Causative Microorganisms and Antibiotics Susceptibility in Neonatal Sepsis at Neonatal Intensive Care Unit: A Longitudinal Study from Diyala Governorate in Iraq

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Abstract

Background: Neonatal sepsis is classified into two types, early-onset and late-onset sepsis, depending on the time of appearance of the clinical features of neonatal sepsis.

Objective: We aim to detect the most common causative organisms of neonatal sepsis and to evaluate the corresponding antibiotics susceptibility in the Diyala governorate.

Patients and Methods: We prospectively collected a convenient sample of 106 sepsis-proven neonates from the neonatal intensive care unit at Al-Batool teaching hospital. We assessed all cases based on clinical features, laboratory investigations, and demographics.

Results: Late-onset neonatal sepsis was predominant (77.4%) among neonates, and it was significantly associated with neonatal prematurity and the mode of delivery at p-values of 0.03 and 0.045 respectively. Premature neonates and those who were the product of cesarean section were more prone to develop late-onset neonatal sepsis with a relative risk of 2.8 and 2.54 respectively. The most common causative microorganism of early-onset neonatal sepsis was found to be Escherichia coli in 45.8% of cases while those causing late-onset neonatal sepsis were mainly due to Gram-negative bacilli represented by Klebsiella pneumonia (46.3%) and Acinetobacter baumannii (24.4%). Multi-drug resistance was evident for most of the causative microorganisms.

Conclusion: To recapitulate, late-onset sepsis appeared was more common among Iraqi neonates, and it was significantly associated with the neonate prematurity and C-section mode of delivery.

Keywords: *Anti-Bacterial Agents; Antibiotics Resistance; Causative Microorganisms; Intensive Care Units; Iraq; Middle East; Neonatal Sepsis; Neonatology.*

Introduction

To date, neonatal sepsis is still a significant cause of neonatal mortality and morbidity, albeit effective modalities of diagnostics and therapeutics implemented by neonatologists worldwide, including those in the developed world [(1)]. Neonatal sepsis is defined as the bacterial invasion of bloodstream causing non-specific systemic manifestations such as fever, respiratory problems, bradycardia or tachycardia, poor feeding, lethargy, irritability, seizures, abdominal distention, and unexplained jaundice [(2)]. Neonatal sepsis is classified into two types, an early-onset and late-onset sepsis, depending on the time of appearance of the signs and symptoms of neonatal sepsis [(1)]. Early-onset neonatal sepsis is diagnosed when the clinical manifestations of neonatal sepsis appear within the first 72 hours of life while the late-onset neonatal sepsis is diagnosed when they appear after the 72 hours of life [(3)]. Early-onset neonatal sepsis is acquired before and during delivery, and it is either a trans-placental or an ascending infection within the birth canal [(4)]. The microorganisms expected to cause early-onset sepsis are prevalent in the maternal genital tract, including Escherichia coli (E. coli) and group B streptococci which are responsible for the majority of cases and may ascend to the amniotic fluid causing chorioamnionitis especially when there is a premature or a prolonged rupture of membranes (PPROM) [(5)]. On the other hand, microbial agents inducing late-onset sepsis are either nosocomial or community-acquired infections and are transmitted to unfortunate neonates [(1-5)]. Many factors predispose the neonates to get an infection [(1)]. Risk factors for early-onset sepsis include maternal infections and febrile illnesses, chorioamnionitis, PPROM, prematurity and low birth weight [(4)]. Risk factors for late-onset neonatal sepsis are invasive procedures, including surgical manipulation, intubation, central venous catheters, resuscitation, mechanical ventilation, and a prolonged stay in the neonatal care units [(4)].

