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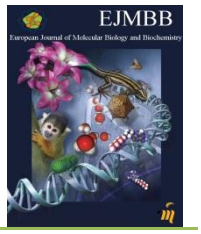

ACINETOBACTER: NO MORE A CHOISY INTRUDER IN NEONATAL SEPSIS

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ABSTRACT

The bacteriological profile of neonatal sepsis is constantly under change with advances in the early diagnosis and treatment of sepsis.Pan-resistant Acinetobacter infection has emerged as an important nosocomial pathogen in the inpatient neonates over the past few years. The primary objective of this study was to find out the prevalence of Acinetobacter species in cases of neonatal septicemia and their antimicrobial susceptibility pattern. This is a prospective study done over a period of one year at Mysore Medical College and Research institute, Mysore, Karnataka, India. Inclusion criteria were neonatal sepsis cases, where *Acinetobacter* species were isolated from blood cultures. In present study incidence of Acinetobacter infection is 6.9%. Antimicrobial susceptibility test showed that 78 isolates were resistant to Ampicillin and Amoxyclav (97.5%).78 (98%) isolates showed multi drug resistance (resistance to ≥ 3 categories of antibiotics), 25(31%) were sensitive to only one antibiotic, 17(21%) were sensitive to only two antibiotics, pan drug resistance was seen 12 (15%) of isolates. Susceptibility to Piperecillin-tazobactem was maximum 68 (85%) followed by Imipenem 60 (75%). Metallobeta lactamase producing strains were detected in 7(8%) isolates. Multidrug resistant Acinetobacter infection is fatal, particularly in premature and low birth weight neonates. Therefore, an effective infection control policy and rational antibiotic use are mandatory in neonatal intensive care areas of each hospital in order to control Acinetobacter infection and improve outcome.

INTRODUCTION

Septicemia remains a significant cause of morbidity and mortality in the newborns, more so in the developing countries [1]. The incidence of neonatal septicemia is 24 per 1000 live births according to National Neonatal Perinatal Database (NNPD) [2].

The bacteriological profile of neonatal sepsis is constantly under change with advances in the early diagnosis and treatment of sepsis and the increased survival of preterm babies [3]. Changing bacterial flora and emergence of resistant strains make it imperative to have knowledge on the prevailing pattern of antimicrobial susceptibility of the etiological agents of septicemia for the appropriate management of the patient. Acinetobacter species are gaining importance as potential pathogens in neonatal septicemia because of their frequent isolation and multidrug resistance. Early diagnosis and appropriate antimicrobial therapy of septicemia are of utmost importance to prevent morbidity and mortality [4]. Increasing rates of Acinetobacter infections may be due to

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lapses in infection- control practices. Institutional birth and preterm birth are identified as the most frequent risk factors. This might be because of multi-drug resistant strains jerking in the hospital environment.(5)Prenatal factors, flora of the delivery room and neonatal intensive care, quality of health care personnel, infection control methods of Neonatal Intensive Care Unit and antibiotics used remains the main determining factors.

With this background the present study was an attempt to find out the prevalence of Acinetobacter species in cases of neonatal septicemia and their antimicrobial susceptibility pattern.

MATERIAL AND METHODS

The present study was conducted in the department of Microbiology, MMC&RI, Mysore and its attached hospitals. Over a period of one year blood samples which were collected suspecting neonatal septicemia were included in the study. All clinical details of the neonates were noted. Blood samples of these neonates were collected with strict aseptic precautions. The samples were inoculated into Brain heart infusion Broth (Hi-Media, Mumbai). The bottles were then incubated aerobically at 37°C and checked for turbidity every day and subcultured according to the standard protocols. The colony characteristics on each culture medium were observed. Suspected colonies of Acinetobacter species were identified & processed by standard biochemical tests. Identification of Acinetobacter species was made on the basis of phenotypic criteria recommended by Gerner-Smidt. (Gram staining, colony morphology, penicillin susceptibility, oxidase, catalase and urease activity, citrate reduction, gelatin hydrolysis, glucose and lactose fermentation) [6].

