EUR REV MED PHARMACOL SCI
2025; 29: 356-374

TRENDS IN BACTERIAL AND FUNGAL BLOODSTREAM INFECTIONS IN SOUTHEAST ASIA: A REVIEW OF BLOOD CULTURE PATHOGENS (2018-2024)

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ABSTRACT – Bloodstream infections (BSIs) pose a significant health burden in clinical settings, contributing to high morbidity and mortality rates worldwide. This review aims to analyze the trends of bacterial and fungal BSI and blood culture pathogen profiles reported in adolescents and adults in Southeast Asian (SEA) countries, drawing from published studies between 2018 and 2024.

A comprehensive literature search was conducted *via* PubMed, Scopus, Web of Science, and Cochrane Library, analyzing 23 studies that included 14,512 patients from 7 SEA countries.

The narrative review highlighted various prevalence rates of bacterial and fungal BSIs among different patient groups: those with indwelling catheters (0.6%-46.9%), sepsis (12.6%-44.5%), and hospitalized patients with other comorbidities (1.1%-29.5%). Blood culture findings revealed that *Escherichia coli* and *Staphylococcus aureus* were the most commonly isolated gram-negative and gram-positive bacteria, respectively, while *Candida* species emerged as the predominant fungal pathogen. Notably, non-*albicans Candida* species were more common than *Candida albicans* in SEA fungemia patients. The overall findings of pathogen distribution in blood cultures from SEA patients are consistent with global surveillance data; however, distinct regional pathogens endemic to SEA, particularly *Burkholderia pseudomallei* and *Talaromyces marneffei*, were also identified.

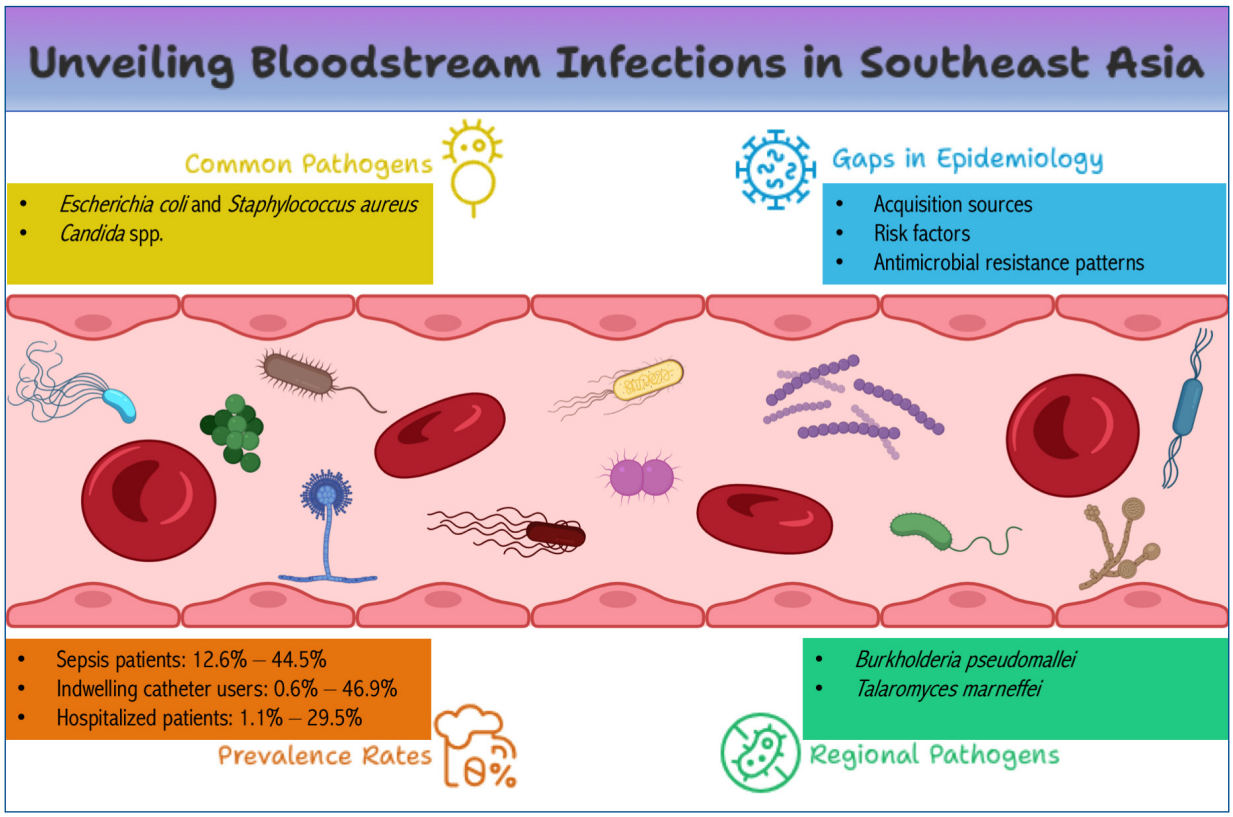
Significant gaps exist in determining bacterial and fungal BSI epidemiology among vulnerable populations, including the acquisition sources, risk factors, antimicrobial resistance patterns, and mortality rates across the SEA region. Overcoming challenges arising from inadequate surveillance and diagnostic capabilities could significantly reduce the BSI burden in the region.

KEYWORDS: Bacteremia, Fungemia, Sepsis, Catheter-related infection, Asian region.

Abbreviations

A. baumannii: *Acinetobacter baumannii*; AMR: Antimicrobial resistance; *B. cereus*: *Bacillus cereus*; *B. pseudomallei*: *Burkholderia pseudomallei*; BD: Becton Dickinson; BSI: Bloodstream infection; *C. albicans*: *Candida albicans*; *C. famata*: *Candida famata*; *C. glabrata*: *Candida glabrata*; *C. krusei*: *Candida krusei*; *C. neoformans*: *Cryptococcus neoformans*; *C. tropicalis*: *Candida tropicalis*; CA: Community-acquired; CCU: Critical care unit; CLABSI: Central line-associated bloodstream infection; CoNS: Coagulase-negative staphylococci; CRBSI: Catheter-related bloodstream infection; *E. cloacae*: *Enterobacter cloacae*; *E. coli*: *Escherichia coli*; *E. faecalis*:

Enterococcus faecalis; *E. faecium*: *Enterococcus faecium*; ESBL: Extended-spectrum beta lactamase; *H. influenzae*: *Haemophilus influenzae*; HA: Hospital-acquired; HCA: Healthcare-associated; HPN: Home Parenteral Nutrition; ICU: Intensive Care Unit; IQR: Interquartile range; *K. pneumoniae*: *Klebsiella pneumoniae*; MDR: multidrug-resistant; MSSA: Methicillin-sensitive *Staphylococcus aureus*; MRSA: Methicillin-resistant *Staphylococcus aureus*; MRCoNS: Methicillin-resistant coagulase-negative staphylococci; NA: Not available; *P. aeruginosa*: *Pseudomonas aeruginosa*; PICC: Peripherally inserted central venous catheter; qSOFA: Quick sequential organ failure assessment; *S. aureus*: *Staphylococcus aureus*; *S. dysgalactiae*: *Streptococcus dysgalactiae*; *S. epidermidis*, *Staphylococcus epidermidis*; *S. pneumoniae*: *Streptococcus pneumoniae*; *S.* Paratyphi: *Salmonella enterica* serotype Paratyphi; *S.* Typhi: *Salmonella enterica* serotype Typhi; SEA: Southeast Asia or Southeast Asian; SIRS: Systemic inflammatory response syndrome; SOFA: Sequential organ failure assessment; spp.: species; *T. marneffei: Talaromyces marneffei*; XDR: Extensively drug resistant.



Graphical Abstract. Unveiling bloodstream infections in Southeast Asia (SEA): Prevalence, epidemiology, and common blood culture pathogens. Created using napkin.ai and Biorender. Karajacob, A. (2025) https://BioRender.com/lakxtb2.

INTRODUCTION

Bloodstream infection (BSI) is defined as a systemic infection arising from a primary or secondary source, which can be confirmed *via* blood culture or non-culture-based microbiological tests with detection of pathogens that are not commensal organisms or contaminants[1]. The clinical manifestations of BSIs are typically non-specific and may include fever, chills, tachycardia, hypotension, fatigue, malaise, and altered mental status. The severity of these symptoms can vary depending on the type of pathogen, site of infection, and the presence of other medical disorders[2]. Moreover, BSIs can be broadly classified into community-acquired (CA), hospital-acquired (HA), and healthcare-associated (HCA) infections in accordance with their acquisition sites[3-6]. The use of invasive devices, such as indwelling urinary and intravascular catheters in BSI management, has also elevated the risk of acquiring catheter-related BSI (CRBSI) or central line-associated BSI (CLABSI)[7,8]. The low clinical positivity rates and prolonged turnaround times of blood cultures, i.e., the current "gold standard" for diagnosing BSI can delay the timely initiation of targeted antibiotic therapy[2]. This often leads to ineffective therapy and extended usage of broad-spectrum antimicrobials, contributing to antimicrobial resistance (AMR) and a higher mortality[9,10].

Recent data highlighted that BSI was the second most common infectious syndrome with global deaths attributable to and associated with AMR, after lower respiratory infections and all related infections in the thorax[11]. Based on data collected by the SENTRY Antimicrobial Surveillance Program from over 200 medical centers in 45 nations (North America, Latin America, Europe and Asia-Pacific) between 1997 and 2016, HA- and CA-BSI attributed to the surge of gram-positive pathogens, such as methicillin-resistant *Staphy-*

lococcus aureus (MRSA) and oxacillin-resistant *S. aureus* in the early 2000s (until 2005 to 2008)[9].

