

Original Article

Trends in neonatal sepsis: bacteriological profile, and antibiotic resistance pattern at a tertiary care hospital in Egypt

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Abstract

Introduction: Neonatal sepsis is a life-threatening bloodstream infection that occurs within the first 4 weeks of life and represents a significant cause of illness and death, especially in developing countries. Regular assessment of the local causative agents and their resistance patterns is important for effective management. This study aimed to determine the microbiological profile of neonatal sepsis and its antibiotic resistance patterns.

Methodology: Our study was conducted on 237 neonates suspected of sepsis. Blood samples were collected and inoculated into BACT/ALERT blood culture bottles. Bacteria causing positive blood cultures were identified conventionally and confirmed to the species level using MALDI-TOF MS. Antibiotic susceptibility patterns were identified using the disk diffusion method in combination with the VITEK® 2 compact system. Data analysis was performed using version 28 of SPSS software.

Results: The overall rate of neonatal sepsis was 33.8% (80/237). Of these, 54 (67.5%) and 26 (32.5%) were caused by Gram-negative and Gram-positive bacteria, respectively. *Klebsiella pneumoniae* 38 (47.5%) was the dominant causative pathogen, followed by coagulase-negative *Staphylococci* (CoNS) 24 (30%). Multidrug resistance (MDR) and extensively drug resistance (XDR) were detected in 82.5% and 10% respectively. An alarmingly high incidence of carbapenem-resistance (90.7%) was detected among Gram-negative bacteria. Methicillin resistance was detected in *S. aureus* and CoNS in 100% and 54.2%, respectively. Tigecycline was the most effective antibiotic for both Gram-positive and Gram-negative bacteria.

Conclusions: Our study showed that neonatal sepsis is mostly caused by MDR pathogens, predominantly *Klebsiella pneumoniae*, urging revised empirical treatments and stricter infection control measures.

Key words: Multidrug resistance (MDR); neonatal sepsis; early-onset sepsis; late-onset sepsis; BACT/ALERT; MALDI-TOF MS.

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Introduction

Neonatal sepsis is defined as a life-threatening bloodstream infection that occurs within the first 4 weeks after birth [1]. In developing countries, it represents a significant cause of illness and death among newborns [2] and requires intense management due to multi-system affection [3].

Based on the onset time, neonatal sepsis is divided into two categories: early-onset and late-onset sepsis [4]. Early-onset sepsis (EOS) occurs within the first 72 hours (three days) after birth and is typically caused by microbes present in the mother's genital tract before or during delivery [5]. Many factors, including vaginal infection or colonization, prematurity, low birth weight, and lack of antenatal care, are commonly reported as risk factors for EOS [6]. Late-onset sepsis (LOS) occurs

after the third day of life and is considered to be either a community- or hospital-acquired infection [7].

Newborns are more vulnerable to bacterial infections than older children due to their immature immune systems. They have a weak inflammatory response to infection, low antibody levels, and reduced complement activity [8]. In addition, newborns in the Neonatal Intensive Care Unit (NICU) are most liable to multidrug-resistant (MDR) bacterial infections due to many factors, including low birth weight, small gestational age, weak immunity, invasive procedures, prolonged antibiotic therapy, prolonged hospital stays (≥ 5 days), and low adherence to infection control measures. Neonatal sepsis caused by MDR organisms was linked to a high rate of mortality [9].

The distribution of pathogenic agents causing

neonatal sepsis varies over time from one country to another, among different locations within the same country, and even within the same setting from time to time. This variation is mainly attributed to changes in antibiotic prescribing practices, the emergence of antibiotic-resistant bacteria, and alterations in lifestyle and healthcare activities [10]. The causative bacteria of neonatal sepsis became more resistant to the commonly used empirical antibiotic agents, making the empirical treatment of these infections much more difficult [11].

It is critical for each NICU to regularly assess the local etiology of sepsis, update antibiotic resistance patterns, and compare findings with clinical profiles to identify the possible risk factors. Such practices will ensure the proper selection of empirical antibiotic therapy and support the development of effective management strategies [12]. Therefore, we aimed to study the onset, bacteriological profile, antibiotic resistance pattern, associated factors, and outcome of neonatal sepsis at Al-Zahraa University Hospital.

Methodology

Sample size determination

The sample size was estimated to be 237 using the online Raosoft® sample size calculator [13]. The parameters included a 5% margin of error, a 95% confidence level, and a 19 % expected response distribution [14]. In 2024, the Egyptian population size was approximately 116.5 million.

Study design

This prospective observational cross-sectional study was conducted on 237 neonates suspected of having neonatal sepsis and admitted to the NICU at Al-Zahraa University Hospital, Cairo, Egypt, during the period from September 2024 to April 2025.

Ethical statement

Our study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine (for Girls), Al-Azhar University, Cairo, Egypt, with approval number 2024092515. Informed consent was obtained from the participant's parents after clarifying the study's aim and safety and before sampling.

