International Journal of Infectious Diseases 17 (2013) e757–e761

Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Seasonal humidity may influence *Pseudomonas aeruginosa* hospital-acquired infection rates

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ARTICLE INFO

Article history:
Received 16 August 2012
Received in revised form 28 February 2013
Accepted 1 March 2013

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Pseudomonas aeruginosa
Humidity
Hospital infection
Seasonality

SUMMARY

Objective: The objective of this study was to determine the association of seasonal climatic conditions with the incidence of *Pseudomonas aeruginosa* infections.
Methods: A retrospective study was carried out to evaluate all infections caused by *P. aeruginosa* in a 660-bed tertiary-care hospital in Brazil over a period of 5 years. To assess seasonal patterns, monthly temperature, relative humidity, and precipitation averages were obtained. Correlations of seasonal variations with infection rates (IR) were determined by Pearson correlation coefficient. Linear regression was used to determine trends, and multivariable linear regression was performed using a Poisson distribution.
Results: A total of 844 cases of *P. aeruginosa* infection were identified for 1 058 501 patient-days during 1826 days (overall IR 7.97/10 000 patient-days). The mean temperature was $18.2 \pm 2.8\,^{\circ}$C, relative humidity was $80.3 \pm 3.6\%$, and precipitation was 104.7 ± 64.38 mm. The Pearson correlation was significant between urinary tract infection and temperature ($R = 0.29$; $p = 0.021$) and precipitation ($R = 0.27$; $p = 0.036$). A correlation was also significant between hospital-associated pneumonia and precipitation ($R = 0.29$; $p = 0.022$) and relative humidity ($R = 0.31$; $p = 0.013$). Relative humidity was associated with a higher IR of other infections caused by *P. aeruginosa*, but it was not possible to build a predictive model when multiple linear regression and Poisson regression were tested.
Conclusion: Climatic conditions are another factor that may interfere with the IR of *Pseudomonas aeruginosa*.

1. Introduction

Temperature, humidity, and precipitation are important determinants of pathogen survival. Many viral and bacterial infections in humans show marked seasonal changes. High ambient temperatures, for instance, provide a supportive environment for food-borne pathogens, whereas higher relative humidity may also affect the stability of air-borne droplets in which viruses travel from person to person.[1]

Pseudomonas aeruginosa is a versatile Gram-negative bacterium that is one of the top three causes of opportunistic human infections.[2,3] *P. aeruginosa* infection is prevalent among patients with burn wounds, cystic fibrosis, acute leukemia, organ transplants, and intravenous drug addiction. Moreover, it is a common nosocomial contaminant, being responsible for 10–20% of infections in most hospitals.

There are several reports of seasonal variations in the incidences of nosocomial infections, the majority of them regarding Gram-negative bacteria.[4] A study performed at the University of Maryland Center observed significant summer peaks in the incidences of infections due to the Gram-negative pathogens *P. aeruginosa*, *Enterobacter cloacae*, *Acinetobacter baumannii*, and *Escherichia coli*.[5] Moreover, Eber et al. have also published the results of a study on inpatients from 132 US hospitals, showing seasonal variations, with peaks in the warmer months of the year, of *Acinetobacter spp*, *E. coli*, and *P. aeruginosa* nosocomial infections.[6] Another study describing seasonal variations in bloodstream infections (BSI) due to *Klebsiella pneumoniae* reported an increase of 41% to 49% on the infection rates (IR) during the warmest months of the year.[7]

Rather than just comparing different types of bacteria, Falagas et al. examined whether lower urinary tract infections (UTIs) are associated with different meteorological parameters. A significant

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1201-9712/$36.00 – see front matter
http://dx.doi.org/10.1016/j.ijid.2013.03.002

correlation was found between visits for lower UTIs and the average higher weekly temperature and decreased relative humidity recorded in the same area.[8] According to these data, seasonality may not interfere solely in the global rates of different bacterial infections, but also in the IR at different body sites. In addition, the study highlights that parameters other than temperature alone, most notably humidity, may interfere in the different rates of infection throughout the year.