The causative microorganisms variate spatially and temporally, and from a population to the other [(1)]. Accurate identification of the source of infection, proper use of antimicrobial agents, and the study of antimicrobial susceptibility play essential roles in the prevention and control of neonatal sepsis and its complications, and this will increase the success rate of management of sepsis while reducing the economic burden on the holistic healthcare system, particularly in developing nations [(6)]. It is imperative to know whether the newborn baby has got sepsis, or not, and to detect the type of causative invasive microorganisms, and to start the treatment as early as possible [(7)]. A first interventional approach will reduce the risk of multidrug-resistant bacteria (MDR) which is defined as resistance to three or more antimicrobial classes [(8)]. To date, there is no single test to diagnose neonatal sepsis with high specificity and sensitivity [(1-3)]. Therefore, diagnostic tests must be in correlated in conjunction with assessing the risk factors and detecting the clinical signs of sepsis. Confirmatory laboratory tests include blood, urine, and cerebrospinal fluid cultures (CSF), as well as ESR, C-reactive protein (CRP), differential leukocyte profile, platelet count, latex agglutination tests and Polymerase Chain Reaction (PCR) [(9)].

In the present study, we aim to detect the causative microorganisms of neonatal sepsis and evaluate the antibiotic resistance in the neonatal intensive care unit in Al-Batool teaching hospital in the Diyala governorate. Our first hypothesis is that late-onset neonatal sepsis is more prevalent in our Neonatal intensive care unit (NICU) and mostly caused by Gram-negative bacilli. The second hypothesis is that multi-drug resistance exists among most of the causative microorganisms.

Materials and Methods

Using a convenient sampling procedure, we prospectively collected 106 sepsis-proven neonates in the neonatal intensive care unit of Al-Batool teaching hospital for the period from the 1st of December 2018 to the 1st of October 2019. We evaluated all the selected cases using clinical examination and laboratory investigations. The laboratory investigations included complete blood count (CBC), C-reactive protein (CRP), blood cultures, and chest x-ray (CXR). All cases enrolled in this study were diagnosed by the presence of at least three out of the following four criteria: 1) Presence of neonatal sepsis risk factors such as prematurity and chorioamnionitis. 2) Presence of two or more signs of the non-specific systemic manifestations such as fever, respiratory problems, bradycardia or tachycardia, poor feeding, lethargy, irritability, seizures, abdominal distention, and unexplained jaundice. 3) Positive CRP and abnormal CBC. 4) Positive culture [(2)]. We also collected data concerning gestational age, the PPROM, mode of delivery, maternal fever, and sex of neonates. A professional laboratory technician collected blood samples from neonates with high clinical suspicion of sepsis for CRP, CBC, and blood culture. The technician collected approximately five cubic centimetres of fresh blood, using aseptic technique, from a peripheral vein from each neonate and sent for biochemical and microbiology studies for cultivation and subsequent processing. Besides, we collected samples of urine and CSF for culture procedures.

The blood samples were cultured under the aerobic condition at 37° C. The cultured blood was observed daily in the first three days to report any visible growth by detecting any one of the following: hemolysis, air bubbles, and coagulation of broth. At the same time, subcultures were made during three successive days on enriched and selective media including blood, chocolate, MacConkey, and mannitol salt agar plates and examined for microbial growth after 24 to 48 hours of incubation. The same procedures were repeated until the 7th day before the blood culture was considered to be free of microorganisms. The obtained bacterial isolates were identified by microbiological methods including colony characteristics, Gram staining, and biochemical properties like catalase, coagulase and DNase production, hemolytic activity on blood agar plates, and growth on mannitol salt agar for Gram-positive bacteria. On the other hand growth on cetrimide agar, citrate utilization, urease, oxidase, and hydrogen sulfide production were used for Gram-negative bacteria [10]. We used VITEK 2 AST-N327 kits (BIOMERIEUX/ France) to validate the identification of Gram-negative bacteria. The results were read using API 32 GN reader. Antibiotics susceptibility was assessed by using the VITEK 2 AST-N327 identification kit in the VITEK 2 compact automated microbial detection system manufactured by bioMérieux France. The tested antibiotics with their minimal inhibitory concentration (MIC) were: Ampicillin 10□g, oxacillin 1□g, gentamicin 10□g, amikacin, vancomycin, ceftriaxone, cefotaxime, ceftazidime and cefoxitin with MIC of 30□g for each, ciprofloxacin 5□g, imipenem and meropenem with MIC of 10□g for each, azithromycin and erythromycin with MIC of 15□g for each, tetracycline (30□g), trimethoprim/ sulfamethoxazole (1.25/23.75□g), fosfomycin (200□g), colistin (4□g), tigecycline (15□g) and piperacillin-tazobactam (100/10□g).

