NIH Public Access
Author Manuscript
Infect Control Hosp Epidemiol. Author manuscript; available in PMC 2014 June 30.

Published in final edited form as:
Infect Control Hosp Epidemiol. 2014 April ; 35(4): 419–422. doi:10.1086/675595.

Outcomes of an Enhanced Surveillance Program for Carbapenem-Resistant Enterobacteriaceae

Margaret Fitzpatrick, MD[1], **Teresa Zembower, MD, MPH**[1], **Michael Malczynski, BS**[2], **Chao Qi, PhD**[3], and **Maureen K. Bolon, MD, MS**[1]

[1]Department of Medicine, Division of Infectious Diseases, Northwestern University Feinberg School of Medicine, Chicago, Illinois

[2]Clinical Microbiology Laboratory, Northwestern Memorial Hospital, Chicago, Illinois

[3]Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, Illinois

Abstract

Optimal surveillance strategies for identifying patients colonized with and at risk for transmitting carbapenem-resistant Enterobacteriaceae (CRE) are urgently needed. We instituted an enhanced surveillance program for CRE that identified unrecognized CRE-colonized patients but failed to identify possible CRE transmissions. We also identified risk factors associated with transmitting CRE.

Controlling the spread of carbapenem-resistant Enterobacteriaceae (CRE) is critical for both acute care and long-term care facilities. The US Centers for Disease Control and Prevention (CDC) recently reported that 3.9% of short-stay hospitals and 17.8% of long-term acute care hospitals (LTACH) had at least 1 hospital-acquired infection due to CRE in 2012, representing a substantial increase over data from 2010.[1] CRE infections tend to occur in severely ill patients, are associated with high mortality rates, and have limited treatment options.[2–4]

The CDC has issued guidelines for identifying and controlling the spread of CRE.[5] Earlier studies have described control of CRE outbreaks using a variety of targeted interventions.[6–10] However, it remains unclear which specific interventions are most effective and feasible to implement on a widespread scale. In this study, we characterized the epidemiology of CRE at a single center and described the outcomes of an enhanced surveillance program of epidemiologically linked contacts of new CRE-infected and CRE-colonized patients. We also reviewed clinical data from CRE-positive patients to identify risk factors associated with transmitting CRE.

© 2014 by The Society for Healthcare Epidemiology of America. All rights reserved.

Address correspondence to: Margaret Fitzpatrick, MD, 645 North Michigan Avenue, Suite 900, Chicago, IL 60611 (margaret-fitzpatrick-0@northwestern.edu).

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Presented in part: IDWeek; San Francisco, California; October 2–6, 2013 (Abstract 42477).

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

METHODS

This was a retrospective cohort study conducted between September 2011 and January 2013 as part of an institutional infection prevention intervention for CRE. The study included hospitalized patients older than 18 years of age with positive CRE cultures from any site and patients screened for CRE as part of the intervention. A patient was defined as having CRE on the basis of nonsusceptibility to any carbapenem. This study was approved by the institutional review board at Northwestern Memorial Hospital (Chicago, IL).

Admission rectal screening for extended spectrum β-lactamase (ESBL) organisms and CRE is performed in all adult intensive care, solid-organ transplant, and hematology-oncology units as part of standard surveillance at our institution. Beginning in September 2011 and in accordance with CDC recommendations, enhanced surveillance for CRE was instituted.[5] CRE-positive patients not under contact isolation were placed in isolation, and surveillance of epidemiologically linked contacts was performed (ring surveillance [RS]). Rectal cultures for CRE were performed for the index patient and all patients hospitalized on the same ward. CRE-positive patients already under contact isolation did not trigger RS.

We identified a possible transmission when a patient screened as part of RS had rectal carriage of CRE with the same organism as the index patient and identical or closely related pulsed-field gel electrophoresis (PFGE) types (3-band difference or less). In addition, we performed a retrospective search for possible transmissions not identified by RS by reviewing epidemiologically linked contacts (ELCs) of new CRE-positive patients (labeled case patients). An ELC of a case patient was defined as any CRE-positive patient who previously spent 24 hours or more on a ward with the case patient before the case patient's acquisition of CRE. A possible transmission occurred if a case patient and an ELC shared the same CRE organism with identical or closely related PFGE types. Although CRE-positive patients discharged before final culture results did not trigger RS, they were included in this expanded search. Electronic medical records were also reviewed to collect clinical data on CRE-positive patients.

