

Gram-Negative Bacteria That Produce Carbapenemases Causing Death Attributed to Recent Foreign Hospitalization

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Overseas travel, as a risk factor for the acquisition of infections due to antimicrobial-resistant organisms, has recently been linked to carbapenemase-producing Gram-negative bacteria. Multiresistant *Klebsiella pneumoniae*, *Escherichia coli*, and *Acinetobacter baumannii* strains were isolated from a wound of a Canadian patient with a recent history of hospitalization in India. This resulted in the initiation of outbreak management that included surveillance cultures. Epidemiological and molecular investigations showed that NDM-1-producing *K. pneumoniae* ST16 and OXA-23-producing *A. baumannii* ST10 strains were transmitted to 5 other patients, resulting in the colonization of 4 patients and the death of 1 patient due to septic shock caused by the OXA-23-producing *A. baumannii* strain. The high rate of false positivity of the screening cultures resulted in additional workloads and increased costs for infection control and clinical laboratory work. We believe that this is the first report of an infection with carbapenemase-producing Gram-negative bacteria resulting in death attributed to a patient with recent foreign hospitalization. We recommend routine rectal and wound screening for colonization with multiresistant bacteria for patients who have recently been admitted to hospitals outside Canada.

Gram-negative bacteria, most notably *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, are among the most important causes of serious hospital-acquired and community-onset bacterial infections in humans, and resistance to antimicrobial agents in these bacteria has become an increasingly relevant problem (1). Of special concern is the development of resistance to the carbapenems, since these agents are often the last line of effective therapy available for the treatment of infections caused by multiresistant *Enterobacteriaceae*, *P. aeruginosa*, and *A. baumannii* (2). Most important is the recognition of isolates that produce carbapenemases, which cause resistance to the carbapenems. Carbapenemases include class A enzymes (i.e., KPC types), class B enzymes, or the metallo- β -lactamases (MBLs [i.e., VIM, IMP, and NDM types]), and class D enzymes, or oxacillinases (i.e., OXA types) (3).

NDM enzymes were first reported for *K. pneumoniae* and *E. coli* strains recovered from a Swedish patient who had been hospitalized in New Delhi, India, previously (4). Recent reports from the Indian subcontinent (including India, Pakistan, and Bangladesh) show that the distribution of NDM β -lactamases among clinical and environmental isolates of Gram-negative bacteria is widespread in these countries (5–8). The majority of NDM-1-producing bacteria (most often *E. coli* and *K. pneumoniae*) are broadly resistant to various drug classes, leaving very limited treatment options (3). Infections with NDM-producing *Enterobacteriaceae* in areas where they are not endemic, such as Canada, have most often been associated with visits to, and hospitalization in, areas of endemicity, such as the Indian subcontinent (9).

A. baumannii is an important nosocomial pathogen associated with a wide range of infections, including respiratory tract, bloodstream, urinary tract, and surgical-site infections (10). The spread of *A. baumannii* between different patients in the hospital setting is difficult to control due to the bacterium's ability to persist in the environment. Therefore, numerous nosocomial intensive-care unit (ICU) outbreaks due to *A. baumannii* have been reported (10). The carbapenemases described in *A. baumannii* include the

MBLs (i.e., VIM, IMP, SIM, and NDM types) and, more commonly, the OXA types (i.e., OXA-23-like, OXA-24-like, OXA-51-like, and OXA-58-like enzymes) (11). OXA-23-like enzymes are the most common carbapenemases described in *A. baumannii* and have been reported in various European, North American, South American, and Asian countries, including India, the United States, and Canada (12). *A. baumannii* strains that produce OXA-type β -lactamases have been responsible for a range of infectious syndromes in military personnel returning to their home countries after being injured in the conflicts in Iraq and Afghanistan (13).

During April 2012, multiresistant *K. pneumoniae*, *E. coli*, and *A. baumannii* strains were isolated from a wound culture from a patient in Edmonton, Canada, with a recent history of hospitalization in India. Infection control precautions and active surveillance were implemented immediately upon the isolation of Gram-negative organisms from the wound culture. However, secondary spread occurred and was associated with the death of another patient. The clinical and infection control aspects of the outbreak were recently presented at IDWeek (14). This study describes the laboratory aspects of screening for carbapenemase-producing bacteria and the molecular characterization of the bacteria involved in the outbreak.

