Timing of conversion to positivity of carbapenemase-producing *Enterobacteriaceae* contacts during a tertiary hospital OXA-48 outbreak.

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Introduction

Isolation and screening of known carbapenemase-producing *Enterobacteriaceae* (CPE) contacts remain crucial factors in the control of spread of these organisms. The optimal duration for which contacts should be screened before being deemed negative is unknown and may vary. Our institution is currently experiencing an OXA-48 CPE outbreak in a variety of different organisms with varying antibiograms and the aim of this study was to assess the duration of screening required to detect the conversion of known contacts to CPE positivity, in order to optimise infection prevention and control management and laboratory resource management.

Methods

A retrospective review was undertaken in an acute tertiary referral hospital with 562 beds, including 14 critical care beds, which treats over 410,000 patients per year. This study was carried out over a 4 year period from July 2013 to July 2017, to investigate the time to detection of CPE positivity among known contacts. An OXA-48 like CPE outbreak occurred from September 2015 onwards. A total of 234 CPE positive cases were identified during this time period. A contact patient was defined as any patient who shared a room or toilet with a patient who was CPE positive. Cases were included where there was a known exposure time to CPE and where there was a negative screen recorded within 7 days of subsequent CPE detection. Upon identification of a new CPE case in our hospital, the patient is immediately isolated with contact precautions and contact tracing is performed. Any contact patients identified subsequently undergo weekly rectal screening for CPE for a minimum of 4 weeks. Currently, rectal screens for the detection of CPE in our hospital are tested by PCR using the FLOW Flex molecular platform (Roche Molecular Diagnostics), which detects IMP-1, KPC, NDM, OXA-48 and VIM carbapenemase genes. Specimens are also cultured on selective CARBA SMART media (Biomérieux). Prior to November 2016, CPE screening was performed using culture methods only. Organisms are identified by MALDI-TOF (Biomérieux) and further evaluated with Rosco disks (Rosco Diagnostica) and meropenem and ertapenem Etest minimum inhibitory concentration (MIC) testing. CPE positive isolates are sent to the Galway University Hospital National Reference Laboratory Services for Selected Pathogens for confirmation and further characterisation.

Results

24 of the 234 patients met the inclusion criteria and were included in the analysis. Of all the exposed patients, 7.4% subsequently tested positive for CPE. The mean time from exposure to detection of CPE was 13 days (range 3-40 days). 11 (45.83%) patients became positive in week 1 following exposure, 4 (16.67%) in week 2, 4 (16.67%) in week 3, 3 (12.50%) in week 4, 1 (4.17%) in week 5 and 1 (4.17%) in week 6. No subsequent CPE conversions occurred after week 6. Therefore, 92% of cases were identified by 4 weeks and 100% by 6 weeks.