Despite advanced healthcare systems in developed nations, significant morbidity and mortality rates due to BSIs have been reported, with incidences ranging between 113 and 204 per 100,000 person-years amongst sepsis and septic shock patients[12]. A systematic analysis from the MICROBE database, covering 204 countries, revealed that BSIs were responsible for 2.91 million global deaths in 2019[13]. There have been a few comprehensive reviews on BSIs in developing nations in Asia, particularly in Southeast Asia (SEA). A 12.5% median prevalence of CA-BSI (ranging from 2.0% to 48.4%) has been documented in a systematic review of 19 African and Asian countries [including three SEA countries, i.e., Thailand, Indonesia, and Cambodia] between 1974 to 2018[14]. Meanwhile, a prospective point prevalence study among 386 adult intensive care units (ICUs) from 22 Asian countries (including 10 SEA countries, i.e., Malaysia, Philippines, Singapore, Thailand, Vietnam, Indonesia, Cambodia, Laos, Brunei, and Timor-Leste) highlighted that sepsis was a common cause of ICU admission, with an overall prevalence of 22.4%, however, detailed information on blood culture pathogens was not reported in that study[15].

The most recent review on CA-bacteremia in febrile children and adults in South and Southeast Asia (including five SEA countries, i.e., Burma, Laos, Philippines, Thailand, and Vietnam) was conducted over a decade ago[16]. In a systematic review of 17 published studies (1990 to 2010), Deen et al[16] reported pathogen isolation in 9% of patients, with proportions ranging from 1% to 51%. S*almonella enterica* serotype Typhi was identified as the most common bacterial pathogen, accounting for 25% and 30% of blood culture isolates in children and adults, respectively, followed by *S. aureus*, *Escherichia coli*, *Streptococcus pneumoniae, Haemophilus influenzae*, and other gram-negative organisms. Additionally, the SEA region has also been described as the global hotspot for AMR[17,18], with the common gram-negative resistant pathogens for HA infections (including HA-BSIs in ICUs) comprising extended-spectrum cephalosporin resistant *E. coli* and *Klebsiella pneumoniae*, carbapenem resistant *K. pneumoniae* and *Acinetobacter baumannii*, and multidrug-resistant (MDR) *Pseudomonas aeruginosa*[10].

In light of the limited recent reviews on bacterial and fungal BSIs in SEA countries[16], this study aims to provide current updates on bacterial and fungal BSI and spectrum of common blood culture pathogens based on published reports between 2018 and 2024 in these countries.

TYPES OF BLOODSTREAM INFECTIONS

Pathogens can be acquired from various anatomic sites before entering the circulatory system. BSIs can be referred to as bacteremia, fungemia, parasitemia, or viremia, depending on the type of pathogen present in the bloodstream. These infections can be broadly classified based on acquisition site, which include CA, HA, and HCA infections[3-6]. CA-BSIs are recognized as the detection of pathogens in the first 48 hours of hospital admission[3]. HA-BSIs are defined as infections acquired from healthcare facilities following 48 hours of hospital admission[3,4]. Meanwhile, HCA-BSIs are described as infections acquired within 48 hours of hospital admission in patients who have had prior exposure to healthcare settings within the last year[5,6].

BSIs can be divided into primary and secondary infections[1]. Primary BSI refers to an infection originating from the bloodstream, with no identifiable source or apparent infections at other anatomical sites (e.g., abdominal, urinary tract, pulmonary system, skin, and soft tissue)[1]. Meanwhile, secondary BSI refers to an identifiable localized infection (e.g., urinary tract infection, pneumonia, and surgical site infection) as the source of infection, which disseminates into the bloodstream[1]. CRBSI is a primary BSI that is clinically defined as a pathogen isolated from the blood culture that originated from the intravascular catheter site[19,20]. Meanwhile, CLABSI refers to primary BSIs occurring within 48 hours of central line insertion and is not related to an infection at another site[7]. The term is used for surveillance purposes and may not account for some BSIs that originate from sources other than the central line[21]. The term CLABSI is used due to the difficulty that arises from the clinical requirements of the patient (the catheter is not always removed), minimal access to advanced microbiological techniques, and strict adherence to procedures by healthcare personnel[21].

RISK FACTORS FOR BLOODSTREAM INFECTIONS

A myriad of risk factors are linked to BSIs, which are supported by previous literature. Patients with meningitis, endocarditis, urinary tract infection, and skin and soft-tissue infection are either predisposed to or have been associated with CA-BSI[10]. Individuals admitted to the ICU have a HA-BSI prevalence rate of 25% to 75% across healthcare settings in regions including North, Central, and South America; Western and Eastern Europe; Asia, the Middle East, Australasia; and Africa[10]. The infections are associated with a wide range of comorbidities (immunocompromised or chronic illness,

e.g., liver diseases), or underlying illnesses including ventilator-associated pneumonia or intra-abdominal infection[10,22,23]. Other vulnerable individuals include neonates[24] and young children[25,26], who have immature and underdeveloped immune systems, as well as the elderly population[27].

Moreover, extended hospitalization frequently results in prolonged exposure to medical devices, such as mechanical ventilators, indwelling urinary and central-line catheters, that may serve as reservoirs for nosocomial pathogens, potentially leading to BSIs[28,29]. Invasive medical procedures can elevate the risk of attaining BSIs by providing potential entry points for pathogens[7,8]. Thus, it is understandable that CRBSIs are a major cause of HA-BSI, with central venous catheters having a 64-times amplified risk of CRBSI in hospitalized subjects, compared to peripheral venous catheters[20,30]. In addition, prior use or misuse of antimicrobials may lead to the development of MDR organisms, which can diminish the efficacy of the treatments and create an environment that is conducive to the proliferation of antibiotic-resistant strains[31]. Prolonged use of antimicrobials may disrupt microbiota, promote pathogen proliferation and entry, and increase the hosts' vulnerability to invasive infections[32].

MATERIALS AND METHODS

In this narrative review, published articles on blood culture-confirmed BSIs between 2018 and 2024 in SEA countries were retrieved using the PubMed, Scopus, Web of Science, and Cochrane Library search engines. Some studies in this review also reported detection of bacterial, fungal, viral, and parasitic organisms based on microscopy, molecular tests, serological tests, and/or next generation sequencing; however, only the bacterial and fungal blood culture results were highlighted in this review. The following medical subject heading terms (MeSH) were used: "bloodstream infections" OR "bacteremia" OR "fungemia" AND "Brunei", "Cambodia", "Indonesia", "Laos", "Malaysia", "Myanmar", "Philippines", "Singapore", "Thailand", "Timor-Leste", and "Vietnam". Studies selected for this review had to fulfil the inclusion criteria requirements, which were English research articles only and reports of adolescents (≥12 years) and adults with the identification of bacterial and fungal causative agents at least to the genus level from blood cultures in SEA patients. The exclusion criteria comprised case reports, conference papers, book chapters, editorials, review articles, and research articles for neonates and children (<12 years). In addition, studies that focused solely on a single pathogen, did not specify the genus or species of the bloodstream pathogens, and used laboratory methods other than blood cultures for diagnosing BSI were excluded. A total of 2,803 articles were retrieved and screened from the databases. Following the removal of duplicates and articles that did not meet the inclusion criteria, 23 research articles remained. These articles involved 14,512 patients from seven different SEA countries, namely Cambodia (1), Malaysia (6), Myanmar (3), Philippines (1), Singapore (2), Thailand (7), and Vietnam (3). The study details are compiled in Table I, and the characteristics of the included studies are displayed in Figure 1. Table II summarizes the blood culture pathogen profile of BSI patients compiled from 10 studies in four SEA countries [Malaysia (n=3), Myanmar (n=2), Thailand (n=3), and Vietnam (n=2)]. The BSI pathogen profiles from the remaining 13 studies could not be extracted for compilation, as it was unclear whether the isolates originated from single or multiple infectious episodes within the same patient. Moreover, most studies reported the number of isolates per species rather than the number of BSI patients infected with each species. Further information regarding the SEA studies in this review is available in **Supplementary Table I-IV**.

BSI PREVALENCE IN SEA COUNTRIES

A total of 23 studies from SEA countries (Figure 1A) analyzed in this review[33-55], which were published between 2018 and 2024 (Figure 1B), reported isolation of bacterial pathogens from blood cultures, while only 15 of these studies simultaneously reported isolation of fungal pathogens (Table I). The prevalence of BSI based on blood cultures ranged from 0.6% to 46.9% across 20 studies, based on the total number of BSI patients with true pathogens in each population (Table I). In addition, nine studies included in this review also reported the acquisition sites of BSIs, with half of the reviewed studies being CA-BSI (n=4)[35,36,47,55], HA-BSI (n=2)[42,54], CA- and HA-BSI (n=2)[33,34], and CA-, HA-, and HCA-BSI (n=1)[49] (Table I).