These seasonal patterns may vary for different diseases, different locations, or different subpopulations. Hence, an understanding of the seasonal fluctuations in diseases is essential to develop efficient strategies for disease prevention and control. There are no reports of studies assessing seasonal variations in nosocomial infections in South America. Furthermore, the number of studies assessing *P. aeruginosa* seasonality is limited, and no studies regarding *P. aeruginosa* solely have yet been published.[4] The present study aimed to determine the association of seasonal climatic conditions with the incidence of *P. aeruginosa* infections, in a tertiary hospital in southern Brazil.

2. Methods

We performed a retrospective study evaluating all infections caused by *P. aeruginosa* from January 2006 to December 2010. The data were obtained from the Hospital Universitário Evangélico de Curitiba, a reference center for trauma, burns, and renal transplantation. This center is a 660-bed tertiary-care hospital in Curitiba, a city located in southern Brazil, with 60 intensive care beds. The institution's ethics committee approved the study.

The IR were obtained from the electronic registers of the service of infection control and hospital epidemiology. This study used the criteria of the Centers for Disease Control and Prevention (CDC, USA) to define cases of nosocomial infection.[9] The infections included in the analysis were classified as: (1) urinary tract infection associated with catheter (UTI), (2) hospital-associated pneumonia (HAP), (3) surgical site infection (SSI), (4) bacteremia and catheter-related infection (BSI), and (5) others, which included tegument infections, meningitis/ventriculitis, and sinusitis. Since IR are confounded by length of stay, we present the rates of infection per 10 000 patient-days. We analyzed monthly rates by site of infection.

To determine whether seasonal variation is associated with *P. aeruginosa* IR, average monthly temperatures (degrees Celsius, °C), relative humidity (percentage, %), and precipitation (millimeters, mm) were obtained from the local weather service, in accordance with local protocols (2006–2010). The measures are performed with hygrometers (relative humidity), pluviometers (precipitation), and thermometers/thermo-hygrometers (temperature).

2.1. Statistical analysis

The associations of seasonal variations and IR were determined by Pearson correlation coefficient. Linear regression was used to determine trends among rates of *P. aeruginosa* infection and seasonal variables. Multiple linear regression and Poisson regression were tested to build a predictive model. The significance level was set at 0.05. All data were stored in Excel (Microsoft, New York, USA) and the statistical analysis was performed using the software R.

3. Results

A total of 844 cases of *P. aeruginosa* infection were identified for 1 058 501 patient-days during 1826 days (overall IR 7.97/10 000 patient-days). There were 258 cases of HAP (IR 2.47/10 000 patients-days), 258 cases of SSI (IR 2.47/10 000 patient-days), 245 UTI (IR 2.36/10 000 patient-days), 64 cases of BSI (IR 0.61/10 000 patient-days), and 19 other infections (IR 0.18/10 000 patient-days). *P. aeruginosa* is considered to be endemic in the institution and there were no outbreaks during the study period. The IR of *P. aeruginosa* during the study period is shown in Figure 1.

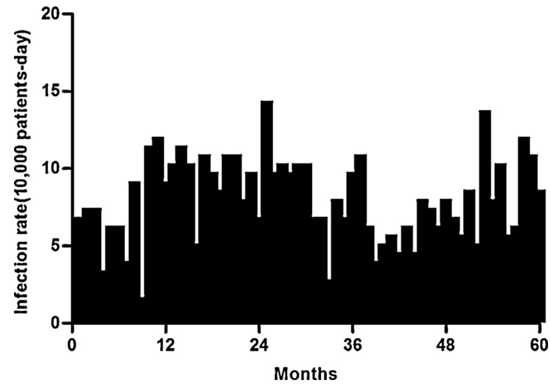

Figure 1. *Pseudomonas aeruginosa* monthly infection rates (IR) during the 5-year study period (2006–2010).

The mean temperature in the city of Curitiba was 18.2 ± 2.8 °C, relative humidity was $80.3 \pm 3.6\%$, and precipitation was 104.7 ± 64.38 mm. Trends in monthly IR at different sites and the average monthly climatic factors are summarized in Figure 2.

The Pearson correlation was significant between UTI and temperature ($R = 0.29$; $p = 0.021$) and precipitation ($R = 0.27$; $p = 0.036$). An association was significant between HAP and precipitation ($R = 0.29$; $p = 0.022$) and relative humidity ($R = 0.31$; $p = 0.013$). All correlations are detailed in the Table 1.

