Letter to the Editor

High Rate of Antimicrobial Resistance in *Pseudomonas aeruginosa* at a Tertiary-Care Teaching Hospital in Southern Brazil

To the Editor:

Pseudomonas aeruginosa is a leading cause of nosocomial infection. An increasing prevalence of multidrug-resistant *P. aeruginosa* has been reported worldwide.[1] The highest rates have been observed in Latin America, especially in Brazil.[2]

Susceptibility patterns may have institutional variations due to multiple factors. Considering this, we performed an analysis of the susceptibility patterns of nosocomial isolates of *P. aeruginosa* to determine the magnitude of resistance to antipseudomonal agents at our institution. We also intended to identify a single susceptibility pattern more frequently associated with multidrug resistance. This kind of phenotypic marker could theoretically be useful to guide individual and institutional prescribing patterns for such strains to predict and prevent the emergence of the multidrug-resistant phenotype.

Clinical and surveillance isolates of *P. aeruginosa* were consecutively collected during September 2002 through July 2003 at Hospital São Lucas, a 600-bed, tertiary-care teaching hospital. Only one sample per patient was analyzed. If the patient had an isolate of multidrug-resistant *P. aeruginosa* following an isolate of non–multidrug-resistant *P. aeruginosa*, the latter was excluded. Strains isolated within 48 hours of patient admission were also excluded.

P. aeruginosa were identified by conventional microbiologic methods.[3] Antibiotic susceptibility tests were performed using the Kirby–Bauer disk-diffusion method according to the guidelines of the National Committee for Clinical Laboratory Standards.[4] Antibiotics tested included amikacin, aztreonam, ceftazidime, ciprofloxacin, imipenem, meropenem, piperacillin/tazobactam, and polymyxin B. Multidrug resistance was defined as resistance to three or more antipseudomonal agents of distinct classes. All statistical analyses were performed using SPSS software for Windows (version 10.0; SPSS, Inc., Chicago, IL). Odds ratios (ORs) and 95% confidence intervals (CI_{95}) were calculated. *P* values were calculated by chi-square.

A total of 189 *P. aeruginosa* isolates were identified during this period. Of those, 10 *P. aeruginosa* isolates were excluded because they were isolated from patients within 48 hours of hospital admission and 16 because they were isolated from patients with previous *P. aeruginosa* isolation (all of them with the same susceptibility pattern). Five isolates (one fully susceptible, two resistant to amikacin and ciprofloxacin, one resistant to amikacin and ceftazidime, and one resistant to ceftazidime and ciprofloxacin) were excluded because the same patients had previous isolates of multidrug-resistant *P. aeruginosa*.

A total of 158 isolates of *P. aeruginosa* were included in the study, corresponding to 7.1% of all bacterial isolates during this period. *P. aeruginosa* was isolated from patients hospitalized in medical and surgical wards. Sixty (38%) of the isolates were obtained from intensive care unit patients.

Ninety (57%) of the strains were resistant to three or more drugs. The most frequent susceptibility pattern defining multidrug resistance was resistance to all tested drugs except polymyxin B (16 strains; 17.8% of the multidrug-resistant *P. aeruginosa*), followed by resistance to amikacin, ceftazidime, ciprofloxacin, imipenem, and meropenem and susceptibility to aztreonam and piperacillin/tazobactam (14 strains; 15.6% of the multidrug-resistant *P. aeruginosa*) and resistance to amikacin, ceftazidime, ciprofloxacin, imipenem, meropenem, and piperacillin/tazobactam and susceptibility to aztreonam (13 strains; 14.4% of the multidrug-resistant *P. aeruginosa*).

P. aeruginosa isolates were more frequently recovered from respiratory secretions (22.2%), followed by urine (21.5%), nasal swabs (15.2%), blood (13.9%), surgical wounds (10.1%), central venous catheters (9.5%), and other secretions (7.6%). There were no statistically significant differences in the sites of isolation between multidrug-resistant *P. aeruginosa* and non–multidrug-resistant *P. aeruginosa* ($P = .40$).

