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Profile of Bacterialisolates in Neonatal Sepsis and Their Drug Resistance Pattern in a Tertiary Care Hospital

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Abstract: ***Background: Neonatal septicemia is responsible for approximately 25% of the neonatal deaths in the world and mostly in developing countries. Increased prevalence of extended spectrum beta-lactamases (ESBLS) and methicillin-resistant Staphylococcus aureus (MRSA) and multiple drug resistant (MDR) strains is a cause of concern in neonatal intensive care units (NICU) worldwide. Objectives: The study aims to find out the bacteriological profile in neonatal sepsis and to study their antimicrobial susceptibility pattern including detection of MRSA and ESBL's. Materials and methods: The study is based on a prospective analysis of all cases admitted to the neonatal intensive care unit (NICU) of a tertiary care hospital, Hassan. Results: In our study out of 250 patients studied, 170 showed blood culture positive, positivity rate being 68%.Gram-negative organisms were isolated in 98 cases(58%), Gram-positive in 72 cases(42%). In gram-negative isolates, 24 cases (14%) were ESBL producers. Methicillin resistance in S. aureus was seen in 15cases (30%). Conclusion: Blood culture is the gold standard in diagnosis and treatment of neonatal septicemia. Multiple antibiotic resistances among neonatal sepsis are currently one of the greatest challenges to the effective management of infections. Therefore, we suggest that surveillance of antimicrobial resistance is necessary.***

Keywords: Neonatal sepsis, Blood culture, MDR, MRSA, ESBL

1. Introduction

Neonatal sepsis is one of the major causes of morbidity and mortality among the newborns in the developing countries. It is a life-threatening clinical emergency that demands urgent diagnosis and treatment.Neonatal sepsis can be defined as "a clinical syndrome characterized by systemic signs and symptoms and bacteremia during the first month of life".[1]

Neonatal septicemia is responsible for approximately 25% of the neonatal deaths in the world and mostly in developing countries. Increased prevalence of extended spectrum beta-lactamases (ESBLs) and methicillin-resistant Staphylococcus aureus (MRSA) and multiple drug resistant (MDR) strains is a cause of concern in Neonatal Intensive Care Units (NICU) worldwide. Septicemia has been classified as early onset septicemia (EOS) and late-onset septicemia (LOS). The microorganisms most common associated with EOS include Group B Streptococcus (GBS), Escherichia coli, coagulase negative Staphylococcus species (CONS), Haemophilus influenza and Listeria monocytogenes.and LOS is caused by CONS, S. aureus, E. coli, Klebsiella spp., Pseudomonas spp., Enterobacter spp., Candida spp., GBS, Serratia spp., Acinetobacter spp. and anaerobes.[2]

Diagnosis and management of sepsis are a great challenge facing neonatologists in NICUs. Clinical diagnosis of presentation is difficult due to nonspecific signs and symptoms. In addition, laboratory diagnosis is time consuming.This matter necessitates the initiation of empiricalantibiotic therapy till the suspected sepsis is ruled out. At thesame time, increasedmultidrug resistant organisms make the treatment options fewer and the effective treatment is delayed.The diversity of organisms causing sepsisvaries fromregion to another and changes over time even in the same place. This is attributed to the changing pattern of antibiotic use and changes in lifestyle.

Many factors contribute to the susceptibility of the neonate tosepsis, which can influence the incidence of neonatal sepsis. Incidence also varies from nursery to nursery depending on conditions predisposing infants to infection.

2. Objectives

a. The study aims to find out the bacteriological profile in neonatal sepsis.
b. To study their antimicrobial susceptibility pattern including detection of MRSA and ESBL's.

3. Materials

The study is based on a prospective analysis of all cases admitted to the neonatal intensive care unit (NICU) of a tertiary care hospital ,Hassan. The study was carried out from March to December 2016.

