

Microbiological Spectrum of Neonatal Sepsis and Antibiotic Susceptibility Patterns

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Abstract:

Background: Newborn sepsis is still considered one of the important causes of morbidity and mortality among infants all around the world. As resistance develops to antibiotics and etiological agents vary with different clinical situations, it is now increasingly difficult to manage neonatal sepsis. Thus, knowledge about microbial flora and antibiotic susceptibility within a particular geographical area has become increasingly important.

Aim: To investigate the cause of sepsis in the microorganisms present in the neonates admitted at the tertiary care hospital.

Methodology: Hospital Level Observational Cross Sectional Study was conducted for one year in 120 babies with clinically confirmed sepsis admitted in NICU of Himalaya Medical College & Hospital, Paliganj, Patna, and Bihar, India. Blood samples from infants suffering from sepsis were subjected to culture and identification by traditional microbial methods. Isolated bacteria the sensitivity test was conducted using the Kirby-Bauer disc diffusion technique. All the data collected was subjected to statistical analysis through SPSS version 25.0.

Results: A total of 40.0% (48/120) had positive blood cultures. The most commonly identified pathogens included *K. pneumoniae* which made up 31.3% of the isolates, *S. aureus* (25.0%), and *E. coli* (16.7%). Gram negative bacilli were the most common group of pathogens, constituting 62.5% of all isolates. Microorganisms showed high sensitivity to meropenem and piperacillin-tazobactam, but were highly resistant to ampicillin. Neonates that were preterm showed significantly more positive cultures than neonates that were not (56.5% vs. 29.7%; $p = 0.008$).

Conclusion: Main bacteria that caused sepsis in babies were mainly Gram-negative organisms, and *Klebsiella Pneumoniae* was the commonest. Continuous surveillance for these organisms is therefore important. It is equally crucial to prevent sepsis among babies through proper antibiotic use.

Keywords: Neonatal sepsis; Microbiological profile; Antibiotic sensitivity; *Klebsiella pneumoniae*; Antimicrobial resistance; NICU.

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Introduction

Neonatal sepsis is known to be the leading cause of infant deaths and illnesses around the world, especially in third-world nations, since there are several issues associated with health-care facility limits and infections acquired in hospitals [1]. Neonatal sepsis, based on the current definition, is an infection that happens in less than 28 days from birth [2]. Premature babies and low body weight newborns tend to develop an infection easier because of weak immunity and sensitivity to invasive procedures performed at neonatal intensive care unit [3]. Despite numerous advances in neonatology, neonatal sepsis continues to be a serious concern in the context of neonatal complications and lengthy hospital stays [4]. Early diagnosis and antibiotic administration can help reduce the mortality rate and improve patient

results; however, different types of microbes can cause infection depending on geographic location and health-care settings [5]. In this case, the growing resistance to antibiotics poses several problems for physicians who have to select the best drug regimen for patients [6]. Regular monitoring of microbial strains and antibiotic susceptibility are critical for implementation of antibiotic stewardship strategies [7]. Given the above discussion, the primary aim of the current study was to examine microbiological aspects of neonatal sepsis and evaluate the antibiogram of isolates at a tertiary care facility [8].

Background of the Study: Neonatal sepsis still ranks among the commonest diseases responsible for neonatal sickness and deaths, especially in developing countries where infection prevalence is

common. Symptoms associated with neonatal sepsis are severe, causing prolonged hospitalization, and raising medical expenses. The microorganisms associated with neonatal sepsis vary from one place to another, as well as according to the health institution. The emergence of microorganisms that have developed resistance to multiple drugs has further complicated the problem. Rapid detection of pathogenic microorganisms and knowledge about their susceptibility to different antibiotics are necessary for instituting appropriate treatment protocols. It is therefore imperative to establish the microbial profile of neonates suffering from sepsis locally and regionally.

Microbiological Profile of Neonatal Sepsis:

Neonatal sepsis may alternatively be called an infection that poses significant danger to life and occurs in infants during their first months of life [9]. Neonatal sepsis is one of the key factors behind many cases of diseases and deaths in infants around the world. Microbial profiling is an identification and analysis of pathogens causing neonatal sepsis [10]. The pathogen organisms found in neonatal sepsis cases include, but are not limited to, Gram negative pathogens such as *K. pneumoniae*, *E. coli*, and *P. aeruginosa*. In addition, the other pathogens include Gram positive pathogens such as *S. aureus* and coagulase-negative staphylococci [11]. There are different geographical patterns for the pathogens because of varied infection and antibiotics use practices [12].

