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Outbreak of IMP-producing carbapenem-resistant *Enterobacter gergoviae* among kidney transplant recipients

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Objectives: The objective of this study was to investigate a prolonged outbreak of carbapenem-resistant *Enterobacter gergoviae* (CREG) involving kidney transplant recipients (KTRs) between 2009 and 2014.

Methods: A case–control study was undertaken. Controls ($n=52$) were selected from CREG-negative KTRs. Surveillance cultures for CREG were collected weekly. Colonization was defined as isolation of CREG from surveillance samples or from clinical specimens, with no evidence of infection. We also investigated infection control practices at the facility.

Results: Of 26 identified cases, 13 had had no known contact with another CREG-positive patient before the first positive culture. Seven patients (27%) developed infection. The site most often colonized was the urinary tract. During the study period two clusters were identified, one in 2009 and another in 2013–14. DNA sequencing revealed bla_{IMP-1} in all CREG tested. No environmental or hand cultures tested positive for CREG. An audit of infection control practices detected flaws in the handling and cleaning of urinary tract devices. Multivariate analysis identified advanced age, ureteral stent use, retransplantation and male gender as risk factors for CREG acquisition.

Conclusions: An outbreak among KTRs caused by an unusual species of MDR bacteria may have resulted from a common source of contamination related to urinary tract devices.

Introduction

Among Gram-negative bacilli, Enterobacteriaceae constitute the most common cause of infection in kidney transplant recipients (KTRs), in whom Enterobacteriaceae typically cause urinary tract infections (UTIs).[1] Although *Escherichia coli* is the species most often isolated, other Enterobacteriaceae species, especially those with MDR strains, have been growing in importance.[2]

Carbapenems are broad-spectrum β-lactam antibiotics that are highly effective against Enterobacteriaceae and are commonly used in the treatment of infections caused by ESBL-producing strains.[3] However, recent studies have reported the emergence of carbapenem-resistant strains of Enterobacteriaceae.[4]

Known risk factors for healthcare-associated infections with carbapenem-resistant Enterobacteriaceae (CRE) include solid organ transplantation (SOT), immunosuppression therapy, mechanical ventilation, prolonged use of invasive devices, use of antimicrobial agents and a high APACHE score.[5–7] In patients with CRE infection, there is often a delay in the introduction of effective therapy, as well as prolonged hospitalization after diagnosis.[7,8] Consequently, high mortality rates (28%–68%) have been reported in cases of CRE infection.[7,8] Among SOT recipients infected with CRE, mortality can be as high as 71% and CRE infection has been shown to be independently associated with an increased risk of death.[3,9–11]

Data related to CRE infection in KTRs are scarce. Most relevant reports deal with *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* (KPC-Kp).[9–11] Such studies have reported that KPC-Kp infection occurs most frequently in the first 2 months after SOT, with a combined incidence of 13%, and that the urinary tract is the most common site of infection. Mortality associated

with CRE infection in SOT recipients reportedly ranges from 33% to 50%.[10,11] Infection with carbapenem-resistant *Enterobacter* spp. is rare in SOT recipients, especially in KTRs, although a few cases have been reported.[2,12] *Enterobacter gergoviae* is an uncommon human pathogen and, to our knowledge, infection with *E. gergoviae* has never been described in SOT recipients.

The aim of this study was to describe an outbreak of carbapenem-resistant *E. gergoviae* (CREG) in KTRs. An additional objective was to investigate possible sources of this microorganism and risk factors for its acquisition.

Methods

Design and setting

This was a case–control study conducted at Hospital das Clínicas, a 1000 bed tertiary care hospital affiliated with the University of São Paulo School of Medicine, in Brazil. KTRs were managed in a urological emergency room and in the kidney transplantation unit, which has a 20 bed adult ward. The median annual number of kidney transplants between 2009 and 2014 was 216.

CREG outbreak

In April 2014, CREG was isolated in five KTRs. Two isolates were from perirectal swabs, which were collected on a weekly basis in the kidney transplantation ward for CRE screening, and three were from clinical cultures. A retrospective review of patient records kept by the Infection Control Department and records of the Microbiology Laboratory revealed that CREG had first been detected in January 2009 and that sporadic cases had since occurred, but only in KTRs. Throughout the study period, surveillance cultures for CRE (from perirectal swabs) had been performed for all patients transferred from other hospitals, as well as on a weekly basis for patients in ICUs. Since September 2012, weekly surveillance cultures had also been collected from patients in the kidney transplantation ward.