Normally distributed continuous data were analyzed with the Student *t* test, and nonparametric data were analyzed with the Mann-Whitney *U* test. Categorical data were analyzed with Fisher exact test. All tests of significance were 2 tailed with $P < .05$ considered significant. All statistical analyses were performed using SPSS, version 21 (Chicago, IL).

RESULTS

Sixty-three patients had a positive CRE culture during the study time period. Twenty-nine patients were under contact isolation and did not trigger RS, and 14 patients were not in contact isolation and did trigger RS. In addition, 14 patients were discharged from the hospital before final culture results, and 3 new CRE-positive patients were missed and did not trigger RS. Table 1 shows the demographic and clinical characteristics of CRE-positive patients. RS screened 174 patients and identified 3 asymptomatic CRE-colonized patients. None of these patients were felt to represent possible transmissions, because their CRE

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

cultures grew different organisms than did the cultures from the index patients who triggered RS. Seven possible transmissions were identified via the search of ELCs and involved 6 CRE-positive source patients; 1 source patient was implicated in 2 possible transmission events (Table 2).

Compared with the control group of CRE-positive patients who did not transmit CRE, CRE-positive patients implicated as source patients in possible transmissions all had a positive clinical culture result (Table 1). They were also older, more likely to have CRE cultured from the respiratory tract, had greater previous antibiotic exposure, and had a higher Charlson comorbidity score, although only age was statistically significant.

DISCUSSION

A better understanding of the epidemiology of CRE and factors associated with its transmission can help inform physicians and infection prevention specialists. In addition to admission screening in high-risk units, we instituted a program of enhanced surveillance, performed on all units, for epidemiologically linked contacts of new CRE-positive patients. This screening identified 3 unrecognized asymptomatic CRE colonizations. Other studies have similarly demonstrated a benefit of additional screening beyond admission surveillance in identifying asymptomatic CRE colonization.[9,10] Earlier identification of CRE positivity may provide both infection control and clinical benefits, because patients known to be CRE colonized may receive timelier active antibiotic therapy with subsequent CRE infections. Despite these benefits, 7 possible transmissions in our study were not identified via RS. RS identifies CRE-colonized patients at a single point in time and is therefore limited in capturing all possible transmissions. Furthermore, the time required to confirm and report CRE culture results provides an opportunity for exposed patients to move between wards or be discharged before RS.

In addition, the risk factors associated with transmitting CRE have not been as thoroughly delineated as risk factors for CRE acquisition. In our cohort, older age, a respiratory source, and a higher degree of comorbidity may have been associated with CRE transmission. Interventions targeted to the ICU, where patients are likely to be older, have a higher degree of comorbidity, and have pneumonia, may be particularly effective at reducing transmission. Furthermore, given that all patients implicated in possible transmissions had clinical CRE cultures, patients with active CRE infections may be more likely to transmit CRE than patients with asymptomatic colonization.

This study has several limitations. First, the small number of possible transmissions impaired detection of a statistical difference in risk factors between patients who may have transmitted CRE and those who did not. Second, the delay between culture acquisition and identification of CRE resulted in many patients with CRE being excluded from the study, which can introduce bias. Third, our study did not examine other potential sources of CRE transmission, such as environmental reservoirs, which may be important contributors to CRE outbreaks.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

In conclusion, RS identified asymptomatically colonized CRE patients, targeting them for earlier isolation and geographical cohorting; however, a number of possible transmissions went unrecognized during the RS intervention. More research is needed to determine whether other surveillance methods, such as regular point prevalence surveys or weekly surveillance in high-risk units, may be more effective than RS.

