Hospital Acquired Blood Stream Infection in an Adult Intensive Care Unit: a Retrospective Case Series

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Abstract

Introduction: Hospital acquired blood stream infections are a common and serious complication in critically ill patients.

Methods: A retrospective case series was undertaken investigating the incidence and causes of bacteraemia on an intensive care unit with a high proportion of postoperative cardiothoracic surgical and oncology patients.

Results: 405 eligible patients were admitted to the intensive care unit over the course of nine months. 12 of these patients developed a unit acquired blood stream infection. The average Acute Physiology And Chronic Health Evaluation II (APACHE II) score of patients, who developed bacteraemia was greater than those who did not (19.8 versus 16.8 respectively). The risk of developing bacteraemia was associated with intubation and higher rates of invasive procedures. The mortality rate amongst the group of patients that developed bacteraemia was 33%. There was a higher proportion of Gram-negative bacteria isolated on blood cultures than in intensive care units reported in other studies.

Conclusion: Critical care patients are at risk of secondary bloodstream infection. This study highlights the importance of measures to reduce the risk of infection in the intensive care setting particularly in patients who have undergone invasive procedures.

Introduction

Hospital acquired blood stream infections (BSI) are a common and serious complication in critically ill patients. Nosocomial infection in intensive care units (ICU) has been shown to have a prevalence as high as one fifth of patients [1]. BSI occur in approximately 7% of all admissions within their first month on ICU [2]. Higher rate of infection in critically ill patients is associated with the use of central venous catheters, invasive ventilation, urinary catheters and other invasive devices and equipment [3,4]. These potentially preventable infections are associated with crude case fatality rates of approximately 40% [5], and increased rates of morbidity and length of ICU stay [6,7].

Central venous catheter-related and ventilator associated pneumonia (VAP) are the most common sources of secondary bacteraemia in critically ill patients [6]. Urinary catheter associated urinary tract infections are another secondary source. ICU acquired BSI are often Gram-positive pathogens such as coagulase-negative staphylococci and Staphylococcus aureus. Escherichia coli and enterococci are also commonly implicated in the development of bacteraemia in critically unwell patients [7,8]. Recent studies during the coronavirus (COVID-19) pandemic have shown higher rates of Gram-negative infection in patients with COVID-19 requiring intensive care [9].

Materials And Methods

Setting
The study was conducted on a 16-bed adult mixed medical and surgical ICU at St Bartholomew's Hospital, which is a tertiary oncology and cardiothoracic centre which can provide extracorporeal membrane oxygenation (ECMO), from August 1st to December 31st 2019. A review of these cases was undertaken due to a high rate of BSI reflected in the Intensive Care National Audit and Research Centre (ICNARC) quarterly report for this period. The observed rate of unit acquired BSI per 1000 patient days was 4.4 compared to an expected rate of 1.8. Eligible patients were all patients admitted to the ICU over this period for a duration of 48 hours or more.

Definitions

Definitions for ICU-acquired BSI were taken from the 2020 Centre for Disease Control (CDC) patient safety component manual [9]. A BSI was defined as the growth of a pathogen in a set of blood culture bottles. An ICU-acquired BSI was defined when the first bottle growth was more than 48 hours after admission to ICU [7]. Positive bacterial culture for coagulase negative staphylococcus was excluded as it was felt likely to relate to contamination not to true bacteraemia.

A venous catheter related BSI was defined as a positive line tip culture in association with an ICU-acquired BSI [10]. A VAP was defined as a pneumonia in patients mechanically ventilated for more than two days, who developed features of infection with positive culture on sputum or bronchoalveolar lavage sample. A urinary catheter associated infection was defined as where an indwelling urinary catheter was in place for more than two days in a patient who developed features of infection with positive culture on a urine sample [10].

Surgical admission was defined as any patient who had undergone a procedure admitted to ICU in the immediate postoperative setting. Immunosuppression secondary to chemotherapy was defined as a patient having undergone chemotherapy within 30 days of their admission to ICU.

