Table 1. Duration of Antimicrobials Among Patients Who Did and Did Not Change Their Code Status

Variable	Patients Not Changing Code Status (n = 96)	Patients ChangingCode Status (n = 36)	*P* Value
Discharged on antimicrobials, no. (%)	36 (37.5)	6 (16.7)	.022
Total duration (days) of antimicrobials (inpatient + outpatient), median (IQR)	9 (4.3–22.3)	6.5 (4–12)	.044
Duration (days) of inpatient antimicrobials, median (IQR)	6 (4–12.8)	5 (4–9.5)	NS

Note. IQR, interquartile range; NS, not significant.

interquartile range [IQR], 3–7) than patients not discharged to hospice (n = 109; median, 7 days; IQR, 4–12). When analyzing by randomization arm, we found no statistically significant difference in discharge on antimicrobial therapy (P = .14). However, patients in the control arm of the study were assigned to usual care, in which they could undergo palliative-care consultation.

Discussion

In a cohort of patients enrolled in a randomized controlled trial of early palliative-care consultation, patients who changed their code status were less likely to be discharged on antimicrobials and to receive overall shorter courses of antimicrobials. This difference was primarily driven by patients transitioning to hospice (n = 23) with 0 of 23 patients discharged on antimicrobials, a number substantially lower than in previous studies.[4]

Palliative care consultants help clarify resuscitation preferences and discuss the risks and benefits of many different therapies for patients at the end of life; antimicrobials are among these. Antimicrobials in patients at the end of life are frequently used but with uncertain benefit.[5,7] Our study suggests that early palliative-care consultation, even when not designed as an antimicrobial stewardship intervention, may nonetheless be effective in reducing antimicrobial consumption in patients at the end of life. Antimicrobial stewardship programs should consider engaging palliative-care providers in the development of end-of-life antimicrobial stewardship efforts.

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A major monoclonal hospital outbreak of NDM-1–producing *Klebsiella pneumoniae* ST340 and the first report of ST2570 in Brazil

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To the Editor—New Delhi metallo-β-lactamase (NDM) is one of the main globally described carbapenemases. It was first reported in 2009 in India.[1] *Providencia rettgeri* was first reported in Brazil in 2013.[2] NDM emergence has been described in Brazil among gram-negative bacteria related to infection or the environment.[3–5] Here, we describe an outbreak of NDM-1–producing *Klebsiella pneumoniae* (KPN) strains ST340 and ST2570 in 50 single isolates from 2 Brazilian hospitals between May 2017 and July 2018 (Figure 1).

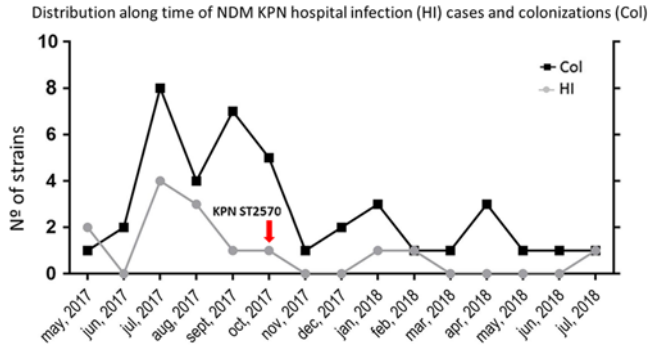

Fig. 1. New Delhi metallo-β-lactamase producing *Klebsiella pneumoniae* (NDM KPN) case distribution along time.

These hospitals belong to a regional medical complex with different locations and professionals. Their microbiology laboratory has applied the same metallo-β-lactamase (MβL) screening procedure with commercial carbapenem disks with and without EDTA (0.1 M) since 2016. Patients admitted are routinely screened for the presence of multidrug-resistant *Enterobacteriaceae*. The lab identified 50 KPN-MβL–positive carbapenem-resistant single strains using the Vitek MS system (bioMeriéux, Marcy-l'Étoile, France). One sample per patient was considered, and the $bla_{\text{NDM-1}}$ gene was detected using multiplex real-time polymerase chain reaction (qPCR).[6]