All *P. aeruginosa* isolates were susceptible to polymyxin B. *P. aeruginosa* isolates showed resistance to ciprofloxacin (59.5% of resistance), imipenem (58.3%), amikacin (57.6%), meropenem (50.0%), ceftazidime (48.7%), piperacillin/tazobactam (38.6%), and aztreonam (33.5%).

Determination of resistance to any antimicrobial drug tested was associated with resistance to three or more drugs (Table 1). Resistance to amikacin was the most common resistance pattern associated with multidrug resistance (OR, 122.00; CI_{95}, 39.05 to 381.16), followed by ceftazidime (OR, 100.21; CI_{95}, 27.94 to 359.46), ciprofloxacin (OR, 81.20; CI_{95}, 27.96 to 235.79), aztreonam (OR, 43.15; CI_{95}, 9.95 to 187.17), piperacillin/tazobactam (OR, 39.27; CI_{95}, 11.42 to 135.07), imipenem (OR, 19.25; CI_{95}, 8.55 to 43.36), and meropenem (OR, 10.03; CI_{95}, 4.75 to 21.17).

Our study demonstrated a high rate of resistance to antipseudomonal agents among nosocomial strains of *P. aeruginosa* compared with multicenter surveillance studies (Table 2).[1,2,5] Resistance to ciprofloxacin and amikacin was higher than that reported in other studies.[1,2,5] Rates of resistance to ceftazidime and piperacillin/tazobactam noted in our study were similar to those reported in Brazil and Latin America,[2,5] but much higher than those in Europe and North America.[1] However, the most remarkable difference was noted in the carbapenem group. Resistance to imipenem and meropenem was almost twice that reported by Sader et al.[5] in Brazilian medical centers. The opposite was observed with aztreonam, which showed lower rates of resistance than in Europe and North America,[1] as well as in Brazil and Latin America.[2,5]

TABLE 1
SUSCEPTIBILITY TO ANTIPSEUDOMONAL AGENTS AMONG MULTIDRUG-RESISTANT AND NON–MULTIDRUG-RESISTANT ISOLATES OF *PSEUDOMONAS AERUGINOSA*

Drug Tested	No. of Isolates: Multidrug Resistant (n = 90)	No. of Isolates: Non–Multidrug Resistant (n = 68)	Total (%)	OR* (CI_{95})	P
Amikacin					
Resistant	84	7	91 (57.6)	122.00 (39.05–381.16)	< .001
Susceptible	6	61	67 (42.4)		
Aztreonam					
Resistant	51	2	53 (33.5)	43.15 (9.95–187.17)	< .001
Susceptible	39	66	105 (66.5)		
Ceftazidime					
Resistant	74	3	77 (48.7)	100.21 (27.94–359.46)	< .001
Susceptible	16	65	81 (51.3)		
Ciprofloxacin					
Resistant	84	10	94 (59.5)	81.20 (27.96–235.79)	< .001
Susceptible	6	58	64 (40.5)		
Imipenem					
Resistant	77	16	93 (58.9)	19.25 (8.55–43.36)	< .001
Susceptible	13	52	65 (41.1)		
Meropenem					
Resistant	65	14	79 (50.0)	10.03 (4.75–21.17)	< .001
Susceptible	25	54	79 (50.0)		
Piperacillin/tazobactam					
Resistant	58	3	61 (38.6)	39.27 (11.42–135.07)	< .001
Susceptible	32	65	97 (61.4)		

OR = odds ratio; CI_{95} = 95% confidence interval.
*For multidrug-resistant *P. aeruginosa* in resistant versus susceptible isolates.

