

Molecular characterisation and epidemiological investigation of an outbreak of *bla*_{OXA-181} carbapenemase-producing isolates of *Klebsiella pneumoniae* in South Africa

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Background. *Klebsiella pneumoniae* is an opportunistic pathogen often associated with nosocomial infections. A suspected outbreak of *K. pneumoniae* isolates, exhibiting reduced susceptibility to carbapenem antibiotics, was detected during the month of May 2012 among patients admitted to a haematology unit of a tertiary academic hospital in Cape Town, South Africa (SA).

Objectives. An investigation was done to determine possible epidemiological links between the case patients and to describe the mechanisms of carbapenem resistance of these bacterial isolates.

Methods. Relevant demographic, clinical and laboratory information was extracted from hospital records and an observational review of infection prevention and control practices in the affected unit was performed. Antimicrobial susceptibility testing including phenotypic testing and genotypic detection of the most commonly described carbapenemase genes was done. The phylogenetic relationship of all isolates containing the *bla*_{OXA-181} carbapenemase gene was determined by pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing.

Results. Polymerase chain reaction analysis identified a total of seven *bla*_{OXA-181}-positive, carbapenem-resistant *K. pneumoniae* isolates obtained from seven patients, all from a single unit. These isolates were indistinguishable using PFGE analysis and belonged to sequence type ST-14. No other carbapenemase enzymes were detected.

Conclusion. This is the first documented laboratory-confirmed outbreak of OXA-181-producing *K. pneumoniae* in SA, and highlights the importance of enforcing strict adherence to infection control procedures and the need for ongoing surveillance of antibiotic-resistant pathogens in local hospitals.

S Afr Med J 2015;105(12):1030-1035. DOI:10.7196/SAMJ.2015.v105i12.9926



Patients infected with multidrug-resistant Enterobacteriaceae were, until recently and with relative success, treated with carbapenems, a class of broad-spectrum β -lactam antibiotics. Of great concern is the over-use of carbapenems in hospitals for treating Gram-negative bacterial infections, which is contributing to the increasing emergence of carbapenem resistance.^[1]

Carbapenem resistance in *Klebsiella* spp. is mainly attributable to the acquisition of carbapenem-hydrolysing β -lactamase enzymes. The Ambler classification scheme is used to separate these enzymes into classes A, B or D.^[3] The OXA-48-like subgroup, of which OXA-181 is a member, are Ambler class D carbapenemases.^[3] OXA-48 was first described in the environmental bacterium *Shewanella* spp., and more recently there have been several reports of this enzyme, mainly in *K. pneumoniae* isolates, from countries in the Middle East, Europe, and northern and southern Africa.^[4-7]

OXA-181, a variant of OXA-48, was first identified in *K. pneumoniae* isolated from a Tanzanian patient.^[7] It differs by just four amino acid substitutions in the active site, yet still confers the same levels of enzymatic hydrolysis of carbapenems as OXA-48.^[7] Several international studies have identified OXA-181-producing Enterobacteriaceae in the UK, the Sultanate of Oman, the Netherlands, Senegal and New Zealand.^[7-12] The genetic location of *bla*_{OXA-181} is

typically on a Tn2013 transposon, immediately downstream of the insertion sequence *ISEcp1B*, carried on a 7.6-Kb, ColE-type plasmid.^[7]

The prevalence of nosocomial infections in African countries has been under-appreciated in the past, and while such outbreaks occurring internationally are frequently reported in the literature, relatively few of these reports originate from developing countries.^[13] However, even in lower-income countries, outbreak reports are necessary to increase awareness in the local medical community and highlight the need for enforced and effective infection prevention and control (IPAC) measures to limit the occurrence and transmission of antibiotic-resistant pathogens. OXA-48-like carbapenem-resistant Enterobacteriaceae are endemic worldwide but had not previously been observed in our hospital. A subsequent report indicates that such organisms had recently been detected in other local institutions.^[6] This outbreak report serves as the first description and characterisation of a single outbreak of carbapenem-resistant *K. pneumoniae* in a haematology unit of a local hospital in Cape Town, South Africa (SA), during the month of May 2012.

