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Factors leading to transmission risk of *Acinetobacter baumannii*

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Abstract

Objective—To identify patient and healthcare worker (HCW) factors associated with transmission risk of *Acinetobacter baumannii* (AB) during patient care.

Setting—Intensive care units (ICU) at a tertiary care medical center

Design—Prospective cohort study

Participants—Adult ICU patients known to be infected or colonized with AB

Measurements and Main Results—Cultures of skin, respiratory tract and the perianal area were obtained from participants and evaluated for the presence of AB. HCW-patient interactions were observed (up to 5 interactions per patient) and activities were recorded. HCW hands/gloves were sampled at room exit (prior to hand hygiene or glove removal) and then evaluated for the presence of AB. Two hundred and fifty four HCW-patient interactions were observed among 52 patients; AB was identified from HCW hands or gloves in 77 (30%) interactions. In multivariate analysis, multidrug-resistant (MDR) AB (Odd Ratio (OR) 4.78, 95% Confidence Interval (CI) 2.14 to 18.45) and specific HCW activities [touching the bed rail (OR 2.19, 95% CI 1.00 to 4.82), performing a wound dressing (OR 8.35, 95% CI 2.07 to 33.63) and interacting with the endotracheal tube or tracheotomy site (OR 5.15, 95% CI 2.10 to 12.60)] were associated with hand/glove contamination.

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Conclusions—HCW hands/gloves are frequently contaminated with AB after patient care. Patient-level factors were not associated with an increased transmission risk; however, having MDR-AB and specific HCW activities led to an increased contamination risk. Our findings reveal a potential selective advantage possessed by MDR-AB in this environment and suggest possible areas for future research.

Keywords

Acinetobacter baumannii; Healthcare-associated Infections; Hospital Epidemiology; Transmission

Acinetobacter baumannii is prevalent among critically ill patients and infection with this organism is associated with increased morbidity, mortality and cost (1, 2). Furthermore, outbreaks are common in intensive care units (ICU) globally (3). Factors associated with the spread of *A. baumannii* from one patient to another are not well defined; yet, identification of risk factors for potential transmission is important and knowledge may be used to develop new strategies aimed at limiting spread. In this study, we assembled a prospective cohort of patients infected or colonized with *A. baumannii* to identify both patient-level and healthcare worker factors associated with the potential for transmission.

Materials and Methods

This study was conducted within intensive care units (ICU) and intermediate care units (IMC) at the University of Maryland Medical Center (UMMC), a tertiary care hospital with an 816-bed capacity located in Baltimore, Maryland. The UMMC has eight adult ICUs: medicine, cardiac, surgical, cardiothoracic, neurosurgical, and three trauma ICUs; and five adult IMC areas. Critical care beds account for more than 30% of all hospital beds. Active surveillance for *A. baumannii* is performed in all study units; in the medical and surgical ICUs all patients are screened at unit admission with a peri-anal culture and patients with an artificial airway also have a sputum culture. In all other units, patients admitted from another facility are similarly screened with peri-anal and sputum cultures. Adult patients located in these areas were screened for study participation. This study was approved by the University of Maryland Baltimore Institutional Review Board.

We used a cohort study design and assembled a prospective cohort of critically ill patients infected or colonized with *A. baumannii* to examine patient and healthcare worker factors associated with potential transmission as measured by presence of *A. baumannii* on healthcare worker hands or gloves after patient care.

Patients who were known to be infected or colonized with *A. baumannii* were eligible for study participation. Initial screening of hospital microbiology reports identified patients with recent (i.e., within the prior 5 days) clinical or infection prevention surveillance cultures positive for *A. baumannii*. The presence of *A. baumannii* was then confirmed via study surveillance cultures on the day of enrollment. All patients included in the final cohort had a least one study surveillance culture positive for *A. baumannii*; those patients whose study surveillance cultures were negative were excluded from the final analysis. Additionally, a group of patients not known to harbor *A. baumannii* were selected at random from the same unit on the same day as *A. baumannii*-positive patients in a ratio of approximately one for

every six cases. The rationale for studying these patients was to ascertain that the baseline prevalence of *A. baumannii* in rooms of patients not colonized or infected with *A. baumannii* is low and thus potential risk of transmission is negligible.