Severity of illness on admission was defined using the APACHE II score.

Data Analysis

Data collected by the ICNARC for our centre over the nine month period was used to identify the ICU-acquired BSI cases. The cases were reviewed retrospectively for demographic, clinical, microbiological and outcome data. Patient notes were analysed by a team made up of four clinicians who were not working in the unit during the period under review. Each case was reviewed by two members of the team independently. The following data was recorded for all patients: age, gender, date of admission, mode of admission, APACHE II score on admission, ICU length of stay, ICU outcome, purpose of admission, microbiological isolates, suspected sources of infection, device insertion and manipulation, and underlying chronic diseases.

Results
From April 1st 2019 to December 31st 2019, 405 patients admitted to ICU were eligible for inclusion. Of those, 12 were diagnosed with a unit acquired BSI giving an observed rate of 3.0%. The mean age was 63.8 years. The male to female ratio in the group of patients diagnosed with BSI was 1:1.

**Risk factors**

Background and admission related risk factors for developing an ICU-acquired BSI are shown in Table 1. The mean ICU admission APACHE II score of patients who developed a unit acquired BSI was 19.8, compared to 16.8 in the patients in the cohort not diagnosed with BSI. Three of the 12 admissions were surgical in nature, while the rest were composed of critically unwell oncological and cardiovascular or respiratory patients. The mean ICU stay of these patients was 28 days.

Of the BSI patients admitted to ICU, five had a malignancy (mostly haematological) and were immunosuppressed having had a recent course of chemotherapy. Three were admitted with neutropenic sepsis. One patient was admitted following a cardiothoracic procedure. Another patient was admitted with decompensated heart failure as shown in Table 2. Two further patients were admitted due to postoperative cardiothoracic complications. Four patients were admitted with heart failure requiring inotropic support (including the previously mentioned patient on chemotherapy) and two patients were admitted for ECMO support for an exacerbation of chronic obstructive pulmonary disease and complete heart block respectively.

All patients who went on to develop a BSI had some form of invasive equipment placed including central venous, arterial and urinary catheters. High risk equipment were considered to be pulmonary artery catheters or central venous lines; of our BSI cases, 67% had high risk equipment placed. 83% were mechanically ventilated at some point during their admission. Five patients who developed a bacteraemia were treated with intravenous steroids. Four of the 12 cases (33%) died.
### Table 1
Patient factors considered to be associated with developing a bloodstream infection on the intensive care unit.

| Factor                                           | Number (percentage) of BSI cases |
|--------------------------------------------------|----------------------------------|
| Surgical Admission                               | 3 (25%)                          |
| Mechanically Ventilated                          | 10 (83%)                         |
| Steroids                                         | 5 (42%)                          |
| Immunosuppression                                | 5 (42%)                          |
| Malignancy                                       | 5 (42%)                          |
| Liver Disease                                    | 1 (8%)                           |
| Chronic kidney disease                           | 2 (17%)                          |
| Chronic obstructive pulmonary disease            | 1 (8%)                           |
| Diabetes mellitus                                | 2 (17%)                          |
| Multiple line changes over the course of patients stay | 2 (17%)                      |
| High Risk Equip/Procedures                       | 8 (67%)                          |

### Timing

There was a range of early and late infections. One patient developed a bacteraemia within the first seven days, six cases subsequently were diagnosed between seven and 14 days, five cases were diagnosed in the following twenty days (Fig. 1).