Objectives

Following the identification of a possible outbreak of carbapenem-resistant *Klebsiella* spp. in a haematology unit in Cape Town, an epidemiological investigation was done to describe the extent of

the outbreak, ascertain possible transmission routes and identify opportunities to prevent further transmission. Laboratory studies were carried out to characterise the molecular basis for carbapenem resistance and the molecular epidemiology of these isolates.

Methods

This was a prospective study, implemented informally in response to the detection on 12 May 2012 of carbapenem-resistant *Klebsiella* spp. from two patients in the haematology intensive care unit (ICU) of a 900-bed tertiary care referral hospital in Cape Town.

The haematology ICU is utilised by high-risk haematology patients, either with haematological malignancies or undergoing stem cell transplants, typically when neutropenic. Patients from both the public hospital and the adjacent private hospital are admitted and nursed in 12 patient isolation rooms by staff from the public or private hospitals, respectively. However, both teams of staff share communal work areas within the unit, including the nurses' station, the sluice room and staff rooms. The unit is supported by infection control staff from both private and public hospitals.

Following the identification of carbapenem-resistant *Klebsiella*, an immediate and intensive outbreak response was implemented. Infection control measures were intensified, patient movement in and out of the affected unit was halted, and 2 weeks later it was closed for decontamination, maintenance and repairs.

A policy for weekly stool or rectal swab surveillance for carbapenem-resistant Enterobacteriaceae for all haematology and oncology inpatients (in either the ICU or the associated wards) was already in place prior to May 2012. Laboratory records were checked for any previous carbapenem-resistant Enterobacteriaceae isolates from both clinical and surveillance specimens. Surveillance was intensified, and stool samples were also obtained from staff members to screen for possible gut carriage. Environmental sampling was not conducted as a previous outbreak suggested very limited benefit.^[14]

For the outbreak a case was defined as a patient with carbapenem-resistant *Klebsiella* isolated from a clinical specimen (provider requested) or surveillance (routine screening) culture from the shared haematology ICU from 1 to 31 May 2012. A retrospective review of hospital records was performed for each case patient admitted before 31 May 2012. Demographic, clinical, and laboratory information was abstracted from case patient charts, with all data being collected in the same manner as in the outbreak reported by Marchaim *et al.*^[15] in 2011. Details of the eight patients included in the outbreak are provided in the 'Results' section.

Ethical considerations

As this study was conducted as an outbreak investigation for IPAC purposes, informed consent of patients was not obtained on the grounds that specimen collection was based on routine clinical practice and infection control requirements. The investigation was approved by the Human Research Ethics Committee of the University of Cape Town (Ref: 534/2012).

Bacterial identification and genotypic typing

All stool specimens or rectal swabs were plated onto MacConkey agar containing 4 µg/mL gentamicin. The resulting colonies were subsequently identified using the Vitek 2 system (GN and N133 card, bioMérieux, France) and their antibiotic susceptibility profiles determined (Vitek 2). All isolates with reduced susceptibility to the carbapenems were screened for phenotypic carbapenemase activity using the modified Hodge test. The minimum inhibitory concentrations of carbapenems available in this hospital (ertapenem, imipenem and meropenem) were determined using the E-test method (bioMérieux, France). All tests were done and interpreted according to the

Clinical Laboratory Standards Institute criteria (CLSI-2012).^[16]

Conventional polymerase chain reaction (PCR) assays were performed using, as template, either total cellular DNA extracted from cultured isolates using the ZR-96 Fungal/Bacterial DNA kit (Zymo Research, Inqaba, South Africa), or total DNA extracted from stool and rectal swab specimens using either the QiaSymphony (QIAGEN, Germany) or ZR fecal DNA Microprep kit (Zymo Research, Inqaba, South Africa). All extractions were carried out as per the manufacturer's instructions. PCR experiments were performed using PCR primers designed to target internal fragments of the current most clinically significant carbapenemase genes (*bla*_{NDM}, *bla*_{VIM}, *bla*_{SPM}, *bla*_{IMP}, *bla*_{KPC}, *bla*_{GES} and *bla*_{OXA-48-like}) (Table 1). The resulting PCR amplicons were purified (QIAquick PCR purification kit, QIAGEN, Germany) and then sequenced. To test for the presence of extended-spectrum β-lactamase (ESBL) (Table 1)^[17-26] genes *bla*_{CTX-M}, *bla*_{SHV} and *bla*_{TEM}, conventional PCR assays using primers designed to target internal fragments of these genes were performed and any resulting PCR amplicons of the expected size were sequenced.

