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Clinical factors associated with bloodstream infection at the emergency department



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Abstract

Background: Bloodstream infection (BSI) is a common urgent condition at the emergency department (ED). However, current guidelines for diagnosis do not specify the juncture at which blood cultures should be taken. The decision whether or not to obtain hemoculture is based solely upon clinical judgment and potential outcomes of inappropriately ordered cultures. This study aimed to find clinical factors present on ED arrival that are predictive of bloodstream infection.

Methods: This study was conducted retrospectively at the ED of a *single tertiary care hospital* in Thailand. We included adult patients with suspected infection based on blood culture who were treated with intravenous antibiotics during their ED visit. Independent positive predictors for positive blood culture were calculated by logistic regression analysis.

Results: A total of 169,578 patients visited the ED during the study period, 12,556 (7.40%) of whom were suspected of infection. Of those, 8177 met the study criteria and were categorized according to blood culture results (741 positive; 9.06%). Six clinical factors, including age over 55 years, moderate to severe CKD, solid organ tumor, liver disease, history of chills, and body temperature of over 38.3 °C, were associated with positive blood culture.

Conclusions: Clinical factors at ED arrival can be used as predictors of bloodstream infection.

Keywords: Bloodstream infection, Bacteremia, Blood cultures, Rapid diagnosis, Emergency department

Background

Bloodstream infection (BSI) is a common urgent condition at the emergency department (ED) [1, 2]. In 2010, the annual incidence of bloodstream infection increased to 38.1 persons per 100,000, and the mortality rate was as high as 50% [3]. Early diagnosis and appropriate antimicrobial therapy are a key to improving patient outcomes [4], particularly among individuals displaying either septic shock or sepsis [5, 6].

Current guidelines recommend obtaining hemoculture in patients suspected of sepsis in order to diagnose BSI

[5, 7], as positive blood culture is an important factor in determining the appropriate antibiotic treatment [5, 8]. However, the guidelines do not specify when blood cultures ought to be procured. Furthermore, the decision as to whether to take hemoculture is based solely upon clinical judgment, which could result in unnecessary cultures [8–10]. There are several predictors of bloodstream infection at the ED such as blood pressure less than 60 mmHg, procalcitonin levels over 2 µg/L, and C-reactive protein > 10 mg/dL [11]. Shapiro et al. developed a clinical score for bloodstream infection at the ED with a decent validation of 83% [12]. However, obtaining this score may require laboratory results, which could result in delayed sepsis management [6]. Hence, this study examined only clinical factors present on ED arrival to

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determine which, if any, were predictive of bloodstream infection.

Methods

Study design and ethical approval

This study was conducted retrospectively as part of an ED infection project at Khon Kaen University's Srinagarind Hospital, a tertiary care hospital with approximately 60,000 annual ED visits. Inclusion criteria were age > 18 years, suspicion of infection based on blood culture collection, and initiation of intravenous antibiotics during the ED visit. Cases with cardiac arrest or trauma, those referred from other hospitals, those who had previously received antibiotics, and those missing clinical data were excluded. The study period took place between January 1st, 2016 and December 31st, 2018. The study protocol was approved by the Khon Kaen University Ethics Committee in Human Research (HE631115).

