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ARTICLE

The epidemiology of the first described carbapenem-resistant *Klebsiella pneumoniae* outbreak in a tertiary care hospital in Saudi Arabia: how far do we go?

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Abstract The purpose of this investigation was to describe the first documented carbapenem-resistant *Klebsiella pneumoniae* (CRKP) outbreak in a tertiary care facility in Saudi Arabia. We initiated a prospective study to follow all cases of CRKP as well as the active surveillance of patients in areas where cases were identified. We also conducted a retrospective review of the microbiology database for any missed cases of CRKP. Pulsed field gel electrophoresis (PFGE) was conducted for the available CRKP isolates. During March 2010, a cluster of eight CRKPs was detected primarily in the adult intensive care unit (ICU). Patients with CRKPs were put under strict contact isolation, along with appropriate infection control measures. A retrospective review of *K. pneumoniae* isolates over the previous 6 months revealed two more CRKPs. The PFGE results during the outbreak period showed that the majority of strains were genetically indistinguishable or closely related. The majority of patients had prolonged hospital stay (91%), indwelling devices (81%), surgical procedures (74%), carbapenem use (62%), and colonization/infection with other multiple drug-resistant organisms (MDROs) (57%). Two-fifths of patients with CRKP had clinical infection and 38% died during the current hospitalization. Contact isolation, hand hygiene, environmental cleaning, and staff education may control CRKP outbreak in the acute care setting, but did not prevent endemicity.

Background

Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is a global concern, leading to healthcare-associated infections

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worldwide. The most important mechanism of resistance is the production of a carbapenemase enzyme that has the ability to hydrolyze carbapenems [1]. Since its first description in North Carolina in 1996 [2], carbapenemase-producing *K. pneumoniae* (KPC) has been identified in 24 states across the US [3]. CRKP is currently seen all over the world [4–6]. There have been no described outbreaks with CRKP reported from Saudi Arabia or Gulf Cooperation Council (GCC) States.

Healthcare-associated infections (HAIs) caused by CRKP may be linked to increased mortality, length of hospitalization, and increased cost [7]. Data from the National Healthcare Safety Network (NHSN; Centers for Disease Control and Prevention [CDC], Atlanta GA, USA) showed that 8.7% of *Klebsiella* isolates causing HAIs in 2006–2007 were carbapenem-resistant compared to just less than 1% in 2000 [8, 9]. Since carbapenems are considered as an effective last line of defense in the treatment of severe infections caused by antimicrobial-resistant *Enterobacteriaceae*, CRKP represent a global threat to the control of HAIs, particularly in the presence of very limited therapeutic options [3]. Moreover, the difficulty of CRKP detection using routine antibiotic susceptibility testing adds to the complexity of the CRKP challenge in the healthcare setting [10]. The CDC recommends aggressive infection control measures to control the CRKP spread in acute care (inpatient) facilities that include early detection and active surveillance [9]. We sought to describe our experience in detecting and containing the first documented CRKP outbreak in Saudi Arabia.

Methods

Setting

The current study was conducted at King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia. KAMC is an approximately 900-bed tertiary care facility that provides healthcare services to about 600,000 Saudi National Guard soldiers, employees, and their families. The care provided ranges from primary and preventive care to tertiary care. KAMC has eight different intensive care units (ICUs) and four step-down units.

Study design

This a retrospective/prospective surveillance study describing the outbreak investigation and containment.

Surveillance and isolation methods

The outbreak was declared after reviewing the first three CRKP isolates at adult ICUs (between March 5th and 13th, 2010). Patients were then placed under strict contact isolation, along with intensified infection control measures and hand hygiene observation. The emerging cluster of CRKP patients were examined prospectively for microbiological and clinical data until discharge or death. The contacts of all clinical cases were screened, minimally through a peri-rectal swab; however, those who were ventilated were also screened through an endotracheal culture and placed under contact isolation until the culture results were available. Included in our study are patients with the first isolate of CRKP related to either a clinical infection or colonization. Patients who were positive by screening surveillance initially and then had invasive disease due to CRKP were reported according to the first positive specimen. The possibility of previously unnoticed CRKP cases was explored through a retrospective review of the microbiology database for any suspected cases of carbapenem resistance among the multiple drug-resistant *K. pneumonia* isolates over the previous 6 months. Commencing March 24th, weekly active surveillance cultures for CRKP were obtained from all ICU patients using rectal swabs and respiratory specimens. In addition, any new admission to the ICU was screened via peri-rectal swab and placed in contact isolation until the results were available. Weekly active surveillance was replaced by monthly active surveillance after declaring the end of the outbreak. Patients who became ready for transfer from the ICU were maintained on contact isolation in the receiving ward until the results became available. Those who were found to be colonized received weekly surveillance cultures until they became negative or until they were discharged.

