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Original Article

Acinetobacter baumannii Infection in the Neonatal Intensive Care Unit

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Abstract

Background: To perform a prospective case control study of blood stream infection to determine the infection rate of *Acinetobacter baumannii* and the risk factors associated with mortality.

Methods: From February 2004 to January 2005, 579 consecutive episodes of blood stream infection were obtained at two neonatal intensive care units Al Nasser and Al Shifa hospitals in Gaza City. Forty (6.9%) isolates of *A. baumannii* were obtained from the neonates under 28 d. Most of the isolates (92%) were from hospitalized patients in the intensive care units.

Results: Community acquired infection was 8%. Sixty three percent of the patients were males. The isolates of *A. baumannii* were resistant to commonly used antibiotics while being sensitive to meropenem (92.5%), imipenem (90%), chloramphenicol (80%), ciprofloxacin (75%), gentamicin (57.5%), ceftriaxone (50%), amikacin (37.5%), cefuroxime and cefotaxime (35%). Over all crude mortality rate was 20% with much higher crude mortality among patients with nosocomial infection. Based on logistic regression, the following factors were statistically significant: weight < 1500g, age < 7 d, mean of hospitalization equal 20 days, antibiotic use, and mechanical ventilation, when compared to the control group ($P< 0.05$).

Conclusion: Infection rate of nosocomial blood stream infection was considerable and alarming in neonatal intensive care unit infants and associated with a significant excess length of NICU stay and a significant economic burden.

Keywords: *Nosocomial infection, Multidrug resistance, Neonatal intensive care unit,* Acinetobacter baumannii

Introduction

Newborns receiving care in neonatal intensive care unit (NICU) are at increased risk of nosocomial infections because of immaturity of the immune system and barrier functions of the skin and gastrointestinal tract, and the invasive diagnostic and therapeutic procedures they undergo (1). Nosocomial infections are those that are acquired in a hospital setting. The center for disease control and prevention (CDC) defines ICU associated infections as those that occur after 48 h of ICU admission or within 48 h after transfer from an ICU (2).

The NICU patients are at high risk nosocomial blood stream infection (NBSI) because of the high acuity, prolonged hospitalization and frequent invasive procedures. Previous studies have found the incidence of NBSI in NICUs to be 5 to 32% (3). Critically ill patients of intensive care units (ICUs) frequently develop nosocomial blood stream infections, which is a leading cause of death in such patients. Debilitated condition of the patient due to underlying diseases, invasive diagnostic and therapeutic procedures and contaminated life support equipment predispose these patients to life threatening BSI. With the spread of multi-resistant bacteria, the treatment of nosocomial BSI has become a challenging task (4).

Bloodstream infections (BSIs) are now ranked as the 10th leading cause of death in the United States, with a recent increase in age-adjusted death rates (5), BSIs also have been associated with increased rates of hospitalization (6,7) increased length of stay (8, 9), and increased hospital costs (10-12). The earliest possible identification of BSI allows for prompt optimization of

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antimicrobial therapy and diminished need for additional diagnostic studies which in turn may serve to decrease both length of stay and cost.

Members of the genus *Acinetobacter* are ubiquitous, free living, small aerobic Gram-negative coccobacilli that prefer moist environment and can be easily obtained from soil, water, food and sewage. They are usually considered to be opportunistic pathogens, and of recent have been reported to cause a number of outbreaks of nosocomial infections in hospitalized patients like septicemia, pneumonia, wound sepsis, endocarditis, meningitis and urinary tract infection (UTI). Although acknowledged to be an opportunist in hospitalized patients, community acquired infections are reported and they can cause suppurative infections in virtually every organ system (13). Interpreting the significance of isolates from clinical specimens is often difficult, because of the wide distribution of *Acinetobacter* in nature and its ability to colonies healthy ambulatory adults exhibit coetaneous colonization and are the most common Gram negative bacilli carried on the skin of hospital personal (13).

A. baumannii has emerged as an important nosocomial pathogen (14). Hospital outbreaks have been described from various geographic areas (15, 16) and this organism has become endemic in some of them. The rate of environmental contamination in the transmission of nosocomial infections in general and in *A. baumannii* infections in particular is well recognized. *A. baumannii* does not have fastidious growth requirements and is able to grow at various temperatures and pH conditions (17). The versatile organism exploits a variety of both carbon and energy sources. These properties explain the ability of *A.* spp. to persist in either moist or dry conditions in the hospital environment, thereby contributing to transmission (18). The nosocomial epidemiology of this organism is complex. Villegas and Hartstein reviewed *Acinetobacter* outbreaks occurring from 1977 to 2000 and hypothesized that endemicity, increasing rate, and increasing of new resistance to antimicrobial drugs in a collection of isolates suggest transmission. These authors suggested that transmission should be confirmed by using a discriminatory genotyping test (19).

