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Full Length Research Paper

Risk factors and outcome of *Acinetobacter* infection in the intensive care unit of a tertiary center in Oyo State, Nigeria

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Acinetobacter **plays an important role in the infection of patients admitted to hospitals.** ***Acinetobacter*** **are free living gram-negative coccobacilli that emerge as significant nosocomial pathogens in the hospital setting and are responsible for intermittent outbreaks in the intensive care unit. The aim of this study was to determine the risk factors and outcome of** ***Acinetobacter*** **infections in patients admitted into the intensive care unit of a tertiary center in Oyo State, Nigeria. A total of one hundred patients were recruited for the study, catheter specimen urine, tracheal aspirate and blood culture were collected aseptically from the patients. The specimens were cultured on blood and MacConkey and the organisms identified using Microbact 12E (0xoid). Fourteen (14%) of the 100 patients recruited into the study developed** ***Acinetobacter*** **infection. Chronic obstructive pulmonary disease, endotracheal intubation, and duration of endotracheal intubation were associated risk factors with only duration of endotracheal intubation specifically an 8 to 14 day period being an independent risk factor for** ***Acinetobacter*****. Six of the patients died of the infection while the remaining eight were discharged from the ICU. The findings that chronic obstructive pulmonary disease and duration of endotracheal intubation being associated with** ***Acinetobacter*** **infection and the attendant mortality associated with the infection should draw attention to this seemingly silent epidemic in our Intensive Care Units so that effective surveillance protocols can be deployed to manage this infection whenever it rears its head.**

Key words: *Acinetobacter*, intensive care unit.

INTRODUCTION

In the last 2 decades, control of hospital-acquired infection caused by multidrug resistant Gram-negative bacilli has proved to be a peculiar problem. An increased incidence of resistant members of the family *Enterobacteriaecea* involved in nosocomial infections was followed by the introduction of newer broad spectrum antibiotics in hospitals and a subsequent increase in the importance of aerobic Gram-negative bacilli. Of the newer pathogens, *Acinetobacter* plays an important role in infection of patients admitted to hospitals. (Gerner-Smidt, 1994).

Acinetobacter is ubiquitous, free-living and fairly stable in the environment. Members of the genus are Gram-negative cocco-bacilli that emerge as significant nosocomial pathogens in the hospital setting and are responsible for intermittent outbreaks (Joshi et al., 2006). Due to their distinct adhesive ability to epithelial cells, they have a predilection to colonize skin, especially

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in the areas of the perineum, inguinal region, axillae, mucous membranes and upper respiratory airway (Silvia Munoz et al., 2008). Over the past two decades, *Acinetobacter* infections have become an increasingly common nosocomial problem. (Silvia Munoz-P et al., 2008; Luis Garcı´a-Garmendia et al., 2001).

In addition to hospitalized patients, community acquired *Acinetobacter* infection is increasingly reported in studies (Villegas and Hartstein, 2003*). Acinetobacter* infections are increasingly implicated in infections in intensive care units and have been cited in up to 17% of ventilator associated pneumonias, second only to *Pseudomonas*, which was responsible for 19% of ventilator associated pneumonia in an ICU (Silvia Munoz et al., 2008). Infections caused by *Acinetobacter* are difficult to control due to multi-drug resistance; this limits therapeutic options in critically ill and debilitated patients especially from intensive care units where their prevalence is most noted (Joshi et al., 2006). The incidence of outbreak is much more in the regions where temperature is hot and humid (Joshi et al., 2006; Silvia Munoz et al., 2008; McDonald et al., 1999). *Acinetobacter* outbreaks have been traced to contamination of respiratory-therapy and ventilator equipment from cross-infection by the hands of health care workers who have cared for colonized, infected patients or touched contaminated fomites (Villegas and Hartstein, 2003; Maragakis et al., 2004).

