Chapter 3
Etiology of Early-Onset Bacterial Sepsis and Antibiotic Resistance in Neonates: A Case Study in an Algerian Neonatal Intensive Care Unit

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3.1 Introduction

Neonatal age represents a critical period in the life of newborns. Globally, an estimated 2.5 million newborns die in the first month of life, approximately 7000 newborn deaths every day in 2018, accounting for 98% of neonatal deaths in developing countries despite recent advances in the health system (World Health Organization [WHO] 2019). The majority of these deaths were caused by infections (35%), prematurity (28%), pregnancy-related complications (24%), and asphyxia (23%) (Alemu et al. 2019).

Neonatal sepsis is an infection involving the bloodstream in infants younger than 28 days old (Singh et al. 2021). It remains one of the greatest causes of morbidity and mortality among neonates, especially in the low-income countries of sub-Saharan Africa, South Asia, and Latin America, with a case fatality risk of 9.8% in the first month of life (Getabelew et al. 2018). According to the onset age of symptoms, neonatal sepsis is divided into early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS refers to sepsis in neonates at or before 72 h of life, and LOS is defined as sepsis occurring after 72 h of life (Singh et al. 2021).

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The causative agents of neonatal sepsis vary across the world; however, according to reports, Gram-negative bacilli (GNB), mainly *Klebsiella* sp. and *Escherichia coli*, are of greater importance in developing countries and group B *Streptococcus* (GBS) in developed countries (Le Doare and Heath 2013).

It is generally assumed that the transmission of pathogens from the female genitourinary system to the newborn or the fetus is the leading cause of EOS. Besides, the infection can also occur in utero or during delivery as they pass through the vaginal tract. Typically, GBS, *E. coli*, coagulase-negative *Staphylococcus*, *Haemophilus influenzae*, and *Listeria monocytogenes* are the primary bacterial pathogens responsible for EOS (Singh et al. 2021; Simonsen et al. 2014). Risk factors for EOS include both maternal and infant factors. These maternal factors include at least dietary intake of contaminated foods, procedures during pregnancy (such as cervical cerclage and amniocentesis), maternal risk factors during labor (prolonged rupture of membranes, vaginal colonization with GBS), and chorioamnionitis. Infant factors include prematurity/low birth weight, congenital anomalies, complicated or instrument-assisted delivery, and low APGAR scores (≤6 at 5 min) (Simonsen et al. 2014).

The WHO guidelines recommend using combination therapy, including gentamicin and benzylpenicillin or ampicillin for at least 7–10 days to manage severe bacterial infection in infants younger than 2 months (WHO 2020). However, these recommendations are based on the common antibiotic susceptibility of the predominant pathogens causing EOS reported in high-income countries (Sivanandan et al. 2011). Understanding the frequency and the drug resistance patterns of bloodstream infections in hospitalized newborns is critical for appropriately directing empiric antimicrobial prescribing and guiding antimicrobial-resistance containment strategies (Larru et al. 2016).

Studies documenting the pathogens causing EOS in African countries are very limited. Thus, local data on the etiology and antibiotic susceptibility of pathogens causing EOS are urgently needed to evaluate the empirical treatment's adequacy and adapt antibiotic regimens to local antibiotic susceptibility patterns. Although various studies have reported the risk factors of neonatal sepsis in different parts of the world, to our knowledge, no study on this topic has been reported in Algeria yet. Thus, we aimed to investigate the risk factors of EOS among neonates admitted to the NICU of the Khalil Amrane University Hospital, Algeria. The study also aimed to identify the pathogens causing EOS and to assess their antibiotic susceptibility patterns.

3.2 Methods

3.2.1 Study Period and Inclusion Criteria

This study was conducted at the NICU of the Khalil Amrane University Hospital, Bejaia, North Algeria. Bejaia city is located on the edge of the Mediterranean Sea with 1,012,274 inhabitants (Algerian census data population statistics projections in

2008). The hospital receives referred patients from all parts of the region, other neighborhood regions, and private clinics.

All neonates aged 72 h or less admitted to the NICU of the Khalil Amrane University Hospital between February and July 2020 were enrolled in this study. This study was approved by the hospital's local ethics committee and conformed to the ethical guidelines of the Declaration of Helsinki. We asked the parents of all neonates to sign a written consent form.

