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Original Article

Use of whole genomic sequencing to detect New Delhi metallo-B-lactamase (NDM)-producing *Escherichia coli* outbreak associated with endoscopic procedures

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Abstract

Background: Whole-genome sequencing (WGS) has emerged as an alternative genotyping tool for outbreak investigations in the healthcare setting. We describe the investigation and control of a New Delhi metallo-B-lactamase (NDM)-producing *Escherichia coli* cluster in Southeast Michigan.

Methods: Michigan Bureau of Laboratories identified several closely related NDM-producing *E. coli* isolates with WGS. An epidemiologic investigation, including case-control study, assessment of infection control practices, and endoscope culturing, was performed to identify source of transmission. Targeted screening of potentially exposed patients was performed following identification of probable source.

Results: Between July 2021 and February 2023, nine patients were identified. Phylogenetic analysis confirmed the isolates were closely related with less than 26 single nucleotide polymorphism (SNP) differences between isolates, suggesting an epidemiological link. Eight (89%) patients had a duodenoscope and/or gastroscope exposure. Cases were compared with 23 controls. Cases had significantly higher odds of exposure to duodenoscopes (odds ratio 15.0; 95% CI, 1.8–142.2; $P = .015$). The mean incubation period, estimated as date of procedure to positive index culture, was 86 days (range, 1–320 days). No lapses in endoscope reprocessing were identified; NDM-producing *E. coli* was not recovered from reprocessed endoscopes or during targeted screening. No additional cases were identified after removal of implicated gastroscopes and replacement of duodenoscope with disposable end caps.

Conclusions: In this investigation, WGS was utilized to identify transmission of an NDM-producing *E. coli* outbreak associated with endoscope exposure. Coupled with epidemiologic data, WGS can facilitate outbreak investigations by rapidly identifying linked cases and potential sources to prevent further transmission.

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Introduction

New Delhi metallo-B-lactamase (NDM, bla_{NDM})-producing carbapenem-resistant *Enterobacterales* (CRE) are a growing threat in the United States, and predominantly occur in patients exposed in healthcare facilities.[1] In less than a decade since NDM was first described in 2009, it was declared an urgent global threat in 2019 by the Centers for Disease Control and Prevention.[2] These bacteria possess significant antimicrobial resistance (AMR), and early detection of an outbreak is difficult.[3] Containment involves implementation of strict infection control measures,[4] and prior outbreaks have been associated with lapses in infection control in long-term acute care and skilled nursing facilities,[5] endoscopic procedures,[6] and contaminated total parenteral nutrition.[7]

Epidemiological surveillance relies on molecular strain typing to determine the genetic relatedness among isolates. Previously, established molecular methods for outbreak surveillance included pulsed-field gel electrophoresis, amplification fragment length polymorphism, and multi-locus sequencing typing.[8] In recent years, whole-genome sequencing (WGS) has emerged as an alternative genotyping tool. Since its inception, United States

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public health has coordinated the use of WGS for bio-surveillance of emerging pathogens at the state level, including CRE.[9] Additionally, WGS is becoming a powerful and attractive tool for epidemiologic investigations and surveillance.[10] When used in conjunction with traditional hospital epidemiologic methods, WGS can quickly determine the source of outbreaks and trace transmission between patients.

Clinical laboratory partners across Michigan are mandated to report carbapenemase-producing CRE cases to public health and are encouraged to submit all CRE isolates to the Michigan Department of Health and Human Services (MDHHS) Bureau of Laboratories (BOL) for routine CRE surveillance, which includes AMR confirmation and WGS on all confirmed non-*Klebsiella pneumoniae* carbapenemase-producing CRE isolates.[11] In September 2021, BOL notified us of two closely related bla_{NDM}-producing *Escherichia coli* isolates from 2 patients who received care in our healthcare facility (HCF) in July 2021. An outbreak investigation was subsequently conducted to identify the source of infection and prevent further transmission. This report describes the role of molecular surveillance in identifying an outbreak of an NDM-producing *E. coli* associated with endoscopic retrograde cholangiopancreatography (ERCP) and esophagogastroduodenoscopy (EGD) at a tertiary HCF in Detroit, Michigan.

