Serratia infections in children

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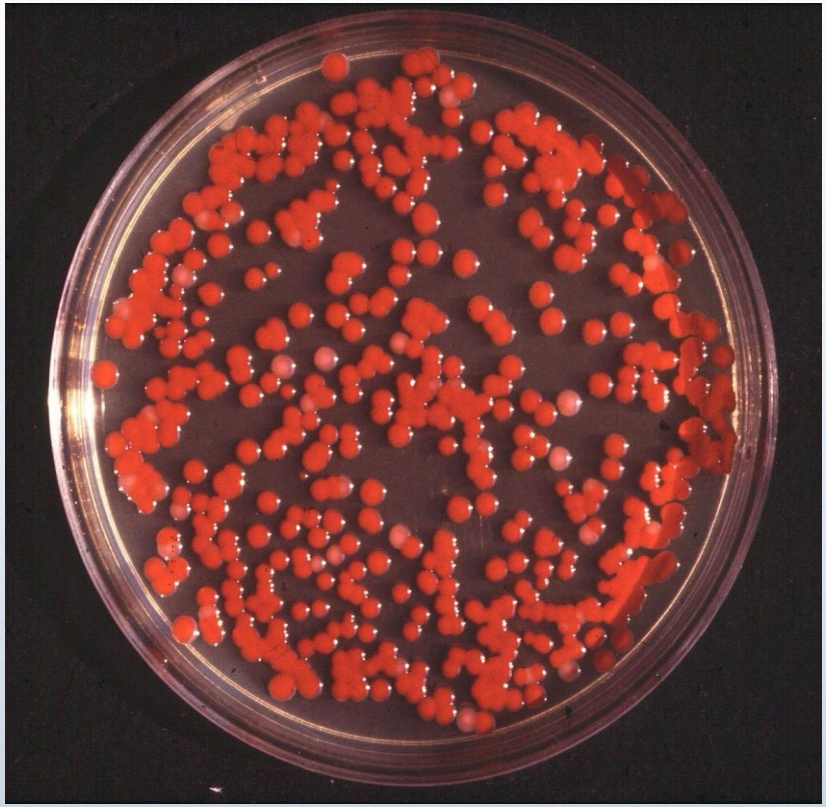
Outline

- Bacteria
- Pathogenesis
- The nature of infections
- About our study
- About our experiences on gram (-) bacteremia
- Management of infections

Bacteria

- Serratia is classified as a member of the family Enterobacteriaceace.
- Straight, motile, catalase-positive, gram-negative rods.
- Consists of 14 recognized species with 2 identified subspecies
- 6 biogroups were recognized according to biochemical characteristics
- The biogroups consist of red pigment (A1, A1/6) and nonpigmented (A3,A4,A5/8) serotypes.

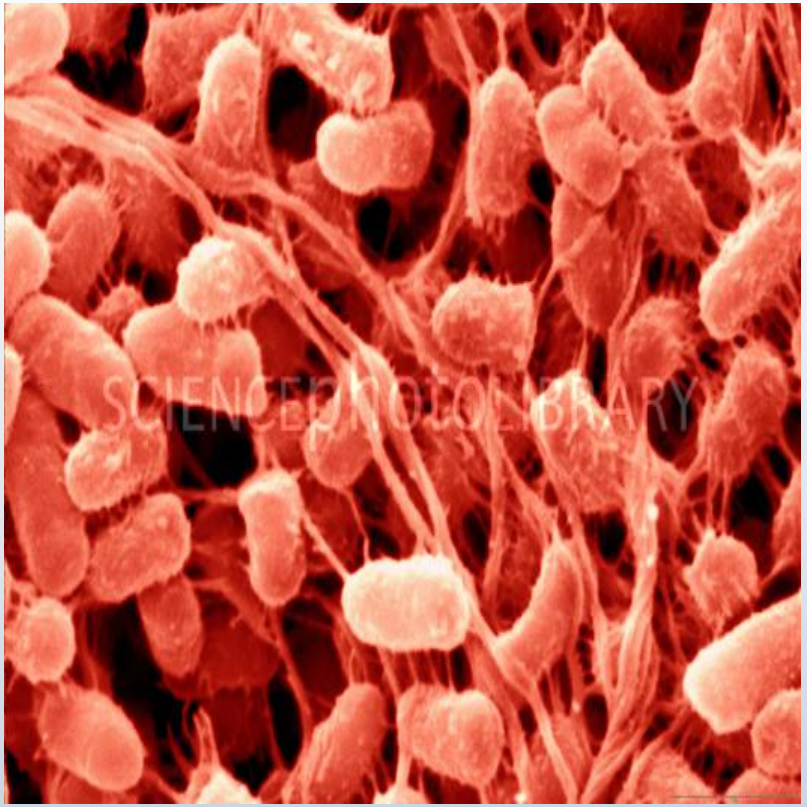


Ochieng et al. Gut Microbes 2014;5:6:729-726; Mahlen SD. Clin Microbiol Rev 2011;24:755-91.

Virulence factors

- S. marcescens is capable of producing well known virulence factors such as fimbriae, quorum sensing systems and various secreted enzymes

- has a potent cytotoxin (ShlA), a secreted pore-forming cytolysin, which is an important factor mediating internalization of S. marcescens and lysis of epithelial cells.



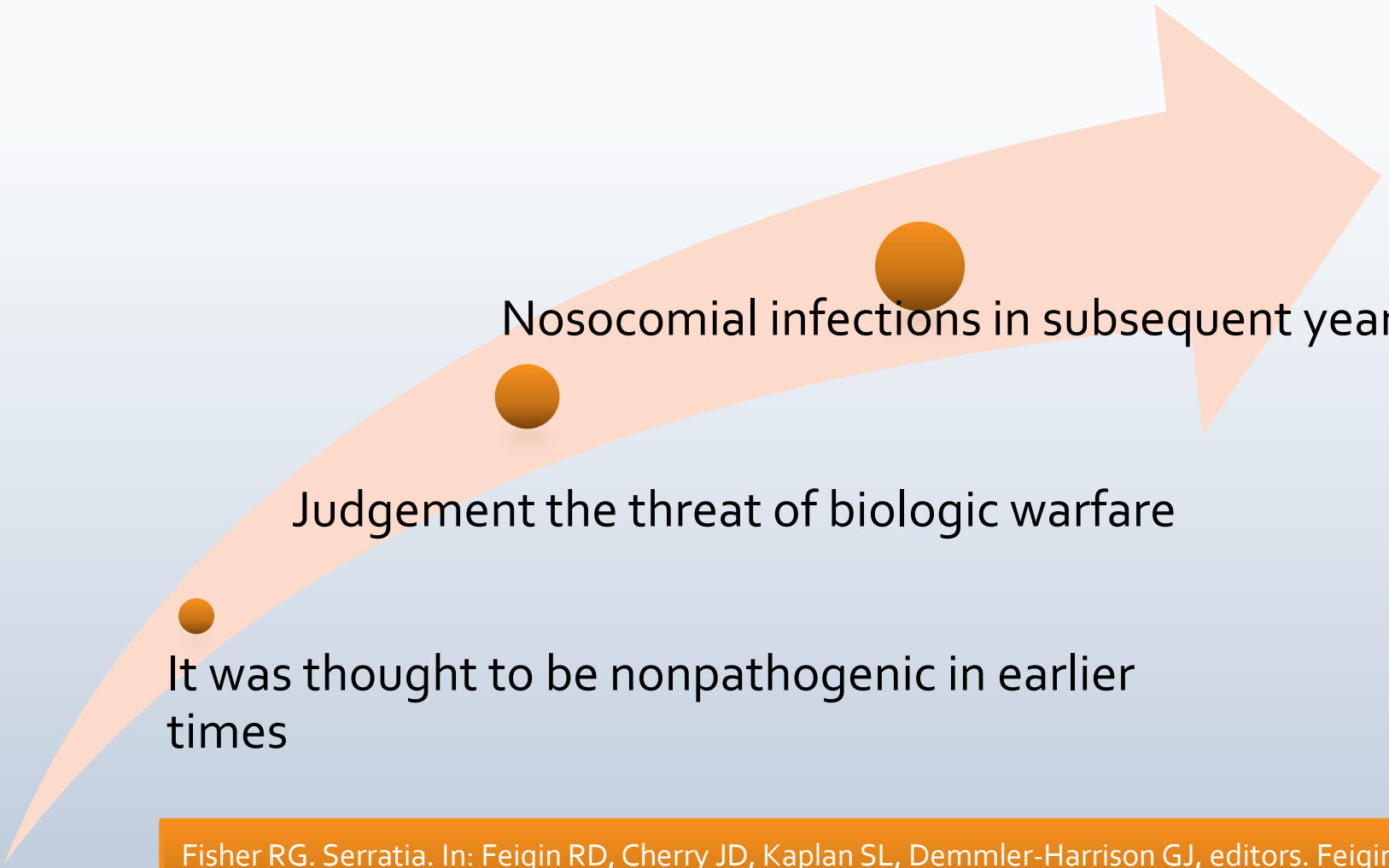
Hertle R, et al. Infect Immun 1999;67:817-25; Hertle R and Schwarz H. BMC Infect Dis 2004;4:16

Human diseases

- S. marcescens
- S. liquefaciens
- S. odorifera
- S. ficara
- S. plymuthica

Fisher RG. Serratia. In: Feigin RD, Cherry JD, Kaplan SL, Demmler-Harrison GJ, editors. Feigin and Cherry's textbook of pediatric infectious diseases. 6th ed. Philadelphia: Saunders Elsevier; 2009. p.1488-1491.

Epidemiological history



Fisher RG. Serratia. In: Feigin RD, Cherry JD, Kaplan SL, Demmler-Harrison GJ, editors. Feigin and Cherry's textbook of pediatric infectious diseases. 6th ed. Philadelphia: Saunders Elsevier; 2009. p.1488-1491.

Clinical aspect

- *Serratia* spp. could cause life-threatening infections such as bacteremia, urinary tract infection, wound infection, pneumonia, meningitis, peritonitis, and conjunctivitis
- Many of them are caused by multiple-drug resistant *Serratia* isolates
- Limited data is available in the literature concerning children with *Serratia* spp. infections.

Leng P, et al. Journal of Hosp Infect 2015; 89: 45-60; Iosifidis E, et al. Am J Infect Control 2012;40:11-5; Ochieng et al. Gut Microbes 2014;5:6:729-726

Our study

Retrospective Investigation of the Infections Caused by Serratia Species in a Tertiary Care Children's Hospital

Aim

The aim of our study was to share our experience about the characteristics, treatment, and outcomes of *Serratia spp.* infection in children at a tertiary care university hospital.