Cases occurring in patients who had not had >48 h contact with another CREG-positive patient in the last 6 months were classified as primary cases, whereas those occurring in patients whose first CREG-positive culture was detected within the first 6 months after they had spent >48 h on the same ward as another CREG-positive patient were classified as secondary cases, suggesting cross-patient transmission. The zone of acquisition was defined as the unit of the hospital in which the patient had stayed within the last ≥3 calendar days before the first CREG-positive culture, or less time for cases in which an invasive device was thought to have played a role in CREG acquisition.[13]

Infection control measures

After the outbreak was identified, control measures were instigated, including hand hygiene training, feedback of data on CREG to clinical staff and audits of infection control practice. Patients with CREG were isolated or cohorted and barrier nursed during both their hospital stay and any readmissions. In addition, the cleaning and sterilization of surgical instruments used in urological procedures, including biopsy guns, was reviewed, as was the reprocessing of single-use medical devices. A protocol for weekly, hospital-wide surveillance for CREG was additionally implemented.

Microbiological analysis

Environmental cultures

Environmental screening and screening for staff carriage was undertaken in May 2014. Swabs were taken from sinks, taps, drains, biopsy guns (trigger and external parts), electric clippers, computers, ultrasound equipment, soap dispensers, blood pressure monitors, urine collection bags, containers used for measuring drain fluid and surfaces within the nurses' stations. Hand swabs were collected from all staff who had been in close contact with KTRs, including the surgeons. Swabs were obtained as staff came on duty to minimize the detection of transient flora.

All environmental samples were cultured in brain heart infusion broth supplemented with meropenem (0.5 mg/L) and incubated overnight at 37°C. Cultures that showed growth were spread onto MacConkey agar and again incubated overnight at 37°C. Suspected colonies were identified using MALDI-TOF MS (MS-VITEK; bioMérieux, Marcy-l'Étoile, France).

Antimicrobial susceptibility testing

An automated susceptibility testing system (VITEK; bioMérieux) was used in order to identify CREG strains among the *E. gergoviae* strains isolated from clinical or perirectal surveillance cultures. MICs were interpreted using CLSI breakpoints.[14] All CREG isolates were analysed by PCR for presence of the bla_{KPC} gene. Tests using imipenem and meropenem discs alone or in combination with EDTA were done to detect metallo-β-lactamase (MBL) enzymes. Presence of bla_{MBL} genes was assessed by multiplex PCR.[15] Sanger sequencing of PCR amplicons following clean-up was carried out to differentiate bla_{IMP} types.

PFGE

After extraction and digestion of whole bacterial DNA with the XbaI restriction enzyme (50 U; New England Biolabs, London, UK), we performed PFGE, using an electric field system (CHEF-DR III; Bio-Rad Laboratories, Hercules, CA, USA), in accordance with the CDC protocol.[16] Running parameters were initially switched to 2.2 s and finally switched to 54.2 s. Total length of time was 19 h, temperature was 14°C and 6 V/cm was used.

Acquired images were analysed with BioNumerics software, version 5.0 (Applied Maths, Sint-Martens-Latem, Belgium). Using the unweighted pair group method with arithmetic mean, we constructed a dendrogram based on the Dice coefficient (1.0% tolerance). Isolates showing ≥80% similarity were classified as being closely related.

Case–control study

As all patients from whom CREG were isolated were KTRs, cases were defined as KTRs with a CREG-positive culture between January 2009 and December 2014. Using a random number table, we selected matched controls (KTRs hospitalized for >72 h on the same ward and at the same time as the matching cases), at a case/control ratio of 1:2.

We analysed the following variables: age; gender; donor type (living or deceased); type of transplantation (single or multiple); retransplantation; diabetes mellitus; SOFA score at admission; type of immunosuppression; dialysis; use of invasive devices (surgical drain, urinary catheter, mechanical ventilator or central venous catheter); antibiotic use; ureteral stent use; having undergone another type of surgery in the last 3 months; kidney biopsy in the last month; length of hospital stay; length of ICU stay; acute cellular rejection and its treatment (plasmapheresis, rituximab, antithymocyte globulin or corticosteroid pulse therapy); antithymocyte globulin induction therapy; surgeon who did kidney transplantation; and colonization with other MDR bacteria. For cases, variables related to exposure time were recorded from admission to the first CREG-positive culture. For controls, these variables were recorded for the total time at risk during the hospital stay. The criteria used in identifying and classifying healthcare-associated infections were those outlined by the US National Healthcare Safety Network.[17]

Statistical analysis

The incidence density was calculated for cases where acquisition was related to kidney transplantation as follows: number of new

cases in the period/number of patient-days in the ward in the same period.

