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Letters to the Editor

Sex bias of *Acinetobacter baumannii* nosocomial infection

To the Editor:

Acinetobacter baumannii is one of the most common nosocomial pathogens isolated in clinical settings worldwide and is often considered to be a serious cause of health care–associated infections. In a retrospective study designed to investigate the clinical characteristics and molecular epidemiology of *Acinetobacter calcoaceticus–A baumannii* complex, we observed a sex bias in 1,600 patients isolated with *A baumannii* in the Fourth Affiliated Hospital of Kunming Medical University, a tertiary care hospital in China, from January 2014-December 2017.

To our surprise, the data showed a significantly increased incidence of *A baumannii* isolations in men (n = 1,179) compared with women (n = 421), with an overall male-to-female ratio of 2.8:1. During the study period, we observed 14,762 patients isolated with gram-negative bacteremia, 27,807 patients with bacteremia, and 60,691 patients with collected specimens. The proportions of men were 65.8%, 53.3%, and 64.3% respectively. After Pearson χ^2 test, statistically, male predominance was observed in patients infected with *A baumannii* strains. Therefore, these results suggest nosocomial *A baumannii* infection is more frequent in men than women. To our knowledge, few studies have been conducted to investigate the sex bias in patients clinically isolated with *A baumannii* bacteremia. Similar trends have also been demonstrated in *Staphylococcus aureus*–associated[1] and *Pseudomonas aeruginosa*–associated[2] investigations. However, one study conversely demonstrated that 60% of *Escherichia coli* bacteremia occur in women, perhaps because of increased *E coli* urinary tract infections in women.[3]

Numerous studies[1-4] have reported that bias direction might be dependent on pathogen and site of infection; however, we did not find a statistically significant sex difference stratified by specimen origin in 1,600 patients isolated with *A baumannii*. In consideration of the immune response associated with testosterone in an anti-inflammatory fashion and the proinflammatory effects of estrogen in nature,[5] we further analyzed whether patient age is involved in the sex difference. However, the data showed a male predominance in most age groups, and the age-associated cutoff value for sex bias in patients infected with *A baumannii* was not observed in the current cohort. An interesting finding was that the age of 49 years might be deemed to be a special point, and male predominance was most obvious in those ≤49 years of age. The difference in incidence between men and women may be because men are generally more active than women and therefore have more opportunities to be exposed to environments containing bacteria.

As listed in Table 1, the resistance rate to all antibiotics excepted tetracycline and aztreonam was statistically significant between men and women. The resistance rates to these 13 antibiotics in men were all higher than in women. To our knowledge, few studies have been published that evaluate whether the resistance rate profiles differ according to sex. Limited information demonstrated the resistance rate to cefoperazone-sulbactam, amoxycillin-clavulanate, imipenem, meropenem, and aztreonam was statistically higher in men isolated with *A baumannii*.[6] However, the sex difference associated with this discrepancy is still unclear. It is possible due to that the nosocomial *A. baumannii* infection was more frequent in men than women in this study. On the other hand, there is general agreement[4,6] that many factors, including different kinetics in men and women, might innately influence infection and progression to disease and basic differences in cell response. Importantly, a recent meta-analysis[7] showed that women in the 16- to 54-year-old age group received a significantly higher number of prescriptions of cephalosporins and macrolides in primary care than men. Male predominance in *A baumannii* nosocomial infection and antibiotic-resistant profiles is found in our and other clinical reports. No study has been conducted to investigate the complicated mechanism.

Table 1
Resistant profiles of *Acinetobacter baumannii* to antibiotics stratified by patients' sex and age, 2014-2017

Antibiotics	Male (n = 1,179)	Female (n = 421)	*P* value
Ampicillin	1,039	347	.003
Piperacillin	972	310	<.001
Amoxicillin-clavulanate	980	318	.001
Ceftazidime	923	295	.001
Ceftriaxone	957	308	.001
Cefepime	962	314	.002
Aztreonam	1,165	416	>.999
Imipenem	912	302	.019
Meropenem	913	303	.024
Gentamicin	926	302	.005
Amikacin	621	187	.003
Ciprofloxacin	971	313	.000
Levofloxacin	687	203	.000
Sulfamethoxazole	742	220	.000
Tetracycline	833	285	.243

Based on these observations and experiments, we hypothesize that men are susceptible to *A baumannii* nosocomial infection and antibiotic resistance. The site of infection and hormonal level possibly play a secondary role in the sex bias. Understanding the molecular mechanisms controlling this sex bias may reveal novel targets to promote host innate defense against *A baumannii* nosocomial infection. Further work is needed to elucidate the complicated mechanisms.