Study population

All neonates aged from 0 to 28 days, either preterm (gestational age < 37 weeks), full term (gestational age = 37-42 weeks), or postdate (gestational age > 42 weeks), who were suspected of having sepsis by presenting one or more of the following signs or

symptoms: elevated body temperature ($\geq 38.0^{\circ}\text{C}$), hypothermia ($\leq 36.5^{\circ}\text{C}$), decreased alertness, seizures, poor feeding, respiratory distress, bulging fontanel, vomiting, yellowing of the skin or eyes (jaundice), and infections at the site of the umbilical stump were included in the study. The study excluded neonates who did not fulfill the inclusion criteria, had negative blood culture results, or displayed fungal growth.

Study setting

This study was performed in a tertiary-level NICU that provides full ventilatory support, invasive monitoring, and multidisciplinary care for critically ill and extremely premature neonates. According to the American Academy of Pediatrics (AAP) guidelines, all neonates referred to the NICU with suspected sepsis received empirical antimicrobial therapy. The antibiotic empirical protocol included ampicillin plus gentamicin for EOS and vancomycin plus cefotaxime or gentamicin for LOS. Blood cultures were withdrawn before antibiotic administration, and the administered antibiotics were adjusted based on the results of culture and sensitivity. Discontinuation of antibiotics was performed in culture-negative cases within 36-48 hours in clinically stable neonates. In our cohort study, some neonates required chest tube insertion to manage pneumothorax, which occurred either spontaneously or as a sequela of meconium aspiration syndrome (MAS).

Data collection

Socio-demographic data, clinical characteristics, and laboratory parameters, including gestational age, sex, sepsis onset, birth weight, premature rupture of membrane (PROM), meconium-stained amniotic fluid (MSAF), hospital stays (in days), endotracheal intubation (ETT), chest tube insertion, central venous line (CVL) insertion, C-reactive protein (CRP) level, and outcome, were collected for each neonate from neonatal case sheets available in hospital records. Sepsis-related death was defined as death occurring within seven days of drawing a positive blood culture sample. The collected data were then analyzed using appropriate statistical methods.

Blood sample collection and culture

Blood samples were collected from all neonates suspected of having sepsis before initiating the antibiotic therapy. Using aseptic technique, 2 mL of blood was withdrawn from a peripheral vein and immediately inoculated on BACT/ALERT® PF Plus pediatric culture bottles with Ref. No. 410853 (BioMérieux, USA), which allows recovery and

detection of aerobic and facultative anaerobic microorganisms. The culture bottles were then transported to the microbiology unit to be incubated in BACT/ALERT 3D 60 (BioMérieux, USA) within 1 hour of the collection. This automated system monitors bacterial growth utilizing a colorimetric sensor, which detects elevated carbon dioxide production resulting from microbial growth. Negative results were considered when the blood culture bottles didn't give a signal for microbial growth after one week of incubation [15].

Bacterial isolation and identification

The blood culture bottles that flagged positive were sub-cultured on blood and MacConkey's agar plates (Oxoid, UK) and incubated aerobically at 37 °C for 24-48 hours. The isolated bacteria were identified conventionally based on culture characteristics, Gram staining, and a series of biochemical tests [16]. Biochemical tests for Gram-positive isolates included catalase, coagulase, DNase agar, and mannitol fermentation. Biochemical assays for Gram-negative isolates included motility assessment, indole production, ornithine decarboxylation, triple sugar iron test, citrate utilization, urease production, and oxidase activity tests [17]. Species-level identification/confirmation of all isolates was performed using Matrix Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) instrument (LT2 Plus, Scientific Analysis Instruments Co., Ltd, UK). The American Type Culture Collection (ATCC) standards were used to ensure the quality of all media and biochemical tests. Commensal organisms such as CoNs were considered true pathogens only when isolated from two separate blood cultures, along with clinical signs indicative of sepsis.

Antimicrobial susceptibility testing (AST)

A broad range of antibiotics was tested using the disk diffusion method. For antibiotics (vancomycin, colistin, and tigecycline) that are not recommended to be tested by the disk diffusion method, the VITEK® 2 (BioMérieux, USA) compact system was used.

Disk diffusion method

Based on Clinical and Laboratory Standards Institute (CLSI) guidelines [18]. The Kirby–Bauer method was conducted on Mueller-Hinton agar (MHA) (Oxoid, UK) plates. A turbidity level equal to 0.5 MacFarland was prepared and then swabbed on MHA plates. Discs of the antibiotics were then added and