We analyzed the data collected by using IBM SPSS version 20, and we expressed the variables as frequencies and percentages. We implemented a Chi-squared test to study the relationship between the onset of neonatal sepsis and each of gestational age, PPROM, mode of delivery, maternal fever, and neonatal gender. We adopted a p-value of 0.05 as the cutoff margin for statistical significance in hypothesis testing.

Results

We collected a convenient sample of 106 neonates who had proven neonatal sepsis, and those patients were admitted to the neonatal care unit at Al-Batool teaching hospital from December 2018 to October 2019. We analyzed our data, using descriptive and inferential statistics, in connection with the onset of neonatal sepsis, possible risk factors, to examine the most common causative bacteria in the early and late-onset neonatal sepsis, and to discover the relative antimicrobial susceptibility. Male neonates were 52 (49.1%), and the female neonates were 54 (50.9%) (Table 1, Figure 1). Among our sample, 24 (22.6%) were of early-onset sepsis, and the remaining 82 (77.4%) were of late-onset sepsis. Preterm neonates accounted for 76 cases (71.7%) and the term neonates attributed to 30 cases (28.3%). PPROM existed in 70 (66%) of cases while the remaining 36 (34%) had an intact membrane. A total number of 67 (63.2%) were a product of cesarean sections, and the remaining 39 (36.8%) were a product of vaginal delivery. There was a history of maternal fever in 69 (65.1%) of cases.

Table 1: Descriptive parameters of the total sample.

Data		Frequency	Percentage
Sepsis	Early-onset	24	22.6%
	Late-onset	82	77.4%
Gestational age	Preterm	76	71.7%
	Term	30	28.3%
State of membranes	Ruptured	70	66.0%
	Intact	36	34.0%
Mode of delivery	Caesarian	67	63.2%
	Normal	39	36.8%
Maternal fever	Present	69	65.1%
	Absent	37	34.9%
Sex	Male	52	49.1%
	Female	54	50.9%

In Al-Batool teaching hospital in Diyala governorate in Iraq, neonates in the neonatal intensive care unit were more prone to develop late-onset sepsis. The most common microorganisms causing late-onset neonatal sepsis included Klebsiella, Acinetobacter baumannii, coagulase-negative staphylococci (Staphylococcus epidermidis, Staphylococcus hominis, and Staphylococcus haemolyticus), Staphylococcus aureus, and Enterobacter species which accounted for 46.34%, 24.4%, 17.1%, 3.7% and 3.7% of the late-onset neonatal sepsis respectively. Early-onset neonatal sepsis was mainly due to E. coli, Staphylococcus hominis, and Klebsiella, which represented 45.8%, 20.8%, and 12.5% of early-onset neonatal sepsis, respectively (Table 2).

Table 2: The causative microorganisms in the early and late-onset neonatal sepsis.