Data collection

A standard data collection form was developed and discussed with infection control staff who were responsible for data collection. Index data was defined as the first date of CRKP isolation from surveillance or clinical cultures. Data collection involved using current and previous patient clinical records, microbiology laboratory records, and, sometimes, contact with the treating physician. Data collected included demographic data, location and duration of hospital stay, clinical presentation (clinical healthcare-associated infections or colonization), clinical severity score, comorbid medical conditions, current antimicrobial therapy, potential risk factors for multiple drug resistance, and outcome data (discharge or death) (Table 1 and 2). Potential risk factors at the index date were clearly defined (as shown in Table 3) before the start of data collection. Death was defined as death occurring during the current hospitalization (up to August 31), irrespective of hospital location at the time of death.

Table 1 Demographic and clinical characteristics of confirmed carbapenem-resistant *Klebsiella pneumoniae* (CRKP) cases at King Abdulaziz Medical City (Riyadh, Saudi Arabia) between September 2009 and August 2010

ID	Age	Sex	PFGE strain	Primary diagnosis on admission*	Hospital transfer	Hospital admission date	Initial admission location*	Index date (first positive)	Admission location at index date	Stay in index location before index date*	Hospital days before index date	Days of current ICU stay	Source of first positive isolate	Presentation of infection	Recent carbapenem intake	History of MDRO	Outcome	Days to outcome
1	76	Male	A1	Acute coronary syndrome	No	02-Sep-09	Ward	01-Dec-09	Ward	Yes	90	12	Wound	Wound infection	Yes	Yes	Death	216
2	68	Female		Liver failure and stroke	No	30-Jan-10	Emergency	23-Feb-10	Adult ICU	Yes	24	29	Respiratory	Colonization	No	No	Death	8
3	40	Female	D	Liver failure and intestinal obstruction	No	12-Dec-09	Emergency	5-Mar-10	Adult ICU	Yes	83	68	Urine	Colonization	Yes	Yes	Death	33
4	22	Male		MVA	Yes	22-Feb-10	Adult ICU	9-Mar-10	Adult ICU	Yes	15	30	Respiratory	Colonization	Yes	Yes	Still in hospital	175
5	28	Male	B1	MVA	No	8-Mar-10	Adult ICU	13-Mar-10	Adult ICU	Yes	5	17	Wound	Wound infection	Yes	Yes	Discharged home	38
6	77	Female	A1	Gastric outlet obstruction	No	21-Jan-10	Emergency	24-Mar-10	ICU step-down	Yes	62	77	Rectal	Colonization	Yes	Yes	Death	31
7	66	Male	A3	Liver failure and hepatitis C	No	11-Feb-10	Adult ICU	27-Mar-10	Liver step-down	Yes	44	63	Blood	BSI	No	Yes	Death	103
8	19	Female	A1	Liver failure and biliary atresia	No	16-Mar-10	Liver step-down	28-Mar-10	Adult ICU	Yes	12	15	Respiratory	Colonization	Yes	Yes	Death	4
9	27	Male	A1	Patellal fracture	No	31.3.2010	Ward	31-Mar-10	Ward	No	0	NA	Wound	Colonization	No	No	Discharged home	4
10	81	Male	A1	UTI and renal impairment	Yes	31-Mar-10	Emergency	6-Apr-10	Adult ICU	Yes	6	5	Rectal	Colonization	No	No	Discharged home	41
11	35	Female		Renal failure	No	30-Mar-10	Emergency	8-May-10	Ward	Yes	39	24	Wound	Wound infection	Yes	No	Discharged home	49
12	43	Male		Calcaneal fracture	Yes	22-Apr-10	Emergency	1-Jun-10	Ward	No	40	NA	Wound	Colonization	Yes	Yes	Discharged home	89
13	72	Female		Shortness of breath	No	18-May-10	Emergency	4-Jun-10	Adult ICU	Yes	17	55	Respiratory	Colonization	Yes	Yes	Death	52
14	72	Female	A1	Infected wound	No	21-Apr-10	Emergency	16-Jun-10	Ward	Yes	56	14	Wound	Infected wound	No	Yes	Discharged home	38
15	32	Female	B1	Epilepsy	No	11-Apr-10	Emergency	7-Jul-10	Ward	No	87	NA	Wound	Abscess	No	No	Still in hospital	55
16	34	Female	A2	MVA	No	5-Jul-10	Adult ICU	18-Jul-10	Adult ICU	Yes	13	32	Respiratory	Colonization	Yes	No	Still in hospital	44
17	60	Female	A2	Heart failure	No	16-Jun-10	Emergency	22-Jul-10	ICU step-down	Yes	36	30	Urine	Colonization	No	No	Death	7
18	31	Female	A1	Abdominal pain during pregnancy	No	15-Jul-10	Adult ICU	15-Aug-10	ICU step-down	Yes	31	46	Catheter tip	BSI	Yes	No	Still in hospital	16
19	52	Male	C	Post-amputation gangrene	No	6-Aug-10	Adult ICU	21-Aug-10	Adult ICU	Yes	15	25	Wound	Gangrene	Yes	Yes	Still in hospital	10
20	81	Male	B2	Parkinsonism	No	22-Aug-10	Emergency	22-Aug-10	Emergency	No	0	1	Urine	Colonization	No	No	Still in hospital	9

