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Epidemiology of *Escherichia coli* bacteraemia in England: results of an enhanced sentinel surveillance programme

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SUMMARY

Background: *Escherichia coli* causes more than one-third of the bacteraemia cases in England each year, and the incidence of these infections is increasing.
Aim: To determine the underlying risk factors associated with *E. coli* bacteraemia.
Methods: A three-month enhanced sentinel surveillance study involving 35 National Health Service hospitals was undertaken in the winter of 2012/13 to collect risk factor information and further details on the underlying source of infection to augment data already collected by the English national surveillance programme. Antimicrobial susceptibility results for *E. coli* isolated from blood and urine were also collected.
Findings: A total of 1731 cases of *E. coli* bacteraemia were included. The urogenital tract was the most frequently reported source of infection (51.2% of cases) with previous treatment for a urinary tract infection being the largest independent effect associated with this infection source. Half of all patients had previous healthcare exposure in the month prior to the bacteraemia with antimicrobial therapy and urinary catheterization being reported in one-third and one-fifth of these patients, respectively. Previous healthcare exposure was associated with a higher proportion of antibiotic non-susceptibility in the blood culture isolates ($P = 0.001$).
Conclusion: Analysis of risk factors suggests the potential benefit of community- and hospital-related interventions, especially the better use of urinary catheters and improved

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antibiotic management of urinary tract infections. As part of the latter strategy, antibiotic resistance profiles need to be closely monitored to ensure that treatment guidelines are up to date to limit inappropriate empiric therapy.

Introduction

Voluntary surveillance identified *Escherichia coli* as the leading cause of bacteraemia in England, with increasing incidence over time despite the overall incidence of bacteraemia being in decline.[1] In 2015, a total of 37,273 cases of *E. coli* bacteraemia were reported to the English mandatory surveillance programme.[2] Thirty-day all-cause mortality in England for this infection was recently estimated as 18.2% (17.8–18.7%), equating to 5220 deaths over a 12-month period.[3] Thus appropriately targeted interventions are required to reduce morbidity and mortality associated with *E. coli* bacteraemia. Whereas English mandatory surveillance of *E. coli* bacteraemia (initiated in 2011) allows better estimation of *E. coli* bacteraemia incidence than was previously possible, detailed epidemiological information is needed to elucidate the reasons behind observed trends.

Following a recommendation from the UK government's Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI), a sentinel surveillance scheme was initiated to augment existing mandatory surveillance.[4] The sentinel programme aimed to gather more detailed risk factor information for patients in the hospital and community settings. Specific data collected included antibiotic consumption, use of urinary catheters, indwelling vascular access and other devices, and invasive procedures prior to the bacteraemia. Additionally we aimed to gather detailed information regarding the clinically identified focus or cause of bacteraemia and antibiotic susceptibility data for the *E. coli* blood and urine cultures.

Methods

Study design

The sentinel study ran in participating English National Health Service (NHS) Trusts (hospitals under the same management board) over the winter of 2012/13. The study was powered to detect with 95% confidence the prevalence of an underlying infection focus or risk factor with a true frequency of at least 10%, based on estimates of the second most prevalent focus (hepatobiliary) reported via mandatory surveillance.[5] As the sampling strategy was clustered (by NHS Trust, not by patient), a design effect was included. This equated to a sample size of 2625 *E. coli* bacteraemia cases; we therefore aimed to recruit 40 Trusts with data collection running over three months. Participating Trusts were selected using simple random sampling. Additionally, two specialist cancer Trusts and six interested Trusts were included *post hoc*.

Cases from the sentinel study were linked to mandatory *E. coli* bacteraemia reports (linked using NHS number, a unique personal identifier), to obtain further patient and specimen information, and to voluntary laboratory reports (linked using a combination of available personal identifiers (NHS number, hospital number, date of birth, gender, encrypted surname) to obtain antibiotic susceptibility data for both *E. coli* blood culture (if not reported by sentinel sites) and urine cultures, one month and one year before the date of the blood culture.[6] Duplicate entries for the same patient within the same episode (considered as 14 days) were removed from analysis with data relating to the earliest specimen retained. This study focused on *E. coli* bacteraemia and for cases of polymicrobial bacteraemia only information pertaining to the *E. coli* isolate was retained.

Data items relating to healthcare exposure prior to the bacteraemia were collected. Specifically, in the previous three days: indwelling vascular access devices (*in situ* or removed), including the type of intravascular device; in the previous seven days: urinary catheterization (*in situ*, inserted, removed, or manipulated), including the type of catheter, insertion method and primary indication for catheterization; in the prior four weeks: other devices (*in situ* or removed), including the type of device and date of insertion; other procedures, including the type and date of procedure; and antimicrobial chemotherapy, including antibiotic name(s), indication, and the treatment area. Patients with more than one healthcare exposure reported or with more than one occurrence of a specific healthcare exposure were included in the study. Previous healthcare exposure in either the community or hospital in the four weeks and one week before bacteraemia was categorized as 'Yes' if at least one of the above data items were selected as 'Yes' or as 'No' if all of the above items were selected as 'No'; otherwise it was coded as 'Not known'. In addition to these data items, the primary focus or reason for the bacteraemia was collected. More detail on data collection can be found in Supplementary Appendix A.

Time of bacteraemia onset based on the days between hospital admission and the taking of a positive blood culture was categorized as follows: on or day after admission (a proxy for community-onset infection); two to six days after admission (proxy for early healthcare-onset infection); seven days or more after admission (proxy for late healthcare-onset infection); from a non-admitted patient.

Information on susceptibility of the *E. coli* blood culture and urine isolates to ciprofloxacin, trimethoprim, co-amoxiclav, third-generation cephalosporins (cefotaxime/ceftazidime), carbapenems (imipenem/meropenem), gentamicin, nitrofurantoin and piperacillin/tazobactam was ascertained using laboratory data reported via the national voluntary surveillance system. The presence of a urine culture in the linked laboratory dataset was taken as a proxy for urinary tract infection (UTI) in the month or year prior to the *E. coli* bacteraemia. Combined susceptibility for blood cultures, using the above antibiotics, was categorized as: 'non-susceptible' if the blood culture was recorded as non-susceptible to at least one of the aforementioned antibiotics; 'susceptible' if the blood culture was recorded as susceptible to all of the aforementioned antibiotics.