According to the WHO recommendations, the suspicion of EOS is based on the presence of the following signs: incapacity to feed, fever, hypothermia, tachypnea, severe chest indrawing, nasal flaring, grunting, lethargy, reduction of movements, poor capillary refill time, bulging fontanelle, convulsions, jaundice, skin pustules, and/or unconsciousness (World Health Organization 2005; Shane et al. 2017).

The Khalil Amrane NICU uses the standard antibiotic regimen for sepsis in neonates and children. This consists of a combination of aminopenicillins, third-generation cephalosporins (3GC) (cefotaxime or ceftazidime), and gentamicin, according to the WHO guidelines for antibiotic use (WHO 2020; Fuchs et al. 2018). In case there was no clinical improvement, an empirical regimen of imipenem in combination with amikacin or ciprofloxacin was initiated.

A minimum of 0.5 ml of blood samples from all neonates suspected of having EOS were sent to the microbiology laboratory for hemoculture and C-reactive protein (CRP) assessment.

3.2.2 Operational Definitions

Clinically suspected sepsis was defined according to the surveillance guidelines published by the Centers for Disease Control and Prevention (CDC), which required a positive blood culture result with signs or symptoms of systemic illness (i.e., fever >38 °C, hypothermia (<36 °C), apnea or respiratory distress, and feeding intolerance). Laboratory-confirmed sepsis was defined as a recognized pathogen isolated from blood culture that was not related to an infection at another site (Horan et al. 2008).

Neonates that develop sepsis in the first 72 h of life were classified as early-onset (Wynn 2016). Premature rupture of membranes (PROM) refers to a patient beyond 37 weeks' gestation who presented with rupture of membranes (ROM) before the delivery (Premature Rupture of Membranes 2020). Preterm birth was defined as live-born neonates delivered before 37 weeks of gestation (Quinn et al. 2016). Low birth weight (LBW) neonates were those with a birth weight of less than 2500 g (Cutland et al. 2017). Neonatal mortality is defined as the number of neonates who died at the NICU throughout the study period (Owusu et al. 2018). Sepsis-related mortality was defined as death with positive blood culture and sepsis or septic shock diagnosis in the same episode.

3.2.3 Data Collection and Analysis

A structured data collection format derived from the WHO Young Infant Study Group's guidelines was used to obtain sociodemographic data and other relevant information (WHO Young Infants Study Group 1999). We collected data about risk factors for EOS, including PROM, meconium-stained liquor, fever within 7 days before delivery, Apgar score, CRP, the weight of the newborn, gestational age, mode of delivery, nutrition, use of a peripheral catheter, and antibiotic treatment. The length of stay in the NICU and mortality were also recorded to assess the outcome.

Data were analyzed using GraphPad Prism 6 (GraphPad Software, La Jolla, CA). Categorical variables such as the history of antibiotic use, history of admission, and risk factors of and maternal-fetal infections were presented proportionally and compared using the chi-squared test or Fisher's exact test. Continuous variables such as gestation age, length of hospital stay, and weight were described as medians (interquartile range (IQR)). Factors that could predict EOS were investigated using multivariate analysis. All factors with a p-value less than 0.05 were considered statistically significant.

3.3 Results

3.3.1 Demographic and Clinical Characteristics

A total of 412 neonates admitted from February to July 2020 were enrolled. Male neonates formed the majority (258; 62.6%) of study participants.

The demographic and clinical characteristics of the patients are summarized in Table 3.1. A total of 137 (33.2%) neonates had birth weights below 2500 g with a median birth weight of 3.0 kg (IQR: 2.1–3.6).

Also, 396 (96.1%) neonates had a peripheral catheter; the median Apgar score after 5 min of birth was 9 (IQR: 8–9). Sixty-five (15.8%) neonates had positive C-reactive protein (CRP).

Concerning neonate feeding, 202 (49.1%) neonates received formula feed, 125 (30.3%) nutrition by a probe, 26 (6.3%) exclusive breast milk, and 59 (14.3%) both breast milk and formula.

The median gestation age was 38 weeks (IQR: 33–39). A total of 217 (52.7%) neonates were delivered by cesarean section (C/S), and 404 (99%) were delivered at NICU public hospital.

Neonates presented perinatal factors including 188 (45.7%) of risk factors for maternal-fetal infections, 127 (30.9%) of PROM (>18 h), 27 (6.4%) of meconium-stained liquor, 28 (6.8%) of fever within 7 days before delivery, and 70 (17%) of mothers who presented gestational diabetes.