PFGE, pulsed field gel electrophoresis; multiple drug-resistant organism (MDRO); ICU, intensive care unit; MVA, motor vehicle accident; index location, adult ICU or ICU step-down; UTI, urinary tract infection

Table 2 Demographic and clinical characteristics of patients with CRKP at King Abdulaziz Medical City (Riyadh, Saudi Arabia) between September 2009 and August 2010

Age (years)	
Mean±SD	50.8±21.8
≤18	0 (0%)
19–59	12 (60%)
≥60	8 (40%)
Sex	
Male	9 (45%)
Female	11 (55%)
Primary diagnosis	
Trauma (MVA or fractures)	5 (25%)
Liver or kidney failure	5 (25%)
Neurological disease	3 (15%)
Gastrointestinal obstruction	2 (10%)
Sepsis	1 (5%)
Other	6 (30%)
Comorbidity	
Surgery	10 (50%)
Hypertension	10 (50%)
Diabetes	9 (45%)
Trauma	6 (30%)
Gastrointestinal disease	5 (25%)
Liver disease	5 (25%)
Heart disease	5 (25%)
Renal disease	4 (20%)
Immunosuppression	3 (15%)
Lung disease	3 (15%)
Stroke	3 (15%)
APACHE III score (median and IQR, days)	67.0 (44.8–95.0)
First admission location	
Emergency rooms	11 (55%)
Adult ICU	6 (30%)
Step-down unit or wards	3 (15%)
Current intensive care admission	17 (85%)
Hospital and ICU stay (median and IQR, days)	
Stay before index date	27.5 (12.3–53.0)
Total ICU stay	29.0 (14.5–50.5)
Total hospital stay	63.0 (34.8–125.8)
Infection presentation	
Colonization	12 (60%)
Clinical infection	8 (40%)
Infected wound	4 (50%)
Bloodstream infection (BSI)	2 (25%)
Other	2 (25%)

SD, standard deviation; IQR, inter-quartile range; APACHE, acute physiology and chronic health evaluation

Table 3 Potential multiple drug-resistant organism (MDRO) risk factors among patients with CRKP at King Abdulaziz Medical City (Riyadh, Saudi Arabia) between September 2009 and August 2010