Isolated bacteria	Early-onset	Late-onset	Frequency	Percentage
Klebsiella	3 (7.3%)	38 (92.7%)	41	38.7%
Acinetobacter baumannii	0 (0%)	20 (100%)	20	18.9%
E. coli	11 (100%)	0 (0%)	11	10.4%
Staphylococcus Epidermidis	1 (12.5%)	7 (87.5%)	8	7.5%
Staphylococcus hominis	5 (71.4%)	2 (28.6%)	7	6.6%
Staphylococcus haemolyticus	0 (0%)	5 (100%)	5	4.7%
Staphylococcus aureus	1 (25%)	3 (75%)	4	3.8%
Enterobacter species	1 (25%)	3 (75%)	4	3.8%
Enterococcus faecalis	0 (0%)	1 (100%)	1	0.9%
Micrococcus luteus	0 (0%)	1 (100%)	1	0.9%
Pseudomonus	0 (0%)	1 (100%)	1	0.9%
Proteus species	1 (100%)	0 (0%)	1	0.9%
Pasturella pnemotropicus	1 (100%)	0 (0%)	1	0.9%
Coagulase-negative staph.	0 (0%)	1 (100%)	1	0.9%
Total	24 (22.6%)	82 (77.4%)	106	100%

This study showed that the onset of the development of neonatal sepsis had a significant relationship with the gestational age and mode of delivery as p-values were equal to 0.03 and 0.045, respectively. Besides, the relative risk for preterm neonates to develop late-onset neonatal sepsis was 2.8 which means that there is a 180% increment in the probability of developing late-onset sepsis with prematurity compared with neonates who are born at full-term, while the relative risk for neonates who were products of cesarean sections to develop late-onset neonatal sepsis was 2.54. Thus they are more likely to develop late-onset neonatal sepsis by 154% more than neonates who were products of vaginal delivery (Table 3).

Table 3: The relation between the onset of neonatal sepsis and the possible risk factors.

Data		Early-Onset	Late-Onset	Total	Chi-square value	P-value	Relative Risk
Gestational age	Preterm	13 (54.2%)	63 (76.8%)	76 (71.7%)	4.699	0.03	2.8
	Term	11 (45.8%)	19 (23.2%)	30 (28.3%)			
	Total	24 (100%)	82 (100%)	106 (100%)			
State of membrane	Ruptured	17 (70.8%)	53 (64.6%)	70 (66%)	0.318	0.573	0.753
	Intact	7 (29.2%)	29 (35.4%)	36 (34%)			
	Total	24 (100%)	82 (100%)	106 (100%)			
Mode of delivery	Caesarian	11 (45.8%)	56 (68.3%)	67 (63.2%)	4.027	0.045	2.54
	Normal	13 (54.2%)	26 (31.7%)	39 (36.8%)			
	Total	24 (100 %)	82 (100%)	106 (100%)			
Maternal fever	Present	19 (79.2%)	50 (61%)	69 (65.1%)	2.704	0.1	0.411
	Absent	5 (20.8%)	32 (39%)	37 (34.9%)			
	Total	24 (100%)	82 (100%)	106 (100%)			
Gender	Male	13 (54.2%)	39 (47.6%)	52 (49.1%)	0.324	0.569	1.3
	Female	11 (45.8%)	43 (52.4%)	54 (50.9%)			
	Total	24 (100%)	82 (100%)	106 (100%)			

The antibiotic resistances of the most common causative microorganisms, which were responsible for causing late-onset neonatal sepsis, were as following as shown in table 4: Klebsiella was resistant to penicillins, cephalosporins, and aminoglycosides, while it was sensitive to azithromycin, colistin, imipenem, and meropenem in 78%, 70.7%, 41.5% and 31.7% of cases respectively. Acinetobacter baumannii was 100% resistant to the tested penicillins, cephalosporins, and aminoglycosides, but it was sensitive to colistin and tigecycline in 95% and 60% of cases respectively. Staphylococcus epidermidis was resistant to the tested penicillins, cephalosporins, and aminoglycosides except for vancomycin since it appeared to be sensitive to vancomycin and tigecycline in 100% of cases respectively. Staphylococcus hemolyticus appeared to be resistant to most of the tested antibiotics, while it was sensitive to tigecycline, ciprofloxacin, and vancomycin in 80%, 60%, and 60% of cases respectively. Staphylococcus aureus was resistant to most of the tested antibiotics, but it was sensitive to ciprofloxacin, tigecycline, and vancomycin in 100%, 75%, and 75% of cases, respectively. Enterobacter species were resistant to most of the tested antibiotics, while it was sensitive to ciprofloxacin, tigecycline, and cefoxitin in 100%, 100%, and 50% of cases respectively.

