/and without (HKE-) nosocomial sepsis

|                                     | HKE (+) n=67 | HKE (-) n=64 | р      |
|-------------------------------------|--------------|--------------|--------|
| Gestational week <sup>*</sup>       | 32±4         | 35±4         | 0.003  |
| Birth weight (gr) <sup>*</sup>      | 1718±863     | 2261±1006    | 0.001  |
| Duration of ventilation (day)*      | 15±13        | 11±12        | 0.272  |
| Duration of TPN (day)*              | 24±14        | 12±12        | 0.0001 |
| Duration of hospitalization (day)*  | 49±25        | 27±19        | 0.0001 |
| Mortality n (%)                     | 22 (32.8)    | 10 (15.6)    | 0.022  |
| C-reactive protein (mg/L)*          | 68.5±57.7    | 47.4±48.3    | 0.025  |
| Neutrophil ratio*                   | 0.23±0.15    | 0.12±0.13    | 0.0001 |
| White blood cell count $(/\mu L)^*$ | 3383±84 3    | 12374±7800   | 0.48   |

\*Mean±standard deviation. TPN: Total parenteral nutrition; HKE: Hospital-acquired infection.

| Table 4. Comparison between mortality and demographic characteristics of the patients |                       |                       |        |  |
|---|-----------------------|-----------------------|--------|--|
|   | Survived (n=99)       | Exited (n=32)         | Р      |  |
| Resuscitation n (%)   | 12 (12.1)             | 13 (40.6)             | 0.002  |  |
| Need for ventilation, n (%)   | 44 (44.4)             | 30 (93.8)             | 0.0001 |  |
| Pathogen Gram (+) / Gram (-), n (%)   | 60 (60.6) / 39 (39.4) | 17 (53.1) / 13 (40.6) | 0.07   |  |
| C-reactive protein (mg/L)   | 54.6±55.2             | 69.4±50.0             | 0.18   |  |
| Neutrophil ratio*   | 0.16±0.14             | 0.23±0.16             | 0.016  |  |

 Table 4.
 Comparison between mortality and demographic characteristics of the patients

 Table 5.
 The relationship between mean values of C-reactive protein, mean platelet volume leukocyte, and platelet counts and mortality

|                                   | Survived (n=99) | Exited (n=32) | Total (n=131) | P,    | <b>P</b> <sub>2</sub> |
|-----------------------------------|-----------------|---------------|---------------|-------|-----------------------|
| White blood cell I. day (/µL)     | 11923±7180      | 15965±10046   | 12887±8101    | 0.015 | 0.357                 |
| White blood cell 5. day (/µL)     | 14604±17478     | 15959±7019    | 14957±15376   | 0.796 |                       |
| Platelet I. day (/µL)             | 171131±120208   | 151656±126999 | 166374±121695 | 0.433 | 0.0001                |
| Platelet 5. day (/µL)             | 226452±115594   | 204078±165456 | 245395±182494 | 0.618 |                       |
| Mean platelet volume 1. day (fL)  | 9.7±1.0         | 9.5±1.1       | 9.6±1.0       | 0.357 | 0.002                 |
| Mean platelet volume 5. day (fL)  | 8.9±0.8         | 8.5±0.9       | 8.8±0.8       | 0.208 |                       |
| C-reactive protein I. day (mg/L)  | 54.6±55.2       | 69.4±50.0     | 58.2±54.2     | 0.18  | 0.0001                |
| C-reactive protein 5. day (mg/L)  | 6.8±11.7        | 19.7±35.0     | 9.7±20.0      | 0.056 |                       |
| C-reactive protein maximum (mg/L) | 81.2±70.4       | 96.2±60.2     | 85.5±67.6     | 0.316 | _                     |

 Table 6.
 Infection markers in gram-positive and gram-negative cases and mortality

|                                   | Gram–Positive (n=77) | Gram-Negative (n=52) | р     |
|-----------------------------------|----------------------|----------------------|-------|
| Gestational weeks                 | 33±5                 | 33±4                 | 0.889 |
| Duration of hospitalization (day) | 36±24                | 42±26                | 0.129 |
| White blood cell I. day (/µL)     | 13641±8532           | 11425±7073           | 0.125 |
| White blood cell 5. day (/µL)     | 12354±4960           | 18119±22567          | 0.22  |
| Platelets I. day (/µL)            | 188182±127808        | 135923±106889        | 0.017 |
| Platelet 5. day (/µL)             | 251456±137936        | 183833±111777        | 0.097 |
| Mean platelet volume 1. day (fL)  | 9.6±0.9              | 9.6±1.3              | 0.683 |
| Mean platelet volume 5. day (fL)  | 8.8±0.9              | 8.8±0.7              | 0.951 |
| C-reactive protein 1. day (mg/L)  | 47.1±52.6            | 74.3±53.9            | 0.005 |
| C-reactive protein 5. day (mg/L)  | 9.7±22.4             | 10.1±17.0            | 0.952 |
| C-reactive protein maximum (mg/L) | 73.6±54.7            | 106.2±82.4           | 0.02  |