Antimicrobial susceptibility testing was performed on Muller Hinton agar by disc diffusion method for the following antimicrobial agents according to the Clinical and Laboratory Standards Institutes guidelines (CLSI):Ampicillin (10µg), Amoxyclav, Cefotaxime (30µg), Ceftazidime (30µg), Ciprofloxacin (5µg), Gentamicin (10µg), Co-trimoxazole (25µg), Pipericillin tazobactem, Amikacin (30µg), Imipenem (10µg). Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 were used as quality control strains [7].

RESULTS

In one year study, 550 blood culture samples yielded growth, of which Acinetobacter isolates were 80 giving an incidence of 6.9%. Out of 80, 15(18.7%) were in NICU which included the new born and ≤ 1 day, 45 (56%) were <7 day old and 20(25%) were >7 days (Table 1). Antimicrobial susceptibility test showed that 78 isolates were resistant to Ampicillin and Amoxyclav (97.5%) (Table 2). 78 (98%) isolates showed multi drug resistance (resistance to ≥ 3 categories of antibiotics), 25(31%) were sensitive to only one antibiotic, 17(21%) were sensitive to only two antibiotics, pan drug resistance was seen 12 (15%) of isolates (Table 3). Susceptibility to Piperecillin-tazobactem was maximum 68 (85%) followed by Imipenem 60 (75%). Metallobeta lactamase producing strains were detected in 7(8%) isolates.

Table 1. Showing age distribution of neonates.

Age in Days	No of cases (n)
≤ 1 day	15(18.7%)
<7 days	45 (56%)
>7 days	20(25%)

Table 2. Resistance pattern of Acinetobacter

Antibiotics	Sensitive	Resistance
Ampicillin	2 (2.5%)	78 (97.5%)
Amoxyclav	2 (2.5%)	78 (97.5%)
Piperecillin and tazobactem	68(85%)	12(15%)
Imipenem	60 (75%)	20(25%)
Ciprofloxacin	38(47.5%)	42(52.5%)
Gentamicin	18(22.5%)	62(77.5%)
Cotrimoxozole	17(21.2)	63(78.8%)
Cefotaxime	15(18.8%)	65(81%)
Ceftazidime	12(15%)	68(85%)

Table 3. Showing multi drug resistance pattern

Groups of drugs	No of isolates
Resistance to ≥ 3 categories of antibiotics	78(98%)
Resistance to ≥ 5 categories of antibiotics	60(85%)
Pan drug resistance	12(15%)

DISCUSSION

Since the last three decades, Acinetobacter species has emerged as an important nosocomial pathogen and have been implicated in wide spectrum of infections, causing significant morbidity and mortality in the patients [8]. The present study was an attempt to correlate the various risk factors and outcome in cases of Acinetobacter neonatal sepsis. In India, the incidence of Acinetobacter sepsis reported varies from 6.5 to 31.5% [9,10]. In the present study, the incidence was 6.9% which is almost similar to other reports from India. A recent study from Pune has reported 10.8% Acinetobacter species from cases of neonatal sepsis [11].

Early onset sepsis syndrome is associated with acquisition of microorganisms from the mother. The most common risk factors associated with early onset neonatal sepsis include premature rupture of membranes (PROM), prolonged rupture of membranes, maternal urinary tract infection, and chorioamnionitis, poor prenatal care, poor maternal nutrition, low socioeconomic status, recurrent abortion etc [12]. Most importantly the repeated anti natal checkup (ANCs) recommended, serves as an important source of nosocomial pathogens like Acinetobacter .Colonization of these multi drug resistant pathogens concurrently lead to early-onset neonatal septicemia. In these situations, "colonization pressure" in mothers who are already colonized or infected with Acinetobacter, can affect the likelihood of cross-transmission to the neonate [13]. In the present study the risk factors for early onset sepsis included PROM in majority of cases followed by meconium aspiration syndrome.