Most neonates (86.9%, 358/412) received antibiotics for a median duration of 7 (3–10) days during their hospitalization. The common antibiotics administrated

Table 3.1 The demographic and clinical characteristics of the patients included in this study

Neonates characteristics	Number	Percent (%)/median
Mean birth weight (kg)	2.84 ± 0.94	3 (IQR: 2.1–3.58)
Birth weight		
<2500 g	137	33.2
≥2500 g	275	66.8
Mean birth size	46.6 ± 5.12	48 (IQR: 43–50)
Sex		
Male	258	62.7
Female	154	37.3
Mean gestational age (weeks)	36.6 ± 3.93	38 (IQR: 33–39)
Gestation age		
Full-term	238	57.8
Premature	174	42.2
Healthcare facility		
NICU public hospital	408	99.0
Private hospital	4	1.0
Perinatal history		
Apgar score (5 min)	8.43 ± 1.21	9 (IQR: 8–9)
Cesarean section	217	52.7
Vaginal delivery	195	47.3
Risk factors of maternal-fetal infections	188	45.7
Premature rupture of membranes (>18 h)	127	30.9
Meconium stained liquor	28	6.8
Fever within 7 days prior to delivery	33	8.0
Gestational diabetes	70	17.0
Nutrition		
Enteral nutrition by a probe	125	30.3
Enteral feeding, exclusive breast milk	26	6.3
Enteral feeding, formula feed only	202	49.1
Enteral feeding, breast milk and formula	59	14.3
Vaccination before admission to the NICU	100	24.2
Use of peripheral catheter	396	96.1
C-reactive protein		
Negative	347	84.2
Positive	65	15.8
Antibiotic treatment in NICU	358	86.9
Type of antibiotics (n = 358)		
Ampicillin (or amoxicillin)	336	93.9
Gentamicin	352	98.3
Amikacin	30	8.3
Third-generation cephalosporins	183	51.1
Imipenem	49	13.7
Ciprofloxacin	14	4.0

(continued)

Table 3.1 (continued)

Neonates characteristics	Number	Percent (%)/median
Vancomycin	5	1.3
Duration of antibiotic therapy	7.87 ± 7.05	7 (IQR: 3–10)
Length of stay in NICU		
<7 days	150	36.4
7–15 days	174	42.2
16–30 days	56	13.6
>30 days	32	7.8
Outcome		
Death	43	10.4
Survival	369	89.6
Causes of death (n = 43)		
Respiratory distress	25	58.1
Prematurity (low birth weight)	6	14.0
Sepsis	5	11.7
Others[a]	7	16.2

[a]Others: renal failure and polymalformative syndrome

were aminopenicillins (ampicillin or amoxicillin) (93.9%, 336/358), gentamicin (98.3%, 352/358), 3GC (51.1%, 183/358), imipenem (13.7%, 49/358), amikacin (8.3%, 30/358), ciprofloxacin (4%, 14/358), and vancomycin (1.3%, 5/358). The combination of aminopenicillins and gentamicin was frequently administered (46.2%), followed by the association of aminopenicillins, gentamicin, and 3GC (33.3%).

A total of 43 (10.4%) neonatal death were recorded resulting from different causes, including respiratory distress (25; 58.1%), prematurity (low birth weight) (6; 14%), sepsis (5; 11.7%), and other causes (renal failure and polymalformative syndrome) (7; 16.2%). Besides mortality, 174 (42.2%), 56 (13.6%), and 32 (7.8%) of neonates had a length of stay of 7–15 days, 16–30 days, and >30 days, respectively.

3.3.2 Profile of Pathogens

Fifty-two bacterial strains were isolated from blood cultures in 49 neonates during the study period giving a culture positivity rate of 11.9% (49/412), of which three neonates presented two different bacterial species per blood culture sample.

The Gram-negative isolates were predominant (78.9%, 41/52) and included *Klebsiella pneumoniae* (n = 35, 67.3%), *Enterobacter cloacae* (n = 3, 5.8%), *Escherichia coli* ($n = 1, 2\%$), *Acinetobacter baumannii* ($n = 1, 2\%$), and *Pseudomonas aeruginosa* (n = 1, 2%).

The Gram-positive bacteria identified were *Enterococcus* spp. (n = 7, 13.4%), coagulase-negative *Staphylococci* (CoNS) (n = 2, 3.9%), *Staphylococcus aureus* (n = 1, 2%), and group B *Streptococci* (GBS) (n = 1, 2%).