In this review, the target group of six studies was individuals with sepsis (Figure 1C), with the BSI prevalence rates ranging from 12.6% to 44.5%[33-38] (Table I). Meanwhile, the CRBSI/CLABSI prevalence was 0.6% to 46.9% (Table I) from eight studies within the SEA region (Figure 1C)[39-46]. Additionally, nine studies reported the prevalence of BSI among hospitalized patients with other comorbidities (Figure 1C), with rates ranging from 1.1% to 29.5% (Table I)[47-55]. These included febrile patients in three studies (3.5%

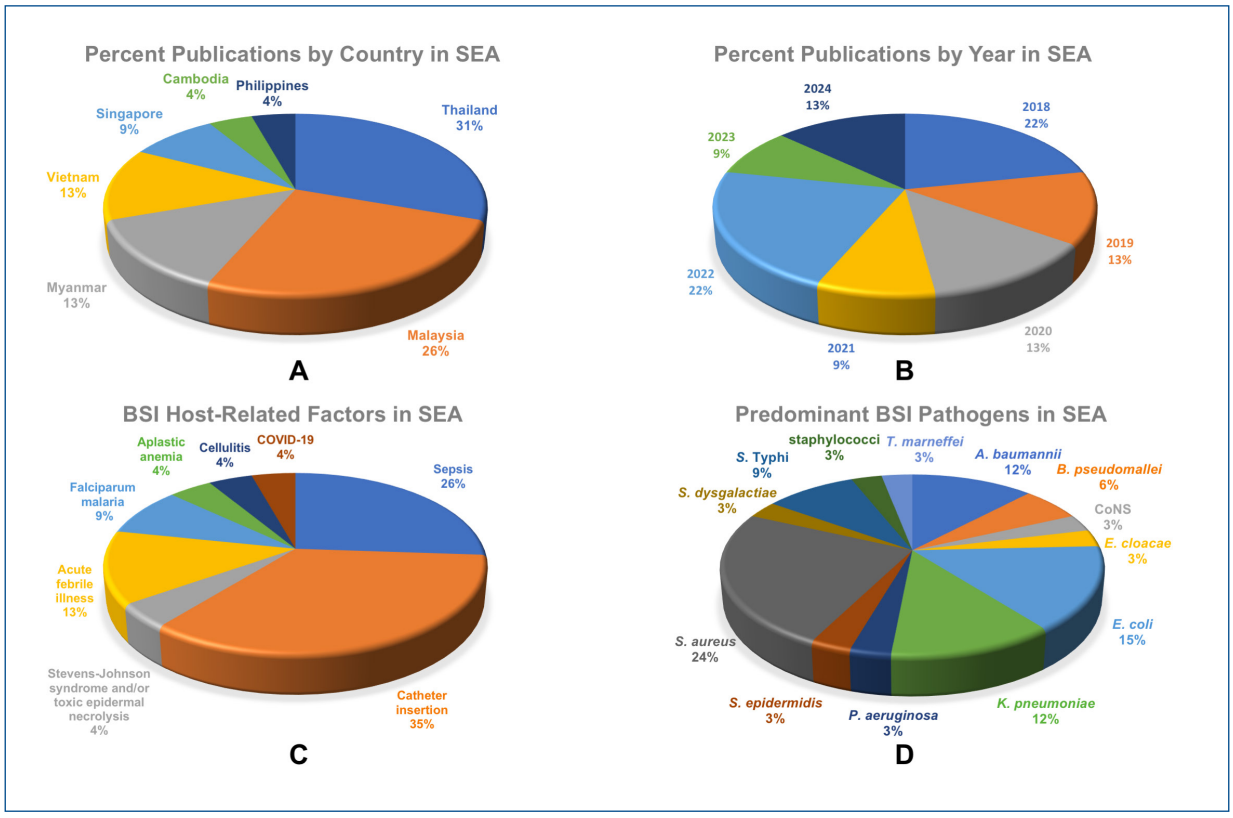


Figure 1. Characteristics of bloodstream infection (BSI) studies in Southeast Asia (SEA; n=23) based on **(A)** country; (**B**) publication year; (**C**) host-related factors; (**D**) predominant BSI pathogens (organisms with the highest isolation rate in each study; % includes drug resistant organisms).

to 9.0%)[47,49,51], as well as patients with falciparum malaria in two studies (1.1% to 20.0%)[48,55], Stevens-Johnson syndrome and/or toxic epidermal necrolysis (29.5%)[50], aplastic anemia (prevalence not reported)[52], cellulitis (1.7%)[53], and COVID-19 (19.0%)[54] in one study each.

BSI PATHOGEN DISTRIBUTION IN SEA COUNTRIES

Regardless of gram-classification, the predominant BSI pathogen in most studies is *S. aureus* (n=8/23 studies; Figure 1D)[39-42,44,47,48,54]. A majority of studies reported *E. coli* (n=7/23)[35-38,48,51,53] and *S. aureus* (n=14/23)[34,35,39-42,44,47-51,54,55] as the predominant gram-negative and gram-positive bacterial pathogens, respectively, and *Candida* spp. as the predominant fungal pathogens (n=10/23)[33,34,38,41,43,45,46,49,50,54] (**Supplementary Table I and II**).

Interestingly, variability in the most commonly isolated bacterial species were also reported in this review (**Supplementary Table I and II**). Frequently reported gram-negative bacteria included *A. baumannii*[34,45,48,50,52], *B. pseudomallei*[33,47,51], *Burkholderia cepacia* complex[43], *Enterobacter cloacae*[48], *H. influenzae*[51], *K. pneumoniae*[39,46,47,54], *Pseudomonas* spp.[40,44], and *P. aeruginosa*[41,42], while gram-positive bacteria included *Bacillus cereus*[52], coagulase-positive staphylococci[36], coagulase-negative staphylococci (CoNS)[45], *Enterococcus faecium*[46,51], methicillin-resistant *Staphylococcus epidermidis*[43], staphylococci[38], *Streptococcus dysgalactiae*[53], and *Streptococcus suis*[37].

Other important pathogens, such as *S.* Typhi, were most commonly isolated in only three studies [Myanmar (n=2), Vietnam (n=1)] in this review[48,49,55]. Three other studies [Cambodia (n=1, 1 isolate), Myanmar (n=1, 3 patients), Thailand (n=1, 2 patients)] also reported isolation of *S.* Typhi but at lower rates[33,35,36]. Intriguingly, the frequent isolation of *B. pseudomallei* in Cambodia[33], Malaysia[34,47], Thailand[36,46,51], and Myanmar[35,49] reflects the endemicity of melioidosis in these countries (**Supplementary Table I and II**). This is a unique regional feature, as this pathogen is rarely reported elsewhere. It was more common in BSI patients with sepsis (n=5 studies), emerging as one of the predominant pathogens in three studies[33,36,47], however, two studies reported its isolation from only one or two sepsis patients[34,35]. *B. pseudomallei* was also identified in BSI patients with acute febrile illness[49,51] and CRBSI[46], though each study reported only a single case of infection.

Among the 15 articles that reported isolation of fungus (Table I), two did not specify the type of fungus isolated[40,44], while three documented non-*Can-*

Table I. Summary of bacterial and fungal BSI studies conducted in SEA countries, 2018-2024.

Study site, period (reference)	No. of patients investigated	Patient characteristics		Blood culture system	Acquisition site	% bacterial and fungal BSI (n)	Predominant bacteria‖	Predominant fungi‖
		Age (years)	Sex					
Sepsis-related BSIs (n=6)								
Takeo Provincial Hospital, Cambodia, 2014 – 2015[33†]	200 adult sepsis patients	Median: 50 Range: 18-83	136 males, 64 females	Aerobic blood culture (unspecified)	CA HA	-	*B. pseudomallei*, *E. coli*	*Non-albicans Candida*
Tertiary hospital, Selangor, Malaysia, 2015 – 2016[34†]	228 adult sepsis patients	Range: <48-67+	137 males, 91 females	Blood culture (unspecified)	CA: 118 HA: 110	-	MDR *A. baumannii*, ESBL K. *pneumoniae*, ESBL *E. coli*, MSSA	*C. tropicalis*, *C. krusei*, *C. glabrata*
Insein General Hospital, Yangon, Myanmar, 2016 – 2017[35]	120 adolescent and adult sepsis patients	Median: 47 IQR: 28-63	52 males, 68 females	Aerobic blood culture (BacT/ALERT, Vitek 2 system)	CA	15.0 (n=18/120)	*E. coli*, *P. aeruginosa*, *S.* Typhi	-
Sunpasitthiprasong Hospital, Ubon Ratchathani province, Thailand, 2013 – 2017[36]	4,989 hospitalized adult patients	Median: 57 IQR: 41-71	2,659 males, 2,330 females	Blood culture (BD BACTEC automated system)	CA	12.6 (n=629/4,989)	*E. coli*, *B. pseudomallei*, coagulase-positive staphylococci	*C. neoformans*, *T. marneffei*, *C. albicans*
108 Military Central Hospital, Hanoi, Vietnam (no study period)[37]	144 naïve and septic patients	Age: 61.4 (SD: 17.4)	106 males, 38 females	Blood culture (BD BACTEC 9120 system, Vitek 2 system)	-	34.0 (n=49/144)	*E. coli*, *K. pneumoniae*, *S. suis*	-
Thong-Nhat Hospital, Ho Chi Minh City, Vietnam, 2018[38‡]	134 adult sepsis and/or septic shock patients	Median: 70 Range: 58-82	66 males, 68 females	Blood culture (unspecified)	-	44.5 (n=53/119)	*E. coli*, staphylococci, *A. baumannii*	*Candida* spp.
Catheter-related BSIs (n=8)								
Universiti Malaya Medical Centre, Kuala Lumpur, Malaysia, 2016 – 2018[39]	50 cuffed and 50 non-cuffed peripherally inserted central catheter adult patients	Mean: 42 (cuffed), 45 (non-cuffed) Range: 26-70 (cuffed), 28-66 (non-cuffed)	30 males, 20 females (cuffed) 30 males, 20 females (non-cuffed)	Blood culture (automated)	-	10.0 (n=5/50, cuffed) 6.0 (n=3/50, non-cuffed)	*K. pneumoniae*, MSSA, MRSA	-
Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia, 2016 – 2018[40]	175 adult hemodialysis patients	Median: 66 (CRBSI), 64 (catheter colonization) IQR: 59-72 (CRBSI), 55-73 (catheter colonization)	54 males, 28 females (CRBSI) 50 males, 43 females (catheter colonization)	Blood culture (unspecified)	-	46.9 (n=82/175)	MSSA, MRCoNS, *Pseudomonas*	Unspecified fungi
Hospital Universiti Sains Malaysia, Kelantan, Malaysia, 2016 – 2017[41]	1,037 and 925 adult patients with central venous catheters pre-and post- the CRBSI intervention program	Mean: 55.53 (SD: 15.50, pre-intervention), 54.61 (SD: 14.94, post-intervention)	36 males, 36 females (pre-intervention); 26 males, 28 females (post-intervention)	Blood culture (BD BACTEC automated system)	-	6.9 (n=72/1,037, pre-intervention) 5.8 (n=54/925, post-intervention)	*S. aureus*, MRCoNS, *E. faecalis* (pre-intervention); *S. aureus*, *E. faecalis*, *P. aeruginosa* (post-intervention)	*C. tropicalis*, *C. albicans* (pre-intervention); *C. tropicalis*, *C. parapsilosis*, *C. haemulonii* (post-intervention)

Table continued

Table I *(Continued)*. Summary of bacterial and fungal BSI studies conducted in SEA countries, 2018-2024.

