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Major Article

Epidemiologic characteristics of health care–associated outbreaks and lessons learned from multiple outbreak investigations with a focus on the usefulness of routine molecular analysis

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Background: Single outbreaks have often been reported in health care settings, but the frequency of outbreaks at a hospital over time has not been described. We examined epidemiologic features of all health care–associated outbreak investigations at an academic hospital during a 5-year period.

Methods: Health care–associated outbreak investigations at an academic hospital (2012-2016) were retrospectively reviewed through data on comprehensive hospital-wide surveillance and pulsed-field gel electrophoresis (PFGE) analysis.

Results: Fifty-one health care–associated outbreaks (annual range, 8-15), including 26 (51%) outbreaks in intensive care units (ICUs), and 263 infected-colonized patients involved in these outbreaks were identified. The frequency of pathogens varied by affected location, specifically multidrug-resistant organisms (20/26 outbreaks, 77% in ICUs vs 2/25 outbreaks, 8% in non-ICUs; $P < .0001$) and gastroenteritis because of *Clostridium difficile*, norovirus, or adenovirus (1/26 outbreaks, 4% in ICUs vs 17/25 outbreaks, 68% in non-ICUs; $P < .0001$). Outbreaks occurred in approximately one-third of all units (37%) with some repeated instances of the same pathogens. Of 16 outbreaks caused by a bacterial pathogen evaluated by PFGE, 12 (75%) included some indistinguishable strains, suggesting person-to-person transmission or a common source.

Conclusions: This study demonstrated epidemiologic characteristics of multiple outbreaks between ICUs and non-ICUs and the value of molecular typing in understanding the epidemiology of health care–associated outbreaks.

Multiple pathogens, including viruses, bacteria, mycobacteria, and fungi, and multiple reservoirs-sources, including health care personnel, patients, visitors, surface environment, medical equipment, air, and water, have been involved in health care–associated outbreaks.[1-5] Health care–associated outbreaks not only may affect patients' morbidity and mortality but also may have severe repercussions in health care operations (eg, ward closure) with the need for time-consuming and potentially expensive interventions.[4]

Single outbreaks caused by a specific pathogen(s) and a source or reservoir have often been reported in hospitals. However, the burden of outbreaks on a hospital over time is still poorly understood. Although there are many publications of outbreak investigations in a single hospital,[4,6] they are likely to be substantially affected by publication bias with larger outbreaks, and those caused by novel reservoirs or routes of transmission, more likely to be published. In addition, concern about health care facility reputation and the risk of legal consequences may interfere with data sharing and obscure the real impact of outbreaks on daily practice in a health care facility.[6,7] To our knowledge, there are no published reports of multiple outbreaks caused by diverse pathogens at an academic medical center and the value of routine molecular typing of pathogens associated with an outbreak over time.

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In this study, we assessed all health care–associated outbreak investigations based on routine practice, examined the value of pulsed-field gel electrophoresis (PFGE) of pathogens involved in outbreaks, and reviewed lessons learned from these multiple investigations at an academic hospital during a 5-year period.

METHODS

This analysis was conducted at an 853-bed tertiary care academic facility with 41 inpatient nursing units. Health care–associated outbreak investigations at our hospital from 2012-2016 were retrospectively reviewed through an institutional health care–associated infection (HAI) database and monthly reports to the hospital infection control committee. Using a laboratory-based pathogen detection system to conduct comprehensive hospital-wide surveillance, outbreak investigations were triggered by an increase in number of infections or pathogens above baseline rate in a unit during a specified period of time; an investigation may also have been triggered by a single case of a rare and epidemiologically important pathogen.[4] In this study, the number of potential health care–associated outbreaks was counted as the number of the corresponding outbreak investigations, including one with only a single case (ie, *Legionella*). Additionally, a health care–associated outbreak identified by molecular typing was defined as (1) cases that overlapped time and space and (2) at least 2 isolates linked by PFGE. Contact tracing associated with exposure investigations of a single patient (eg, varicella, tuberculosis) with a communicable disease were excluded from analysis. Variables in the outbreak investigations included year, duration of outbreak, location, pathogen, presence or absence of HAI, type of specific HAI, number of patients infected-colonized, number of health care personnel involved, presence or absence of PFGE with number of isolates and number of different patterns when PFGE was performed, and brief summary of infection control measures and interventions.

Comprehensive hospital-wide surveillance for all HAIs, including all sites defined by the Centers for Disease Control and Prevention, was conducted through a chart review of each patient in accordance with the Centers for Disease Control and Prevention criteria.[8] Our HAI surveillance included components of laboratory reports of positive culture results, results of serologic testing or molecular-based diagnostic tests, clinical reports of infections, morbidity and mortality conferences, and autopsies. HAIs are classified into one of the following 5 major infections with 14 specific infection sites: bloodstream infections, urinary tract infections, respiratory tract infections (pneumonia and lower respiratory tract infections), surgical site infections, and other type of HAIs (gastrointestinal infections; eye, ear, nose, throat, or mouth infections; skin and soft-tissue infections; cardiovascular system infections; bone and joint infections; central nervous system infections; reproductive tract infections; and systemic infections). All surveillance data of HAIs and outbreak investigations during the study period were entered into an electronic database. This study was approved by the Institutional Review Board of University of North Carolina at Chapel Hill.