Microbiological profiling is vital in informing intervention measures that improve neonatal health [13]. Identification of the pathogens through laboratory diagnosis ensures development of personalized management procedures based on the causative pathogen. Such information is helpful in choosing effective antibiotics [14]. The presence of pathogens locally plays a big role in making decisions when it comes to prescribing empirical antibiotics. It is important to have constant monitoring of the profile of the microbes so that decisions can be made in light of the growing problem of antimicrobial resistance [15].

Objectives of the Study

1. To estimate the frequency of cases of culture-positive neonatal sepsis in neonates who were hospitalized in the NICU.
2. To ascertain the microbial profile of bacteria involved in neonatal sepsis.
3. To investigate the antibiogram patterns of bacteria isolated from patients with neonatal sepsis.
4. To examine any relationship between certain neonatal factors such as gestational age and culture-positive neonatal sepsis.

Methodology: The current study was undertaken to assess the microflora associated with neonatal sepsis and analyze the antimicrobial resistance patterns of the isolates. The study aimed at generating comprehensive information on the etiology of neonatal sepsis and antimicrobial resistance trends, which are important aspects of modern medicine.

Study Design: This study employed the methodology of an observational hospital-based cross-sectional study design. Patients diagnosed clinically with sepsis and satisfying predetermined inclusion criteria were recruited sequentially into the study.

Identification of causative agents and their antibiotic resistance profiles was determined through blood cultures and antibiotic sensitivity testing.

Study Area: This study was performed in the NICU and Department of Microbiology of Himalaya Medical College & Hospital, Paliganj, Patna, and Bihar, India.

Study Duration: This study was carried out within a duration of one year.

Study Participants: In the present research, the sample consisted of infants that had been admitted to the NICU unit and displayed clinical symptoms of sepsis.

Inclusion Criteria

- Neonates aged 0-28 days who are admitted into the NICU and presenting with clinical symptoms indicating sepsis.
- Neonates for whom blood culture investigations were advised by the treating physician.
- Neonates from whom parental or guardian consent had been obtained for their involvement in the study.

Exclusion Criteria

- Neonates who have previously been on long-term antibiotics before drawing the blood sample.
- Neonates with inadequate or contaminated blood samples.
- Neonates whose parents or guardians refused consent for participation.
- Neonates with incomplete clinical or laboratory records.

Sample Size: For the purpose of the study, a total of 120 neonates who exhibited clinical symptoms suggestive of sepsis were selected through consecutive sampling.

Procedure: Written informed consents were obtained from the participants' parents or guardians before enrolling in the study. Information related to demographic profile and medical history such as

age, gender, birth weight, gestational age, mode of delivery, and medical symptoms were recorded through a pre-tested questionnaire form.

After applying necessary precautionary measures, blood sample measuring around 1-2 ml was withdrawn from the patients before giving them any antibiotic drugs. The blood cultures were performed in suitable media, and incubation of samples was done according to established laboratory procedures. Isolated bacteria were identified by using biochemical techniques in laboratory settings.

In determining the sensitivities of antibiotics used for isolated bacterial species, Kirby-Bauer disc diffusion method was performed on Mueller Hinton agar plate following CLSI guidelines. Antibiotic drugs frequently administered to newborn babies were analyzed for their effectiveness.

Statistical Analysis: Data analysis involved using statistical tools such as Microsoft Excel and SPSS

version 25.0 software packages. For the description of categorical data, frequency and percentage distributions were used. Continuous data were represented using means and standard deviations. Correlation of variables with each other was done using tests such as Chi-square or Fisher’s exact test when required. A level of significance was set at $p < 0.05$ for all analyses conducted.

Results

Characteristics of study subjects are shown in Table 1 below. Out of the total number of 120 infants studied, 60.0% (n = 72) were male while 40.0% (n = 48) were female. In addition, out of the total number of 120 infants in the study, 61.7% (n = 74) were full term babies while 38.3% (n = 46) were preterm babies. Birth weight (underweight babies with weight less than 2500 grams at delivery) was found to occur in 43.3% (n = 52) of the cases Neonate.