3.4 Antimicrobial Susceptibility

Different antibiotic resistance rates of *Enterobacterales* strains (n = 39) were recorded toward ampicillin (79.4%, 31/39), amoxicillin-clavulanate (79.4%, 31/39), cefotaxime (69.2%, 27/39), gentamicin (53.9%, 21/39), amikacin (28.2%, 11/39), cefoxitin (7.7%, 3/39), and ciprofloxacin (5.1%, 2/39). However, all *Enterobacterales* isolates were susceptible to imipenem.

The *A. baumannii* isolate was resistant to ciprofloxacin and susceptible to imipenem, while the *P. aeruginosa* isolate was resistant to imipenem.

Concerning the Gram-positive bacteria, the *Staphylococcus* spp. isolates were oxacillin-resistant except for one isolate. The seven *Enterococcus* spp. isolates were vancomycin-susceptible, and the GBS isolate was penicillin-resistant.

3.5 Predictors of Early-Onset Bacterial Sepsis

We investigated different factors that could predict EOS using multivariate analysis. Thus, low gestational age, low birth weight (<2500 g) and size, gestational diabetes, enteral nutrition by a probe, and antibiotic use (amikacin, 3GC, imipenem, and ciprofloxacin), were significantly associated with neonatal EOS. Sex, Apgar score, perinatal history, peripheral catheter use, and CRP were not associated with EOS (Table 3.2).

3.6 Discussion

The epidemiology of each NICU is different, and each unit should know its trend. To our knowledge, this study is the first report evaluating the EOS from NICU in Algeria.

In our study, neonates hospitalized in a precarious clinical state often present serious pathologies that may justify the use of invasive procedures. Our study assessed the risk factors influencing EOS and revealed that the probability of a neonate developing EOS increased with low birth weight.

NICU stays are among the most expensive hospitalizations. In this study, EOS significantly extended the length of hospital stay in affected neonates compared to those without EOS. Atif et al. reported that the mean additional NICU stay was 9.2 days, and the mean additional fixed cost was $769. Besides, the mean

Table 3.2 Predictors of early-onset bacterial sepsis

Characteristics	Neonates with EOS ($n = 49$)	Neonates with no-EOS ($n = 363$)	*P*-value
Mean gestational age (weeks)	33.9 ± 4.4	36.9 ± 3.72	<0.001
Mean birth weight (kg)	2.27 ± 1.03	2.92 ± 0.90	<0.001
Birth weight			
<2500 g	31 (63.2%)	106 (29.2%)	<0.001
≥2500 g	18 (36.8%)	257 (70.8%)	
Mean birth size	44.0 ± 5.09	46.9 ± 5.03	<0.001
Sex			
Male	32 (65.3%)	226 (62.2%)	0.68
Female	17 (34.7%)	137 (37.8%)	
Gestation age			
Full-term	15 (30.7%)	223 (61.4%)	<0.001
Premature	34 (69.3%)	140 (38.6%)	
Healthcare facility			
NICU public hospital	49 (100%)	359 (98.9%)	1
Private hospital	0 (0%)	4 (1.1%)	
Perinatal history			
Apgar score (5 min)	8.10 ± 1.21	8.47 ± 1.20	0.049
Cesarean section	22 (44.9%)	195 (53.8%)	0.25
Vaginal delivery	27 (55.1%)	168 (46.2%)	
Risk factors of maternal-fetal infections	24 (6.7%)	164 (45.1%)	0.62
Premature rupture of membranes (>18 h)	19 (38.8%)	108 (29.8%)	0.2
Meconium stained liquor	1 (2%)	27 (7.4%)	0.23
Fever within 7 days before delivery	4 (8.1%)	29 (8.0%)	1
Gestational diabetes	3 (6.1%)	67 (18.4%)	0.031
Nutrition			
Enteral nutrition by a probe	30 (61.3%)	95 (26.1%)	<0.001
Enteral feeding, exclusive breast milk	2 (4%)	24 (6.7%)	
Enteral feeding, formula feed only	15 (30.7%)	187 (51.5%)	
Enteral feeding, breast milk and formula	2 (4%)	57 (15.7%)	
Use of peripheral catheter	49 (100%)	347 (95.6%)	0.24
C-reactive protein			
Negative	38 (77.6%)	309 (85.1%)	0.17
Positive	11 (22.4%)	54 (14.9%)	
Antibiotic treatment in NICU	47 (96.0%)	311 (85.7%)	0.046
Type of antibiotics			
Ampicillin (or amoxicillin)			