Study site, period (reference)	No. of patients investigated	Patient characteristics		Blood culture system	Acquisition site	% bacterial and fungal BSI (n)	Predominant bacteria‖	Predominant fungi‖
		Age (years)	Sex					
Sultan Ahmed Shah Medical Centre, Malaysia, 2019 – 2020[42]	578 adult patients from the medical, surgical and CCU/ICU wards	Mean: 59.56 (SD: 12.9, Pre-COVID), 62.08 (SD: 13.6, During COVID)	190 males, 131 females (Pre-COVID) 177 males, 80 females (During COVID)	Blood culture (unspecified)	HA	0.6 (n=2/321, Pre-COVID); 0.8 (n=2/257, During COVID)	MRSA, *E. faecalis* (Pre-COVID); MRSA, *P. aeruginosa* (During COVID)	-
University of the Philippines – Philippine General Hospital, Philippines, 2018 – 2019[43§]	707 adult kidney disease patients with a central venous catheter for hemodialysis	Median: 54	401 males, 306 females	Blood culture (unspecified)	-	27.9 (n=197/707)	Methicillin-resistant *S. epidermidis*, *B. cepacia* complex, *A. baumannii*	*Candida spp.*
Singapore General Hospital, Singapore, 2010 – 2012[44]	677 adult end stage renal disease patients on hemo-dialysis via catheters	Mean: 57.5 (SD: 11.8)	404 males, 273 females	Blood culture (unspecified)	-	16.2 (n=110/677)	MSSA, CoNS, MRSA	Unspecified fungi
Ramathibodi Home Parenteral and Enteral Nutrition Referral Center, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, 2002 – 2014[45§]	72 adults with intestinal failure receiving home parenteral nutrition through a central venous catheter	Mean: 56.2 (SD: 15.7)	33 males, 39 females	Blood culture (unspecified)	-	13.9 (n=10/72)	CoNS, *S. aureus*, *A. baumannii*	*Candida spp.*
Khon Kaen University's Srinagarind Hospital, Thailand, 2020 – 2021[46]	50 adults with triple-lumen central venous catheters clinically suspected with CRBSI	Median: 60 IQR: 53 – 74	30 males, 20 females	Blood culture (BacT/ALERT Virtuo®, Vitek 2 system)	-	28.0 (n=14/50)	XDR *K. pneumoniae*, *E. faecium*	*C. albicans*, *C. glabrata*
BSI in hospitalized patients with various underlying comorbidities (n=9)								
Teluk Intan Hospital, Perak, Malaysia, 2016[47¶]	309 hospitalized adults with acute febrile illness	Median: 47 IQR: 29 – 62	171 males, 138 females	Aerobic blood culture (BD BACTEC 9240 system)	CA	7.0 (n=15/214)	*K. pneumoniae*, *B. pseudomallei*, *S. aureus*	-
Insein General Hospital, Yangon, Myanmar, 2016 – 2017[48]	20 adults with falciparum malaria	Median: 28 IQR: 19 – 35	19 males, 1 female	Aerobic blood culture (BD BACTEC-plus, Vitek system)	-	20.0 (n=4/20)	*E. coli*, *S.* Typhi, *A. baumannii*, *E. cloacae*, *S. aureus*	-
Yangon General Hospital, Yangon, Myanmar, 2015 – 2016[49]	947 febrile adolescents and adults	Median: 37 IQR: 12 – 94	501 males, 446 females	Aerobic blood culture (BacT/ALERT 3D 60 Microbial Detection system, Vitek 2 system)	CA: 76 HCA: 6 HA: 8	9.5 (n=90/947)	*S.* Typhi, *E. coli*, *S.* Paratyphi	*C. tropicalis*, *C. albicans*, *C. famata*
Singapore General Hospital, Singapore, 2003 – 2016[50]	176 adults with Stevens-Johnson syndrome and/or toxic epidermal necrolysis	Median: 41 IQR: 44 – 71	72 males, 104 females	Aerobic and anaerobic blood culture (unspecified)	-	29.5 (n=52/176)	*A. baumannii*, *S. aureus*	*Candida* spp.

Table continued

Table I *(Continued)*. Summary of bacterial and fungal BSI studies conducted in SEA countries, 2018-2024.

Study site, period (reference)	No. of patients investigated	Patient characteristics		Blood culture system	Acquisition site	% bacterial and fungal BSI (n)	Predominant bacteria‖	Predominant fungi‖
		Age (years)	Sex					
Chiangrai Prachanukroh Hospital, Chiangrai, Thailand, 2006 – 2008[51]	200 adults with acute undifferentiated fever	Median: 41 IQR: 29 – 52	114 males, 80 females, 6 unspecified	Blood culture (unspecified)	-	3.5 (n=7/200)	*H. influenzae,* *S. aureus,* *B. pseudomallei,* *E. coli,* *E. faecium*	*T. marneffei*
Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University, Chiang Mai, Thailand, 2010 – 2015[52†]	67 adults with aplastic anemia	Median: 51 Range: 15 – 87	37 males, 30 females	Blood culture (unspecified)	-	-	*A. baumannii,* *P. aeruginosa,* *B. cereus*	*Aspergillus* spp.
Ramathibodi Hospital, Bangkok, Thailand, 2018 – 2022[53]	1,560 adult patients with cellulitis	Mean: 65.79 (SD: 15.78, 47 patients with compli-cations), 57.51 (SD:18.97, 1513 patients with no complications)	599 males, 961 females	Blood culture (unspecified)	-	1.7 (n=27/1,560)	*S. dysgalactiae,* *S. hominis,* *E. coli*	-
Tertiary care referral centre, Southern Thailand, Thailand, 2020 – 2022[54]	252 hospitalized adults with COVID-19	48 BSI patients Median: 61 IQR: 52 – 69 204 non-BSI patients Median: 62 IQR: 47 – 73	126 males, 126 females	Blood culture (unspecified)	HA	19.0 (n=48/252)	ESBL *K. pneumoniae,* MSSA, MDR *A. baumannii*	C. *tropicalis*
Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam, 1991 – 2003[55]	845 adults with severe falciparum malaria	9 bacteremic patients Median: 47 Range: 17 – 60 836 non-bacte-remic patients Median: 31 Range: 15 – 79	-	Aerobic blood culture (manual and BD BACTEC 9050 automated analyser)	CA	1.1 (n=9/845)	*S.* Typhi, *S. aureus*	-

A. baumannii, *Acinetobacter baumannii*; *B. cereus*, *Bacillus cereus*; BD, Becton Dickinson; *B. cepacia*, *Burkholderia cepacia*; *B. pseudomallei*, *Burkholderia pseudomallei*; BSI, bloodstream infection; CA, community-acquired; *C. albicans*, *Candida albicans*; *C. famata*, *Candida famata*; *C. glabrata*, *Candida glabrata*; *C. krusei*, *Candida krusei*; *C. neoformans*, *Cryptococcus neoformans*; *C. tropicalis*, *Candida tropicalis*; CCU, critical care unit; CoNS, coagulase-negative staphylococci; CRBSI, catheter-related bloodstream infection; *E. cloacae*, *Enterobacter cloacae*; *E. coli*, *Escherichia coli*; *E. faecalis*, *Enterococcus faecalis*; *E. faecium*, *Enterococcus faecium*; ESBL, extended-spectrum beta lactamase; HA, hospital-acquired; HCA, healthcare-associated; *H. influenzae, Haemophilus influenzae*; ICU, intensive care unit; IQR, interquartile range; *K. pneumoniae*, *Klebsiella pneumoniae*; MDR, multidrug-resistant; MSSA, methicillin-susceptible *Staphylococcus aureus*; MRCoNS, methicillin-resistant coagulase-negative staphylococci; MRSA, methicillin-resistant *Staphylococcus aureus*; *P. aeruginosa*, *Pseudomonas aeruginosa*; *S. aureus*, *Staphylococcus aureus*; *S. hominis*, *Staphylococcus hominis*; *S. epidermidis*, *Staphylococcus epidermidis*; *S. dysgalactiae*, *Streptococcus dysgalactiae*; *S. suis*, *Streptococcus suis*; *S.* Paratyphi, *Salmonella enterica* serotype Paratyphi; *S.* Typhi, *Salmonella enterica* serotype Typhi; spp., species; *T. marneffei*: *Talaromyces marneffei*; XDR, extensively drug-resistant.

†BSI rate was not reported, as the data was not available in terms of number of patients (refer to **Supplementary Table I**). ‡BSI rate was reported based on blood cultures collected from only 119 patients. §BSI rate was not calculated in the original article; however, the number of patients were available for calculation in this review. ¶BSI rate was reported out of 214 patients who had pathogen isolated from various anatomical sites. ‖BSI pathogens with the three highest isolation rates; however, certain studies included more than three pathogens when isolation rates were equal.

dida species (*Aspergillus*, *Cryptococcus neoformans* and *Talaromyces marneffei*) as the most frequently cultured organisms from BSIs[36,51,52]. This review found that two Thai studies[36,51] reported *T. marneffei* BSI in hospitalized patients, including three cases without organ dysfunction, three with sepsis, and two human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)-positive patients with acute febrile illness.