The primary exposure variable was the identification of *A. baumannii* from patient study surveillance cultures (number of cultures positive). At enrollment, the following cultures were obtained from each participant: skin, peri-anal, respiratory tract and wounds (when applicable). These sites were chosen as they are the most commonly described habitat of *A. baumannii* colonization among hospitalized patients (4, 5). Skin cultures were obtained using a sterile Dual Tip BactiSwab (Remel, Lenexa, KS) and sampling bilateral axilla and groin with a single composite swab. Peri-anal samples were obtained in a standardize manner previously described(6). Suctioned sputum samples were obtained from patients with an artificial airway during routine suctioning using a closed tracheal suction procedure(5). In all other patients, the respiratory tract was sampled via culture of the oropharynx using Fisherfinest cotton swab (Fisher, Waltham, MA). For patients with skin and soft tissue wounds, each wound was cultured separately using a Dual Tip BactiSwab. Additional patient-level exposure variables were collected via review of the medical record and include the presence of medical devices, antibiotic exposure and the presence of comorbidities (Charlson score(7)). Patients were assessed for infection as a result of the *A. baumannii* trigger culture using Centers for Disease Control and Prevention National Healthcare Safety Network Criteria(8).

The primary outcome of this study is the identification of *A. baumannii* on healthcare worker hands or gloves after patient care and is considered a proxy for the potential for pathogen transmission in this and other studies (9, 10). For each cohort member, up to five unique healthcare worker-patient interactions were observed ideally within 24–36 hours of patient sample collection. After providing patient care, healthcare worker hands or gloves (if worn) were cultured using a sterile Dual Tip BactiSwab in a standardized method previously described (9). Additional data regarding the healthcare worker and the healthcare worker-patient interaction were collected including: healthcare worker type, duration of time spent in room, and healthcare worker activities.

After collection, skin, peri-anal, oropharyngeal and wound swabs were all processed using similar methodology. A swab was used to process sputum samples following standard laboratory procedures. Swabs were initially suspended in BHI broth and incubated for 24 hours at 37°C. They were then sub-cultured to ChromAgar *Acinetobacter* agar (Gibson Laboratories, Lexington, KY); and incubated at 37°C for 48 hours. Red colonies identified on the ChromAgar *Acinetobacter* agar were identified as *A. baumannii* via the Vitek II system (bioMerieux, Durham, NC).

Susceptibility testing was performed by disk diffusion in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines (11, 12). Susceptibility to tigecycline was interpreted using published Food and Drug Administration guidelines for *Enterobacteriaceae* (12). Polymixin B was interpreted using the CLSI breakpoints for *Pseudomonas aeruginosa*. Multidrug resistance was defined with standard definitions as an isolate that was resistant to one or more agents in three or more antimicrobial categories (13).

Risk factors for potential transmission, including number of study surveillance sites positive (the primary exposure variable), were evaluated by generalized linear mixed models to take into account correlated patient data. Potential confounding variables were examined in a bivariate analysis also using generalized linear mixed models. Covariates that were significant at the P <0.10 level were then added to the model and retained in the final model if they were significant at the P<0.05 level. All analyses were performed using SAS version 9.4 (The SAS Institute, Cary, NC).

Results

Sixty patients with a known history of *A. baumannii* infection or colonization within the past 5 days and 10 patients without a known history of *A. baumannii* were consented to participate in this study from January 2013 to April 2015. Ten of the 60 *A. baumannii*-positive patients were excluded from the cohort: for two not all study surveillance cultures (primary exposure) were not obtained, two were missing healthcare worker cultures (primary outcome) and six did not culture positive for *A. baumannii* from the study surveillance cultures. Two patients without a known history of *A. baumannii* were found to have *A. baumannii* from study surveillance cultures at the time of study enrollment and were considered part of the cohort for analysis. Thus 52 patients were included in the final cohort for analysis (Table 1).