Methods

Field investigation

Case definition: A case was defined as an NDM-producing *E. coli* isolate that was closely related by WGS to the outbreak strain, recovered from a patient hospitalized in our HCF between July 1, 2021 and February 28, 2023.

Initial case finding and case description: The initial 2 cases were hospitalized at our HCF in July 2021 and subsequently became symptomatic. The first patient developed peritonitis during the index hospitalization, and the second patient presented to an outside HCF with sepsis and bacteremia 1 month later. The CRE isolates were sent to BOL for further testing and were identified as closely related to NDM-producing *E. coli*. Upon further review, 3 additional patients who were admitted to our HCF between August and September were identified. Medical record review revealed that all patients underwent ERCP procedures with 2 duodenoscopes prior to the onset of infection. We subsequently reviewed all reported CRE cases in our database since January 2020 but no additional NDM cases were identified.

Additional case findings: Between November 2021 and February 2023, four additional cases were identified; the final case was detected at an inpatient rehabilitation facility 5 days after the patient was discharged from our HCF.

Case-control study: A case-control study was performed to identify risk factors for NDM-producing *E. coli* carriage. All consecutive patients with a history of non-NDM-producing carbapenem-resistant *E. coli* who were hospitalized between January 2020 and April 2023 were selected as controls. Patient characteristics, prior antibiotic exposure, units of stay and operating rooms, procedures, and healthcare staff exposures were evaluated.

Exposure screening: MDHHS recommended screening healthcare contacts to identify cases, including roommates, high-risk patient contacts who overlapped with the cases on the same inpatient units, and patients who were exposed to shared duodenoscopes and gastroscopes. One hundred thirty-six patients exposed to the implicated duodenoscopes (May 2021-November 2021) and 1097 to gastroscopes (May 2021-March 2023) were notified and offered CRE screening.

Infection control practices and environmental assessment: A detailed assessment of endoscopic procedures, reprocessing of equipment, infection prevention and control (IPC) practices, and cleaning of environment were performed in the endoscopy suites. Interviews of endoscopy personnel and direct observation of endoscope cleaning and reprocessing were conducted by the IPC team. The implicated endoscopes were sequestered and sent to a reference laboratory for inspection and cultures; Tween-based solution was used as extraction fluid for duodenoscopes and sterile water for gastroscopes.[12]

Laboratory analysis

Isolate identification: Identification of *E. coli* and antimicrobial susceptibility patterns were determined using MALDI-TOF mass spectrometry and Vitek (bioMerieux, Durham NC), respectively, in our clinical microbiology laboratory. Carbapenemase gene detection for clinical isolates suspected of harboring metallo-beta-lactamase genes (i.e., meropenem/vaborbactam and/or ceftazidime/avibactam resistance) was performed using Cepheid GeneXpert® (Sunnyvale, CA). All isolates were sent to MDHHS BOL for AMR confirmation and WGS. Rectal swabs of exposed patients were also sent to BOL for CRE screening.

WGS and assembly, phylogenetic tree analysis: Sequence data were generated by extracting DNA with the Qiagen DNeasy Blood and Tissue Kit (Germantown, MD) library prep with the Nextera Flex kit (Illumina, San Diego, CA), and sequencing on the Illumina MiSeq platform. A core-SNP alignment was made by trimming reads with Trimmomatic (Illumina),[13] mapping reads to the IMT16316 genome (Genbank accession GCA_002587005.1), and core SNPs were selected using Snippy.[14] The tree was made using IQ-TREE[15] and the tree scale is in nucleotide substitutions per site. AMR-associated genes were detected by first assembling sequencing reads using Shovill[16] and then applying ABRicate.[17] Sequence reads are available in the National Center for Biotechnology Information under BioProject PRJNA659498. Visualizations were made using the *ggtree* and *ggplot* packages in R v4.0.4 (R Core Team, Vienna, Austria).