Although relative humidity was associated with a higher IR for other infections caused by *P. aeruginosa*, it was not possible to build a predictive model when multiple linear regression and Poisson regression were tested.

4. Discussion

The main determinants of temporal variations in disease manifestations are related to: host susceptibility, periodicity in pathogen abundance and transmissibility, and the ever-changing environment that can support or repress a host or pathogen.[1] Thus, to develop efficient strategies for disease prevention and control, it is important to have an understanding of the main determinants of temporal variations and their interactions.

Among the several Gram-negative bacteria reported to be affected by seasonality, *Acinetobacter* species are the most commonly described to be subject to seasonal variations. For instance, there are reports of increases in overall bloodstream and pneumonia infections caused by acinetobacter species during the warm months in the Northern Hemisphere (July-October). There are also reports of increases in overall bloodstream and pneumonia infections caused by *Acinetobacter* species during the warm months in the Northern Hemisphere (July–October).[10] However, the authors highlight the need for caution with regard to the epidemiological studies regarding *A. baumannii* due to the quality of the epidemiological data and the difficulty in identifying this organism.[4] The same, therefore, can be inferred for other epidemiological studies regarding the seasonality of Gram-negative bacterial infections.

In contrast to *Acinetobacter spp*, studies specifically regarding the seasonality of *P. aeruginosa* are limited, and more data on the seasonal variations of these bacteria are yet to be published. A case–control study performed over a 3-year period comparing hematology–oncology outpatients with and without central-line-associated