Table 1. Primer sequences used in this study

Primer	Sequence (5' - 3')	Gene	Reference
Carbapenemases			
GESF	ATGCGCTTCATTCACGC	<i>bla</i> _{GES}	17
GESR	GCTCAGGATGAGTTGTG	<i>bla</i> _{GES}	17
IMIF	ATTGACACTCCATTAC	<i>bla</i> _{IMI-1}	18
IMIR	AACAACCAGTTTTGC	<i>bla</i> _{IMI-1}	18
NDMF	GGTTTGCGGATCTGGTTTTTC	<i>bla</i> _{NDM-1}	19
NDMR	CGGAATGGCTCATCACGATC	<i>bla</i> _{NDM-1}	19
OXA48F	CGTGTATTAGCCTTATCG	<i>bla</i> _{OXA-48-like}	20
OXA48R	CGCTAACCACTTCTAGG	<i>bla</i> _{OXA-48-like}	20
VIMF	GTGAGTATCCGACAGTC	<i>bla</i> _{VIM-1}	18
VIMR	GAGCAAGTCTAGACCG	<i>bla</i> _{VIM-1}	18
KPCF	TGTCACTGTATCGCCGTC	<i>bla</i> _{KPC-1}	21
KPCR	CTCAGTGCTCTACAGAAAACC	<i>bla</i> _{KPC-1}	21
SPMF	CTGCTTGGATTATGGGCGC	<i>bla</i> _{SPM-1}	22
SPMR	CCTTTTCCGCGACCTTGATC	<i>bla</i> _{SPM-1}	22
Extended-spectrum β-lactamases			
CTXMIF	CGCTTTGCGATGTGCAG	<i>bla</i> _{CTX-M-1}	17
CTXM1R	ACCGGATATCGTTGGT	<i>bla</i> _{CTX-M-1}	17
SHVC	AGAAGGGTTATTCTATTTGTGCG	<i>bla</i> _{SHV}	17
SHVD	TCTTTCCGATGCCGCCAGTCA	<i>bla</i> _{SHV}	23
DEB	ATGAGTAAACTTGGTCTGAC	<i>bla</i> _{TEM}	24
3061TEM	AGGAAGCAAAGCTGAAAGGAATCAAATTTGG	<i>bla</i> _{TEM}	25
Insertion sequence			
ISEcp1F	GCAGGTCTTTTCTGCTCC	<i>ISEcp1</i> transposase	26
ISEcp1R	TTTCCGAGCACCGTTTGC	<i>ISEcp1</i> transposase	26

To describe the genomic arrangement of the identified *bla*_{OXA-181} genes in positive isolates in relation to the *ISEcp1B* gene, which had previously been shown to be associated with the OXA-181 gene,^[7] conventional PCR was carried out using primers designed to amplify an internal fragment of the insertion element, *ISEcp1B*, and an internal portion of the OXA-181 gene (Table 1). The resulting PCR amplicons were purified (QIAquick PCR purification kit) and then sequenced to confirm sequence identity.

The relatedness of the *Klebsiella* isolates was investigated using pulsed-field gel electrophoresis (PFGE) according to a previously published protocol with minor changes.^[27] Total genomic DNA was digested, *in situ*, with XbaI (New England Biolabs Inc., UK) and the resulting DNA fragments were separated by electrophoresis using a 1% w/v, 0.5 × TBE-agarose gel in a CHEF-DR1 GeneNavigator apparatus (GE Healthcare, USA) with a ramped pulse time of 5 - 60 seconds, over 21 hours, at a constant voltage of 200 V, in 0.5 × TBE buffer maintained at 14°C. The resulting restriction profiles were analysed using GelCompar II version 5.1 software (Applied Maths, Belgium). A dendrogram indicating the UPGMA clustering between the isolates was created using the Dice similarity coefficient. The band tolerance and optimisation were set at 1.0% and a similarity threshold of ≥80% was used to define related clusters.^[28]