Statistical analysis

Patient characteristics were summarized using descriptive statistics; counts and percentages were used for categorical variables and median with interquartile range for continuous variables. Bivariate analyses were performed to assess for associations between patient exposures and NDM *E. coli* carriage. Chi-square or Fisher's exact tests were used to compare categorical variables; the Mann Whitney-*U* test was used to compare non-parametric continuous variables. Unadjusted odds ratio and 95% CIs for each exposure were calculated. All *P*-values were 2-sided; statistical significance was defined as $P < .05$. Analyses were performed using SPSS software, version 28.0.1 (IBM, Armonk, NY).

Results

Field investigation

Case patients: A total of 9 cases who were admitted to our HCF were identified between September 2021 and March 2023 (Table 1 and Fig. 1). The median age was 64 years (interquartile range 46–75) and 67% were female. The mean incubation period, estimated as the date of the procedure with the implicated endoscope to positive index

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Table 1. Characteristics of patients with NDM-1 isolated in culture

Case #	Age, years	Gender	Co-morbidities	EGD/ERCP Indication	Implicated Scope	Incubation Period (days)	Index Specimen Type	Outcome
1	64	Female	Liver transplant recipient	Bile leak	Duodenoscope A Duodenoscope C	1	Peritoneal fluid	Alive
2	69	Male	Metastatic colorectal cancer	Tumor-related obstruction	Duodenoscope A Gastroscope A	30	Blood	Deceased
3	50	Female	Liver transplant recipient	Bile leak	Duodenoscope A Duodenoscope C Gastroscope B	2	Blood	Alive
4	79	Male	Metastatic lung cancer	Ascending cholangitis	Duodenoscope B	6	Tracheal aspirate	Deceased
5	84	Female	Choledocholithiasis	Bile leak	Duodenoscope A Duodenoscope B Gastroscope A	120	Peritoneal fluid	Alive
6	62	Male	Choledocholithiasis	Ascending cholangitis	Duodenoscope C	2	Peritoneal fluid	Alive
7	39	Female	Primary sclerosing cholangitis	Biliary stricture	Duodenoscope A Gastroscope A	320	Urine	Alive
8	71	Female	Liver transplant recipient	Bile leak	Gastroscope A	231	Peritoneal fluid	Deceased
9	41	Female	Cirrhotic liver disease	Esophageal varices	Gastroscope A Gastroscope B	62	Urine	Alive

EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography.