Figure 1. Flow Diagram of Cases

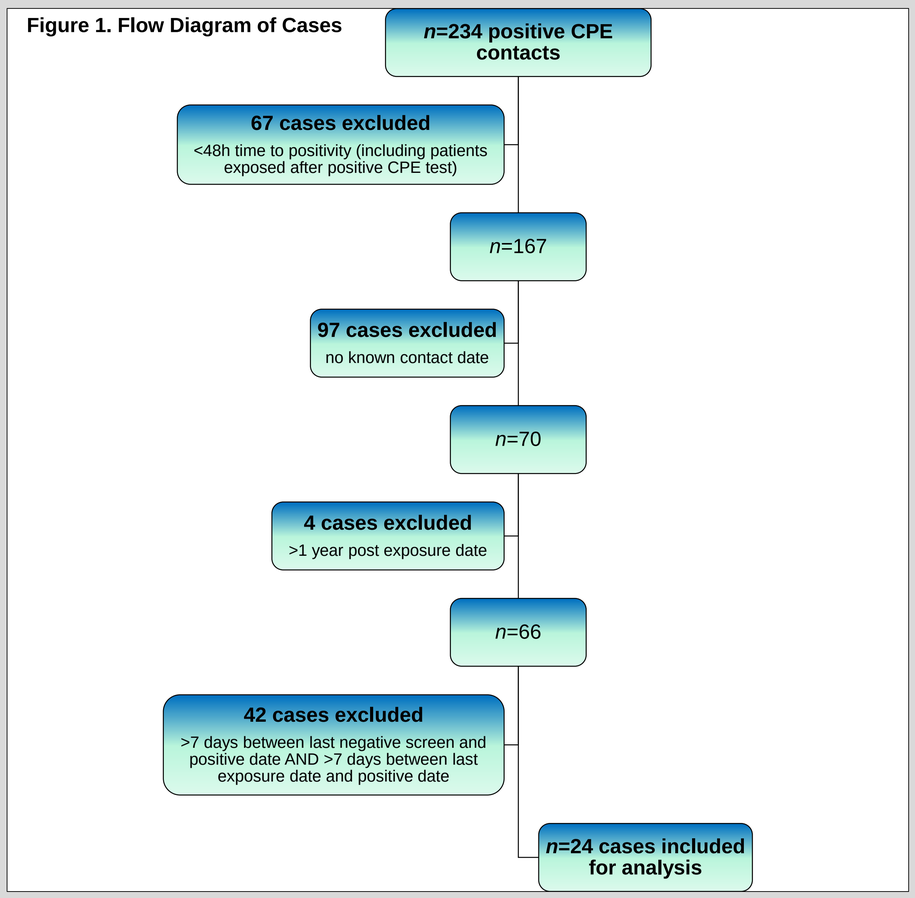
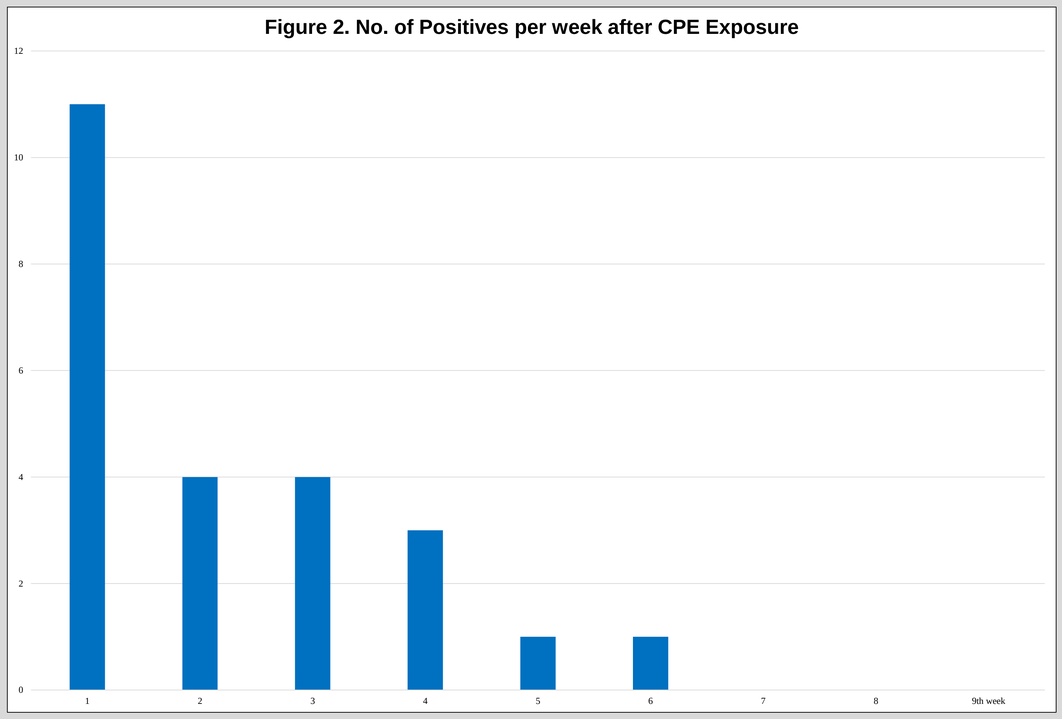


Figure 2. No. of Positives per week after CPE Exposure



Discussion

Recent ESCMID guidelines advise that the prevalence of possible cross-transmission of Gram negative bacilli among patients is difficult to evaluate but that studies in the ICU population report percentages ranging from 23% to 53% of patients' contacts.[1]

Screening contact patients in order to rapidly identify cross-transmission has been shown in multiple studies to be an important factor in limiting the spread of CPE.[2-4]

New guidance from the World Health Organisation advises that contacts of CRE colonised or infected patients should undergo surveillance cultures, as early recognition of colonisation helps to identify patients at-risk of subsequent CRE infection and allows the early introduction of infection prevention and control measures in order to prevent further transmission.[5]

Public Health England advise screening contact patients on a weekly basis for a period of 4 weeks but recognise that some institutions may wish to take a more aggressive approach. Duration of carriage is felt to be a function of the particular strain and species and therefore this four week period is arbitrary but felt to be pragmatic given the lack of evidence.[6]

Harvey et al carried out a study of time from exposure to detection of CPE contacts during a clonal outbreak of VIM-4 *K. pneumoniae* and found that 7 weeks of screening would be required to detect all conversions to positivity, similar to our findings, but suggested a longer period of screening, for up to 12 weeks in order to additionally facilitate the surveillance of contacts of contacts.[7]

For logistical and resource optimisation purposes, CPE contacts in our institution are currently screened for 4 weeks from time of exposure before being deemed negative for CPE and removed from isolation. The question is raised as to whether these patients should be isolated and screened for a longer duration, for example for up to 6 weeks. According to our data, screening for 4 weeks from time of exposure captures 92% of contacts that convert to CPE positive cases, with a requirement to screen for at least 6 weeks to detect all cases. Duration of screening and isolation needs to be determined with respect to what is practical for an individual institution with an awareness that time to detection of CPE following exposure may be variable and that vigilance for conversion should be maintained for a prolonged period in CPE contacts.

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