Of the remaining 10 articles, four did not specify fungal pathogens up to the species level (*Candida* spp.)[38,43,45,50], highlighting limitations in laboratory diagnostic practices and/or resources in distinguishing between different *Candida* species. Five studies documented non-*albicans Candida* species as the predominant fungal pathogens[33,34,41,49,54], while only one study highlighted *Candida albicans* as the main fungal agent in BSIs[46].

A smaller evaluation, including 10 studies from four SEA countries in this review was also performed to obtain detailed information on blood culture pathogen profiles (Table II). Among the 10,168 patients analyzed in Table II, 937 blood culture isolates were identified in 933 (9.2%) BSI patient samples[34-37,39,41,48,51,53,55]. *E. coli* was the predominant isolate, accounting for 25.6% (n=239/933) of isolates in adolescents and adults (Table II). Other common pathogens included *B. pseudomallei* (16.5%, n=154/933), *K. pneumoniae* (6.6%, n=62/933), and *S. aureus* (5.9%, n=55/933) (Table II). Moreover, the distribution of BSI pathogens across 933 patient samples highlighted that Thailand (71.1%) had the highest relative percentage of bacterial and fungal pathogens, followed by Malaysia (20.4%), Vietnam (6.2%), and Myanmar (2.4%; Table II).

BLOOD CULTURE DIAGNOSTIC SYSTEMS USED IN BSI IN SEA COUNTRIES

Studies analyzed in this review had sample collection performed between 1991 to 2022. These samples were collected in one or more aerobic and/or anaerobic blood culture bottles following routine procedures in the respective laboratories. A total of six studies performed only aerobic culture[33,35,47-49,55], one performed both aerobic and anaerobic culture[50], while the remaining 16 studies did not specify culture conditions[34,36-46,51-54].

Moreover, a total of 14 studies did not specify the type of blood culture system used routinely for laboratory diagnosis of BSI[33,34,38-40,42-45,50-54], while six used Becton Dickinson (BD) BACTEC™ automated blood culture systems [models 9050 (n=1), 9120 (n=1), 9240 (n=1), unspecified (n=3)][36,37,41,47,48,55], and three used bioMérieux BacT/ALERT® automated microbial detection systems [3D 60 Microbial Detection System (n=1), VIRTUO (n=1), unspecified (n=1)][35,46,49] (Table I). Blood culture samples were also processed manually in one study in Vietnam (between 1991 and 1997)[55].

Sepsis diagnostic criteria in SEA countries

A total of 10 studies in this review used either the systemic inflammatory response syndrome (SIRS) (n=2)[33,34] or Sepsis-3 (n=8) criteria to recruit patients with sepsis[35-38,46,47,49,53] (**Supplementary Table I**). The sequential organ failure assessment (SOFA) diagnostic tool under the Sepsis-3 guidelines was used in three studies[37,38,46]. Quick SOFA (qSOFA) was used in four studies[35,47,49,53], while one study used modified SOFA scores[36].

SOURCE OF BLOODSTREAM INFECTIONS IN SEA COUNTRIES

Expectedly, *E. coli* predominated among the most commonly isolated sepsis pathogens in four studies [Myanmar (n=1), Thailand (n=1), Vietnam (n=2)][35-38], followed by *B. pseudomallei* (Cambodia, n=1 study)[33], MDR *A. baumannii* (Malaysia, n=1 study)[34], and staphylococci (Vietnam, n=1 study)[38] (Table I). While among CRBSI pathogens, *S. aureus* (including MRSA) was most commonly observed in five studies [Malaysia (n=4), Singapore (n=1)][39-42,44], followed by *K. pneumoniae* [2 studies; Malaysia (n=1), Thailand (n=1)][39,46], *P. aeruginosa* (Malaysia, n=1 study)[42], methicillin-resistant *S. epidermidis* (Philippines, n=1 study)[43], and CoNS (Thailand, n=1 study)[45] (Table I). Analysis of the overall BSI blood culture pathogen profile amongst hospitalized patients with other comorbidities was not possible in this study, as the patients belonged to distinct subgroups that could not be combined to accurately represent pathogen distribution. Hence, each study was discussed separately to understand their respective pathogen profiles in the later section of this review.

Sepsis-related bloodstream infection (n=6 studies)

Six of the 23 SEA studies in this review documented BSIs in sepsis patients[33-38]. A single-center study in rural Cambodia reported that gram-negative organisms, *B. pseudomallei* (n=8/20 isolates) and subsequently *E. coli* (n=5/20), were the main bloodstream pathogens in 200 hospitalized adult sepsis patients who were severely ill[33]. Meanwhile, a study conducted at a Malaysian tertiary hospital revealed that 56 bloodstream isolates were cultured from 228 adult ICU sepsis patients[34]. This study also reported that a major source of isolated MDR organisms was from blood samples[34]. MDR *A. baumannii*, methicil-

Table II. Blood culture pathogen profile of BSI patients from 10 studies in SEA, 2018-2024.

Pathogen profile	Overall (n=933 patient samples; %)	Malaysia[34,49,41] (n=190; 20.4%)	Myanmar[35,48] (n=22; 2.4%)	Thailand[36,51,53] (n=663; 71.1%)	Vietnam[37,55] (n=58; 6.2%)
Gram-negative	**598 (56.6)**	**91 (8.6)**	**21 (2.0)**	**439 (41.6)**	**47 (4.5)**
Gram-negative *Enterobacteriaceae*					
Non-*Salmonella Enterobacteriaceae*					
Escherichia coli[†]	239 (25.6)	14 (1.5)	8 (0.9)	193 (20.7)	24 (2.6)
Klebsiella spp.[‡]	66 (7.1)	24 (2.5)	-	29 (3.1)	13 (1.4)
K. pneumoniae[†]	62 (6.6)	20 (2.1)	-	29 (3.1)	13 (1.4)
Acinetobacter spp.	29 (3.1)	15 (1.6)	1 (0.1)	12 (1.3)	1 (0.1)
A. baumannii[§]	18 (1.9)	15 (1.6)	1 (0.1)	1 (0.1)	1 (0.1)
Enterobacter spp.	12 (1.3)	5 (0.5)	2 (0.2)	5 (0.5)	-
E. cloacae[†, ¶]	7 (0.8)	5 (0.5)	2 (0.2)	-	-
Proteus spp.	6 (0.6)	2 (0.2)	-	4 (0.4)	-
P. mirabilis	2 (0.2)	2 (0.2)	-	-	-
Morganella morganii	2 (0.2)	1 (0.1)	-	-	1 (0.1)
Serratia marcescens	2 (0.2)	1 (0.1)	-	1 (0.1)	-
Pantoea spp.	1 (0.1)	1 (0.1)	-	-	-
Salmonella enterica					
Salmonella spp.	1 (0.1)	1 (0.1)	-	-	-
S. enterica serotype Typhi	9 (1.0)	-	4 (0.4)	2 (0.2)	3 (0.3)
Non-typhoidal *Salmonella*	9 (1.0)	-	-	8 (0.9)	1 (0.1)
S. enterica serotype Paratyphi	1 (0.1)	-	1 (0.1)	-	-
Other gram-negatives					
Burkholderia spp.	159 (17.0)	7 (0.8)	1 (0.1)	151 (16.2)	-
B. pseudomallei	154 (16.5)	2 (0.2)	1 (0.1)	151 (16.2)	-
B. cepacia	5 (0.5)	5 (0.5)			
Pseudomonas spp.	38 (4.1)	8 (0.9)	4 (0.4)	26 (2.8)	-
P. aeruginosa	12 (1.3)	8 (0.9)	4 (0.4)	-	-
Aeromonas spp.	9 (1.0)	1 (0.1)	-	6 (0.6)	2 (0.2)
A. hydrophilia	2 (0.2)	1 (0.1)	-	-	1 (0.1)
A. sobria	1 (0.1)	-	-	-	1 (0.1)
Achromobacter xylosoxidans	4 (0.4)	4 (0.4)	-	-	-
Stenotrophomonas maltophilia	4 (0.4)	4 (0.4)	-	-	-
Ralstonia mannitolilytica	2 (0.2)	2 (0.2)	-	-	-
Haemophilus influenzae	2 (0.2)	-	-	1 (0.1)	1 (0.1)
H. influenzae type B	1 (0.1)	-	-	-	1 (0.1)
Mycoplasma pneumoniae	1 (0.1)	1 (0.1)	-	-	-
Neisseria meningitidis	1 (0.1)	-	-	-	1 (0.1)
Vibrio vulnificus	1 (0.1)	-	-	1 (0.1)	-
Gram-positive	**276 (29.6)**	**88 (9.4)**	**2 (0.2)**	**175 (18.8)**	**11 (1.2)**
Staphylococcus spp.	125 (13.4)	58 (6.2)	2 (0.2)	62 (6.6)	3 (0.3)
Coagulase-positive staphylococci	108 (11.6)	47 (5.0)	2 (0.2)	56 (6.0)	3 (0.3)
S. aureus[‖]	55 (5.9)	47 (5.0)	-	3 (0.3)	3 (0.3)
Coagulase-negative staphylococci[††]	17 (1.8)	11 (1.2)	-	6 (0.6)	-
S. hominis	3 (0.3)	-	-	3 (0.3)	-
S. epidermidis	2 (0.2)	-	-	2 (0.2)	-
S. haemolyticus	1 (0.1)	-	-	1 (0.1)	-
Streptococcus spp.	107 (11.5)	1 (0.1)	-	98 (10.5)	8 (0.9)
Group A *Streptococcus* (*S. pyogenes*)	28 (3.0)	-	-	27 (2.9)	1 (0.1)
Group B *Streptococcus* (*S. agalactiae*)	31 (3.3)	-	-	31 (3.3)	-
S. pneumoniae	18 (1.9)	-	-	17 (1.8)	1 (0.1)
Group D *Streptococcus*	7 (0.8)	-	-	7 (0.8)	-
S. dysgalactiae	4 (0.4)	-	-	4 (0.4)	-
S. suis	4 (0.4)	-	-	-	4 (0.4)
S. sanguinis	2 (0.2)	1 (0.1)	-	-	1 (0.1)
S. mitis	1 (0.1)	-	-	-	1 (0.1)
Other streptococci	12 (1.3)	-	-	12 (1.3)	-

Table continued

Table II *(Continued)*. Blood culture pathogen profile of BSI patients from 10 studies in SEA, 2018-2024.