Two hundred fifty-four healthcare worker-patient interactions were observed for the 52 cohort patients. *A. baumannii* was identified from a culture of the healthcare worker hand or gloves in 77 of the 254 interactions (30.3%). Healthcare workers from whom *A. baumannii* was identified on the hands or gloves after patient care spent more time in the room for the observed episode of care and were more likely to have interacted with specific items in the room [e.g. bedrail (p<0.01) and supply cart (p<0.01)] or performed specific activities [e.g. wound dressing (p<0.01), bathing or hygiene (p<0.01) and manipulation of the endotracheal tube(p<0.01)]; see Table 2 for detailed description of the bivariate analysis. Patient level factors, including number of clinical sites positive for *A. baumannii*, infection versus colonization, presence of medical devices or wounds were not associated with a greater potential risk of transmission. Forty interactions were observed for the 8 patients not known to harbor A. baumannii; *A. baumannii* was recovered from one of 40 (3%) interactions.

The results of the multivariable analysis used to measure the association between patient and healthcare worker factors and the risk for potential *A. baumannii* transmission as measured by identification of *A. baumannii* on healthcare worker hands or gloves are presented in Table 3. Patients colonized or infected with multidrug-resistant (MDR) *A. baumannii* had a greater risk for potential transmission; odds ratio (OR) 4.78, 95% confidence interval (CI) 2.14 to 18.45. Additionally, specific healthcare worker activities, such as touching the bed rail (OR 2.19, 95% CI 1.00 to 4.82), performing a wound dressing (OR 8.35, 95% CI 2.07 to 33.63) and interacting with the endotracheal tube or tracheotomy site (OR 5.15, 95% CI 2.10 to 12.60) were associated with a greater risk of potential transmission.

Eighty-one percent (42/52) of cohort patients harbored a MDR strain *A. baumannii*. A secondary analysis was performed restricted to only these patients and results were similar;

i.e. the same healthcare worker activities were found to be a risk for transmission (data not shown).

We also examined the sensitivity of identifying *A. baumannii* from the study clinical cultures using a "gold standard" of *any culture positive* and found that the skin swab was positive in 69% (35/51) of the patients, perianal 59% (30/51) and respiratory tract 71% (36/51). If samples are combined, sensitivity increased to 90% (46/51) for skin plus either perianal or respiratory tract and 94% (48/51) for perianal plus respiratory tract. One of the 52 cohort patients was excluded from this analysis as the only positive *A. baumannii* culture was from a wound culture.

Discussion

To our knowledge, this is the largest prospective cohort study of patients colonized or infected with *A. baumannii* to examine the potential for transmission based on healthcare worker hand or glove contamination; and the first to also consider patient-level factors. In this prospective cohort study, we found that healthcare workers who provide care for patients known to be infected or colonized with *A. baumannii* exit the room with *A. baumannii* on their hands or gloves 30% of the time and thus the potential for transmission with this organism is high. These findings are remarkably consistent with previous studies using similar methodologies, which showed hand or glove contamination with *A. baumannii* to be 33% to 39% (9, 14).

In comparison to studies investigating the transmission potential of other organisms (e.g. methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant Enterococci (VRE)), *A. baumannii* appears to have a greater potential for transmission; 30% compared to approximately 20% for the other organisms. Reasons for this are unclear. Additionally, we found that that there is a greater risk for transmission if the patient harbors a MDR strain of *A. baumannii*, which to our knowledge has not been previously shown. Studies comparing transmission of antibiotic-resistant bacteria versus antibiotic-susceptible bacteria are surprisingly uncommon in the literature. In a similar study performed in nursing homes, MRSA transmission was more common than MSSA transmission to healthcare worker gowns or gloves even when controlling for other risk factors including level of colonization (unpublished data, Roghmann MC).

