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Clinical and economic impact of contaminated blood cultures within the hospital setting

Y.M. Alahmadi [a], M.A. Aldeyab [a,*], J.C. McElnay [a], M.G. Scott [b], F.W. Darwish Elhajji [a], F.A. Magee [b], M. Dowds [b], C. Edwards [b], L. Fullerton [c], A. Tate [c], M.P. Kearney [b]

[a] Clinical and Practice Research Group, School of Pharmacy, Queen's University Belfast, Belfast, UK
[b] Northern Health and Social Care Trust, Ballymena, Antrim, UK
[c] Iskus Health Ltd, Dublin, Ireland

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SUMMARY

Blood cultures have an important role in the diagnosis of serious infections, although contamination of blood cultures (i.e. false-positive blood cultures) is a common problem within the hospital setting. The objective of the present investigation was to determine the impact of the false-positive blood culture results on the following outcomes: length of stay, hotel costs, antimicrobial costs, and costs of laboratory and radiological investigation. A retrospective case–control study design was used in which 142 false-positive blood culture cases were matched with suitable controls (patients for whom cultures were reported as true negatives). The matching criteria included age, comorbidity score and month of admission to the hospital. The research covered a 13-month period (July 2007 to July 2008). The findings indicated that differences in means, between cases and controls, for the length of hospital stay and the total costs were 5.4 days [95% CI (confidence interval): 2.8–8.1 days; $P < 0.001$] and £5,001.5 [$7,502.2; 95% CI: £3,283.9 ($4,925.8) to £6,719.1 ($10,078.6); $P < 0.001$], respectively. Consequently, and considering that 254 false-positive blood cultures had occurred in the study site hospital over a one-year period, patients with false-positive blood cultures added 1372 extra hospital days and incurred detrimental additional hospital costs of £1,270,381 ($1,905,572) per year. The findings therefore demonstrate that false-positive blood cultures have a significant impact on increasing hospital length of stay, laboratory and pharmacy costs. These findings highlight the need to intervene to raise the standard of blood-culture-taking technique, thus improving both the quality of patient care and resource use.

Introduction

Since bloodstream infections have a significant impact on morbidity and mortality within hospitalised patients, accurate blood culture data have an important role in the diagnosis of serious infections.[1–3] However, contamination of blood cultures (i.e. false-positive blood cultures) is a common problem within hospital care and represents approximately half of all positive blood cultures.[4–6] In order to decide whether a microbial isolate from a blood culture is a pathogen or a contaminant, several clinical and laboratory approaches have been proposed. These include clinical features such as fever; the proportion of blood culture sets that are positive as a function of the number of sets obtained; the identity of the micro-organism itself; the number of culture vials within a culture set that show growth and the time it takes for growth to be detected once a blood culture is received in the laboratory.[7] False-positive blood cultures have been associated with unnecessary antibiotic use, additional laboratory tests and increased length of hospital stay, thus incurring significant additional hospital costs, and exposing the patient to unnecessary treatments and unnecessarily prolonged hospital stay.[4,6,8] Several techniques have been employed to minimise the risk of contamination of blood cultures. These include the use of venepuncture

* Corresponding author. Address: Clinical and Practice Research Group, School of Pharmacy, Queen's University Belfast, Belfast BT9 7BL, UK. Tel.: +44 28 90972033; fax: +44 28 90247794.
E-mail address: maldeyab02@qub.ac.uk (M.A. Aldeyab).

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protocols, antiseptic preparations and a dedicated phlebotomist or blood culture teams to obtain the blood culture sample from patients.[5,9] However, given the fact that none of the currently available skin disinfectants are able to eliminate all bacteria, a zero or even close to zero blood contamination rate is not possible to achieve.[7,10] Although it has been recommended that target rates for blood culture contamination should not exceed 3%, the contamination rate in many institutions actually exceeds 7%.[4,11–13]

The objective of the present investigation was to determine the impact of the false-positive blood culture results on the following outcomes: length of stay, hotel costs, antimicrobial costs, and costs of laboratory and radiological investigation.

Methods

The present work was carried out in the form of an audit as part of the hospital's clinical service development programme and therefore ethical approval was not required. The study was registered with, and approved by, the Trust's research and development department. The author is an honorary member of staff within the Trust.

Setting and study period

The study was carried out in Antrim Area Hospital in Northern Ireland, a 426-bedded district general teaching hospital serving a population of about 420 000. The hospital provides all acute, general medical and surgical services, supports a range of outpatient facilities and acts as a centre for the coordination of health service provision throughout a defined geographical area in Northern Ireland. The study was conducted retrospectively over a 13-month period, from July 2007 to July 2008.

