clindamycin and ciprofloxacin[4] than of invasion by community-associated, multidrug-susceptible SCC*mec* IV–harboring MRSA.[6] Even though our inference is limited by lack of strain and SCCmec typing, the findings are consistent with our recent identification of SCC*mec* type II in MRSA-colonizing nares and oropharynges of acute-care and long-term admissions of psychiatric patients.[9] We also analyzed a time series of 15 years using a robust statistical model to detect sudden changes in trends.

In a classic article, Deurenberg and Stobberingh[10] describe the blurring of distinctions between CA- and HA-MRSA and argue for a pure molecular definition, based on SCC*mec* typing. Because strain typing is not widely available, especially in low-to-middle income countries, careful long-term follow-up of resistant profiles may provide a reasonable proxy for detecting ecological changes in MRSA infections. Those trends also have therapeutic relevance. Although TMP/SMX is not a reasonable choice for treating MRSA BSI, other less-severe infections (eg, skin infections or phlebitis) acquired during hospital admissions may benefit from that antimicrobial. Further studies combining long-term analysis of time series with molecular typing may provide insights on the past, present, and future of healthcare-associated infectious caused by MRSA.

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Retrospective analysis of multidrug-resistant clinical and environmental isolates for the presence of the colistin-resistance gene *mcr-1*

Kara J. Levinson PhD, MPH[1], Mackenzie E. Collins BS[1], Anne M. Lachiewicz MD[2], Andy J. Koltun MS[3], Mark D. Sobsey PhD[3], Elizabeth Christenson PhD[3], Jill R. Stewart PhD[3] and Melissa B. Miller PhD[1,4]

[1]Clinical Microbiology Laboratory, UNC Health, Chapel Hill, North Carolina, [2]Department of Infectious Diseases, University of North Carolina School of Medicine, Chapel Hill, North Carolina, [3]Gillings School of Global Public Health, Department of Environmental Sciences & Engineering, University of North Carolina, Chapel Hill, North Carolina and [4]Pathology and Laboratory Medicine, University of North Carolina School of Medicine, Chapel Hill, North Carolina

To the Editor—Carbapenem-resistant Enterobacterales (CRE) are a public health threat due to increased mortality, cost, and transmissibility of these infections. Although colistin is rarely considered as a last-resort antibiotic to treat CRE infections, increasing reports of plasmid-mediated colistin-resistant CRE isolates worldwide[1] are concerning. Resistance to colistin is conferred by *mcr* genes and was first linked to the *mcr-1* gene.[2] Since the initial *mcr-1* report from 2005, researchers have screened isolate collections for *mcr-1* and have found plasmid-mediated colistin resistant strains in animal and human populations.[2] At the time of this study, 4 clinical isolates containing the *mcr-1* gene were identified in the United States,[3] which has since increased to 55 isolates in at least 21 states.[4] The overall prevalence, distribution, and impact of *mcr-1* remain unclear.

In North Carolina, more than half of hospitals have reported CRE infections,[5] yet resistance to colistin has not been systematically examined. Given the active agriculture industry within the state, the potential to identify *mcr-1* among clinical and

Author for correspondence: Kara J. Levinson, E-mail: Kara.Levinson@tn.gov, or Melissa B. Miller, E-mail: Melissa.Miller@unchealth.unc.edu.

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Table 1. Summary of Clinical and Environmental Isolates Screened for *mcr-1*–Mediated Colistin Resistance