Received 12 February 2013 Returned for modification 10 April 2013

Accepted 14 April 2013

Published ahead of print 22 April 2013

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doi:10.1128/AAC.00297-13

MATERIALS AND METHODS

Index patient. A 62-year-old female (patient A) was admitted with a post-operative wound infection to a surgical ward in a Canadian hospital in Edmonton, Alberta, Canada, on 31 March 2012. She was housed in a room shared with three other patients. She had just returned from India after being admitted to a hospital in that country for a prolonged period. Multiresistant *A. baumannii* (AB01), *K. pneumoniae* (Kp01), and *E. coli* (Ec01) strains were cultured from thigh tissue obtained on 1 April 2012 during surgical debridement. *K. pneumoniae* (Kp02) was cultured from a rectal screening swab obtained from this patient on 3 April 2012.

Screening of patients for carbapenemase-producing bacteria. Surveillance cultures (i.e., from rectal, wound, ostomy, and endotracheal suction specimens) were used to identify all epidemiologically linked patients who may have become colonized. This procedure was directed by the Infection Prevention and Control (IPC) team and formed part of contact tracing and unitwide prevalence screening. Those screened included inpatients in the same wards/units as the index patient and subsequent case patients. Surveillance cultures were undertaken weekly for all patients on the affected units until negative screening cultures were obtained for two consecutive weeks. Roommates and unit contacts of case patients also had surveillance specimens collected before discharge. In addition, inpatients of surgical units were screened before transfer to another service within the hospital. No environmental or health care worker screenings were performed. An incident case was defined as the isolation of any carbapenemase-producing Gram-negative organism in clinical or surveillance cultures from 1 April 2012 to 25 May 2012. Clinical specimens were obtained from body sites as directed by an attending physician for the clinical management of a patient. Active surveillance cultures were performed on stool, rectal swabs, ostomy output, wound swabs, and endotracheal suction specimens as requested by the hospital's IPC team and involved a total of 410 patients.

Screening swabs obtained from patients were placed in a Copan M40 Transystem containing Amies gel transport medium. Stool and endotracheal suction specimens were submitted in sterile containers without transport medium. The Centers for Disease Control and Prevention (CDC, Atlanta, GA) protocol was used to screen for carbapenemase-producing Gram-negative bacteria (15). The specimens were inoculated into 5 ml of Trypticase soy broth (TSB) containing a 10- μ g-meropenem disk and were incubated overnight (at 35°C, in ambient air), and 100 μ l was then plated onto a MacConkey agar (MAC) plate and was streaked for isolation. The MAC plate was incubated overnight (at 35°C, in ambient air) and was then examined for growth. Single colonies of Gram-negative bacilli were subcultured to a MAC plate containing a meropenem disk (10 μ g). Non-meropenem-susceptible isolates underwent identification and susceptibility testing using a Vitek 2 instrument (Vitek AMS; bioMérieux Vitek Systems Inc., Hazelwood, MO). The identification of *A. baumannii* was confirmed by using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) (Vitek AMS; bioMérieux Vitek Systems Inc., Hazelwood, MO) and detection of chromosomal OXA-51-like carbapenemases (16).

Susceptibility testing. Antimicrobial susceptibility was determined with MicroScan Neg MIC panels (type 38; Siemens, Burlington, ON, Canada). The MICs of the following drugs were determined: amoxicillin-clavulanic acid (AMC), piperacillin-tazobactam (TZP), ceftioxin (FOX), ceftriaxone (CRO), ceftazidime (CAZ), aztreonam (ATM), imipenem (IPM), meropenem (MER), ertapenem (ERT), amikacin (AMK), gentamicin (GEN), tobramycin (TOB), ciprofloxacin (CIP), trimethoprim-sulfamethoxazole (SXT), and tigecycline (TIM). Additional tests for susceptibility to colistin (COL) were performed using Etest methodology according to the manufacturer's instructions (bioMérieux, Marcy l'Etoile, France). Throughout this study, results were interpreted using the 2012 CLSI criteria for broth dilution (17). The European Committee for Antimicrobial Susceptibility Testing (EUCAST) breakpoint (for *K. pneumoniae* and *E. coli*) was used for COL, and the FDA breakpoint was used for TIM.

