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RESEARCH ARTICLE

A retrospective study on antibiotic sensitivity pattern of pathogens isolated from blood culture in cases of late-onset neonatal sepsis at a neonatal intensive care unit

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ABSTRACT

Background: Despite significant advancement in neonatal intensive care, the incidence of late-onset neonatal sepsis (LONS) remains a major cause of neonatal morbidity and mortality. The causative organisms and their susceptibility to antibiotics vary in different regions; which forms a basis in the selection of empiric antibiotic in suspected cases of sepsis. **Aims and Objectives:** To determine the drug sensitivity pattern of the commonly isolated pathogens in LONS. **Materials and Methods:** This study was done after obtaining approval from the Institutional Human Ethical Committee of JJM Medical College Davangere. The blood culture sensitivity data of all neonates admitted and treated as cases of LONS over a period of 2 years (December 2013 to December 2015) at the neonatal intensive care unit of Bapuji Hospital were studied retrospectively. **Results:** A total of 212 neonates admitted were suspected cases of LONS. 51.88% of them were blood culture positive, with 78.18% of the isolated organisms being Gram-positive and 24 (21.81%) Gram-negative. The most frequently isolated organism was coagulase-negative *Staphylococcus aureus* (78.18%) followed by *Klebsiella pneumoniae* (10.9%). 71.25% of these organisms showed resistance to ampicillin, and 56.25% showed resistance to gentamicin which is the World Health Organization recommended an empirical choice of antibiotics. **Conclusion:** Our study has shown an increasing trend of resistance to the commonly prescribed first-line empiric antibiotics such as ampicillin and gentamicin. Hence, periodic surveillance of antibiotic susceptibility is of prime importance to choose the right empiric antibiotic.

KEY WORDS: Neonatal Sepsis; Empiric Antibiotics; Antibiotic Sensitivity Pattern

INTRODUCTION

Sepsis is one of the most common causes of neonatal morbidity and mortality. It is responsible for about 30–50% of the total neonatal deaths in developing countries.[1] India contributes to around one-quarter of all neonatal deaths in the world and more than half (52%) of these are estimated to occur due to infections.[2] Neonatal mortality due to sepsis is largely preventable with rational antimicrobial therapy and aggressive supportive care.

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According to the onset of age; neonatal sepsis is divided into early onset neonatal sepsis (EONS) and late ONS (LONS). EONS presents within first 72 h of life. The source of infection is generally the maternal genital tract. LONS usually presents after 72 h of age. The source of infection is either nosocomial or community-acquired and neonates usually presented with septicemia, pneumonia, or meningitis.[3] The incidence of LONS has increased in parallel with the improved survival of premature infants, especially in those with very low birth

weight, indicating the role of hospitalization and life-sustaining medical devices in the pathogenesis of neonatal LONS.[4,5]

Infection Society of America has begun to refer to a group of nosocomial pathogens as *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* "(ESKAPE) pathogens." ESKAPE is an acronym for the group of bacteria, encompassing both Gram-positive and Gram-negative species, made up of ESKAPE species.[6,7] These bacteria are common causes of life-threatening nosocomial infections and are characterized by potential drug resistance mechanisms.[8]

A timely and accurate diagnosis of LONS is of utmost importance, given the mortality rate and long-term adverse outcomes associated with LONS. However, diagnosing neonatal infection is challenging, since clinical signs and symptoms are often slight and nonspecific for a particular infection. Therefore, in cases of suspected sepsis, 2 or 3 days empirical antibiotic therapy should begin immediately after cultures have been obtained without awaiting the results. Ampicillin (or penicillin) plus gentamicin is currently recommended by World Health Organization (WHO) as first-line antimicrobials for both EONS and LONS.[9] An ideal choice of antimicrobial agents is to cover the most common pathogens without providing selection pressure for antibiotic resistance, which embarks the need for understanding the pattern of causative pathogens and their susceptibility pattern in a given region.

Hence, this study was conducted with the aim to determine the microbiological characteristics (causative organisms and their antimicrobial susceptibility) in suspected cases of LONS.

MATERIALS AND METHODS

This study was done after obtaining the approval from Institutional Human Ethical Committee of JJM Medical College, Davangere, and in collaboration with the Department of Neonatology. The study was conducted retrospectively, where the blood culture sensitivity data of all neonates admitted as suspected cases of LONS over a period of 2 years, i.e., between December 2013 and December 2015 were documented and analyzed. Neonates with surgical problems, major congenital malformations, on antibiotics or those whose mothers have received antibiotics before delivery, were excluded from the present study. Blood culture was done by standard microbiological techniques in all the cases, and the reports were analyzed.