Secondary Aims

- To identify the risk factors
- To determine the best management approach
- To implement necessary control measures

Materials and Methods

- Retrospective study
- January 2008- December 2016 on patients who were aged between 1 month and 18 years, and those who had a positive culture with *Serratia* spp. were enrolled in the study
- Patients who were determined to have colonization with *Serratia* spp. were excluded.
- The patients were then categorized into two groups as community-acquired infection (CAI) and healthcare-associated infection (HAI).

Materials and Methods

- The investigation was reviewed and approved by the ethical committee of Hacettepe University Faculty of Medicine, Ankara, Turkey (no.03/2017).
- Potential variables associated with the infections included: age, gender, medical history, laboratory findings; type and antimicrobial susceptibility of the isolated bacteria; length of hospital stay; dose and duration of antimicrobial treatment including beta-lactam antibiotics; penicillin derivatives, cephalosporins, monobactams, carbapenems and fluoroquinolones, aminoglycosides, anaerobicidal agents and glycopeptides; and exposure to more than one of the antibiotics studied.

Definitions

Infection Colonization

- Infection was based on the clinical and laboratory findings of individual patients, imaging results, and the isolation of *Serratia* spp from blood, urine, wound, sputum, cerebral spinal fluid or peritoneal fluid
- colonization is used for a condition where a bacteria that is not thought to be causing disease is isolated from a non-sterile site without causing infection

CAI

- was defined as the identification of a significant pathogen in a blood culture taken within 48 hours of presentation to the emergency department (in the absence of admission to the hospital in the previous month)

HAI

- was defined as a new-onset infection on or after 3rd hospital day

www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf ; Pirofski LA and Csadevall A. Lancet Infect Dis. 2002; 2: 628-635; Revelas A, Niger Med J. 2012; 53: 59-64; CDC /NHSN (http://www.microcsalud.us.es/web/docencia/master/medicina/infecciones-nosocomiales/temas/2015/01/CDC%20NHSN%20HAI%20Definitions.pdf)

Outcome parameters

clinical response	• resolution of fever (temperature <38° C), leukocytosis (WBC <10,000), and local signs and symptoms of infection
microbiological response	• eradication of the organism that caused the infection, which was proven by repeated negative cultures at the end of the therapy
treatment failure and relaps	• defined as a lack of resolution or worsening of the signs and symptoms of infection • defined as recurrence of the infection with the same microorganism at any site of the body within a month after the discontinuation of the therapy

Hachem RY, et al. Antimicrob Agents Chemother. 2007; 51: 1905-11 ; Ozsurekci Y, et al. Diagn Microbiol Infect Dis 2016;85:233-8.

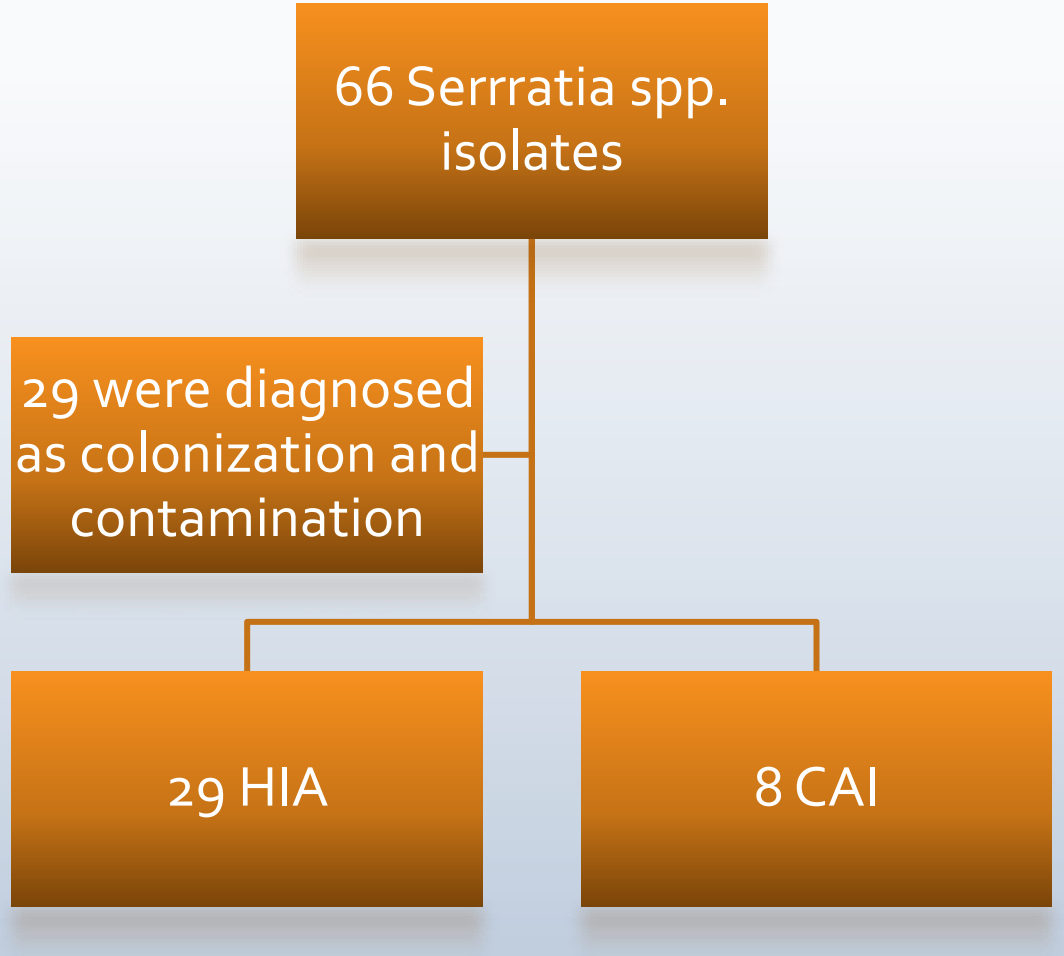
Microbiological and moleculary method

- BD Phoenix (BD Diagnostics System, Sparks, MD) automated system used both for identification and antimicrobial susceptibility testing (AST) of the isolates between November 2010 and June 2013
- MALDI-TOF-MS and antimicrobial susceptibility testing was performed by using VİTEK 2 (bioMérieux, Marcy-l'Étoile, France) system after June 2013
- The clonal relationship of the strains were investigated by with pulse-field gel electrophoresis (PFGE)

CLSI Criteria 2014 ; Durmaz R, et al. Jpn J Infect Dis 2009;62:372-377.

Results and Discussion

Distribution of Serratia spp. isolates



Recent studies showed that

- Serratia marcescens is a common enteric bacterium generally thought not to be pathogenic.
- It is a widely distributed saprophytic bacterium and causes diseases in plants as well as wide range of hosts including invertebrate and vertebrate.
- With S. marcescens being the most commonly isolated species, accounting for 92% of all isolated Serratia in human infections.
- 65 % of all Serratia infections were community-based

Almuneef MA, et al. Clin Infect Dis 2001;32:220-7; Laupland KB, et al. Eur J Clin Microbiol Infect Dis 2008;27:89-95; Mahlen SD. Clin Microbiol Rev 2011;24:755-91.

Infection types

- A range of infections such as blood stream infections (BSI), pneumoniae, urinary tract infection, and wound infection have been associated with this organism.
- S. marcences may affect in rare cases central nervous system.
- Serratia bacteremia (56.7%, n=21) was the most common type of infection among the patients in the present study.

de Vries JJ, et al. Infect Control Hosp Epidemiol 2006;27:1153-8; Voelz A, et al. Int J Hyg Environ Health 2010;213:79-87.

Infection Types

Underlying diseases				NA
None	4 (10.8)	3 (10.3)	1 (12.5)	
Pulmonary disease	9 (24.3)	7 (24.1)	2 (25)	
Immunodeficiency	6 (16.2)	4 (13.8)	2 (25)	
Neurogycal diseases	6 (16.2)	5 (17.2)	1 (12.5)	
Malignancies	5 (13.5)	5 (17.2)	0	
Other*	7 (18.9)	5 (17.2)	2 (25)	
Infection types				NA
Bacteremia	21 (56.7)	21 (72.4)	0	
CRBSI	11 (52.3)	11 (52.3)	0	
Urinary tract infection	5 (13.5)	3 (10.3)	2 (25)	
Wound infection	4 (10.8)	2 (6.9)	2 (25)	
Meningitis	2 (5.4)	1 (3.4)	1 (12.5)	
Peritonitis	2 (5.4)	0	2 (25)	
Pneumonia	2 (5.4)	1 (3.4)	1 (12.5)	
Central venous catheter	20 (54.1)	20 (82.8)	0	0.001
Surgery	16 (43.2)	13 (44.8)	3 (62.5)	1.00
Trauma	2 (5.4)	1 (3.4)	1 (12.5)	0.3
Urinary catheter	5 (13.5)	5 (17.2)	0	0.5
VPS	2 (5.4)	1 (3.4)	1 (12.5)	0.3
Burn	1 (2.7)	1 (3.4)	0	1.00
Hemodialysis	1 (2.7)	1 (3.4)	0	1.00
Periton dialysis	2 (5.4)	0	2 (25)	**0.04**
Mechanical ventilation	10 (27)	10 (34.5)	0	0.07
Broad spectrum antibiotic usage	15 (40.5%)	15 (51.7)	0	**0.01**

Bloodstream Infections (BSI)

- Hospital-acquired bloodstream infections are an increasing cause of morbidity and mortality in patients.
- Each year, approximately 250.000 cases occur in the USA, most of which (64%) are associated with the use of intravascular catheters.
- In fact, indwelling catheterization was reported as being an important risk factor of Serratia marcescens infection in as early as 1972 (Henjyoji et al., 1971).

Chemaly RF, et al. Am J Infect Control 2011;39:521-4; Wisplinghoff H, et al. Clin Infect Dis 2004;39:309-17; Henjyoji EY, et al. J Trauma. 1971; 11: 417-421.