Table 4: The antibiotic resistance of common organisms, based on blood culture, in late-onset sepsis.

Antibiotics	Klebsiella	Acinetobacter baumannii	Staph. Epidermidis	Staph. hemolyticus	Staph. aureus	Enterobacter species
Ampicillin	41 (100%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Oxacillin	41 (100%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Amoxicillin	41 (100%)	20 (100 %)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Ceftriaxone	41 (100%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Cefotaxime	40 (97.6%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Ceftazidime	39 (95.1%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Cefoxitin	38 (92.7%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	2 (50%)
Gentamicin	40 (97.6%)	20 (100%)	7 (87.5%)	5 (100%)	3 (75 %)	4 (100%)
Amikacin	33 (80.5%)	20 (100%)	8 (100%)	4 (80%)	4 (100%)	4 (100%)
Vancomycin	41 (100%)	20 (100%)	0 (0%)	2 (40%)	1 (25%)	4 (100%)
Azithromycin	9 (22%)	14 (70%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Erythromycin	41 (100%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Imipenem	24 (58.5%)	18 (90%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Meropenem	28 (68.3%)	20 (100%)	8 (100%)	5 (100%)	4 (100%)	3 (75%)
Tetracycline	22 (53.7%)	19 (95%)	3 (37.5%)	5 (100%)	4 (100%)	4 (100%)
Metheprime	41 (100%)	20 (100%)	1 (12.5%)	1 (20%)	3 (75%)	4 (100%)
Ciprofloxacin	33 (80.5%)	20 (100%)	5 (62.5%)	2 (40%)	0 (0%)	0 (0%)
Fosfomycin	41 (100%)	20 (100%)	7 (87.5%)	5 (100%)	3 (75%)	4 (100%)
Colistin	12 (29.3%)	1 (5%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)
Tigecycline	32 (78%)	8 (40 %)	0 (0%)	1 (20%)	1 (25%)	0 (0%)
Tazocin	29 (70.7%)	17 (85%)	8 (100%)	5 (100%)	4 (100%)	4 (100%)

On the other hand, the antibiotic resistances of the most common causative microorganisms, which were responsible for causing early-onset neonatal sepsis, were as following as shown table 5: E. coli was resistant to the tested penicillins, cephalosporins and aminoglycosides except for amikacin since it appeared to be sensitive to meropenem, imipenem, amikacin and ciprofloxacin in 90.9%, 81.8%, 81.8% and 63.6% of cases respectively. Staphylococcus hominis was resistant to most of the tested antibiotics, but it showed 100% sensitivity to each of tigecycline and methepreme. Proteus species were 100% resistant to the tested antibiotics except for amikacin, meropenem, fosfomycin, and tazocin, where they were 100% sensitive for these antibiotics. Pasteurella pneumotropica was 100% resistant to the tested antibiotics except for amikacin and meropenem since it appeared to be 100% sensitive for each one of them.

Table 5: The antibiotic resistance of common organisms, based on blood culture, in early-onset sepsis.