In the statistical analysis, we used the χ^2 test or Fisher's exact test, as indicated, and calculated odds ratios for dichotomous variables, whereas we used the Mann–Whitney test for continuous variables. Variables showing $P \leq 0.2$ in a univariate analysis were included in a multivariate analysis, which was performed by stepwise logistic regression. Variables that then reduced the −2 log likelihood or showed $P \leq 0.05$ were retained in the model. All statistical analyses were performed with the Statistical Package for the Social Sciences, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Clinical characteristics and epidemiology analysis

Twenty-six cases were identified during the study period. As depicted in Figure 1, we identified two clusters, one in 2009 (5 cases, 1 of which was classified as secondary) and another in the 2013–14 period (14 cases, 12 of which were classified as secondary). The incidence of CREG per quarter ranged from zero to 2.68/1000 KTR-days in the kidney transplantation ward. No more cases were identified after August 2014.

As shown in Table 1, CREG acquisition was traced to two units: the kidney transplantation ward, in 22 cases (84.6%); and the urological emergency room, in 4 cases (15.4%). One of the patients in the latter group had a hospital stay of <3 days and had been submitted to urinary catheterization before culture collection, but had not been hospitalized within the preceding 6 months. The median time between the kidney transplantation procedure and CREG acquisition was 25.5 days; 15 (57.7%) cases acquired CREG in the first month after kidney transplantation.

Of the 26 CREG-positive patients, 18 (69.2%) were male, 15 (57.7%) had received a deceased-donor kidney, 20 (76.9%) acquired CREG in first 60 days after kidney transplantation and 19 (73.1%) did not develop CREG infection.

In 19 cases (73.1%) CREG was identified in a urine sample, whereas it was identified in a perirectal swab sample in 5 (19.2%). Only one patient had CREG isolated in urine and perirectal swab samples. Of the 21 patients in whom CREG was isolated from samples other than perirectal swab samples, 13 (61.9%) had at least one negative perirectal swab culture for CRE after CREG isolation.

Seven patients developed CREG infection (five UTIs and two organ-space surgical infections), but none developed bacteraemia. Three were treated with a carbapenem/polymyxin combination and four received monotherapy (with imipenem, ciprofloxacin, amikacin and polymyxin E, respectively). In all seven cases, the CREG infection resolved, although one patient died during the hospital stay in which CREG was acquired (Table 1).

In five cases (19.2%), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) and CREG were isolated in the same urine sample, although the former were rare at our facility. In six patients, other MDR bacteria were isolated, including carbapenem-resistant *K. pneumoniae* ($n=2$), vancomycin-resistant *Enterococcus* spp. ($n=2$), a combination of carbapenem-resistant *K. pneumoniae*