incubated aerobically at 37°C for 18 hours. All antibiotic discs (Oxoid, UK) used were chosen according to CLSI recommendations and availability and included ampicillin (10 µg), ampicillin/sulbactam (10/10 µg), piperacillin (100 µg), piperacillin/tazobactam (100/10 µg), cefazolin (30 µg), cefoxitin (30 µg), cefotaxime (30 µg), ceftazidime (30 µg), cefepime (30 µg), imipenem (10 µg), meropenem (10 µg), gentamicin (10 µg), tobramycin (10 µg), amikacin (30 µg), ciprofloxacin (5 µg), levofloxacin (5 µg), trimethoprim-sulfamethoxazole (1.25/23.75 µg), tetracycline (30 µg), and minocycline (30 µg) for Gram-negative isolates. For Gram-positive isolates, the following antibiotic discs, including penicillin (10 µg), ampicillin (10 µg), ampicillin/sulbactam (10/10 µg), cefoxitin (30 µg), imipenem (10 µg), meropenem (10 µg), gentamicin (10 µg), ciprofloxacin (5 µg), levofloxacin (5 µg), moxifloxacin (5 µg), trimethoprim-sulfamethoxazole (1.25/23.75 µg), tetracycline (30 µg), erythromycin (15 µg), clindamycin (2 µg), quinupristin/dalfopristin (15 µg), and linezolid (30 µg), were used. Based on inhibition zones of the tested antibiotics, the bacterial isolates were classified into sensitive or resistant after interpretation according to the CLSI recommendations [18]. Multidrug resistance (MDR) was defined as un-susceptibility to at least one antibiotic agent in \geq different antibiotic categories; extensively drug resistance (XDR) was defined as resistance against all antibiotics except one or two classes, while pan drug resistance (PDR) was defined as un-susceptibility to all antimicrobial agents in all antibiotic classes [19]. For Gram-positive bacteria, methicillin-resistant coagulase-negative *Staphylococci* (MR CoNS) were reported if the diameter of the inhibition zone around the cefoxitin disk was \leq 24 mm, while methicillin-resistant *S. aureus* (MRSA) was reported if the diameter of the inhibition zone around the cefoxitin disk was \leq 21 mm [18].

Minimal Inhibitory Concentration (MIC) Testing

Minimum inhibitory concentrations (MICs) of the tested antibiotics were determined using the automated VITEK® 2 compact system, with the aid of AST GP67, AST GN73, and AST GN222 cards, with MIC results interpreted according to CLSI breakpoints [18].

Statistical Analysis

Version 28 of the SPSS software (IBM Corp., USA) was utilized to analyze the data. Descriptive measures, including mean and median, were used to summarize the quantitative data. Count (frequency) and percent (%) were used to describe the categorical data. The chi-

square (χ^2) test was utilized to evaluate associations between categorical data [20]. The variables that showed statistical significance in the univariate analysis were entered into a multivariate logistic regression model using the forward conditional method to detect risk factors of neonatal death [21]. A $p < 0.05$ was considered statistically significant.

Results

Prevalence of culture-positive neonatal sepsis

This study was conducted on 237 neonates admitted with suspected septicemia to the NICU at Al-Zahraa University Hospital during the study period. Eighty (33.8%) neonates showed confirmed sepsis based on positive blood culture results. Each neonate with confirmed sepsis experienced only one episode, and one pathogenic organism was isolated per case.

Demographic and clinical data of the septic participants

Among neonates with confirmed sepsis, gestational ages ranged from 33 to 41 weeks, with a mean of 37.2

Table 1. Socio-demographic and clinical characteristics of neonates with bacteremia (n = 80).

Characteristics	Frq (n = 80)	%
Term		
Full Term	54	67.5
Pre-Term	26	32.5
Sex		
Female	24	30.0
Male	56	70.0
Onset		
Early	56	70.0
Late	24	30.0
Birth weight		
< 2.5	14	17.5
≥ 2.5	66	82.5
Premature rupture of membranes		
Yes	24	30.0
No	56	70.0
Meconium-stained Amniotic Fluid		
Yes	11	13.8
No	69	86.3
Hospital stays		
≤ 7 days	48	60.0
> 7 days	32	40.0
Endotracheal tube		
Yes	42	52.5
No	38	47.5
Chest tube		
Yes	8	10.0
No	72	90.0
Central Venous Line		
Yes	72	90.0
No	8	10.0
C-Reactive Protein		
Positive	74	92.5
Negative	6	7.5
Outcome		
Death	26	32.5
Discharge	54	67.5

Data are displayed in the form of frequency and percentages.

Table 2. Distribution of the isolated pathogens.

Isolates	Frq (n = 80)	%
Gram-negative bacteria (n = 54)		
<i>Klebsiella pneumoniae</i>	38	47.5
<i>Acinetobacter baumannii</i>	16	20
Gram-positive bacteria (n = 26)		
<i>Staphylococcus hemolyticus</i> (CoNS)	10	12.5
<i>Staphylococcus hominis</i> (CoNS)	7	8.75
<i>Staph epidermidis</i> (CoNS)	7	8.75
<i>Staph aureus</i>	2	2.5

Data are displayed in the form of frequency and percentages.

weeks. Birth weights varied from 1.7 to 4 kg, with a mean of 3 kg. Hospital stay durations ranged from 3 to 17 days, with a mean of 7.1 days. EOS was reported in 70% of cases, while LOS was found in 30%. The overall sepsis rate was higher among males (70%) than among females (30%). Approximately one-third (26, 32.5%) of the septic cases died, whereas the other 54 (67.5%) cases were discharged. Table 1 illustrates all relevant socio-demographic and clinical characteristics of neonates with sepsis-positive blood cultures.

