ORIGINAL ARTICLE

Clustering of *Serratia marcescens* infections during six years: Epidemiology and risk factors for mortality

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ABSTRACT

Background: *Serratia marcescens* is responsible for hospital-associated infections found in clusters and outbreaks. Based on a previous outbreak in our institution, we aimed to evaluate epidemiological characteristics and risk factors for mortality of patients with *S. marcescens* infection in the previous five-year period.

Method: A retrospective analysis of the patients with *S. marcescens* colonization and infection between January 2008 and December 2012 was included. Data included demographical characteristics, co-morbidities, and invasive procedures performed were obtained from the computer databases, the microbiology laboratory, and infection control surveillance data. Data were plotted monthly on process control charts including Exponentially Weighted Moving Average (EWMA) statistics.

Results: We identified 378 patients colonized or infected with *S. marcescens* between January 2008 and December 2012. The median age of patients was 57 years (0-90 years). Of all hospitalized patients 60 (21.7%) expired and 216 (78.2%) survived. Previous ICU stay, respiratory failure, loss of consciousness, total parenteral nutrition, mechanical ventilation, intubation, central catheterization, urinary catheterization, hemodialysis, previous use of antibiotics were significant risk factors for mortality. Multivariate analysis showed that mortality risk of *Serratia* infection increased threefold for hemodialysis patients and fivefold for intubated patients. A mean monthly level of *Serratia* infections hospital-wide identified from process control chart statistics was 6.3 and ranged from 5.2-8.8 over five years. For ICU cases the mean was 1.9 and ranged over five years from 1.1 to 3.3.

Conclusions: *S. marcescens* is an opportunistic pathogen associated with significant mortality. We documented that *S. marcescens* strains persisted over prolonged periods causing cluster of infections. Clinicians should consider that small clusters of *S. marcescens* infections are the tip of the iceberg and may be a predictor of an outbreak.

KEY WORDS

Serratia marcescens, cluster, intensive care units, outbreak

INTRODUCTION

Serratia marcescens is responsible for hospital-associated infections found in clusters and outbreaks (1). We have previously reported outbreaks of postoperative empyema due to *S. marcescens* that was recognized in the intensive care unit (ICU) of our Division of Thoracic Surgery between 3 and 19 March 2013 related to a contaminated portable suction machine (2). All isolates were found to be identical by repetitive sequence-based polymerase chain reaction. Based on this outbreak, we aimed to evaluate epidemiological characteristics and risk factors for mortality of patients with *S.marcescens* infection in the previous five-year period. We also reviewed clustering of *S. marcescens* infections in the past years and the pattern of *S. marcescens* outbreaks in our institution.

METHODS

We performed a retrospective study at Erciyes University Hospital. Patients with *S. marcescens* colonization and infection were included between January 2008 and December 2012. Data included demographical characteristics, co-morbidities and invasive procedures performed was obtained from computer databases, the microbiology laboratory and infection control surveillance data. A retrospective data analysis was conducted to evaluate the risk factors for 30-day mortality.

We utilized process control charts to plot all *S. marcescens* infections in an attempt to visually demonstrate the statistics and identify the rapid increases in the number of cases (3). Data were plotted monthly on process control charts including Exponentially Weighted Moving Average (EWMA) statistics.

Statistical analysis: The statistical analysis was performed using SPSS software version 16 (USA). The chi-square test was used for the categorical variables. Mann-Whitney U test was used to determine the differences between the two groups. Univariate and multiple binary logistic regression analyses (model: backward Wald) were performed to analyze the effects of variables. The level of significance was set at $p < 0.05$ for all tests.

FIGURE 1: Serratia infections hospital-wide between 2008 to 2012 presented in EWMA statistics