### Table 2
Reasons for admission to the intensive care unit for patients who developed a unit acquired bloodstream infection.

| Reason for admission to intensive care unit | Number of cases (percentage) |
|--------------------------------------------|------------------------------|
| Decompensated heart failure                | 4 (33%)                      |
| Post-operative complications                | 3 (25%)                      |
| Neutropaenic sepsis                         | 3 (25%)                      |
| Complete heart block                        | 1 (8%)                       |
| Infective exacerbation of chronic obstructive pulmonary disease | 1 (8%) |
Microbiology

13 pathogenic isolates were grown on blood culture in total (Fig. 2). *Escherichia coli* was the most common causative pathogen (three cases), with one of these cases being an extended spectrum beta lactamase (ESBL) producing organism. There were two cases of *Serratia* and two cases of *staphylococcus aureus* (one Methicillin-sensitive *Staphylococcus aureus* (MSSA) and one Methicillin-resistant *Staphylococcus aureus* (MRSA)). One patient grew an enterococcus and *E. coli* simultaneously. Three cases were multi-drug resistant organisms: ESBL E. Coli, MRSA and vancomycin resistant enterococcus (VRE). Nine of the 13 cases were Gram-negative microorganisms. It should be noted that all patients on arriving in our ITU were screened for MRSA. However, it is unclear from the documentation whether the patient who developed an MRSA bacteraemia was decolonised on identification of a positive MRSA swab twenty-five days prior to their first positive blood culture. The case of the VRE BSI did not have screening for VRE.

Source of infection

For the patients with an ICU-acquired BSI, a focus of infection was identified with growth of the same pathogen on other culture samples (sputum, urine or line tip) in five cases. The most commonly confirmed sources of BSI were VAP and line associated with two cases of each. There was a single case of urinary-catheter associated BSI. Seven cases of BSI did not grow the same pathogen on any another culture sample. However, based on clinical findings, one case of BSI was suspected to be urinary catheter acquired, one was identified as being due to a line infection and one was felt to be secondary to an infected a pacemaker device (Fig. 3). Following review of the clinical cases and cultures results the suspected source of BSI remained unclear for four cases.

Discussion

The range of pathogens causing BSI in this cohort of patients is in keeping with those seen in other intensive care units. This study demonstrated a higher incidence of Gram-negative pathogens causing bacteraemia compared to larger scale studies, which have shown a predominance of Gram-positive organisms [2, 8].

Line associated bacteraemia was the most common cause of secondary BSI, followed by VAP and urinary catheter associated infections. In the cases of line associated infection, the notes were reviewed to verify if lines had been inserted using aseptic technique. In two of the three cases the documentation surrounding the venous catheter insertion was unsatisfactory. For the patients found to have BSI secondary to VAP, documentation of VAP care bundle use was reviewed. In both cases of BSI secondary to VAP, there was inadequate documentation of the VAP care bundle. All patients were screened for MRSA on admission to ICU. It was not clear from the documentation whether the patient who acquired an MRSA bacteraemia had received appropriate eradication therapy. The patient who developed VRE bacteraemia
did not have VRE screening. In patients with persistent pyrexia of unknown origin, all patients had devices or lines removed or replaced where possible.

BSI is an important cause of morbidity and mortality in ICU. This is reflected in the mortality rate of 33% in this patient cohort. The importance of thorough clinical examination and septic screen testing to identify a source of infection to guide targeted antimicrobial therapy is key. Patients on ICU are at high risk of secondary infection. This study highlights the importance of aseptic technique during line and catheter insertion, vigilant line care, VAP care bundles.

**Study limitations**

The authors recognise the exclusion of coagulase-negative staphylococcus blood cultures may have underestimated the true rate of unit-acquired BSI. Also, any case that may have had a positive blood culture within 48 hours of discharge from the ICU would not have been identified in this study. The case reviews would have been enhanced by access to nursing documentation to assess the documentation of the VAP care bundles and MRSA decolonisation. In four cases of BSI no cause of infection was identified. Review of the notes in these cases did not reveal any further information as to the cause of the bacteraemia.

**Conclusion**

This study demonstrates a higher proportion of Gram-negative bacteraemia compared to large scale ICU studies in the literature where Gram-positive pathogens predominated. This may be attributed to our cohort of patients many of who were immunosuppressed or post-operative cardiothoracic patients. Our mortality rate for patients with BSI did not differ from rates seen in other intensive care units.

During the COVID-19 pandemic it has been noted that the rate of Gram-negative BSI in patients with COVID-19 infection requiring ICU care has been high. This study provides useful baseline data of the rates of BSI in an ICU prior to the pandemic.

