ORIGINAL ARTICLE

ACINETOBACTER INFECTIONS AS AN EMERGING THREAT IN INTENSIVE CARE UNITS

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Background: Nosocomial infections caused by *Acinetobacter* species (*Spp.*) is an emerging threat in health care setups especially intensive care units (ICU). The objective of this observational study was to determine the pattern of *Acinetobacter* infections and its association with length of stay in patients admitted to our medical ICU from January to August 2011. **Methods:** All patients above 16 years of age with stay of more than 48 hours were checked for any development of new infections not present or incubating at the time of admission. Nosocomial infections were documented in the light of clinical findings and lab results. Data was analysed using statistical software SPSS 15.0. **Results:** A total of 146 patients had a stay of at least 48 hours; frequency of nosocomial infection was 30.8% out of which 57.8% were *Acinetobacter* infections. Respiratory system was most commonly involved. *Acinetobacter* Spp showed high resistance (96.2%) to penicillins, cephalosporins and even extended spectrum antibiotics including carbepenems, quinolones and piperacillin plus tazobactam. Extended drug resistance was seen in 92.3% isolates; while we found high susceptibility to tigecycline (88.5%) and polymyxins (100%). *Acinetobacter Spp.* infected patients had mean length of stay (LOS) of 12.92 days when compared to patients with other nosocomial infections and no infection with mean LOS of 7.05 days (p=0.05) and 4.86 days (p=0.00) respectively. **Conclusions**: *Acinetobacter* Spp infections increase with longer duration of stay in ICU. Emergence of multi-drug and extended-drug resistant *Acinetobacter* Spp is alarming and overwhelming at this rate for already stretched out health system with its economic and health implications.

Keywords: *Acinetobacter*, medical ICU, nosocomial Infection, multi-drug resistant, hospital acquired infection

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INTRODUCTION

Acinetobacter is a gram-negative aerobic, non-motile, encapsulated and non-fermentative coccobacillus first described in 1911, belongs to the family Neisseriaceae. Frequently, it can be misidentified as Neisseria or Moraxella species on gram staining.[1] More than 20 species of *Acinetobacter* species (*Spp.*) has been reported.[2] However, the most common one known to cause major nosocomial infections in the ICU is *Acinetobacter baumannii*, making up to 80 percent of total *Acinetobacter* clinical isolates reported worldwide.[3] In humans *Acinetobacter Spp.* have been implicated in a wide spectrum of infections including pneumonia, meningitis, bacteraemia, soft tissue infections, surgical site infections, peritonitis, endocarditis, catheter-related infections and urinary tract infections. These infections mostly occur in critically-ill patients.[2]

Acinetobacter species are noted for their intrinsic resistance to multiple antibiotics. The chromosomally encoded AmpC cephalosporinase is common to all strains of *Acinetobacter*. baumannii. In addition recent emergence of the OXA enzymes confer carbapenem resistance. Other mechanisms of resistance include outer membrane protein changes, aminoglycoside-modifying enzymes, topoisomerase mutations and efflux pumps.[4] In addition, *Acinetobacter* organisms have dessication-tolerant properties, which account for its ubiquitous nature in the environment.

Acinetobacter became a concern in the ICUs in the United States; it was cited as the cause of 17 percent of cases of ventilator-associated pneumonias in a Guatemalan ICU, second only to *Pseudomonas* which caused 19 percent of cases.[5]

Infections with *Acinetobacter* tend to occur more commonly in debilitated patients in ICUs and among residents of long-term care facilities particularly facilities caring for ventilator-dependent patients. Additional risk factors include recent surgery, central vascular catheterization, tracheostomy, mechanical ventilation, enteral feeding, and treatment with third generation cephalosporin, fluoroquinolone, or carbapenem antibiotics.[6]

Data on *Acinetobacter Spp.* infections is lacking on local and national level in Pakistan. Most studies have been on the prevalence of microbial flora in general but not in specific on *Acinetobacter* infections in critical care units.[7,8] Studies can help recognize its magnitude at regional and local level and prevent possible outbreaks of this infection.[9] Moreover local studies can suggest regional epidemiological data and proper choice of antibiotics

in critically ill patients thus preventing delays in institution of effective therapy early.