Distribution of the isolated pathogens

Among all isolated pathogens (80), Gram-negative bacteria were detected in 54/80 (67.5%), whereas Gram-positive bacteria were found in 26/80 (32.5%). Among the Gram-negative isolates, *Klebsiella pneumoniae* was the most frequently isolated pathogen, 38/80 (47.5%), followed by *Acinetobacter baumannii*, 16/80 (20%). Most Gram-positive isolates were CoNS 24/80 (30%), followed by *Staphylococcus aureus* 2/80 (2.5%). Table 2 provides the overall distribution of isolated pathogens.

Association between different types of organisms and neonatal characteristics

The distribution of isolated pathogens varied significantly across different clinical variables. *Klebsiella pneumoniae* was the most prevalent organism overall. While *Klebsiella pneumoniae* was significantly reported in full-term infants (51.9%) and in EOS cases (55.4%), *Acinetobacter baumannii* was more frequent in cases with prolonged hospitalization (> 7 days) (37.5%). There was no significant correlation between these two Gram-negative organisms and the other clinical data of the patients. Similarly, no significant association was found concerning Gram-positive bacteria and the neonatal data as presented in Table 3.

Table 3. Association between different types of organisms and neonatal data.

Characteristic	Organism type								P
	CoNS (n = 24)		<i>Staph aureus</i> (n = 2)		<i>Klebsiella pneumoniae</i> (n = 38)		<i>Acinetobacter baumannii</i> (n = 16)		
	n	%	n	%	n	%	n	%	
Full term (n = 54)	18	33.3	2	3.7	28	51.9	6	11.1	0.036*
Male (n = 56)	16	28.6	2	3.6	28	50.0	10	17.9	0.730
Early onset sepsis (n = 56)	17	30.4	2	3.6	31	55.4	6	10.7	0.011*
Low birth weight (< 2.5 kg) (n = 14)	4	28.6	0	0.0	6	42.9	4	28.6	0.786
Premature rupture of membranes (n = 24)	8	33.3	0	0.0	8	33.3	8	33.3	0.151
Meconium-stained amniotic fluid (n = 11)	3	27.3	0	0.0	6	54.5	2	18.2	1
Hospital stays > 7 days (n = 32)	9	28.1	0	0.0	11	34.4	12	37.5	0.008*
Endotracheal intubation (n = 42)	12	28.6	0	0.0	20	47.6	10	23.8	0.495
Chest tube insertion (n = 8)	0	0.0	0	0.0	6	75.0	2	25.0	0.170
Central venous line insertion (n = 72)	22	30.6	2	2.8	32	44.4	16	22.2	0.350
Positive C-reactive protein (n = 74)	22	29.7	2	2.7	34	45.9	16	21.6	0.548

Data are displayed in the form of frequency and percentages; p is statistically significant at < 0.05.

Table 4. Antibiotic resistance pattern of the obtained Gram-negative isolates.

Antibiotic	Bacterial resistance rate to antimicrobial agents (%)				Total n (%)
	<i>Klebsiella pneumoniae</i> (n = 38)		<i>Acinetobacter baumannii</i> (n = 16)		
	n*	%*	n*	%*	
Ampicillin	38	100	NA*	NA*	38 (100)
Ampicillin/sulbactam	38	100	16	100	54 (100)
Piperacillin	38	100	16	100	54 (100)
Piperacillin/tazobactam	34	89.5	16	100	50 (92.6)
Cefazolin	38	100	NA*	NA*	38 (100)
Cefoxitin	31	81.6	NA*	NA*	31 (81.6)
Cefotaxime	38	100	16	100	54 (100)
Ceftazidime	38	100	16	100	54 (100)
Cefepime	38	100	16	100	54 (100)
Imipenem	33	86.8	16	100	49 (90.7)
Meropenem	32	84.2	16	100	48 (88.9)
Ciprofloxacin	32	84.2	16	100	48 (88.9)
Levofloxacin	30	78.9	14	87.5	44 (81.5)
Gentamicin	21	55.3	16	100	37 (68.5)
Tobramycin	26	68.4	16	100	42 (77.8)
Amikacin	22	57.9	11	68.8	33 (61.1)
Colistin	5	13.2	2	12.5	7 (13.0)
SXT	34	89.5	16	100	50 (92.6)
Tetracycline	9	23.7	6	37.5	15 (27.8)
Tigecycline	4	10.5	2	12.5	6 (11.1)
Minocycline	10	26.3	2	12.5	12 (22.2)

Data are presented as numbers and percentages; n* = number of resistant isolates; %* antibiotic resistance rate. NA: not applicable; SXT: trimethoprim-sulfamethoxazole.

Table 5. Antibiotic resistance pattern of the obtained Gram-positive isolates.