References

1. Centers for Disease Control and Prevention. Vital signs: carbapenem-resistant Enterobacteriaceae. MMWR Morb Mortal Wkly Rep. 2013; 62:165–170. [PubMed: 23466435]
2. Correa L, Martino MD, Siqueira I, et al. A hospital-based matched case-control study to identify clinical outcome and risk factors associated with carbapenem-resistant *Klebsiella pneumoniae* infection. BMC Infect Dis. 2013; 13:80. [PubMed: 23398691]
3. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. Clin Infect Dis. 2011; 53:60–67. [PubMed: 21653305]
4. Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant *Klebsiella pneumoniae* infection and the impact of antimicrobial and adjunctive therapies. Infect Control Hosp Epidemiol. 2008; 29:1099–1106. [PubMed: 18973455]
5. Centers for Disease Control and Prevention. [Accessed December 10, 2012.] CRE tool-kit: guidance for control of carbapenem-resistant Enterobacteriaceae (CRE). 2012. http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html. Published June 21, 2010
6. Chitnis AS, Caruthers PS, Rao AK, et al. Outbreak of carbapenem-resistant Enterobacteriaceae at a long-term acute care hospital: sustained reductions in transmission through active surveillance and targeted interventions. Infect Control Hosp Epidemiol. 2012; 33:984–992. [PubMed: 22961017]
7. Munoz-Price LS, Hayden MK, Lolans K, et al. Successful control of an outbreak of *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* at a long-term acute care hospital. Infect Control Hosp Epidemiol. 2010; 31:341–347. [PubMed: 20175685]
8. Schwaber MJ, Lev B, Israeli A, et al. Containment of a countrywide outbreak of carbapenem-resistant *Klebsiella pneumoniae* in Israeli hospitals via a nationally implemented intervention. Clin Infect Dis. 2011; 52:848–855. [PubMed: 21317398]
9. Calfee D, Jenkins SG. Use of active surveillance cultures to detect asymptomatic colonization with carbapenem-resistant *Klebsiella pneumoniae* in intensive care unit patients. Infect Control Hosp Epidemiol. 2008; 29:966–968. [PubMed: 18754738]
10. Snitkin ES, Zelazny AM, Thomas PJ, et al. Tracking a hospital outbreak of carbapenem-resistant *Klebsiella pneumoniae* with whole-genome sequencing. Sci Transl Med. 2012; 4:148ra116.

NIH-PA Author Manuscript NIH-PA Author Manuscript NIH-PA Author Manuscript

TABLE 1

Clinical Characteristics and Risk Factors Associated with Carbapenem-Resistant Enterobacteriaceae (CRE)–Positive Patients Transmitting CRE

Variable	CRE-positive patients			Univariate analysis, OR (95% CI)	*P*
	All (*n* = 41)	Who may have transmitted CRE (*n* = 6)	Who did not transmit CRE (*n* = 35)		
Demographic characteristic					
Age, mean (±SD), years	58 (15)	75 (15)	57 (15)	…	.01
Female sex	23 (48)	4 (67)	19 (54)	1.68 (0.27–10.43)	.68
Infection/colonization					
Organism[a]					
Klebsiella pneumoniae	35 (85)	6 (100)	29 (83)	…	.57
Other	7 (17)	0	7 (20)	…	.33
Culture site					
Urine	19 (46)	1 (14)	18 (51)	0.19 (0.02–1.79)	.19
Respiratory	10 (24)	3 (50)	7 (20)	4.0 (0.66–24.25)	.14
Rectal	7 (17)	0	7 (20)	…	.57
Blood	2 (5)	1 (17)	1 (3)	6.8 (0.36–126.9)	.27
Abdominal	1 (2)	0	1 (3)	…	>.99
Bone/wound	2 (5)	1 (17)	1 (3)	6.8 (0.36–126.9)	.27
CRE cultured from another site	34 (83)	4 (67)	30 (86)	0.33 (0.05–2.33)	.27
Hospital acquired[b]	24 (59)	5 (83)	19 (54)	4.21 (0.45–39.86)	.37
Healthcare exposures					
Previous hospital, LTACH, or skilled nursing facility exposure	39 (95)	6 (100)	33 (94)	…	>.99
Hospital stay in previous 3 months	34 (83)	5 (83)	29 (83)	1.03 (0.10–10.52)	>.99
LTACH stay in previous 6 months	7 (17)	2 (33)	5 (14)	3.0 (0.43–20.95)	.27
Skilled nursing facility stay in previous 6 months	16 (39)	2 (33)	14 (40)	0.75 (0.12–4.66)	>.99
Transferred from another hospital or LTACH	18 (44)	3 (50)	15 (43)	1.33 (0.24–7.56)	>.99
Central venous or arterial catheter	27 (66)	5 (83)	22 (63)	2.96 (0.31–28.14)	.65
Foley catheter or other urinary diversion[c]	32 (78)	6 (100)	26 (74)	…	.31
Other foreign material[d]	17 (41)	2 (33)	15 (43)	0.67 (0.11–4.13)	>.99
Mechanical ventilation	18 (44)	4 (67)	14 (40)	3.0 (0.48–18.65)	.38