Study design

The first stage involved a review of the microbiology laboratory records of patients whose blood cultures yielded growth over the study period. For the purposes of this study, a blood culture set was defined as 'any one blood drawing, regardless of the number of sample bottles filled', and a blood culture episode was defined as 'the 48-hour period beginning when a blood culture was drawn'.[4] All sets drawn within the first 48 h of the primary sample were therefore considered part of the initial episode.[4] The second stage of the study involved matching the 142 (see sample size calculation section below) false-positive blood culture cases identified in stage 1 with suitable controls (patients whose cultures were reported as true negative) matched for age (two categories: 19–64 years and >64 years), comorbidity score (calculated using the Charlson Index)[14] and month of admission to the hospital, over the 13-month study period (July 2007 to July 2008). The hospital microbiology department records were used to identify a list of all potential cases and controls over the same study period (July 2007 to July 2008); this generated a list of 281 potential case patients and 5254 potential control patients. Using the latter list, and in order to minimise potential bias, control patients were chosen based on the alphabetical order (as described elsewhere) of their surnames.[15] To allow performance of the economic analysis, antimicrobial costs, microbiology laboratory costs and daily hotel costs for each directorate were determined.

Blood culture processing

The microbiology laboratory within the hospital recommends that blood for cultures is drawn using an aseptic technique as follows. The venepuncture site is disinfected with ChloraPrep® (2% w/v chlorhexidine gluconate in 70% isopropyl alcohol) and the septum of the blood culture bottles with 70% isopropyl alcohol. The standard for routine blood cultures is a minimum of two sets (three sets for suspected infective endocarditis) drawn from different peripheral venous sites in order to optimise recovery of organisms and to assist the physician in determining the clinical significance of certain isolate(s). Blood drawn from a single venepuncture is regarded as a single set regardless of how many blood culture bottles are inoculated; routinely this is an aerobic and an anaerobic bottle for adults. To facilitate this, blood culture collection boxes, sterile gloves and a sharps box are available in each clinical area. The box includes the blood culture bottles, a sterile procedure kit (a butterfly vacutainer with adapter, forceps, cotton wool balls, disposable tourniquet, adhesive dressing, and clinical waste bag), alcohol swabs and ChloraPrep®.

When bacterial growth is detected in a blood culture bottle, an aliquot of broth is drawn for microscopic examination with a Gram stain and subculture using standardised techniques. All positive Gram stain results are telephoned the same day to the ward with preliminary and definitive identification and antimicrobial sensitivities telephoned to the ward as they become available. This is followed by a written report.

Definition of contamination

Whereas many bacterial isolates from blood cultures are frequently recognised as a cause of bacteraemia, there are a number of organisms which may be a pathogen or a contaminant. These include *Corynebacterium* species, *Bacillus* species (other than *Bacillus anthrax*), *Propionibacterium acnes*, coagulase-negative staphylococci (CoNS), viridans group streptococci and *Clostridium perfringens*.[7,16] Based on the standard of a minimum of two blood culture sets being drawn from different peripheral venous sites, samples are defined as contaminated if a single blood culture set is positive for these microorganisms or if multiple blood culture sets are positive but different species and/or antibiotic sensitivity resistance patterns are obtained from different sets and the results of the blood culture are not compatible with the clinical condition of the infected patient. If only one set of blood cultures is received, the preliminary identification results without antibiotic sensitivities is issued to the ward with a request for a clinical evaluation and a further set of blood cultures.

Sample size calculation

To detect a difference in length of stay $\geq$3 days in one group compared with the other, based upon a standard deviation of 9 days (as determined from Bates *et al.*[4]), with 80% power and 5% significance level, a total of 284 individuals are required, i.e. 142 cases and 142 controls.

Statistical analyses

Medians and interquartile ranges were calculated for the total length of hospital stay and total costs, as these variables were not normally distributed. Means for differences between cases and controls in relation to total length of hospital stay and total costs were compared using paired sample *t*-test (using SPSS® version 17 for Windows) as within paired difference data were normally distributed.

Results

Over the study period, 142 patients who had false-positive blood culture (cases) were matched and compared with 142 patients who had true-negative blood culture (controls).