Table 1: Demographic and Clinical Characteristics of Study Participants

Variable	Category	Frequency (n)	Percentage (%)
Sex	Male	72	60.0
	Female	48	40.0
Gestational Age	Preterm	46	38.3
	Term	74	61.7
Birth Weight	<2500 g	52	43.3
	≥2500 g	68	56.7
Onset of Sepsis	Early-onset (<72 h)	78	65.0
	Late-onset (≥72 h)	42	35.0
Mode of Delivery	Vaginal	70	58.3
	Cesarean Section	50	41.7

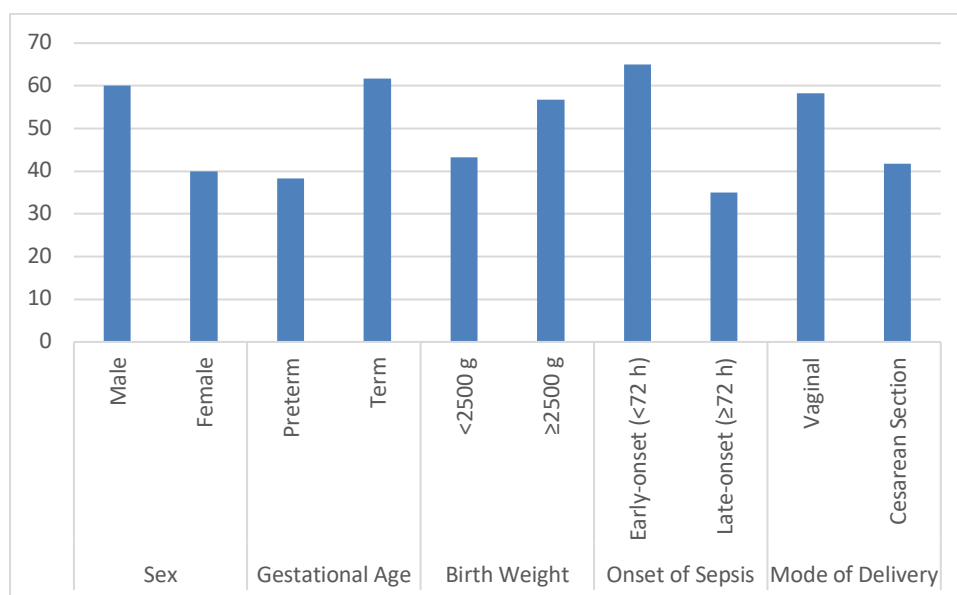


Figure 1: Graphical Representation of the Percentage of Demographic and Clinical Characteristics of Study Participants

Blood culture outcomes in the studied neonates are presented in Table 2 below. In the current study sample comprising 120 neonates with suspicion of

sepsis, positivity of blood cultures was recorded in 48 neonates (40.0%). The other 72 patients (60.0%) did not grow any bacteria in culture tests. Although

the moderate blood culture positivity could indicate previous administration of antibiotics, low presence of bacteria, or limitations of blood cultures in

diagnosis, it demonstrates the critical importance of blood culture for establishing neonatal sepsis diagnosis.

Table 2: Blood Culture Results among Study Participants

Blood Culture Result	Frequency (n)	Percentage (%)
Positive	48	40.0
Negative	72	60.0
Total	120	100.0