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Outbreak of bloodstream infections because of *Serratia marcescens* in a pediatric department

Elias Iosifidis MD, MSc [a], Evangelia Farmaki MD, PhD [b], Natalia Nedelkopoulou MD [b], Maria Tsivitanidou MD [c], Maria Kaperoni RN, MSc [d], Vassiliki Pentsoglou RN [d], Spyros Pournaras MD, PhD [e], Miranta Athanasiou-Metaxa MD, PhD [b], Emmanuel Roilides MD, PhD [a,d,*]

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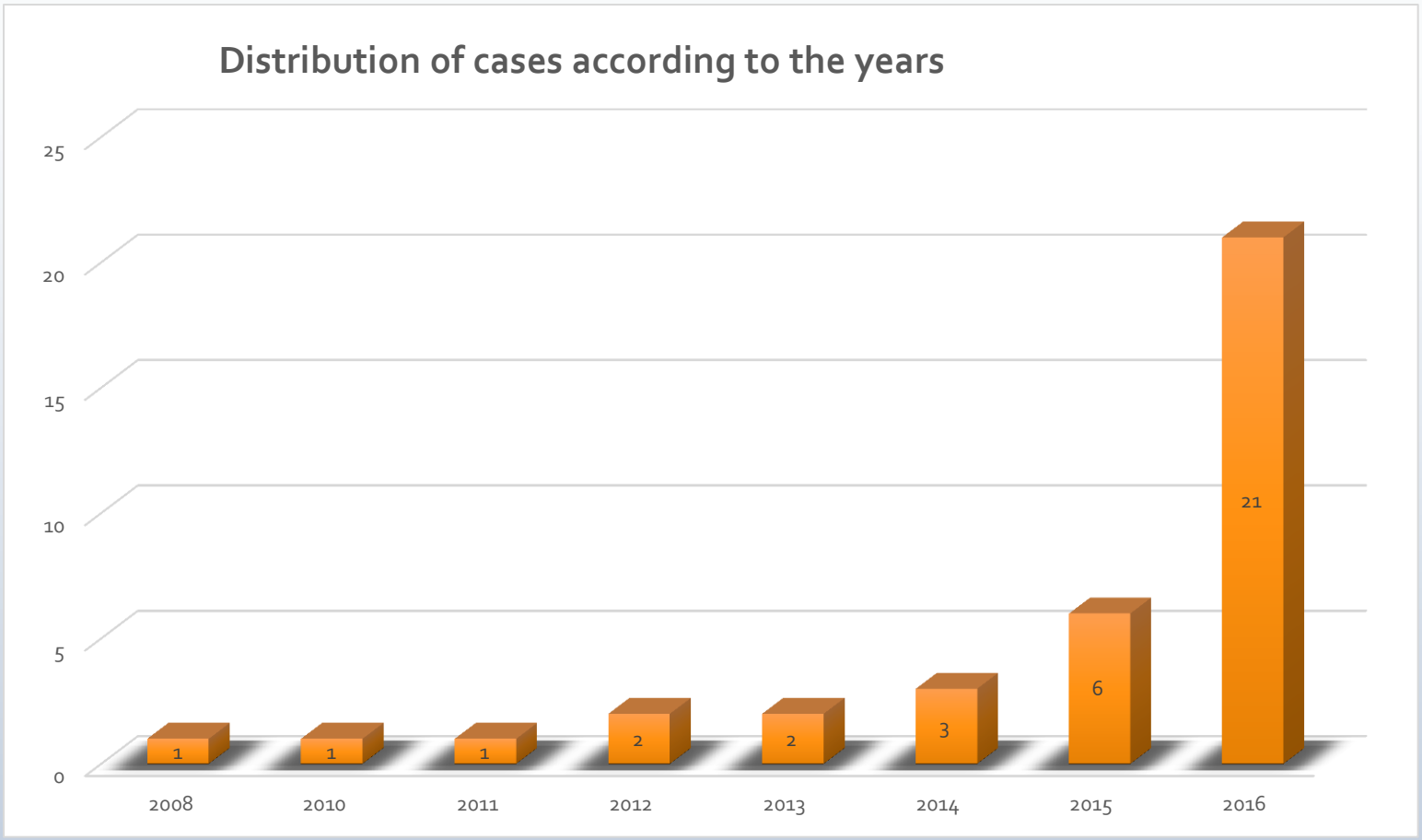
[b] *First Department of Pediatrics, Aristotle University, Thessaloniki, Greece*
[c] *Microbiology Department, Hippokration Hospital, Thessaloniki, Greece*
[d] *Infection Control Committee, Hippokration Hospital, Thessaloniki, Greece*
[e] *Microbiology Department, University of Thessaly, Larisa, Greece*

- The first BSI outbreak caused by S. marcescens in children were reported in the study, particularly associated with change of vascular access sites.

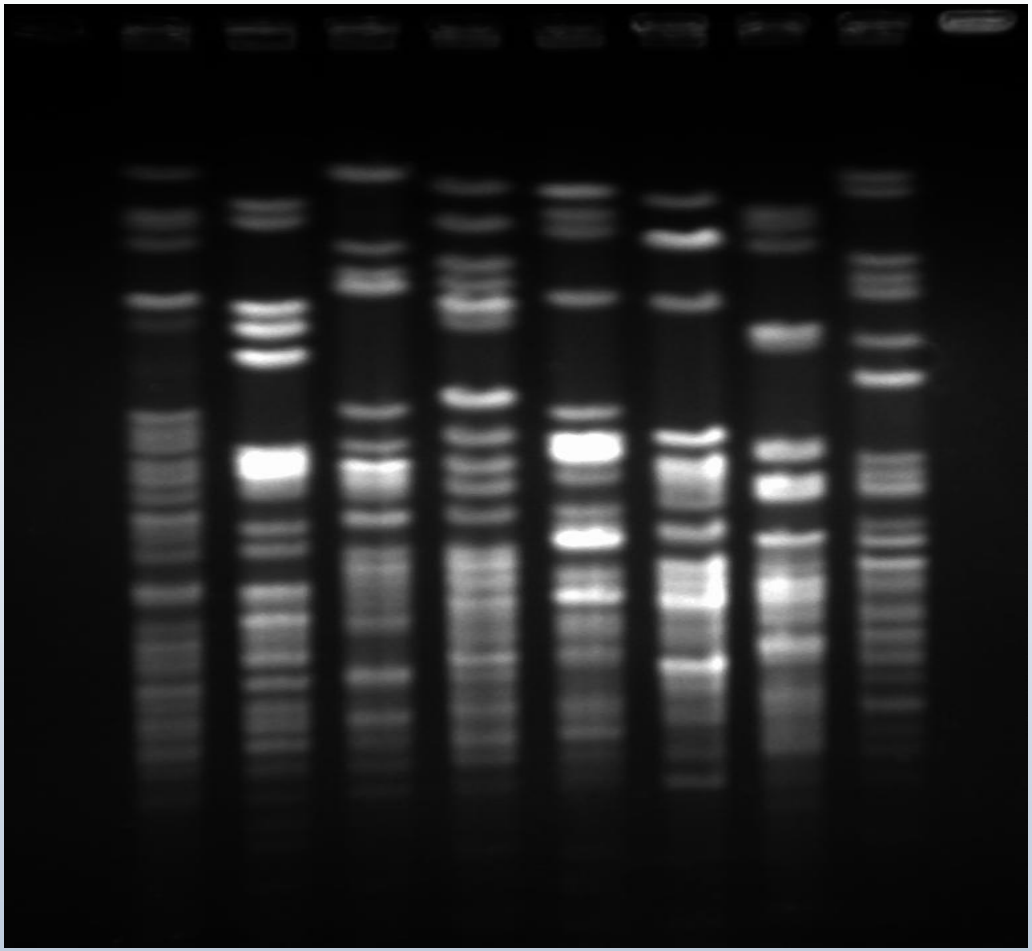
In the present study

- 57.1% (n=12) of the patients with bacteremia were detected in 2016.
- Eight of the strains from 2016 could be reached and we performed PFGE analysis to understand clonal relation.

Distribution of infections according to years



PFGE image of 8 bloodstream isolates



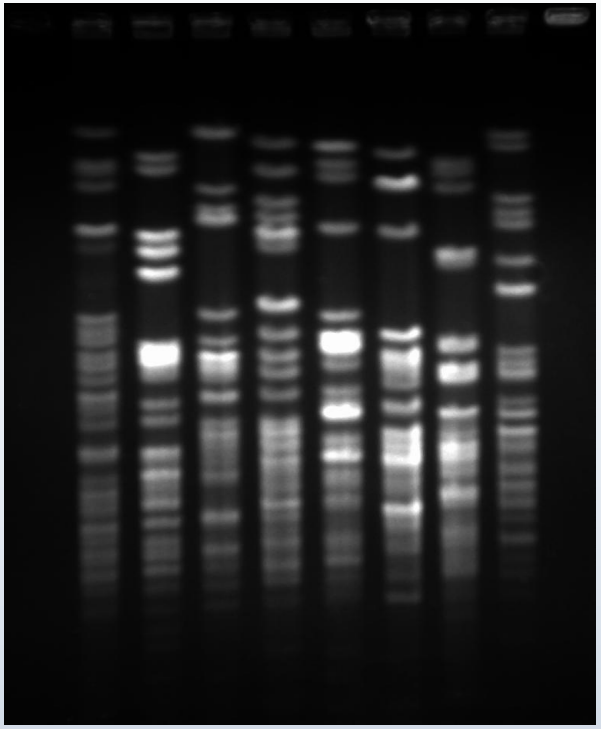
Serratia marcescens bacteremia because of contaminated prefilled heparin and saline syringes: A multi-state report

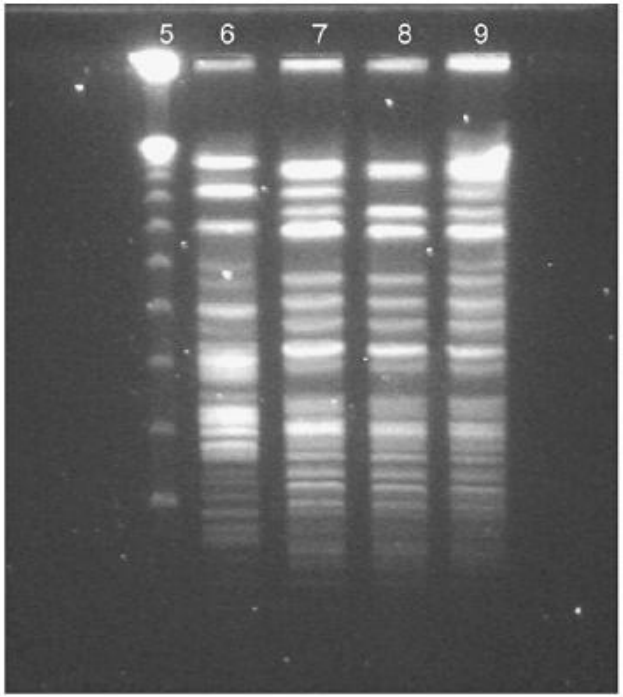
Roy F. Chemaly, MD, MPH,[a] Dhanesh B. Rathod, MD,[a] Monica K. Sikka, MD,[b] Mary K. Hayden, MD,[b] Mark Hutchins, MD,[c] Tracy Horn, RN,[c] Jeffery Tarrand, MD,[a] Javier Adachi, MD,[a] Kim Nguyen, MT,[a] Gorden Trenholme, MD,[b] and Issam Raad, MD[a]
Houston, Texas; Chicago, Illinois; and Lincoln, Nebraska

- November 2007-January 2008, 162 cases were reported across 9 states in USA.
- Prefilled heparin and salin syringes were found to be responsible for outbreaks in different centers in USA.

