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Acinetobacter species, antimicrobial resistance, colistin, children, PICU

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## Culture Sensitivity Pattern and Outcome of Acinetobacter Infection among Children Admitted in the Paediatric Intensive Care Unit of A Tertiary Care Hospital in Eastern India

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### Abstract

Acine to bacter species, resistant to most of the available antimicrobials, is a threat to pediatric population. It is now being frequently detected as a cause of hospital acquired infection, which can cause pneumonia, septicemia, meningitis, urinary tract and wound infections. We sought to find the prevalence of Acinetobacter infection, pattern of drug sensitivity and outcome of patients admitted in the paediatric intensive care unit of a tertiary care hospital in last 12 months. A prospective observational study was conducted over a total of 1004 patients admitted in Paediatric Intensive Care Unit(PICU)of our hospital over a period of 1 year. Data were collected and interpreted in Microsoft Excel using standard statistical analysis. Among the 1004 blood culture reports Acinetobacter species found in 28 (2.7%) patients. Acinetobacter found sensitive to colistin (42.85 %), minocycline (35.71%), cefoperazone-sulbactam (28.57%), amikacin (25%), trimethoprim/sulfamethoxazole (14.28%). It shows resistance to piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, gentamicin, ciprofloxacin, levofloxacin. These patients shows a wide spectrum of illness like pneumonia (35.71%), meningitis (21.42%), urinary tract infection (14.28%), multi organ dysfunction syndrome (10.71%), or both pneumonia with meningitis in a same patient (17.85%). Among these patients some required mechanical ventilation (35.71%) and ionotropic support (28.57%). After 42 days of treatment with antibiotics majority of them was cured 20(71.42%). But unfortunately, some of them died 8(28.57%) in the course of treatment. Among the discharged patients some showed long term sequelae 3(37.5%) like delayed developmental milestones, requirement of anticonvulsants, bronchiectasis, gait abnormality, malnutrition.

## INTRODUCTION

Management of Acine to bacter species infections is a challenge as it has the ability to survive in adverse condition and its ability to persist for long periods of time on surfaces makes it a frequent cause for healthcare-associated infections and multiple outbreaks<sup>[1,2]</sup>. The spectrum of infections include pneumonia, bacteremia, meningitis, urinarytract infection and wound infection. Beijerinck, a Dutch microbiologist, isolated the organism from the soil by enrichment in calcium acetate containing minimal medium on 1911 and named it *Micrococcus calcoaceticus*<sup>[3]</sup>. Genus *Acinetobacter* was first established on 1971. Bouvet and Grimont, distinguish 12 DNA (hybridization) groups or genospecies, in 1986, based on DNA relatedness criteria and named some species including *A. baumannii*, *A. calcoaceticus*, *A. haemolyticus*, *A. jobsonii*, *A. junii* and *A. looffii*<sup>[4]</sup>. At present, more than 25 Species of *Acinetobacter* have been identified by DNA-DNA hybridization. Among these species, *A. calcoaceticus*, *A. baumannii*, *Acinetobacter* genomic species 3 and Acine to bacter genomic species13 TU, are closely related and are difficult to distinguish them separately by phenotypic tests alone. They have been grouped as the *A. calcoaceticus*-*A. baumannii* complex<sup>[5,6]</sup>. 80% of the clinical infections caused by *Acinetobacter* species are due to this group of organism<sup>[7-10]</sup>. *Acinetobacter* is a 'multidrug resistant' (MDR) organism because it is resistant to three classes of antimicrobial agents- all penicillin's and cephalosporins (including inhibitor combinations), fluoroquinolones and amino glycosides<sup>[11]</sup>. If it shows resistance to carbapenems along with above class of antimicrobials then it is termed as 'extensive drug resistant' (XDR). XDR *Acinetobacter* species. that shows resistance to polymyxins and tigecycline, is termed as 'pandrug resistant' (PDR)<sup>[12]</sup>. As *Acinetobacter* is resistant to multiple antimicrobials, early investigation and proper susceptible antimicrobial treatment is necessary to combat this organism. For this proper knowledge of antimicrobial susceptibility of *Acinetobacter* for a particular area is necessary before setting guidelines for antimicrobial therapy.

**Aims and Objectives:** Hence, there is a need for surveillance to understand the trends of antibiotic susceptibility profile of *Acinetobacter* in a particular area. This study was therefore done to determine prevalence of this infection, its susceptibility pattern and outcome of this infection in pediatric intensive care unit in a tertiary care hospital.