Potential risk factors at index date*	
Prolonged hospital stay (≥5 days)	18 (90%)
Recent antimicrobial therapy (last month)	17 (85%)
Recent indwelling device	16 (80%)
Recent admission to ICU (last month)	15 (75%)
Recent surgical procedure	13 (72%)
Recent mechanical ventilation	14 (70%)
Previous hospitalization (last 3 months)	12 (63%)
Previous MDRO (last month)	12 (60%)
Immunosuppression	8 (44%)
Recent endoscope	5 (26%)
Recent trauma	4 (21%)
Transferred from another hospital	3 (15%)
CRKP patient in an adjacent room	1 (5%)
CRKP patient in the same room	0 (0%)
Recent burns	0 (0%)
Prior antimicrobial use**	
Carbapenem	12 (60%)
Antianaerobic	10 (50%)
Colistin	9 (45%)
Fluoroquinolones	7 (35%)
Vancomycin	7 (35%)
Tigecycline	3 (15%)
Cephalosporins III	2 (10%)
Aminoglycoside	1 (5%)
Tazocin	1 (5%)
Previous MDRO	
Acinetobacter	4 (20%)
Pseudomonas	3 (15%)
MRSA	2 (10%)
VRE	1 (5%)
Outcome	
Death	8 (40%)
Discharged home	6 (30%)
Still in hospital	6 (30%)
Cause of death	
Septic shock	5 (71%)
Liver/kidney failure	4 (57%)
Cardiopulmonary arrest	4 (57%)
Days before death	
Mean±SD***	56.8±72.1
Median and IQR***	32.0 (7.3-90.3)

*Risk factors presence over the last 2 weeks, unless mentioned otherwise

**For at least 2 days over the last month

***Abbreviations as per Table 2

Microbiological examination and clonal analysis

K. pneumoniae isolates were identified using the standard laboratory methods of the Clinical and Laboratory Standards Institute (CLSI) guidelines [11]. The identification of *K. pneumoniae* to the species level was done using the MicroScan WalkAway system (Siemens) and then confirmed using API 20E. Antimicrobial susceptibility testing was determined using the MicroScan WalkAway system (Siemens) and confirmed using the disk diffusion method and E-test (AB Biodisk). Minimum inhibitory concentration (MIC) breakpoints of carbapenems (meropenem and or imipenem) were defined according to the 2009 CLSI guidelines [11]. *K. pneumoniae* isolates found to have elevated MICs of carbapenems or with reduced disk diffusion zone sizes were tested for the presence of carbapenemases by use of the modified Hodge test (MHT) [12]. Carbapenemase production was detected by using meropenem disks; when the test isolate produced the enzyme and allowed the growth of a carbapenem-susceptible strain (*E. coli* ATCC 25922) towards a carbapenem disk, it was considered as positive. Pulsed field gel electrophoresis (PFGE) was done for the genotyping of *K. pneumoniae* isolates as previously described [13, 14].

Data analysis

The distribution of *K. pneumoniae* isolates by carbapenem resistance was plotted over time. Categorical data were presented as a percentage, while continuous data were presented as mean and standard deviation or median and interquartile range, as appropriate. SPSS software (release 18.0, SPSS Inc., Chicago, IL, USA) was used for the statistical analyses.

Results

In the year between September 2009 and August 2010, 20 (1.17%) out of 1,706 *K. pneumoniae* isolates detected at KAMC (Riyadh) were CRKP (Fig. 1). The epidemic curve showed a clear outbreak peak that did not resolve completely, creating an endemic pattern (Fig. 1). CRKP isolates were detected in samples from wound (40%), respiratory tract (25%), urine (15%), and other sites, including blood and the rectum (20%).

