Original Article

Microbiological Patterns Among Neonates Suffering from Late Neonatal Sepsis and to Specify the Antibiotic Susceptibility

Bacteriological Profile and Antibiotic Susceptibility in Neonatal Sepsis

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ABSTRACT

Objective: To assess the microbiological patterns among neonates suffering from late neonatal sepsis and to specify their antibiotic susceptibility.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Department of Neonatology Department Of Recep Tiyyap Erdogan Hospital Muzafargarh between 1st January 2016 and 1st January 2021.

Materials and Methods: All medical records of neonates who developed or presented after a stay of 48 hours in a hospital setting and presented with signs and symptoms of sepsis and their blood cultures reported between 1st January 2016 and 1st January 2021 were included in the study. Data was retrieved from REDCap and analyzed by using SPSS version 26.0.

Results: A total of 103 (23.9%) patients' blood cultures were found positive, and of these, 38 (36.3%) were coagulase negative staphylococci, 5 (4.8%) were Actinobacteria, 7(6.8%) were E.coli, 17(16.5%) were Klebsiella pneumoniae, 13(12.62.%) were Pseudomonas aeruginosa, 18 (17.4%) gram positive cocci, 2 (1.94%) were streptococcus, 1(0.97%) proteus vulgaris, 1 (0.97%) MRSA, and 1 (0.97%) were enterococcus species. It is observed that overall microbes show high resistance towards common antimicrobials, including ampicillin, amoxicillin, cefotaxime, tobramycin, and ceftazidime.

Conclusion: The results of this study clearly show that the microbes are resistant to commonly available antibiotics and hence antibiotic stewardship is necessary in resource poor countries like Pakistan.

Key Words: Antibiotic Susceptibility, Neonatal Sepsis, MRSA

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INTRODUCTION

Birth asphyxia, prematurity, and neonatal sepsis are the three main causes of neonatal mortality worldwide.[1] Traditional classifications of sepsis include early-onset (occurring within 72 hours of birth) and late-onset sepsis (beyond 72 hours). The majority of late-onset infections are caused by hospital-acquired organisms, in contrast to early neonatal infections, which are typically acquired by maternal vaginal tract germs.

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Late onset sepsis can be community acquired, but the majority of cases are of hospital acquired infections. In South Asian healthcare data, the cumulative incidence of culture-positive sepsis was 15.8 per 1000 live births (95% CI 12.7 to 18.8, n=15 reports). This is roughly two to four times more than what is recorded in upper income nations like the United States and Uk.[2,3] In comparison to developed countries, it is 4 to 10 times greater.[2,3]

This overall scenario is a result of poverty, inadequate access to appropriate interventions, especially facility births, and egregious inequality in the provision of healthcare. Most hospital acquired infections are documented in wealthy countries among significant numbers of very high risk, extremely low birthweight (1000 g) infants who frequently go unresuscitated in undeveloped countries.[4] In many developed countries, coagulase-negative staphylococci (CONS) and gram-positive bacteria are the main causes of late-onset newborn sepsis, while gram-negative bacteria are more frequently responsible in underdeveloped nations. The variety of microorganisms that cause late-onset

newborn sepsis varies geographically and with time in the same location. [5,6]

According to an article by M Jeeva Sankar and colleagues, one of the most prevalent organism type was a gram-negative one (63%) with the top three being Klebsiella spp. (23%), Escherichia coli (14%), and Acinetobacter spp. (8%) Staphylococcus aureus and Coagulase-negative Staphylococci made up 20% and 9%, respectively, of the Gram-positive bacteria. Gram negative bacteria had a greater mortality rate than Gram - positive cocci (11.9%; 95% CI 10.5 to 13.3%). The most prevalent bacteria among the 703 isolates from community - based settings were Klebsiella spp (25%), E coli (15%), and S aureus (12%).[7] In the last decade, it has been observed that there is high antibiotic resistance among gram–negative hospital acquired neonatal sepsis. Isolates are about 60 -70% multidrug resistant. [8]

As our hospital is looking after both inborn neonates as well, we also take care of referrals. We found that there is tremendous antibiotic resistance particularly among the neonates that are being referred from both private and government institutes in the current study, investigators aimed to examine the microbiological patterns of late neonatal sepsis and to specify their antibiotic susceptibility. We have aimed to see which etiological agents are responsible for late onset sepsis and their resistance pattern. The objective of this study was to assess the microbiological patterns among neonates suffering from late neonatal sepsis and to specify their antibiotic susceptibility.

MATERIALS AND METHODS

A retrospective study was undertaken at the Department of Neonatology, Recep Tiyyap Erdogan Hospital Muzafargarh. Exemption from ethical approval was granted by the institute review board of Indus Hospital and Health Network with reference # IHHN_IRB_2021_08_013.

Data and medical records of the neonates were extracted from the hospital's database after the administration's approval was obtained. All cases of neonatal admissions to Neonatal ICU with suspicion of neonatal sepsis between 1st January 2016 and 1st January 2021 were included in the study.