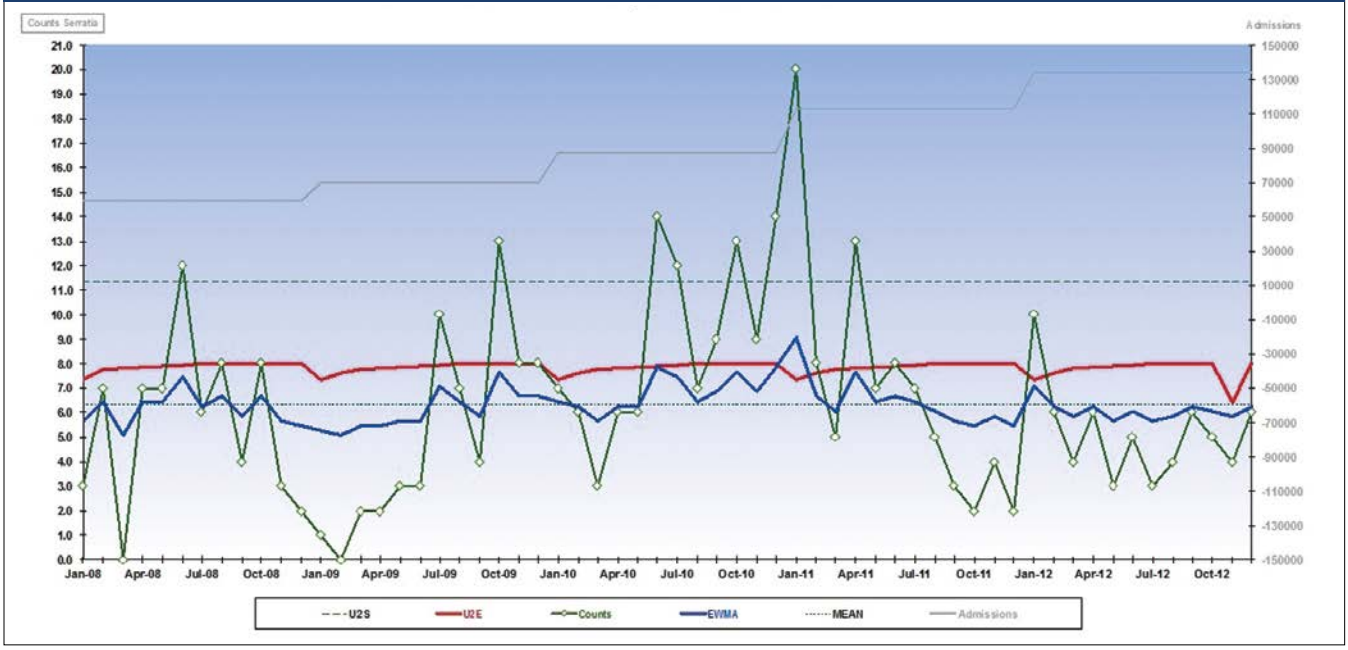
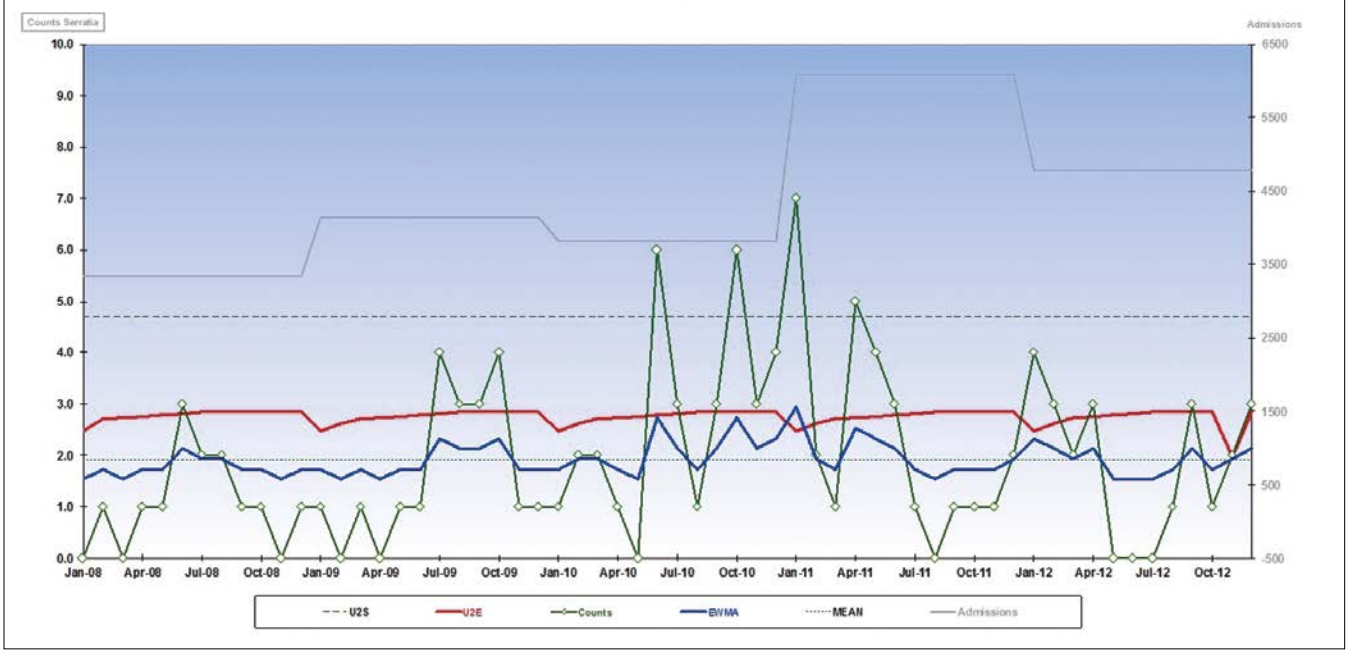