Pathogen Profile	Overall (n=933 patient samples; %)	Malaysia[34,49,41] (n=190; 20.4%)	Myanmar[35,48] (n=22; 2.4%)	Thailand[36,51,53] (n=663; 71.1%)	Vietnam[37,55] (n=58; 6.2%)
Enterococcus spp.	25 (2.7)	16 (1.7)	-	9 (1.0)	-
E. faecalis	14 (1.5)	12 (1.3)	-	2 (0.2)	-
E. faecium	4 (0.4)	3 (0.3)	-	1 (0.1)	-
Bacillus spp.	6 (0.6)	5 (0.5)	-	1 (0.1)	-
B. cereus	1 (0.1)	-	-	1 (0.1)	-
Corynebacterium spp.	5 (0.5)	4 (0.4)	-	1 (0.1)	-
C. amycolatum	3 (0.3)	3 (0.3)	-	-	-
C. jeikeium	1 (0.1)	1 (0.1)	-	-	-
C. striatum	1 (0.1)	-	-	1 (0.1)	-
Micrococcus luteus	2 (0.2)	-	-	2 (0.2)	-
Propionibacterium spp.	3 (0.3)	3 (0.3)	-	-	-
P. acnes	1 (0.1)	1 (0.1)	-	-	-
Actinobacteria	1 (0.1)	1 (0.1)	-	-	-
Lysinibacillus fusiformis	1 (0.1)	-	-	1 (0.1)	-
Other gram-positives	1 (0.1)	-	-	1 (0.1)	-
Fungi	**38 (4.1)**	**14 (1.5)**	**-**	**24 (2.6)**	**-**
Candida spp.	20 (2.1)	14 (1.5)	-	6 (0.6)	-
C. tropicalis	8 (0.9)	8 (0.9)	-	-	-
C. albicans	4 (0.4)	1 (0.1)	-	3 (0.3)	-
C. parapsilosis	3 (0.3)	2 (0.2)	-	1 (0.1)	-
C. glabrata	1 (0.1)	1 (0.1)	-	-	-
C. haemulonii	1 (0.1)	1 (0.1)	-	-	-
C. krusei	1 (0.1)	1 (0.1)	-	-	-
Other *Candida*	2 (0.2)	-	-	2 (0.2)	-
Talaromyces marneffei	8 (0.9)	-	-	8 (0.9)	-
Cryptococcus neoformans	7 (0.8)	-	-	7 (0.8)	-
Fusarium spp.	1 (0.1)	-	-	1 (0.1)	-
Unspecified fungi	2 (0.2)	-	-	2 (0.2)	-
Other polymicrobial infections	**25 (2.7)**	**-**	**-**	**25 (2.7)**	**-**

[†]Extended-spectrum beta-lactamase producing isolates included *E. coli* (n=7 patients), *K. pneumoniae* (n=10 patients), and *E. cloacae* (n=1 patient). [‡]One study reported isolation of multidrug-resistant *Klebsiella* spp. (n=1 patient). [§]Two studies reported isolation of multidrug-resistant *A. baumannii* (n=11 patients). [¶]One study documented carbapenem-resistant *E. cloacae* (n=1 patient). [‖]A total of six BSI patients (n=3 studies) were reported to have methicillin-resistant *S. aureus.* [††]A total of nine BSI patients (n=1 study) were reported to have methicillin-resistant coagulase-negative staphylococci.

lin-sensitive *S. aureus* (MSSA), extended-spectrum beta lactamase (ESBL) producing *E. coli*, ESBL *K. pneumoniae*, and non-ESBL *E. coli* were the most prevalent organisms[34]. Other MDR organisms were also noted in this study, such as ESBL *E. cloacae* and MRSA, which were detected at a lower rate[34]. A Myanmar study found that 15.0% (n=18/120) of adolescents and adults admitted from the community with sepsis had CA-BSI[35]. Of those patients, 94% had gram-negative pathogens in their blood cultures, mainly *E. coli* and *P. aeruginosa*[35]. Expectedly, individuals with bacteremia (56%, n=10/18) had a significantly higher probability of death (p=0.005) compared to individuals with culture-negative samples (24%, n=24/102)[35].

Moreover, a study in a resource-limited tertiary-care hospital in Northeast Thailand reported a CA-BSI prevalence of 12.6% (n=629/4,989) in hospitalized adult patients with systemic manifestations of infection within 24 hours of admission[36]. Pathogens were isolated from 522 (13.7%) and 107 (9.0%) of patients with (sepsis) and without organ dysfunction, respectively[36]. Male gender, older age, relocation from another medical facility, greater modified SOFA score, concurrent disorders, and a positive blood culture for pathogenic organisms were all significantly associated with mortality[36]. This study highlighted that *E. coli* and *B. pseudomallei* were the most prevalent bacteria in blood cultures[36]. Similar to Ye Lynn et al[35] in Myanmar, Thai CA-bacteremia patients were

also significantly associated (p<0.001) with an increased 28-day mortality rate (24%, n=196/819)[36].

Hospitalized sepsis patients in two Vietnamese studies had BSI prevalence rates ranging from 34.0% to 44.5%[37,38], however, the infection origin was not indicated. Trung et al[37] reported BSIs in 34.0% of 144 naïve and septic patients, highlighting *E. coli* and *K. pneumoniae* as the main pathogens. Meanwhile, BSIs were reported in 44.5% of sepsis patients (n=53/119) in another cross-sectional study, with *E. coli* and staphylococci as the prevailing pathogens[38]. Nguyen-Hoang and Bui[38] further highlighted that the frequency of successful empirical antimicrobial treatment outcomes did not significantly vary between culture-positive or negative blood cultures. In contrast, Trung et al[37] reported that the use of empirical antibiotic therapy significantly reduced the positivity rates of blood cultures, decreasing from 42.9% in untreated sepsis patients to 27.2% in those who had received antimicrobial treatment (p=0.049).

Remarkably, fungemia in sepsis patients was concurrently observed across four studies [Cambodia (n=1), Malaysia (n=1), Thailand (n=1), Vietnam (n=1); Table I][33,34,36,38]. Isolation of fungal pathogens was relatively lower compared to bacterial pathogens in sepsis patients with BSI. Studies in Cambodia[33], Malaysia[34], and Vietnam[38] highlighted that fungal blood cultures were mostly positive with *Candida* spp. (Table I). The type of *Candida* species was not reported (15.2% in 134 patients) in the Vietnamese study[38], while non-*albicans Candida* spp. were the predominant blood culture pathogens in two studies from Cambodia[33] and Malaysia[34] (Table I). The Cambodian study[33] did not specify the exact *Candida* species (n=1/20 isolates), while the Malaysian study[34] reported six cases of candidemia, with *Candida tropicalis* identified as the main fungal pathogen (n=4/228 patients), followed by *Candida krusei* and *Candida glabrata* with one case each (**Supplementary Table I and II**). In contrast, Hantrakun et al[36] reported 22 fungemia cases (n=22/4,989 patients) in the Thai study, with *C. neoformans* and *T. marneffei* identified as the prevailing pathogens in seven and six cases respectively, followed by *C. albicans* in an additional three cases (**Supplementary Table I and II**).

Catheter-related bloodstream infection (CRBSI; n=8 studies)

Currently, there are no prior reviews on CRBSI prevalence within the SEA region. Hence, a comprehensive review is essential to obtain actual prevalence data to support the development of targeted infection control strategies. In a Malaysian study, 10.0% and 16.0% of patients with cuffed tunneled peripherally inserted central venous catheters (PICCs; n=5/50) and non-cuffed tunneled PICCs (n=8/50), respectively, developed bacteremia[39]. The majority of these patients (89.0%) were on long-term antibiotics[39]. Both patient cohorts had three bacterial species, with *K. pneumoniae* predominating in blood cultures, followed by MSSA and MRSA isolates[39]. The latter catheter design was reported to have decreased risk of CRBSI and was significantly associated with prolonged duration of indwelling catheter utilization[39]. A higher CRBSI prevalence of 46.9% (n=82/175) was documented in another Malaysian study regarding hemodialysis patients, which also isolated MSSA, in addition to methicillin-resistant CoNS (MRCoNS) and *Pseudomonas* as the predominant pathogens[40]. It was reported that patients with gram-negative blood cultures, elevated initial C-reactive protein levels, and catheter salvation were more likely to have poor outcomes, while having diabetes, polymicrobial infections, and a femoral vein catheter site was significantly linked to recurrence of CRBSI[40]. In another reviewed study, hospitalized adults with central venous catheters in a Malaysian tertiary institution exhibited a 6.94% CRBSI prevalence before the implementation of an intervention program, and a reduction to 5.83% after the intervention[41]. Pathogens with the highest distribution comprised of *S. aureus*, MRCoNS and *Enterococcus faecalis* in the pre-intervention group, while *S. aureus*, *E. faecalis*, and *P. aeruginosa* were isolated in the post-intervention group[41]. Additionally, an increase in HA-CLABSI from 0.6% (n=2/321) to 0.8% (n=2/257) was observed among hospitalized Malaysian patients during the COVID-19 pandemic[42]. MRSA was cultured prior and during COVID-19, however, *E. faecalis* was only isolated before the pandemic, while *P. aeruginosa* was detected during the pandemic[42]. CLABSI rates showed a slight increase during the COVID-19 pandemic, which aligns with global trends due to increased catheter use and strained healthcare resources during the pandemic[56].