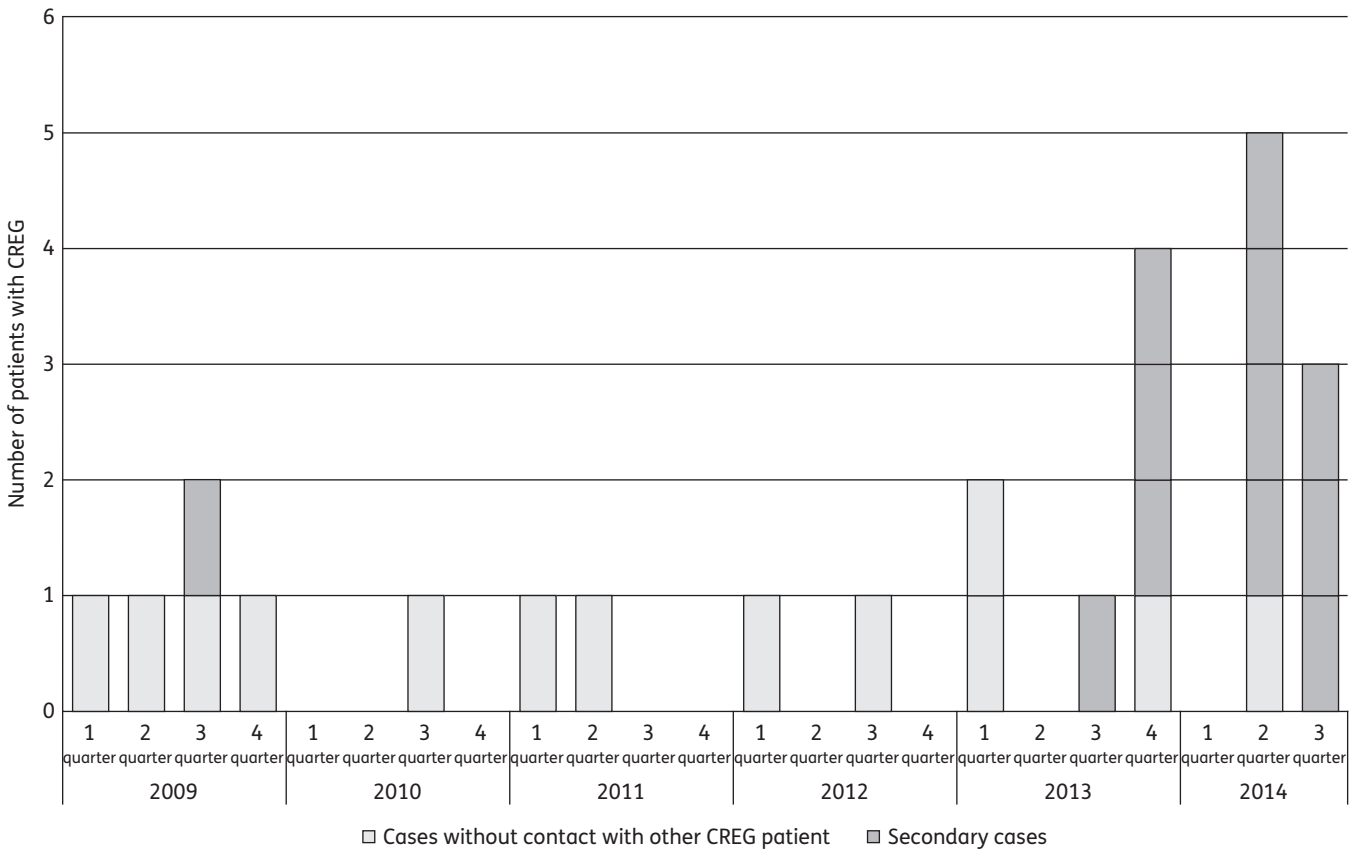

Figure 1. Distribution of primary and secondary cases of CREG acquisition between 2009 and 2014, by quarter.

Table 1. Description, treatment and outcomes of 26 KTRs with positive cultures for CREG

Case	Gender	Date of first CREG-positive culture (dd/mm/yyyy)	Zone of CREG acquisition	Acquisition classification	Time (days)[a]	Culture material	Manifestation	PS culture	PFGE subtype	Treatment	Outcome
1	female	05/01/2009	KT ward	primary	37	urine	colonization	SNC	clone A	none	discharge
2	male	30/06/2009	UER	primary	40	urine	UTI	negative	clone B	imipenem + polymyxin B	discharge
3	male	30/07/2009	KT ward	primary	23	urine	colonization	negative	clone B	none	discharge
4	female	24/09/2009	KT ward	secondary	26	urine	UTI	SNC	NP	ciprofloxacin	discharge
5	male	28/12/2009	KT ward	primary	6	urine	colonization	SNC	clone B	none	discharge
6	male	16/09/2010	KT ward	primary	1006	urine	colonization	SNC	NP	none	death
7	female	05/02/2011	UER	primary	275	urine	colonization	SNC	clone A	none	discharge
8	female	13/04/2011	KT ward	primary	25	urine	colonization	SNC	clone A	none	discharge
9	female	17/02/2012	KT ward	primary	234	urine	UTI	negative	clone A	imipenem + polymyxin B	discharge
10	female	08/08/2012	KT ward	primary	4	PS	colonization	positive	clone A	none	discharge
11	male	04/01/2013	KT ward	primary	53	urine	SSI	positive	clone A	imipenem	discharge
12	male	24/02/2013	UER	primary	2420	urine	UTI	SNC	clone A	amikacin	discharge
13	female	18/09/2013	KT ward	secondary	35	urine	SSI	negative	clone A	meropenem + polymyxin E	discharge
14	male	05/11/2013	KT ward	primary	6	PS	colonization	positive	NP	none	discharge
15	female	22/11/2013	KT ward	secondary	16	urine	colonization	negative	clone A	none	discharge
16	male	01/12/2013	KT ward	secondary	8	urine	colonization	negative	clone A	none	discharge
17	male	13/12/2013	KT ward	secondary	15	urine	colonization	negative	clone A	none	discharge
18	male	08/04/2014	KT ward	secondary	31	PS	colonization	positive	NP	none	discharge
19	male	13/04/2014	KT ward	secondary	11	CB	colonization	negative	clone A	none	discharge
20	male	17/04/2014	UER	secondary	43	urine	colonization	negative	clone A	none	discharge
21	male	19/04/2014	KT ward	primary	4	DF	colonization	negative	NP	none	discharge
22	male	29/04/2014	KT ward	secondary	41	PS	colonization	positive	NP	none	discharge
23	male	10/06/2014	KT ward	secondary	971	PS	colonization	positive	clone A	none	discharge
24	male	03/08/2014	KT ward	secondary	16	urine	colonization	negative	NP	none	discharge
25	male	07/08/2014	KT ward	secondary	18	urine	UTI	negative	clone A	polymyxin E	discharge
26	male	14/08/2014	KT ward	secondary	4243	Urine	colonization	negative	clone A	none	discharge