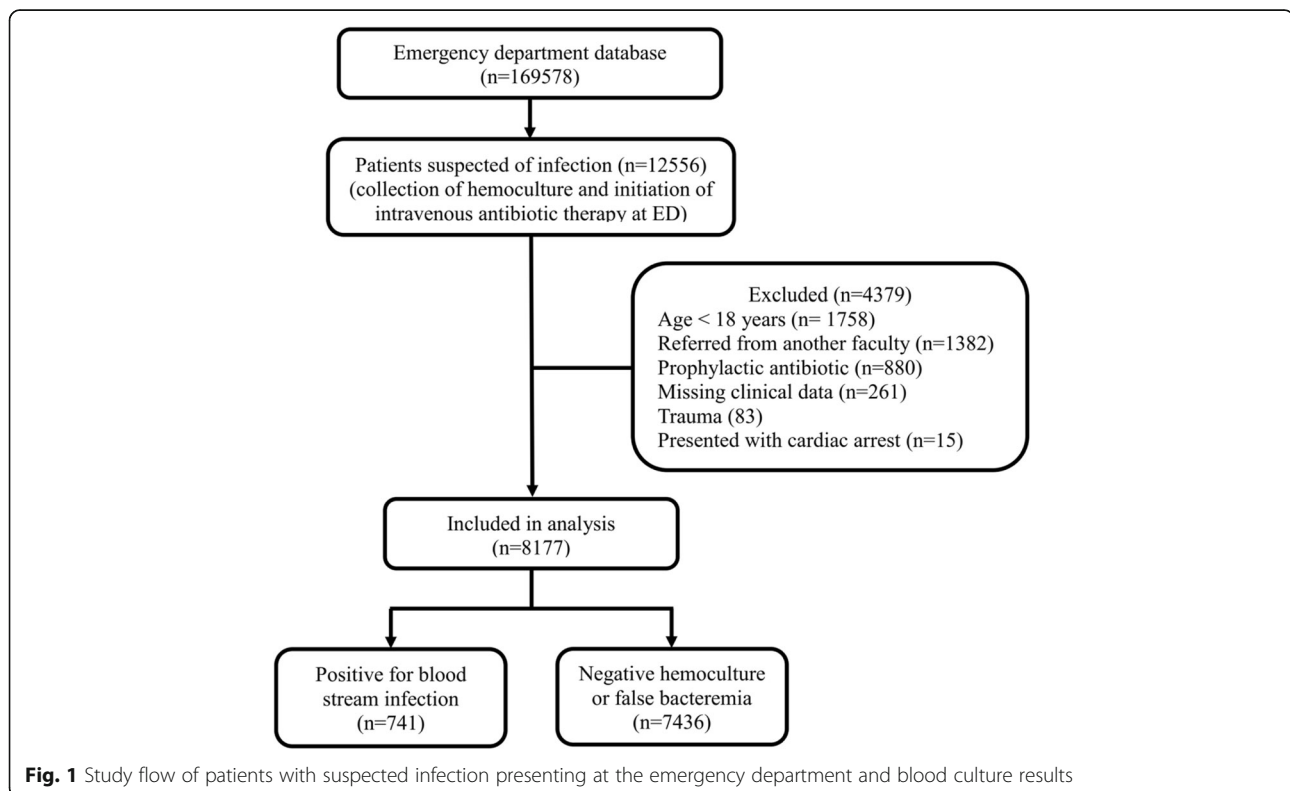
Source of data and microbiological methods

Blood cultures at the ED each consist of two aerobic bottles. Those with a pathogen similar to at least one sample with clinical relevance were considered positive for bloodstream infection. Pathogens (e.g., coagulase-negative Staphylococci, *Corynebacterium* spp., *Propionibacterium* spp., Viridans group streptococci, *Micrococcus* spp., and *Bacillus* spp.) were considered as such if they were isolated

from a patient twice or more consecutively with clinical relevance [7, 13, 14]. Clinical data of eligible patients were retrieved from the computerized hospital database and chart records. Data were subsequently categorized as comorbid conditions, ED arrival parameters, and parameters beyond the initial hour following presentation at the ED. Comorbid conditions were defined according to the Charlson Comorbidity Index (CCI) [15]. ED arrival parameters included history of fever or chills, vital signs, and sepsis scores including Systemic Inflammatory Response Syndrome (SIRS) score, quick Sepsis-related Organ Failure Assessment (qSOFA), and National Early Warning Score (NEWS). Parameters beyond the initial hour post ED arrival included white blood cell count and lactate levels.