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The mean age and median comorbidity scores (i.e. the matching criteria) were similar for both cases and controls (mean age: 66 years; median comorbidity: 1). Out of the 142 cases and 142 controls, 51% and 59% were male, respectively. Blood was drawn from an intravascular line in 48% of cases (20 from 42 patients for whom this information was available) and in 8% of controls (4 from 53 patients for whom this information was available). The median length of stay in hospital from admission to sample taken was similar in both cases and controls (one day). The median length of stay in hospital from admission to discharge was 13 and 8 days in cases and controls, respectively. General characteristics of the study population are listed in Table I. Median hotel costs for cases were £5,060 compared with £1,890 for controls. Median antibiotic use and median microbiology test charges for cases and controls were £157 vs £14 and £120 vs £32, respectively. Details of the charges for cases and controls are shown in Table II. Differences in means, between cases and controls, for the length of hospital stay and the total costs were 5.4 days (95% CI: 2.8–8.1 days; $P < 0.001$) and £5,001.5 [$7,502.2; 95% confidence interval (CI): £3,283.9 ($4,925.8) to £6,719.1 ($10,078.6); $P < 0.001$], respectively. Patients with false-positive blood cultures added 1372 extra hospital days and incurred additional hospital costs of £1,270,381 ($1,905,572) per year when compared with the true-negative controls. In a more conservative estimate for the latter, i.e. by considering the lower boundary of the 95% CI, patients with false-positive blood cultures added 711 extra hospital days and incurred additional hospital costs of £834,111 ($1,251,167) per year.

Over a one-year period (July 2007 to June 2008) in the study site hospital, a total of 5447 blood cultures were processed by the hospital laboratory department, of which 594 (10.9%) were reported as positives (i.e. either true positive or false positive). Of the 594 blood cultures, 254 were identified as false-positive blood cultures contributing to 42.8% of the total positives. The blood culture contamination rate in Antrim Area Hospital over a one-year period (July 2007 to June 2008) was 4.7% (254/5447). Most of the studied false-positive cases ($N = 142$) occurred in the intensive care unit (ICU) (59 patients; 41.55%), followed by medical wards (55 patients; 38.73%), accident and emergency (16 patients; 11.27%), surgical wards (7 patients; 4.93%) and obstetrics and gynaecology (5 patients; 3.52%).

Table I
General characteristics of cases and control patients (July 2007 to July 2008)

Characteristics	False positive (142 cases)	True negative (142 controls)
Mean (SD) age (years)	66 (18)	66 (17)
19–64	55 (39)	54 (38)
>64	87 (61)	88 (62)
Sex		
Male	73 (51%)	84 (59%)
Female	69 (49%)	58 (41%)
Comorbidity score at admission[a]	1 (0–2)	1 (0–2)
Length of stay in hospital from admission to sample taken in days[a]	1 (0–4)	1 (0–2)
Length of stay in hospital from admission to discharge in days[a]	13 (6–23)	8 (4–15)
Sample drawn from intravascular line (42 cases; 53 controls)	20 (48%)	4 (8%)
Sample drawn peripherally (42 cases; 53 controls)	22 (52%)	49 (92%)
Underlying mental diseases	11 (8%)	13 (9%)
Sample drawn at weekends	28 (20%)	40 (28%)

[a] Median (interquartile range).

Table II
Detailed charges for cases and control patients during the study period (July 2007 to July 2008)

Cost variable	False positive (142 cases)	True negative (142 controls)
Antibiotic (£)	157 (17–406)	14 (2–101)
Microbiology test (£)	120 (23–286)	32 (9–73)
Radiology test (£)	0 (0–35)	14 (14–49)
Biochemistry test (£)	16 (4–40)	14 (7–23)
Haematology test (£)	22 (4–71)	21 (13–27)
Hotel costs (from sample taken to discharge; £)	5,060 (1,787–10,595)	1,890 (1,080–3,786)
Total costs (£)	5,873 (2,031–12,077)	2,103 (1,239–4,311)

Values are median (interquartile range).

Discussion

Although blood culture has been widely recognised as the most appropriate laboratory test for the diagnosis of serious infections in patients, interpretation of blood culture results may be complicated by the occurrence of contaminants, leading to a significant impact on hospitalised patients and incurring additional healthcare costs. To our knowledge, this is the first study which has used Charlson comorbidity index as an integral criterion for matching cases with controls. Measuring comorbidity is considered an essential step in indicating the burden of the disease and, thus, providing risk adjustment criteria for case-mix purposes.[17] The comorbidity index has also been shown to have a significant relationship with length of hospital stay.[18] In addition, the controls for the purposes of this study were selected from all true-negative blood-cultured patients hospitalised during the study period. This helped ensure that controls were representative of the population that produced the cases, thus minimising potential bias.