PFGE was performed for selected bacterial pathogens based on likelihood of an epidemiologic link (eg, >3 pathogens overlapping in time and location). We reviewed all PFGE analyses performed during the study period. Environmental sampling of the hospital and hand sampling of health care personnel depended on ongoing situation of an outbreak or type of pathogen.

Statistical analyses were performed by 2-tailed Fisher test using JMP 11 (Statistical Analysis System, Cary, NC); $P \leq .05$ was considered to be statistically significant.

RESULTS

Fifty-one health care–associated outbreaks (annual range, 8-15), including 26 (51%) outbreaks in ICUs and 25 (49%) outbreaks in non-ICUs, were identified during the study period. The annual number of outbreaks was almost constant except for 2015 with an increase in gastroenteritis, whereas epidemiologic features (eg, pathogen type) in these outbreaks substantially differed by year (Fig 1). Outbreaks occurred in 15 units (36.6% of all 41 inpatient units). Of the 26 outbreaks in ICUs, 12 (46.2%) and 7 (26.9%) occurred in the burn ICU and the neonatal ICU, respectively. Of the 25 outbreaks in non-ICUs, 6 (24%) occurred in the bone marrow transplant unit. An outbreak of *Stenotrophomonas maltophilia* involved multiple nursing units. Overall, 30 (58.8%) outbreaks were terminated within 1 month, whereas 4 (7.8%) continued for >6 months (ie, 1 methicillin-resistant *Staphylococcus aureus* [MRSA] outbreak in the neonatal ICU, 1 carbapenem-resistant *Enterobacteriaceae* [CRE] outbreak in the burn ICU, 2 multidrug-resistant *Pseudomonas* outbreaks in the burn ICU). The frequency of outbreaks sustained over 2 months was significantly higher in ICUs than in non-ICUs (Table 1), and the burn ICU accounted for 52.6% (10/19) of these prolonged outbreaks in ICUs.

The frequency of pathogens varied greatly by affected location, specifically multidrug-resistant organisms (MDROs) in ICUs (MRSA, CRE, and multidrug-resistant *Pseudomonas aeruginosa*) and gastroenteritis in non-ICUs (*Clostridium difficile*, norovirus, and adenovirus) (Fig 2, Table 1). Of 34 bacterial outbreaks, an MDRO (22 outbreaks, 64.7%) was the most frequent, followed by *C difficile* (7 outbreaks, 20.6%). Eleven viral outbreaks included 7 (63.6%) norovirus gastroenteritis, 2 adenovirus gastroenteritis, 1 enterovirus meningitis, and 1 influenza respiratory infection, whereas 75% of all fungal outbreaks (3/4) were caused by *Rhizopus* spp. A pseudo-outbreak of *Ralstonia insidiosa* via a contaminated sonicator occurred in a laboratory during the study period. The frequency of outbreaks of repeated pathogens at the same location was 63%, and outbreaks in ICUs significantly tended to reoccur more commonly than those in non-ICUs (Table 1).

Of the 51 outbreaks, 47 (92.2%) resulted in HAIs. Gastroenteritis (n = 18, 35.3%) was the most common type of infection, followed by pneumonia (n = 9, 17.6%), bloodstream infection (n = 8, 15.7%), and skin and soft-tissue infection (n = 8, 15.7%), whereas there were no HAIs identified in 4 (7.8%) investigations. The type of HAIs differed significantly within or outside an ICU (Table 1). Overall, 263 infected-colonized patients (median, 4; range, 1-20) were involved in health care–associated outbreaks. There was no statistical

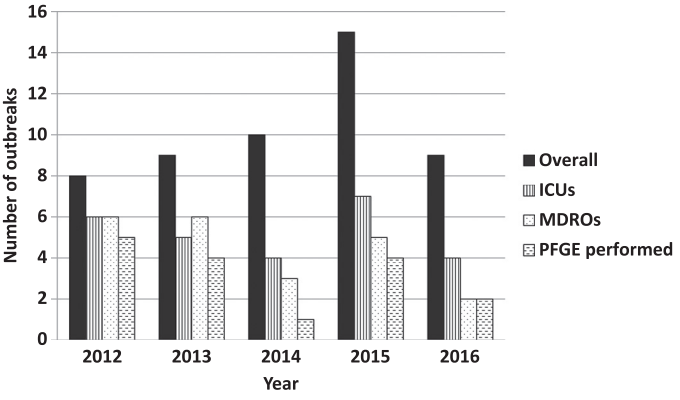

Fig 1. Annual trends in health care–associated outbreak investigations at an academic hospital, 2012-2016. *ICU*, intensive care unit; *MDRO*, multidrug-resistant organism; *PFGE*, pulsed-field gel electrophoresis.