Chemaly RF, et al. Am J Infect Control 2011;39:521-4; Blossom D, et al. Arch Intern Med 2009;169:1705-11; Su JR, et al. Infect Control Hosp Epidemiol 2009;30:593-5; Chemaly RF, et al. Infect Control Hosp Epidemiol 2009;30:1237-8

PFGE image of 8 bloodstream isolates





Our data (Turkey)

Lane	Source of isolate	Culture date	PFGE type
5	Standard (λ)	NA	NA
6	Sporadic strain at center 2	12/2007	Unrelated
7	Strain from a prefilled heparin syringe at center 2	12/2007	Related to the SM8 subtype (1-band difference)
8	Strain from a prefilled saline syringe at center 2	1/2008	Related to the SM8 subtype (2-band difference)
9	Strain from prefilled heparin syringe at center 1 (SM8)	11/2007	Closely related to the strains in Lane 7 & 8

Molecular analysis with PFGE showed that S. marcences isolates recovered from the case patients are not belonged to the same clone, that is, isolates were genetically different.

Risky periods

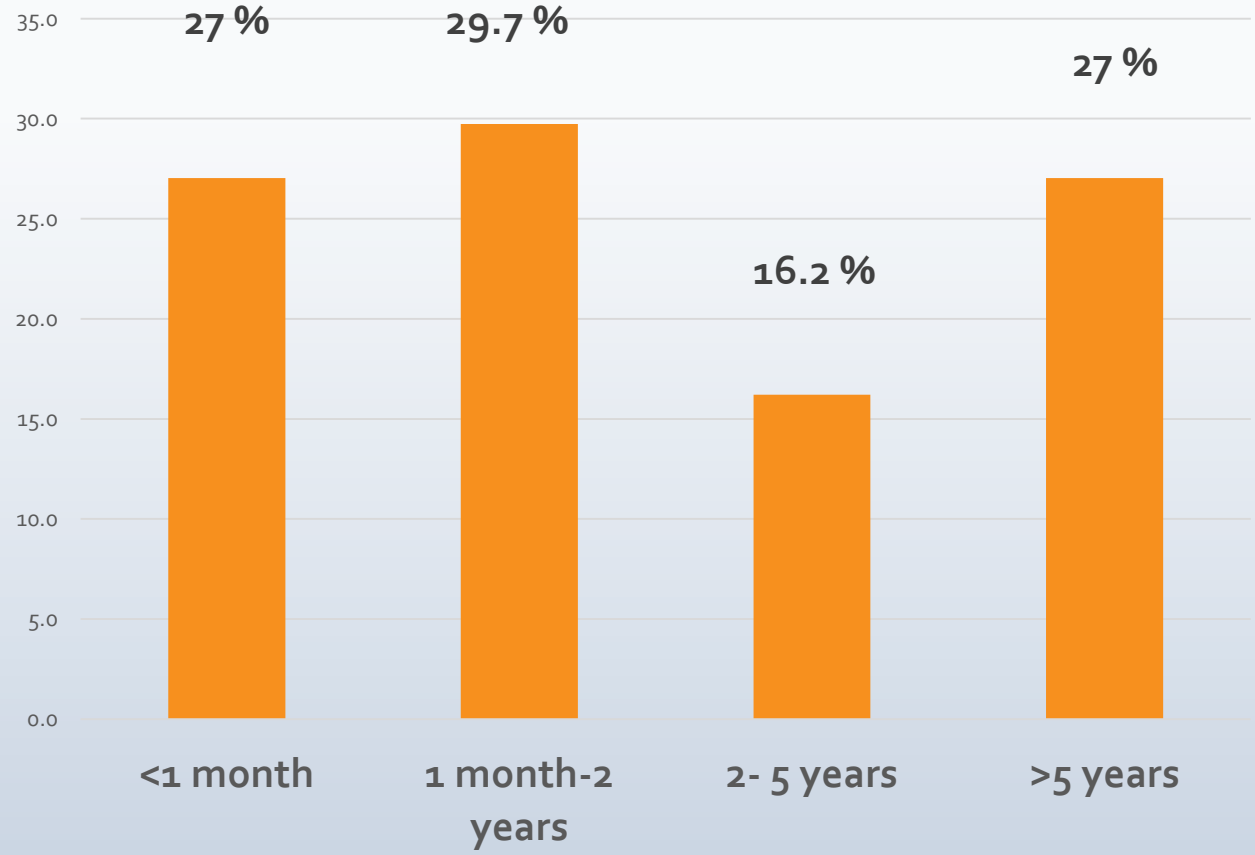
- S. marcescens is more likely to infect neonates than adults.
- Outbreaks of S.marcescens in pediatric patients involve mainly critically ill children hospitalized in neonatal or pediatric intensive care units.

Friedman ND, et al. Am J Infect Control 2008;36:22-28; Maragakis LL, et al. Infect Control Hosp Epidemiol 2008;29:418-23; Voelz A, et al. Int J Hyg Environ Health 2010;213:79-87; Dessi A, et al. J Chemother 2009;21:493-9; Khanna A, et al. J Clin Diagn Res 2013;7:243-246; Fleisch F, et al. Clin Infect Dis 2002; 34: 767-73.

Demographics and clinical characteristics of patients

Characteristics	Total cases (n=37)	Hospital acquired	Community acquired	*p* value
Demographics				
Age (months; median: minimum-maximum)	20 (0-210)	13 (0-210)	82 (0-204)	0.09
Gender (male)	23 (62.2)	17 (58.6)	6 (75)	0.68
None	4 (10.8)	3 (10.3)	1 (12.5)	
Pulmonary disease	9 (24.3)	7 (24.1)	2 (25)	
Immunodeficiency	6 (16.2)	4 (13.8)	2 (25)	
Neurogycal diseases	6 (16.2)	5 (17.2)	1 (12.5)	
Malignancies	5 (13.5)	5 (17.2)	0	
Others*	7 (18.9)	5 (17.2)	2 (25)	

Age distribution



Risk factors for nosocomial infections

- Long-term hospitalization
- Mechanical ventilation
- Organ transplantation
- Misuse of drug vials
- İllicit narcotic use
- Contaminated hands of healthcare workers

Leng P, et al. J Hosp Infect 2015;89:46-50; Ostrowsky BE, et al. N Engl J Med 2002;346:1529-1537.

Risk factors

- All of the HAI group and in total 15 patients (40.5%) had broad spectrum antibiotic usage in the previous 30 days.
- There were statistical difference between HAI and CAI groups in terms of central venous catheter, periton dialysis, broad spectrum antbiotic usage.

Risk factors

Infection types				NA
Bacteremia	21 (56.7)	21 (72.4)	0	
CRBSI	11 (52.3)	11 (52.3)	0	
Urinary tract infection	5 (13.5)	3 (10.3)	2 (25)	
Wound infection	4 (10.8)	2 (6.9)	2 (25)	
Meningitis	2 (5.4)	1 (3.4)	1 (12.5)	
Peritonitis	2 (5.4)	0	2 (25)	
Risk factors				
Central venous catheter	20 (54.1)	20 (82.8)	0	**0.001**
Surgery	16 (43.2)	13 (44.8)	3 (62.5)	1.00
Trauma	2 (5.4)	1 (3.4)	1 (12.5)	0.3
Urinary catheter	5 (13.5)	5 (17.2)	0	0.5
VPS	2 (5.4)	1 (3.4)	1 (12.5)	0.3
Burn	1 (2.7)	1 (3.4)	0	1.00
Hemodialysis	1 (2.7)	1 (3.4)	0	1.00
Periton dialysis	2 (5.4)	0	2 (25)	**0.04**
Mechanical ventilation	10 (27)	10 (34.5)	0	0.07
Broad spectrum antibiotic usage	15 (40.5)	15 (51.7)	0	**0.01**
Non-marcescens	5 (13.5)	4 (17.2)	0	

Outbreaks are found to be associated with

- Magnesium sulphate solution
- Tap water
- Soap tablets, medicated liquid soap
- Barbers and razors
- Laryngoscopes
- Bronchoscopes
- Oscillators

Leng P, et al. J Hosp Infect 2015;89:46-50; Chemaly RF, et al. Am J ınfect Control 2011;39:521-524; Kirschke DL, et al. N Engl J Med 2003;348:214-220; Liu D, et al. J Hosp Infect 2011;77:175-176; Sunenshine RH, et al. Clin Infect Dis 2007;45:527-533; Macdonald TM, et al. Pediatr Crit Care Med 2011;12:e282-286

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Outbreak of *Serratia marcescens* postoperative infection traced to barbers and razors