## MATERIALS AND METHODS

This prospective observational cohort study was conducted in the pediatric intensive care unit, of our tertiary care hospital over a period of 1 year from May

2022-April 2023. Informed consent was taken from parents of each patient and approval taken from Research and Ethical committees of our institute. During the study period, all the patients admitted in pediatric intensive care unit in our tertiary care center were taken for screening of *Acinetobacter*. Acine to bacter is a hospital acquired infection and especially suspected in patients having symptoms of pneumonia, bacteremia, meningitis, urinarytract infection and wound infection. So two blood culture samples were sent from all the patients. 2ml Blood was collected aseptically before starting of antibiotics and added to each bottles containing 25ml of Brain heart broth (Hi Media, Mumbai, India). These culture vials were incubated at 37 degree Celsius for 7 days. Subcultures was taken in MacConkey agar and sheep blood agar on day 2 and day 7. If same organism is isolated from both broths then it was considered as pathogenic and if one broth obtained the organism or mixed growth was obtained, then it was taken as contaminated.

Acine to bacter was taken for culture sensitivity for antibiotics, namely-piperacillin/tazobactam, ceftazidime, cefoperazone/sulbactam, cefepime, imipenem, meropenem, amikacin, gentamicin, ciprofloxacin, levofloxacin, minocycline, colistin and trimethoprim/sulfamethoxazole. Windows Version SPSS used for data entry and analysis. Mean and standard deviations (SD) were calculated for study variables. To compare two groups Chi-square or Fisher's exact was used.  $P < 0.05$  was taken as statistically significant.

## RESULTS AND DISCUSSIONS

A total 1004 patients were admitted in pediatric intensive care unit during this 1 year time period. Two blood culture samples were sent for all these patients. Out of these 1004 samples, 648 samples were blood culture positive (64.5%) and 28 (2.78%) samples were found to be positive for Acine to bacter species. Among these 28 (2.78%) culture positive patients, 17 (56%) were male and 11 (44%) female.

Table 1 shows that, 12 out of 28 blood culture report of *Acinetobacter* was sensitive to colistin which is 42.85%. 10 out of 28 Acine to bacter species were sensitive to minocycline which is 35.71%. 8 out of 28 blood culture shows sensitivity to cefoperazone/sulbactam which is 28.57%. 7 out of 28 were amikacin sensitive (25%). And 4 out of 28 were sensitive to trimethoprim/sulfamethoxazole (14.28%). Acine to bacter species shows resistance to majority of antimicrobials like Piperacillin/Tazobactam, Ceftazidime, Cefepime, Imipenem, Meropenem, Gentamicin, Ciprofloxacin and Levofloxacin.

Table 2 shows that out of 28 patients with Acine to bacter Infection 10 shows features of pneumonia, 6 shows features of meningitis, 4 having urinary tract infection, 5 have both pneumonia and meningitis and

**Table 1. Culture sensitivity pattern of Acinetobacter species (Total cases n= 28)**

1. Colistin, n (%)	12 (42.85%)
2. Minocycline, n (%)	10 (35.71%)
3. Cefoperazone/Sulbactam, n (%)	8 (28.57%)
4. Amikacin, n (%)	7 (25%)
5. Trimethoprim/Sulfamethoxazole, n (%)	4 (14.28%)
6. Piperacillin/Tazobactam, n (%)	Resistant for all samples, 28 (100%)
7. Ceftazidime, n (%)	Resistant for all samples, 28 (100%)
8. Cefepime, n (%)	Resistant for all samples, 28 (100%)
9. Imipenem, n (%)	Resistant for all samples, 28 (100%)
10. Meropenem, n (%)	Resistant for all samples, 28 (100%)
11. Gentamicin, n (%)	Resistant for all samples, 28 (100%)
12. Ciprofloxacin, n (%)	Resistant for all samples, 28 (100%)
13. Levofloxacin, n (%)	Resistant for all samples, 28 (100%)

**Table 2. Disease pattern in Acinetobacter Infection (Total cases n= 28)**

Presentation	Number (percentage)
1. Pneumonia	10 (35.71%)
2. Meningitis	6 (21.42 %)
3. Urinary tract Infection	4 (14.28%)
4. Both Pneumonia and Meningitis	5 (17.85 %)
5. Multi Organ Dysfunction Syndrome	3 (10.71%)

**Table 3. Hospital course of children with Acinetobacter infection (Total cases n= 28)**

1. Requirement of Mechanical Ventilation	10 (35.71%)
2. Requirement of Ionotropic Support	8 (28.57%)
3. Death	8 (28.57%)
4.Recovery	20 (71.42%).
5. Long term sequelae	3 (37.5%)

3 presented with features of multiorgan dysfunction syndrome.