Multilocus sequence typing (MLST), specific for *Klebsiella*, was performed using seven housekeeping genes as reference loci (*rpoB*, *gapA*, *mdh*, *pgi*, *phoE*, *infB*, and *tonB*) according to the method described by Diancourt *et al.*,^[29] with minor amendments. Allele and sequence types were determined using the Institut Pasteur MLST online database for *K. pneumoniae*.^[30]

Results
Outbreak investigation

Review of laboratory records showed that no carbapenem-resistant Enterobacteriaceae had been detected prior to 12 May 2012. A total of 340 rectal swabs or stool specimens, from patients and staff members, were collected and screened for carriage of carbapenem-resistant Enterobacteriaceae. A total of eight patients with carbapenem-

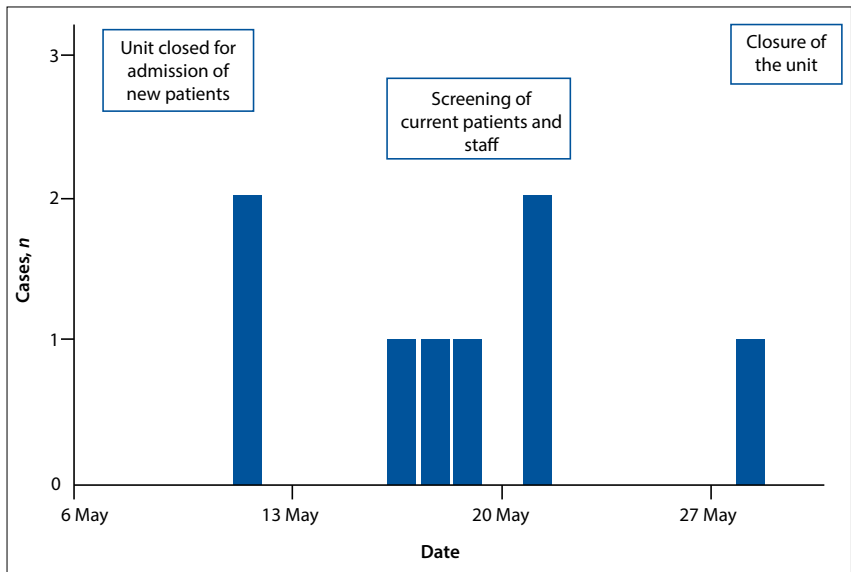


Fig. 1. Timeline and transmission opportunities among the patients during the outbreak. A transmission opportunity was deemed to have occurred if two patients were in the same ward during the same time period.