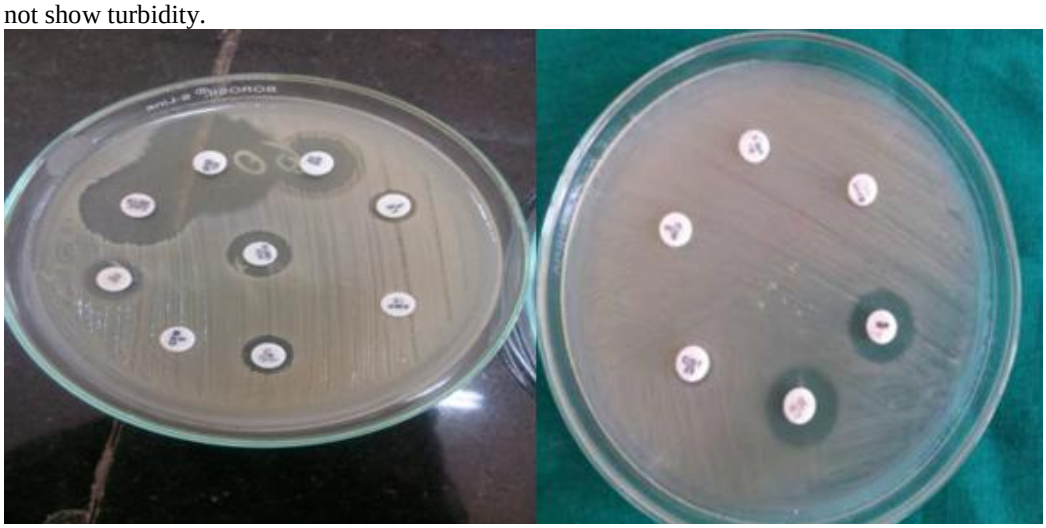
Inclusion criteria: Neonates clinically suspected of having sepsis, temperature >99ºF or <95ºF, respiratory rate>60 per minute, abnormal cry, refusal of feed, drowsy or unconscious, septic focus on skin or umbilicus, diarrhea and seizures.
Exclusion criteria: Neonates already on antibiotics and with diagnosis of intra-uterine infection and congenital anomalies were excluded from the study. [3]

4. Methodology

Blood culture sample included a single sample collected from a peripheral vein or artery under aseptic conditions.

The local site was cleansed with 70% alcohol and Povidone iodine (1%), followed by 70% alcohol again. Blood cultures was done in a brain heart infusion biphasic medium. Approximately, 1 ml of blood was inoculated into the brain heart infusion broth and incubated at 37˚c. subcultures was done on sheep blood agar and Macconkey agar at the earliest visual detection of turbidity or blindly on days 1, 4, and 7 ,if the bottles did not show turbidity.

Antibiogramwas done using appropriate antibiotics by Kirby-Bauer disc diffusion method. Isolated staphylococcus aureuswas tested for methicillin resistance usingcefoxitin disc (30µg) and ESBL producers were detected using combined disc method.



[Antibiotic sensitivity plate with ESBL producer (with CAZ+CAC)] [Antibiotic sensitivity plate with MRSA (tested with cefoxitin disc)]

5. Results

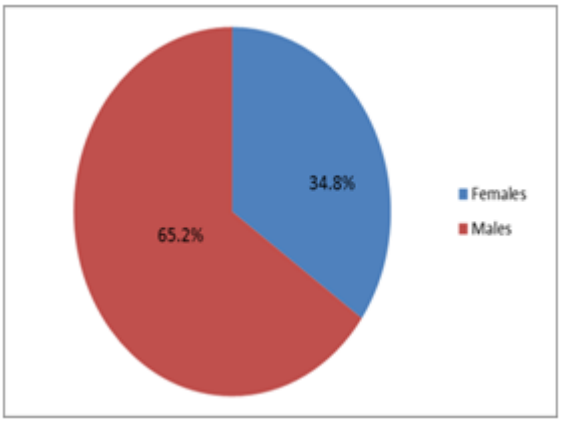
Total 250 patients were studied during the study period.Out of which 170 showed blood culture positive, positivity rate being 68%. Among the culture positive cases, there were 112 (65.2%) male and 58(34.8%) females. Male to female ratioof 1.9: 1.

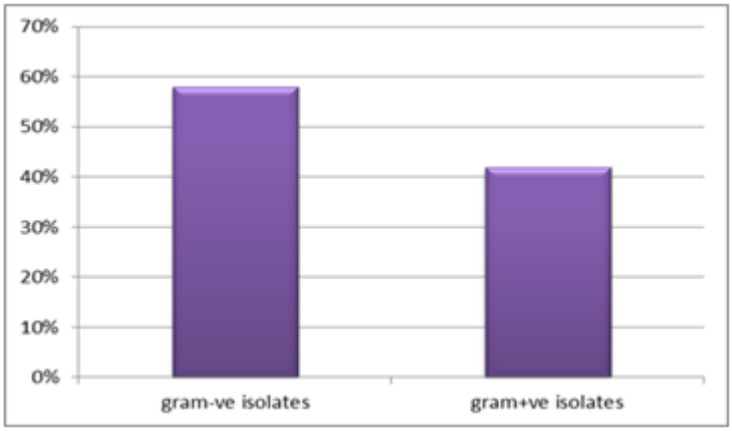
Gram-negative organisms were isolated in 98 cases(58%), Gram-positive in 72 cases(42%).In gram-negative isolates, 24cases (14%) were ESBL producers. Methicillin resistance in S.aureus was seen in as high as 15cases (30%) resistance.