Late-onset sepsis syndrome occurs at 4-90 days of life and is acquired from the care giving environment. The babies who were born in hospitals showed a higher isolation of *Acinetobacter* spp. This might be because of the multidrug resistant strains which were existent in the hospital environment [14]. Late neonatal sepsis is most commonly acquired from the hospital environment, practices and procedures like central venous catheterization (duration of >10 d), nasal cannula or continuous positive airway pressure (CPAP) [15]. The major maternal risk factors presented were LSCS and preterm labour. A study done by Caroline Signore et al says that elective cesarean delivery is associated with greater risk of neonatal respiratory morbidity and fetal laceration, neonatal sepsis, intracranial hemorrhage, intrapartum asphyxia, and neonatal encephalopathy [16].

The fetal risk factors were low birth weight, prematurity, perinatal asphyxia, fetal distress, iv catheterization, mechanical ventilation and hospital stay of more than 8 days.

CDC indicates that infections with MDR Acinetobacter are independently associated with the adverse clinical outcomes of prolonged hospital and ICU lengths of stay compared with the outcomes for uninfected patients and those infected with drug-susceptible Acinetobacter. We observed a significant association between Acinetobacter blood stream infection and above risk factors. It is highly alarming to note the levels of drug resistance in these isolates. It indirectly predicts that the isolate is of hospital origin and poses a great threat for the neonate and rises a concern in the management

Acinetobacter spp. has the reputation of causing outbreaks in intensive care units [17]. Resistances to major antimicrobial drugs as well as resistance to desiccants and disinfectants are the major factors that make it a successful and persistent hospital pathogen [18]. Multidrug-resistant Acinetobacter has been reported worldwide and is now recognized as one of the most difficult health care-associated infections to control and treat.

The likelihood of maternal and neonatal deaths is further magnified with the critical accumulation of risks such as unplanned, unwanted and unsupported pregnancy, delivering without being attended to by skilled health professionals (i.e. midwives, nurses and doctors), not securing proper postpartum and newborn care for the mother and her newborn, respectively which leads to the serious complications with prolonged hospital stay which give an access for the secondary infections multi drug resistant bacteria [19].

Acinetobacter remained as a successful nosocomial pathogen because of its ability to stay in the environment for prolonged periods [20]. Airborne transmission and patient-to-patient transmission have also been demonstrated. However, although the hands of hospital personnel, coupled with contamination of environmental surfaces and medical equipment, may play a role in the spread during an outbreak, it seems likely that the infected patient forms the primary reservoir of infection, with such patients shedding extremely large numbers into their surrounding environment [21]. Acinetobacter is emerging as an important pathogen in traditional and nontraditional healthcare settings. Its ability to infected healthy hosts and its propensity to develop antimicrobial drug resistance have caused concern among the infectious diseases community [22].

In our study the multidrug resistant Acinetobacter is on a inclined phase with 78 (98%) isolates resistant to ≥ 3 categories of antibiotics. It is documented that the prior use of third-generation cephalosporins (especially ceftazidime), fluoroquinolones, and carbapenems is associated with the subsequent development of MDR. In our study we have reported pan drug resistance of all the antibiotics we used which is an alarm to recognize Acinetobacter as an XDR bacteria and immediate and appropriate measures should be considered to prevent the spread of the same both at the hospital as well as community levels. Clinicians should be aware of drug resistance patterns of the isolates that render them to provide an effective patient care.

CONCLUSION

Multi-drug resistant nosocomial Acinetobacter septicemia may cause severe clinical disease in neonates

that is associated with a high mortality. The increase in the infection rate due to a particular pathogen may be due to lapses in infection-control measures, resulting in an increase in cross-transmission between patients. Therefore, continuous bacteriological surveillance, implementation of infection control policies, careful disinfection of intensive care equipment, and rational antibiotic use are required to control such infections.

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