β -Lactamase identification. The presence of carbapenemase was determined with the modified Hodge test (MHT) (17) and the MBL Etest (bioMérieux, Marcy l'Etoile, France) according to the manufacturer's instructions. PCR amplification for *bla*_{CTX-M}, *bla*_{KPC}, *bla*_{VIM}, *bla*_{IMP}, *bla*_{NDM}, *bla*_{OXA-48-like}, *bla*_{OXA-23-like}, *bla*_{OXA-24-like}, *bla*_{OXA-51-like}, and *bla*_{OXA-58-like} was carried out on the isolates with a GeneAmp thermal cycler, model 9700 (Applied Biosystems, Norwalk, CT), using PCR conditions and primers described previously (16, 18–20). *bla*_{CTX-M}, *bla*_{NDM}, *bla*_{OXA-48-like}, and *bla*_{OXA-23-like} were sequenced using PCR conditions and primers described previously (19, 21, 22).

Plasmid-mediated quinolone resistance determinants. The *qnrA*, *qnrS*, and *qnrB* genes were amplified by multiplex PCR (23). *aac(6')-Ib* and *qepA* were amplified in a separate PCR using primers and conditions described previously (24, 25). The variant *aac(6')-Ib-cr* was further identified by digestion with BstF51 (New England Biolabs, Ipswich, MA).

16S rRNA methylation. Genes coding for 16S rRNA methylases were amplified using a multiplex PCR described by Doi and Arakawa (26).

PFGE. The *E. coli* and *K. pneumoniae* isolates were examined for genetic relatedness by pulsed-field gel electrophoresis (PFGE) following the extraction of genomic DNA and digestion with XbaI using the standardized *E. coli* (O157:H7) protocol established by the CDC, Atlanta, GA (27). The *A. baumannii* isolates were examined for genetic relatedness by PFGE following the extraction of genomic DNA and digestion with ApaI as described previously (28). Subsequent PFGE analyses were performed on a CHEF Mapper apparatus (Bio-Rad Laboratories, Hercules, CA). PFGE banding patterns were analyzed with BioNumerics software (Applied Maths, Kortrijk, Belgium), and relatedness was calculated using the UPGMA (unweighted-pair group method using average linkages) algorithm, with the Dice coefficient for assessment of the similarity of bands. Cluster designations were based on the criteria of Tenover et al. (29).

MLST. Multilocus sequence typing (MLST) was performed on the *K. pneumoniae* isolates by using seven conserved housekeeping genes (*gapA*, *infB*, *mdh*, *pgi*, *phoE*, *rpoB*, *tonB*) as described previously (30). MLST was performed on the *E. coli* isolate by using seven conserved housekeeping genes (*adh*, *fumC*, *gyrB*, *icd*, *mdh*, *purA*, *recA*). A detailed protocol of the MLST procedure for *E. coli*, including allelic type and sequence type (ST) assignment methods, is available at MLST Databases at the ERI, University College Cork (<http://mlst.ucc.ie/mlst/dbs/Ecoli>). MLST was performed on the *A. baumannii* isolates by using seven conserved housekeeping genes (*cpn60*, *fusA*, *gltA*, *pyrG*, *recA*, *rplB*, *rpoB*). A detailed protocol of the MLST procedure for *A. baumannii*, including allelic type and ST assignment methods, is available at the Institut Pasteur website (http://www.pasteur.fr/recherche/genopole/PF8/mlst/primers_Abaumannii.html).

RESULTS

Summary of the nosocomial outbreak. The details of the clinical presentations, nosocomial outbreak, and infection control procedures were recently presented at IDWeek, San Diego, CA (14). Outbreak management was initiated immediately upon the identification of multiresistant Gram-negative bacteria in the index patient (patient A).