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

Variable	CRE-positive patients			Univariate analysis, OR (95% CI)	*P*
	All (*n* = 41)	Who may have transmitted CRE (*n* = 6)	Who did not transmit CRE (*n* = 35)		
Duration of previous antibiotic treatment, median (range), days	5 (0–76)	8 (6–10)	4 (0–76)	…	.09
ICU at onset	17 (41)	4 (67)	13 (37)	3.39 (0.54–21.11)	.2
Clinical/laboratory					
Age-adjusted Charlson comorbidity score, median (range)	6 (1–14)	7 (5–11)	4 (1–14)	…	.10
Active malignancy	8 (20)	1 (17)	7 (20)	0.8 (0.08–7.99)	>.99
History of transplantation	7 (17)	0	7 (20)	…	.57
Current immunosuppression[e]	17 (42)	3 (50)	14 (40)	1.95 (0.37–10.2)	.68
Diabetes mellitus	16 (39)	2 (33)	14 (40)	0.75 (0.12–4.67)	>.99
Renal dysfunction[f]	20 (49)	4 (67)	16 (46)	2.38 (0.38–14.7)	.41
Liver dysfunction[g]	9 (22)	1 (17)	8 (23)	0.68 (0.07–6.65)	>.99
Clinical outcome					
Hospital mortality	10 (24)	2 (33)	8 (23)	1.69 (0.26–10.97)	.62
Hospital LOS, median (range), days	19 (3–196)	28 (15–42)	19 (3–196)	…	.44
Time to mortality, median (range), days	12 (0–29)	16 (15–16)	8 (0–29)	…	.41

NOTE. Data are no. (%) of patients, unless otherwise indicated. ICU, intensive care unit; LOS, length of stay; LTACH, long-term acute care hospital; MDRO, multidrug resistant organism; OR, odds ratio.

[a] One patient grew both carbapenem-resistant *K. pneumoniae* and *Enterobacter aerogenes* from the same culture. Other organisms were *Enterobacter aerogenes, Enterobacter gergorviae, Klebsiella oxytoca,* and *Escherichia coli*.

[b] Culture obtained 48 hours or more after hospital admission.

[c] Ileal conduit or suprapubic catheter.

[d] Tracheostomy, percutaneous gastrostomy tube, automatic implantable cardioverter defibrillator/permanent pacemaker, ventriculoperitoneal shunt, bioprosthetic mechanical and aortic valves, abdominal mesh, prosthetic knee joint, and inferior vena cava filter.

[e] Receipt of immunosuppressive therapy at the time of culture.

[f] Chronic kidney injury, dialysis, or increase in creatinine level of 0.5 mg/dL or 50% at time of culture from a previous value recorded any time during the hospital stay.

[g] Any liver function test 3 times the upper limit of normal or greater at time of culture.

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

TABLE 2

Summary of Possible Carbapenem-Resistant Enterobacteriaceae Transmissions

Transmission number	Identified via RS or search of ELC	Source patient type of clinical culture	No. of days case patient shared on ward with source patient	Case patient in isolation	Source patient in isolation	Organism
1	ELC	Blood	3	Yes	Yes	*Klebsiella pneumoniae*
2	ELC	Wound	2	Yes	Yes	*K. pneumoniae*
3	ELC	Respiratory	3	No	No	*K. pneumoniae*
4	ELC	Urine	3	No	Yes	*K. pneumoniae*
5	ELC	Respiratory	3	No	Yes	*K. pneumoniae*
6	ELC	Urine	9	No	Yes	*K. pneumoniae*
7	ELC	Respiratory	3	No	Yes	*K. pneumoniae*

NOTE. ELC, epidemiologically linked contacts; RS, ring surveillance.