Antibiotics	E. coli	Staph. hominis	Proteus species	Pasteurella pneumotropica
Ampicillin	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Oxacillin	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Amoxicillin	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Ceftriaxone	9 (81.8%)	7 (100%)	1 (100%)	1 (100%)
Cefotaxime	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Ceftazidime	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Cefoxitin	8 (72.7%)	7 (100%)	1 (100%)	1 (100%)
Gentamicin	9 (81.8%)	7 (100%)	1 (100%)	1 (100%)
Amikacin	2 (18.2%)	7 (100%)	0 (0%)	0 (0%)
Vancomycin	11 (100%)	6 (85.7%)	1 (100%)	1 (100%)
Azithromycin	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Erythromycin	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Imipenem	2 (18.2%)	7 (100%)	1 (100%)	1 (100%)
Meropenem	1 (9.1%)	7 (100%)	0 (0%)	0 (0%)
Tetracycline	9 (81.8%)	6 (85.7%)	1 (100%)	1 (100%)
Metheprime	6 (54.5%)	5 (71.4%)	1 (100%)	1 (100%)
Ciprofloxacin	4 (36.4%)	0 (0%)	1 (100%)	1 (100%)
Fosfomycin	11 (100%)	7 (100%)	1 (100%)	1 (100%)
Colistin	9 (81.8%)	7 (100%)	0 (0%)	1 (100%)
Tigecycline	11 (100%)	0 (0%)	1 (100%)	1 (100%)
Tazocin	6 (54.5%)	7 (100%)	0 (0%)	1 (100%)

Discussion

Neonatal sepsis remains the major cause of morbidity and mortality in most of the neonatal intensive care units internationally. Hence, we should continually update our knowledge on the causative microorganisms, possible risk factors, and the emergence of multi-drug resistance microbial strains which drastically affect the outcome of management. Physicians should aim to facilitate the emergence of a potential empirical antibiotic therapy depending on the knowledge of their epidemiological factors and the antimicrobial susceptibility in connection with spatial and temporal epidemiology of neonatal sepsis [(6)]. Our study showed that the Iraqi in the Diyala governorate were more susceptible to develop late-onset neonatal sepsis (77.4%). Besides, the onset of the development of neonatal sepsis had a significant relationship with the gestational age and mode of delivery as p-values were equal to 0.03 and 0.045, respectively. Thus premature neonates were more prone to develop late-onset neonatal sepsis than term neonates as the relative risk was 2.8, and those who were the product of cesarean section appeared to be at a higher risk of developing late-onset neonatal sepsis as the relative risk was 2.54. Furthermore, multi-drug resistance was a problem for most of the causative microorganisms. The most common causative microorganism of early-onset neonatal sepsis was Escherichia coli in 45.8% of cases, and the second most common causative microorganism was Staphylococcus hominis which is a member of coagulase-negative staphylococcus and present in 20.8% of cases. In contrast, those causing late-onset neonatal sepsis were principally Gram-negative bacilli, represented by Klebsiella pneumonia (46.34%), Acinetobacter baumannii (24.4%), and coagulase-negative staphylococci (17.1%).