RESULTS

A total of 212 neonates were admitted as suspected cases of LONS. 136 were males and 76 were females.

Culture sensitivity reports of 212 cases included were studied. A total of 110 cases were culture positive.

Out of 110 bacterial isolates, 78.18% (86) were Gram-positive and 21.81% (24) were Gram-negative.

The most frequently isolated organism was coagulase-negative *S. aureus* (78.18%) followed by *K. pneumoniae* (10.90%), *Pseudomonas*, *Acinetobacter,* and *Enterococci* [Figure 1 and Table 1].

All isolates showed low sensitivity to ampicillin, amikacin, and gentamicin, moderate sensitivity to cefotaxime, ceftriaxone, ciprofloxacin and maximum sensitivity to imipenem, meropenem, and linezolid [Figures 2-4].

DISCUSSION

Findings in Our Study

Early diagnosis and empirical treatment with antibiotics are essential for the prevention of morbidity and mortality of neonatal sepsis in neonatal intensive care unit.[10] In our study, the culture positivity rate was found to be 51.88%. The distribution

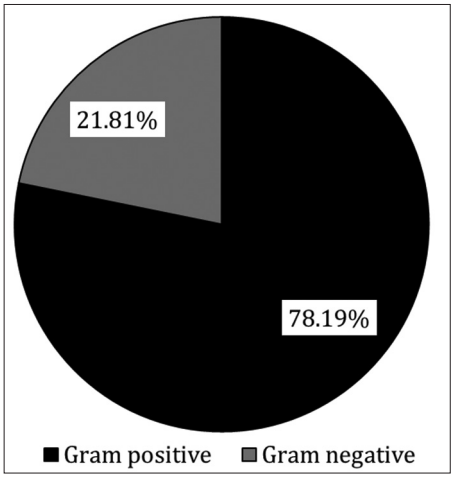

Figure 1: Distribution of organisms

Table 1: Distribution of organisms (ESKAPE group)

Bacterial isolate	*n* (%)
Coagulase-negative *Staphylococcus aureus*	86 (78.18)
Klebsiella	12 (10.90)
Pseudomonas	6 (5.45)
Acinetobacter	4 (3.63)
Enterococci	1 (0.90)
Escherichia coli	1 (0.90)
Total	110 (100)

ESKAPE: *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter*

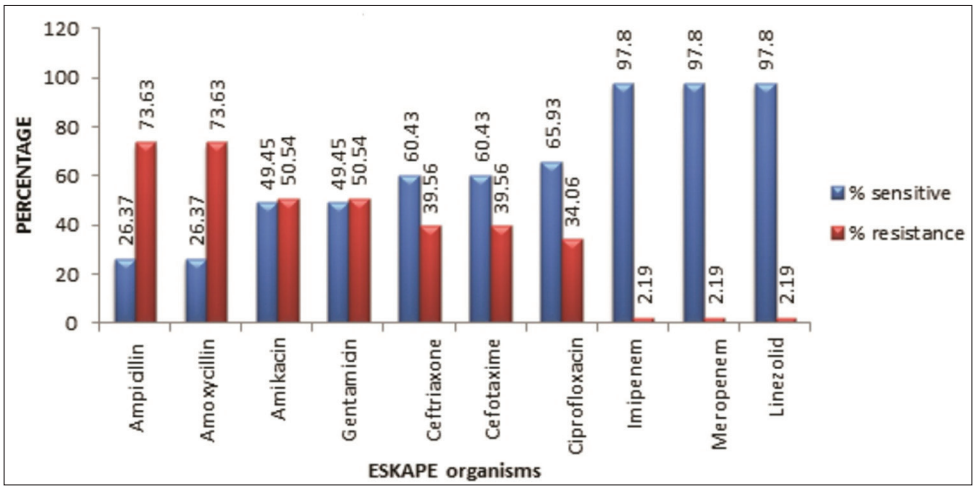

Figure 2: Sensitivity pattern of *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* organisms to various drugs