Statistical analysis

Eligible patients were categorized into two groups based on whether their blood culture results were positive or negative. Descriptive statistics were used to compare differences in studied variables between the two groups. Factors associated with positive blood culture were calculated via logistic regression analysis. Univariate and multivariate logistic regression were applied to calculate the unadjusted/adjusted odds ratios (95% confidence interval) of each factor. All statistical analyses were performed using STATA version 10.1 (College Station, Texas, USA).



Results

Patient characteristic and microbiology data

A total of 169578 patients visited the ED during the study period, of which 12556 (7.40%) were suspected of infection according to the hospital database. After exclusion, 8177 individuals met the study criteria and were categorized according to blood culture results as either positive for bloodstream infection (741 patients; 9.06%) or negative/non-pathogen bacteremia (7436 patients; 90.94%), as shown in Fig. 1. Almost all variables studied differed significantly between groups (Table 1), with the exception of AIDS prevalence (2.16% in the positive group and 1.44% in the negative group; p 0.125). The most common Gram-negative and positive pathogens were *Escherichia coli* (274 patients; 36.98%) and *Streptococcus* (76 patients; 10.26%), respectively.

Clinical factors predictive of bloodstream infection

There were four significant comorbid conditions, two factors at ED arrival, and three factors beyond the first hour (Table 2). The six significant predictors for positive blood culture on ED arrival were age over 55 years, moderate to severe CKD, solid organ tumor, liver disease, history of chills, and body temperature over 38.3 °C. Liver disease had the highest adjusted odds ratio at 2.04 (95% CI of 1.59, 2.61). The adjusted odds ratio of independent factors ranged from 1.33 to 2.04 (Table 2). Beyond the first hour after ED arrival, lactate level and white blood cell count were both significant factors, with adjusted odds ratios ranging from 1.10 to 2.48.

Discussion

The positive blood culture rate in this study (9.06%) was comparable with those in previous studies (up to 12.4%)

Table 1 Baseline characteristics of patients with suspected infection presenting at the emergency department categorized by blood culture results

| | ALL patients (n = 8177) n (%) | Positive blood culture (n = 741) n (%) | Negative blood culture (n = 7436) n (%) | p-value |
|---|-------------------------------|--|---|---------|
| Demographics | | | | |
| Age, yrs. –median (range) | 62 (18–100) | 62 (18–100) | 64 (18–100) | < 0.001 |
| Male | 4275 (52.28) | 415 (56.01) | 3860 (51.90) | 0.003 |
| CCI –median (range) | 3 (0–13) | 4 (0–13) | 3 (0–13) | < 0.001 |
| Comorbidity | | | | |
| Age > 55 years | 5231 (63.97) | 537 (72.47) | 4694 (63.13) | < 0.001 |
| Hypertension | 2149 (26.28) | 235 (31.71) | 1914 (25.74) | < 0.001 |
| Solid organ malignancy | 1878 (22.97) | 231 (31.17) | 1647 (22.15) | < 0.001 |
| Diabetes mellitus | 1729 (21.14) | 194 (26.18) | 1535 (20.64) | < 0.001 |
| Liver disease | 1190 (14.55) | 191 (25.78) | 999 (13.43) | < 0.001 |
| Moderate to severe CKD | 639 (7.81) | 86 (11.61) | 553 (7.44) | < 0.001 |
| AIDS | 123 (1.50) | 16 (2.16) | 107 (1.44) | 0.125 |
| History of chills | 515 (6.30) | 101 (13.63) | 414 (5.57) | < 0.001 |
| Clinical presentation at triage zone | | | | |
| Respiratory rate > 22/min | 5369 (65.66) | 573 (77.33) | 4796 (64.50) | < 0.001 |
| Temperature > 38.3 °C | 2658 (32.51) | 349 (47.10) | 2309 (31.05) | < 0.001 |
| Heart rate > 120/min | 921 (11.26) | 105 (14.17) | 816 (10.97) | < 0.001 |
| Hypotension (SBP < 90 or MAP < 65 mmHg) | 611 (7.47) | 96 (12.96) | 515 (6.93) | < 0.001 |
| Met Sepsis criteria | | | | |
| SIRS \geq 2 | 6149 (75.20) | 651 (87.85) | 5498 (73.94) | < 0.001 |
| qSOFA \geq 2 | 1230 (15.04) | 140 (18.89) | 1060 (14.25) | < 0.001 |
| NEWS \geq 7 | 2917 (35.67) | 259 (34.95) | 1759 (23.66) | < 0.001 |
| Lactate values | | | | |
| | (n = 4694) | (n = 575) | (n = 4119) | |
| First lactate, mmol/L–median | 1.88 (0.01–28.33) | 2.50 (0.01–18.71) | 1.80 (0.01–28.33) | < 0.001 |
| First lactate > 2 mmol/L | 2193 (46.72) | 383 (51.69) | 1810 (23.34) | < 0.001 |