In the study site hospital, blood culture contamination rate (4.7%) was lower than rates usually reported at teaching hospitals, which were shown to exceed 7%.[4,12,13] A comparison of the characteristics of patients included in this research project showed that both cases and controls were comparable in terms of the matching criteria, i.e. age, and comorbidity index (Table I). The findings of this study showed statistically significant differences in means between cases and controls, in relation to length of hospital stay and total costs, of 5.4 days and £5,001.5 ($7,502.2), respectively. These findings confirm other reports which documented an association between contaminated samples and unnecessary antibiotic use, additional laboratory tests and increased length of hospital stay, and consequently increased hospital costs.[4,6,8,12] Bates *et al.* carried out an investigation to determine the extent to which false-positive blood cultures increase hospital resource utilisation.[4] In their study, false-positive blood cultures, compared with negative blood cultures, were associated with an increased length of stay by 4.5 days (median: 12.5 vs 8 days respectively) and increased total costs by $4,385 (median: $13,116 vs $8,731 respectively). In another two studies aimed at demonstrating the clinical and economic impact of contaminant blood cultures, the authors reported that contaminants were associated with an increase in length of hospital stay by 3 days (median: 8 vs 5) and 1 day (median: 5 vs 4), and additional hospital charges by $8,750 (median: $23,908 vs $15,158) and $8,720 (median: $27,472 vs $18,752) per patient, respectively.[6,12]

In Antrim Area Hospital, and using the estimated additional charges per patient associated with a false-positive blood culture, the prevention of the occurrence of the reported 254 false-positive blood cultures would have resulted in opportunity cost of £1,270,381 ($1,905,572) per year. Even when considering the most conservative cost estimate (i.e. by considering the lower boundary of the 95% CI of the cost), the financial impact of false-positive cultures of £834,111 ($1,251,167) is significant. In this study, the percentage of false-positive blood cultures represented 42.8% of all positive blood cultures, confirming findings by others.[4–6] Of note, the blood culture contamination rate (4.7%) in the study site

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hospital would need to be reduced by about 36% in order to achieve the recommended target rate of <3%.[5] Importantly, a relatively high percentage of the false-positive cases (41.55%) resulted from cultures taken in the ICU, which is recognised to be among the most expensive of hospital wards. Further research is needed to study determinants and trends in contamination in ICUs, and to determine the impact of false-positive cultures on ICU resources, i.e. additional length of ICU stay and overall cost. These findings highlight the need for effective interventions to reduce rates of false-positive blood cultures, and via these to minimise costs and promote more timely patient discharge from hospital. Techniques which have been employed to minimise the risk of contamination of blood cultures include the use of adequate venepuncture protocols, the use of more effective skin antiseptic preparations, the use of commercial blood culture collection kits, and blood cultures taken by a dedicated phlebotomist.[5,7,9,12] The latter, combined with feedback of blood culture contamination rates, has proved effective in reducing overall contamination.[19] Such interventions are likely to be cost-effective, bearing in mind the considerable saving that could be achieved, but a full economic analysis of new approaches will be required. A decrease in unnecessary use of antibiotics would also be a significant outcome which could assist in the hospital's drive to control the spread of antimicrobial resistance. The findings indicated that samples drawn from an intravascular line were more likely to be contaminated (Table I), highlighting a possible association between levels of contaminated blood cultures and the method of sample collection.

The study has some limitations. Firstly, the estimated charges associated with contaminants in the study site hospital may not be directly generalisable to other hospitals since this study was conducted in a single medium-sized teaching hospital, and other hospitals may vary in their healthcare practices and charges. However, the increase in length of hospital stay, observed in this study due to false-positive culture results, is likely to be comparable among hospitals.

Secondly, a relatively high percentage of the false-positive cases resulted from cultures taken in the ICU. Since the ICU is considered among the most expensive wards in hospitals and ICU patients may have long hospital stays, our study may have been strengthened by matching for site of sampling. This was not possible due to difficulties in achieving sufficient numbers of control patients. However, our additional hospital cost estimates were similar to additional hospital charges presented by others.[6,12] In addition, a subset of matched cases and controls was extracted from the total study population to include only patients whose blood culture was not taken in the ICU (i.e. 70 cases and 70 controls). Analysis of data for these latter cases, using the Wilcoxon signed rank test, showed similar results to the full study cohort. Differences in medians, between cases and controls, for the length of hospital stay and the total costs were 5 days (95% CI: 2–10; $P < 0.001$) and £5,839 [$8,759; 95% CI: £3,725 ($5,588) to £8,242 ($12,363); $P < 0.001$], respectively. Thirdly, it was not possible to exclude the possible effect of clinical confounding factors, although the matching of patients' comorbidities would help to minimise their impact.

In conclusion, the findings of this study demonstrated the impact of false-positive blood cultures on increasing hospital length of stay, laboratory costs and antimicrobial costs. Future research should aim at further investigation of factors influencing levels of blood culture contamination and possible ways to intervene in order to successfully decrease the occurrence of false-positive results.

Conflict of interest statement

L. Fullerton and A. Tate are employed by Iskus Health Ltd. The company develops and supplies kits, components and systems to improve blood culture outcomes.

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None.

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