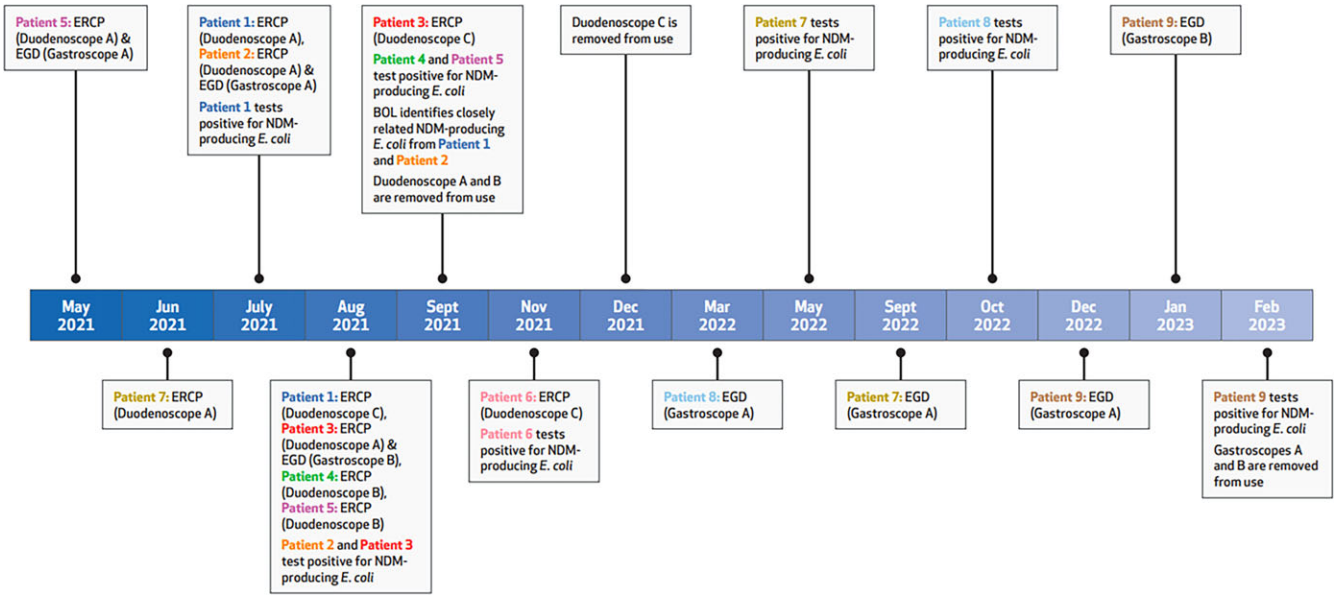

Figure 1. Timeline of outbreak investigation with procedures, NDM-producing *E. coli* detection, and removal of endoscopes.

culture, was 86 days (range, 1–320 days). Six patients had a clinical infection and three were determined to be colonized. Intra-abdominal fluid (44%) and blood (33%) were the most common sources. Patient 5, the suspected index case, was originally from India and had a history of extended-spectrum beta-lactamase (ESBL)-producing *E. coli and* non-ESBL *E. coli* bacteremia; however, there were no reported overnight health care stays or invasive procedures outside the United States. Patient 7 had an ESBL-producing *E. coli* urinary tract infection prior to the NDM diagnosis. Three patients subsequently died, but only one death was determined to be related to NDM infection.

During the investigation, epidemiological tracing of the cases revealed no temporal overlap of patient rooms. The first 7 patients had 1 or more ERCP procedures with the 3 implicated duodenoscopes between May and November 2021. Patient 5 underwent ERCP twice with duodenoscopes A and B in May and August of 2021, respectively; 5 additional cases were traced to these duodenoscopes. Duodenoscope C, initially used in Patients 1 and

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Table 2. Comparison of clinical characteristics and risk factors for NDM infection

Characteristics	Cases (n = 9)	Controls (n = 23)	Unadjusted Odds Ratio (95% CI)	*P*-value
Median age (IQR) years	64 (46–75)	64 (57–71)	N/A	.74
Male sex	3 (33%)	15 (65%)	3.8 (0.74–19.1)	.13
Length of stay, days	22 (8–43)	43 (14–61)	N/A	.30
Previous antibiotic use in 90 days, *n* (%)	7 (78%)	23 (100%)	4.3 (2.2–8.2)	.073
• BL/BLI	3 (33%)	14 (61%)	.32 (.06–1.6)	.24
• Cephalosporin	5 (56%)	19 (83%)	.26 (.05–1.4)	.18
• Carbapenem	4 (44%)	12 (52%)	.73 (.16–3.5)	1.0
• Fluoroquinolone	0	3 (13%)	.69 (.54–.88)	.54
• TMP/SMX	0	3 (13%)	.69 (.54–.88)	.54
• Aminoglycoside	0	2 (9%)	.7 (.55–.89)	1.0
Unit of stay, *n* (%)				
• MICU	0	8 (35%)	.63 (.46–.85)	.07
• SICU	2 (22%)	5 (22%)	1.03 (.16–6.6)	1.0
• Medical GPU	4 (44%)	4 (17%)	3.8 (.69–20.8)	.18
• Surgical GPU	3 (33%)	23 (26%)	1.4 (.27–7.5)	.69
Operating room, *n* (%)				
• Room A	1 (11%)	3 (13%)	.83 (.08–9.3)	1.0
• Room B	3 (33%)	1 (4%)	11.0 (.96–125.8)	.06
• Room C	1 (11%)	0	.26 (.14–.47)	.28
• Room D	1 (11%)	0	.26 (.14–.47)	.28
Procedure, *n* (%)				
• ERCP	8 (89%)	8 (35%)	15.0 (1.8–142.2)	**.015**
• EGD	8 (89%)	11 (48%)	8.7 (.94–81.5)	.05
• Other endoscopy	5 (56%)	4 (17%)	5.9 (1.1–32.5)	.075
• Bronchoscopy	1 (11%)	3 (13%)	.83 (.08–9.3)	1.0
• Endotracheal intubation	3 (33%)	13 (56%)	.39 (.08–1.9)	.43
• TEE	2 (22%)	1 (4%)	6.3 (.5–80.2)	.18
Staff Exposure, *n* (%)				
• Staff A	1 (11%)	1 (4%)	2.8 (.15–49.4)	.49
• Staff B	1 (11%)	1 (4%)	2.7 (.15–49.4)	.49
• Staff C	2 (22%)	1 (4%)	6.3 (.49–80.2)	.18
• Staff D	2 (22%)	2 (9%)	3.0 (.4–25.5)	.57
• Staff E	4 (44%)	3 (13%)	5.3 (.89–31.9)	.076
• Staff F	2 (22%)	0	.23 (.12–.45)	.07
• Staff G	2 (22%)	0	.23 (.12–.45)	.07
E coli in the past 1 year, *n* (%)	2 (22%)	13 (57%)	.22 (.04–1.3)	.12
ESBL-producing *E coli* in the past year, *n* (%)	2 (22%)	11 (48%)	.31 (.05–1.8)	.25
CRE *E. coli* in the past year, *n* (%)	0	2 (9%)	.7 (.55–.89)	1.0