PS, perirectal swab; KT, kidney transplantation; SNC, sample not collected; UER, urological emergency room; SSI, surgical site infection; CB, catheter blood; DF, drain fluid; NP, not performed.
[a]Time from transplantation to CREG acquisition.

and vancomycin-resistant *Enterococcus* spp. ($n=1$), and carbapenem-resistant *Acinetobacter baumannii* ($n=1$).

The audit of infection control practices detected flaws in the process of cleaning and sterilizing the biopsy gun. The biopsy gun was used on several patients in a day and the process of cleaning and sterilizing was performed only at the end of each day. Another notable mistake was the urine collectors used by the patients. Another notable procedural flaw identified was that the urine collectors used by the patients lacked identification and were left in a communal bathroom, resulting in individual collectors being shared between patients. Moreover, there was no supervision of the cleaning process, with patients being advised to clean the urine collectors themselves after each use. Recommendations to adjust those processes were made.

Table 2. Drug susceptibility of *E. gergoviae* strains isolated from 26 KTRs

Antibiotic	Susceptibility		Resistant strains, *n* (%)
	MIC range (mg/L)	50th percentile MIC (mg/L)	
Imipenem	≤1 to ≥16	8	21 (80.8)
Meropenem	≤1 to ≥16	≥16	22 (84.6)
Polymyxin	<0.5	<0.5	0 (0)
Ertapenem	4 to ≥8	≥8	26 (100)
Tigecycline	0.5 to ≥8	2	5 (20.0)
Gentamicin	≤1 to ≥16	≥16	20 (76.2)
Amikacin	≤2 to ≥64	≥64	15 (57.1)
Ciprofloxacin	1 to >4	≥4	25 (95.2)

Microbiology characteristics and PFGE analysis

All isolated CREG strains were susceptible to polymyxin. Among the carbapenems tested, more strains were susceptible to imipenem than to any other. The proportion of amikacin-resistant strains increased progressively during the study period (Table 2). All *E. gergoviae* isolates were confirmed to be MBL producers by use of the imipenem and meropenem plus EDTA discs. The PCR for bla_{KPC} was negative in all strains and the bla_{IMP} genes were detected in all *E. gergoviae* isolates. DNA sequencing identified bla_{IMP-1} in all *E. gergoviae* isolates. PFGE analysis was performed for 19 strains; 16 (84.2%) presented profile A and 3 (15.8%) presented profile B (Figure 2).

Environmental investigation

Thirty-six environmental samples were collected and none tested positive for CREG. Other Enterobacteriaceae were detected in five environmental samples (Table 3): two from computers, one from a soap dispenser and four from bathroom sink drains. Twenty-three hand samples were collected and none tested positive for CREG, but seven tested positive for other Enterobacteriaceae (Table 3): four from transplant surgeons, two from nurses and one from a nephrologist.