The objective of this study was to determine the pattern of *Acinetobacter* infections and its association with length of stay in patients admitted to our intensive care unit.

MATERIAL AND METHODS

This observational study was conducted at medical intensive care unit of our institute. All patients consecutively admitted from January 2011 to August 2011 having age above 16 years and who stayed for more than 48 hours in intensive care unit were included in the study. Data was collected from patient files and lab database system and checked for any development of new infections irrelevant to that of at admission in view of baseline culture and sensitivities. Temperature along with other vitals, complete blood picture, urine analysis, x-rays, culture and sensitivities (blood c/s, urine c/s, tracheal/sputum c/s, stool c/s and other site specific sampling), indwelling catheters (Central venous, arterial and Foley's catheter), endotracheal intubations and any other procedures were looked for in all patients for clinical evidence of infection. Samples were cultured on blood agar and brain-heart infusion agar for *Acinetobacter Spp.* Susceptibility was tested using disc diffusion method according to the guidelines of Clinical and Laboratory Standards Institute (CLSI), 2009.[10] Nosocomial infection was documented in the light of Centre of Disease Control (CDC) Guidelines.[11] Patients were included only once in the study, regardless of the number of times *Acinetobacter* organisms were isolated. The first *Acinetobacter* culture isolate was considered. Pattern of *Acinetobacter* infection was documented in terms of frequency, type of organ system involved and its susceptibility. Susceptibility of *Acinetobacter Spp.* in documented infections was recorded based on culture and sensitivity reports. Length of stay in ICU was compared between patients with and without nosocomial infection. Independent samples t-test was used to compare means. *P* value of less than or equal to 0.05 was considered statistically significant. Data was analyzed with the help of statistical software SPSS Ver.15.0.

Any infection acquired in intensive care unit by a patient after 48hrs, not present or incubating at the time of admission was labelled as nosocomial infection. Multi-Drug Resistant (MDR) *Acinetobacter Spp.* was defined as the isolate resistant to at least three classes of antimicrobial agents - all penicillins and cephalosporins (including inhibitor combinations), fluroquinolones, and aminoglycosides. Extensive-Drug Resistant (XDR) *Acinetobacter Spp.* was defined as the isolate that is resistant to the three classes of antimicrobials described above (MDR) and shall also be resistant to carbapenems. Pan-Drug Resistant (PDR) *Acinetobacter Spp.* was defined as the isolate XDR that is resistant to polymyxins and tigecycline in addition to above.[12]

RESULTS

During 8 months period, out of 400 total admissions in our medical intensive care unit (ICU), 146 patients (n=146) had age above 16 years and stay greater than 48 hours. The mean age was 57.98 (Range: 22–89 years), 83 (56.8%) were males and 63 (43.2%) were females. Demographic and clinical characteristics of patients are summarized in table-1.

Nosocomial infections were seen in 45 (30.8%) patients, among this 26 (57.8%) patients had *Acinetobacter* Spp infection with overall percentage of 17.8%. Respiratory system was the most common system involved affecting 20 (76.9%) patients followed by blood stream and wound site infections in 3 (11.5%) patients each. Infected system involvement is summarized in table-2. No urinary or gastrointestinal infections were seen with *Acinetobacter Spp.*