Antibiotic	Bacterial resistance rate to antimicrobial agents (%)				Total (n = 26) n (%)
	CoNS (n = 24)		<i>Staph aureus</i> (n = 2)		
	n*	%*	n*	%*	
Penicillin	24	100	2	100	26 (100)
Ampicillin	24	100	2	100	26 (100)
Ampicillin/sulbactam	22	91.7	2	100	24 (92.3)
Cefoxitin	13	54.2	2	100	15 (57.7)
Imipenem	13	54.2	2	100	15 (57.7)
Meropenem	13	54.2	2	100	15 (57.7)
Ciprofloxacin	12	50.0	2	100	14 (53.8)
Levofloxacin	12	50.0	2	100	14 (53.8)
Moxifloxacin	10	43.5	2	100	12 (46.2)
Gentamicin	10	41.7	2	100	12 (46.2)
SXT	12	50.0	1	50.0	13 (50)
Tetracycline	12	50.0	0	0.0	12 (46.2)
Tigecycline	0	0.0	0	0.0	0 (0.0)
Erythromycin	18	75.0	2	100	20 (76.9)
Clindamycin	16	66.7	2	100	18 (69.2)
Quinupristin/dalfopristin	2	8.3	0	0.0	2 (7.7)
Linezolid	0	0.0	0	0.0	0 (0.0)
Vancomycin	0	0.0	0	0.0	0 (0.0)

Data are presented as numbers and percentages; n* = number of resistant isolates; %* antibiotic resistance rate. CoNS: coagulase-negative *Staphylococci*; SXT: trimethoprim-sulfamethoxazole.

Table 6. Distribution of MDR and XDR among the obtained organisms.

Resistance level	CoNS (n = 24)		<i>Staph aureus</i> (n = 2)		<i>Klebsiella pneumoniae</i> (n = 38)		<i>Acinetobacter baumannii</i> (n = 16)		p
	n	%	n	%	n	%	n	%	
Sensitive	6	25	0	0	0	0	0	0	
MDR	18	75	2	100	32	84.2	14	87.5	0.003*
XDR	0	0	0	0	6	15.8	2	12.5	
MR-CoNS	13	54.2	0	-	-	-	-	-	
MRSA	-	-	2	100	-	-	-	-	< 0.001*
CR	-	-	-	-	33	86.8	16	100	

Data are displayed in the form of counts and percentages; p is statistically significant at < 0.05. MR-CoNS: methicillin-resistant coagulase-negative *Staphylococci*; CR: carbapenem resistance.

Antibiotic resistance pattern of the obtained isolates
Gram-negative bacteria

Table 4 illustrates the resistance patterns of Gram-negative isolates. All *Acinetobacter baumannii* and *Klebsiella pneumoniae* isolates (100%) were resistant to many beta-lactam antibiotics, including ampicillin, ampicillin/sulbactam, piperacillin, cefazolin, cefotaxime, ceftazidime, and cefepime. In addition, all *Acinetobacter baumannii* isolates (100%) were unsusceptible to many other antibiotics, including imipenem, meropenem, ciprofloxacin, gentamicin, and tobramycin. The lowest resistance rates among both organisms were reported against tigecycline (11.1%), colistin (13%), and minocycline (22.2%).

Gram-positive bacteria

Table 5 illustrates the antibiotic resistance rates among Gram-positive isolates. For CoNS, the highest resistance rates were reported against penicillin, ampicillin (100% for each), ampicillin/sulbactam (91.7%), erythromycin (75%), and clindamycin (66.7%), while the lowest resistance rates were reported

against tigecycline, linezolid (0% for each), and quinupristin/dalfopristin (8.3%). Only two *S. aureus* isolates were obtained and confirmed as MRSA. These two isolates were resistant to many tested antibiotics across several classes, including beta-lactams, aminoglycosides, quinolones, and macrolides. However, they exhibited sensitivity to tetracycline, tigecycline, quinupristin/dalfopristin, vancomycin, and linezolid.

Prevalence of MDR and XDR among the obtained isolates

Collectively, 66 out of 80 isolates (82.5%) were MDR and 8 (10%) were XDR, while the remaining 6 isolates (7.7%) were sensitive. All XDR isolates were Gram-negative, while all sensitive isolates were CoNS. No PDR isolates were observed. MDR and carbapenem resistance were significantly higher in *Acinetobacter baumannii*, while XDR was significantly higher in *Klebsiella pneumoniae*. Table 6 illustrates the distribution of MDR, XDR, and the resistance mechanisms among the obtained organisms.

Table 7. Relation between different variables with neonatal outcome.