Acinetobacter baumannii, Acinetobacter calcoaceticus and *Acinetobacter lwoffii* are the species most frequently reported in clinical literature (Silvia Munoz et al., 2008). There are some data to suggest that the proportion of intensive care unit (ICU)-acquired pneumonia cases being found to be due to *A. baumannii* is actually increasing. In large surveillance studies from the United States between 5 and 10% of cases of ICU-acquired pneumonia were due to *A. baumannii* (McDonald et al., 1999). Data on *Acinetobacter* in Africa is largely limited to South Africa at the present time, although there are scattered reports from other countries in Africa (Lowman et al., 2008).

In addition to lengthy stay in the ICU, risk factors for colonization and infection are recent surgery, central vascular catheterization, tracheostomy, mechanical ventilation, enteral feedings, and treatment with third-generation cephalosporin, fluoroquinolones, or carbapenems antibiotics (Silvia Munoz et al., 2008). The study of Husni and co-workers establish clear-cut evidence of an association between some antimicrobial agents and *A. baumannii* infection (Husni et al., 1999). It was shown that indiscriminate use and abuse of antimicrobials led to the selection of drug resistant strains.

Acinetobacter infection in literature is associated with high morbidity, mortality and increased length of hospital stay especially amongst patients in ICU, this has been attributed to its ability to acquire and up regulate resistance genes (Silvia Munoz et al., 2008). Despite the fact that patients in the ICU of the University College Hospital Ibadan have similar associated risk factors (mechanical ventilation, tracheostomy, exposure to antibiotics particularly third generation cephalosporins, quinolones, carbapenems, prolonged hospital stay, multiple invasive procedures) they are not isolated in the hospital. (Husni et al., 1999). The aim of this study was to determine the risk factors and outcome of *Acinetobacter* infections in ICU patients in the University College Hospital Ibadan.

MATERIALS AND METHODS

Study area

This cross sectional study was carried out in the University College Hospital (UCH) Ibadan, Nigeria. The University College Hospital is a 850 bedded tertiary health institution with a 12 bedded ICU and which has a monthly turnover of 25 patients.

Study population

This consists of patients who were admitted in the intensive care unit of the University College Hospital. A total of 100 patients were recruited into the study, this population of patients comprises of patients who have had surgery, on ventilators or intubation and prior history antibiotic use. Ethical approval was obtained from the University of Ibadan, University College Hospital joint ethical committee.

Methods of data collection

Verbal and written informed consent was sought and obtained from spouse, parent or caregiver of each subject; thereafter relevant medical history, socio-demographic data and other information obtained from the care giver and case files were entered into a semi-structured close-ended questionnaire.

Laboratory methods

The tests were carried in the Bacteriology laboratory of the University College Hospital.

Specimen collection and transport

Tracheal aspirate, blood, urine were collected from all recruited patients for microscopy, culture and sensitivity. Specimens were collected using aseptic technique to prevent contamination. For optimal results, specimens were collected in clean sterile, wide bore containers. The samples were collected in patients who had spent at least 48 h in ICU.

Culture and identification

The specimens were inoculated on selective and non-selective media. The specimen was inoculated on MacConkey agar and blood agar and incubated at 35-37°C for 18-24 h. *Acinetobacter* species grew on MacConkey agar appearing as a non-lactose

fermenter.

Characterization

All Gram-negative coccobacilli isolated were tested for catalase and motility. All catalase positive, non-motile Gram negative coccobacilli were subjected to an oxidase test. All oxidase negative organisms were inoculated into peptone broth for about 30 min. Subsequently 1 ml of the broth was inoculated into the various cups of Microbact Identification kit and incubated for 18-24h. After the stated period, Gram negative coccobacilli were identified as *Acinetobacter* spp based on the reactions on the identification panel which was read with the help of the identification software that accompanies the kit. Ventilator-associated pneumonia is defined as pneumonia occurring more than 48 h after patients have been intubated and received mechanical ventilation.

Data analysis

All data were analyzed using the Statistical Package for the Social sciences (SPSS) version 15.0. Data were presented using frequency tables, charts, as appropriate and cross tabulation to study relationships and association between variables. Statistical significance was set at 5%. A logistic regression was conducted to identify factors independently associated with *Acinetobacter* infection.