During March 2010, staff of the infection control and microbiology laboratory noticed the emergence of a cluster of CRKP isolates ($n=7$) in mainly adult ICU patients. Patients with CRKP were put under strict contact isolation, along with appropriate infection control measures for staff and visitors. These include intensifying hand hygiene compliance, starting CRKP active surveillance, activating within hospital transfer precautions, enhancing concurrent and terminal cleaning of patients' rooms, and staff education. Whenever feasible, respiratory therapists, nursing staff, and nursing aids were also cohorted during their shifts and on a rotating basis, to care exclusively for CRKP patients under contact isolation. Careful review of *K. pneumoniae* isolates over the previous 6 months revealed two previously unnoticed CRKPs; one in late February 2010 and another one in early December 2009. Admission and periodic active surveillance cultures showed a decrease but persistence of CRKP isolates in following months. Reviewing patients' records during the outbreak period through May 2010 showed that all patients with CRKP but one had stayed for some time in adult ICUs before the index date (Fig. 2). All the study isolates were tested with the MHT and were positive (showing cloverleaf-like indentation). PFGE results were available for 15 (75%) out of 20 isolates. Review of the PFGE results during the outbreak period showed that the majority of outbreak strains were genetically indistinguishable or closely related (Fig. 3). Isolates 1, 6, 8, 9, 10, 14, and 18 are 100% identical and closely related to 16 and 17 (similarity 97.15%), with isolate 7 having 90.91% similarity. Isolates 5 and 15 are 100% identical and closely related to 20 (similarity 97.15%). Isolate 19 is 77% similar to 5, 15, and 20. Isolate 3 is a distant similarity of 67% with the other 14 isolates.

The majority of patients were initially admitted to emergency rooms (55%) and adult ICUs (30%). About 15% of the patients were transfers from other hospitals. The admitted patients were 55% females and 45% males. The majority of patients (60%) were aged 19 to 59 years (mean±standard deviation [SD] 50.8±21.8). Their primary admission diagnoses were trauma including motor vehicle accident (25%) and liver or kidney failure (25%). The median APACHE III score was 67. The main comorbid conditions were surgery (50%), hypertension (50%), diabetes (45%), trauma (30%), and gastrointestinal disease, liver disease, and heart disease (25% each). CRKP patients required, on average, 63 days of hospital stay, 27.5 of them before the index date. The majority (85%) of patients required ICU admission during their hospital stay, with a median of 29 days of ICU stay. Two-fifths (40%) of patients presented with clinical infection. Out of those patients who presented with clinical infection, 50% had wound infections and 25% had bloodstream infection.

Many of the potential risk factors for developing multiple drug-resistant organisms (MDROs) were observed in CRKP patients (Table 3). The majority (90%) of CRKP patients spent at least 5 days in the hospital (the majority of which were in the ICU) prior to the index date. The majority (85%) of CRKP patients received antimicrobial therapy (for at least 2 days) during the month prior to the index date. Carbapenem (60%), antianaerobics (50%), colistin (45%), fluoroquinolones (35%), and vancomycin (35%) were the

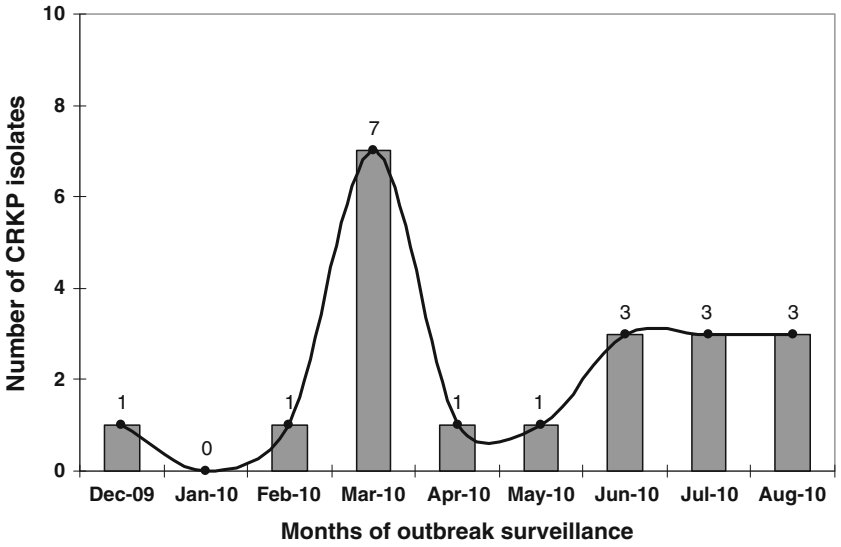

Fig. 1 Number and distribution of confirmed carbapenem-resistant *Klebsiella pneumonia* (CRKP) cases at King Abdulaziz Medical City (Riyadh, Saudi Arabia)

frequently used medications by CRKP patients. Half (50%) of the CRKP patients had previous colonization/infection with MDROs during the month prior to the index date, with *Acinetobacter* and *Pseudomonas* being the most frequently encountered MDROs. In addition, the majority of CRKP patients had recent history of indwelling devices, surgical procedures, and mechanical ventilation.