CKD chronic kidney disease, SBP systolic blood pressure, MAP mean arterial pressure, SIRS Systemic Inflammatory Response Syndrome, qSOFA quick Sepsis-related Organ Failure Assessment, NEWS National Early Warning Score

Table 2 Factors associated with positive blood culture in patients suspected of infection presenting at the emergency department

| Factors | Unadjusted Odds Ratio (95% CI) | ^a Adjusted Odds Ratio (95% CI) | p-value |
|------------------------------------|--------------------------------|---|---------|
| Comorbid conditions | | | |
| Age > 55 | 1.54 (1.30–1.81) | 1.33 (1.04–1.72) | 0.02 |
| Sex | 0.84 (0.73–0.99) | 0.94 (0.78–1.13) | 0.52 |
| Emergency severity index level | 0.62 (0.55–0.70) | 0.87 (0.71–1.13) | 0.18 |
| CCI | 1.13 (1.09–1.06) | 0.98 (0.92–1.04) | 0.46 |
| Liver disease | 2.24 (1.87–2.67) | 2.04 (1.59–2.61) | < 0.01 |
| Diabetes mellitus | 1.36 (1.15–1.62) | 1.08 (0.89–1.30) | 0.45 |
| Moderate to severe CKD | 1.63 (1.28–2.08) | 1.68 (1.22–2.32) | 0.01 |
| Solid organ tumor | 1.59 (1.35–1.87) | 1.40 (1.09–1.80) | 0.01 |
| Hypertension | 1.34 (1.13–1.57) | 1.14 (0.92–1.41) | 0.24 |
| On arrival parameter | | | |
| History of Chills | 2.67 (2.12–3.38) | 1.94 (1.43–2.62) | < 0.01 |
| Temperature > 38.3 °C | 1.40 (1.32–1.50) | 1.77 (1.39–2.25) | < 0.01 |
| Heart rate > 120 /min | 1.01 (1.00–1.01) | 0.96 (0.73–1.26) | 0.76 |
| SBP < 90 or MAP < 65 | 2.01 (1.59–2.54) | 1.22 (0.86–1.71) | 0.26 |
| Respiratory rate > 22/min | 1.03 (1.02–1.04) | 0.89 (0.71–1.26) | 0.32 |
| SIRS criteria ≥ 2 | 2.5 (2.03–3.20) | 1.21 (0.94–1.53) | 0.26 |
| qSOFA criteria ≥ 2 | 1.79 (1.49–2.15) | 1.20 (0.94–1.53) | 0.15 |
| NEWS ≥ 7 | 1.73 (1.47–2.04) | 0.93 (0.73–1.18) | 0.53 |
| Beyond first hour parameter | | | |
| ^b Lactate level | 1.13 (1.10–1.16) | 1.10 (1.07–1.14) | < 0.01 |
| WBC > 11,000 /microliter | 1.31 (1.12–1.52) | 1.28 (1.03–1.59) | 0.03 |
| WBC < 3000 /microliter | 2.30 (1.70–3.13) | 2.48 (1.68–3.66) | < 0.01 |

CCI Charlson Comorbidity Index, CKD chronic kidney disease, SBP systolic blood pressure, MAP mean arterial pressure, SIRS Systemic Inflammatory Response Syndrome; qSOFA quick Sepsis-related Organ Failure Assessment, NEWS National Early Warning Score, WBC white blood cell

^a adjusted by the studied factors shown in this table

^b initial lactate level in mmol/L.