Distribution of Isolated Organisms

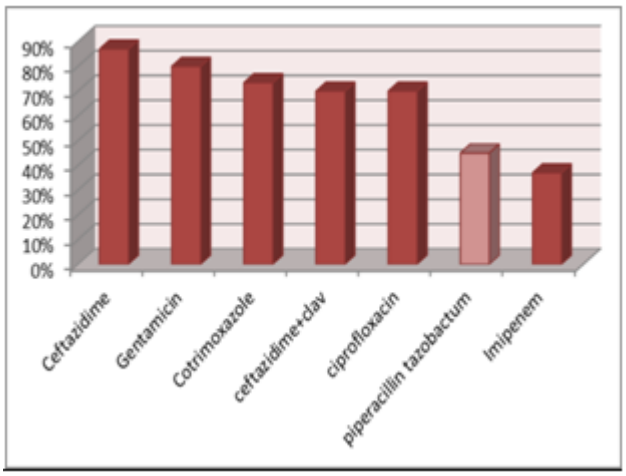
Organisms	Frequency of isolation
Klebsiella	32 (16%)
CONS	20(10%)
Acinetobacter	47(24%)
Staph. aureus	42(22%)
E.coli	12(6%)
Candida	18(9%)
Enterococci	14(7%)
Others(citrobacter , pseudomonas, micrococci, diphtheroids)	12(6%)
Total	197

Gender-wise distribution Percentage of isolates

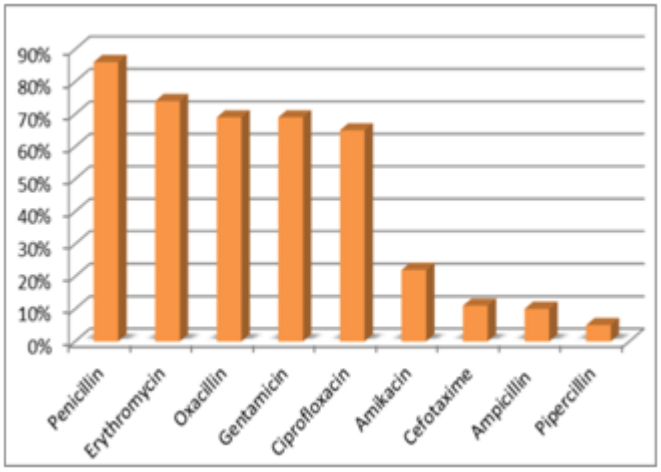




Antibiotic resistance among Gram negative isolates



Antibiotic resistance among Gram-positive isolates



Among Gram-negative isolates, Acinetobacterspp(24%) was commonest organism isolated followed by Klebsiella spp. (16%), E.coli(6%), and others(6%). While in Gram-positive isolates,Staphylococcus aureuswas most common (22%) followed by Coagulase negative Staphylococci (CONS) (10%) and Enterococci spp. (7%).

A preponderance of male infants is apparent in almost all studies of sepsis in newborns. In our study also, culture positivity was more in male infants.

Present study showed penicillin resistance in 80% isolates. Increased resistance was also noticed against Gentamicin, Erythromycin, Cephalosporins and Oxacillin which are commonly used for empirical therapy among Gram positive organisms.

Gram-negative organisms showed high resistance to the third generation Cephalosporins. They also showed high resistance to Cotrimoxazole, Gentamicin and Ciprofloxacin

ESBL production was detected in 24 (14%) of the cases of GNB that includedKlebsiella 14(8%) and E.coli 10(6%). 30% S.aureus isolates were found to be methicillin – resistant.

6. Discussion

Septicemia in neonates refers to generalized bacterial infection documented by positive blood culture in the firstfour weeks of life [4] and is one of the four leading causes of neonatal mortality and morbidity in India.[5-7]

Neonatal septicemia continues to be a major problem for neonates in neonatal intensive care units around the world.[8] Neonatal mortality rate is one of the indicators for measuring the health status of a nation.[9] There could be various reasons for neonatal mortality but septicemia continues to be a major cause of neonatal mortality and morbidity worldwide. Incidence varies from country to country, but it is much higher in developing countries than in developed nations.[9] According to World Health Organization (WHO)estimates, there are about 5 million neonatal deaths a year, with 98% occurring in developing countries.[10]