FIGURE 2: Serratia infections from Adult Intensive Care Unit between 2008 to 2012 presented in EWMA statistics



RESULTS

We identified 378 patients colonized or infected with *S. marcescens* between January 2008 and December 2012. Of all patients with *S. marcescens* 17% (66/378) were outpatients and the remaining 83% (312/378) were inpatients from internal medicine, surgery, pediatrics and intensive care units. Overall, 51% of strains were isolated from the ICU patients.

The median age of patients was 57 years (0-90 years). Of all hospitalized patients 60 (21.7%) expired and 216 (78.2%) survived. Previous ICU stay, respiratory failure, loss of consciousness, total parenteral nutrition, mechanical ventilation, intubation, central catheterization, urinary catheterization, hemodialysis, previous use of antibiotics were significant risk factors for mortality. Multivariate analysis showed that mortality risk of *Serratia* infection increased threefold for hemodialysis patients and fivefold for intubated patients (Table 1).

A hospital-wide mean monthly level of *Serratia* infections identified from process control chart statistics was 6.3 and ranged from 5.2-8.8 over five years (Figure 1). For ICU cases the mean was 1.9 and ranged over five years from 1.1 to 3.3 (Figure 2). Charted EWMA statistics illustrate fluctuations in

TABLE 1: Univariate and multivariate analysis of risk factors for mortality of *Serratia marcescens* infections

Risk factors	Died patients n: 60 (21.7 %)	Survived patients n: 216 (78.3 %)	P	Multiple analysis OR (95% CI)	P
Age	60 (0-84)	57 (0-90)	0.157		
Male gender	18 (30.0)	66 (30.6)	1.000		
Internal medicine	6 (10.0)	54 (25.0)	**0.001**		
Surgical units	8 (13.3)	70 (32.4)			
Intensive care units	40 (66.7)	68 (31.5)			
Pediatrics	6 (10.0)	24 (11.1)			
Previous ICU stay	46 (76.7)	89 (41.2)	**0.001**		
Transfer from another institution	3 (5.0)	27 (12.5)	0.107		
Transfer between units	16 (26.7)	32 (14.8)	0.036		
Malignancy	15 (25.0)	54 (25.0)	1.000		
Multiple body trauma	4 (6.7)	11 (5.1)	0.747		
COPD	6 (10.0)	13 (6.0)	0.385		
Previous use of steroids	8 (13.3)	31 (14.4)	1.000		
Diabetes mellitus	9 (15.0)	34 (15.7)	1.000		
Unconsciousness	8 (13.3)	9 (4.2)	**0.015**		
Cardiac failure	5 (8.3)	13 (6.0)	0.555		
Immune-suppression	2 (3.3)	7 (3.2)	1.000		
Respiratory failure	38 (63.3)	67 (31.0)	**0.001**		
Renal failure	12 (20.0)	18 (8.3)	**0.017**		
Total parenteral nutrition	23 (38.3)	41 (19.0)	**0.002**		
Mechanical ventilation	44 (73.3)	73 (33.8)	**0.001**		
Transfusion	29 (48.3)	71 (32.9)	0.034		
Surgery	25 (41.7)	77 (35.6)	0.450		
Enteral feeding	22 (36.7)	34 (15.7)	**0.001**		
Urinary catheterization	46 (76.7)	115 (53.2)	**0.002**		
Hemodialysis	12 (20.0)	15 (6.9)	**0.005**	3.071 (1.267-7.447)	0.013
Intubation	44 (73.3)	73 (33.8)	**0.001**	5.244 (2.750-9.998)	0.001
Tracheostomy	13 (21.7)	33 (15.3)	0.327		
Drainage	5 (8.3)	18 (8.3)	1.000		
Thorax tube	9 (15.0)	41 (19.0)	0.572		
Central venous catheterization	32 (53.3)	54 (25.0)	**0.001**		
Bronchoscopy	5 (8.3)	7 (3.2)	0.142		
Arterial catheterization	18 (30.0)	33 (15.3)	**0.014**		
Percutaneous endoscopic gastrostomy	5 (8.3)	10 (4.6)	0.330		
Nasogastric drainage	27 (45.0)	46 (21.3)	**0.001**		
Previous use of antibiotics	50 (83.3)	136 (63.0)	**0.003**		
Aminoglycosides	7 (11.7)	20 (9.3)	0.624		
Beta-lactams	28 (46.7)	78 (36.1)	0.177		
Glycopeptides	10 (16.7)	26 (12.0)	0.386		
Carbapenems	19 (31.7)	41 (19.0)	0.050		
Quinolones	4 (6.7)	15 (6.9)	1.000		
Cephalosporins	18 (30.0)	58 (26.9)	0.744		
Other antibiotics	17 (28.3)	32 (14.8)	0.021		
Site of infection					
Blood stream infection	49 (22.7)	9 (15.0)	**0.001**		
Urinary system infection	28 (13.0)	2 (3.3)			
Pleural fluid	31 (14.4)	5 (8.3)			
Endotracheal aspirates/sputum	55 (25.5)	33 (55.0)			
Others	53 (24.5)	11 (18.3)			
Length of hospital stay before infection	11 (1-472)	7 (1-138)	**0.024**		
Length of ICU stay before infection	20 (1-472)	23 (1-254)	0.244		