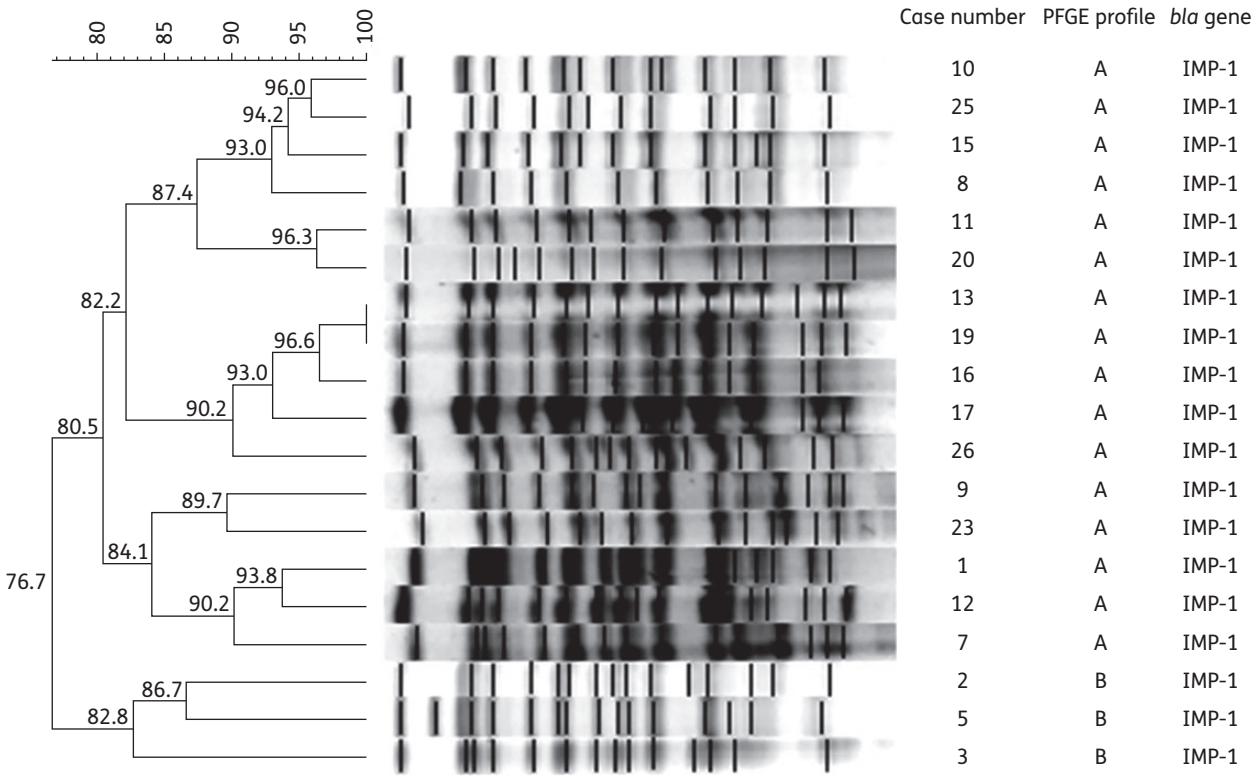

Figure 2. PFGE of genomic DNA, digested with restriction enzyme XbaI, of CREG isolates. The dendrogram was based on the Dice coefficient, with the unweighted pair group method with arithmetic mean clustering.

Table 3. Bacteria isolated from environmental cultures (total number of samples collected = 36) and from cultures of healthcare worker hand samples (total number of samples collected = 23)

Type of sample	Microorganism	Source of sample collection	Number of isolates
Environmental	*Pseudomonas aeruginosa*	bathroom sink drain	2
	Enterobacter cloacae	bathroom sink drain, computer screen and computer keyboard	3
	Pseudomonas putida	bathroom sink drain	1
	Stenotrophomonas maltophilia	bathroom sink drain	1
	Klebsiella pneumoniae	bathroom sink drain	1
	Leclercia adecarboxylata	soap dispenser	1
Healthcare worker hand (professional category)	*Citrobacter koseri*	nephrologist ($n=1$)	1
	Klebsiella oxytoca	surgeon ($n=2$); assistant nurse ($n=1$)	3
	Serratia marcescens	surgeon ($n=1$); assistant nurse ($n=1$)	2
	Citrobacter braakii	surgeon ($n=1$)	1

Case–control study

Univariate analysis identified certain risk factors for CREG acquisition by KTRs: male gender; retransplantation; had been submitted to a surgery by Surgeon 2; ureteral stent use; CRPA colonization; and having undergone another type of surgery in the last 3 months. The variables that remained significant in the multivariate analysis were male gender, advanced age, retransplantation and ureteral stent use (Table 4); the Hosmer–Lemeshow test for the final model had *P* 0.89.

Discussion

Although not a common human pathogen, *E. gergoviae* has been implicated in cases of primary bacteraemia, traumatic endophthalmitis, neonatal sepsis, abdominal abscess, pneumonia, osteomyelitis and UTI.[18–23] The reported frequency of such cases is higher among immunocompromised hosts, such as neonates and patients infected with HIV, as well as those with haematological malignancy, lung cancer or liver failure. In two previous reports of CREG infection, the outcomes were unfavourable.[19,22] Although the outbreak described in the present study also involved immunocompromised patients, the frequency of infection was low and the success rate of antibiotic therapy was high, which allows us to infer that *E. gergoviae* has low virulence. In support of that hypothesis is our finding that none of the CREG-positive patients developed a bloodstream infection.