A Filipino single-center study detected CRBSI in 27.9% (n=197/707) of adult kidney disease patients undergoing hemodialysis, and observed that autoimmune disease, dialysis more than three times per week, insertion of central venous catheters for blood transfusion or intravenous therapy, renal hypoperfusion, drug-induced nephropathy, and hypertensive kidney disease are key risk factors for CRBSI[43]. Organisms, such as methicillin-resistant *S. epidermidis*, *B. cepacia* complex, and *A. baumannii* were in higher distribution, while MDR pathogens represented 44.5% of isolates from these CRBSI patients[43]. A Singaporean single-center study highlighted a 16.2% (n=110/677) CRBSI prevalence in adults undergoing hemodialysis for

renal replacement therapy *via* a vascular catheter, with MSSA, CoNS, and MRSA as the main pathogens, while fungi were isolated at a much lower rate[44]. Clinical variables, such as prolonged duration of indwelling catheters, were significantly associated with the development of CRBSI[44]. Moreover, diagnosis of CRBSI was also significantly related to a higher mortality rate in this patient cohort[44].

Two Thai studies highlighted a higher central venous catheter BSI prevalence, ranging between 13.9% (n=10/72) and 28.0% (n=14/50)[45,46]. Pichitchaipitak et al[45] noted that extended periods of Home Parenteral Nutrition (HPN), cyclic HPN infusion, and the use of hospital-based compounded Parenteral Nutrition formulations were significant risk factors associated with CRBSIs. Contrarily, Deawtrakulchai et al[46] claimed that there were no identified risk factors significantly related to CRBSIs among patients with triple-lumen central venous catheters. Though, this analysis reported that the first positive blood culture from individual bottles had a significantly shorter time to positivity and higher sensitivity compared to pooled blood cultures for CRBSI diagnosis[46]. Both Thai studies had slightly different pathogen distributions and isolation rates. Pichitchaipitak et al[45] mainly detected CoNS, *S. aureus*, and *A. baumannii*, while Deawtrakulchai et al[46] primarily detected extensively drug-resistant (XDR) *K. pneumoniae* and *E. faecium*.

Importantly, fungemia in CRBSI patients was simultaneously identified in six of eight reviewed CRBSI studies [Malaysia (n=2), Philippines (n=1), Singapore (n=1), Thailand (n=2); Table I][40,41,43-46], with much lower rates compared to bacteremia rates in CRBSI patients. Two studies (Malaysia, n=3/87 isolates; Singapore, n=2/113 isolates) did not specify the fungus isolated[40,44], two studies (Philippines, n=4/204 isolates; Thailand, n=2/26 isolates) identified the fungal pathogens up to the genus level (*Candida* spp.)[43,45], while the remaining two studies [Malaysia, n=3/72 patients (pre-intervention), n=5/54 patients (post-intervention); Thailand n=3/19 isolates] reported the isolation of *C. albicans*, *C. glabrata*, *Candida haemulonii*, *Candida parapsilosis,* and *C. tropicalis*[41,46] (**Supplementary Table I and II**). Among these isolates, *C. albicans* and *C. tropicalis* were the predominant fungal pathogens[41,46].

Bloodstream infection in hospitalized patients with other comorbidities (n=9 studies)

This review highlights the importance of hospitalized patients with BSI of unknown origin, as identifying the causative pathogens is essential for selecting effective antimicrobial therapy, enhancing patient recovery, and monitoring emerging resistance trends. At a tertiary hospital in rural Malaysia, 7.0% (n=15/214) of hospitalized adults with acute febrile illness (>38ºC) exhibited CA-BSI, with *K. pneumoniae*, *B. pseudomallei*, and *S. aureus* as the predominant pathogens[47]. Elevated procalcitonin biomarker levels discriminated between culture-confirmed bacteremia patients and patients with scrub typhus, as the former patient group was observed to have significantly increased levels (p<0.001)[47].

Furthermore, a study in a tertiary hospital in Myanmar reported a slightly higher BSI prevalence of 9.5% (n=90/947) in febrile (>38ºC) patients, which mainly comprised of CA-BSI (84.4%), followed by HA- (8.9%), and HCA- (6.7%) BSI[49]. Among these patients, 5.6% (n=5/90) were also reported to have septicemia (sepsis patients with BSI)[49]. The spectrum of top causative organisms primarily included *S.* Typhi, followed by *E. coli* and *Salmonella enterica* serotype Paratyphi[49]. Antimicrobial susceptibility results highlighted that ESBL-producers included *E. coli* and *K. pneumoniae*, while multidrug resistance was observed in *E. coli* (n=17/20), *K. pneumoniae,* and *Acinetobacter* spp., and extensive drug resistance was only observed in *E. coli*[49]. Additionally, the variety of fungal pathogens in this cohort was relatively limited (3 species) compared to the bacterial pathogens (13 species)[49]. Interestingly, non-*albicans Candida* spp. (*C. tropicalis* and *C. famata*) were isolated in higher proportion compared to *C. albicans*[49]. Essentially, acute febrile patients in this review shared similar BSI pathogen distribution, despite differences in the predominant pathogen and isolation rates attributable to host and geographical-related factors.

Meanwhile, in Thailand, 3.5% (n=7/200) of hospitalized adults with acute undifferentiated fever were diagnosed with BSI, with the predominance of *T. marneffei*, and lower but equal isolation rates of different bacteria (*H. influenzae*, *S. aureus*, *B. pseudomallei*, *E. coli,* and *E. faecium*)[51]. The mortality rate was 4.5% (nine deaths), of which two were attributable to BSI (patients infected with *T. marneffei* and *H. influenzae*)[51].

In a Singaporean single-center study, 29.5% (n=52/176) of hospitalized adults with Stevens-Johnson syndrome and/or toxic epidermal necrolysis were diagnosed with BSI[50], and predominantly displayed *A. baumannii* and *S. aureus*. Patients with BSI had significantly increased ICU admission (p<0.0005), extended hospital lengths of stay (p<0.0005), and greater mortality rates (p<0.0005), as well as having higher odds of invasive mechanical ventilation and dialysis[50]. Additionally, underlying factors, such as cellulitis in hospitalized Thai adult patients have led to a

BSI prevalence of 1.7% (n=27/1,560), with higher pathogen proportions of *S. dysgalactiae*, *Staphylococcus hominis,* and *E. coli*[53]. The study also developed a Ramathibodi Necrotizing Fasciitis/Bacteria (RAMA-NFB) Prediction score, with a higher predictive power (82.78%) compared to qSOFA (62.70%) in identifying high-risk cellulitis patients who may develop complications of necrotizing fasciitis and bacteremia[53].

Other comorbid diseases, including aplastic anemia, falciparum malaria, and COVID-19, have been reported to predispose individuals to BSI. In a Thai study, *A. baumannii*, *P. aeruginosa*, and *B. cereus* were the main bacterial organisms isolated from blood cultures of 67 aplastic anemia patients, in addition to the isolation of the fungus *Aspergillus* spp.[52]. Moreover, studies in Myanmar[48] and Vietnam[55] observed a 20.0% (n=4/20) and 1.1% (n=9/845) BSI prevalence, respectively, amongst hospitalized subjects with falciparum malaria upon admission. Despite the small number of patients in the Myanmar study[48], the peripheral parasite count was significantly lower in bacteremic patients, compared to non-bacteremic patients. Interestingly, *S.* Typhi was most commonly isolated from CA-bacteremia patients in the Vietnamese study[55], while equal isolation rates of different gram-negative (*E. coli*, *S.* Typhi, *A. baumannii*, and *E. cloacae*) and gram-positive bacteria (*S. aureus*) were noted in the Myanmar study, though the infection origin was not specified[48].

In another Thai study, 19.0% (n=48/252) of hospitalized COVID-19 patients were predisposed to HA-BSI (nosocomial), with a significantly higher mortality rate (62.5%) compared to non-BSI patients[54]. Frequently isolated pathogens included ESBL *K. pneumoniae,* MSSA, and MDR *A. baumannii*, while the fungal isolation rate (*C. tropicalis*) was much lower[54]. The significant predictors of BSI in this study included being male, methylprednisolone use, administration of 6-12 mg/day dexamethasone cumulative dosage, and leukocytosis during admission[54].

DISCUSSION

This review highlights varying prevalence rates of bacterial and fungal BSIs reported among different patient groups: sepsis (12.6%-44.5%), those with indwelling catheters (0.6%-46.9%), and hospitalized patients with other comorbidities (1.1%-29.5%) within the SEA region between 2018 and 2024. The last review about CA-BSI pathogens in South and Southeast Asia was reported over a decade ago[16]. In that analysis, only three studies involving patients suspected of sepsis were conducted in the SEA region (Philippines and Vietnam)[16]. Unfortunately, the etiological agents were not characterized based on patient risk factors[16]. As a result, the actual BSI pathogen profiles among sepsis and indwelling catheter patients in SEA countries alone remain unknown, highlighting a significant knowledge gap in understanding regional pathogen distributions.