All neonates who developed or presented after a stay of 48 hours in a hospital setting and presented with signs and symptoms of sepsis and their blood cultures reported were included in the study. Neonates with marked dysmorphism and complex congenital heart diseases were excluded. Blood cultures were taken for all neonates with suspected late onset clinical sepsis. Clinical sepsis was defined as the presence of any of the signs suggestive of sepsis clinically. such as lethargy, apnea, tachypnea, tachycardia, hypotension, temperature instability, poor feeding, poor perfusion, abdominal distension, plus positive septic screen. [9]

Approximately 1 ml of blood was obtained for culture with antiseptic precautionary measures from a vein in the arm as well as a central vein. Using a Peds Plus Vial, a BACTEC 9050 automated device carried out the culture. Gram staining was done for any culture that showed a positive result, and subcultures were carried out on the proper media based on the results of the Gram stain: Mac Conkey agar and 5% sheep blood agar for Gram negative and positive organisms, and Sabouraud's dextrose agar and 5% sheep blood agar for yeast isolates. All negative containers were cultured once on blood agar and then discarded after being incubated in the apparatus for up to seven days. [6]

Data was retrieved from REDCap and analyzed by using SPSS version 26.0. Qualitative data is presented in terms of frequencies and percentages, and quantitative data is presented in terms of mean and standard deviation

RESULTS

During the study period, 430 patients' blood cultures with clinically suspected sepsis were sent, out of which 103 (23.9%) patients' blood cultures were found positive .The following results are of positive blood cultures in neonates. The mean gestational age of the neonates having positive blood cultures was 34 □ 3.121, with a minimum age of 26 weeks and maximum age of 42 weeks. The mean weight of patients in grams was 2129 □ 850.035 grams, with a minimum weight of 745 grams and a maximum weight of 5000 g.

Table No.1: Perinatal Parameters of the Subjects

Variable	Values	
Gestational Age (Mean □□SD)	34 □ 3.121	
Gestational age groups	26-36.6 weeks	82 (79.6%)
	37-41.6 weeks	20(19.41%)
	Greater than 42 weeks	1 (1%)
Weight	2129 □ 850.035 grams	
Gender	Male	63(63%)
	Female	40(38.83%)
Duration of rupture of membranes	Less than 12 hours	87(84.5%)
	Greater than 12 hrs	16 (15.5%)
Mode of Delivery	c section,	57 (55.3%)
	SVD	46(44.7%)
Place of Delivery	Our setup	63 (61.2%)
	Other setups	40(38.8%)

Regarding the gestational age, 82 (79.6%) were between the ages of 26-36.6 weeks, 20 (19.41%) neonates were between 37-41.6 weeks, and only 1 (1%) had a gestational age greater than 42 weeks. The majority of the patients were males, 63 (63%), and 40(38.83%) were females. 16 (15.5%) patients had ruptured membranes for greater than 12 hours, whereas 87 (84.5%) had ruptured membranes for less than 12 hours. Regarding liquor, 90(87.4%) had clear liquor, whereas 13(12.6%) had meconium-stained liquor.

The majority of the neonates were delivered via c section, 57 (55.3%), whereas 46(44.7%) were delivered via SVD. 63 (61.2%) neonates were delivered at our setup, whereas 40 (38.8%) were delivered at other setups and were referred to our hospital. 78 (75.7%) had births attended by trained personnel, whereas 25 (24.3%) had no trained birth attendant at the time of birth.

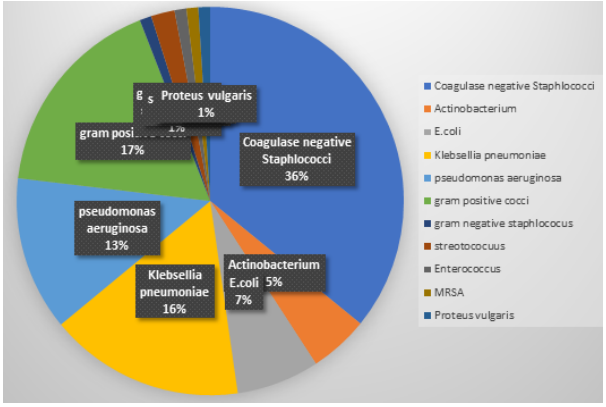

Figure No.1: Distribution of Bacterial Organisms Found in Cultures Among Neonates