In the present study, the most common site of CREG infection was the urinary tract. Although none of the seven CREG-infected patients required retreatment, five (71%) had positive cultures after treatment. In other studies of KTRs, the urinary tract has also been shown to be the most common site of CRE infection and the reported UTI recurrence rate is high (11%–50%).[10–12]

Although Enterobacteriaceae are common agents of infection after kidney transplantation, there have been few outbreaks of these bacteria in kidney transplantation units.[1] Martins *et al*.[24] reported a monoclonal outbreak of ESBL-producing *K. pneumoniae* on a kidney transplantation ward, in which ESBL-producing *K. pneumoniae* infection was detected in six KTRs. The authors suggested that the outbreak was caused by cross-contamination. A reported outbreak of OXY-2-producing *Klebsiella oxytoca* in a renal transplant unit was also monoclonal.[25] However, an outbreak of *Enterobacter cloacae* susceptible only to carbapenem on a paediatric kidney transplantation ward was found to be polyclonal and most of the cases occurred in the late post-transplant period.[26] Therefore, there is no prevailing model for Enterobacteriaceae outbreaks among KTRs.

In the present study, the incidence of CREG was bimodal. We assume that, during the two high-incidence periods, the main means of CREG transmission was through cross-contamination between patients in the same ward. However, given that the outbreak period was long, that the incidence of CREG was low during most of the period and that (despite the size of the hospital) the bacteria were restricted to a specific population, a common source of CREG is highly probable. Although our microbiological investigation of the environment failed to identify a common source, the inappropriate infection control practices identified could explain the persistence of CREG among the KTRs. Such practices included inadequate cleaning of biopsy guns, inappropriate reprocessing of surgical instruments, sharing of urine collectors and inefficient disinfection of devices between uses. It is well known that environment cultures have low sensitivity. Although outbreaks with an identified source are more likely to be published, many outbreaks failed to identify specific causes, and bundles of measures are usually effective in controlling these outbreaks.

Our findings that most patients did not develop infection and that the infections detected were of low severity allow us to predict that any common source would have had a small inoculum and possibly low pathogenicity. Another argument supporting the existence of a common source (that was eliminated after infection control measures had been taken) is the frequency of co-colonization by CRPA, which is not a common agent at our facility and is typically associated with outbreaks caused by environmental contamination.[27,28]

Many outbreaks of *P. aeruginosa* or Enterobacteriaceae have been attributed to contamination during urological procedures,[29,30] The contaminated materials have ranged from forceps tips to a urodynamic system pressure dome, an endoscopic camera, an operating room table and a biopsy needle guide.[27–30] Although other outbreaks have been epidemiologically related to urology procedures, environmental cultures have not linked

Table 4. Univariate and multivariate analysis of the risk of CREG acquisition among KTRs