outbreaks isolated throughout various parts of the hospital, but underline that outbreaks are driven primarily by the ICU. The peak of outbreak activity in ICU occurred in June 2008 and remained within statistical control limits until July 2009, when another peak recurred until it was controlled in November 2009. From that point onward, it remained under the upper limit but did not decline to zero until May 2010. The outbreak spiked in ICU rapidly in June 2010 remaining above statistical control limits until February and March 2012. After six months of zero cases the outbreak over the upper EWMA limit commenced in January 2012 and continued into April 2012 and again in September, November and December 2012. There were 10 months out of a total 48 months when no cases occurred.

The resistance rate of *S. marcescens* clinical isolates to ertapenem was 1.7% (3/172), imipenem 2.2% (6/268), amikacin 4.3% (12/276), ciprofloxacin 11.3% (31/274), cephotaxime 26.9% (35/130), cefepime 15.3 (42/274) and ampisilin/sulbactam 4.45 % (9/202).

DISCUSSION

S. marcescens is an opportunistic pathogen associated with significant mortality. Infections caused by this bacterium have become a significant concern for its ability to cause hospital outbreaks, especially in ICUs and neonatal units (1,4). In this study, we retrospectively analyzed hospital-wide epidemiology of Serratia infections; its distribution among wards, antimicrobial resistance, clustering patterns and predictors of mortality.

Individuals at risk for *Serratia* infection tend to be inpatients with a prolonged hospital stay and history of invasive procedures. In our study, 17% of isolates were obtained from outpatients. However, while *S. marcescens* is a rare cause of community-onset infections, some part of them is considered to be health care associated. Antibiotic resistance is increased among patients with *S. marcescens*. High resistance rates to third-generation cephalosporins were previously reported from Taiwan and Korea (6,7). Though resistant strains have been associated with adverse outcomes, lower resistance and mortality rates were found in this study. Several risk factors were associated with 30-day mortality due to *S. marcescens* infections (7,8). In this study, the variables independently associated with 30-day mortality were history of hemodialysis and intubation.

One of the limitations of the study was that we did not perform molecular and epidemiologic analysis of clonal relatedness among *S. marcescens* strains. Since such analysis is costly, we took the advantage of using EWMA to detect suspected outbreaks retrospectively. Small clusters of *S. marcescens* infections are potential predictors of outbreaks (5). Clustering of cases in the ICU where we achieved several consecutive months of zero cases suggests that interventions need to be implemented early and be continuously reinforced.

In conclusion, *S. marcescens* is an opportunistic pathogen associated with significant mortality. We documented that *S. marcescens* strains persisted over prolonged periods causing cluster of infections. These clustered cases require early detection and intervention to prevent outbreaks. Clinicians should consider that small clusters of *S. marcescens* infections are the tip of the iceberg and may be predictors of a likely outbreak.

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