compared and their mean values were calculated (Table 5). Platelet counts on the first day were found to be statistically significantly lower relative to the fifth day (p=0.0001).

The first day CRP and MPV values were statistically significantly higher when compared with the fifth-day CRP and MPV values (p=0.002; p=0.0001, respectively). In the group of exited sepsis cases the mean leukocyte count on the first day of sepsis was found to be statistically significantly higher than the survived group (p=0.015). The data are included in Table 5.

Microorganisms grown in the blood culture of our cases were evaluated under the categories of gram-positive and gram-negative species. In two patients Candida albicans was grown in culture media, and they were excluded from the evaluation because of their small number (1 of 2 patients in whom Candida spp. was isolated was lost during follow-up, and the other responded to the treatment). One hundred and twenty-nine patients were evaluated. Gram-positive microorganisms were isolated in 77 patients (59.7%) and gram-negative pathogens in 52 (40.3%) patients. When compared with cases with sepsis caused by gram-positive microorganisms, in cases with sepsis where gram-negative pathogens were isolated, CRP values on the 1 st day and maximum CRP values were statistically significantly higher (p=0.005, p=0.02), and platelet counts on the 1<sup>st</sup> day were statistically significantly lower (p=0.002, p=0.017). The findings are shown in Table 6.

## DISCUSSION

Neonatal sepsis is one of the causes of serious mortality and morbidity.<sup>[1]</sup> The definitive diagnosis of neonatal sepsis is made by early isolation of the active pathogen in blood culture.<sup>[3]</sup> In our study, early- and late-onset neonatal sepsis rates were very close to each other among patients followed up in the neonatal intensive care unit with the diagnosis of sepsis. In the study of Gürsu et al.<sup>[12]</sup> 46.6% of sepsis patients were diagnosed with early-onset neonatal sepsis and 53.4% of them as late-onset sepsis similar to our study.

In comparison of sepsis groups according to gestational age and birth weights; the mean gestational age of the early-onset neonatal sepsis group was statistically significantly higher than the late-onset sepsis group (p=0.037). The birth weight averages of the early –onset neonatal sepsis group was statistically significantly higher than the late-, and very late-onset group (p=0.006). Also in the study by Kara et al.<sup>[13]</sup> gestational ages of babies with late-onset neonatal sepsis were higher compared to the other groups, but unlike our study, babies who were born under 33 weeks of gestation had not received the diagnosis of early-onset neonatal sepsis.

Mortality rates of neonatal sepsis have been reported to range between 2–4% in term and late preterm babies. It has been reported to be 25% for early-onset sepsis and 18% for late-onset sepsis in preterm babies.<sup>[10,14]</sup> In our study, the mortality rate due to sepsis was detected as 24.4%. In our cases with early-onset neonatal sepsis, the mortality rate was 17.9%, while it was 31.1% in late-onset neonatal sepsis and 33.3% in very late-onset neonatal sepsis without any i significant intergroup difference (p=0.206).The mortality rates of 13%, and 36.5% were reported by Türkmen et al.<sup>[15]</sup> and Kara et al.,<sup>[13]</sup> respectively. In our study, we found higher or lower mortality rates compared to various studies which we interpreted this discrepancy to relatively higher number of preterm infants included in our study.

While the mortality rate was 18% in sepsis cases where gram-positive bacteria were isolated, we found the mortality rate to be 37.1% in cases where gram-negative bacteria were isolated which was compatible with the literature data.<sup>[9]</sup> In the study of Türkmen et al.,<sup>[15]</sup> mortality rates were found to be 9.6% and 19.2% in patients where gram-positive and gram-negative bacteria were isolated, respectively. In the study of Gürsu et al.,<sup>[12]</sup> mortality rates were 41.1%, and 18.2% in patients whose blood cultures demonstrated growth of gram-positive, and gram-negative bacteria, respectively.