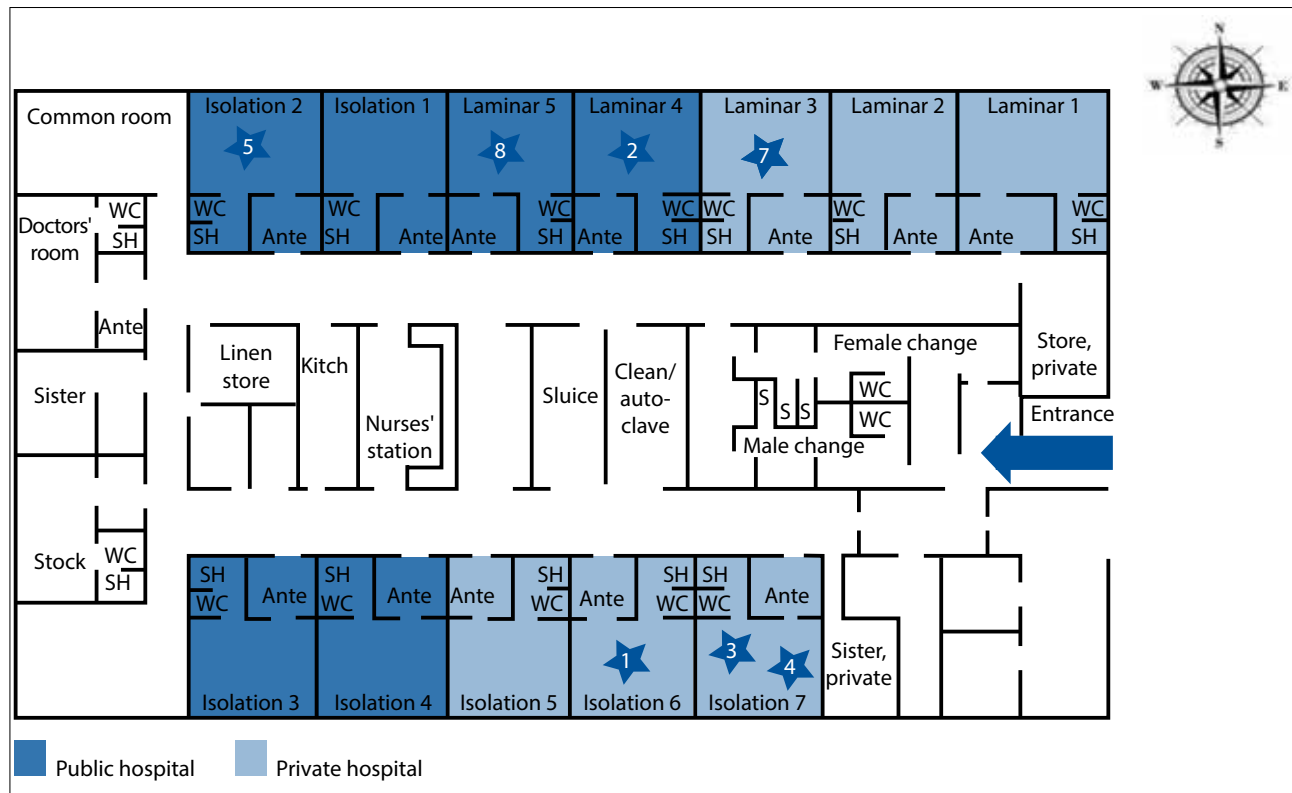


Fig. 2. Floor plan of the shared haematology ICU in the hospital, showing the location of the patients identified with carbapenem-resistant *Klebsiella* during May 2012. Starred rooms indicate locations of affected case patients. (WC = water closet (toilet); S/SH = shower.)

resistant *Klebsiella* were identified from 12 to 31 May 2012. The eight patients were either infected (blood culture, $n=1$) or colonised (pus swab, stool, sputum or tracheal aspirate, $n=7$). No carbapenem-resistant Enterobacteriaceae were identified from the rectal swab specimens submitted by the healthcare workers (HCWs). A timeline of the outbreak is depicted in Fig. 1.

Patient characteristics

A summary of the patients' demographic and clinical information is provided in Table 2. The median age was 48 years (range 30 - 77 years) and half of the patients were male. The median hospitalisation time was 16 days (range 3 - 29 days). All patients had underlying malignancies, were receiving cancer chemotherapeutic treatment and had been previously exposed to multiple antibiotics, placing them at high risk for acquiring nosocomial infections.

A timeline for detection of carbapenem-resistant *Klebsiella* isolates indicated that the outbreak occurred over a 2-week period from 12 to 28 May. The floor plan of the affected ICU indicates the placement of 7 of the 8 patients (Fig. 2). Patients 1, 2, 3, 4, 7 and 8 were either placed in the same room as a previous case or in adjacent rooms in close proximity to communal areas, while patient 5 was in close proximity to the doctors' room and a common staff room. Seven of the eight patients were admitted to the shared haematology unit for the duration of their hospital stay. The remaining patient (patient 6), who had a respiratory tract colonisation, was identified in a separate

ICU, but could be epidemiologically linked to patient 1 because he was transferred and admitted to the bed adjacent to patient 6. Patient 1 died from a bloodstream infection (6 hours post transfer), and 8 days later a carbapenem-resistant *K. pneumoniae* was cultured from an endotracheal specimen from patient 6.

Infection control

During the inspection of the IPAC practices in the affected ICU, breaches in contact precaution including lack of use of aprons and gloves by HCWs before entering patient rooms, incorrect disposal of these items and poor hand hygiene were observed. In addition, incorrect signage relating to standard IPAC practices and inadequate signage for patients about contact precautions was also documented.