BL/BLI, beta-lactam/beta-lactamase inhibitor; CRE, carbapenem-resistant Enterobacterales; EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography; ESBL, extended-spectrum beta-lactamase; medical GPU, medical general patient unit; MICU, medical intensive care unit; SICU, surgical intensive care unit; surgical GPU, surgical general patient unit; TEE, trans-esophageal echocardiogram; TMP/SMX, trimethoprim/sulfamethoxazole.

3 after their NDM infection, was implicated in Patient 7. Although Patient 8 had 4 prior ERCPs, the implicated duodenoscopes were not used. However, Patient 8 had an EGD with gastroscope A that was used in three cases previously. Patient 9 did not have an ERCP but did have 2 EGDs with gastroscopes A and B that were used in five cases previously. Cases or their relatives, if they were deceased, were notified of the exposure. See Fig. 1 for the timeline of the investigation.

Case-control study: Overall, 9 cases and 23 controls had similar demographic characteristics, length of stay, unit of stay, operating room, and staff exposures (Table 2). Endoscopic retrograde cholangiopancreatography duodenoscopes were used on 8 (89%)

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Table 3. Infection control assessment and control measures

Infection Control Assessment/Observation
Endoscopy Suites • Gaps in general IPC practices, such as proper hand hygiene and storage of personal items, were noted • Direct observation of equipment reprocessing procedures was performed • Interviews of endoscopy personnel revealed high turnover rate of dedicated environmental services personnel, leading to lack of standardization of workflow for room turnover or cleaning • Protein test to detect residual proteins after high-level disinfection was disrupted during the COVID-19 pandemic due to swab shortages • Disposable or single-use duodenoscopes were not routinely used for patients with prior history of multidrug-resistant organisms • Inspection/repair logs of all implicated endoscopes were reviewed • Environmental surveillance cultures performed on all implicated endoscopes
Other measures • Multidisciplinary incident team, including administrative leaders, IPC, laboratory services, Clinical Engineering, and environmental services, was assembled • Screening for CRE was offered to all patients who underwent endoscopic procedure with the implicated endoscopes during the outbreak period
Infection Control Measures
Endoscopy Suites • Ongoing staff education to ensure adherence to IPC practices • Corrective measures for equipment reprocessing procedures were implemented • Protein testing was expanded to include all channeled scopes • Indications for disposable duodenoscopes were emphasized to the proceduralists • All implicated endoscopes were removed from further use • Duodenoscopes were upgraded to a contemporary design with disposable end caps
Other measures • Team members from IPC, endoscopy suites, and reprocessing conducted weekly environmental of care rounds to monitor process improvement measures

cases and 8 (35%) controls (unadjusted odds ratio 15.0; 95% CI, 1.8–142.2; $P = .015$). Although gastroscope use did not reach statistical significance, they were more commonly used in cases than controls (unadjusted odds ratio 8.7; 95% CI, .94–81.5; $P = .05$).