The details of the outbreak and the chronological summary of events are given in Fig. 1 and Table 1. In brief, the index patient underwent surgery in India for a fractured femur that subsequently became infected and did not respond to treatment. Eventually, she discharged herself and flew back to Edmonton, Canada, where she was admitted to the surgical ward (unit 1), sharing a room with 3 other patients, on 31 March 2012. Between 3 April and 9 May 2012, several multiresistant Gram-negative bacteria were cultured from 6 different patients in 3 different units. On 3 April, *K. pneumoniae* (Kp03) was cultured from a rectal swab from patient B, and *A. baumannii* (AB02) was cultured from a rectal swab from patient C. Patients B and C were roommates of patient A in unit 1.

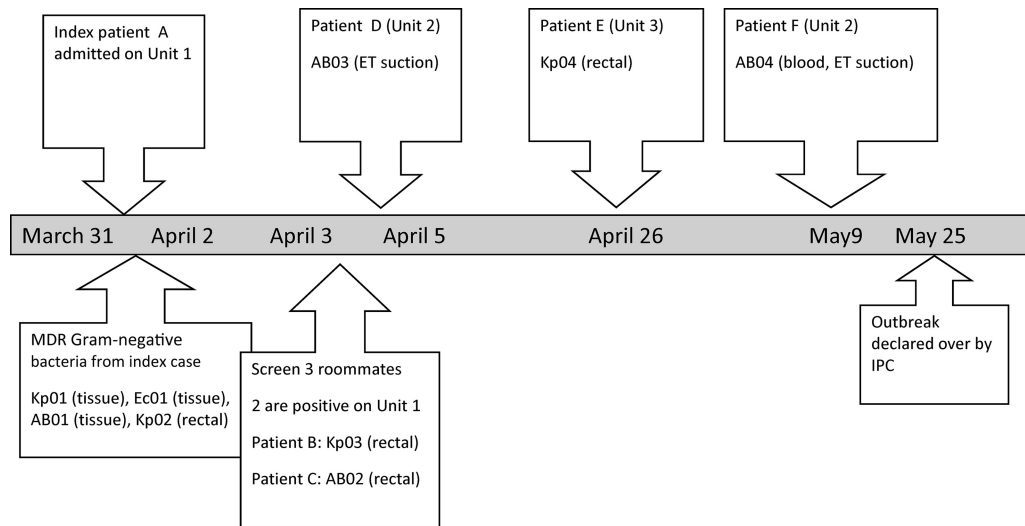


FIG 1 Timeline of events in the nosocomial outbreak with multidrug-resistant (MDR) Gram-negative bacteria. ET, endotracheal.

A. baumannii (AB03) was cultured from an endotracheal specimen collected on 4 April from patient D in unit 2. Patient D had no symptoms or signs of pulmonary infection. Patient D stayed briefly in the same unit as patient A and was then transferred to unit 2. *K. pneumoniae* (Kp04) was cultured from a rectal swab collected on 26 April from patient E in unit 3. Patient E was briefly admitted to unit 2. *A. baumannii* (AB04) was cultured from an endotracheal specimen and blood collected on 8 May from patient F in unit 2. Patient F developed septic shock and organ failure, was transferred to the intensive-care unit, and died a few hours later. None of patients B, C, D, E, and F had a history of hospitalization in a foreign country or of travel to a foreign country in the preceding 12 months.