Overall, 45 isolates were identified from hospital 1, and 5 were identified from hospital 2. Among them, 41 were from surveillance cultures (rectal swabs) and 9 were from clinical samples (5 urine, 3 blood and 1 tracheobronchial aspirate). At the moment of isolation, 14 of these 50 patients had a diagnosis of hospital-acquired infection (HAI) according to established criteria (7 nonventilation pneumonia, 4 bloodstream, 2 catheter, and 1 skin and soft-tissue infections). In 5 of 14 patients, NDM-KPN was potentially associated with the HAI (3 blood and 2 urine cultures). In 5 of the 14 HAI patients, other microorganisms were considered causative agents, and in 4 these patients, no agents were isolated from infections (NDM KPN from surveillance only). At admission, 7 of the 14 HAI patients presented with community infections, 4 with orthopedic or trauma, and 2 with neurological conditions. Also, 5 of these 14 HAI patients had multiple comorbidities. Notably, 7 of these 14 patients were later discharged with improved conditions, and 7 of these patients died during their hospital stay.

Antimicrobial susceptibility testing was performed by Vitek 2 System (bioMeriéux), and high-level resistance was detected for all β-lactams, ciprofloxacin, and gentamicin (ie, using the guidelines of the Clinical Laboratory Standards Institute [CLSI]). All strains were susceptible to colistin (minimum inhibitory concentration [MIC], ≤2 μg/mL), and 40 of 50 were resistant to tigecycline (MIC, >2 μg/mL) (ie, using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria). ESβLs (ie, bla_{TEM}, bla_{SHV}, and $bla_{\text{CTX-M}}$) and quinolone resistance genes (*qnr*S) were detected in all isolates. A molecular investigation was performed using pulsed field gel-electrophoresis (PFGE), and multilocus sequence typing (MLST). PFGE showed 2 different patterns, A and B. Pattern A was found in 44 of 45 strains from hospital 1 and in 5 of 5 strains from hospital 2. Only 1 strain from hospital 1 showed a distinct PFGE pattern (pattern B). MLST was performed in 5 KPN strains, 4 belonging to pattern A and 1 belonging to pattern B. Also, 4 pattern A strains belonged to the same ST340, clonal complex 258 (CC258). The pattern B strain belonged to ST2570, a different and nonphylogenetically related strain.

The first (or index) case occurred in hospital 1 in May 2017 on a female patient hospitalized at an isolation unit. This patient had many comorbidities (ie, diabetes, hypertension, Alzheimer disease, and previous hemorrhagic stroke) and was admitted to the hospital due to urinary tract infection. On May 21, 2017, she was diagnosed with nonventilation pneumonia and presented both KPN and *Enterobacter cloacae* from blood cultures. Despite therapy, she died during hospitalization on July 1, 2017. The KPN isolate belonged to PFGE pattern A and ST340.

Various studies have demonstrated that the KPN phylogenetic lineage belonging to CC258 (including ST258, ST11, ST340, and ST437) is vastly adapted to human populations and to hospital infections.[7] Previous reports of KPN ST340 and ST11 carrying NDM and other resistance mechanisms (ESβLs and *qnr* genes) have been documented in Brazil.[4,5] The emergence and spread of NDM KPN is worrying and represents a new worldwide challenge because it may carry several high-level antimicrobial resistance mechanisms.

The KPN pattern B and ST2570 strain was recovered from a blood culture of a patient hospitalized on a different unit in hospital 1 on October 6, 2017. This patient was initially hospitalized on September 20, 2017, due to a skin and soft-tissue infection and various comorbidities (ie, human immunodeficiency virus [HIV], treated tuberculosis, and chronic obstructive pulmonary disease [COPD]) and with many previous hospital passages. The blood culture was positive for NDM KPN on October 6, 2017, and the HAI was a skin and soft-tissue infection. Unfortunately, this patient was sent to the intensive care unit (ICU) and died 15 days later, despite medical care and antimicrobial therapy (including meropenem and polymixin B). Notably, the detection of the KPN ST2570 isolate seems relevant. Eibach et al[8] described ESβL-producing KPN ST2570 in samples from local and imported poultry in Ghana. To the best of our knowledge, this is the first human case (bloodstream infection and sepsis) caused by an NDM-KPN ST2570. It has been shown that NDM plasmid-bearing microorganisms might have significant environmental presence,[9,10] which could be gene sources to other species. We do not know which role the ST2570 isolate played in this outbreak, but it presence raises an interesting discussion, especially in a patient with multiple comorbidities and admittances. Could distinct KPN lineages adapted to poultry be the linkage between CC258 and environmental NDM isolates?