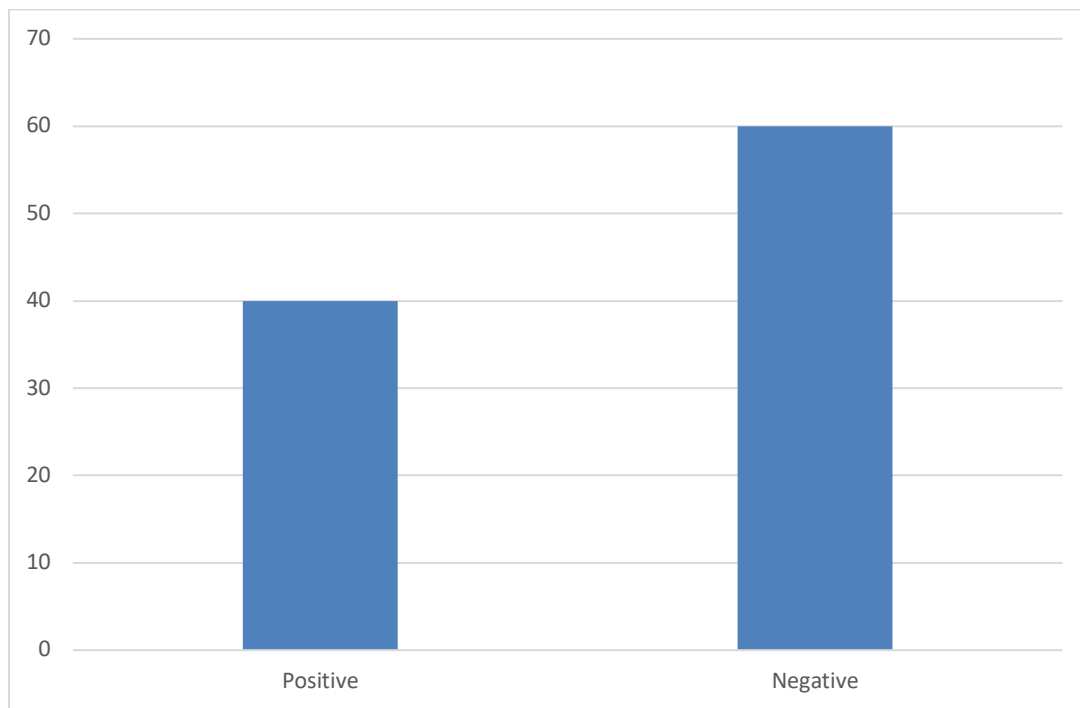


Figure 2: Graphical Representation of the Percentage of Blood Culture Results among Study Participants

In Figure 3 below, the frequency of the bacteria isolated from the patients' positive cultures can be seen. In the total number of 48 positive cultures, the *K. pneumoniae* accounted for 31.3% (n=15),

while the *S. aureus* comprised 25.0% (n=12). Meanwhile, *E. coli* accounted for 16.7% (n=8) of the cultures, and the coagulase-negative staphylococci consisted of 12.5% (n=6).

Table 3: Distribution of Bacterial Isolates among Culture-Positive Cases (n = 48)

Organism Isolated	Frequency (n)	Percentage (%)
<i>Klebsiella pneumoniae</i>	15	31.3
<i>Staphylococcus aureus</i>	12	25.0
<i>Escherichia coli</i>	8	16.7
Coagulase-negative Staphylococci (CONS)	6	12.5
<i>Pseudomonas aeruginosa</i>	4	8.3
<i>Acinetobacter</i> spp.	3	6.2
Total	48	100.0

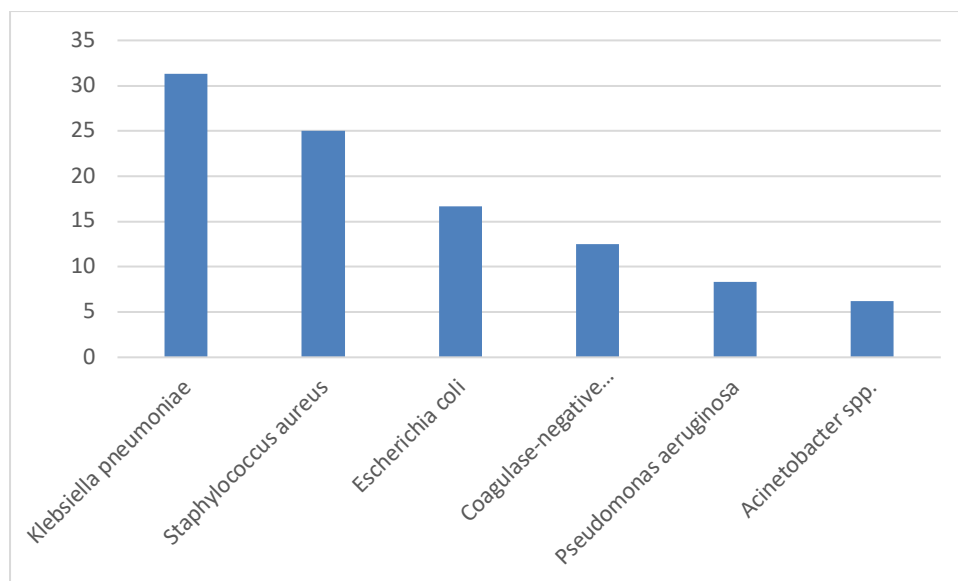


Figure 3: Graphical representation of the Percentage of Distribution of Bacterial Isolates among Culture-Positive Cases

From the data presented in Table 4, it can be noted that Gram-negative bacteria comprised a higher number than others with regard to the percentage of weight. The percentage contribution of Gram-negative bacteria stood at 62.5% (n=30), whereas for Gram-positive bacteria, it stood at 37.5% (n=18). The results suggest that there exists an increased prevalence of infections due to Gram-negative bacteria in the NICU setting.=