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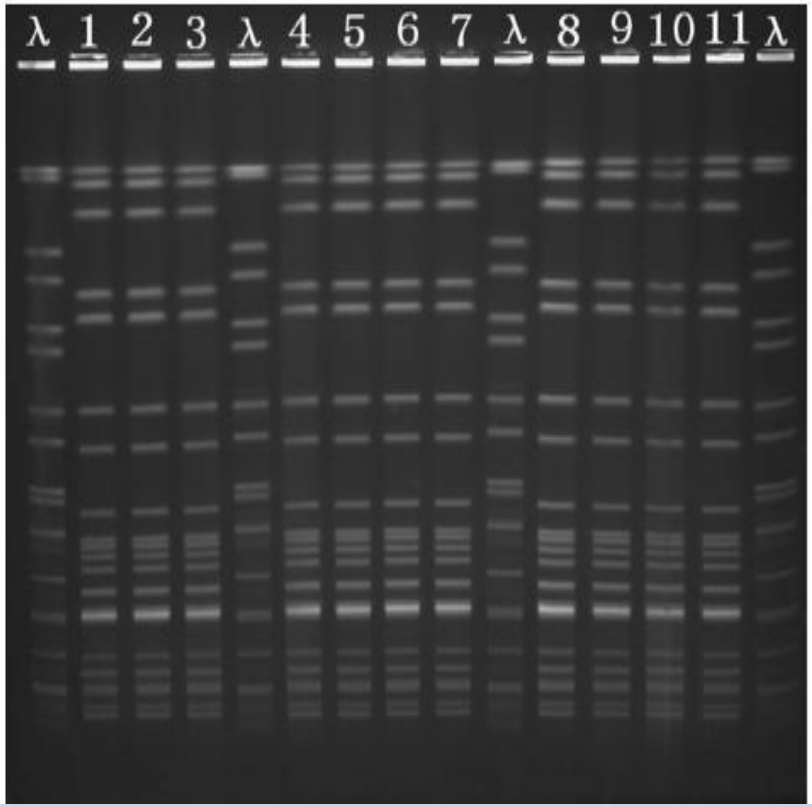
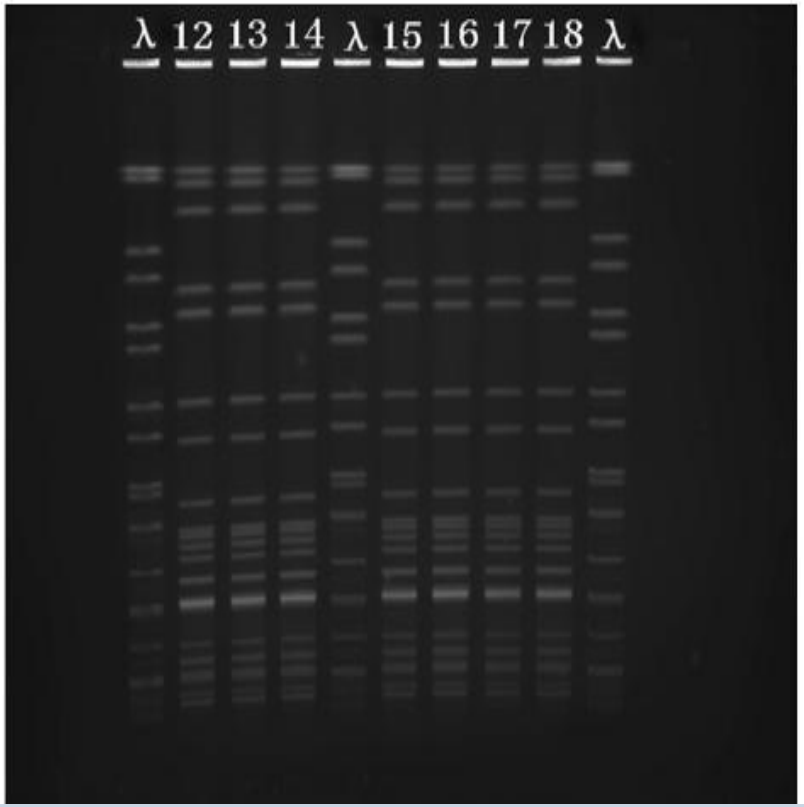
Table I
Results of case–control study

	Cases ($N = 14$) (%)	Controls ($N = 28$) (%)	OR	95% CI	*P*-values
Age (years)	52.29 ± 15.38	48.46 ± 12.12	1.024	0.972–1.078	0.384
Gender (male)	9 (64.29%)	19 (67.86%)	0.853	0.221–3.291	1
Transfusion	2 (14.3)	0 (0.0)	–[a]	–[a]	0.106
Chronic diseases (*N*, %)	7 (50.0)	8 (26.6)	2.5	0.661–9.456	0.193
Hypertension (*N*, %)	6 (42.9)	6 (21.4)	2.75	0.684–11.053	0.169
Diabetes (*N*, %)	3 (21.4)	2 (7.1)	3.545	0.518–24.258	0.313
Coronary disease (*N*, %)	1 (7.1)	2 (7.1)	1	0.083–12.074	1
Urinary catheter (*N*, %)	14 (100.0)	27 (96.4)	–[a]	–[a]	1
Gastric tube (*N*, %)	4 (28.6)	3 (10.7)	3.333	0.629–17.653	0.197
Tracheal cannula (*N*, %)	12 (85.7)	18 (64.3)	3.333	0.618–17.970	0.277
Drainage (*N*, %)	11 (78.6)	12 (42.9)	4.889	1.113–21.473	0.028
Central venous catheter (*N*, %)	1 (7.1)	1 (3.6)	2.077	0.120–35.894	1
Ventilator	2 (14.3)	1 (3.6)	4.5	0.371–54.543	0.254
Exposure to the two barbers	12 (85.7)	2 (7.1)	78	9.785–621.789	<0.0001
Duration of antibiotic therapy (days)	20.93 ± 12.797	4.11 ± 3.315	1.492	1.116–1.911	<0.0001
Duration of hospital stay (days)			1.265	1.090–1.468	0.002
Duration of fever (days)	10.14 ± 7.89	2.04 ± 3.71	1.275	1.092–1.487	0.002
Number of operations	1.57 ± 0.938	1 ± 0	–[a]	–[a]	0.004


λ 1 2 3 λ 4 5 6 7 λ 8 9 10 11 λ


λ 12 13 14 λ 15 16 17 18 λ

Outcome of S.marcescens infections

- S. marcescens can cause HAIs with significant impact on morbidity and mortality.
- The rates of morbidity and mortality might have reached up to 39-50 %.
- Moreover, BSI caused by S. marcescens constitute difficult-to-treat infections and can lead to life-threatening events associated with high morbidity and mortality rates in pediatric patients as well as adults.
- Little is known about the pediatric cases with S. marcescens without outbreak.

Yu WL, et al. J Microbiol Immunol Infect 1998;31:171-179; Friedman ND, et al. Am J Infect Control 2008;36:22-28; Maragakis LL, et al. Infect Control Hosp Epidemiol 2008;29:418-23; Voelz A, et al. Int J Hyg Environ Health 2010;213:79-87; Dessi A, et al. J Chemother 2009;21:493-9

Outcome parameters of the present study

Microbiologic response on the third day	30 (81)	25 (86.2)	5 (62.5)	0.15
Microbiologic response at the end of the therapy	24 (100)	21 (100)	3 (100)	-
Clinical reponce on the sixth day	33 (89.2)	26 (89.7)	7 (87.5)	1.00
Clinical response at the end of the therapy	37 (100)	29 (100)	8 (100)	-
Infectious related mortalty	0	0	0	NA
Overall mortality	2	2	0	NA
ICU stay	18 (48.6)	17 (58.6)	1 (12.5)	0.08

Resistance pattern

- Reduced susceptibility of S. marcescens to various antimicrobials has been documented, and outbreaks of even multiresistant strains have been reported, especially in adult populations and critically ill patients.
- In this study, our isolates were in vitro susceptible to common antimicrobials used for S. marcescens, including cephalosporins, carbapenems, and aminoglycosides.

Ostrowsky BE, et al. N Engl J Med 2002;346:1529-37; Bagattini M, et al. J Hosp Infect 2004;56:29-36.

Susceptibility pattern (%)

				Penicillins			Cephalosporins				Carbapenems				Aminoglycosides		Others	
Bacteria	Clinical specimens	Sources	No. Isolates	Ampicillin	Ampicillin-sulbactam	Piperacilline-tazobactam	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone	Ertapenem	Imipenem	Meropenem	Carbapenems	Amikacin	Gentamicin	Ciprofloxacin	Colistin
Serratia spp.	Blood	HAI	21	R	95	65	R	85	85	85	85	100	85	85	80	80	95	R
		CAI	0															
	UTI	HAI	3	R	100	100	R	100	100	100	100	100	100	100	100	100	100	R
		CAI	2	R	100	100	R	100	100	100	100	100	100	100	100	100	100	R
	Wound	HAI	2	R	50	50	R	100	100	100	100	100	100	50	50	100	100	R
		CAI	2	R	66.6	100	R	100	100	100	100	100	100	100	100	100	100	R
	CSF	HAI	1	R	0	100	R	100	100	100	100	100	100	100	100	100	100	R
		CAI	1	R	100	0	R	0	0	0	100	100	100	100	0	100	100	R
	Periton	HAI	0	R	100	0	R	100	100	100	100	100	100	100	100	100	100	R
		CAI	2	R	100	50	R	50	50	100	100	100	100	100	100	100	100	R
	Sputum	HAI	1	R	100	100	R	100	100	100	100	100	100	100	100	100	100	R
		CAI	1	R	100	100	R	100	100	100	100	100	100	100	100	100	100	R

R; intrinsic resistance, NA; not applicated, HAI;hospital acquired infection, CAI; community acquired infection, UTI; Urinary tract infection, CSF;

Dicision of antimicrobials

- It is stated that cephalosporins should be avoided in the treatment of severe *Serratia marcescens* infections due to their propensity to induce the chromosomal AmpC enzyme.
- Otherwise, carbapenems are stable to these enzymes and should be considered as the first choice antibiotics for empiric or definitive treatment of sepsis in patients with multidrug-resistant *Serratia marcescens*.
- It is important to be aware of the treatment options during outbreak periods as well as in normal circumstances due to antibiotic resistance.

Crivaro V, et al. J Hosp Infect 2007; 67: 135-141; David MD, et al. J Hosp Infect 2006; 63: 27-33.

Our antimicrobial choices

Antibiotics used				NA
Meropenem, amikacin	14 (37.8)	13 (44.8)	1 (12.5)	
Meropenem, ciprofloxacin	4 (10.8)	4 (13.8)	0	
Meropenem, amikacin, ciprofloxacin	4 (10.8)	4 (14.8)	0	
Cefalosporin and/or amikacin	6 (16.2)	2 (6.9)	4 (50)	
Meropenem	2 (5.4)	1 (3.4)	1 (12.5)	
Sulbactam ampicillin	2 (5.4)	2 (6.9)	0	
Others	5 (13.5)	3 (10.3)	2 (25)	
Outcome				
Microbiologic response on the third day	30 (81)	25 (86.2)	5 (62.5)	0.15
Microbiologic response at the end of	24 (100)	21 (100)	3 (100)	-

Treatment challange?

- The challenge of the treatment is natural resistance patterns of microorganisms to benzylpenicillin, oxacillin, cefaclor, cefazolin, cefuroxime, numerous macrolides, lincosamides, streptogramins, glycopeptides, rifampicin and fusidic acid.
- Moreover *Serratia* spp. has an innate resistance to colistin and reduced susceptibility to tigecycline which are used for carbapenem-resistant bacteria.
- For this reason treatment options for resistant infections are extremely limited.

Gruber TM, et al. J Antimicrob Chemother 2015; 70: 1026-30; Stock I, et al. Int J Antimicrob Agents 2003; 22: 35-47.

Table 1
Characteristics of case and control patients

Characteristic	Cases, n = 4	Controls, n = 29	Total, N = 33	*P* value
Age, median (range)	2.5 (9 mo-3.5 yr)	3.5 (2 mo-11 yr)	2.5 (2 mo-11 yr)	NS
Male sex	2	18	20	NS
Fever at admission	3	20	23	NS
Intravenous administration of antimicrobials	4	22	26	NS
Penicillins	1	2	3	
β–Lactams/β-lactamase inhibitors	3	6	9	
Second generation cephalosporins	1	2	3	
Third-generation cephalosporins	2	9	11	
Aminoglycosides	3	2	5	
Glycopeptides	1	3	4	
Fluoroquinolones	2	1	3	
Clindamycin	1	1	2	
Intravenous administration of anticonvulsants	1	0	1	NS
Intravenous administration of fluids				
Number of patients	4	26	30	NS
Duration, median (range), days	27 (18-46)	5 (1-37)	5 (1-46)	<.05
Vascular access changes				
Number, median number (range)	12 (4-12)	2 (1-7)	2.5 (1-12)	<.05
Thrombophlebitis	1	0	1	NS

Iosifidis E, et al. Am J Infect Control 2012;40:11-15.