Variable	Neonatal Outcome				p
	Died (n = 26)		Discharge (n=54)		
	n	%	n	%	
Preterm	14	53.8	12	22.2	0.005*
Male	16	61.5	40	74.1	0.252
Early onset sepsis	18	69.2	38	70.4	0.917
Low birth weight (< 2.5 kg)	10	38.5	4	7.4	0.001*
Premature rupture of membranes	6	23.1	18	33.3	0.348
Meconium-stained amniotic fluid	0	0.0	11	20.4	0.013*
Hospital stays > 7 days	12	46.2	20	37.0	0.436
Endotracheal intubation	24	92.3	18	33.3	< 0.001*
Chest tube insertion	6	23.1	2	3.7	0.013*
Central venous line insertion	24	92.3	48	88.9	1
Positive C-reactive protein	24	92.3	50	92.6	1
Isolated bacteria					
Gram-positive	6	23.1	20	37.0	
Gram-negative	20	76.9	34	63.0	0.212
CoNS	6	23.1	18	33.3	
<i>Staph aureus</i>	0	0.0	2	3.7	
<i>Klebsiella pneumoniae</i>	14	53.8	24	44.4	0.653
<i>Acinetobacter baumannii</i>	6	23.1	10	18.5	
Antibiotic resistance					
MDR	24	92.3	50	92.6	
Sensitive	2	7.7	4	7.4	1

Data are displayed in the form of numbers and percentages; p is statistically significant at < 0.05.

Table 8. Multivariate logistic regression for prediction of neonatal mortality.

Death	<i>p</i>	AOR	95% CI	
			Lower	Upper
ETT	< 0.001*	25.452	4.927	131.489
Chest tube	0.049*	< 0.001	1.013	83.678

p is statistically significant at < 0.05. ETT: endotracheal tube; AOR: adjusted odd ratio; CI: confidence interval.

Neonatal sepsis outcomes and determinants of mortality

Out of 80 septic cases, 26 (32.5%) cases died, whereas the other 54 (67.5%) cases were discharged. Preterm birth was significantly higher among neonates who died compared to those who survived (53.8% vs. 22.2%, $p = 0.005$). Infants with low birth weight (< 2.5 kg) were significantly more represented among the mortality group compared to the survival group (38.5% vs. 7.4%, $p = 0.001$). A paradoxical finding emerged regarding meconium-stained amniotic fluid, where it was significantly more frequent among neonates who survived compared to those who died (20.4% vs. 0.0%, $p = 0.013$). Endotracheal intubation and chest tube insertion were significantly more frequent among neonates who died than among those who survived (92.3% vs. 33.3%, $p < 0.001$; and 23.1 vs. 3.7, $p = 0.013$, respectively). On the other hand, no significant differences in outcomes were observed for sex, sepsis onset, duration of hospital stay, premature rupture of membranes, central venous line placement, C-reactive protein levels, type of organism, or multidrug-resistant infection status as presented in Table 7.

Variables that were statistically significant in the univariate analysis ($p < 0.05$), including premature birth, low birth weight, endotracheal intubation, and chest tube insertion, were entered into a multivariate logistic regression model using the forward conditional method to identify independent predictors of mortality. Endotracheal intubation and chest tube placement were reported to be risk factors of neonatal death (AOR = 25.452, 95% CI = 4.927–131.489, $p \leq 0.001$; AOR = 0.001, 95% CI = 1.013–83.678, $p = 0.049$), respectively, as shown in Table 8.

Discussion

Neonatal sepsis is considered one of the critical causes of illness and mortality, specifically in countries with low- and middle-income. This infection occurs in infants within the earliest 4 weeks of life and has been identified as a critical problem worldwide. Treating such infections successfully becomes difficult in settings with limited resources, and the growing resistance to antibiotics globally makes treating these infections harder [22].

The distribution of pathogenic agents causing

neonatal sepsis and their antibiotic resistance patterns varies within the same setting from time to other. The microbial agents causing neonatal sepsis developed resistance to the frequently used empirical antibiotics [2]. Accordingly, identifying the current common pathogens causing this infection and their updated antibiotic resistance patterns will help in the proper selection of empirical antibiotic therapy and support the development of effective management strategies.

In the current study, eighty (33.8%) neonates showed confirmed sepsis based on positive blood culture results. A similar result was reported in Nigeria by Shobowale *et al.* [23], who showed that 34% of neonates had positive blood cultures. In Ethiopia, a study performed by Fenta *et al.* [24] documented a similar result at a rate of 27.2%. A lower rate was reported by another Egyptian study done by Gaballah *et al.* [14], who reported that sepsis was confirmed only in 19% of neonates. Another study conducted in Ghana by Aku *et al.* [25] reported much lower results of culture-positive sepsis at a rate of 17.3%. This discrepancy in results may be caused by variations in study settings, sample size, neonatal characteristics, research methodology, sampling techniques, and period of study.