Among 26 patients with documented *Acinetobacter* infection, *Acinetobacter Spp.* was found to be resistant in all patients (100%) against beta lactam penicillin (*ampicillin*), while in 25 (96.2%) out of 26 patients it showed resistance to second and third generation cephalosporins (*ceftazidime*, *cefepime*, *cefixime* and *ceftriaxone*). Resistance level was seen less when combination with inhibitor like *sulbactam* was used with cephalosporins; in our case *cefoperazone* with *sulbactam* was checked, showing resistance in 19 (73.1%) of these patients. In 25 (96.2%) of these patients *Acinetobacter* Spp showed resistance against most commonly used extended spectrum antibiotics including carbepenems (*meropenem* and *imipenem*), quinolones (*ciprofloxacin* and *levofloxacin*) and *piperacillin plus tazobactam.* On the other hand it showed resistance in only 50% of patients against *amikacin.* Susceptibility was found better to *glycylcycline* (tigecycline) and *polymyxin* (colistin) up to 88.5% and 100% respectively, while *Acinetobacter Spp.* isolates showed extended drug resistance in 24 (92.3%) patients. Detailed susceptibility results with respect to organ system involved are given in table-II. *Acinetobacter Spp.* infections were seen significantly increased with the increase in length of stay (LOS) in ICU. Mean length of stay was 12.92 days in patients with *Acinetobacter* infection compared to 7.05 days in patients with other nosocomial infections (p=0.05) and 4.86 days in patients with no infection (p=0.00) as shown in table-3.

Table-1: Demographics of Patients

Characteristics	Total Patients n=146 (100%)
Mean age	57.98yrs (R=22-89)
Gender	
Male	83 (56.8%)
Female	63 (43.2%)
Type of Admission	
Emergency	83 (56.8%)
Medical Wards	53 (36.3%)
Surgical wards	8 (5.5%)
Other Hospital	2 (1.4%)
Organ-System Effected	
Pulmonary	57 (39%)
Renal	22 (15.1%)
Neurologic	19 (13%)
DIC/Shock	15 (10.3%)
Cardiac	12 (8.2%)
Gastro	12 (8.2%)
Hematologic	3 (2.1%)
Endocrine	2 (1.4%)
Trauma	2 (1.4%)
Poisoning	2 (1.4%)
Mean length of stay	6.58 days (R=2–52)
Outcome	
Alive	111 (76%)
Dead	34 (23.3%)
LAMA (Left against medical advice)	01 (0.7%)

Table-2: Spectrum and Susceptibility of *Acinetobacter* Spp Infections.

Susceptibility		Type Of Infection			
		Respiratory (n=20) 76.9%	Blood (n=3) 11.5%	Wounds (n=3) 11.5%	Total (26) 100%
Cephalosporins	R	19 (95%)	3 (100%)	3 (100%)	25(96.2%)
	S	1 (5%)	0 (0%)	0 (0%)	1 (3.8%)
Cefoperazone + Sulbactam	I	2 (10%)	0 (0%)	0 (0%)	2 (7.7%)
	R	15 (75%)	2 (66.7%)	2 66.7%)	19 (73.1%)
	S	3 (15%)	1 (33.3%)	1 (33.3%)	5 (19.2%)
Ampicilin	R	20 (100%)	3 (100%)	3 (100%)	26 (100%)
Quinolones	R	19 (95%)	3 (100%)	3 (100%)	25 (96.2%)
	S	1 (5%)	0 (0%)	0 (0%)	1 (3.8%)
Carbapenem	R	19 (95%)	3 (100%)	3 (100%)	25 (96.2%)
	S	1 (5%)	0 (0%)	0 (0%)	1 (3.8%)
Amikacin	I	3 (15%)	1 (33%)	0 (0%)	4 (15.4%)
	R	10 (50%)	2 (66.7%)	1 (33.3%)	13 (50%)
	S	7 (35%)	0 (0%)	2 (66.7%)	9 (34.6%)
Piperacillin+ Tazobactam	R	19 (95%)	3 (100%)	3 (100%)	25 (96.2%)
	S	1 (5%)	0 (0%)	0 (0%)	1 (3.8%)
Tigecycline	R	2 (10%)	1 (33.7%)	0 (0%)	3 (11.5%)
	S	18 (90%)	2 (66.7%)	3 (100%)	23 (88.5%)
Colistin	S	20 (100%)	3 (100%)	3 (100%)	26 (100%)

