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Hospital microbiology laboratory practices for Enterobacteriaceae: Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN) annual survey, 2015 and 2016

Alicia Shugart, MA, **Maroya Spalding Walters, PhD, ScM**, **Lindsey M. Weiner, MPH**, **David Lonsway, MmedSc**, and **Alexander J. Kallen, MD, MPH**

Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract

We analyzed clinical microbiology laboratory practices for detection of multidrug-resistant Enterobacteriaceae in US short-stay acute-care hospitals using data from the National Healthcare Safety Network (NHSN) Annual Facility Survey. Half of hospitals reported testing for carbapenemases, and 1% performed routine polymyxin susceptibility testing using reference broth microdilution.

Reliable clinical microbiology laboratory data are critical for patient treatment and for surveillance and control of multidrug-resistant organisms (MDROs) such as carbapenem-resistant Enterobacteriaceae (CRE). The reference standards and microbiologic test methods that clinical laboratories use can influence MDRO detection. Despite this potential for variation, US short-stay acute-care hospital (ACH) laboratory practices have not been previously described.

Methods

We assessed laboratory practices using data from the NHSN Patient Safety Component Annual Hospital Survey (OMB No. 0920–0666),[1] which collects information about hospital characteristics and practices, including clinical microbiology testing. The respondent, typically the hospital's infection preventionist,[2] is instructed to consult the hospital's laboratory lead for applicable questions.[1]

The analysis was limited to clinical microbiology laboratory practices for Enterobacteriaceae. All ACHs that reported for calendar years 2015 and 2016 by July 1, 2017, were included; more than 90% of US ACHs completed this survey each year.

Author for correspondence: Alicia Shugart, Centers for Disease Control and Prevention, Roybal Campus, 1600 Clifton Road, MS A31, Atlanta, GA 30329. ashugart@cdc.gov.

PREVIOUS PRESENTATION: Similar data for calendar years 2014 and 2015 have been presented: Shugart A, Weiner LM, Lonsway D, et al. Hospital Microbiology Laboratory Practices: CDC NHSN Annual Survey, 2014 and 2015. In addition, an oral presentation of these data was given at the SHEA Annual Conference 2017 on March 29, 2017, in St Louis, Missouri.

Conflicts of interest. All authors report no conflicts of interest relevant to this article.

Psychiatric hospitals were excluded. Data were analyzed using SAS version 9.4 software (SAS Institute, Cary, NC). The Pearson χ^2 test with minimum significance of $P < .05$ was used to assess differences between survey years. Results are presented for 2016; 2015 results were reviewed to evaluate changes over time and are presented where they differed significantly from 2016 results.

Results

General practices

Overall, 4,745 and 4,685 hospitals completed the 2015 and 2016 surveys, respectively. In 2016, most were nonspecialty hospitals (n = 3,409, 73%). Others were critical access hospitals (n = 886, 19%), specialty hospitals (n = 154, 3%), surgical hospitals (n = 122, 3%), and governmental hospitals (n = 114, 2%). Overall, 1,736 (37%) were teaching hospitals. The median hospital size was 100 beds (interquartile range [IQR], 27–225).

In 2016, 2,904 hospitals (62%) reported that their antimicrobial susceptibility testing (AST) was performed at an onsite laboratory, a small but significant decrease from 3,037 hospitals (64%) in 2015 ($P = .04$). Among hospitals using an offsite laboratory, the number using an affiliated laboratory increased to 1,130 (63%) in 2016 from 1,023 (60%) in 2015 ($P = .03$), while the number using a commercial or reference laboratory decreased to 651 (37%) in 2016 from 685 (40%) in 2015 ($P = .03$).

For primary AST for Enterobacteriaceae, in 2016, 4,520 hospitals (97%) reported using automated testing instruments (ATI), including Vitek (bioMèrieux, Marcy-l'Étoile, France), Microscan (Microscan, Renton, Washington), BD Phoenix (Becton Dickenson, Franklin Lakes, NJ), and Sensititre (Thermo Scientific, Waltham, MA). Disk diffusion (1.3%) and broth microdilution (0.8%) were rarely reported.