TABLE 2
PATTERNS OF *PSEUDOMONAS AERUGINOSA* RESISTANCE TO ANTIPSEUDOMONAL AGENTS IN DIFFERENT STUDIES

Drug	% of Isolates Resistant: Current Study	Sader et al.,[5] 2001*	Andrade et al.,[2] 2003†	Gales et al.,[1] 2001‡: Europe	Gales et al.,[1] 2001‡: United States
Amikacin	57.6	44.2	34.6	21.1	3.4
Aztreonam	33.5	57.3	58.7	44.4	37.7
Ceftazidime	48.7	40.5	43.7	28.4	21.9
Ciprofloxacin	59.5	41.3	50.1	32.4	24.7
Imipenem	58.9	30.2	37.8	28.4	19.1
Meropenem	50.0	25.6	35.6	26.2	9.1
Piperacillin/tazobactam	38.6	29.2	35.1	26.2	13.4

*Included Brazilian medical centers from Rio de Janeiro, Florianópolis, São Paulo, and Porto Alegre.
†Included medical centers from Brazil, Argentina, Chile, Colombia, Mexico, Uruguay, and Venezuela.
‡Included many medical centers from Europe and the United States.

The higher rates of resistance to antipseudomonal agents noted in our study seem to represent an increasing prevalence of resistance in *P. aeruginosa* as reported from other Latin American hospitals during the past few years.[2] This could be due to interinstitutional and intrainstitutional spread of multidrug-resistant *P. aeruginosa* clones (a hypothesis that is under investigation) or to local prescribing patterns, although there do not seem to be important differences in these patterns from other tertiary-care institutions (unpublished data).

We believe that the exclusion of five non–multidrug-resistant strains did not cause any important bias in our study because their inclusion would not likely cause major changes in the final results.

The current study failed to find a single antibiogram of multidrug resistance in our isolates because multiple patterns were involved. A prospective study would be able to follow the evolution of the susceptibility pattern of particular strains, using molecular typing, and would provide better understanding of how susceptibility profiles evolve to multidrug resistance. Although also associated with multidrug resistance, resistance to carbapenem drugs, especially meropenem, was less frequently associated with multidrug resistance at this institution.

Increasing resistance in *P. aeruginosa*, particularly that seen in Brazilian and Latin American centers,

https://doi.org/10.1086/503487 Published online by Cambridge University Press

is of great concern because it has clinical and public health implications. Susceptibility patterns can have institutional variations and local surveillance is encouraged.

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HOSPITAL ACQUIRED INFECTION:
REQUEST FOR COLLABORATIVE RESEARCH PARTNERS (TO GENERATE DATA FOR PUBLICATION)

- **MRSA**
- **VRE**
- ***Acinetobacter* spp.**
- ***Clostridium difficile***
- **viruses**
- **fungi**

1. There is increasing evidence that the environment is contributing significantly to the spread of hospital acquired infection. (This contrasts with the historic view that the environment did not contribute to infection acquisition rates.)

2. There is also evidence that the hospital environment is contaminated with nosocomial pathogens and conventional cleaning methods are not effective.

3. BIOQUELL's RBDS hydrogen peroxide vapor technology has been shown to be a safe and highly effective way of eradicating nosocomial pathogens[1] from the hospital environment. At the end of the process the vapor is catalytically converted to water and oxygen, hence there are no problematic residues.

4. BIOQUELL's RBDS technology has already been deployed in more than 1000 rooms/ zones in pharmaceutical companies and hospitals in Europe and Asia - including intensive care units full of modern, sensitive electronic equipment.

5. **BIOQUELL is seeking collaborative research partners who are currently experiencing a nosocomial outbreak (or cluster), and who have good, detailed, historic infection acquisition data.** We wish to carry out scientific research with such partners to investigate the link between environmental contamination and infection acquisition rates - and specifically to demonstrate that following the eradication of the pathogen from the environment using BIOQUELL's technology, then the infection acquisition rate falls.

6. BIOQUELL's hydrogen peroxide vapor technology is scalable and portable - and can be deployed on a worldwide basis.

If you are interested in participating in such a collaborative research study or would like further information on BIOQUELL's technology then please contact Jon Otter, Lead Microbiologist, at BIOQUELL (jon.otter@bioquell.com).

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[1] French GL, Otter JA, Shannon KP, Adams NMT, Parks MJ, Watling D. Tackling contamination of the hospital environment by methicillin-resistant *Staphylococcus aureus* (MRSA): a comparison between conventional terminal cleaning and hydrogen peroxide vapour decontamination. *J Hosp Infect* 2004;**57**:31-37.

https://doi.org/10.1086/503487 Published online by Cambridge University Press