Active surveillance cultures. Over a period of 55 days, the clinical microbiology laboratory received 442 screening specimens from 410 patients. The true-positive rate (i.e., the proportion of carbapenemase producers) was 1.1% (5/442). The 5 true-positive specimens were from patients B through F. Sixty-three percent of specimens (278/442) had no growth, while 35.7% (158/442) grew organisms that subsequently proved not to be resistant to the carbapenems. One specimen grew carbapenem-resistant *Enterobacter cloacae* that tested negative for carbapenemases by phenotypic and genotypic tests. The subsequent growth from the TSB containing a 10- μ g-meropenem disk resulted in 246 different isolates that required further workup; 5 were true positives, and

241 included the following bacteria: 203 *Enterobacteriaceae* that subsequently tested susceptible to MER by disk diffusion, 21 *Pseudomonas aeruginosa* isolates that tested susceptible to MER, 3 *P. aeruginosa* isolates intermediate to MER, 3 *P. aeruginosa* isolates that tested resistant to MER but were negative for carbapenemases, 1 *Pseudomonas fluorescens* isolate, 4 *Stenotrophomonas maltophilia* isolates, 2 yeast isolates, and 4 *Enterococcus* spp. This part of the investigation required an additional 120 technologist hours, with an estimated laboratory cost of Can\$7,000.

Susceptibility testing and β -lactamases. Table 2 shows the results of susceptibility and molecular tests for carbapenemase-producing bacteria. Kp01 was susceptible to AMK (MIC, 16 μ g/ml), GEN (MIC, 2 μ g/ml), TIM (MIC, 2 μ g/ml), and COL (MIC, 0.25 μ g/ml); Kp02, Kp03, and Kp04 were susceptible only to COL (MIC, 0.5 μ g/ml); Ec01 was susceptible to TIM (MIC, 1 μ g/ml) and COL (MIC, 0.12 μ g/ml); AB01, AB02, AB03, and AB04 were susceptible to COL (0.12 μ g/ml). The TIM MIC for Kp02, Kp03, and Kp04 was 4 μ g/ml.

Kp01 tested positive by the modified Hodge test and the MBL Etest; Kp02, Kp03, and Kp04 were negative by the modified Hodge test and the MBL Etest; Ec01 was negative by the modified Hodge test and positive by the MBL Etest. AB01, AB02, AB03, and AB04 tested positive by the MBL Etest and the modified Hodge test using IPM as the substrate. PCR results showed that Kp01 was positive for *bla*_{NDM}, *bla*_{CTX-M β} and *bla*_{OXA-48-like}, and sequencing identified the *bla*_{NDM}

TABLE 1 Clinical characteristics of the patients involved in the outbreak

Patient	Age (yr)	Sex	Admitting diagnosis	Organism(s) isolated	Date of culture	Unit	Specimen ^a
A	62	F	Femoral fracture with deep postoperative infection	<i>K. pneumoniae</i> (Kp01)	1 Apr.	1	Tissue
				<i>E. coli</i> (Ec01)	1 Apr.		Tissue
				<i>A. baumannii</i> (AB01)	1 Apr.		Tissue
				<i>K. pneumoniae</i> (Kp02)	3 Apr.		Rectal
B	83	F	Ankle fracture requiring operative fixation	<i>K. pneumoniae</i> (Kp03)	3 Apr.	1	Rectal
C	69	F	Infected thigh requiring incision and drainage	<i>A. baumannii</i> (AB02)	19 Apr.	1	Rectal
D	58	M	Intra-abdominal sepsis due to perforated viscus	<i>A. baumannii</i> (AB03)	4 Apr.	2	ET suction
E	80	M	Ischemic bowel due to small-bowel obstruction	<i>K. pneumoniae</i> (Kp04)	26 Apr	3	Rectal
F	74	M	Segmental resection for pulmonary nodule	<i>A. baumannii</i> (AB04)	8 May	2	ET suction, blood

^a ET, endotracheal.

TABLE 2 Susceptibilities and molecular characteristics of carbapenemase-producing bacteria