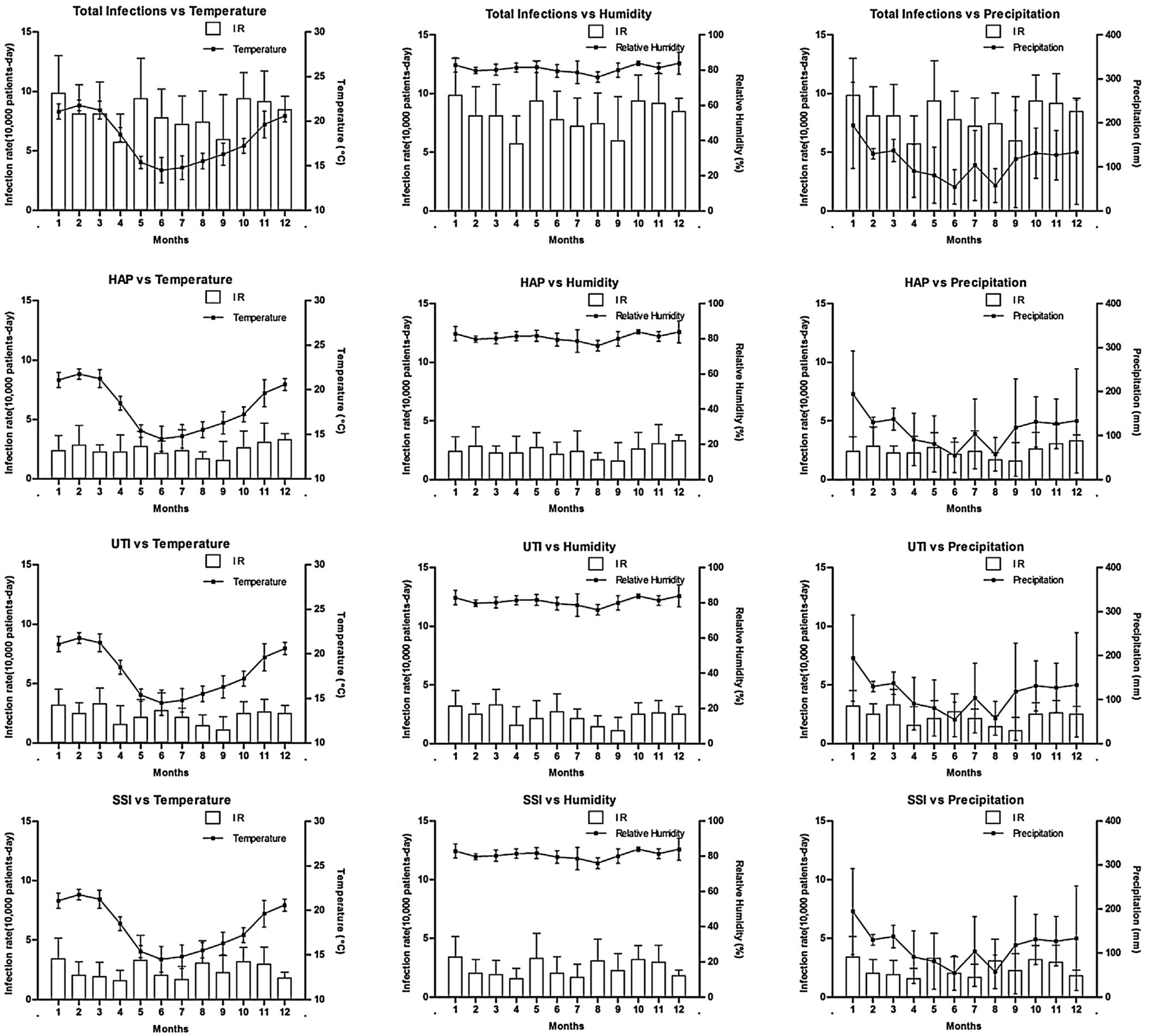

Figure 2. Association between different climatic factors and the monthly infection rates (IR) of *Pseudomonas aeruginosa* throughout the 5-year study period (2006–2010). Each number on the *x*-axis corresponds to a month of the year. The error line of each column and point is the standard deviation associated with the same month in different years of the study period. The *y*-axis corresponds to the values of the climatic factor analyzed.

BSI, identified a significant increase in BSIs caused by *Pseudomonas spp*, during the summer months (May–October).[11] In addition, trends for seasonal variations in Pseudomonas peritonitis (summer peak) have already been reported in the literature.[12] Even though these studies have reported important data on *Pseudomonas spp* seasonality, they are not specific to *P. aeruginosa* and include other species of the genus *Pseudomonas* as well.

Other studies have indirectly assessed the effect of seasonal variations in *P. aeruginosa* IR together with other Gram-negative bacteria. Perencevich et al., after collecting over 26 624 unique clinical cultures of both Gram-negative and Gram-positive bacteria from 1998 to 2005, concluded that significantly higher rates of infection from different Gram-negative pathogens were observed during the summer months.[5] A 17% increase in the monthly rates of infection caused by *P. aeruginosa* and *A. baumannii* was seen for each 10 °F increase during the warm months (May–September).[5]

After assessing 844 cases of *P. aeruginosa* infection in a tertiary hospital in southern Brazil, we were unable to establish a seasonal pattern for *P. aeruginosa* infections during the summer months. Although our sample size is smaller (Perencevich et al. evaluated 3373 *P. aeruginosa* cultures during a 96-month period), we emphasize that, for the same infectious agent, infection rates recorded at different locations and with different subpopulations may present different patterns of incidence.

Conversely, after stratifying the infections by site, we found that there was a significant association between UTI infections caused by *P. aeruginosa* and temperature ($R = 0.29$; $p = 0.021$) and precipitation ($R = 0.27$; $p = 0.036$). There are also other reports regarding higher UTI infection rates for different pathogens including *P. aeruginosa*, during the warmer periods of the year.[13,14] However, different from the present study, those studies assessed community-acquired and not nosocomial UTIs caused by not only *P. aeruginosa* but also other bacteria. Even though mostly related to community-acquired UTIs, the study by Falagas et al. showed a significant correlation between medical visits for lower UTIs and average higher weekly temperature and decreased relative

Table 1
Correlation of infection rates (IR) caused by *Pseudomonas aeruginosa* at different sites according to climatic conditions between 2006 and 2010