Neonatal sepsis is broadly divided into two types according to age of onset: Early-onset sepsis (<72 hrs) and late-onset sepsis (≥72 hrs-28 days). Early-onset sepsis is acquired during fetal life, delivery, or at the nursery.[11] Neonatal sepsis is caused by a variety of Gram-positive as well as Gram-negative bacteria, and sometimes yeasts.[8] The spectrum of organisms that causes neonatal sepsis changesover times and varies from region to region. This is due to thechanging pattern of antibiotic use and changes in lifestyle.[12]

The uncertainty surrounding the clinical approach to treatment of neonatal septicemia can be minimized by periodic epidemiological surveys of aetiological agents and their antibiotic sensitivity patterns leading to recognition of the most frequently encountered pathogens in a particular geographical area. For effectual management of septicemia cases, study of bacteriological profile along with the antimicrobial sensitivity pattern plays a noteworthy role.

The bacteriological profile of septicemia keeps changing with the passage of time from region to region and hospital to hospital, in the same city or country. The emergence of resistant bacteria in NICU settings leads to failure in the treatment of neonatal septicemia. To supplement the management of septicemia in neonates, we need to do longitudinal surveillance of the NICUs and formulate periodic guidelines for empirical treatment. In recent years, there has been a lot of improvement in medical facilities and as a result, the survival rate of the preterm and LBW babies has improved. But at the same time, these neonates with immature immune defenses are exposed to NICU flora for a longer duration.

The bacteriological profile has changed worldwide from predominant Gram-negative to a predominant Gram-positive bacteria isolation.[13-18] Many recent studies have reported the emergence of some new emerging organisms such as CONS, NFGO (non fermentor group of organisms), and Candida spp. as acause of neonatal septicemia.[4, 20-23]

Blood culture positivity in our study was 68%,which was high and similar to results found by Kumhar GD et al. Iroy

et al., and Kairavi .J.Desai et al[[24,25]],Mehmood et al[[25]], (2002) study was 4.76%, ShawCk et al[[26]], (2007) study was 54.64%, Bhattacharjee et al[[27]], (2008) study was 48%, Dias et al[[28]],(2010) study was 32% .

Our study showed a preponderance of Gram-negative isolates 58% versus 42%, Gram-positive isolates. Shah et al.[[1]], showed gram-negative 52% and gram positive 45% .Nayak et al[[30]]; showed 61.33% were gram negative isolates while 28% were gram positive isolates.

Our study showed S. aureus (22%) and CONS (10%) as the most common Gram-positive organisms which is quite similar as compared to other studies conducted by Agnihotri et al[[4]]. where S.aureus (35%) and Sundaram et al[[19]]. S.aureus (23%) and CONS (6.3%).

Both Gram-positive and Gram-negative isolates showed a high resistance to Cephalosporins, penicillin and gentamicin in the current study, it was observed that antibiotic resistance among the Gram –positive isolates was highest to penicillin (80%) followed by erythromycin.Similar reports of high resistance to Ampicillin (71%) were reported by Bhat et al[[20]].
In the present study, 30% S.aureus isolates were found to be methicillin –resistant, compared to 11.1% reported by Kaistha et al. [[29]], 41% by Thakur et al[[2]] .

Gram-negative isolates showed a high resistance to all Cephalosporins which is similar to the resistance pattern reported by Agnihotri et al[[4]] and Bhat et al.[[20]]

7. Conclusion

It is evident from this study that Gram-negative organisms (Klebsiella, Acinetobacter, E.coli), CONS, and S. aureus are the leading cause of neonatal sepsis in this study, and most of them are resistant to multiple antibiotics. Therefore we suggest that surveillance of antimicrobial resistance is necessary. Also, an antibiotic policy should be formulated in the hospital. Depending on the antibiotic sensitivity pattern of the isolates, antibiotics should be used. Furthermore, we advise that health education be provided to the public on the dangers of indiscriminate use of antibiotics, which is currently considered to be menace in our society and which has been responsible for the ineffectiveness of most commonly used antibiotics such as penicillin and ampicillin, as observed in our study.

Neonatal sepsis is an important cause of neonatal mortality and it depends upon the age of onset of sepsis, upon the etiologic agent and their resistant pattern. Implementation of infection control measures, periodic epidemiological surveillances in NICU's, strict aseptic measures like hand washing ,maintaining separate medicinal trays for each patient, fumigation of NICU's, restricted entry by health personnels, restricting the use of broad spectrum antibiotics,rotation of antibiotics and rationalizing the use of antibiotics can decreaseantibiotic resistance. Early diagnosis and specific treatment can reduce neonatal mortality and morbidity.

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