Exposure screening: Three patients exposed to the duodenoscopes and 197 exposed to the gastroscopes returned for screening, but no additional cases were detected. Of note, Patient 7 was among the exposed patients notified in 2021 but declined screening at the time.

Infection control practices and environmental assessment: The IPC assessment focused on endoscope reprocessing (Table 3). No breaches were identified in the reprocessing of duodenoscopes and gastroscopes. Observations occurred in two endoscopy suites where the procedures were performed. Precleaning, manual cleaning, high-level disinfection (HLD) using automated endoscope reprocessors with RAPICIDE™ High-Level Disinfectant (Cantel Medivators, Conroe, TX), rinsing, drying, and storage were performed according to healthcare industry standards. The automated endoscope reprocessors were functioning properly and maintenance was up to date.

The inspection/repair logs of all implicated endoscopes were reviewed. The scopes had been inspected, repaired, and rebuilt numerous times. For example, Duodenoscope A was serviced 14 times for various reasons, including failed leak testing and broken elevator, and fully disassembled multiple times since 2016. Gastroscope B was purchased in 2018 and serviced 31 times for mechanical/physical damage or fluid invasion. It was completely rebuilt in February 2023; the insertion tube and all internal components were replaced at that time. It was sent out for repair again 1 month later.

The scopes were inspected for visible debris and damage prior to extraction method by the reference lab. Duodenoscope A had visible internal debris and damage but not the other scopes. Multiple organisms, including *Candida parapsilosis, Micrococcus* species, *Pseudomonas aeruginosa*, *Staphylococcus auricularis,* and *epidermidis,* were recovered from all the endoscopes. However, *E. coli* was not recovered.

Infection prevention and control measures: All implicated endoscopes were removed from further use (Table 3). Our duodenoscope inventory was upgraded to a contemporary design with disposable end caps as per the Food and Drug Administration recommendations in January 2022, and the older models were retired.

Laboratory Analysis: WGS was performed on 10 available NDM *E. coli* isolates (including two isolates from Patient 5). All isolates were classified as sequence type 648 and harbored NDM-5 carbapenemase genes, in addition to bla_{NDM}, $bla_{\text{TEM-1B}}$, $bla_{\text{OXA-1B}}$, and $bla_{\text{CTX-M-15}}$ antibiotic resistance genes. Phylogenetic analysis confirmed the 10 isolates (2 from a single case) were closely related with less than 26 single nucleotide polymorphisms (SNPs) differences between isolates (Fig. 2), consistent with a plausible epidemiologic linkage (Fig. 3).

Discussion

This report describes the detection of NDM *E. coli* outbreak associated with endoscopic procedures using WGS. The NDM *E. coli* strains were closely related according to the WGS analysis, suggesting possible dissemination through a common source. Our epidemiologic investigation and case-control analysis suggested that exposure to duodenoscopes and/or gastroscopes was associated with transmission in all cases despite the negative endoscope cultures for the pathogen in question. No other source of transmission was identified after an extensive investigation.

This investigation uniquely highlights the importance of WGS for surveillance and epidemiologic investigation to identify an otherwise unknown nosocomial outbreak and halt subsequent transmission. WGS has been used for molecular strain typing and phylogenetic analysis during outbreaks for a variety of pathogens.[18–20] However, utilizing WGS for ongoing, routine surveillance of healthcare-associated outbreaks is currently less common but has been reported for Vancomycin-resistant enterococci,[21]