Almost 28 yr ago, researchers observed acquired resistance of *A. baumannii* to antimicrobial drugs commonly used at that time, among them aminopenicillins, ureidopenicillins, first and second generation cephalosporins. cephamycins, most aminoglycosides, chloramphenicol, and tetracyclines (20).

In the current study we intend to study the occurrence of *A. baumannii* infection among NICUs patients, and to assess characteristics and risk factors for multi-drug resistant *A. baumannii* acquisition during hospitalization

Materials and Methods

We made a case control study from Feb 2004 to Jan 2005. This study was performed at the neonatal intensive care units of Al Shifa and Al Nasser hospitals. A case was defined as any infant hospitalized in the NICU who developed *A. baumannii* after 48 h of admission to NICU or after transfer from it and confirmed by laboratory examinations, and other neonates hospitalized during the same period with no diagnosis of blood stream infection syndrome were the controls. The localization of the cases in the incubators was recorded; an individual record was filled out with the nursing staff.

Venous blood was obtained from NICU newborns by nursing staff by means of aseptic techniques. Briefly 0.2 ml of blood were drawn into bottles containing 10 ml of supplemented trypticase soy broth and incubated at 37º C.

Blood from bottles showing positive growth index was gram stained and those with gram negative rods or coccobacilli were subcultured on sheep blood and MacConkey agar plates and incubated aerobically for 24 h at 37º C. Isolates were identified as *A. baumannii* by a negative oxidase test, catalase positive reactions and Analytical Profile Index (API 20E) system updated profile (Biomerieux SA, France). Multiple blood culture yielding the same organism from the same patient was considered to be a single infection. The following variables were recorded: age, sex dates of

admission and discharged from NICU, diagnosis on admission, birth weight, gestational age, detailed informatives on intensive procedures and treatment before and after the onset of blood stream infection was based on definition of CDC (21).

The antibiotic susceptibility of *A. baumannii* isolates were determined by the disk diffusion method on Mueller Hinton agar plates with using calibrated inoculum of the isolates based on McFarland Standard with the following antibiotics: cephalexin, amoxicillin, piperacillin, ampicillin, trimethoprime-sulfamethoxazole, cefaclor, cefuroxime, cefotaxime, ceftriaxone, gentamicin, amikacin, ceftazidime, ciprofloxacin, chloramphenicol, imipenem, and meropenem. We defined *A. baumannii* as multidrug resistant (MRD) when the organism was resistant to three antibiotics out of four of the following: ceftazidime, ciprofloxacin, gentamicin, and imipenem (22).

Data were analyzed using SPSS version 13. Categorical variables were analyzed using $\chi 2$ test. All tests were two-tailed with $P< 0.05$ considered significant.

Results

Blood specimens from 579 neonates were collected form which forty patients with *A. baumannii* infection were reported from the neonates less than 28 d. The incidence density was 40 (6.9 %).

Study population subjects were 92.5% from Al Shifa hospital, meanwhile the rest (7.5%) were from Al Nasser NICU.

The study patients' characteristics and risk factors are displayed in Table 1. Case patients were similar to their matched control patients with respect to mean age (under 28 d). The patient group had the mean age 9.3±5.8 with median age 8.0, while the control group had the mean age 10.8±5.8 with median age 10.0.

The groups were similar in their coexist conditions in the neonatal incubators. Hospital events differed between case patients and controls. Case patients which had statistically significant, were more likely to have received mechanical ventilation OR= 3.5, to have received antibiotics OR= 6.0, and to have central venous catheter (CVC) OR= 10.5.

Several variables tended to be more associated with case patients but the values did't reach statistical significant like weeks of gestation, and sex.

Overall crude mortality rate was 5 of 40 (12.5%), median of patient hospitalization at 20 d, OR= 3.1, P= 0.003; 12 d, OR= 0.48, P= 0.16 and 8 d OR= 0.46, P= 0.06.

The strains of *A. baumannii* were found to be highly resistant to several of the antimicrobial drugs examined (Table 2) particularly the cephalosporins (Cephalexin). Intermediate resistant was observed to aminoglycosides, chloramphenicol and ciprofloxacin. In addition a small number of bacterial strains were resistant to impenem and meropenem. Despite a small number of bacterial strains were resistant to impenem and meropenem, fifteen strains were considered as multidrug resistant strains from both hospitals, which constituted of 37.5% of the total isolated strains.