We speculate that among the MDR *A. baumannii* recovered in this analysis at UMMC, the presence of genetic determinants conferring resistance to environmental disinfectants, biocides, or genes tolerating desiccation may be present (15). (16, 17). Among these genotypes, either increase expression of intrinsic efflux pumps or factors leading to increased biofilm production could be the mechanism responsible for prolonged carriage and dissemination of MDR *A. baumannii* strains. Our study identifies the "tip of the iceberg" and reveals that among *MDR A. baumannii* these determinants, in addition to antibiotic resistance, could be contributing to transmission dynamics. We believe that these findings warrant further investigation; if confirmed these findings could highlight challenges with *A. baumannii*, with respect to outbreak propensity(3). If MDR isolates are more likely to be transmitted than susceptible-*A. baumannii*, even among patients who are colonized only and

not infected, it would suggest the need to identify these organisms through screening programs and utilize vigilant transmission prevention strategies.

While the risk for transmission was greater when the patient harbored a MDR strain of *A. baumannii*, we found it interesting that patient-level factors were not associated with an increased potential risk for transmission. Prior to undertaking the study, we hypothesized that burden of organism, as measured by the number of clinical sites from with *A. baumannii* was identified, would be associated with an increased potential for transmission. Although we did not identify it as a risk factor for *A. baumannii* transmission in this study, it is possible that if we had performed quantitative cultures of the patient samples we may have seen a relationship between higher burden and transmission potential. If this were the case, however, one might suspect that factors that may impact the overall quantity of organism (such as antibiotic exposure, infection versus colonization or the presence of wounds and devices) would also be associated with an increased transmission risk, which was not seen in this study.

We found that several specific healthcare worker activities were associated with an increased risk for potential transmission including touching the bed rail, performing wound care, and interacting with the endotracheal tube or tracheotomy site. Morgan and colleagues previously examined risk factors for potential *A. baumannii* transmission, although they did not adjust for patient-level factors and had a small patient sample size, and similarly found that performing a wound dressing or interacting with the ventilator tubing, as well as duration of time in room, were risks for glove contamination (9, 14). Other studies, looking at different organisms, have had similar findings(9, 10, 14, 18–21). Together, these studies suggest several areas for focus to reduce the spread of organisms including emphasis on wound and respiratory care techniques.

Hand hygiene and Contact Precautions, which include glove use, have been a mainstay of infection prevention for several decades (22). These findings highlight the need for strict adherence to hand hygiene expectations, particularly after contact with a patient or their environment as well as after glove use. Recently, several factors, such as cost, waste and the potential for adverse events, have led many to re-consider Contact Precautions and their application (23). In a recent report, 30 US hospitals do not use Contact Precautions for the control of endemic MRSA or VRE instead relying on syndromic precautions and Standard Precautions (23). While we believe that novel approaches to the implementation of Contact Precautions is an area of needed study, our data would suggest that a patient-based syndromic approach to precautions for Gram-negative pathogens such as *A. baumannii* is ill advised given the risk of transmission from contact with the environment (e.g. the bed rail). Instead, further research into specific healthcare worker activities and how enhanced precautions at these times may reduce transmission is needed. Additionally, in this study population, we found that 20% of patients not known to harbor *A. baumannii* indeed were colonized, suggesting a significant unidentified burden. That, together with the high frequency of hand/glove contamination would support consideration of approaches which emphasize hand hygiene and/or glove use (e.g., Universal Gloving)(24, 25).

All 52 cohort patients were sampled at multiple clinical sites to ensure identification of *A. baumannii* which is known to have multiple potential habitats in the clinical setting. Subsequently, we examined the sensitivity of each site for identification of *A. baumannii* compared to a gold standard of having *A. baumannii* identified from any site and found that the sensitivity of any one site was lower than when combining at least two potential sites, similar to findings reported by Ayats et al in 1997 (4).