RESULTS

A total of 100 patients were recruited into the study over a period of 9 months. The age of the patients range from 2 to 95 years. Majority of the patients (40%) were in the 31-40 year age group while the 10-20 year age group constituted the least age group (4%). There were 52 males and 48 males, giving a male to female ratio of 1.08:1. Eighty one (81%) of the patients were admitted from the Accident and Emergency unit while 19% were from other wards in the hospital (Table 1).

Acinetobacter spp was isolated from fourteen (14%) of the total number of patients recruited into the study and was responsible for 14% of infections in the ICU based on evaluation of clinical charts. It represented 9% of the isolates from all the specimens collected during the study period (Table 1). Twelve (86%) of the isolates were recovered from tracheal specimens while 1(7%) was from urine and blood specimens each. Eleven (79%) of the isolates were *A. baumannii* while the others were *A. iwoffi* (14%) and *A. calcoaceticus* (7%) (Table1).

Clinical characteristics

Six (11.5%) of the males had *Acinetobacter* infection compared with eight (16.7%) observed among the females. There is no significant difference in the prevalence of *Acinetobacter* infection between both sexes (P-value= 0.460). Eighty-seven (87%) of the patients in the intensive care unit were mechanically ventilated. Thirteen (14.9%) of the patients who were mechanically ventilated developed *Acinetobacter* infection as compared to 1(7.7%) who was not mechanically ventilated but had *Acinetobacter* infection. Mechanical ventilation was not a risk factor for the development of *Acinetobacter* infection. (Table 2, P-value=0.482).

Of the patients studied, 11% were diabetic while 21% were hypertensives. Diabetes mellitus and hypertension did not contribute significantly to *Acinetobacter* infection (Table 2). Of the three patients who had chronic obstructive pulmonary disease (COPD) two (66.7%) developed *Acinetobacter* infection. There was a positive association between COPD and development of *Acinetobacter* infection (Table 2, P- value=0.008). Ionotropic support, steroid use and use of Immunosuppressants did not impact significantly on the likelihood of having *Acinetobacter* infection. Mode of nutrition, renal support, length of stay in ICU, peripheral, central venous cannulation and history of blood transfusion also did not contribute statistically to likelihood of *Acinetobacter* infection (Table 2).

Two (9.1%) of the patients who had a tracheostomy developed *Acinetobacter* infection compared to twelve (15.4%) of the patients who did not have tracheostomy tube but developed *Acinetobacter* infection. Also Presence of an endotracheal tube and the duration of endotracheal intubation also were risk factors for *Acinetobacter* infection (Table 3). Multivariate Logistic Regression done for risk factors with P value of less than or equal to 0.1, only the following factors fit into the model: Fever, endotracheal intubation, duration of endotracheal intubation and length of stay in ICU. Only duration of endotracheal tube was an independent risk factor for *Acinetobacter* infection (Table 4). Outcome of *Acinetobacter* infection in the ICU, of the fourteen patients with *Acinetobacter* infection six of the patients succumbed to the infection while eight of the patients were discharged from the ICU after prolonged duration of antibiotherapy.

DISCUSSION

Prevalence of *Acinetobacter* infection in this study was 14%, this prevalence is higher than reports from similar studies carried out in France (Jolly-Guillou, 2005) who reported 9% and Iregbu et al. (1999) who reported 4.6%. The higher prevalence in this study may due to sample location with the ICU having a lot of patients with debilitating illnesses and also attention to infection control practices may not have been strictly adhered to. *Acinetobacter* consisted of 9% of all isolates in the study, this finding is low compared to 14.5% obtained by Kessaris et al. (2006), 13.9% by Lul et al. (2009) but higher than 8.4% reported by Oberoi et al. (2009) and 3% reported by Iregbu et al. (1999).

In this study 12(86%) of the isolates were recovered from tracheal aspirate. This is similar to the 87% obtained

Table 1. Distribution of socio-demographic data and selected variables.