Extended-spectrum cephalosporin and carbapenem susceptibility testing methods

From 2015 to 2016, the proportion of hospitals reporting that their laboratories assessed cephalosporin and monobactam resistance in Enterobacteriaceae using the Clinical Laboratory Standards Institute's (CLSI) pre-2010 minimum inhibitory concentration (MIC) interpretative criteria decreased (n = 1,377 [29%] vs n = 1,150 [25%], respectively; $P < .0001$). Similarly, 1,252 hospitals (26%) used CLSI's pre-2010 MIC interpretative criteria for detecting CRE in 2015, compared to 1,063 hospitals (23%) in 2016 ($P < .0001$). Of those using pre-2010 MIC interpretative criteria for CRE, 464 hospitals (44%) reported not testing for carbapenemases.

Overall, 2,329 hospitals (50%) reported testing Enterobacteriaceae for carbapenemases. Phenotypic tests (eg, modified Hodge test [MHT]) were more frequently reported (n = 1,865, 80%) than molecular tests (n = 422, 18%; $P < .0001$); 170 hospitals (7%) reported using both phenotypic and molecular methods (Table 1). Most hospitals (n = 1,697, 73%) reported changing carbapenem susceptibility results to resistant if a carbapenemase was detected. This practice was more common among hospitals using pre-2010 interpretative criteria than those using more recent interpretative criteria (n = 496 [83%] vs n = 1,201 [69%], respectively; $P < .0001$).

Polymyxin susceptibility test methods

Testing gram-negative bacilli for polymyxin susceptibility was reported by 1,885 hospitals (40%). Methods reported included Etest (bioMèrieux, Marcy-l'Étoile, France; n = 920, 49%), disk diffusion (n = 474, 25%), ATI (n = 452; 24%), and broth microdilution (n = 63, 3%).

Discussion

This is the first national assessment of laboratory practices for Enterobacteriaceae among ACHs. A small but significant increase in the use of offsite laboratories was observed in 2016. Capacity to detect carbapenemase-producing organisms and to identify colistin resistance in hospital laboratories was limited, impairing efforts to prevent the spread of highly drug-resistant Enterobacteriaceae.

Although most hospitals used onsite laboratories, this proportion decreased in 2016. Among facilities that completed the same survey for 2014, more facilities using onsite laboratories reported receiving MDRO results rapidly than facilities using offsite laboratories.[2] Increased reporting times can delay infection control interventions, such as contact precautions. Regardless of laboratory location, facilities should implement procedures to ensure that identification of targeted MDROs is rapidly communicated to the appropriate clinical and infection control staff.

In 2010, the CLSI lowered Enterobacteriaceae carbapenem MIC breakpoints,[3,4] which increased sensitivity for carbapenemase-producing isolates. However, 6 years later, nearly 25% of laboratories reported using pre-2010 breakpoints. Delays may be linked to the overwhelming popularity of ATIs for primary AST of major pathogens; it can take years for ATI manufacturers to develop and the US Food and Drug Administration (FDA) to clear updated ATI panels.[4] Once they are commercially available, laboratories may not promptly acquire and implement them. The CLSI recommends that laboratories using the pre-2010 break-points test for and interpret carbapenemase-producing isolates as carbapenem resistant. Overall, 11% of hospital laboratories were not following this guidance, which likely resulted in underdetection of CRE and missed infection control opportunities. Further work, potentially led by public health agencies, is needed to update and improve susceptibility testing in local clinical laboratories.

Half of facilities reported that their laboratories did not test for carbapenemases. Those that used newer carbapenem breakpoints were less likely to test for carbapenemases, which although consistent with clinical testing recommendations,[3] indicates that fewer facilities used testing for infection control purposes. In 2016, the Centers for Disease Control and Prevention (CDC) launched the Antibiotic Resistance Laboratory Network (ARLN) to expand mechanism testing of carbapenem-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* to 50 state public health laboratories, 5 local public health laboratories, and Puerto Rico.[5] Initiatives like ARLN aim to ensure that testing for carbapenemases is widely available, even if clinical laboratory testing capacities shrink. These public health laboratories and their associated health departments' healthcare-associated infection

programs may also serve as a resource to improve testing practices at laboratories in their jurisdictions.