Critical care patients are at high risk of infection and the importance of measures to reduce the risk of secondary infection through comprehensive ICU care including line insertion and care VAP care bundles remain key.

**Abbreviations**

- APACHE II Acute Physiology And Chronic Health Evaluation II
- BSI Blood Stream Infection
- ICU Intensive Care Units
- VAP Ventilator Associated Pneumonia
COVID-19 Coronavirus
ECMO Extracorporeal Membrane Oxygenation
ICNARC Intensive Care National Audit And Research Centre
CDC Centre For Disease Control
ESBL Extended Spectrum Beta Lactamase
MSSA Methicillin-Sensitive Staphylococcus Aureus
MRSA Methicillin-Resistant Staphylococcus Aureus
VRE Vancomycin Resistant Enterococcus

Declarations

Funding

This study received no external funding.

Conflicts of Interest

The authors declare that they have no conflict of interest.

Availability of data and material

Excel sheets with which data was collected on and calculations made can be provided on request.

Code availability (software application or custom code)

Not applicable.

Authors' contributions

The first four authors reviewed their, evenly distributed, allocated cases and identified the relevant information for the purposes of this paper. Consultant Mary White oversaw this work.

Ethics approval

The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Consent for publication

Not applicable.
References

1. J. Vincent and e. al., "The Prevalence of Nosocomial Infection in Intensive Care Units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee," The Journal of the American Medical Association, pp. 639-44, 1995.

2. M. Garrouste-Orgeas and e. al., "Excess Risk of Death from Intensive Care Unit—Acquired Nosocomial Bloodstream Infections: A Reappraisa," Clinical Infectious Diseases, vol. 42, no. 8, p. 1118–1126, 2006.

3. L. Soufir and e. al., "Attributable morbidity and mortality of catheter-related septicemia in critically ill patients: A matched, risk-adjusted, cohort study," Infection Control and Hospital Epidemiology, vol. 20, no. 6, pp. 396-401, 1999.

4. J. O'Horo and e. al., "Arterial catheters as a source of bloodstream infection: a systematic review and meta-analysis.," Critical Care Medicine, vol. 42, no. 6, pp. 1334-1339, 2014.

5. J. R. Prowle and e. al., "Acquired Bloodstream Infection in the Intensive Care Unit: Incidence and Attributable Mortality," Critical Care, vol. 15, no. 2, 2011.

6. M. Bassetti and e. al., "Bloodstream Infections in the Intensive Care Unit," Virulence, vol. 7, no. 3, pp. 267-279, 2016.

7. K. B. Laupland and e. al., "Intensive-care-unit-acquired bloodstream infections in a regional critically ill population," The Journal of Hospital Infection, vol. 58, no. 2, pp. 137-145, 2004.

8. V. De Santis and e. al., "Bacteraemia incidence, causative organisms and resistance patterns, antibiotic strategies and outcomes in a single university hospital ICU: continuing improvement between 2000 and 2013," Journal of Antimicrobial Chemotherapy, vol. 70, no. 1, pp. 273-278, 2015.

9. A. Sturdy et al. Severe COVID-19 and healthcare-associated infections on the ICU: time to remember the basics? J Hosp Infect. 2020. 105 (4): 593-595.

10. C. Centre for Disease Control, "National Healthcare Safety Network (NHSN)," January 2020. [Online]. Available: https://www.cdc.gov/nhsn/PDFs/pscManual/pcsManual_current.pdf. [Accessed 10 07 2020].

11. CCN, Critical Care Network, Ventilator Care Bundle, July 2020 [Online]. Available: https://www.londonccn.nhs.uk/managing-the-patient/respiratory/ventilator-care-bundle/

Figures
Figure 1

Histogram showing the timing of the day of admission on the intensive care unit when the first positive blood culture occurred in patients with a unit acquired blood stream infection.

Figure 2
Pie-chart showing the distribution of pathogenic isolates for patients identified as having a unit acquired bloodstream infection.