Type of Organism	Total Isolates	Isolates Tested[a]	Organism (No. of Isolates Tested)	Extensively Resistant[b]	Positive for *mcr-1* Gene
Multidrug resistant	405	387	*C. freundii* (5)	6	0
			C. werkmani (1)		
			Citrobacter spp. (1)		
			E. aerogenes (3)		
			E. cloacae/asburiae (9)		
			E. cloacae complex (3)		
			E. coli (302)		
			K. oxytoca (2)		
			K. pneumoniae (51)		
			M. morganii (2)		
			P. mirabilis (4)		
			R. ornithinolytica (1)		
			S. marcescens (3)		
Carbapenem-resistant Enterobacterales (CRE)	100	100	*C. freundii* (5)	12	0
			E. aerogenes (5)		
			E. cloacae/asburiae (30)		
			E. cloacae complex (6)		
			E. hormaechei (1)		
			Enterobacter spp. (6)		
			E. coli (12)		
			K. oxytoca (1)		
			K. pneumoniae (29)		
			M. morganii (1)		
			P. rettgeri (1)		
			S. marcescens (2)		
			S. odorifera (1)		
Burn unit	133	126	*C. freundii* (1)	9	0
			C. koseri (10)		
			E. aerogenes (6)		
			E. cloacae/asburiae (43)		
			E. coli (2)		
			K. pneumoniae (3)		
			M. morganii (1)		
			P. mirabilis (20)		
			S. marcescens (40)		
Industrial hog operations	18	18	*E. coli* (18)	0	0
Municipal sewage	55	46	*C. amalonaticus* (1)	0[c]	0
			C. braaki (1)		
			C. farmerii (1)		
			C. freundii (1)		
			E. cloacae/asburiae (12)		
			E. coli (8)		
			K. oxytoca (6)		
			K. pneumoniae (14)		
			S. marcescens (2)		
Total	711	677		27	0

[a]Met MDR criteria and grew in culture from frozen stock.[b]Resistant to all 5 drug classes tested, including (1) extended-spectrum cephalosporins (cefepime, ceftriaxone); (2) fluoroquinolones (ciprofloxacin, levofloxacin); (3) aminoglycosides (gentamicin, tobramycin, amikacin); (4) carbapenems (meropenem, ertapenem); (5) piperacillin/tazobactam (if ceftriaxone was intermediate or resistant, piperacillin/tazobactam was considered resistant).[c]Screened and isolated based on extended-spectrum β-lactamase (ESBL)– and *Klebsiella pneumoniae* carbapenemase (KPC)–mediated resistance, not evaluated for extensive resistance.

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environmental isolates may be higher with more opportunity for transmission between animal and human populations. To address this, we screened clinical and environmental isolates for *mcr-1* to determine the prevalence and dissemination of colistin resistance among MDR organisms.

Methods

Study inclusion criteria included an isolate (1) identified as a member of *Enterobacterales* via biochemicals or mass spectrometry, (2) with antimicrobial susceptibility results, and (3) with drug resistance to ≥3 drug classes (ie, multidrug-resistant or MDR). Clinical isolates were obtained from the UNC Clinical Microbiology Laboratory and were determined to be MDR or CRE as part of routine patient care. Additional clinical isolates were obtained from archived MDR isolates collected from surveillance swabs of burn unit patients. Bacterial isolates were collected from December 2015 to May 2018.

To determine whether MDR strains containing *mcr-1* were circulating in the environmental microbial population, we screened isolates collected from surface water of industrial hog operations in eastern North Carolina, and drug-resistant *Escherichia coli* isolates were collected from UNC Hospitals and Chapel Hill–Carrboro community sewage. Based on previous studies that screened clinical isolate collections, we expected the prevalence of *mcr-1* to be ~1%.[6] Thus, by screening clinical and environmental MDR isolates, we sought to increase the likelihood of identifying *mcr-1*–positive strains.

To verify individual isolates containing the *mcr-1* gene could be detected when pooled and screened, we established the limit of detection (LOD) using 2 *mcr-1*–positive *E. coli* strains as controls. We made a dilution series, performed polymerase chain reaction (PCR), 100 μL of each dilution was plated onto sheep blood agar, and incubated overnight at 35°C to calculate colony-forming units (CFU/mL). We were able to reproducibly detect *mcr-1* if present in an individual sample at ≥925 CFU/mL, which is considerably lower than the CFU present in pools of bacterial isolates.