Jiang et al. (2014) mentioned that late-onset neonatal sepsis occurred in 71.9% of cases, and late-onset neonatal sepsis was more common in premature infants [(11)]. In Kosovo, Julia (2018) found that the incidence rate of neonatal sepsis was 18.9% among them, 63.6% were EOS, and 34.6% were LOS [(12)]. In Norway, Ronnestad (2005) reported that the incidence of LOS was 19.7% among neonates with low birth weight less than 1500gm and the most common pathogens were coagulase-negative staphylococci followed by *Candida* species [(13)]. In Croatia, Stemberger and tešović (2012) found that preterm infants were more prone to both EOS and LOS and the most common causative agents of EOS were gram-negative rods including E. coli, Klebsiella species, and Pseudomonas while those causing LOS were staphylococci and enterococci [(14)]. Similarly, Gowda et al. (2017) found that late-onset neonatal sepsis had a significant relationship with the prematurity [(15)]. Kilani Basamad (2000) reported that E. coli was the most common causative agent of early-onset sepsis [(16)]. In Australia, Braye et al. (2019) stated that E. coli and GBS were the most common causative agents of EOS in preterm and term babies, respectively [(17)]. Berardi A. et al. (2019) mentioned that LOS was significantly associated with prematurity in Italian and the most common causative organisms were coagulase-negative staphylococci, E. coli, Staphylococcus aureus and Enterobacteriaceae [(18)]. In India, Dudeja (2020) stated that in developing countries the more commonly encountered pathogens in causing neonatal sepsis were Gram-negative organisms represented by Acinetobacter and Klebsiella species, as well as E. coli [(19)]. In 2011, Stoll and coworkers stated that the most significant pathogen in preterm infants was E. coli [(20)]. Jiang and colleagues (2014) declared that the most encountered microorganism in the early onset neonatal sepsis were group B streptococci and E. coli [(11)]. In 2015, Ansari and collaborators confirmed that the coagulase-negative staphylococcus, Staphylococcus aureus, Acinetobacter species, and Klebsiella pneumoniae were the most common etiological agents of late-onset neonatal sepsis [(21)]. Jiang et al. (2014) stated that among the most common pathogens causing late-onset neonatal sepses were Klebsiella pneumoniae and Acinetobacter baumannii [(11)]. On the other hand, Lee and associates (2004) stated that they did not encounter E. coli septicemia since early-onset neonatal sepsis was minimal in their study sample [(22)]. Arild Rønnestad and Tore Gunnar Abraha (1998) found that coagulase-negative staphylococci were the main causative organism in the early and late-onset neonatal sepsis [(23)]. Berger et al. (1998) reported that the most common pathogen causing early-onset sepsis was group B streptococcus [(24)].

These heterogeneities of the results from those existing studies might associate with the geographic and temporal variations of specific populations, and other differences related to demographics, ethnicity, the climate, and the environment, and the overall status of the healthcare system. Our study has some limitations, including the relatively small sample size from a single tertiary healthcare centre using a covenant sampling method, the implementation of convenient sampling, and the lack of random selection of patients. Hence, future studies, including randomized controlled trials and meta-analytic studies in combination with predictive modelling and machine learning algorithms, are essential [25]. Furthermore, the prolonged hospital stay, improper application of infection control programs, overcrowding of neonates, and the improper use of empirical therapy might be the aetiology behind the increment in the incidence rate of late-onset neonatal sepsis and the spread of hospital-acquired infections in our hospital. Therefore, regular and vigilant monitoring, evaluation of the neonatal intensive care unit measures, and reviewing the proper use of antimicrobial therapies are necessary to prevent and eliminate late-onset neonatal sepsis.

Conclusions

Late-onset neonatal sepsis appeared to be more common in our tertiary healthcare institute than early-onset neonatal sepsis. Klebsiella pneumonia, Acinetobacter baumannii, staphylococcus epidermidis, and Staphylococcus haemolyticus were the most common causative microorganisms. Late-onset neonatal sepsis appeared to be significantly associated with the prematurity and caesarian section. The increment in the incidence of late-onset neonatal sepsis and the antimicrobial resistance, including the horrific multi-drug resistance, necessitates the avoidance of overcrowding of neonates in intensive care units, minimizing the use of invasive interventional, the unnecessary use of broad-spectrum antibiotics, and the prolonged duration of treatment. Indeed, the application of infection control programs in the neonatal intensive care unit is critical to prevent and the development of neonatal sepsis.

Conflicts of Interest: The authors declare no conflict of interest.

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Ethical Considerations

The ethics committee and the institutional review board of Al-Batool teaching hospital approved the study in 2018. The authors carried out the work described in this manuscript following the Code of Ethics of the World Medical Association (Declaration of Helsinki) on medical research involving human subjects, the EU Directive (210/63/EU), and the uniform requirements for manuscripts submitted to biomedical journals and the ethical principles defined in the Farmington Consensus of 1997. We acquired informed consent from the parents, or the guardians, of each patient. The patients were not subjected to further risk, and we dealt with their information dealt with complete confidentiality, and only the data curator had access to them, while other researchers were blinded.

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