(continued)

Table 3.2 (continued)

Characteristics	Neonates with EOS ($n = 49$)	Neonates with no-EOS ($n = 363$)	*P*-value
Yes	44 (89.8%)	292 (80.4%)	0.11
No	5 (10.2%)	71 (19.6%)	
Gentamicin			
Yes	46 (93.9%)	306 (84.2%)	0.074
No	3 (6.1%)	57 (15.8%)	
Amikacin			
Yes	16 (32.7%)	14 (3.9%)	<0.001
No	33 (67.3%)	349 (96.1%)	
Third-generation cephalosporins			
Yes	35 (71.4%)	148 (40.8%)	<0.001
No	14 (28.6%)	215 (59.2%)	
Imipenem			
Yes	27 (55.1%)	22 (6%)	<0.001
No	22 (44.9%)	341 (94%)	
Ciprofloxacin			
Yes	27 (55.1%)	22 (6%)	<0.001
No	22 (44.9%)	341 (94%)	
Vancomycin			
Yes	2 (4%)	3 (0.9%)	0.11
No	47 (96%)	360 (99.1%)	
Duration of antibiotic therapy	15.6 ± 10.2	6.83 ± 5.79	<0.001

[a]Others: renal failure and polymalformative syndrome

cumulative extra cost per patient was $1315 (Atif et al. 2008). Previous studies showed an average extra stay of 5.2 days (Leroyer et al. 1997), 16 days (Abdel-Wahab et al. 2013), and 24 days (Mahieu et al. 2001) for infected neonates.

The mortality rate of neonates at the Khalil Amrane NICU in Algeria was low compared to some studies conducted in other African countries. Thus, the overall percentage of neonatal mortality reported at the neonatal inpatient unit at the Komfo Anokye Teaching Hospital in Ghana was 20.2% (Owusu et al. 2018). In their study, Demisse et al. reported a mortality rate of 14.3% among all admitted neonates in the NICU of the University of Gondar Referral Hospital, Northwest Ethiopia (Demisse et al. 2017). In their systematic review of clinical risk factors for mortality in infants under 12 months of age hospitalized for sepsis or severe infections in low−/middle-income countries, Liang et al. reported very high mortality rates, ranging from 14.6% to 36.0% of admitted neonates. Prematurity and low birth weight were significantly associated with mortality (Liang et al. 2018). These differences could be attributed to many factors, including the healthcare system of the African countries, treatment and care access, the nutritional statute of both mothers and newborns, and the immunity statute of people.

The distribution of the strains per species showed that *K. pneumoniae* accounted for 64.8% ($n = 35$) of all isolates recorded in this study. It is assumed that GBS and

E. coli are the most frequently involved organisms in EOS, accounting for approximately 70% of infections. The remaining pathogens are other *Streptococci*, *S. aureus*, *Enterococcus* spp., *Haemophilus influenzae*, and *Listeria monocytogenes* (Simonsen et al. 2014; Bizzarro et al. 2005; Stoll et al. 1996).

In this study, GNB, especially *K. pneumoniae*, are the leading pathogens causing EOS. Our study constitutes the first report on the microbiological etiology of EOS in Algeria. Our data are in line with some studies published in other African countries. For example, Mulinganya et al. in the Democratic Republic of Congo found that 82% of pathogens isolated from EOS were Gram-negative, of which *E. cloacae* complex (42%), *K. pneumoniae* (18%), and *Serratia marcescens* (12%) were the most prevalent (Mulinganya et al. 2021). Similarly, in the systematic review and meta-analysis conducted by Okomo et al., the authors reported that *Klebsiella* (42%), *E. coli* (19%), and *S. aureus* (14%) were the most prevalent pathogens causing neonatal sepsis (Okomo et al. 2019).

Only one GBS strain was isolated in the current study. This result is in line with the previously cited works of Mulinganya et al. and Okomo et al. They reported one case (1/660) and two cases (2/90), respectively (Mulinganya et al. 2021; Okomo et al. 2019). Our finding is somehow contradictory to what is assumed in the literature, of which GBS is one of the leading neonatal sepsis pathogens globally, which could have an exceptionally high burden of disease in Africa (Sinha et al. 2016; Edmond et al. 2012). WHO recommended using GBS vaccination as a potential control strategy to reduce the GBS EOS in low- and middle-income countries (Giersing et al. 2016). However, in light of our results, we think that GBS vaccination would not be necessary as a strategy to reduce EOS in Bejaia.