Table 3 depicts the hospital course and outcome of children with Acine to bacter sepsis. 10 out of 28 patients required mechanical ventilation which is 35.71%. Out of 28 patients 8 required ionotropic support. 20 out of 28 patients discharged on completion of 42 days of antibiotic. Unfortunately despite all measures taken, 8 patients out of 28 died during course of treatment.

3 out of 8 discharged patients shows long term consequences like delayed developmental milestones, requirement of anticonvulsants, bronchiectasis, gait abnormality and malnutrition.

In our study period a total of 1004 patients were admitted in pediatric intensive care unit in our tertiary care hospital. All these patients were screened for Acinetobacter infection by obtaining 2 blood culture sample from each patient. Out of 1004 blood culture report 28 (2.78%) were found to be positive for Acine to bacter spp. On gender comparison male gender was found to be predominant which was 17 (56 %) cases out of 28 cases and female patients was only 11 (44%) cases out of 28 cases. On antibiotic sensitivity testing Acinetobacter was found to be sensitive to colistin (42.85%), minocycline (35.71%), cefoperazone-sulbactam (28.57), amikacin (25%), trimethoprim/sulfamethoxazole (14.28%). But it is resistant to most of the other antibiotics like piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, gentamicin, ciprofloxacin, levofloxacin. Acine to bacter shows a wide spectrum of disease in these patients like Pneumonia (35.71%), Meningitis (21.42%), Urinary tract Infection (14.28%), Multi Organ Dysfunction Syndrome (10.71%), or both Pneumonia and Meningitis in a same patient (17.85%).

Among these patients some required of mechanical ventilation 10 (35.71%) and requirement of ionotropic support 8 (28.57%). All these patients were treated for 42 days of antibiotics according to culture sensitivity report. After completion of treatment majority of them was cured 20(71.42%). But unfortunately, some of them died 8(28.57%) despite receiving treatment with sensitive antibiotics. On long term follow up of the discharged patients some showed long term sequelae 3(37.5%) like delayed developmental milestones, requirement of anticonvulsants, bronchiectasis, gait abnormality, malnutrition. Recent articles related to Acinetobacter were searched in PUBMED, Google Scholar, and Cochrane Library. These articles shows Acinetobacter is a concern to health care system due to its multi drug resistance pattern. Though Acine to bacter is resistant to multiple antibiotics but with proper blood culture sensitivity report and using sensitive antibiotics we can overcome this burden. In our study we used 42 days course of sensitive antibiotics according to blood culture sensitivity report for Acinetobacter. With this strategy approximately 71.42% patients was cured and discharged. But after receiving sensitive antibiotic 28.57% patients failed to survive. We received blood culture report after 7 days which was the main limitation of our study as we were unable to start susceptible antibiotics before 7 days. Some patients deteriorated in these 7 days who failed to respond to empirical antibiotics during this period and these patients were either died in the course of treatment or showed long term sequelae. So in every patients 2 blood culture sample should be sent for culture and sensitivity. Furthermore we can use advanced culture system for fast culture sensitivity report like chromogenic agar. However if possible, a 6 monthly

antibiogram report should be made to check Acine to bacter sensitivity for antibiotics available locally to combat this organism.

## CONCLUSION

Acine to bacter species contribute to a high percentage of sepsis among children admitted in Pediatric Intensive Care Unit(PICU) of anytertiary care hospital.They are resistant to most of the common antibiotics used in PICU like piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, gentamicin, ciprofloxacin and levofloxacin.In our study we found Acine to bacter to be sensitive to colistin, minocycline, cefoperazone-sulbactam, amikacin and trimethoprim/sulfamethoxazole.They shows a wide spectrum of disease like Pneumonia, Meningitis, Urinary tract Infection and Multi Organ Dysfunction Syndrome. Most of them recovered well with sensitive antibiotics for six weeks. Few cases get complicated, required respiratory and inotropic support and ultimately expired. So if we identify this deadly organism early in the course of the disease then there will be better chance of recovery with appropriate antibiotics therapy sensitive to this multi resistant organism.

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