The recent identification of the plasmid-mediated colistin resistance gene *mcr* has increased the importance of identifying colistin-nonsusceptible isolates[6]; however, only 1% of hospitals indicated that their laboratories used reference broth microdilution, which is the currently recommended method.[7] The most commonly reported methods included Etest and disk diffusion, both of which are discouraged due to inaccurate results obtained with polymyxins.[7] Notably, 24% of facilities reported using an ATI for colistin susceptibility, despite the absence of an FDA-cleared automated test.[7] This lack of availability of polymyxin AST hampers detection of *mcr*-carrying isolates; undetected dissemination of *mcr* could increase the prevalence of colistin resistance among Enterobacteriaceae. Further work is needed to identify risk factors to better target colistin AST to identify isolates for *mcr* screening. Colistin susceptibility testing is available through the ARLN, and results from this work will be useful to better define this issue.

This analysis has several limitations. Data are self-reported to NHSN and are not validated by the CDC. Although respondents are instructed to confer with their laboratory's lead, limited laboratory expertise or communication could result in incomplete or incorrect responses, particularly among hospitals that used offsite laboratories.

Nearly all US ACHs completed the survey for 2015 and 2016; therefore, these data are the most complete representation of clinical microbiology laboratory practices for Enterobacteriaceae currently available. Clinical microbiology laboratories should prioritize implementation of current CLSI breakpoints. Laboratories should also develop a strategy for routine carbapenemase testing, either in-house or through the ARLN. Hospital epidemiologists, infection control staff, and clinicians should be aware of the limitations of their laboratories' practices when interpreting results. Additionally, public health surveillance and prevention programs should consider current clinical laboratory practices when developing programs and interpreting data.

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Table1.

Carbapenemase Testing Practices for Enterobacteriaceae[a]

Carbapenemase Testing Practices for Enterobacteriaceae	Facilities, No. (%)	Facilities Using Pre-CLSI MIC Interpretative Criteria, No. (%)	Facilities Using 2010 or More Recent CLSI MIC Interpretative Criteria, No. (%)
Total	4,685 (100)	1,063 (23)	3,622 (77)
Did not perform carbapenemase testing	2,356 (50)	464 (44)	1,892 (52)
Performed carbapenemase testing[b]	2,329 (50)	599 (56)	1,730 (48)
Phenotypic testing[b]	1,865 (80)	537 (90)	1,328 (77)
Modified Hodge test (MHT)	1,568 (84)	503 (94)	1,065 (80)
Etest	229 (12)	42 (8)	187 (14)
Carba NP test	132 (7)	14 (3)	118 (9)
Metallo-β-lactamase (MBL) screen	65 (3)	11 (2)	54 (4)
CIM or mCIM	24 (1)	1(0)	23 (2)
Molecular testing (eg, PCR)[b]	422 (18)	91 (15)	331 (19)
Testing method unspecified[b]	212 (9)	18 (8)	194 (92)
If carbapenemase is detected:			
Change susceptible carbapenem results to resistant	1,697 (73)	496 (83)	1,201 (69)
Report carbapenem MIC results without an interpretation	167 (7)	47 (8)	120 (7)
No change is made to interpretation of carbapenem results	465 (20)	56 (9)	409 (24)

Note. CLSI, Clinical and Laboratory Standards Institute; MIC, minimum inhibitory concentration; CIM, carbapenem inactivation method; mCIM, modified carbapenem inactivation method; PCR, polymerase chain reaction.

[a]CLSI carbapenem MIC interpretative criteria used, reported by short-stay acute-care hospitals to the National Healthcare Safety Network in 2016.

[b]Respondents were instructed to report all test methods that were routinely used for carbapenemase detection; sum of carbapenemase testing methods may exceed 100%.