In our study, a higher rate of EOS was reported in 70% of cases, and LOS was documented in 30%. The overall sepsis rate was higher among males (70%) than among females (30%). Approximately one-third (26, 32.5%) of the septic cases died, whereas 54 (67.5%) cases were discharged. This comes in accord with another study performed in Ethiopia by Fenta *et al.* [24], who found that 72% (48/67) of sepsis cases were EOS. In addition, Aku *et al.* [25] in Ghana reported EOS at a rate of 54%. The relatively high incidence of EOS in our study may be explained by several factors, including maternal risk factors (such as chorioamnionitis, inadequate intrapartum antibiotic prophylaxis, and limited antenatal screening for maternal infections), the characteristics of the study population, and local infection control practices. Meanwhile, an Egyptian study done by Gaballah *et al.* [14] reported EOS among 39.6% of cases and LOS in 60.4% of cases, with most cases of EOS (63%) being males, while the majority of LOS (61.5%) were females. Another Egyptian study conducted by Salama

et al [26] concluded that LOS was more common (58.8%) than EOS. Males represented 56.2% of premature neonates, and a high death rate (51.6%) was reported, especially among EOS. In Poland, a study conducted by Golińska *et al.* [27] documented a lower rate of EOS, 8.3% (29/349), compared to the high rate of LOS, 91.7% (320/349). In addition, a study performed in Germany by Tessema *et al.* [28] reported comparable findings with EOS at a rate of 13.4%. Certain countries may attribute these lower EOS rates to the use of antibiotics during obstetric care.

In our study, the most frequent pathogens were Gram-negative bacteria identified in 54/80 (67.5%) of cases, while Gram-positive bacteria were found in 26/80 (32.5%). Many studies conducted in different countries reported similar results with high prevalence of Gram-negative bacteria at rates of 73.6%, 62%, 75%, and 77%, respectively [14,26,29,30]. On the contrary, a study conducted in Ethiopia by G/Eyesus *et al* [31] revealed that Gram-positive organisms were the most isolated bacteria (67.5%). In addition, two other studies in Nigeria and India reported higher rates of Gram-positive bacteria [32,33]. In Europe, various studies have also reported a high prevalence of Gram-positive bacteria. For instance, a study conducted in Sweden by Oldendorff *et al.* [34] found that CoNS was the most frequently identified pathogen, accounting for 53.8%, followed by *S. aureus* at 24.9%, and Group B Streptococci (GBS) at 13.7%. Similarly, another study conducted in Slovenia by But *et al.* [35] reported that Gram-positive bacteria were identified in 57% of neonatal sepsis cases, with an even higher prevalence noted in LOS cases (88%). The most common pathogens identified there were GBS (25%), followed by CoNS (15%) and *S. aureus* (13%).

In this study, the most frequent isolated Gram-negative pathogen was *Klebsiella pneumoniae*, 38/80 (47.5%), followed by *Acinetobacter baumannii*, 16/80 (20%). Most Gram-positive isolates were CoNS 24/80 (30%), followed by *S. aureus* 2/80 (2.5%). Similar findings were reported by other Egyptian studies, which informed that *Klebsiella spp.* and CoNS were the most common isolated pathogens [26,36]. In addition, many other studies reported that *K. pneumoniae* was the most common isolated pathogen, accounting for 33.3%, 45.3%, and 54%, respectively [30,37,14]. The high prevalence of *Klebsiella pneumoniae* supports its significant role in nosocomial transmission, which can be attributed not only to a lack of hygienic practices and infection control measures but also to its ability to form biofilms, which facilitates colonization of medical devices, thereby enhancing its persistence and

resistance within the hospital environment.

Our results revealed a different distribution of pathogens between EOS and LOS. While *Klebsiella pneumoniae* was significantly reported in EOS cases, 31/56 (55.4%), *Acinetobacter baumannii* was more frequent in LOS cases, 10/24 (41.7%). Different results were reported by Almohammady *et al.* [37], who stated that *Klebsiella pneumoniae* was equally detected among both EOS and LOS cases. In addition, Sherif *et al.* [38] documented that the primary cause of EOS was *Klebsiella spp.* and *E. coli*, while the predominant cause of LOS was CoNS and *S. aureus*. Another study conducted in Saudi Arabia documented that 33.3% of EOS cases were caused by Group B Streptococcus, while 47.2% and 17.9% of LOS cases were caused by *Staphylococci* and *Klebsiella spp.*, respectively [39]. The observed discrepancies between results may be due to practices of healthcare workers towards infection control measures, maternal preparation, type of delivery, and study settings.

In this study, all *Klebsiella pneumoniae* and *Acinetobacter baumannii* isolates exhibited 100% resistance against many beta-lactam (ampicillins, cephalosporins) antibiotics. Additionally, all *A. baumannii* isolates were resistant to fluoroquinolones (ciprofloxacin), carbapenems (meropenem, imipenem), and aminoglycosides (gentamicin, tobramycin). The minimal resistance rates were documented against tigecycline (11.1%), colistin (13%), and minocycline (22.2%). In accordance with our results, Mohsen *et al.* [36] documented high resistance of Gram-negative bacteria to ampicillins and cephalosporins. Another Egyptian study conducted by Almohammady *et al.* [37] reported a 100% resistance rate of *Klebsiella spp.* towards many beta-lactam antibiotics associated with low susceptibility to amikacin, ciprofloxacin, and gentamicin at rates of 12%, 12%, and 6%, respectively. They also reported that *A. baumannii* isolates were resistant to ampicillins, cephalosporins, and carbapenems (imipenem, meropenem) with high susceptibility to polymyxin only. Moreover, Gaballah *et al.* [14] reported high resistance of *Klebsiella spp.* towards beta-lactam antibiotics with a much lower resistance rate to colistin (5%) and tigecycline (1%). On the other hand, G/Eyesus *et al.* [31] in Ethiopia reported a lower rate of resistance, with 94.4% of *K. pneumoniae* isolates sensitive to amikacin and 87.2% of isolates sensitive to gentamicin and ciprofloxacin.