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Conflicts of interest: None to report.

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Risk factor for infection in spine surgery: Are the results correct?

To the Editor:

In a previous issue of the *American Journal of Infection Control*, Gu et al. reported a prospective cohort of 1764 patients who underwent instrumented spinal procedures. In their univariate analysis, the only risk factor for surgical site infection (SSI) with statistical significance was reason for surgery, but in multivariate analysis, they found that 8 factors were associated with SSI (Table 1). Using the data published by Gu et al., we calculated odds ratios (ORs) and *P*-value (chi-square test), calculations were performed using EpiInfo 7 statistical software.

We found that surgeon level, reason for surgery, and morbid obesity were significantly associated with SSI and that intraoperative antibiotic use was associated with no development of SSI. Bivariate analysis highlighted that surgical location, diabetes mellitus, and current smoking could be risk factors for SSI presentation, studies with larger sample size could test these associations.

Additionally, our results showed that unadjusted ORs were very different compared to the adjusted ORs reported by the authors (Table 1). We think that the inclusion of 44 variables into the logistic regression model was undesirable. Considering that only 58 patients in this study[1] had an SSI, the inclusion of so many variables into a logistic regression model could lead to interactions, confounding, and overadjustment that can affect the validity of the results.[2,3]

We suggest that, in studies of factors associated with diseases, before multivariate analysis, researchers calculate association measures like OR and relative risk[4] with their respective confidence intervals.

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Table 1
Risk factors for SSI after instrumented spine surgery

Variable	OR (95% CI)	*P*-value*	Adjusted OR† (95% CI)	*P*-value†
Overweight	1.29 (0.69-2.43)	0.42	–	–
Obesity	1.8 (0.89-3.8)	0.09	–	–
Morbid obesity	3.2 (1.15-8.94)	0.02	–	–
Surgical location (cervical vs other)	1.43 (0.80-2.55)	0.22	3.17 (1.95-5.13)	<0.001
Surgeon level (other versus architer)	1.71 (1.01-2.90)	0.04	1.83 (1.19-2.81)	0.0006
Surgical approach (posterior vs other)	1.27 (0.63-2.53)	0.50	5.59 (2.08-15.04)	0.001
Season in which surgery was performed (summer vs other)	1.34 (0.78-2.29)	0.29	2.16 (1.17-4.00)	0.014
Reasons for surgery (degenerative vs other)	2.19 (1.10-4.36)	0.02	1.46 (1.08-1.96)	0.13
Autograft for fusion and fixation	1.55 (0.91-2.63)	0.10	2.12 (1.11-4.04)	0.022
Gender (male)	1.30 (0.77-2.20)	0.33	–	–
Preoperative stay (≥3 d)	1.81 (0.97-3.38)	0.06	–	–
Diabetes mellitus	2.14 (0.95-4.82)	0.06	–	–
Steroid use	1.57 (0.79-3.15)	0.20	–	–
Current smoking	1.99 (0.92-4.29)	0.07	–	–
Age (≥60y)	0.54 (0.227-1.07)	0.07	–	–
Preoperative antibiotic use	0.95 (0.45-2.04)	0.90		
Intraoperative antibiotic use	0.04 (0.02-0.08)	0.00	–	–
Postoperative antibiotic use	2.00 (0.85-4.68)	0.11		
Drainage use	2.52 (0.90-7.00)	0.07	–	–
Platelet count upper limit	1.86 (0.92-3.74)	0.08	–	–

OR, odds ratio; *CI*, confidence interval.
*chi-square test.
†Published results of Gu et al.[1]