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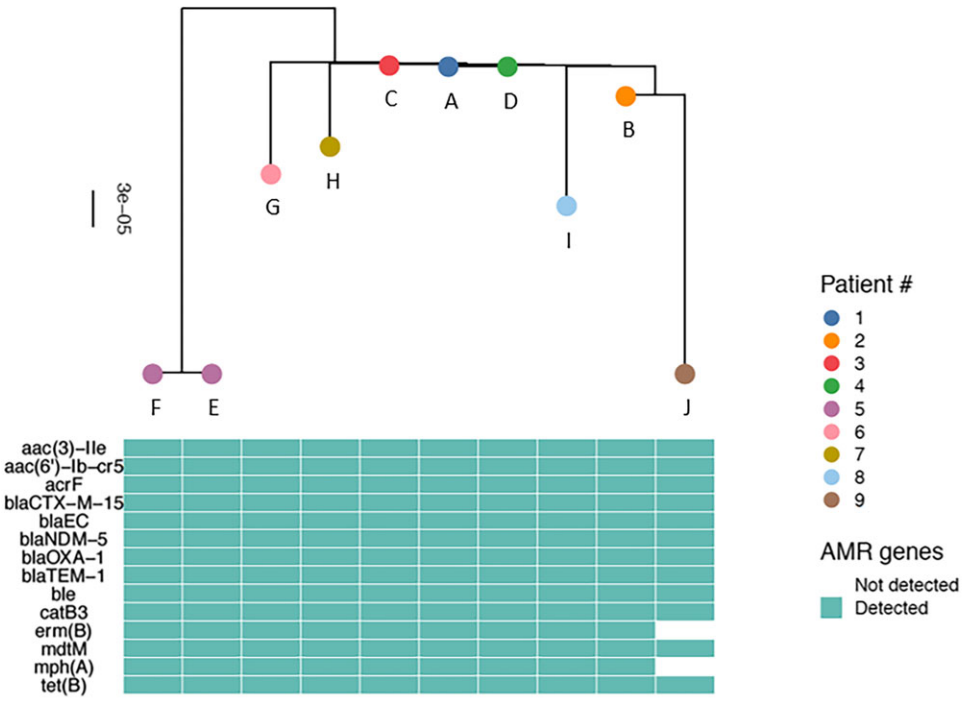

Figure 2. Core single nucleotide polymorphism (SNP)-based phylogenetic tree.

Core single nucleotide polymorphism (SNP)-based maximum-likelihood phylogenetic tree of isolates involved in the investigation, with presence of acquired antimicrobial-resistance associated genes.

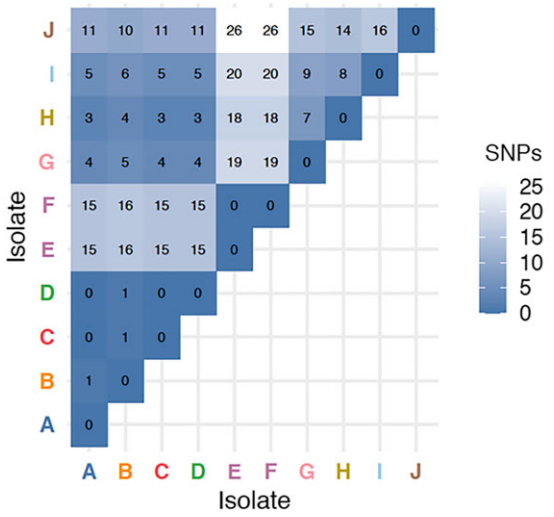

Figure 3. Single nucleotide polymorphism (SNP) matrix of isolates depicting pairwise SNP distances.

carbapenem-resistant *K. pneumoniae*[22] and *Pseudomonas aeruginosa*.[23] It may play an important role in detecting occult outbreaks due to organisms with prolonged and variable incubation periods as illustrated in this report and previous studies.[21–23]

Collaboration and coordination among state health departments and HCFs to identify occult nosocomial outbreaks and detect and limit the transmission of emerging pathogens and multidrug resistant organisms is paramount. CRE colonization can be prolonged, with persistent intermittent shedding of organisms, and infection can follow a long incubation period.[24,25] While the incubation period varied among cases, the organism was detected more than six months after the procedure in two patients. Early identification is critical to implement isolation precautions in hospitalized patients and prevent subsequent transmission. As a result of the WGS data, we were able to determine the likely source of the outbreak and focus efforts on prevention, potentially saving time and resources on the investigation.