Table 1: Characteristic and risk factors for *A. baumannii* infection in neonates

Risk factor		Cases	Controls	OR	*P*
Weight at birth	>1500g	15	70		
	≤1500g	25	30	3.89	0.001<
Sex	Females	15	45		
	Males	25	55	1.36	0.42
Age	>7 d	21	72		
	≤ 7 d	19	28	2.33	0.027
Weeks of gestation	26-29	5	15	0.81	0.70
	30-33	10	25	1.0	1.0
	34-36	25	60	1.11	0.78
Median of hospitalization	20 d	25	35	3.1	0.003
	12 d	5	23	0.48	0.16
	8 d	10	42	0.46	0.06
Antibiotic used		36	60	6.0	0.001<
Utilization of Central Venous Catheter (CVC)		29	20	10.5	0.001<
Mechanical ventilation		24	30	3.5	0.001<
Mortality		5	14	0.88	0.81

P<0.05 statistically significant

Table 2: Distribution of antimicrobial susceptibility pattern among *Acinetobacter baumannii* isolates (n= 40)

Antimicrobial agents	Number of susceptible isolates	Percentage of susceptibility
Cephalexin	0	0
Amoxicillin	1	2.5
Piperacillin	4	10
Ampicillin	6	15
SXT*	9	22.5
Cefaclor	12	30
Cefuroxime	14	35
Cefotaxime	14	35
Ceftriaxone	20	50
Gentamycin	23	57.5
Amikacin	15	37.5
Ceftazidime	12	30
Ciprofloxacin	30	75
Chloramphenicol	32	80
Imipenem	36	90
Meropenem	37	92.5

*SXT: trimethoprime-sulfamethoxazole

Discussion

We performed a case-control study intending to determine the occurrence of *A. baumanni* as well as the multidrug resistant strains present in NICUs. The infection rate in this study was 6.9% of the total BSI (579) recorded in the NICU during 1 yr. The new borne examined in this study presented a risk factors for contracting sepsis. The most predominant factors were: submission to invasive procedures mechanical ventilation, utilization of central venous catheter, presence of conditions such as prematurity, and very low birth weight. Greenberg et al. (23) in a study performed at a university hospital in Negev, Southern Israel, concluded that the risk factors of prematurely and very low birth weight significantly influenced the incidence of sepsis in comparison to that seen in neonates from the general population.

In relation to birth weight Fanaroff et al. (24) reported a significant decreasing in the risk of septicemia with increasing birth weight in a study performed with infants weighing between 501 to 1500 g get births from eight participating centers in the USA. The observation reported was in agreement with our results.

The reported cases of neonatal infection caused by *A. baumanni* made it as important pathogens. To define the risk factors for the acquisition of infection we compared the case infant group with a randomly selected group of control infants. The following factors were significant weight ≤1500 g, duration of hospitalization for 20 d, use of ceftazidime. These same risk factors were described by McDonald (25) and Melamed (26).

Although the infection caused by *A. baumannii* was not traced to a common source, and may be attributed to such sources like respiratory equipment, mattresses, suction catheters, laryngoscopes, gloves, and air conditioner. Though the dissemination of this pathogen is facilitated by its prolonged survival on inanimate surfaces, high colonization rates among hospitalized patients, and frequent contamination of health care workers.

Our results highlight that because of the infants in NICU are exposed to central vascular catheters, a major risk factor NBSI emphasis should be given to the guidelines of Centers for Disease Control and Prevention for prevention of catheter related BSI (21). Major areas of emphasis include: educating and training of personnel who inserts and maintains catheters, using maximal sterile barrier precautions during central venous catheter insertion, using a 2% chlorhexidin preparation for skin antisepsis, avoiding routine replacement of central venous catheters as a strategy to prevent infection and using antiseptic/antibiotic impregnated short-term central venous catheters if the rate of infection is high (21).

The high resistance rates found in this study may be associated with the high frequency at which these antimicrobial drugs were used for both prophylactic and therapeutic treatment of hospitalized newborns. This practice have may exerted selective pressures leading to the emergence of multidrug resistant strains (27, 28) which in turn may have stimulated the acquisition of genes encoding resistance mechanisms via horizontal transfer mechanisms between environment. It is of

particular interest that in this study a significant number of patients received antimicrobial drugs before positive blood culture presentation, (empiric use), due to clinical manifestations suggestive of sepsis.

It was clearly from the results obtained that invasive procedures, empiric antibiotics, prolonged hospitalization, and extremely low birth weight, increase the risk of infection. To control infections, prolonged use of broad-spectrum antibiotics is often encountered, which leads to the resurgence of multidrug-resistant organisms. Therefore, preventive antibiotics should be used as little as possible, while therapeutic antibiotics should be specific and used as short period of time as possible. The combined use of various antibiotics should likewise be judicious. In conditions wherein the use of antibiotics is necessary, rotating antibiotic regimens has been suggested and may be a way to solve this problem.

In conclusion, our study showed that infection rate of NBSI is considerable and alarming in NICU infants and associated with a significant excess length of NICU stay and a significant economic burden especially in developing countries such as Palestine. We recommend that special attention should be given to the continuing education of the nursing personnel, and the quality of care for these neonates, via making hospital administrators and policy makers more sensitive to the needs of adopting a continuous monitoring and surveillance of NBSI.

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