Archived isolates were cultured at 35°C on MacConkey agar. To extract DNA, single colonies were placed in nuclease-free water, boiled for 10 minutes, and centrifuged; this extract was used as the PCR template. Real-time PCR was performed using the 2x Taq Man DNA Universal Mastermix kit (Applied Biosystems, Foster City, CA), and primers and probes (Biosearch Technologies, Petaluma, CA) previously published to detect DNA internal to the *mcr-1* gene.[7] To screen a large number of isolates in a cost-effective manner, extracted DNA was pooled into groups of 20 isolates and tested for the presence of *mcr-1*. Positive pools were retested in individual PCR reactions to identify positive isolates. Two *E. coli* strains (0494 and 0495) containing the *mcr-1* gene from the CDC and FDA Antibiotic Resistance Isolate Bank served as positive controls.

Results

In total, 711 clinical and environmental MDR isolates were screened, including 638 clinical patient isolates, 17 industrial hog operation and 1 control site MDR or confirmed β-lactamase–producing isolates, and 55 hospital and municipal sewage isolates. Among the 711 isolates, 677 isolates met the study inclusion criteria and grew in culture from frozen stock. Clinical isolates grew from a range of culture types including 389 isolates from urine, 44 from blood, 34 aerobic/anaerobic isolates, 21 respiratory isolates, 1 sterile fluid isolate, and 124 isolates from burn unit surveillance. All 677 isolates were tested by PCR, and none were positive for the *mcr-1* gene.

Discussion

Colistin is one of few remaining antibiotics to treat MDR infections. Thus, understanding dissemination of *mcr-1*–mediated colistin resistance in microbial populations is vital. Although we did not identify any *mcr-1*–containing isolates in our screen, the lack of detectable colistin resistance still provides valuable information for patient and public health. This absence suggests a low prevalence of *mcr-1*–mediated colistin resistance in the microbial population circulating in North Carolina. In March 2019, the first clinical isolate positive for *mcr-1* in North Carolina was detected,[8] further supporting our screen findings and low prevalence in the state.

Very low prevalence of *mcr-1* is consistent with findings in similar studies, such as a screen of 1,000 environmental Shiga toxin–producing *E. coli* isolates in the agricultural region of California, identified by PCR that did not detect *mcr-1* or *mcr-2*.[9] Similarly, a screen of cecal contents in >2,000 food animals identified only 2 samples (<0.1%) positive for *mcr-1*.[10]

Our report provides the first assessment of *mcr-1* dissemination in North Carolina. The absence of *mcr-1* positive isolates detected in clinical and environmental settings provides valuable data to inform clinicians, pharmacists, and epidemiologists of the risk associated with colistin in the treatment of MDR organisms. Transmission of colistin resistance via *mcr-1* remains a significant threat worldwide and highlights the importance of continued surveillance to track the spread of MDR organisms.

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Is it time for us to account for the impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections?

Mohamad G. Fakih MD, MPH[1], Lisa K. Sturm MPH, CIC[1], Rama V. Thyagarajan MD, MPH, CIC[2] and Kristin E. Mondy MD, FACP[2]

[1]Quality Department, Clinical and Network Services, Ascension, St. Louis, Missouri and [2]Division of Infectious Diseases, Department of Medicine, Dell Medical School, University of Texas at Austin, Austin, Texas