		UTI	HAP	SSI	BSI	Other	Total	Temp	Precip	RH
UTI	*R*	**1**	0.353	0.028	−0.234	−0.168	0.553	0.297	0.272	0.189
	p-Value		0.006	0.834	0.072	0.199	0	0.021[a]	0.036[a]	0.147
HAP	*R*	0.353	**1**	0.075	−0.008	0.043	0.665	0.162	0.295	0.318
	p-Value	0.006		0.571	0.949	0.744	0	0.217	0.022[a]	0.013[a]
SSI	*R*	0.028	0.075	**1**	0.161	0.408	0.659	−0.035	−0.091	0.022
	p-Value	0.834	0.571		0.218	0.001	0	0.791	0.489	0.866
BSI	*R*	−0.234	−0.008	0.161	**1**	0.225	0.237	−0.149	−0.193	−0.187
	p-Value	0.072	0.949	0.218		0.084	0.068	0.256	0.139	0.152
Other	*R*	−0.168	0.043	0.408	0.225	**1**	0.336	−0.081	0.019	0.224
	p-Value	0.199	0.744	0.001	0.084		0.009	0.539	0.888	0.085
Total	*R*	0.553	0.665	0.659	0.237	0.336	**1**	0.146	0.169	0.229
	p-Value	0	0	0	0.068	0.009		0.267	0.197	0.078
Temp	*R*	0.297	0.162	−0.035	−0.149	−0.081	0.146	**1**	0.328	0.114
	p-Value	0.021	0.217	0.791	0.256	0.539	0.267		0.011	0.387
Precip	*R*	0.272	0.295	−0.091	−0.193	0.019	0.169	0.328	**1**	0.685
	p-Value	0.036	0.022	0.489	0.139	0.888	0.197	0.011		0
RH	*R*	0.189	0.318	0.022	−0.187	0.224	0.229	0.114	0.685	**1**
	p-Value	0.147	0.013	0.866	0.152	0.085	0.078	0.387	0	

R, Pearson correlation coefficient; UTI, urinary tract infection; HAP, hospital-associated pneumonia; SSI, surgical site infection; BSI, blood stream Infection; Temp, temperature; Precip, precipitation; RH, relative humidity.
[a] Statistically significant *p* values.

humidity.[8] Besides showing the importance of meteorological parameters other than just temperature, the findings of Falagas et al. could in part explain some of the seasonal variations observed with BSI, because, in many studies, UTI was the most common primary source of infection.[4,8]

In the present study, we also identified a significant association between HAP and precipitation ($R = 0.29$; $p = 0.022$) and relative humidity ($R = 0.31$; $p = 0.013$). Although we did not find many studies associating these variables, Liang and Miao evaluated both precipitation and relative humidity as markers of morbidity in childhood pneumonia.[15] Future studies could assess these variables as potential incidence predictors of *P. aeruginosa* hospital-acquired pneumonia.

Potential explanations for the correlation between these seasonal variables and the incidences of infection due *P. aeruginosa* remain elusive. A clue could be that *P. aeruginosa* is an aquatic organism and is associated with summer peaks. Regardless of the mechanisms responsible for infection, recognition of this link between the physical environment and the incidences of pathogenic infections among hospitalized patients may influence diagnosis strategies, empirical therapies, and infection control prevention programs, thus improving patient care.

Our study has limitations. Besides not having a control group, our evaluations were also limited to one specific Gram-negative pathogen only, meaning we were unable to explore the impact of seasonal fluctuations on a greater scale. Additionally, the majority of our data were obtained from one tertiary center, hence conclusions from our study may not be inferred for all hospitals. Finally, this study represents an epidemiological survey, and as such we were unable to analyze specific patient characteristics or disease that might have contributed to the observed trends.

The seasonal variability in the infection rate will stimulate new studies and possible strategies to decrease infection rates. For instance, temperature can interfere with human activities, which could account for the seasonal variability. The modification of environmental temperature or humidity is a potentially valid method for controlling infection rates.[16] Freeman et al. suggest surveillance during the periods in which the IR were reported to increase. Furthermore, the authors also recommend performing studies during these periods in order to evaluate the colonization rates and to determine the bacterial charge during alterations in temperature.[17] These theories are promising, but have not as yet been evaluated. According to our study, a drier environment could decrease Pseudomonas infection.

In conclusion, we identified incremental changes in the incidences of specific infections due to *P. aeruginosa* associated with seasonal changes in temperature, humidity, and precipitation. Taking into consideration the limitations of this study, our findings may lead to a better understanding of changes in disease occurrences and may be important for building efficient strategies for disease prevention and control.

Funding: This study received no financial support.

Conflict of interest: The authors have no commercial relationships or other affiliations that might constitute a conflict of interest (e.g., pharmaceutical stock ownership, consultancy, advisory board membership, relevant patents, or research funding).

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