WHO has provided guidelines for the management of common childhood illnesses. These guidelines recommended supplying ampicillin and gentamicin for at least 2 days in neonates with known risk factors for infection and reassessing them. Treatment should only be continued if there are signs of sepsis (or positive blood culture). It recommends hospitalization and IM or IV antibiotic therapy with a combination of gentamicin and benzylpenicillin or ampicillin for at least 7–10 days in infants aged <2 months who fulfill the case definition of severe bacterial infection (Fuchs et al. 2018).

In this study, the WHO's recommendations were applied to treat newborns before a definitive etiologic diagnosis was available. Empiric antibiotic therapy for suspected sepsis was started with broad-spectrum antibiotics, of which the combination of ampicillin or amoxicillin for 7–10 days and gentamicin or amikacin for 2 days was the more commonly administered. The antibiotics were administered in doses to achieve a bactericidal concentration in the blood according to the newborn weight. Once a pathogen has been identified in the blood culture, antibiotic treatment is restricted and targeted to the isolated bacteria.

We noticed that the *Enterobacterales* strains isolated from blood cultures in our study were highly resistant to penicillin/amoxicillin (85%), gentamicin (62.5%), and cefotaxime (70%). Thus, our results imply revisiting the use of aminopenicillins, gentamicin, and cefotaxime as first-line antibiotics, as high rates of resistance

were reported. Besides, the Gram-positive strains isolated in this study were also resistant. For example, the *Staphylococcus* spp. isolates were resistant to oxacillin.

Extending the duration of antibiotic use is one of the consequences of nosocomial infections. We found a mean extended antibiotic use of 8.4 days in neonates with EOSs compared with neonates without EOS. The excess use of antibiotics has important implications for NICU patients, for whom the risk of acquiring antibiotic-resistant nosocomial pathogens may be further amplified. From our experience, inappropriate and prolonged broad-spectrum antibiotic therapy and non-investigation of neonatal patients treated with antibiotics are very common in Algeria, and this undoubtedly contributes to the emergence and amplification of resistance in hospitals. If the neonate is treated with the inappropriate antibiotic, the sepsis may progress rapidly, and the patient may develop severe sepsis or septic shock. Correct diagnosis and adequate treatment represent the main determinants of patient outcomes (Folgori and Bielicki 2019). In this study, 22 (6%) neonates were treated with imipenem when they did not need to be treated with a carbapenem molecule (no-EOS). Some studies reported that reducing unnecessary antibiotic use in NICU effectively reduced antibiotic exposure without affecting the quality of care, which occurred in parallel with a reduction in length of stay and multidrug-resistant organisms (Cantey et al. 2016; McCarthy et al. 2018; Yin et al. 2021). The frequent use of imipenem could select for carbapenemase producers in the future. In this respect, we reported in a previous study in the same NICU that the prevalence of fecal carriage of *Enterobacterales* strains producing the OXA-48 carbapenemase was 1.6% (7/422) (Mairi et al. 2019). Furthermore, intestinal colonization by multidrug-resistant (MDR) bacteria also plays a role as a risk factor for infection. According to literature data, up to 50% of newborns colonized by MDR bacteria can develop sepsis (Yap et al. 2016; Lukac et al. 2015).

In addition, blood cultures are the gold standard for establishing a diagnosis of neonatal sepsis, despite being positive in a minority of patients with suspected sepsis, particularly EOS. It is important to note that false-negative blood cultures may occur due to a small volume (less than 1 ml) of blood inoculated for culture, low levels of bacteremia, and prenatal antibiotic use (Zea-Vera and Ochoa 2015). However, in the presence of clinical signs and laboratory markers that are consistent with an infection, the antimicrobial treatment is frequently prolonged beyond 48 h. Thus, increased antibiotic use can contribute to developing and spreading resistant pathogens in the NICUs (Oeser et al. 2020).

We are conscious that our study has some limitations regarding sample size and duration. However, this study, which constitutes the first report from Algeria, highlights the importance of determining the etiology of pathogens causing EOS and their antibiotic susceptibility patterns to rapidly address a correct antibiotic treatment regimen. Furthermore, the results obtained from this study may contribute to better management of neonatal sepsis in the first 3 days of life and the development of local policies based on local epidemiological information. Currently, the use of molecular diagnostics such as real-time PCR will provide an opportunity to improve our understanding of the etiology of EOS, thus limiting therapeutic failures in the NICUs in developing countries.

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