Table No.2: The Results of Sensitivity and Resistance to Specific Drugs

Antibiotics	Sensitive	Resistant
Ampicillin	20(20%)	80(80.%)
Amoxicillin	31(31%)	69(69%)
Gentamicin	66(66%)	34(34%)
Amikacin	85(85%)	15(15%)
Tobramycin	36(36%)	64(64%)
Cefotaxime	34(34%)	66(66%)
Ceftazidime	37(37%)	63(63%)
Meropenem	67(67%)	33(33%)
Imipenem	63(63%)	37(37%
Cefoperazone Plus Sulbactam	58(58%)	42(42%)
Chloramphenicol	70(70%)	30(30%)
Piperacillin/Tazobactam	59(59%)	41(41%)
Colistin	64(64%)	36(36%)
Ciprofloxacin	64(64%)	36(36%)
Co-trimoxazole	36(36%)	64(64%)
Ertapenem	42(42%)	58(58%)
Ceftriaxone	47(47%)	53(53%)

Out of the 103 positive cultures, 38 (36.3%) were coagulase negative. Staphylococci 5 (4.8%) were Actinobacteria, 7(6.8%) were E.coli, 17(16.5%) were Klebsiella pneumoniae, 13(12.62.%) were Pseudomonas aeruginosa, 18 (17.4%)) gram positive cocci, 2 (1.94%) were streptococcus, 1(0.97%) proteus vulgaris ,1(0.97%) MRSA ,1(0.97%) were enterococcus species as illustrated in the Figure 1.

The susceptibility and resistance pattern are presented in Table 2. It is observed that overall microbes showed high resistance towards common antimicrobials including ampicillin, amoxicillin, cefotaxime, tobramycin, and ceftazidime.

DISCUSSION

Neonatal sepsis is a major health concern in developing countries such as Pakistan. [10] Timely diagnosis and prompt administration of empirical antibiotics is necessary while the results of the blood culture are awaited. The range of organisms that cause newborn sepsis evolves over time and also differs by area. Regular assessment for microbiological species and vulnerability patterns can eliminate any confusion about the treatment strategy for treating newborn sepsis, allowing an acceptable choice of antibacterial drugs for initial therapy to be outlined and re-evaluated in a timely fashion.[11]

In our study, 16 (16%) were coagulase negative staphylococci in this study, and they are the most common organisms isolated in the present study. Contrary findings were reported by several other authors including Bhat et al. (90.8%) and Shrestha et al. (60.64%). [12,13]

The low prevalence of CoNS infection in the current study, which is typically linked to central lines, and the rarity of Group B Streptococcus infection in Pakistan can both be blamed for the low frequency of gram-positive infection.[5] In neonatal sepsis, Pseudomonas aeruginosa was found in 13% of patients in our study. Another study from south India (33.2%) produced similar findings.[12] While another research claimed that Klebsiella was the most prevalent organism. [14] Staphylococcus aureus was cited by some writers as being the most prevalent organism. [15] Additionally, the bacterial flora that causes early-onset newborn sepsis has undergone a significant alteration as a result of intrapartum antibiotic prophylaxis.

The current study's low rate of enterococci disease (1%) is comparable to the findings of Bhat et al. (2.2%). [12] In polymicrobial sepsis, the connection of two distinct species did not follow any particular pattern. It's possible that a newborn already sick with one microbe picked up the second one from the hospital setting, or that both of the bacteria were picked up there. Most earlier research either did not recognize the importance of polymicrobial sepsis or did not take into account the second organism in a culture that was already

positive.[16] The incidence of polymicrobial sepsis was not studied in this research.

In a study published recently by Pokhrel et al., a total of 69 (20.5%) neonates who were admitted to the NICU had culture-positive sepsis. [17] Out of these, 47 (68.1%) were preterm babies. The majority of the bacteria isolated were gram-negative, with Klebsiella species making up the majority (n = 23, 33.3%). Klebsiella was found to be resistant to typically used antibiotics, including Cefotaxime, Gentamicin, Ciprofloxacin, Ofloxacin, and Chloramphenicol. [17]

The prevalence of polymicrobial sepsis and the clinical outcome of newborn septicemia must be correlated. The issue of antibiotic resistance is pervasive. [18-20] Numerous Gram positive and Gram negative microorganisms in the current investigation also displayed varied resistance to many of the therapeutically helpful medicines. Recent studies have also noted the increased incidence of resistance to routinely used antibiotics. The current study shows that the commonly used antibiotic ampicillin is resistant in about 80% of cultures and that chloramphenicol is sensitive in about 70% of cultures.

There are, however, some limitations to this study. Firstly, it is a retrospective study conducted at a single center. Moreover, the classification of sepsis (early/late sepsis) has not been taken into consideration. In addition to these limitations, individual microbes' drug sensitivity has also not been taken into consideration in this study.

CONCLUSION

We conclude that neonatal sepsis is a grave medical problem in our region. The results of this study clearly show that the microbes are resistant to commonly available antibiotics and hence antibiotic stewardship is necessary in resource poor countries like Pakistan.

Author's Contribution:

Concept & Design of Study:	Sana Arshad, Athar Razzaq
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Revisiting Critically:	Sana Arshad, Athar Razzaq
Final Approval of version:	Sana Arshad, Athar Razzaq

Conflict of Interest: The study has no conflict of interest to declare by any author.

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