Variable	Number	Percent
Age (Years)		
<10	13	13.0
10-20	4	4.0
21-30	13	13.0
31-40	30	30.0
41-50	20	20.0
51-60	10	10.0
>60	10	10.0
Sex		
Male	52	52.0
Female	48	48.0
Source of Isolate		
Tracheal Aspirate	12	86.0
Urine	1	7.0
Blood	1	7.0
Species Distribution		
Acinetobacter baumannii	11	79.0
Acinetobacter Iwoffi	2	14.0
Acinetobacter calcoaceticus	1	7.0
Source of Admission		
A/E	82	82.0
Ward	18	18.0

A/E, Accident and emergency.

by Lul et al. (2009) but much higher than 46.5% reported by Popescu et al. (2011) these results are in conformity with the present study where the respiratory tract is the most frequent site of isolation of *Acinetobacter spp* in ICU patients (Lul et al., 2009; Popescu et al., 2011; Alsan and Klompas, 2010). The high rate of recovery from the respiratory tract may be due to the invasive procedures that were carried out in the respiratory tract in the process of maintaining the airway. Risk factors for *Acinetobacter* infection reported by Dijkshoorn et al. (2007) were previous surgery and antibiotic use but this was contradicted in this study. Other risk factors implicated in other studies such as length of ICU stay, urethral catheterization, mechanical ventilation, diabetes mellitus, mode of nutrition were dispelled in this study (Garnacho-Montero et al., 2005; Özdemir et al., 2011; Deris et al., 2011). Duration of endotracheal intubation, chronic obstructive pulmonary disease were risk factors associated with *Acinetobacter* infection identified in this study (Garnacho-Montero et al., 2005; Özdemir et al. 2011; Deris et al., 2011).

Severe underlying diseases, invasive diagnostic and therapeutic procedures used in ICUs have been demonstrated to predispose patients to severe infections with *A. baumannii (*Jarousha et al., 2008). Residents of long-term care facilities, particularly ventilator-dependent patients are also at increased risk. The identification of ICU stay as a strong risk factor is not unexpected. A longer stay in a high-risk unit has been identified as a risk factor in previous studies (Lone et al, 2009). In this study 42.9% of patients who developed *Acinetobacter* infections spent between 8-14 days in the ICU; this is similar to that reported by Husni et al. (1999) where the mean time was 12.4 days. The wide array of intrinsic and acquired resistance determinants that have emerged in *A. baumanni* have justifiably brought it great scientific attention as determined by the Infectious Diseases Society of America (Ecker et al., 2008). *A. baumannii* is one of the "red alert" pathogens that greatly threaten our current antibacterial armoury. Prior to the 1970s, it was possible to treat *Acinetobacter* infections with a range of

Table 2. Relationship between selected risk factors and *Acinetobacter* infection.

Parameter	Presence of *Acinetobacter*			
	Yes	No	Total	P- value
Sex				
Male	6(11.5%)	46(88.5%)	52(100%)	0.460
Female	8(16.7%)	40(83.3%)	48(100%)	
Primary diagnosis				
Medical	3(3%)	22(22%)	25(25%)	
Surgical	2(2%)	12(12%)	14(14%)	0.678
Neurosurgical	8(8%)	44(44%)	52(52%)	
Obs/gynae	1(1%)	8(8%)	9(9%)	
Mechanical ventilation				
Yes	13(14.9%)	74(85.1%)	87(100%)	0.482
No	1(7.7%)	12(92.3%)	13(100%)	
Diabetes mellitus				
Yes	2 (18.2%)	9 (81.8%)	11 (100%)	0.672
No	12 (13.5%)	77 (86.5%)	89 (100%)	
Hypertension				
Yes	3 (14.3%)	18 (85.7%)	21 (100%)	0.966
No	11 (13.9%)	68 (86.1%)	79 (100%)	
Chronic obstructive pulmonary disease				
Yes	2 (66.7%)	1 (33.3%)	3 (100%)	0.008
No	12 (12.4%)	85 (87.6%)	97 (100%)	
Immunosuppressant use				
Yes	1 (50.0%)	1 (50.0%)	2 (100%)	0.138
No	13 (13.3%)	85 (86.7%)	98 (100%)	
Nutrition				
Enteral	2 (11.8%)	15 (88.2%)	17 (100%)	0.771
Parenteral	12 (14.5%)	71 (85.5%)	83 (100%)	

antibiotics, including aminoglycosides, β-lactams, and tetracyclines. However, resistance to all known antibiotics has now emerged in *A. baumannii*, thus leaving the majority of today's clinicians in unfamiliar territory.