We report the first major outbreak of NDM KPN in hospitals from a single city in Brazil. Most isolates belonged to a well-adapted and documented CC258 (ST340). One case was caused by a distinct and not phylogenetically related ST2570. This outbreak highlights the relevance of monoclonal isolate dissemination between environments, despite hospital control policies. Apparently, monoclonal dissemination of well-adapted isolates takes place before plasmid dissemination to other clones or species.

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Putative horizontal transfer of carbapenem resistance between *Klebsiella pneumoniae* and *Kluyvera ascorbata* during abdominal infection: A case report

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To the Editor—The emergence of KPC-producing *Enterobacter* has led to the development of serious infections related to high levels of mortality and morbidity worldwide.[1,2] The rapid spread of KPCs is linked to multiple elements, such as plasmid-borne genes and the dissemination by international travelers; these bacteria are frequently multidrug resistant, causing untreatable infections.[3,4] *Kluyvera* spp is a genus of gram-negative rods of the Enterobacteriaceae family.[5] Although it is a commensal of the human gut microbiota,[6] *Kluyvera* spp has the potential to cause septic shock, urinary tract infections, catheter-associated bloodstream infections, and abdominal infections.[7] Here, we report a case of a plasmid-mediated horizontal transfer from a *Klebsiella pneumoniae* isolate to a *Kluyvera ascorbata* isolate during abdominal infection. The patient approved the data submission.

A 43-year-old male patient was admitted to the Hepatobiliary and Pancreatic Surgical Division from a hospital in the South Region of Brazil in October 2016. He was asymptomatic but had an incidental type 1 biliary cyst that was discovered during ultrasonography. Magnetic resonance imaging (MRI) with cholangiopancreatography was performed for adequate evaluation and showed an abnormal pancreatobiliary junction, as well. In November 2016, the patient underwent a cholecystectomy and total resection of the cyst, with closure of distal part of the main bile duct inside the pancreas, accompanied by Roux-en-Y hepaticojejunostomy to provide proper biliary drainage. The pathology report showed no malignancy in surgical specimen. After 48 hours, the patient was evaluated with postoperative pancreatitis and signs of sepsis, therefore piperacillin/tazobactam treatment was started. The patient continued to present clinical deterioration and needed parenteral nutrition; he was consequently transferred to the intensive care unit (ICU). Blood cultures were negative and abdominal computerized tomography (CT) showed abdominal collections. CT-guided drainage of pancreatic fluid was performed and cultures were negative. Nevertheless, antimicrobial treatment with meropenem was started and continued for 14 days without resolution. A second CT-guided drainage procedure was performed at the end of December, and the bacteriological culture yielded a multisusceptible *Enterococcus faecalis*; a *Kluyvera ascorbata* resistant to ampicillin and second-generation cephalosporin but susceptible to carbapenem, and multidrug-resistant *Klebsiella pneumoniae*, including resistance to tigecycline and carbapenem. Antibiotics were adjusted to vancomycin, meropenem, and ertapenem plus polymyxin B with clinical improvement but without complete bacterial clearance. After 17 days, a third CT-guided drainage was performed, and the bacterial culture yielded 1 *K. ascorbata* isolate resistant to carbapenem. A fourth CT-guided drainage was performed after 15 days, and the culture yielded *K. ascorbata* susceptible to carbapenem and *K. pneumoniae* resistant to carbapenem. Antibiotic treatment was adjusted to polymyxin B, tigecycline, and sulfametoxazol-trimetoprim, and the patient was evaluated with signs of controlled infection. After 14 days, the antibiotic treatment was suspended, and a final CT showed no signs of abdominal collections. The patient was discharged and was followed as an outpatient.

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