Isolate no.	Organism	Susceptibility ^a (MIC [$\mu\text{g/ml}$])		Phenotypic test result					PMQR ^c determinant(s)	16S rRNA methylase
		NS	S	MHT	MBL Etest	β -Lactamases	PFGE pattern ^b	MLST		
Kp01	<i>K. pneumoniae</i>	TZP (>64/4), FOX (>32), CRO (>32), CAZ (>16), ATM (>16), IPM (>8), MER (>8), ERT (>4), TOB (>8), CIP (>2), SXT (>2/38)	AMK (16), GEN (2), TIM (2), COL (0.25)	Positive	Positive	NDM-1, CTX-M-15, OXA-181	A	ST1972	<i>qnrS</i> , <i>aac6'-Ib-cr</i>	Negative
Kp02	<i>K. pneumoniae</i>	TZP (>64/4), FOX (>32), CRO (>32), CAZ (>16), ATM (>16), IPM (>8), MER (>8), ERT (>4), GEN (>8), TOB (>8), AMK (>32), CIP (>2), SXT (>2/38), TIM (4)	COL (0.5)	Negative	Negative	NDM-1, CTX-M-15	B	ST116	<i>qnrB</i> , <i>aac6'-Ib-cr</i>	Negative
Kp03	<i>K. pneumoniae</i>	TZP (>64/4), FOX (>32), CRO (>32), CAZ (>16), ATM (>16), IPM (>8), MER (>8), ERT (>4), GEN (>8), TOB (>8), AMK (>32), CIP (>2), SXT (>2/38), TIM (4)	COL (0.5)	Negative	Negative	NDM-1, CTX-M-15	B	ST116	<i>qnrB</i> , <i>aac6'-Ib-cr</i>	Negative
Kp04	<i>K. pneumoniae</i>	TZP (>64/4), FOX (>32), CRO (>32), CAZ (>16), ATM (>16), IPM (>8), MER (>8), ERT (>4), GEN (>8), TOB (>8), AMK (>32), CIP (>2), SXT (>2/38), TIM (4)	COL (0.5)	Negative	Negative	NDM-1, CTX-M-15	B	ST116	<i>qnrB</i> , <i>aac6'-Ib-cr</i>	Negative
Ec01	<i>E. coli</i>	TZP (>64/4), FOX (>32), CRO (>32), CAZ (>16), ATM (>16), IPM (>8), MER (>8), ERT (>4), GEN (>8), TOB (>8), AMK (>32), CIP (>2), SXT (>2/38)	TIM (1), COL (0.12)	Negative	Positive	NDM-1, CTX-M-15	NP	ST410	<i>aac6'-Ib-cr</i>	Negative
AB01	<i>A. baumannii</i>	TZP (>64/4), CAZ (>16), ATM (>16), IPM (>8), MER (>8), AMK (>32), GEN (>8), TOB (>8), CIP (>2), SXT (>2/38)	COL (0.12)	Positive	Positive	OXA-23, OXA-51	C	ST110	<i>aac6'-Ib-cr</i>	<i>armA</i>

AB02	<i>A. baumannii</i>	TZP (>64/4), CAZ (>16), ATM (>16), IPM (>8), MER (>8), AMIK (>32), GEN (>8), TOB (>8), CIP (>2), SXT (>2/38)	COL (0.12)	Positive	Positive	OXA-23, OXA-51	C	ST10	<i>aac6'-Ib-cr</i>	<i>arrnA</i>
AB03	<i>A. baumannii</i>	TZP (>64/4), CAZ (>16), ATM (>16), IPM (>8), MER (>8), AMIK (>32), GEN (>8), TOB (>8), CIP (>2), SXT (>2/38)	COL (0.12)	Positive	Positive	OXA-23, OXA-51	C	ST10	<i>aac6'-Ib-cr</i>	<i>arrnA</i>
AB04	<i>A. baumannii</i>	TZP (>64/4), CAZ (>16), ATM (>16), IPM (>8), MER (>8), AMIK (>32), GEN (>8), TOB (>8), CIP (>2), SXT (>2/38)	COL (0.12)	Positive	Positive	OXA-23, OXA-51	C	ST10	<i>aac6'-Ib-cr</i>	<i>arrnA</i>

^a NS, nonsusceptible (resistant or intermediate); S, sensitive; TZP, piperacillin-tazobactam; FOX, cefoxitin; CRO, ceftriaxone; CAZ, ceftazidime; ATM, aztreonam; IPM, imipenem; MER, meropenem; ERT, ertapenem; GEN, gentamicin; TOB, tobramycin; AMK, amikacin; CIP, ciprofloxacin; SXT, trimethoprim-sulfamethoxazole; TIM, tigecycline; COL, colistin.