In addition to complete resistance to carbapenems, CRKP isolates had 90–100% resistance to cephalosporins, fluoroquinolones, and aminoglycosides. They were still generally susceptible to colistin (79%) and glycylcyclines (67%). The most frequently used mediations at the index date were carbapenem (55%), colistin (50%), fluoroquinolones (40%), tigecycline (40%), and tazocin (25%). CRKP

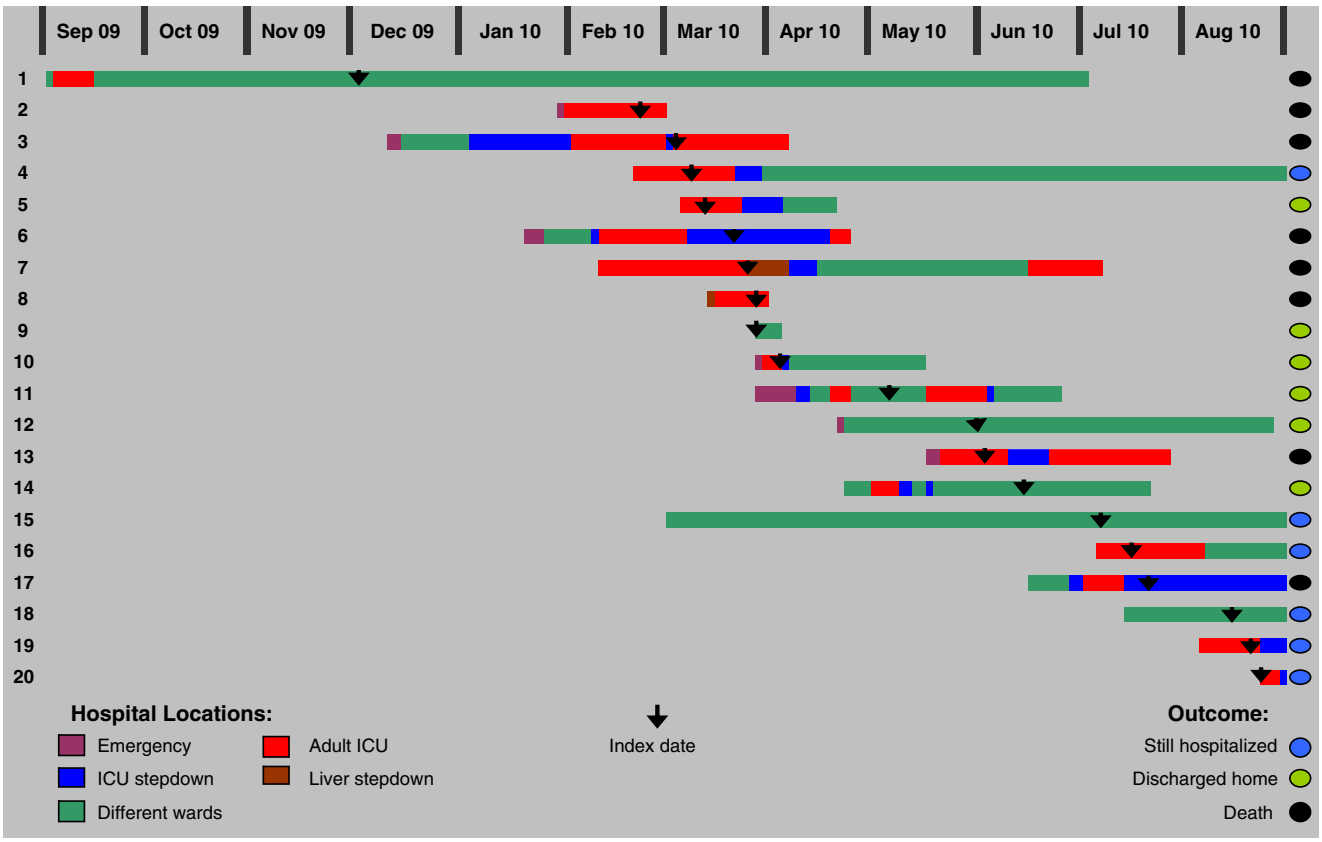

Fig. 2 Location and duration of hospitalization and outcome of CRKP at King Abdulaziz Medical City (Riyadh, Saudi Arabia) between September 2009 and August 2010