Contents lists available at ScienceDirect

Journal of Global Antimicrobial Resistance

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

Antimicrobial resistance patterns of Gram-negative bacteria isolated from bloodstream infections in an Iranian referral paediatric hospital: A 5.5-year study

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Table 1
Antimicrobial resistance of Gram-negative blood culture isolates.

Organism		GEN	AMK	SXT	IMP	CAZ	CIP	TZP	AMP	FEP	CTX
Enterobacter aerogenes	N/Total	13/21	13/22	4/22	0/16	3/3	–	9/22	5/5	17/22	19/21
	%	62	59	18	0	100	–	41	100	77	90
Enterobacter cloacae	N/Total	14/76	17/76	16/76	4/61	2/4	0/2	38/77	28/29	19/76	50/76
	%	18	22	21	7	50	0	49	97	25	66
Escherichia coli	N/Total	57/185	41/188	140/189	11/143	8/12	1/3	77/191	47/49	114/191	144/188
	%	31	22	74	8	67	33	40	96	60	77
Salmonella group D	N/Total	1/6	–	5/24	0/9	–	–	1/8	6/16	4/7	5/23
	%	17	–	21	0	–	–	13	38	57	22
Haemophilus spp.	N/Total	–	3/8	10/19	6/27	0/1	0/3	1/11	4/6	5/11	4/18
	%	–	38	53	22	0	0	9	67	45	22
Acinetobacter baumannii[a]	N/Total	54/64	36/49	15/18	53/63	54/62	44/49	53/64	–	52/62	12/12
	%	84	73	83	84	87	90	83	–	84	100
Pseudomonas aeruginosa[b]	N/Total	22/73	12/53	15/15	15/73	18/72	–	16/72	–	18/54	2/2
	%	30	23	100	21	25	–	22	–	33	100
Klebsiella pneumoniae	N/Total	161/260	167/259	153/257	39/218	17/21	0/5	155/258	33/33	198/260	224/261
	%	62	64	60	18	81	0	60	100	76	86
Serratia marcescens	N/Total	59/150	68/148	14/149	6/91	2/2	0/2	72/148	–	66/148	123/149
	%	39	46	9	7	100	0	49	–	45	83
Salmonella group C	N/Total	–	–	1/2	–	–	–	–	0/1	–	0/2
	%	–	–	50	–	–	–	–	0	–	0
Total	N/Total	381/835	357/803	373/771	134/701	104/177	45/64	422/851	123/139	493/831	583/752
	%	46	44	48	19	59	70	50	88	59	78

GEN, gentamicin; AMK, amikacin; SXT, trimethoprim/sulfamethoxazole; IMP, imipenem; CAZ, ceftazidime; CIP, ciprofloxacin; TZP, piperacillin/tazobactam; AMP, ampicillin; FEP, cefepime; CTX, cefotaxime.

[a] Susceptibility of *A. baumannii* to GEN, AMK, SXT, IMP, CAZ and CIP was determined by the broth microdilution method.

[b] Susceptibility of *P. aeruginosa* to GEN, AMK, IMP and CAZ was determined by the broth microdilution method.

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Coproduction of KPC-2 and IMP-10 in Carbapenem-Resistant *Serratia marcescens* Isolates from an Outbreak in a Brazilian Teaching Hospital

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We describe an outbreak caused by KPC-2- and IMP-10-producing *Serratia marcescens* isolates in a Brazilian teaching hospital. Tigecycline was the only active antimicrobial agent tested. The bla_{IMP-10} gene was located in a new class 1 integron, named *In*990, carried by a nonconjugative plasmid, in contrast to bla_{KPC-2}.

Accepted Manuscript

Title: Current epidemiology of resistance among Gram-negative bacilli in pediatric patients in Turkey

Authors: Kubra Aykac, Yasemin Ozsurekci, Sevgen Tanir Basaranoglu, Mustafa Senol Akin, Ali Bulent Cengiz, Asiye Bicakcigil, Banu Sancak, Ates Kara, Mehmet Ceyhan

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Reference: JGAR 472

Table 2. Gram-negative Bacteria in Isolates, % Susceptible

				Penicillins			Cephalosporims				Carbapenems				inoglycosides	Fluoroquinolone	Other	
Organism	Sources	Clinical specimens	No. Isolates	Ampicillin	Ampicillin-sulbactam	Piperacillime-tazobactam	Cefazolin	Cefepime	Ceftazidime		Ertapenem	Imipenem	Meropenem	Carbapenems	Gentamicin	Ciprofloxacin	Trimethoprim-sulfamethoxazole	Colymicin
E. Coli	IP	Blood	67	6.5	0	64.1	44.4	41.8	46.6	4	88.7	90.4	92.3	90.9	8	71.2	50.8	27.8	96.2
	OP		11	40	100	81.8	83.3	77.8	62.5		90.9	100	90.9	90.9	0	90.9	90.9	60	100
	IP	CSF	10	0	20	25	42.9	0	66.7		100	100	100	100		60	70	28.6	100
	OP		4	0	0	80	100	33.3	66.7		100	100	100	100	0	100	100	100	100
Enterobacter spp.	IP	Blood	34	R	R	82.6	R	80.6	74.1	6	82.4	78.3	84.4	82.4		85.3	79.4	75.9	100
	OP		1	R	R	100	R	100	100	1	100	100	100	100	0	100	100	100	100
	IP	CSF	3	R	R	100	R	100	100	1	100	100	100	100	0	33.3	100	100	100
	OP		1	R	R	100	R	100	100	1	100	100	100	100	0	100	100	100	100
A. baumannii	IP	Blood	42	NA	40.7	57.1	NA	41.4	50	1	NA	50	51.2	52.4	1	52.4	62.5	81.1	82.1
	OP		2	NA	NA	100	NA	100	100	1	NA	100	100	100	0	100	100	100	100
	IP	CSF	7	NA	40.7	20	NA	16.7	28.6	N	NA	28.6	28.6	28.6	9	28.6	28.6	66.7	100
	OP		1	NA	NA	100	NA	100	100	N	NA	100	100	100	0	100	100	100	100
Klebsiella spp.	IP	Blood	134	R	2.9	43.3	22.7	37.5	39	3	66.9	73.1	74.6	70.1	2	55.6	67.7	54	94.5
	OP		4	R	NA	100	100	75	50	1	100	100	100	100	0	75	75	100	100
	IP	CSF	7	R	13.8	14.3	NA	14.3	0		71.4	66.7	71.4	71.4		71.4	85.7	83.3	100
	OP		3	R	100	66.7	100	100	100	1	100	100	100	100	0	100	100	100	100
Pseudomonas spp	IP	Blood	44	R	R	56.8	R	71	73.5		R	65.9	63.6	61.4	2	77.3	70	R	97.7
	OP		1	R	R	100	R	100	100		R	100	100	100	0	100	100	R	100
	IP	CSF	10	R	R	77.8	R	100	77.8		R	66.7	77.8	70	0	70	66.7	R	100
	OP		0	R	R	NA	R	100	NA		R	NA	NA	NA	A	NA	NA	R	100

S. rubidaea

- He is a 15-month-old boy with malignancy.
- S. rubidaea was cultured in his blood while he had a diagnosis of febrile neutropenia.
- He was treated with meropenem and amikacin and discharged in a good condition.

S. odorifera

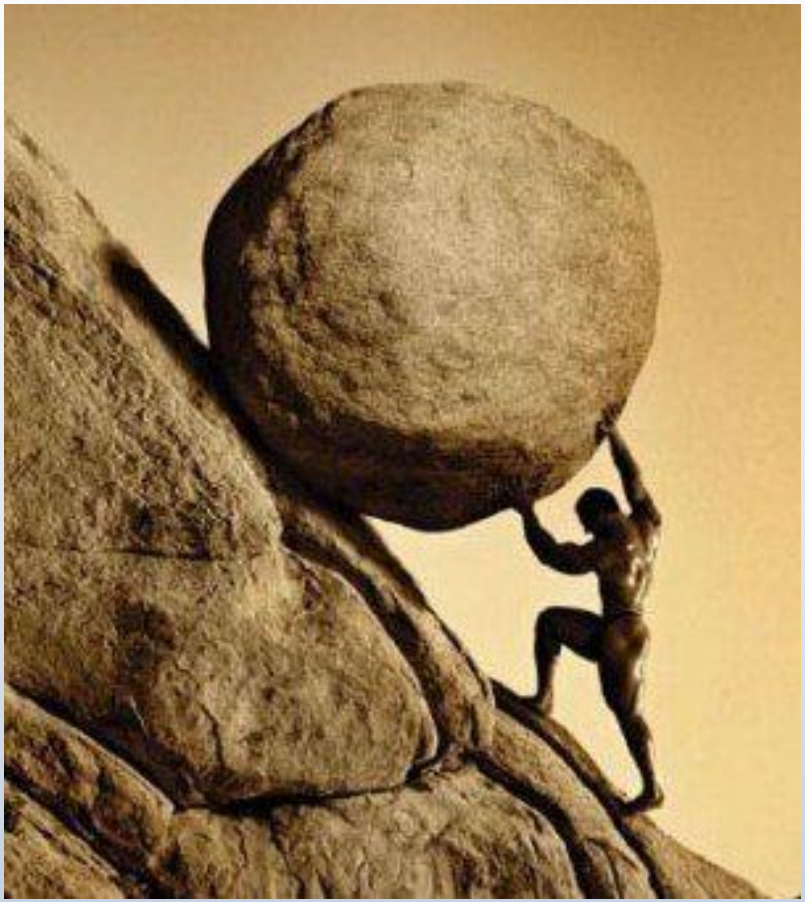
- S. odorifera was a three-year-old boy with a diagnosis of hemophilia A.
- He had catheter-related bloodstream infection with S. odorifera.
- He was treated with cefepime and amikacin and discharged in a good condition.

Consequently,

Prompt recognition and initiation of appropriate empiric antimicrobial therapy as well as favorable antimicrobial susceptibility profile of the causative organism may have contributed to the absence of mortality in this study.

A huge struggle in Hacettepe

What can we do for favorable antimicrobial susceptibility profile of the organisms in hospital setting?