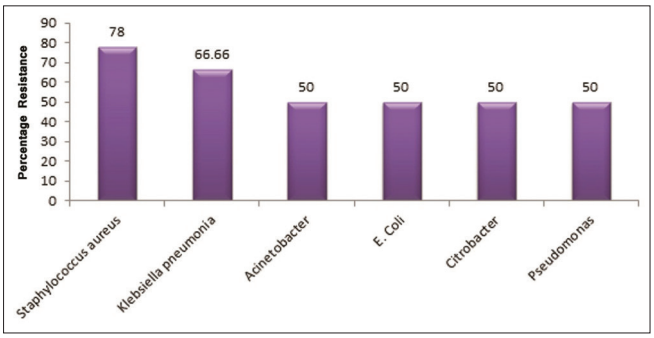

Figure 3: Susceptibility pattern of organisms to ampicillin

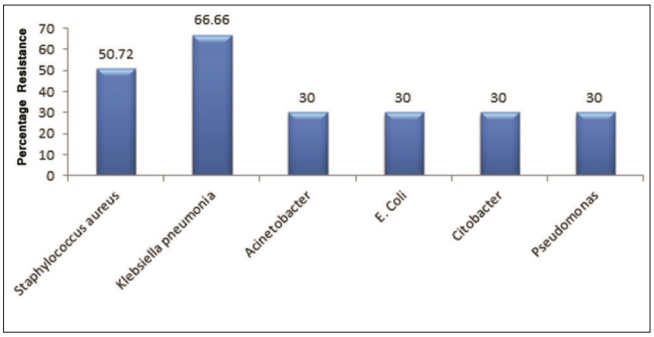

Figure 4: Susceptibility pattern of organisms to gentamicin

of organisms causing LONS showed that Gram-positive organism, i.e., coagulase-negative staphylococci (CoNS) as major cause contributing to 78.18% of culture-positive cases. *K. pneumoniae* was the most common Gram-negative organism (10.90%) and the second most frequent after CoNS in the study. The other organisms isolated were Pseudomonas, Acinetobacter and enterococci, Citrobacter, which constitute the ESKAPE group of pathogens. In our study, all the isolates were resistant to penicillin. Ampicillin, gentamicin had the lowest sensitivity to all bacterial isolates. Moderate sensitivity was observed for third-generation cephalosporins such as ceftriaxone and cefotaxime. Highest sensitivity was recorded with meropenem, imipenem, and linezolid (98% sensitivity).

Findings of Other Similar Studies

The culture positivity rates in our study were 51.88% while that in Shah *et al*.[11] study was 31.75%, Shaw *et al*.[12] study was 54.64%, and Bhattacharjee *et al*.[13] study was 32%. There are various factors which can influence the blood culture positivity rates and hence it is highly variable from place to place. Cultures positive with potential pathogens that may also be contaminants are far more difficult to interpret, the most common of which is CoNS. These results must always be interpreted in the specific clinical context in which they are seen.[14] CoNS were the most frequently isolated organism in our study followed by *Klebsiella* which is similar to a study done by Gandhi *et al*.[15] CoNS have emerged as the predominant pathogens of LOS, accounting for 53.2–77.9% of LOS in industrialized countries, and 35.5–47.4% in some developing regions.[16] Infection with CoNS is usually hospital-acquired spreading through indwelling catheters or central lines. The distribution pattern of causative organisms varies from one region to another and also may change over time within the same hospital due to demographic characteristics of patients, microflora colonization of the nosocomial environment and the policy of antibiotic use.[5] These organisms, through a wide variety of mechanisms, are developing resistance to the commonly used antibiotics. Ampicillin, gentamicin had the lowest sensitivity to all bacterial isolates. Which is similar to the findings of a study done by Tallur *et al*.[17]

Highest sensitivity was recorded with meropenem, imipenem, and linezolid (98% sensitivity). Which is similar to the findings of a study done by Bilal *et al.* in adults where ESKAPE organisms isolated from endotracheal tube showed maximum sensitivity to imipenem.[18]

Strengths and Limitations of the Study

The study was focused to identify the pathogenic organisms causing LONS, which is increasing despite the aseptic precautions taken in tertiary centers, which increases the

morbidity and duration of the hospital stay. The limitations of this study are the small sample size and being a retrospective study it was difficult to retrieve all the relevant clinical data which could have given more inputs regarding other contributing factors for the development of LONS.

CONCLUSION

With the advancement of neonatal intensive care, the risk of neonates acquiring LONS is increasing. Since LONS is usually hospital-acquired, prevention measures should be employed with an emphasis on proper hand hygiene and evaluation of other potential reservoirs as sources of bacterial acquisition and transmission. However, early suspicion and treatment of neonatal sepsis with empirical antibiotics are essential to reduce neonatal morbidity and mortality. At present, ampicillin and gentamicin are recommended by the WHO as the first-line empirical antibiotics in the management of LONS. The increasing resistance to the commonly used antibiotics reflects the inadvertent use of antibiotics. Hence, it is important to periodically update the pattern of prevailing strains and their drug susceptibility in a region to restrict and rationalize the use of antibiotics.

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