[11, 16]. Subjecting low-risk patients to unnecessary blood culture may yield false positives and increase healthcare costs [12]. As previously reported [12, 17–19], fever and older age are independently associated with positive blood culture at the ED. Although body temperature over 38.3 degrees celsius is one criterion included in the SIRS score [5], only 47.10% of patients in this group had positive cultures (Table 1). The proportion of patients in the positive group with respiratory rate over 22 times/min was higher than that of those with high body temperature (77.33% vs 47.10%). However, this difference was not significant after adjustment for other factors (Table 2). This implies that body temperature alone may not be an adequate indicator of positive blood culture and that it should, instead, be considered in combination with the other five independent factors.

History of chills, which is an indicator of pyrogenic cytokines, is another predictor of positive blood culture. Previous studies by Tokuda et al. and Holmqvist et al. showed history of chills to be associated with positive

blood culture, regardless of severity (mild to shaking) [20, 21]. However, these studies had smaller populations and adjusted for fewer other variables than did our study. The former adjusted for only age and body temperature ($n = 526$), while the latter adjusted for age, sex, vomiting, and antibiotic use ($n = 479$).

This study's findings regarding co-morbid diseases and laboratory tests differed from those of some previous studies [17, 18]. One study, for example, found that the prevalence of liver cirrhosis, chronic kidney disease, and malignancy did not differ significantly between those with and those without positive blood culture [17], whereas our study found a correlation between these comorbid diseases and blood culture positivity. These differences may have been due to our larger study population or the fact that we used clinical factors (with no laboratory results) to predict positive blood cultures in order to allow for more rapid assessment of risk. However, there have been other studies that have reported findings similar to ours [19, 22–24]. For example, one previous study found that cirrhotic patients had a higher

incidence of bloodstream infection than non-cirrhotic patients [24].

Strengths and limitations

In this study, we enrolled a large population to determine predictors for positive blood culture in ED patients with suspicion of infection. However, there were some limitations to this study. Although we employed a large sample size, clinical data were missing in some cases due to the retrospective study design. Such cases were excluded (261 patients). Second, blood cultures were performed based on the judgement of the attending physicians at a single ED. Further studies are thus required to validate and confirm the results of this study. Finally, the results may not be universal for other setting such as community hospitals [25, 26].

Conclusions

Six clinical factors, including age over 55 years, moderate to severe CKD, solid organ tumor, liver disease, history of chills, and body temperature of over 38.3 °C were associated with blood culture positivity. Consideration of these clinical factors may allow for more rapid assessment of positive blood culture risk in ED patients suspected of infection.

Abbreviations

AUROC: Associated area under the ROC; BSI: Bloodstream infection (BSI); CCI: Charlson Comorbidity Index; CKD: Chronic kidney disease; ED: Emergency department; +LR: Positive likelihood ratio; -LR: Negative likelihood ratio; MAP: Mean arterial pressure; NEWS: National Early Warning Score; qBSI score: Quick Bloodstream Infection score; ROC curve: Receiver operating characteristic curves; SIRS: Systemic Inflammatory Response Syndrome (SIRS); SBP: Systolic blood pressure

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Authors' contributions

Conceptualization and Methodology: P.P., N.L. and K.A.; data validation: P.P., N.L. and K.L.; data curation and investigation: P.P., K.A. and S.S.; writing—original draft and formal analysis: P.P., K.S. and V.C.; writing—review and editing: All authors; supervision: P.P. and K.A. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study period took place between January 1st, 2016 and December 31st, 2018 using study protocols approved by the Khon Kaen University Ethics Committee in Human Research (HE631115).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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