In our study, the mean gestational week of the cases was  $33\pm5$  weeks, and the mean time interval between the onset of sepsis and its diagnosis was  $11\pm10$  days. In the study of Bulut et al.,<sup>[16]</sup> the mean gestational week was  $35.4\pm4.2$  weeks, and the mean time interval between the onset of sepsis and its diagnosis was  $7.0\pm5.7$  days. The gestational weeks of the patients in our study were not so long.

The order of frequency of microorganisms causing sepsis in newborns varies according to different countries and different centers in the same country. In our study, most frequently *S. aureus* was isolated from blood cultures in early-onset sepsis. In the study of de Bont,<sup>[17]</sup> Berger<sup>[18]</sup> et al., Group B *Streptococci* were found to be the most common pathogen in early-onset neonatal sepsis. Unlike western countries, Group B *Streptococci* were not detected in our study. In Western Europa CNS was the most common pathogen in late-onset neonatal sepsis.<sup>[9]</sup> In our study, *S. aureus, Klebsiella spp* and CNS were most frequently isolated in blood cultures of infants diagnosed with late-onset sepsis. In the study of Berger et al.,<sup>[18]</sup> the most common pathogen in late-onset neonatal sepsis iwas *S. epidermidis*.

In this study, most of the infections were hospital-acquired and the mortality rate was 32.8%. Mortality rate in hospital-induced sepsis; 15.9% of Taş et al.;<sup>[19]</sup> 33.3% of Belet et al.,<sup>[20]</sup> Makhoul<sup>[21]</sup> and his friends were 16.9%. In our study, the mortality rate was found to be high in infants with HKE, and we linked this to the high rate of preterm infants.

The most common microorganism isolated in blood cultures of the patients with hospital-acquired sepsis was CNS, while the most frequently detected pathogen in non-hospital-acquired infections was *S. aureus*. In a study conducted in the Netherlands, CNS was the most frequently found pathogen in hospital-acquired infections. <sup>[22]</sup> The mean length of hospital stay was  $49\pm25$  days in patients with nosocomial sepsis, which was found to be statistically significantly longer than the non-nosocomial sepsis group. In the study of Kuzucu et al.,<sup>[23]</sup> the length of hospital stay due to hospital-acquired infections increased by 23 days.

In our study, there was no statistically significant difference between the leukocyte counts on the first and fifth days of the patients with sepsis, while platelet counts on the first day were significantly lower than the platelet values on the fifth day (p=0.0001). Berger et al.<sup>[18]</sup> found that in 45.5% of the patients thrombocytopenia accompanied neonatal sepsis. In the study of Bulut et al.<sup>[16]</sup> this rate was found as 46.9%. In our study, in 37.4% of the patients with neonatal sepsis concomitant thrombocytopenia was detected at the time of diagnosis

In our study, the first day CRP and MPV values were statistically significantly higher than the fifth-day CRP and MPV values (p<0.05). On the first day, the mean MPV was found to be 9.6±1.0 fL. In the study of Oncel et al.,<sup>[4]</sup> the mean MPV in patients with sepsis was 8.57±0.67 fL, whereas in the study of Patrick et al.,<sup>[24]</sup> the average value of MPV in patients with late-onset sepsis was 12.63 fL.

In the study of Vander Lelie et al.,<sup>[25]</sup> increases in MPV were detected in 13 of 25 patients, but the control MPV values observed one week after treatment were within the normal range. In our study, it was found that MPV values may have a diagnostic value in patients with sepsis. However, it did not provide sufficient information about

causative pathogen (gram-positive/negative) isolated in blood culture, so MPV values were not predictive in terms of mortality.

In our study, the mean values of CRP on the 1st day of sepsis and maximum CRP values of the group where gram-positive pathogens were grown in blood culture were found to be statistically significantly lower than the group where gram-negative microorganisms were isolated in blood culture (p=0.005, p=0.02). Our data support the data reported by Oncel et al.<sup>[4]</sup>

In conclusion, according to our study, risk of sepsis-related mortality increases in patients with late- onset, hospital- acquired, gram-negative sepsis demonstrating a high number of leukocytes on the 1st day, and the increased CRP on the  $5^{\rm th}$  day.

Although the incidence of neonatal sepsis has decreased compared to previous years, sepsis is still a serious cause of mortality and morbidity in all newborn units.

## **Ethics Committee Approval**

Ethical approval was obtained before the study was performed from Dr. Lütfi Kırdar Training and Research Hospital Clinical Research Ethics Committee (date: 03.10.2012, no: B104İSM4340029/1009/84).

#### Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

#### Authorship Contributions

Concept: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Design: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Supervision: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Fundings: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Materials: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Data: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Analysis: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Literature search: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Writing: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.; Critical revision: M.B., Y.A., F.N., N.Ç., M.Ö., Ö.G.

#### **Conflict of Interest**

None declared.

## REFERENCES

- Hedegaard SS, Wisborg K, Hvas AM. Diagnostic utility of biomarkers for neonatal sepsis--a systematic review. Infect Dis (Lond) 2015;47:117-24. [CrossRef]
- Thaver D, Zaidi AK. Burden of neonatal infections in developing countries: a review of evidence from community-based studies. Pediatr Infect Dis J 2009;28:S3–S9. [CrossRef]
- Chauhan N, Tiwari S, Jain U. Potential biomarkers for effective screening of neonatal sepsis infections: An overview. Microb Pathog 2017;107:234–42. [CrossRef]
- Oncel MY, Ozdemir R, Yurttutan S, Canpolat FE, Erdeve O, Oguz SS, et al. Mean platelet volume in neonatal sepsis. J Clin Lab Anal 2012;26:493–6. [CrossRef]
- Guida JD, Kunig AM, Leef KH, McKenzie SE, Paul DA. Platelet count and sepsis in very low birth weight neonates: is there an organ-

ism-specific response?. Pediatrics 2003;111:1411-5. [CrossRef]

- Hornik CP, Benjamin DK, Becker KC, Benjamin DK Jr, Li J, Clark RH, et al. Use of the complete blood cell count in early-onset neonatal sepsis. Pediatr Infect Dis J 2012;31:799–802. [CrossRef]
- Cortese F, Scicchitano P, Gesualdo M, Filaninno A, De Giorgi E, Schettini F, et al. Early and Late Infections in Newborns: Where Do We Stand? A Review. Pediatr Neonatol 2016;57:265–73. [CrossRef]
- Sharma P, Kaur P, Aggarwal A. Staphylococcus aureus- the predominant pathogen in the neonatal ICU of a tertiary care hospital in amritsar, India. J Clin Diagn Res 2013;7:66–9. [CrossRef]
- Ferrieri P, Wallen LD. Neonatal bacterial sepsis. In: Gleason CA, Devaskar SU, editors. Avery's Diseases of the Newborn. 9th ed. Philadelphia: Elsevier Saunders; 2012. p. 538–51. [CrossRef]
- Edwards MS. Clinical features, evaluation, and diagnosis of sepsis in term and late preterm infants. Available at: https://www.uptodate.com/contents/clinical-features-evaluation-and-diagnosis-ofsepsis-in-term-and-late-preterm-infants. Accessed Apr 7, 2020.
- Perrone S, Lotti F, Longini M, Rossetti A, Bindi I, Bazzini F, et al. C reactive protein in healthy term newborns during the first 48 hours of life. Arch Dis Child Fetal Neonatal Ed 2018;103:F163–F6. [CrossRef]
- Gürsu HA, VitrinelA, Cömert S, Ağzıkuru T, Aksoy F, Akın Y, et al. Neonatal sepsisli olgularımızın prospektif değerlendirilmesi. Bakırköy Tıp Dergisi 2007;3:89–93.
- Kara H, Ertuğrul S, Gündoğuş N, Akpolat N, Özmen Ö. Yenidoğan yoğun bakım ünitesindeki kültür ile kanıtlanmış sepsisli hastaların değerlendirilmesi. Dicle Tıp Dergisi 2015;42:355–60. [CrossRef]
- Pammi M. Treatment and prevention of bacterial sepsis in the preterm infant <34 weeks gestation. Available at: https://www.uptodate.com/contents/treatment-and-prevention-of-bacterial-sepsis-inpreterm-infants-less-than34-weeks-gestation. Accessed Apr 7, 2020.
- Türkmen MK, Telli M, Erişen S, Güzünler M, Eyigör M. Neonatal sepsisli olguların değerlendirilmesi ve antibiyotik duyarlılıklarının belirlenmesi. ADÜ Tıp Fak Derg 2010;11:15–20.
- Bulut MO, Bulut İK, Büyükkayhan D, İçağasıoğlu D, Gültekin A, Toksoy HB, et al. Neonatal sepsisli olguların retrospektif olarak değerlendirilmesi. CÜ Tıp Fak Derg 2005;27:63–8.
- de Bont ES, Martens A, van Raan J, Samson G, Fetter WP, Okken A, et al. Tumor necrosis factor-alpha, interleukin-1 beta, and interleukin-6 plasma levels in neonatal sepsis. Pediatr Res 1993;33:380–3.
- Berger C, Uehlinger J, Ghelfi D, Blau N, Fanconi S. Comparison of C-reactive protein and white blood cell count with differential in neonates at risk for septicaemia. Eur J Pediatr 1995;154:138–44.
- Taş DB, Can D, Genel F, Atlıhan F, Oral R. Prematüre servisinde sepsis etkenleri ve kültür antibiyogram sonuçlarının değerlendirilmesi. Ege Pediatri Bülteni 2000;7:15–23.
- Belet N, Küçüködük Ş, Sezer T, Yıldıran A, Tanyeri B. Ondokuz Mayıs Üniversitesi Tıp Fakültesi yenidoğan ünitesinde izlenen nozokomiyal sepsis olguları. Türk Pediatri Arşivi 2000;35:256–60.
- Makhoul IR, Sujov P, Smolkin T, Lusky A, Reichman B. Epidemiological, clinical, and microbiological characteristics of late-onset sepsis among very low birth weight infants in Israel: a national survey. Pediatrics 2002;109:34–9. [CrossRef]
- 22. van der Zwet WC, Kaiser AM, van Elburg RM, Berkhof J, Fetter WP, Parlevliet GA, et al. Nosocomial infections in a Dutch neonatal intensive care unit: surveillance study with definitions for infection specifically adapted for neonates. J Hosp Infect 2005;61:300–11.
- Kuzucu Ç, Gülcan H, Üzüm İ, Durmaz B. Bir yenidoğan ünitesinde hastane kaynaklı sepsislerde etken mikroorganizmalar ve antibiyotik duyarlılıkları. Ankem Derg 2004;18:5–8.
- Patrick CH, Lazarchick J. The effect of bacteriemia on automa¬ted platelet measurements in neonates. Am J Clin Pathol 1990;93:391–4.
- Van der Lelie J, Von dem Borne AK. Increased mean platelet volume in septicaemia. J Clin Pathol 1983;36:693–6. [CrossRef]