We focused our initial investigation on duodenoscopes given previously reported higher rates of contamination and transmission associated with these devices.[26] However, gastroscopes were also subsequently implicated in additional cases and may have contributed to transmission events within the first seven cases.

Our study also re-emphasizes the well-established association of CRE transmission following endoscopy and ERCP procedures.[27] Following a large outbreak of NDM-producing *E. coli* at an HCF in northeastern Illinois [1], additional outbreaks have been reported worldwide.[26,28–31] The incidence of infection associated with these devices is reportedly 1 in 1.8 million procedures,[32] likely an underestimation. The intricate design and delicate materials of flexible endoscopes make them difficult to clean and disinfect.[26,30–34] It is estimated that the microbial contamination rate of reusable duodenoscopes is as high as 15%.[30]

Bacterial contamination and infection-transmission associated with these devices due to endoscope reprocessing breaches, device defect or device-specific factors, and lapses in infection control practices have been reported.[1,26] However, several outbreaks have occurred despite adherence to reprocessing protocols or in the absence of endoscope defects. Occult internal damage within endoscopes may be implicated in transmission of infection in some settings.[26,31]

Since we did not identify any lapses in endoscope reprocessing, we investigated other potential contributing factors. There was concern for wear and tear, and the repair logs of the endoscopes revealed that

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all the implicated endoscopes were frequently sent out for repairs over their lifespan. Despite HLD, high-concern pathogens associated with human disease, including *P. aeruginosa* and *C. parapsilosis,* were recovered from the endoscopes. Although NDM-1-producing *E. coli* was not recovered from the endoscopes, this could be explained by a lower bioburden following several rounds of HLD and lag time from the procedure to testing of the scopes.

Studies suggest lifetime usage, not endoscope age, is a better predictor of the extent of damage.[31] Repeated use and reprocessing of flexible duodenoscopes can result in occult damage, and limited access to cleaning leads to the development of microbial biofilms and persistent contamination of bacteria after standard reprocessing. In two published studies, visual inspection of endoscope working channel with a borescope revealed widespread occult damage and debris, which can potentially impact the adequacy of endoscope reprocessing.[35,36] Notably, the "life expectancy" and normal "wear and tear" of endoscopes are not well defined, and guidance on when to replace or retire these devices is limited.

Given the potential for damage and risk of contamination due to ineffective reprocessing or fluid invasion, the duodenoscopes used in our HCF were recalled by the manufacturer in December 2021.[37] After we transitioned to duodenoscopes with disposable end caps the following month, there are ongoing discussions regarding leasing instead of purchasing gastroscopes, establishing a preventative maintenance program for scope inspection using borescopes, and reporting or escalating issues.

Environmental assessment identified inconsistencies in practice during routine and terminal cleaning of some shared equipment in the endoscopy suites. The outbreak occurred during the COVID-19 pandemic when there were staffing and supply shortages. Efforts are being made to increase environmental services support and standardize room cleaning workflows. There is ongoing education to ensure adherence to IPC practices with emphasis on hand hygiene, routine and terminal cleaning of some shared equipment, and scope handling to reduce the risk of contamination.

There are several limitations to this investigation. Although all patients with endoscopic exposure were notified, just 16.5% returned for screening, and the exact attack rate is unknown. It is possible that the number of affected patients is underestimated. Furthermore, endoscope reprocessing occurred after patients were exposed; however, prior observations and audits did not identify any gaps in practices. Due to the small number of cases, gastroscope use did not reach statistical significance for association with acquisition of NDM-producing *E. coli*. Additionally, a case-control study was limited by low power; and a multivariable analysis was not conducted.

Conclusions

This outbreak highlights the importance of utilizing WGS with epidemiologic data to detect nosocomial outbreaks, identify potential sources of infection, and limit the transmission of multidrug resistant organisms among patients. It also illustrates the risk of bacterial contamination and infection-transmission associated with endoscopes despite adherence to reprocessing protocols due to endoscope defects. HCFs should consider transitioning to newer duodenoscope models to reduce the risk of contamination and infection.

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