The BSI prevalence of sepsis patients in this review was broader compared to previous sepsis studies[10,15]. Li et al[15] focused on sepsis pathogens from ICU patients in Asia, including SEA, highlighting that 2.1% (n=106/4,980 patients) of these patients presented with primary bacteremia[15]. Sepsis pathogens were recovered from various infection sites, including the respiratory tract, abdomen, urinary tract, skin or soft tissue, neurological system, bloodstream (primary bacteremia), bones and joints, as well as from catheter-related infections, systemic infections, and infective endocarditis[15]. In that study, gram-negative bacteria were identified in 51.8% of patients, with *K. pneumoniae, A. baumannii*, and *E. coli* being the most common[15]. Gram-positive bacteria were accounted in 20.2% of patients, predominantly *Enterococcus* species and *S. aureus*[15]. Fungal infections were observed in 13.3% of cases, mainly involving *Candida* species[15]. Unfortunately, the source of infection was not specified for these sepsis pathogens. Meanwhile, Timsit et al[10] documented a BSI range of 29.8% to 39.8% in adult patients with sepsis or septic shock from randomized trials between 2008 to 2017 across Australia, Finland, France, Hong Kong, New Zealand, North America, and the Republic of Ireland, however the pathogen species was not discussed. Essentially, identifying the causative BSI pathogen is crucial for improving clinical management and reducing sepsis morbidity and mortality[57].

Interestingly, the CRBSI prevalence in this review was also slightly higher compared to recent single center studies conducted in China, Ghana, India, and Spain (between 1994 and 2022), with prevalence rates ranging from 1.02% to 39.25%[58-61]. However, global CRBSI prevalence rates were not available for comparison. Instead, catheter-related infections accounted for the majority (21%) of BSIs in a prospective, multicenter investigation (EUROBACT-1) involving 1,156 patients from 162 ICUs across 24 countries (not including SEA countries) between 2009 and 2011[22].

Evidently, the bacterial pathogen trends of sepsis and catheter-related BSI patients in this review were typical[10,20,62], aside from *B. pseudomallei.* The overall bloodstream pathogen profile in this review was consistent with a report from the SENTRY antimicrobial surveillance program, whereby *S. aureus* and *E. coli* were the predominant causes of BSI worldwide in a 20-year surveillance study from over

200 medical centers in 45 nations (1997 to 2016)[9]. Moreover, detecting *B. pseudomallei* BSI is crucial due to its association with melioidosis, a disease with high mortality rates, especially in SEA, South Asia, China, northern Australia, and Taiwan[63-66]. The increased susceptibility to melioidosis in patients with diabetes, excessive alcohol consumption, and chronic kidney disease is likely attributed to impaired innate immune response, particularly dysfunction of neutrophils and other phagocytic cells, which affect their ability to mobilize, migrate, attach, ingest, and eliminate pathogens[66-68]. To contrast, Deen et al[16] reported *S.* Typhi as the predominant bacterial pathogen (30%) in CA-BSIs from South Asia and SEA, while it was only documented in three studies in this review[48,49,55]. Together with fungal infection, the altered epidemiology of invasive salmonellosis in SEA has been attributed to the rising socioeconomic development and the growing HIV/AIDS prevalence[69].

The fungal BSI pathogen trend in this review was similar to global isolation rates, whereby *Candida* spp. were also highlighted as the main BSI fungal pathogens (n=216/222 isolates) across 16 medical centers (USA, France, Germany, Ireland, Italy, Mexico, and South Korea) in the SENTRY Antimicrobial Surveillance Program between 2012-2017, accounting for 3.1% of bacterial and fungal BSIs[70]. The higher prevalence of non-*albicans Candida* spp. compared to *C. albicans,* as noted in the reviewed SEA studies, is a matter of concern given the emergence of antifungal resistance[71], especially in light of recent reports of *Candida auris* in SEA[72]. The disparities in *Candida* species isolation between each study in this review could also be due to differences in demographic characteristics, geographical settings, socioeconomic status, acquisition site (HA or CA), and source of infection[9,70].

Another unique BSI fungal pathogen in the SEA region is *T. marneffei*[36,51], which is endemic and commonly associated with the tropical Asian climate[73]. Researchers from talaromycosis endemic regions have called for its recognition as a neglected tropical disease on a global scale[73]. Talaromycosis poses a significant mortality risk, especially for HIV-infected individuals, with prevalence rates ranging from 0.13% to 26.76%, and fatality rates reaching up to 40% in endemic regions such as China, Vietnam, Thailand, and India[74].

The WHO AWaRe (Access, Watch, Reserve) classification plays a pivotal role in global AMR monitoring and in promoting the responsible use of antibiotics. It prioritizes the management of common sepsis-causing pathogens, including *E. coli*, *S. aureus* (including MRSA), *K. pneumoniae*, non-typhoidal *Salmonella*, *S.* Typhi, *S.* Paratyphi, *Streptococcus pyogenes*, *S. pneumoniae*, *A. baumannii*, *P. aeruginosa*, *Neisseria meningitidis*, *B. pseudomallei* (in South-East Asia and Australia), *Listeria monocytogenes* (maternal sepsis), *S. agalactiae* (maternal sepsis), and ESBL and carbapenemase multidrug-resistant organisms[75]. Inclusion of *T. marneffei* and other pathogens with significant regional impact in the AWaRe classification would support more effective diagnosis, treatment, and surveillance of the diseases in SEA countries.

Blood culture contamination was only mentioned in nine articles in this review, with varying definitions of true BSI[33,35,36,46-49,51,55]. Contaminants in these articles were excluded from the analysis of BSI prevalence rates. However, only seven studies specified the genus or species of organisms that were classified as contaminants[36,46-49,51,55]. Some studies considered *Bacillus* spp.[36,46,47,49], *S. epidermidis*[48,55], CoNS[36,46,47,49,51], *B. cepacia*[55], *Micrococcus* spp.[36,49], *Corynebacterium* spp.[36,49], alpha-hemolytic streptococci[36], diptheroids[36], *Propionibacterium* spp.[36], *Achromobacter* spp.[49], *Brevibacterium* spp.[49], *Dermacoccus* spp.[49], and *Kocuria* spp.[49], as skin commensals and/or culture contaminants, which were excluded from true bacteremia rates. However, in one study, CoNS was considered to be a pathogen if it was isolated from more than one blood culture within 48-hour hospital admission[50], while other studies (n=6) included CoNS as a pathogen without specification[34,40,41,44-46].

The overall BSI prevalence in SEA countries may be underestimated, as many studies were excluded in this review due to missing patient demographic data (e.g., number of patients, age range, BSI prevalence), limited focus on a single organism as opposed to a broader range of pathogens, or incomplete pathogen identification (genus and species). Moreover, pathogen acquisition sites, such as CA-, HA-, and/or HCA-BSI, and AMR data can assist in understanding the epidemiology, pathogenesis, and management of BSIs[10], however, only less than half of the studies in this review provided this information, highlighting gaps in data collection. BSI prevalence rates in SEA countries may also be impacted by unreported cases, lack of clinical suspicion, or the inability to culture and identify fastidious and slow growing pathogens (e.g., *Rickettsia*, *Leptospira*, *Mycobacterium* spp.) due to limited access to advanced diagnostic tests, such as polymerase chain reaction, enzyme-linked immunosorbent assay, indirect immunofluorescence assay, and next generation sequencing, in resource-constrained settings.

Additionally, the restriction of the search strategy to articles published between 2018 and 2024 may have led to the exclusion of relevant studies from some SEA countries (Brunei, Indonesia, Laos, and Timor-Leste) that did not publish blood culture data within this timeframe. The included

studies, however, comprised data collected between 1991 and 2022, highlighting a discrepancy between the publication date criteria and the actual study periods. This limitation may impact the overall representativeness of the review findings, as BSI trends and pathogen distributions tend to remain stable over extended periods, while antimicrobial susceptibility patterns may evolve. The challenges of this review also include the difficulty in finding BSI studies in SEA with homogeneous populations or standardized clinical and laboratory diagnostic techniques, notably blood culture systems. The differences in the inclusion and exclusion criteria of the subjects in each study (i.e., age, gender, comorbidities) further add heterogeneity and inconsistencies, which may affect the outcomes and interpretation of research findings.

CONCLUSIONS

Research on BSI epidemiology is crucial to guide clinical diagnosis, antimicrobial treatment, and patient management. Most BSI studies included in this review focused on patients with indwelling catheters, followed by those with sepsis and other underlying medical conditions. While *E. coli* and *S. aureus* were the most common BSI pathogens, other regionally significant bacterial and fungal pathogens were also identified from blood cultures of sepsis patients, underscoring the importance of ongoing surveillance and improvements in diagnostic and therapeutic approaches. These variations likely stem from the complex interplay of demographic, host, and pathogen-related factors. Given the dynamic and evolving nature of microbial populations, continuous and vigilant monitoring of blood cultures and antibiotic resistance patterns is pivotal to prevent potential disease outbreaks in the SEA region and to optimize antimicrobial stewardship programs tailored to regional needs.

Conflict of Interest
The authors declare that they have no conflict of interest to disclose.

Funding
This work was supported by the Ministry of Science, Technology and Innovation (MOSTI), Government of Malaysia under the Technology Development Fund 1 (Ted 1) grant (TDF07211415: MOSTI002A-2022TED1 and MOSTI002B-2022TED1). The funders had no role in the conceptualization, design, data collection, analysis, decision to publish, or preparation of the manuscript.

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Availability of Data and Materials
All data generated or analyzed during this study are included in this published article and its supplementary information files.

Informed Consent
Informed consent was not required for this review as there was no original data collection involving human participants.

Ethics Approval
Ethics approval was not required as this review article summarized and analyzed existing published literature.

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Acknowledgements
We would like to thank Universiti Malaya and the Ministry of Science, Technology and Innovation (MOSTI), Malaysia, for their support in this publication.

AI Disclosure
Artificial intelligence from the website https://www.napkin.ai/ was used to partially generate the graphical abstract in this review.

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