Microbiological characterisation of *Klebsiella* isolates

A total of eight carbapenem-resistant *Klebsiella* isolates (seven *K. pneumoniae* and one *K. oxytoca*) were identified. All eight isolates exhibited a multidrug-resistance phenotype with resistance to ampicillin, co-amoxiclav, cefuroxime, cefoxitin, cefotaxime, ceftazidime, cefepime, gentamicin, amikacin, tigecycline, co-trimoxazole, nalidixic acid and ciprofloxacin, and were susceptible to colistin only. Carbapenem minimum inhibitory concentration (MIC) patterns are shown in Table 2. The isolates demonstrated variable susceptibility to imipenem with reduced susceptibility to both meropenem (range 8 - >32 mg/L) and ertapenem (all

>32 mg/L). The modified Hodge test was positive for all eight isolates.^[31]

Conventional PCR for OXA-48 and OXA-48-like genes generated amplicons of the expected size for all eight isolates. Subsequent sequence analysis revealed that all eight PCR positive isolates had 100% homology with *bla*_{OXA-181}, a genetic variant of *bla*_{OXA-48}. Similar results were obtained from DNA extracted from the corresponding rectal swabs or stool samples. No amplicons were obtained for the other carbapenemase genes screened: *bla*_{NDM}, *bla*_{VIM}, *bla*_{IMP}, *bla*_{KPC}, *bla*_{SPM} and *bla*_{GES}. All eight isolates were positive on ESBL PCR screening for *bla*_{CTX-M}, *bla*_{TEM} and *bla*_{SHV} (with the exception of *K. oxytoca*, which did not contain *bla*_{SHV}), as shown in Table 2.

Genetic arrangement of the *bla*_{OXA-181}

Using the forward primer targeting ISEcp1B and the reverse primer internal to *bla*_{OXA-181}, an amplicon of the expected size was obtained, suggesting these genes are associated in all eight isolates.

Phylogenetic analysis

To establish the relatedness of the seven *K. pneumoniae* isolates, PFGE analysis was carried out. *K. pneumoniae* isolate 4 was not viable. The resultant PFGE fingerprints of six of the *K. pneumoniae* isolates, patients 1, 2, 3, 5, 6, and 8, were indistinguishable (100% identity) and were assigned to cluster A (Fig. 3). Two contemporary *K. pneumoniae* isolates, one from another ward (carbapenem susceptible) and one from another local hospital (carbapenem

Table 2. Demographic information, PCR and microbiological results of patients identified with carbapenem-resistant *Klebsiella* spp.

Patient identity	Isolate identity	Date of isolation	Gender	Age (y)	Specimen type	Clinical outcome	MIC (mg/L)			MHT	Carbapenemase genes	
							EP	IP	MP		<i>bla</i> _{OXA-181}	ESBL genes
Case 1	<i>K. pneumoniae</i>	12/05/2012	M	77	Blood	Deceased	>32	6	16	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM} , <i>bla</i> _{SHV}
Case 2	<i>K. pneumoniae</i>	12/05/2012	M	36	Stool	Survived	>32	4	>32	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM} , <i>bla</i> _{SHV}
Case 3	<i>K. pneumoniae</i>	17/05/2012	M	44	Stool	Survived	>32	1.5	8	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM} , <i>bla</i> _{SHV}
Case 4	<i>K. pneumoniae</i>	18/05/2012	F	52	Stool	Deceased*	N/D	4	N/D	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM} , <i>bla</i> _{SHV}
Case 5	<i>K. pneumoniae</i>	19/05/2012	F	57	Stool	Survived	>32	8	>32	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM} , <i>bla</i> _{SHV}
Case 6	<i>K. pneumoniae</i>	21/05/2012	F	51	Tracheal aspirate	Survived	>32	4	>32	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM} , <i>bla</i> _{SHV}
Case 7	<i>K. oxytoca</i>	21/05/2012	F	41	Stool	Survived	>32	>32	16	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM}
Case 8	<i>K. pneumoniae</i>	24/05/2012	M	30	Stool & pus swab	Survived	>32	4	16	+	<i>bla</i> _{OXA-181}	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM} , <i>bla</i> _{SHV}

EP = ertapenem; IP = imipenem; MP = meropenem; MHT = modified Hodge test.
*Died from causes unrelated to *K. pneumoniae* infection.