## Kültür Kanıtlı Sepsis Tanısı Alan Yenidoğan Olguların Değerlendirilmesi

**Amaç:** Yenidoğan sepsisi tanı ve tedavisindeki gelişmelere rağmen, bebeklerde önemli bir morbidite ve mortalite nedeni olmaya devam etmektedir. Bu çalışmada, yenidoğan ünitesinde kan kültüründe etken izole edilip sepsis tanısı konulan hastaların demografik verilerini, sepsis nedeni olan mikroorganizmalar ve tanı aldıkları andaki akut faz reaktanlarını değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** Hastanemiz yenidoğan yoğun bakım ünitesinde üç yıllık süre boyunca, klinik ve laboratuvar bulgularıyla birlikte, kan kültürü pozitif sepsis tanısı almış olan 131 olgu geriye dönük olarak değerlendirildi.

**Bulgular:** Sepsisli olguların tanı aldığı zaman alınan kan kültüründe üretilen mikroorganizmalara bakıldığında 36 hastada ile en yüksek oranda (%27.5) *Staf. aureus* izole edildiği görüldü. Bu olguların 19'u metisilin dirençli *S. aureus* idi. Yirmi altı hastada (%19.8) *Klebsiella spp.* saptandı. 13 olguda *Klebsiella pneumonia*, iki olguda *Klebsiella oxytoca* izole edilirken, 11 olguda ESBL pozitifliği tespit edildi. Sepsisli olgularınızda kültür alımının birinci gününde trombosit değerlerinin beşinci gün trombosit değerlerine göre anlamlı düşük; kültür alınan birinci gün CRP ve ortalama trombosit volümü (MPV) değerlerinin beşinci gün CRP ve MPV değerlerine göre anlamlı yüksek olduğu saptandı (p<0.05). Çalışmamızda kan kültüründe gram pozitif etken izole edilen grubun kan kültürü alındığı birinci gün CRP ve maksimum CRP değerlerinin ortalaması kan kültüründe gram negatif mikroorganizma izole edilen gruptan istatistiksel olarak anlamlı derecede düşük bulundu (p<0.05).

**Sonuç:** Bu çalışma ile ünitemizde yenidoğanlarda sepsise en sık neden olan mikroorganizmaları; etkene yönelik olarak (gram pozitif veya gram negatif) ve hastane kökenli olup olmamasına göre sepsis tablolarında, sepsis belirteçlerinde farklılık olduğunu belirledik.

Anahtar Sözcükler: C-reaktif protein; mortalite; neonatal; ortalama trombosit volümü; sepsis.