R=*Resistant*, **S**=*Sensitive*, **I**=*Intermediate*

Table-3: Nosocomial Infections and length of stay in ICU

Nosocomial infection	Total patients (n)	Mean LOS (Days)	SD	Independent *t*-test Sig.(2-tailed)
No infection	101	4.86	3.231	*p*=0.000
Acineto-Infection	26	12.92	11.980	
Other infections	19	7.05	4.743	*p*=0.050

DISCUSSION

Acinetobacter associated nosocomial infections in critically ill patients are on the rise.[13,14] Its multi-drug resistant (MDR) phenotype is capable of acquiring new mechanisms of resistance and nosocomial outbreaks.[15]

In our study the frequency of nosocomial infection was 30.8% comparable to some recent local studies showing frequency of 29.13% and 39.7% respectively.[16,17] *Acinetobacter* Spp infections accounts for 57.8% of these infections which seems to be rising worldwide.[14,18,19]*Acinetobacter* infections most frequently involve the respiratory tract of intubated patients and *Acinetobacter* pneumonia has been more common in critically ill patients in Asian (range 4–44%) and European (0–35%) hospitals than in United States hospitals (6–11%). A higher proportion of *Acinetobacter* isolates were resistant to *aminoglycosides* and *piperacillin/tazobactam* in Asian and European countries than in the United States. The data suggest that *Acinetobacter* infections are a growing threat affecting a considerable proportion of critically ill patients especially in Asia and Europe.[20]

Most common system involved in our study by *Acinetobacter* infection was respiratory system which is comparable to above and studies from Pakistan[7] India[21] and Turkey[22] followed by blood and wound infections. In our study *Acinetobacter Spp.* showed 100% resistance to beta lactam penicillin (*ampicillin*), 96.2% to second and third generation cephalosporins (*Ceftazidime, cefepime, cefixime* and *ceftriaxone*) and extended spectrum antibiotics (*Carbepenems, quinolones* and *piperacillin plus tazobactam*), 73.1% against *cefoperazone* with *sulbactam* combination and 50% resistance against amikacin. High susceptibility was found against *tigecycline* and *polymyxin* (*Colistin*) 88.5% and 100% respectively. These results were found similar to studies done by Erdem *et al*.[22] There are not many local studies suggesting the susceptibility patterns of *Acinetobacter* Spp. One study suggests the increasing resistance to *cephalosporins* and *carbapenems*[23] and similarly another one from Aneela *et al* suggested very high resistance against *ceftazidime* (100%), *amikacin* (91%), *ciprofloxacin* (88%) and to *imipenem* (86%).[7] With increased length of stay chances of acquiring these nosocomial infections increases. *Acinetobacter Spp.* infection tend to be associated with longer duration of stay as seen in our study and others.[24,25] Vice versa these infections can increase morbidity, length of stay and mortality.[24] Extended drug resistance was seen in 92.3% *Acinetobacter* isolates in our study that is comparably high and it may be due to dubious definition of multi

and extended drug resistant *Acinetobacter Spp.* However studies do show already increasing resistance and high figures for nosocomial infection caused by multi drug resistant *Acinetobacter Spp.* as in study by Kempf *et al*[25] and others.[21,22,26] No pan resistant *Acinetobacter Spp.* was seen in our study. We have observed good susceptibility to *doxycycline* comparable to *tigecycline* in our study but due to its limited data, we didn't include it in our study.

CONCLUSION

This study shows pattern of *Acinetobacter Spp.* infection in our setup. *Acinetobacter Spp.* infections tend to increase with the increase in length of stay in ICU. Extended resistant *Acinetobacter Spp.* warrants urgent attention. This increases morbidity, mortality and healthcare costs because of extended length of stay, use of more potent/toxic and more expensive drugs especially in intensive care units. This calls in for the review of our local, national and universal infection control policies and practices before it takes its toll on already stretched out health system.

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