Conclusion

The intensive care unit is responsible for life support services to patients from diverse specialties; it has a high rate of isolation of multidrug resistant organisms that pose therapeutic problems to both the managing clinicians and clinical microbiologists. The 14% prevalence of *Acinetobacter* infection in the ICU of the University College Hospital, Ibadan, Nigeria, though in keeping with reports from other climes is quite high and suggest a poor infection control practice in the ICU. Risk factors identified in this study were chronic obstructive pulmonary disease and duration of endotracheal intubation. On logistic regression analysis only duration of endotracheal intubation was an independent risk factor for *Acinetobacter* infection. So policies for infection control in patients on ventilators for prolonged periods should be developed.

Table 3. Relationship between selected risk factors and *Acinetobacter* infection.

Parameter	Presence of *Acinetobacter*			
	Yes	No	Total	P-Value
Endotracheal intubation				
Yes	14(17.1%)	68 (82.9%)	82 (100%)	0.05
No	0 (0.0%)	18 (100.0%)	18 (100%)	
Duration of endotracheal Intubation (days)				
<7	2 (5.1%)	36 (94.9%)	38 (100%)	
8 to 14	5 (20.8%)	17 (79.2%)	23 (100%)	0.05
>14	5 (22.7%)	16 (77.3%)	21 (100%)	
Ionotropic support				
Yes	3 (20.0%)	12 (80.0%)	15 (100%)	0.465
No	11 (13.0%)	74 (87.0%)	85 (100%)	
Renal support				
Yes	1 (25.0%)	3 (75.0%)	4 (100%)	0.518
No	13 (13.5%)	83 (86.5%)	96 (100%)	
Blood transfusion				
Yes	8 (16.3%)	41 (83.7%)	49 (100%)	0.511
No	6 (11.8%)	45 (88.2%)	51 (100%)	
Peripheral cannula				
Yes	14 (14.1%)	86 (85.9%)	100(100%)	0.685
No	0 (0%)	0 (0%)	0(0%)	
Central venous catheter				
Yes	3 (25.0%)	9 (75%)	12(100%)	0.242
No	11(12.5%)	77 (87.5%)	88(100%)	
Urinary catheter				
Yes	14(14.4%)	83(85.6%)	97(100%)	0.478
No	0(0%)	3(100%)	3(100%)	
Drain				
Yes	2(33.3%)	4 (66.7%)	6(100%)	0.159
No	12(12.8%)	82 (87.2%)	94(100%)	
Tracheostomy				
Yes	2(9.1%)	20 (90.9%)	22(100%)	0.452
No	12(15.4%)	66 (84.6%)	78(100%)	
Length of Stay(days)				
<7	3(6.4%)	44 (93.6%)	47(100%)	
8-14	6(19.4%)	25 (80.6%)	31(100%)	0.111
>14	5(22.7%)	17 (77.3%)	22(100%)	
Steroid use				
Yes	3 (17.6%)	14 (82.4%)	17 (100%)	0.634
No	11 (13.3%)	72 (86.7%)	83 (100%)	

Table 4. Logistic regression analysis of risk factors to rule out confounders.

Parameter	B	P-value	O.R	C.I
Fever				
<1 week	1			
>1 week	-0.351	0.802	0.704	0.045 - 10.937
Endotracheal tube duration				
<7 days	1	0.087		
8 to 14 days	2.057	0.033	7.819	1.179 - 51.882
> 14	1.671	0.075	5.318	0.846 - 33.431
Endotracheal tube				
Yes	1			
No	-18.777	0.999	0.000	0.000
Length of ICU Stay				
< 1 week	1	0.237		
1 to 2 weeks	-1.390	0.088	0.249	0.05 - 1.231
2 to 3 weeks	0.791	0.484	2.205	0.241 - 20.260
> 3 weeks	-19.781	0.999	0.000	0.000

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