In this study, the count of *S. aureus* isolates was extremely low to compare their susceptibility pattern with other studies, while CoNS were the most frequent Gram-positive isolates, demonstrating 100% resistance

rates against penicillin and ampicillin, 91.7% to ampicillin/sulbactam, and no resistance was reported against vancomycin, tigecycline, and linezolid. Our findings agreed with a study conducted in Nepal by Manandhar *et al.* [40], who reported a 100% resistance rate of CoNS to ampicillin. Sherif *et al.* [38] reported nearly similar results with high resistance to ampicillin (85%) and cloxacillin (94%). A similar result regarding vancomycin and linezolid was documented by Pokhrel *et al.* [30] and Almohammady *et al.* [37].

In our study, MDR was detected in 82.5% of isolates, with all *Acinetobacter baumannii* isolates being carbapenem-resistant (100%) and showing the highest rate of MDR. XDR was detected in 10% of isolates, with *Klebsiella pneumoniae* exhibiting a significantly higher rate. Similarly, another study conducted in Ethiopia by Sherif *et al.* [38] documented a high rate of MDR (84%) among neonatal sepsis, with all isolates of *Acinetobacter spp.* (100%) and 95% of *Klebsiella spp.* being MDR. In addition, Pokhrel *et al.* [30] in Nepal documented a similar higher rate of MDR (73.9%) among neonatal sepsis, with MDR Gram-negative bacteria representing the highest rate (80.8%). In contrast, Almohammady *et al.* [37] and Gaballah *et al.* [14] reported lower findings of MDR at rates of 69.7% and 65%, respectively. In Poland, a study done by Golińska *et al.* [27] reported that the prevalence of MDR microorganisms varied depending on the diagnosis. Methicillin-resistant CoNS was detected in both EOS and LOS at rates of 60% and 92.4%, respectively. In Gram-negative bacteria, ESBL production was observed in 25% of EOS and 19.6% of LOS cases.

In this study, approximately one-third (32.5%) of the septic neonates died. Compared to our findings, Salama *et al.* [26] showed a higher mortality rate of 51.6%, while Sherif *et al.* [38] and Fenta *et al.* [24] reported much lower mortality rates at 7% and 4.8%, respectively. The death rate was extremely higher in preterm infants ($p = 0.005$), in infants with low birth weight ($p = 0.001$), in those with endotracheal intubation ($p < 0.001$), and with chest tube placement ($p = 0.013$). Multivariable logistic regression was used to evaluate the association between neonatal death and these factors. Endotracheal intubation and chest tube placement were observed to be risk factors of neonatal death (AOR = 25.452, 95% CI = 4.927–131.489, $p \leq 0.001$, and AOR ≤ 0.001 , 95% CI = 1.013–83.678, $p = 0.049$), respectively. Another Egyptian study conducted by ElMashad *et al.* [41] reported a lower neonatal mortality rate (15.5%). Regarding risk factors, they reported similar results, with preterm delivery,

underweight at birth, and mechanical ventilation being significantly associated with a high death rate. In Ethiopia, a study conducted by Abiy *et al.* [42] found that low birth weight (< 2,500 g) and prematurity were significant predictors of neonatal mortality.

While the current study provides valuable data on the microbiological profile, their susceptibility, and critical MDR trends at our study site, it was not without limitations. Only two *Candida spp.* were identified during our study period; their exclusion may have minimal impact on the overall conclusions of the study. Additionally, being a single-center study, the findings may not be generalizable to other regions in Egypt. Furthermore, resistance patterns and microbial profiles change over time, and the results may not accurately reflect future trends without continuous surveillance.

Conclusions

Gram-negative bacteria, predominantly *Klebsiella pneumoniae*, made up the majority of sepsis-causing isolates. The alarming rates of carbapenem resistance among Gram-negative bacteria, as well as methicillin resistance among *Staphylococci spp.*, represent significant therapeutic challenges. Our study calls for the immediate implementation of enhanced infection control measures and routine antimicrobial resistance surveillance. Optimizing empirical treatment protocols based on localized susceptibility patterns, coupled with antimicrobial stewardship programs, is critical to facing this growing threat.

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Authors contributions

SMA: conceptualization, methodology, investigation, data curation, formal analysis, writing-original draft, and writing-review and editing. SE: conceptualization, enrolling the patients, methodology, investigation, and data curation. MMA: enrolling the patients, methodology, investigation, and data curation. ENAM: conceptualization, enrolling the patients, formal analysis, writing-review and editing. SAAS: conceptualization, methodology, writing-original draft, and writing-review and editing. All authors have approved the final version of the manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Conflict of interest

No conflict of interest is declared.

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