Focus to risks

Tanır Basaranoglu et al. Italian Journal of Pediatrics (2017) 43:79
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Italian Journal of Pediatrics

RESEARCH Open Access

A comparison of blood stream infections with extended spectrum beta-lactamase-producing and non-producing *Klebsiella pneumoniae* in pediatric patients

Sevgen Tanır Basaranoglu[1*], Yasemin Ozsurekci[1], Kubra Aykac[1], Eda Karadag Oncel[1], Asiye Bıcakcigil[2], Banu Sancak[2], Ali Bulent Cengiz[1], Ates Kara[1] and Mehmet Ceyhan[1]

Table 1 Demographic characteristics of patients, risk factors and outcome

	ESBL (+) $n = 69$	ESBL (−) $n = 42$	p
Gender[a]			0.99
Male	37(63.8)	21(36.2)	
Female	24(61.5)	15(38.5)	
Age (months)[b]	4.9(1.7–26)	16.4(3.1–69.1)	0.04
Total length of hospitalization (days)[b]	56(32–89)	34(21–71)	0.03
Length of stay in hospital before infection (days)[b]	33(11.5–59.5)	11.5(0–26)	0.001
Duration of treatment for infection (days)[b]	16(11–21.5)	17(12–23)	0.66
Underlying medical condition/disease[a]			NA
Hematologic malignancy	7(11.4)	8(22.2)	
Oncologic malignancy	6(9.8)	10(27.2)	
Congenital heart anomalies	8(13.1)	4(11.1)	
Primary immunodeficiencies	2(3.2)	1(2.7)	
Neurologic/Metabolic disease	10(16.3)	4(11.1)	
Gastrointestinal disease	9(14.7)	6(16.6)	
Prematurity	6(9.8)	1(2.7)	
Others	13(21.3)	2(5.5)	
Mechanical ventilation[a]	31(81.6)	7(18.4)	0.005
Presence of central venous catheter[a]	34(60.7)	22(39.3)	0.90
Prior surgery[a]	33(66)	17(34)	0.57
Polymicrobial bacteremia[a]	6(42.9)	8(57.1)	0.19
Prior chemotherapy associated neutropenia[a]	15(46.9)	17(53.1)	0.058
Prior *K. pneumoniae* colonization[a]	7	5	NA
Prior antibiotic use[a]			
Broad spectrum cephalosporins	21(75)	7(25)	0.16
Fluoroquinolones	15(75)	5(25)	0.29
Carbapenems	25(61)	16(39)	1.0
Aminoglycosides	47(77)	14(23)	0.001
Glycopeptides	35(71.4)	14(28.6)	0.11
Use of more than one of the antibiotics studied[a]	52(75.4)	17(24.6)	0.001

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Bloodstream infections in children caused by carbapenem-resistant versus carbapenem-susceptible gram-negative microorganisms: Risk factors and outcome

Yasemin Ozsurekci [a,*], Kubra Aykac [a], Ali Bulent Cengiz [a], Sevgen Tanır Basaranoglu [a], Banu Sancak [b], Sevilay Karahan [c], Ates Kara [a], Mehmet Ceyhan [a]

Table 2
Overall outcome of patients with Gram-negative microorganism bloodstream infection with and without carbapenem resistance.

	No. (%)		
Outcome	CSGN (n = 66)	CRGN (n = 31)	*P value*
Clinical response at			
Day 6	50 (75.8)	11 (35.5)	**0.001**
End of the therapy	55 (83.3)	17 (54.8)	**0.002**
Microbiological response			
Day 6	48 (72.7)	16 (51.6)	**0.006**
End of the therapy	29 (43.9)	10 (32.3)	**0.004**
Treatment Failure	12 (18.2)	12 (38.7)	**0.03**
Relapse	4 (6.1)	2 (6.5)	**0.03**
Infection-related mortality	7 (10.8)	10 (32.3)	**0.01**
Overall mortality	13 (19.7)	11 (35.5)	0.09

Table 1
Demographic and clinical characteristics of patients with Gram-negative microorganism bloodstream infection with and without carbapenem resistance.

	CSGN (n = 66)	CRGN (n = 31)	*P value*
Age [months; median(IQR)]	25 (5–82)	20 (5–122)	0.99
Sex (n, %)			0.82
Male	41 (62.1)	20 (64.5)	
Female	25 (37.9)	11 (35.5)	
Service (n, %)			0.74
ICU	13 (19.7)	7 (22.6)	
Others*	53 (80.3)	25 (83.3)	
Treatment duration during infection [days; median(IQR)]	15 (11–21)	15 (5–25)	0.75
Total length of stay in hospital before infection [days; median(IQR)]	11 (2–24)	35 (12–58)	**0.002**
Total length of stay in hospital from infection to discharge [days; median(IQR)]	23 (13–42)	19 (3–52)	0.76
Underlying disease (n, %)			0.16
Malignancies	27 (40.9)	11 (35.5)	
Neurologic/metabolic disorders	7 (10.6)	8 (25.8)	
Immunosuppressed situations	8 (12.1)	1 (3.2)	
Others**	24 (36.4)	11 (35.5)	
Isolated pathogen (n, %)			0.39
Acinetobacter spp.	5 (7.6)	2 (6.4)	
E. coli	22 (33.3)	6 (19.4)	
Klebsiella spp.	25 (37.9)	18 (58.1)	
Pseudomonas spp.	6 (9.1)	3 (9.7)	
Enterobacter spp.	8 (12.1)	2 (6.4)	
Medication history and medical devices existed at the beginning of infection (n, %)			
Central venous catheter	42 (63.6)	25 (80.6)	0.09
Mechanic ventilation	8 (12.1)	4 (12.9)	0.91

Table 3
Multiple logistic regression models for outcome.

Outcome and variable	OR (95% CI)	*P value*
Clinical response on day 6		
Resistance Pattern (CRGN/CSGN)	0.248 (0.089–0.692)	**0.008**
Presence of mechanical ventilation	0.201 (0.049–0.822)	**0.02**
Extended spectrum antibiotic usage prior to infection	0.375 (0.140–1.003)	0.05
Clinical response at the end of therapy		
Extended spectrum antibiotic usage prior to infection	0.120 (0.035–0.412)	**0.001**
Treatment duration during infection	0.938 (0.882–0.997)	**0.04**
Microbiological response at day 6		
Treatment duration during infection	1.185 (1.079–1.303)	< **0.001**
Microbiological response at the end of therapy		
Total length of stay in hospital from infection to discharge	1.023 (1.007–1.039)	**0.005**
Treatment failure		
Resistance Pattern (CRGN/CSGN)	2.871 (0.906–9.098)	0.07
Treatment duration during infection	1.077 (1.015–1.143)	**0.01**
Total length of stay in hospital from infection to discharge	0.940 (0.894–0.988)	**0.02**
Extended spectrum antibiotic usage prior to infection	4.004 (1.292–12.415)	**0.01**
Presence of mechanical ventilation	5.083 (1.029–25.116)	**0.04**
Infection related mortality		
Extended spectrum antibiotic usage prior to infection	36.382 (1.065–1242.897)	**0.04**
Total length of stay in hospital before infection	2.029 (1.187–3.470)	**0.02**

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ORIGINAL ARTICLE

Can procalcitonin be a diagnostic marker for catheter-related blood stream infection in children?☆

Yasemin Ozsurekci[a,*], Kamile Oktay Arıkan[a], Cihangül Bayhan[a], Eda Karadağ-Öncel[a], Ahmet Emre Aycan[a], Venhar Gürbüz[a], Gülşen Hasçelik[b], Mehmet Ceyhan[a]

Table 1 Patients' demographics and clinical characteristics.

	Proven CRBSI ($n=24$)	Not proven CRBSI ($n=25$)	p
Age [month; mean ± SD (Min.–Max.)]	67.2 ± 71.7 (3.0–252.0)	78.2 ± 63.1 (2.0–245.0)	0.24[a]
Gender			0.14[b]
Female [*n* (%)]	11 (45.8)	6 (24)	
Male [*n* (%)]	13 (54.2)	19 (76)	
Primary admission diagnosis			0.39[b]
Hematological [*n* (%)]	12 (50)	15 (60)	
Nephrological [*n* (%)]	4 (16.7)	1 (4.0)	
Immunological [*n* (%)]	2 (8.3)	2 (8.0)	
Gastroenterological [*n* (%)]	3 (12.5)	1 (4.0)	
Other [*n* (%)]	3 (12.5)	6 (24.0)	
WBC count [$10^3/\mu L$; median (IQR)]	5.20 (0.9–13.0)	1.7 (0.8–5.4)	0.17[c]
Platelet [$10^3/\mu L$; median (IQR)]	118.0 (43.0–237.2)	111.0 (22.0 –214.5)	0.83[c]
CRP [mg/dL; median (IQR)]	5.63 (1.17–12.45)	2.10 (0.73–8.5)	0.33[c]
PCT-Kryptor [ng/mL; median (IQR)]	1.77 (0.30–4.96)	0.28 (0.17–0.68)	0.03[c,d]
PCT-RTA [ng/mL; median (IQR)]	1.76 (0.71–3.13)	0.57 (0.26–1.00)	0.03[c,d]
Mortality [n (%)]	2 (8.3)	0 (0)	N/A

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Original Article

Presepsin: A new marker of catheter related blood stream infections in pediatric patients☆

Sevgen Tanır Basaranoglu*, Eda Karadag-Oncel, Kubra Aykac, Yasemin Ozsurekci, Ahmet Emre Aycan, Ali Bulent Cengiz, Ates Kara, Mehmet Ceyhan

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Table 1
Characteristics of patient and control groups.

	Proven CRBSI (Group 1a) n = 36	Suspected CRBSI (Group 1b) n = 22	Control (Group 2) (n = 80)	*p*
Age (years) (mean ± SD)	6.5 ± 5.8	5.9 ± 4.2	6.5 ± 4.4	0.72
Gender				0.12
Male (n, %)	21 (58.3)	16 (72.7)	39 (48.7)	
Underlying diagnosis, (n,%)				0.18
Hematologic malignancy	12 (33.3)	12 (54)		
Oncologic malignancy	2(5.5)	3(13.6)		
Renal disease	3 (8.3)	2 (9)		
Gastrointestinal disease	4 (11)	1 (4.5)		
Primary immunodeficiency	5 (14)	1 (4.5)		
Congenital heart defects	3 (8.3)	3 (13.6)		
Others	7 (19.4)	–		
Presepsin [pg/ml; median (min-max)]	1679 (1048–2935)	1832 (1004–2895)	479 (295–1585)	1.0[a] <0.001[b] <0.001[c]
PCT [ng/ml; median (min-max)]	0.89 (0.07–402)	0.485 (0.15–135.4)		0.68[a]
CRP [mg/dl; median (min-max)]	2.70 (0.17–44)	2.98 (0.21–16.4)		0.73[a]
WBC [10^3/μL; median (min-max)]	4.4 (1.0–36.9)	2.3 (2.0–29.6)		0.62[a]

PCT: Procalcitonin, CRP: C-reactive protein, WBC: White blood cell count. SD:Standard deviation.