Table 4: Gram-wise Distribution of Isolates

Type of Organism	Frequency (n)	Percentage (%)
Gram-negative bacteria	30	62.5
Gram-positive bacteria	18	37.5
Total	48	100.0

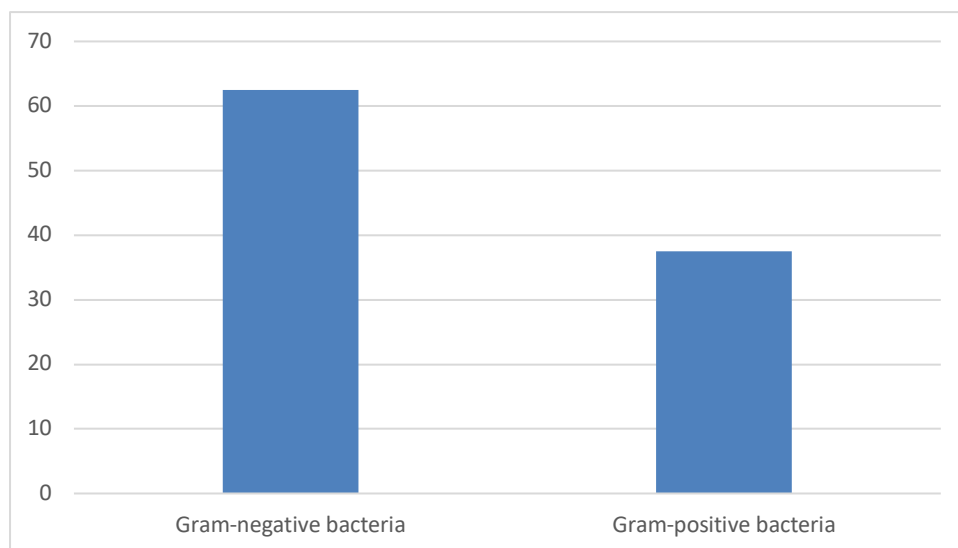


Figure 4: Graphical representation of the Percentage of Gram-wise Distribution of Isolates

Table 5 highlights the antibiogram of the predominant bacterial isolates.

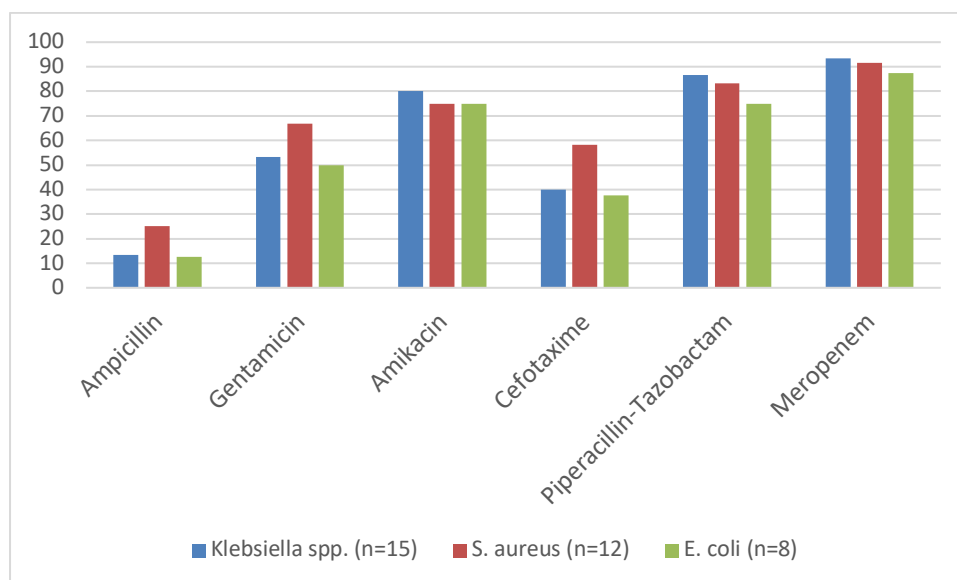
Susceptibility towards meropenem was noted to be very high for Klebsiella spp., Staphylococcus aureus and E. coli, all at 93.3%, 91.7% and 87.5% respectively. At the same time, piperacillin-

tazobactam demonstrated good effectiveness towards several bacteria at 75.0% to 86.7%.

Conversely, the resistance levels were very high towards ampicillin where low susceptibility ranged from 12.5% to 13.3%. This is indicative of increasing resistance of neonatal.