To the Editor—We read with interest the recent study by Weiner-Lastinger et al[1] on the impact of coronavirus disease 2019 (COVID-19) pandemic on nationally reportable healthcare-associated infections (HAIs). This is the largest and most comprehensive study evaluating national performance on HAIs during the pandemic using National Healthcare Safety Network (NHSN) data. They compared the standardized infection ratios (SIRs) for reportable infections in different quarters of 2019 to their corresponding quarters in 2020. Overall, the COVID-19 pandemic was associated with significant increases in many reportable HAIs. The changes varied per quarter, but by the fourth quarter of 2020, there was a 47% increase in central line-associated bloodstream infections (CLABSI), a 34% increase in LabID hospital-onset (HO) methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia, a 45% increase in ventilator associated events, and a 19% increase in catheter-associated urinary tract infections (CAUTI). On the other hand, there was a decrease in colon surgery SSIs (8%) and abdominal hysterectomy SSIs (13%), as well as LabID HO *Clostridioides difficile* infection (CDI, 5.5%). The effect of the COVID-19 pandemic during the second and third quarters of 2020 was less visible. The pandemic was not as widespread compared to the last quarter of the previous year. These findings are important because they reflect the sensitivity of the different NHSN measures to the pandemic.

The pandemic has revealed future opportunities when evaluating and following the progress of HAIs in US hospitals. First, our current measures and their risk adjustment may not adequately reflect the impact of the COVID-19 pandemic on patient risk (whether intrinsic or extrinsic factors).[2] Traditionally, the risk adjustment incorporated into the SIR includes facility, unit characteristics, and a few patient factors.[3] The current baseline has been adjusted to the performance in 2015 and assumes that no large changes in population characteristics have occurred. Second, incorporating community and preferably hospital and unit level COVID-19 prevalence as a factor may help better evaluate HAI risk adjustment in corresponding hospitals. COVID-19 surges and inpatient caseloads have been associated with higher mortality[4] and CLABSI.[5] Reviewing the national study,[1] CLABSI and HO-MRSA bacteremia for specific states like Michigan and New Jersey exhibited significant increases in the second quarter of 2020 but not the third quarter, consistent with the early surges. Moreover, the currently submitted measures do not identify the proportion of patients with COVID-19 developing HAI infection (reporting COVID-19 status with each HAI remains optional). Third, the SIR does not account for drastic changes in device utilization or changes in volumes of procedures. A few years ago, the CDC introduced the standardized utilization ratio (SUR) to evaluate device utilization.[6] Compared with 2019, central-line and urinary catheter utilization increased by 7% and 9%, respectively, whereas a much more pronounced change in ventilator SUR, up to 30%, was observed. These findings underscore the importance of devising new measures that account for the overall population risk.[7] Finally, the analysis of the national data was limited by including only hospitals with complete surveillance data. Over the first 2 quarters of 2020, there was a 12%–14% reduction in reporting CLABSIs, CAUTIs, HO-CDIs, and HO-MRSA bacteremia cases. On the other hand, hospitals had larger reductions in reporting SSIs (colon 25%–27% and abdominal hysterectomy 32%–36%). The interruption in reporting was more notable at the state level, with 61% of hospitals in the state of New Jersey and 41% in the state of New York not reporting CLABSI for the second quarter of 2020. The attrition in reporting may underestimate the impact of the pandemic on HAIs because hospitals with large numbers of COVID-19 patients (and subsequently higher HAI rates) may have ceased reporting due to other priorities.

Examining specific HAIs, the pandemic has helped us better understand the susceptibility of the measures to significant changes in patient characteristics and care. For example, CLABSI is a very sensitive measure to changes in population and practices. Changes in central-line care, duration of use, and patient characteristics heavily affect its outcomes. We have reported that hospitals with COVID-19 patients representing >10% of admissions had 2.4 times more CLABSI events than those with <5% COVID-19 cases. Proportionately, COVID-19 patients had >5 times more CLABSI events than patients not infected with COVID-19.[5] Similarly, HO-MRSA bacteremia events may be heavily affected by the increase in intravascular device infections, ventilator-associated pneumonias, and hospital-acquired pneumonias in COVID-19–infected patients.[8] On the other hand, the NHSN CAUTI definition is more dependent on culturing practices, preexisting prevalence of bacteriuria, antimicrobial pressure, and is less susceptible

Author for correspondence: Mohamad G. Fakih, E-mail: Mohamad.Fakih@ascension.org
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