There are several limitations to our study. Firstly, although this is the largest prospective cohort of its kind, this study has the limitation of being performed at a single center and having a small overall number of patients which may limit generalizability and affect power to identify potential associations. Secondly, clustering of healthcare worker-patient interactions may also affect power. We limited the overall number of interactions per cohort member to only 5 and adjusted for clustering the analysis. Thirdly, additional factors, including quantitative cultures to determine organism burden, were not measured and may be associated with the potential for transmission. Fourthly, although we seek to better understand transmission of A. baumannii, this is notoriously difficult to determine in the clinical setting and thus we have used the proxy of healthcare worker hand/glove contamination as a measure of potential risk of transmission. Lastly, identification of possible molecular mechanisms responsible for dissemination was not investigated (further studies are planned).

Conclusions

Healthcare worker hands and gloves are frequently contaminated with *A. baumannii* after providing patient care. While patient characteristics did not predict transmission, MDR *A. baumannii* and specific healthcare worker activities including touching near patient surfaces (i.e. bed rail), performing wound care, and interacting with the respiratory tract in patients with an artificial airway increased transmission risk. Future research should focus on determining the molecular basis responsible for dissemination as well as gaining a deeper understanding of specific behaviors associated with transmission and prevention strategies aimed specifically at high risk behaviors. Additionally, strategies to improve hand hygiene and an evidenced-based approach to the use of gowns and gloves are needed.

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Table 1

Acinetobacter baumannii (AB) Cohort Characteristics

	AB-Positive patients (N = 52)
Age, mean (SD)	54.5 (15)
Men, No. (%)	36 (69)
Location ICU (versus IMC), No. (%)	45 (87)
Surgical ICU	5 (10)
Neurocare ICU	5 (10)
Medical ICU	16 (31)
Neuro-trauma ICU	8 (15)
Multi-trauma ICU	8 (15)
Select-trauma ICU	3 (6)
Neurotrauma IMC	5 (10)
Multitrauma IMC	2 (4)
Charlson Comorbity Index, mean (SD)	2.8 (3)
Artificial airway, No (%)	41 (79)
Urinary catheter, No. (%)	29 (56)
Central venous catheter, No. (%)	43 (83)
Wounds, No. (%)	27 (52)
Diarrhea, No. (%)	28 (54)
Antibiotics, No. (%)	46 (88)
Source of AB-positive culture (i.e. non-study culture), No. (%)	
Infection control perianal surveillance	9 (17)
Blood	1 (2)
Respiratory	31 (60)
Wound	5 (10)
Other	6 (11)
Infection (versus colonization), No. (%)	29 (56)
Multidrug-resistant AB, No. (%)	42 (81)
Study surveillance culture positive for AB - by site, No (%)	
Skin	
Peri-anal	35 (67)
Respiratory	30 (58)
Wound	36 (69)
	13 (25)

	AB-Positive patients (N = 52)
Length of stay in days, median (interquartile range)	25 (35)
In-hospital mortality, No. (%)	8 (15)

Table 2
Factors Associated with Transmission Risk

The proportion of the total healthcare worker (HCW)-patient interactions observed in which a transmission risk was identified (i.e. *Acinetobacter baumannii* (AB) was identified from HCW hands/gloves) and those in which no transmission risk was identified (i.e. No AB from HCW hands/gloves). Results from bivariate analysis* showing patient- and HCW -level factors and their association with transmission risk.