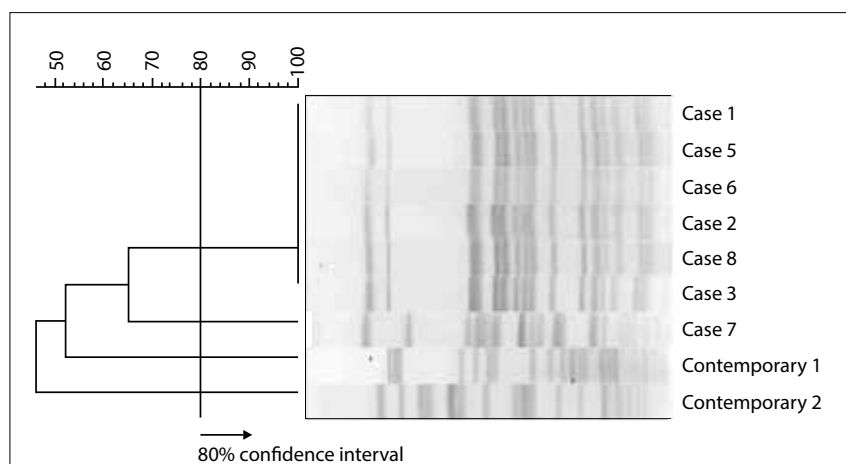


Fig. 3. Dendrogram and PFGE DNA fingerprints generated by *Xba*I restriction enzyme treatment of OXA-181-producing *K. pneumoniae* isolates (patient cases 1, 5, 6, 2, 8, 3) and one *K. oxytoca* (patient case 7). Two contemporary *K. pneumoniae* isolates, one from another ward (carbapenem-susceptible, contemporary isolate) and one from another local hospital (carbapenem-resistant, contemporary isolate 2) were included in the analysis as outliers.

resistant) were included in the analysis and shown to be unrelated to cluster A. The *K. oxytoca* isolate from patient 7 was, as expected, genetically distinct from all the *K. pneumoniae* strains tested. Since the six *K. pneumoniae* isolates had the same PFGE profile, MLST analysis was only carried out on two representative *K. pneumoniae* isolates, case numbers 6 and 4. The results were analysed using the Pasteur database and showed that these two strains are both members of sequence type ST14.

Discussion and conclusions

This study describes the first documented nosocomial outbreak of *bla*_{OXA-181}-producing, carbapenem-resistant *K. pneumoniae* and *K. oxytoca* isolated from a local tertiary academic hospital in Cape Town. Resistance to the clinically significant carbapenem antibiotics by enzymatic hydrolysis has been described in Enterobacteriaceae worldwide, and recently the class D β -lactamase, OXA-48 and its variants have been detected more frequently.^[4] While the *bla*_{OXA-181} gene has previously been identified in several clonally unrelated *K. pneumoniae* isolates from SA, India, Singapore, the Netherlands and New Zealand,^[4-12] this is the first report describing an outbreak of *bla*_{OXA-181} in SA. To our knowledge this is the first identification of a *bla*_{OXA-181}-producing *K. oxytoca* isolate. Although it remains unclear where this organism originated, and since no international travel link could be established for any of the patients, there is evidence to suggest that OXA-181 may have been prevalent in a nearby private sector hospital that could have been a possible source of this organism in the community.^[6] The profiles

of six of the *K. pneumoniae* isolates, patients 1, 2, 3, 5, 6, and 8, were indistinguishable and were assigned to cluster A. Two contemporary *K. pneumoniae* isolates, one from another ward (carbapenem-susceptible) and one from another local hospital (carbapenem-resistant), were included in the analysis and shown to be unrelated to cluster A. PFGE is no longer considered the gold standard for genetic typing because of its lack of discrimination. Therefore, to characterise the genetic background of this clone further, MLST of two representative isolates from cluster A, spanning the defined outbreak period, were selected. MLST indicated that these two isolates belonged to sequence type ST14. *K. pneumoniae* ST14 has on two previous occasions been associated with ESBLs and not with metallo- β -lactamases or serine carbapenemases, as was observed in these isolates.^[10,11]