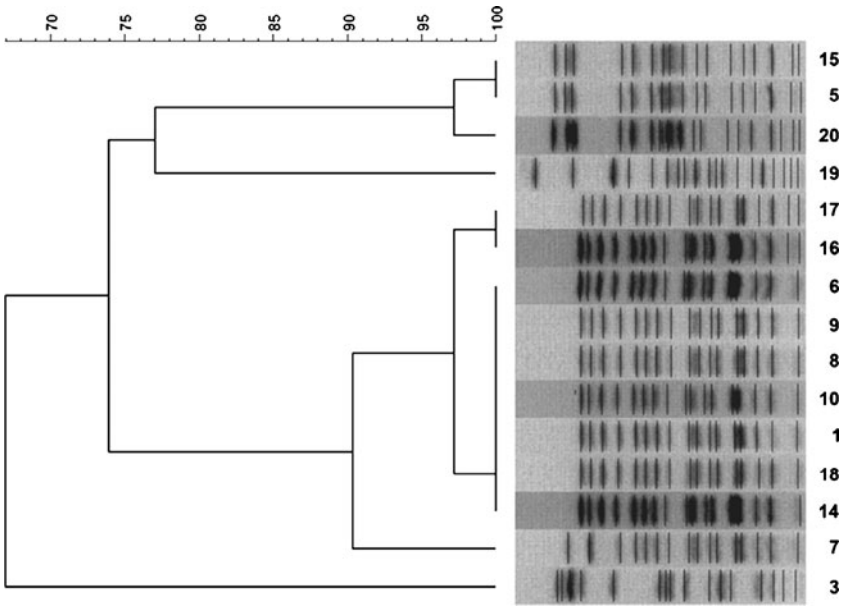

Fig. 3 Dendrogram based on pulsed-field gel electrophoresis (PFGE) of DNA restriction fragments of representative CRKP outbreak isolates (n=15). The dendrogram is shown on the left, with the percentage homology score indicated on top (0–100%). Actual pulsed field gel electrophoresis (PFGE) fingerprints are given on the immediate right of the dendrogram. Computer analysis of *Xba* I-digested isolates was performed using BioNumerics software (Applied Maths BVBA, Keistraat 120, 9830 Sint-Martens-Laten, Belgium)

patients required, on average, 24 days of antimicrobial therapy. By the end of August 2010, 8 (40%) of the CRKP patients died, 6 (30%) were discharged home, and 6 (30%) were still hospitalized (Table 3). The majority of deaths (75%) happened during the outbreak period through May 2010 and only 3 (38%) of the deaths happened within 4 weeks from the index date. Death happened at a median of 32 days from the index date. The most frequent causes of death were septic shock (71%), liver or kidney failure (57%), and cardiopulmonary arrest (57%).

Discussion

In this paper, we described our experience in detecting and containing the first documented CRKP outbreak in Saudi Arabia. As per CDC guidelines [9], we retrospectively reviewed the microbiological and clinical records of all *K. pneumoniae* isolates 6 months prior to the outbreak, as well as started active surveillance cultures. Active surveillance was shown to be very effective in controlling CRKP outbreak [15]. To early detect new CRKP isolates and to limit within-hospital spread, we have decided to keep CRKP active surveillance cultures to the routine workup done for all new ICU admissions. Unlike the outbreak setting, the effectiveness of active surveillance to limit the spread of CRKP and other multidrug-resistant *Enterobacteriaceae* in the non-outbreak setting is controversial [16–18]. Considering the cost benefit, we stopped monthly active surveillance cultures 3 months after declaring the end of the outbreak.