Observations of HCW-patient interactions				
Variable	**Transmission risk identified: AB positive HCW cultures N=77; n (%)**	**No Transmission risk identified: AB negative HCW cultures N=177; n (%)**	**Odd Ratio (95% Confidence Interval)**	**P-value**
Patient-level Factors				
Study Culture Positive (No. Sites Positive of skin, respiratory or perianal)				
Wound only	2 (3)	3 (2)	Ref	0.75
1	18 (23)	47 (27)	0.51 (0.03, 7.80)	
2	35 (45)	90 (51)	0.51 (0.04, 7.41)	
3	22 (29)	37 (21)	0.82 (0.05, 12.53)	
Infection (versus colonization)	45 (58)	95 (54)	1.23 (0.56, 2.72)	0.60
Multidrug-resistant *A. baumannii*	69 (90)	137 (77)	2.77 (0.95, 8.06)	0.06
Charlson comorbidity index (mean, SD)	2.8 (2)	2.8 (3)	1.00 (0.86, 1.16)	1.00
Artificial airway	65 (84)	135 (76)	1.84 (0.69, 4.91)	0.22
Urinary catheter	41 (53)	101 (57)	0.95 (0.44, 2.05)	0.89
Central venous catheter	63 (82)	152 (86)	0.66 (0.23, 1.89)	0.43
Wound(s)	38 (49)	92 (52)	0.89 (0.40, 1.95)	0.77
Diarrhea	35 (45)	97 (55)	0.65 (0.31, 1.38)	0.26
Antibiotics	76 (99)	163 (92)	7.65 (0.70, 83.81)	0.10
HCW-Factors				
HCW type				
Nurse	36 (47)	61 (34)	Ref	0.01
Physician	17 (22)	41 (23)	0.59 (0.25, 1.37)	
Patient Care Technician	5 (6)	15 (8)	0.45 (0.13, 1.61)	
Respiratory Therapist	11 (14)	10 (6)	2.05 (0.64, 6.58)	
Physical/Occupational	1 (1)	6 (3)	0.38 (0.03, 4.47)	
Therapist	7 (9)	42 (24)	0.16 (0.05, 0.49)	
Other				

Observations of HCW-patient interactions				
Variable	**Transmission risk identified: AB positive HCW cultures N=77; n (%)**	**No Transmission risk identified: AB negative HCW cultures N=177; n (%)**	**Odd Ratio (95% Confidence Interval)**	**P-value**
Time in room, minutes (median, IQR)	6.0 (9)	4.0 (6)	1.06 (1.01, 1.10)	0.01
HCW interaction with environment **Interactions with non-significant sites not shown (sink, bedside table, vital sign monitor, door handle, intravenous medication pump, ventilator and floor)*				
Bedrail	39 (51)	62 (35)	2.83 (1.36, 5.88)	< 0.01
Supply cart	34 (44)	44 (25)	2.57 (0.40, 3.28)	< 0.01
HCW Interaction with Patient **Interactions that were non-significant are not shown (obtaining vital signs, urinary catheter drainage, administering parenteral medications, intravenous medication pump)*				
Physical exam	32 (42)	53 (30)	1.89 (0.97, 3.67)	0.061
Wound dressing	13 (17)	6 (3)	8.81 (2.50, 31.05)	<0.01
Bathing hygiene	9 (12)	10 (6)	3.78 (1.12, 12.78)	0.032
Endotracheal tube or tracheotomy site	25 (32)	24 (14)	4.40 (1.92, 10.08)	< 0.01

†Bivariate analysis using generalized linear mixed models to account for patient clustering.

Table 3

Factors Associated with Potential Transmission of *Acinetobacter baumannii* Multivariate, Generalized Linear Mixed Model, Regression

Variable	OR (95% CI) N=254
Study Culture Positive (No. Sites Positive)	
0	1.67 (0.07, 41.24)
1	Ref
2	1.42 (0.45, 4.52)
3	1.94 (0.50, 7.49)
Multidrug-Resistant *A. baumannii*	
No	Ref
Yes	4.78 (1.24, 18.45)
HCW touched bed rail	
No	Ref
Yes	2.19 (1.00, 4.82)
HCW performed wound dressing	
No	Ref
Yes	8.35 (2.07, 33.63)
HCW interacted with endotracheal tube/tracheotomy site	
No	Ref
Yes	5.15 (2.10, 12.60)