All OXA-181-containing isolates in this study were resistant to carbapenems and positive for carbapenemase production by the modified Hodge test. The co-production of OXA-181 with ESBL enzymes and the accumulation of additional β -lactamase genes in Enterobacteriaceae has been shown to collectively produce an elevated multidrug-resistance phenotype.^[4,7,9,10] A probable explanation for the uncharacteristically high carbapenem resistance levels observed with these isolates was the presence of additional ESBL genes. Furthermore, the OXA-181 gene was shown to be linked to the *ISEcp1B* element, which has been shown to up-regulate gene expression and allow for gene mobilisation.^[7] Further investigations are underway to determine the plasmid types of these isolates to better elucidate reasons for its successful spread.

The IPAC report documented inadequate infection control practices among healthcare staff in the shared haematology unit, and it is possible that this breakdown in infection control practices contributed to the spread of this organism between patients, either directly via the hands of staff or via fomites. It was observed among HCWs that breaches in contact precautions, including the lack of aprons and gloves prior to entering patient rooms, as well as the incorrect disposal of these items, and overall poor hand hygiene could have contributed to the spread of this organism. HCWs were encouraged to submit faecal samples for the screening of gut carriage of carbapenem-resistant Enterobacteriaceae as a possible source of the outbreak. This investigation could not rule out transmission in other communal areas, such as the radiology department or procedure rooms used for implanting medical devices. Further case-control analysis of patient and provider risk factors would have strengthened this investigation. In addition, this study could not clearly identify an index patient, given the inconsistent compliance with surveillance screening policy prior to the outbreak. The following recommendations were made based on the IPAC report from this investigation: stricter adherence to laboratory screening for antibiotic-resistant organisms from routine surveillance rectal swabs of new patients, both on admission and weekly follow-up, as well as the re-education and adherence to IPAC among all staff (temporary and full time). Additionally, improved IPAC signage practices that will increase awareness among hospital staff, the identification of IPAC awareness champions and developing a multidisciplinary team to maintain awareness should be considered. Ultimately, timely identification of the organism, swift unit closure and a reduction in patient movement coupled with strict contact precautions for colonised patients were effective in limiting further transmission of this isolate, as there were no new cases identified after 28 May. However, given the ongoing circulation of patients between local hospitals, and the potential for long-term asymptomatic carriage, it is likely that carbapenem-resistant *Klebsiella* will be reintroduced in the future. Vulnerable patients with haematological malignancies are likely to manifest infections as a result of multidrug-resistant organisms, including carbapenem-resistant *Klebsiella*.

In summary, this outbreak demonstrates the importance of active surveillance coupled with rapid and accurate molecular genotypic testing in enabling the detection and subsequent control of carbapenemase-

producing *Klebsiella*. This work highlights the necessity of not only ensuring that effective infection control measures are in place to identify and limit the spread of such organisms, but also the added value molecular screening offers in confirming an outbreak by determining the molecular epidemiology of the bacterial isolates and the prevalence of resistance genes circulating in our hospitals and communities.

Author contributions. All authors were involved in the conceptualisation of the study. RKJ, CM, MS, CB and MRM collected the data. MRM, MS, SW and CB investigated the outbreak. RKJ, CM, MS, CB, MN, MRM, and SW carried out the data analysis and interpretation. RKJ and MRM drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgements. We acknowledge the National Health Laboratory Service Microbiology Division, Department of Medical Microbiology, University of Cape Town, as well as Sisters Morris, Engelbrecht and Boonzaaier, local infection control sisters and Seymour Williams and Alexander Kallen of the Centers for Disease Control and Prevention, USA. In addition, we acknowledge that the data for the MLST online database for *K. pneumoniae* are publicly available at <http://www.pasteur.fr/mlst>.

Funding. This work was supported by the Global Disease and Detection Funding, Centre for Opportunistic Tropical and Hospital Infections, National Institute for Communicable Diseases and the National Health Laboratory Service, Johannesburg.

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Accepted 28 September 2015.