Table 5: Antibiotic Sensitivity Pattern of Major Isolates (%)

Antibiotic	Klebsiella spp. (n=15)	S. aureus (n=12)	E. coli (n=8)
Ampicillin	13.3	25.0	12.5
Gentamicin	53.3	66.7	50.0
Amikacin	80.0	75.0	75.0
Cefotaxime	40.0	58.3	37.5
Piperacillin-Tazobactam	86.7	83.3	75.0
Meropenem	93.3	91.7	87.5
Vancomycin	—	100.0	—

**Figure 5: Graphical representation of the Percentage of Antibiotic Sensitivity Pattern of Major Isolates**

Below is the table illustrating the association between gestational age and positive results for blood culture associated with neonatal sepsis.

According to this study, 56.5% (n=26/46) of neonates who were born preterm had neonatal sepsis, while only 29.7% (n=22/74) had sepsis in cases where deliveries took place at term. The

result showed statistical significance ($\chi^2=7.12$, p=0.008).

Therefore, premature births were significantly correlated with higher vulnerability to neonatal sepsis. Preterm newborns tend to have a poorly developed immune system.

Table 6: Association between Gestational Age and Culture Positivity

Gestational Age	Culture Positive n (%)	Culture Negative n (%)	Total	χ^2	p-value
Preterm	26 (56.5)	20 (43.5)	46	7.12	0.008*
Term	22 (29.7)	52 (70.3)	74		
Total	48	72	120		

*Statistically significant (p < 0.05)

Discussion

The objective of this research was to study the microbiological profile along with antibiotic sensitivity pattern of the pathogens isolated from the cases of sepsis among neonates admitted at a tertiary care hospital (Oo et al., 2021) [16]. The results indicate that 40.0% of neonates with suspicion of neonatal sepsis were positive on culture. These results demonstrate that a relatively high burden of sepsis cases exists among neonates in the studied environment (Weldu et al., 2020) [17]. Furthermore, there was a male predominance (60.0%) among the studied population. In addition,

it was found that the majority of the cases (65.0%) were early onset sepsis cases, implying that neonatal infection commonly occurs during the early stages after delivery (Abdelsalam et al., 2020) [18]. Moreover, preterm neonates comprised 38.3% of the total participants enrolled in this study. This information plays an important part in assessing the risk profile of infants in the neonatal period.

From the microbiological testing done, it is clear that *K. pneumoniae* was the main cause of sepsis among the neonates, with a positivity rate of 31.3%. Others include *S. aureus* and *E. coli*, whose positivity rates stood at 25.0% and 16.7%,

respectively. The Gram-negative group had 62.5% of all the cultures obtained, meaning that such pathogens predominate when it comes to neonatal sepsis in this setting. Identifying the causative bacterial species responsible for neonatal sepsis is vital, especially when it comes to making decisions regarding antibiotic therapy. Constant microbiological profiling can be helpful in future decisions concerning neonatal infections (Sawhney et al., 2015) [19].

The results indicated high susceptibility to the antibiotics on the various organisms, whereby meropenem exhibited high susceptibility, with 93.3%, 91.7%, and 87.5% sensitivities to *Klebsiella* spp., *S. aureus*, and *E. coli*, respectively. Similarly, Piperacillin-tazobactam revealed high sensitivities (Li et al., 2020) [20]. On the other hand, ampicillin showed relatively lower sensitivities. There exists a significant correlation between gestational age and culture positivity. Preterm babies exhibited much higher culture positivity rates compared to those of term neonates (56.5% vs. 29.7%; $p = 0.008$). Understanding the associations between various risk factors and neonatal infection is necessary for adopting optimal management strategies and interventions.

Conclusion

From the findings of this study, there is continued sepsis incidence in NICU-infants admitted within hospitals. The incidence of sepsis showed that the positive blood culture cases comprised 40.0%. Based on the microbiologic analysis of the isolates, it indicates that there is an increased prevalence of gram-negative microorganism at 62.5%, where *Klebsiella pneumoniae* was identified as the most prevalent pathogen, while *Staphylococcus aureus* and *Escherichia coli* were secondary.

On the other hand, there was excellent effectiveness shown by meropenem and piperacillin/tazobactam in treating the pathogens identified; however, resistance occurred when using ampicillin to treat the pathogens. This represents a great public health issue, considering the increased rate of antibiotic resistance worldwide. Furthermore, it showed that preterm infants have high susceptibility to developing culture-positive sepsis compared to term infants ($p=0.008$).

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