^b NP, not performed.

^c PMQR, plasmid-mediated quinolone resistance.

enzyme as NDM-1, the *bla*_{CTX-M} enzyme as CTX-M-15, and the *bla*_{OXA-48-like} enzyme as OXA-181. Kp02, Kp03, Kp04, and Ec01 were positive for *bla*_{NDM} and *bla*_{CTX-M}, and sequencing identified the *bla*_{NDM} enzyme as NDM-1 and the *bla*_{CTX-M} enzyme as CTX-M-15. AB01, AB02, AB03, and AB04 were positive for *bla*_{OXA-23-like} and *bla*_{OXA-51}, and sequencing identified the *bla*_{OXA-23-like} enzyme as OXA-23. The *A. baumannii* isolates were negative for MBLs by use of a different multiplex PCR (31).

Molecular characterization and typing. PFGE showed that Kp02 was indistinguishable from Kp03 and Kp04 but was not related to Kp01. MLST identified Kp02, Kp03, and Kp04 as ST16, while Kp01 belonged to ST972 (Table 2). PFGE showed that AB01, AB02, AB03, and AB04 were indistinguishable from each other, and MLST identified them as ST10 (Table 2). Ec01 belonged to ST410. The presence of the different plasmid-mediated quinolone resistance determinants and 16S rRNA methylation is shown in Table 2.

DISCUSSION

Easy access to air and ground transportation is making it possible for people to travel to different countries and continents in a matter of hours or days, whether as tourists (medical, business, study, or recreational), immigrants, refugees, asylum seekers, or migrant workers (9). Overseas travel, as a risk factor for the acquisition of infections due to antimicrobial-resistant organisms, has recently been linked to infections due to CTX-M-producing *E. coli* strains or to various carbapenemase-producing Gram-negative bacteria (9).

Kohlenberg and colleagues described an outbreak of OXA-23-producing *A. baumannii* over a 10-month period at a German hospital that involved 32 patients in 5 intensive-care units and 2 regular wards (32). The index patient had been transferred to the German hospital by an ambulance flight from Thailand, where he had been hospitalized after a motor vehicle accident. Hrabak and colleagues reported an NDM-1-producing *A. baumannii* isolate from a patient transferred from a hospital in Egypt to the Czech Republic (33). A second *A. baumannii* isolate that produced NDM-1 was recovered 6 days later from the airways of another patient sharing the same room. That patient died due to respiratory failure; however, it was not clear if his death was due to the *A. baumannii* infection. MLST showed that both isolates belonged to ST1, which represents the epidemiologically successful European clone I. A report from the CDC described the spread of NDM-producing *K. pneumoniae* from an index patient to 2 other patients (34). One month prior to being admitted to a hospital in Rhode Island, the index patient had been hospitalized in Vietnam. Lowe and colleagues from Toronto, Canada, analyzed a cluster of patients infected or colonized with NDM-producing *K. pneumoniae* over a 15-month period and identified 2 index patients who were responsible for the transfer of 2 different clones to 7 contacts. One of the index patients had previously received medical care in India (35).

We describe the characteristics of carbapenemase-producing *Enterobacteriaceae* and *A. baumannii* strains that were linked to an index patient who had been hospitalized in India recently when she injured her leg while on vacation. Epidemiological and molecular investigations showed that NDM-1-producing *K. pneumoniae* ST16 and OXA-23-producing *A. baumannii* ST10 were transmitted to 5 other patients, even after infection control precautions and active surveillance had been implemented. One of

these patients died due to septic shock caused by the same OXA-23-producing *A. baumannii* strain. We believe this is the first report to describe infection with multiresistant Gram-negative bacteria resulting in death attributed to a patient with recent foreign hospitalization.