[a] Group1a vs Group 1b.

[b] Group 1a vs Group 2.

[c] Group 1b vs Group 2.

Last options

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Is colistin effective in the treatment of infections caused by multidrug-resistant (MDR) or extremely drug-resistant (XDR) gram-negative microorganisms in children?

Yasemin Ozsurekci [a,*], Kubra Aykac [a], Ali Bulent Cengiz [a], Cihangul Bayhan [a], Banu Sancak [b], Eda Karadag Oncel [a], Ates Kara [a], Mehmet Ceyhan [a]

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Hindawi
Case Reports in Infectious Diseases
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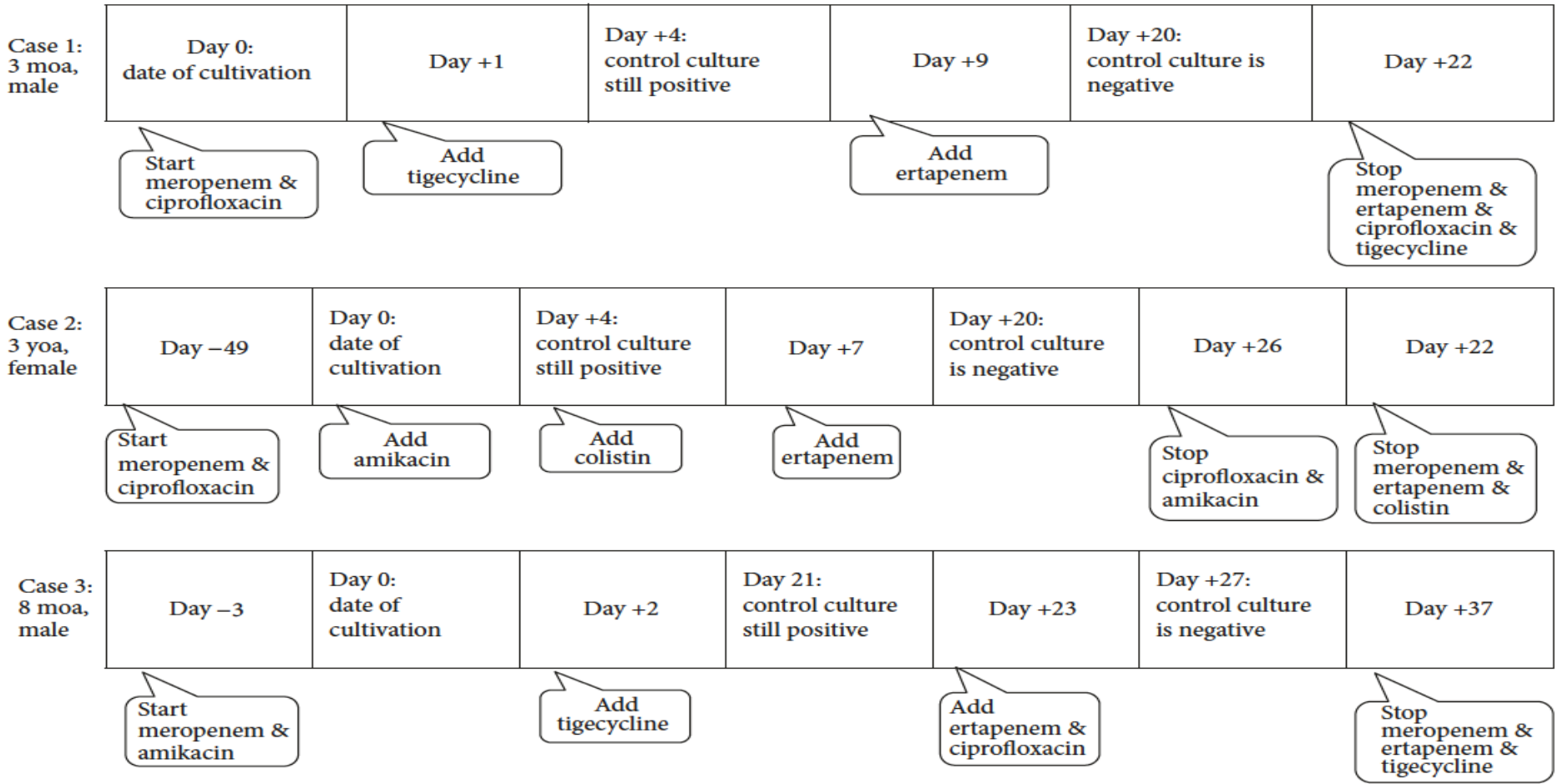
Case Report

Add-On Therapy with Ertapenem in Infections with Multidrug Resistant Gram-Negative Bacteria: Pediatric Experience

Sevgen Tanır Basaranoglu, Yasemin Ozsurekci, Kubra Aykac, Kamile Oktay Arıkan, Ayse Buyukcam, Ali Bulent Cengiz, Mehmet Ceyhan, and Ates Kara



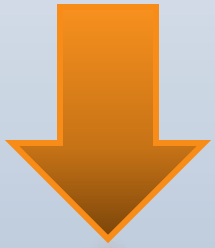
Limitations of the study

- It was retrospective in nature
- It is possible that we missed relevant clinical information, as a result.
- We do not have a chance to keep and investigate all the clinical isolates to figure out that what is going on really?
- The major limitation of this study is that there is no testing for potential environmental sources or any other human source.

Conclusion

Rational antibiotic usage

- Previous extended-spectrum antibiotic usage is a risk factor for acquisition of Gram-negative bacterial infections in children in our study consistantly with our previous findings besides the data from literature (Maltezou et al., Pediatr Infect Dis 2013; 32:151-4; Tsai et al., Pediatrics 2014;133:e322-9).
- There should be a checkpoint for reasonable antibiotic usage in hospitals.



Antibacterial stewardship in Hacettepe

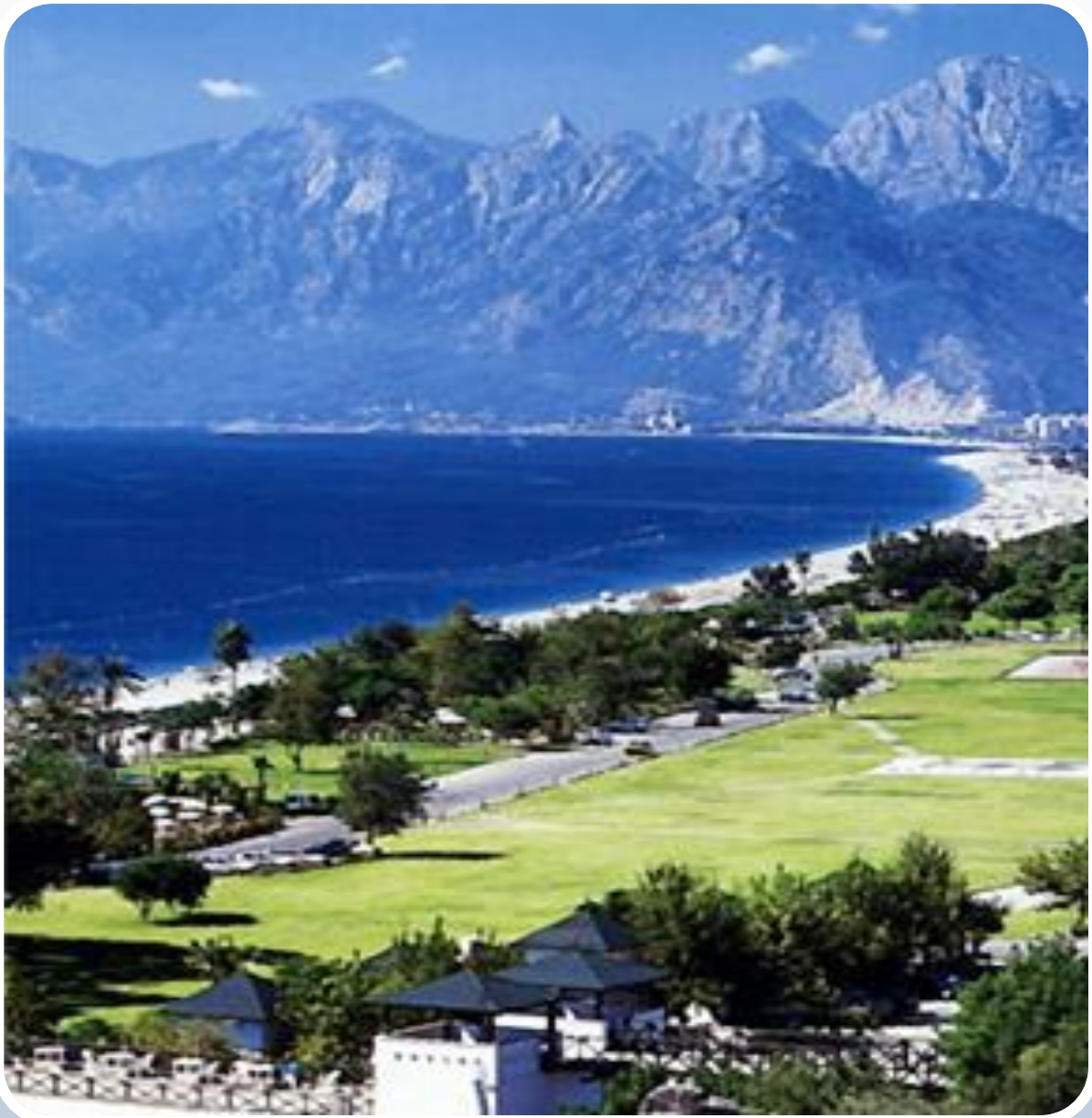
- Pyxis MedStation™ system which is an automated antibiotic dispensing system was used in our huspital.
- Approval from the pediatric infectious disease department is taken before starting each course of antibiotics in our hospital.

Infection control strategies in Hacettepe

- We have not detected any *Serratia* spp. outbreak during the study period.
- Our hospital was accredited by the Joint Commission International in 2011. Infectious control precautions are carried out by a team.
- Education about infection control precautions is given routinely by this team.
- They verify that precautions are used by all staff, in all care settings, at all times and for all patients whether the infection is known to be present or not.

Summary

- Rational antibiotic consumption and infection control precautions might contribute to decrease the levels of antibiotic resistance and infectious-related mortality in patients with serratia infections.
- It is important for each hospital to be aware of its own local antibiotic resistant rates for the appropriate management of Serratia infections (Active surveillance).
- It is important the strict adherence to infection control policies, particularly hand hygiene to combat the infections.



Thank you…