Variable	Cases ($n=26$)	Controls ($n=52$)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	*P*	OR (95% CI)	*P*
Demographic characteristics						
age (years), median (range)	56 (18–69)	47 (22–72)		0.15	1.05 (1.01–1.11)	0.02
male gender, *n* (%)	19 (73.1%)	23 (44.2%)	3.42 (1.23–9.54)	0.02	3.53 (1.09–11.38)	0.03
diabetes mellitus, *n* (%)	9 (34.6%)	13 (25%)	1.59 (0.57–4.42)	0.37		
KT procedure characteristics						
deceased donor, *n* (%)	15 (57.7%)	34 (65.4%)	0.72 (0.28–1.90)	0.51		
combined transplant, *n* (%)	0	4 (7.7%)	0.92 (0.85–1.00)	0.30		
retransplantation, *n* (%)	7 (26.9%)	5 (9.6%)	3.46 (0.98–12.27)	0.05	7.00 (1.24–39.04)	0.03
KT performed by a less experienced surgeon, *n* (%)	7 (26.9%)	4 (7.7%)	4.42 (1.16–16.86)	0.04		
Healthcare assistance in the period of CREG acquisition						
antithymocyte globulin use, *n* (%)	13 (50%)	22 (42.3%)	1.36 (0.53–3.51)	0.52		
SOFA score at admission, median (range)	4 (1–6)	4 (0–7)	0.77 (0.28–2.11)	0.95		
another type of surgery in the last 3 months, *n* (%)	24 (92.3%)	35 (67.3%)	5.83 (1.23–27.59)	0.02		
renal biopsy in the last 30 days, *n* (%)	16 (61.5%)	37 (71.2%)	0.65 (0.24–1.75)	0.39		
ureteral stent use, *n* (%)	15 (57.7%)	11 (21.2%)	5.08 (1.83–14.15)	0.001	3.99 (1.28–12.43)	0.02
central venous catheter use, *n* (%)	22 (84.6%)	37 (71.2%)	2.23 (0.66–7.57)	0.27		
abdominal drain use, *n* (%)	14 (53.8%)	18 (34.6%)	2.20 (0.84–5.75)	0.10		
length of urinary catheter use (days), median (range)	6 (0–25)	5 (0–29)		0.15		
length of hospital stay (days), median (range)	10 (1–43)	18 (3–160)		0.56		
ICU admission, *n* (%)	8 (30.8%)	19 (36.5%)		0.38		
dialysis, *n* (%)	15 (57.7%)	26 (50%)	1.36 (0.53–3.52)	0.52		
acute cellular rejection, *n* (%)	5 (19.2%)	17 (32.7%)	0.49 (0.16–1.52)	0.21		
corticosteroid pulse therapy, *n* (%)	4 (15.4%)	18 (34.6%)	0.34 (0.10–1.15)	0.11		
plasmapheresis, *n* (%)	2 (7.7%)	7 (13.5%)	0.54 (0.10–2.78)	0.71		
treatment with cephalosporin, *n* (%)	12 (46.2%)	25 (48.1%)	0.93 (0.36–2.38)	0.87		
treatment with carbapenem, *n* (%)	5 (19.2%)	17 (32.7%)	0.49 (0.16–1.52)	0.29		
another healthcare-associated infection, *n* (%)	9 (34.6%)	23 (44.2%)	0.67 (0.25–1.77)	0.42		
colonization by CRPA, *n* (%)	5 (19.2%)	1 (1.9%)	12.1 (1.34–110.3)	0.01		
colonization by other MDR bacteria, *n* (%)	11 (42.3%)	20 (38.5%)	1.17 (0.45–3.06)	0.74		

KT, kidney transplantation.

the causative agents to the environment.[31,32] In our study, none of the urological procedures, surgical instruments or operating rooms was employed exclusively in KTRs; only the surgical team was exclusive, which led us to focus our investigation on the kidney transplantation ward and on a possible kidney transplantation staff member colonized by CREG.

Another unique feature of this outbreak is the CREG producing carbapenemase IMP, all of them belonging to the same PFGE cluster. IMP is an enzyme not commonly found in Enterobacteriaceae and the majority of reports of Enterobacter harbouring IMP-1 are from Asia and Oceania.[33,34] Conversely, IMP carbapenemases are frequently described in *P. aeruginosa*, including in Brazil, which also corroborates the hypothesis of a common source for this outbreak and the possible transfer of the bla_{IMP} gene between these two bacteria.[35] To our knowledge this is the first description of IMP-producing *Enterobacter* in Brazil.

Our finding that male gender was a risk factor for infection following kidney transplantation was surprising, because such infection, especially UTI, is typically more common among females.[36] Although we found no difference between genders in terms of the surgical materials used or procedures performed, urine collection devices are gender-specific. In addition, each room on our kidney transplantation ward has two beds and a shared bathroom, which favoured cross-contamination only between patients of the same gender. Although this finding had a plausible explanation, it is always possible that this association was aleatory due to the small number of cases in the present outbreak.

Advanced age is a known risk factor for infection in the general population (because of immunosenescence) and has been associated with a higher incidence of infections such as UTIs and surgical site infections, as well as with an increased risk of infection with MDR bacteria, in KTRs.[2,37] Our findings regarding advanced age and CREG acquisition are in agreement with those of previous studies of such agents in KTRs.

We also found that retransplantation was a risk factor for CREG acquisition. Patients undergoing retransplantation are known to be at higher risk of bacterial infections, particularly UTIs.[37] Many factors contribute to this risk, including aggressive immunosuppression therapy, multiple surgical procedures and a high number of anatomical abnormalities of the bladder.

Another risk factor for CREG acquisition identified in our case–control study was the use of a ureteral stent, which is common after kidney transplantation and has previously been identified as a risk factor for UTI in general.[38] The use of a ureteral stent permits biofilm formation and facilitates bacterial growth. Assuming a common source with a small inoculum, we believe that ureteral stent use increased the risk of CREG acquisition/persistence among the patients evaluated in our study.

Here, we have described an outbreak of CRE among KTRs, likely attributable to a common source that was not identified, but the modification of deficiencies in infection control procedures successfully controlled the outbreak.

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Transparency declarations

None to declare.

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