Of special interest was the fact that the index patient was colonized/infected with 2 different isolates of NDM-producing *K. pneumoniae* (belonging to ST16 and ST972). However, only the ST16 isolate was transmitted to other patients. *K. pneumoniae* ST16 was first described in Paris during the early 2000s (30) and had been responsible for nosocomial outbreaks of CTX-M-15-producing *K. pneumoniae* in Sweden (36) and Denmark (37) during the mid- to late 2000s. This sequence type had also been reported with KPC-2 from Brazil (38) and with OXA-48 from Spain (39). *A. baumannii* ST10 with acinetobacter-derived cephalosporinase (ADC) from companion animals and horses in Switzerland had been described previously (40).

Active surveillance screening of patients played an important role in managing and eventually controlling this outbreak. We chose to use the CDC screening procedure for carbapenemase-producing Gram-negative bacteria because of its cost-effectiveness and the fact that all supplies were readily available in our laboratory (15). The sensitivity of this method compares well to that of CHROMagar chromogenic media for the detection of carbapenemase-producing Gram-negative bacteria (41). However, we found the CDC screening method labor-intensive, with high breakthrough growth (i.e., 35.7%) and slow turnaround (a minimum of 2 days for negative specimens and longer for positive specimens). Isolates from surveillance cultures were reported to Infection Control on day 1 (including those that subsequently tested negative for carbapenemases). The high rate of false positivity of the screening cultures resulted in additional workloads, closure of hospital beds and wards, and increased costs for infection control and the clinical laboratory. Collaboration and good communication between the Infection Prevention and Control team and the clinical laboratories were crucial to the successful investigation and control of this outbreak.

The phenotypic confirmation tests, such as the MBL Etest and the modified Hodge test (MHT), performed poorly during our investigation. Previous evaluations of the MHT have shown that this method reliably detects KPC- and OXA-48-producing isolates (42). Unfortunately, the MHT performs poorly in the detection of MBL-producing isolates (3). This would explain why Kp01 tested positive by the MHT while the other *K. pneumoniae* isolates tested negative. Interestingly, the OXA-23-producing *A. baumannii* isolate tested positive by the MBL Etest, a result attributed to the destabilization of OXA dimers by EDTA and/or to the antimicrobial activity of EDTA against certain isolates of *A. baumannii* (43, 44). We believe that the presence of carbapenemases among Gram-negative bacteria is an infection control emergency and that the detection of these bacteria in clinical laboratories is a critical step required for the appropriate management of patients and for infection prevention and control efforts. We urgently need rapid, cost-effective phenotypic methods, such as the Carba NP test, that will reliably detect carbapenemases in all Gram-negative bacteria (45).

The European Centre for Disease Prevention and Control has developed a communication platform tool dedicated to antimicrobial resistance (AMR) in health care-associated infections (HAI), which is referred to as the Epidemic Intelligence Informa-

tion System (EPIS) AMR-HAI. EPIS AMR-HAI allows experts in national risk assessment bodies within the European Union to rapidly and securely exchange information related to microorganisms with emerging antimicrobial resistance that have a potential impact in the European Union (9). We recommend that similar communication platforms be established in different provinces and states on the North American continent to ensure the timely communication of emerging antimicrobial resistance mechanisms among public health officials, infection control practitioners, and clinical microbiologists.

In order to prevent the introduction and spread of multiresistant bacteria from travelers returning to their home countries, it is essential to rapidly identify patients colonized or infected by these bacteria (9, 46). We recommend that patients recently admitted to hospitals in areas of endemicity be screened, by culture of rectal and wound specimens using CHROMagar, for colonization with multiresistant bacteria. We further recommend careful attention to routine infection control measures (i.e., hand hygiene, cleaning of shared equipment, effective environmental cleaning) with consideration of preemptive contact isolation for patients with a recent history (i.e., 6 months) of foreign hospitalization. Such measures will help to prevent nosocomial outbreaks with multiresistant Gram-negative bacteria, which will ultimately save lives.

ACKNOWLEDGMENTS

J.D.D.P. previously received research funds from Merck and Astra Zeneca. All other authors have nothing to declare.

This work was supported by a research grant (73-6350) from Calgary Laboratory Services.

We thank Sharla Manca and Amber-Leah Wolfe for their assistance during the outbreak investigation.

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