As shown in other studies [17, 19], reinforcing infection control measures together with contact isolation of patients colonized or infected with CRKP were successful in controlling the CRKP outbreak in our hospital. Staff education focused on the resistant nature of the CRKP organism and the absolute importance of staff adherence to infection control recommendations. Hand hygiene was an essential element of these measures, and we were able to increase its compliance at adult ICUs from 79.5% in March 2010 to 85–95% during the following months (data not shown). Nevertheless, infection control staff had to deal with some cultural and logistic challenges. Convincing the patient and his/her visitors with standard infection control measures is not always easy, especially when the patient is colonized. Cohorting respiratory therapists, nursing staff, and nursing aids was not always possible due to logistic reasons. Keeping the same level of infection control measures compliance at weekends is another challenge.

CRKP in the current study had 90–100% resistance to most of the commonly used antimicrobial agents, including carbapenems, cephalosporins, and fluoroquinolones, leaving very limited therapeutic options to treat severe hospital infections. Our isolates were, however, still generally sensitive to colistin and, to a lesser extent, to glycylcyclines [20, 21]. Recent reports showing the emergence of colistin-resistant CRKP in some parts of the world are alarming [21–23]. Although it is nephrotoxic, colistin is considered, by far, to be the only therapeutic choice currently available, as glycylcyclines have relatively low peak serum concentration to treat certain severe hospital infections, such as bloodstream infections [24]. Judicious use of antimicrobial agents may be seen as a long-term measure to reduce CRKP and other Gram-negative MDROs. The establishment of a comprehensive antimicrobial stewardship program, on the other hand, is a project worthy of leadership attention and support. As a consequence of CRKP outbreak, we initiated an antimicrobial use and resistance database in our ICUs to monitor carbapenem and other broad-spectrum antimicrobial use.

Quick and adequate detection of CRKP is critical for the success of infection control measures. The detection of CRKP-producing bacteria based only on susceptibility testing is not easy, due to the heterogeneous expression of β-lactam resistance [10]. As per CDC recommendations [9], we used the MHT to confirm suspicious isolates based on the MICs breakpoints of the 2009 CLSI guidelines. Since the test is time-consuming and required reading expertise, securing results at the right time from an infection control point of view was sometimes challenging. The 2010 CLSI guidelines have overcome this problem by lowering the MICs for carbapenems, eliminating the need to perform the confirmatory MHT. The down side to this, however, is the large number of isolates that would mandate a larger number of patients to be placed on contact isolation according to an MDRO isolation policy. Therefore, we decided to continue to use the 2009 CLSI guidelines with all suspicious isolates to be reviewed by the director of the microbiology laboratory in order to decide on the need for the MHT.

The reported mortality in patients with CRKP is striking. It ranged between 40% and 70% [7, 25, 26]. Mortality in the current study was 38%. This crude mortality is probably overestimating the impact of CRKP and is confounded by multiple comorbidities. Only 38% of our CRKPs presented as HAI. It is estimated that about one-third to one-half of crude mortality associated with CRKP were actually attributable to CRKP infection [25, 26]. The high frequency of potential risk factors of MDROs in our CRKP patients is in agreement with previous reports describing CRKP risk factors, including prolonged hospital stay, prior hospitalization, prior antimicrobial intake, current stay in the ICU, recent surgery, and the use of a ventilator or indwelling device [7, 26, 27].

Conclusion

Reinforcing infection control measures together with contact isolation of patients colonized or infected with carbapenem-resistant *Klebsiella pneumoniae* (CRKP) were successful in controlling the CRKP outbreak, but did not prevent endemicity. Since CRKP has limited therapeutic options and is associated with high mortality, we have decided to focus on limiting the spread by continuing to carry out CRKP active surveillance cultures for all new intensive care unit (ICU) admissions. The need for new effective antibiotics against pan-resistant, Gram-negative, multiple drug-resistant organisms (MDRO) is now more critical than ever before.

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Author participation H.H.B., S.M.A.J., C.F., Y.A., A.A., and M.S. were actively involved in the outbreak management, collecting, and revising the data. A.E.-S. was involved in the data analysis and preparation of the manuscript. A.A.A.-Q., M.N.A.-A., and H.T.A. were involved in running the PFGE and the analysis. H.H.B. and A.E.-S. prepared and edited the final manuscript. All authors approved the final version of the manuscript.

Ethical approval This work was conducted after obtaining Institutional Review Board (IRB) approval from King Abdullah International Medical Research Center (KAIMRC), King Saud University for Health Sciences, Riyadh, Saudi Arabia.

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