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REVIEW

Bacteremia in the Gulf Cooperation Council Region: A Review of the Literature 2013–2023

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Abstract: Bloodstream infections (BSIs) are amongst the leading healthcare-associated infections (HCAIs), and their comprehensive evaluation and management are of global and regional importance. This narrative review examines and reports data on BSIs from the Gulf Cooperation Council (GCC) region covering the period between 2013 and 2023. The reviewed literature demonstrated that BSIs were frequently associated with critical care settings such as the Intensive Care Unit (ICU) and were often associated with invasive lines and devices [such as central-line associated BSI (CLABSI)]. Fever was the main presenting symptom, while diabetes mellitus and hypertension were the common associated comorbidities. High mortality rates were reported for BSIs, particularly when caused by multidrug-resistant (MDR) Gram-negative pathogens. There was a wide range of antimicrobial resistance rates reported across the region; however, carbapenem-resistance rates exceeding 30% were reported for *Pseudomonas aeruginosa, Acinetobacter baumannii* and *Klebsiella pneumoniae*. Few publications included molecular mechanisms of carbapenem resistance; however, when mechanisms were reported they were dominated by OXA-48. In conclusion, the lack of structured surveillance programs and networks to monitor microbiological phenotypic and genotypic patterns as well as clinical outcomes across the region means there is paucity of uniform data on BSIs across the GCC region. To bridge this gap, we recommend timely surveillance programs for the monitoring of resistance and outcomes.

Keywords: bacteremia, bloodstream infection, Gulf, review, antimicrobial

Introduction

Bacteremia is defined as the presence of viable bacteria in the bloodstream acquired from a variety of sites, such as the urinary tract, respiratory system, or through the breach of gastrointestinal mucosa or skin and soft tissue barriers.[1] The resulting bacteremia might be transient and asymptomatic, where the body clears the bacterial burden without interventions with no subsequent harm, or may lead to an established bloodstream infection (BSI).[1] BSI is facilitated through specific bacterial virulence factors that allow the transmission of pathogens to the bloodstream, evading multiple defense barriers and subsequent survival to manifest as clinical disease.[2] Globally, BSIs are considered a significant healthcare burden with an estimation of 575,000–677,000 episodes annually in North America and greater than 1,200,000 in Europe, as well as being ranked amongst the top seven causes of mortality in North America and Europe.[3] The clinical presentation of BSIs is variable since it can present as either primary bacteremia with direct invasion into the bloodstream, or secondary, where the infection is related to other primary infection sites such as urinary or respiratory tracts.[1,4,5] One of the important features of BSIs is the ability of the bacteria to infect distant organs through hematogenous spread, seeding to remote sites such as

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cardiac valves, bone tissues and brain parenchyma, causing infections such as infective endocarditis, osteomyelitis and brain abscesses.[6,7] Central lines are also associated with BSI and for the correct evaluation of central-line associated infections (CLABSIs), the Centers for Disease Control and Prevention (CDC) guidance advocates establishing appropriate eligibility criteria: presence of a central line for more than two consecutive days and the isolation of pathogens consistent with CLABSI.[4]

The hallmark for the initial diagnosis of a BSI is a positive blood culture, used to confirm the presence of bacteremia; therefore, the evaluation can be confounded by the spurious contamination by skin commensals such as coagulase-negative staphylococci and *Corynebacterium* spp.[4,8] Such possible contamination should be carefully evaluated before the initiation of appropriate management. Major causes of Gram-positive bacteremia are *Staphylococcus aureus*, coagulase-negative staphylococci as well as *Streptococcus* and *Enterococcus* species.[9] Bacteremia caused by Gram-negative bacteria are dominated by *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Acinetobacter baumannii*. In contrast to Gram-positive bacteremia, the appropriate management of Gram-negative bacteremia can be difficult due to the escalating challenges of antimicrobial resistance (AMR).[10] Multidrug-resistant (MDR) pathogens are a prominent challenge especially in healthcare-associated infections (HCAIs) and amongst patients with multiple comorbidities and in critical care settings.[5,11] In general, BSIs are associated with significant morbidity and mortality,[12] which is amplified in the presence of MDR particularly if associated with HCAIs.

Risk factors associated with a BSI include comorbidities such as diabetes mellitus and an immunocompromised state such as patients with organ transplants, recipients of chemotherapy or people living with HIV.[13–16] In addition, patients with organ dysfunction such as heart failure, chronic respiratory and end stage renal disease (particularly those on assisted supportive devices or receiving dialysis) are at increased risk.[15,16] Old age and being resident in a long-term facility are independent risks for developing a BSI with directly increased mortality.[15,16] Although BSIs can be insidious, typical symptoms include fever, chills and rigors accompanied by raised inflammatory markers and are associated with tachypnoea and hypotension.

As the effective treatment of bacterial BSI is of global and regional importance, focus has been directed towards improving surveillance and monitoring. In the Gulf Cooperation Council (GCC) region, expert working groups have been deliberating to consolidate appropriate therapeutic recommendations and specific guidance considering regional challenges such as variability of local infrastructure and resistance patterns, the availability of novel antimicrobials, and expertise.[17] This narrative study will review data on non-transient bacteremia (BSI) from the GCC region published between 2013 and 2023. The alphabetically arranged region includes Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates.

Methods

Search Strategy

A literature search was conducted for English-language articles published between May 2013 and May 2023 using medical search engines PubMed (Medline®), PubMed Central and Embase®. Search protocol terms included "bacteraemia", "bacteremia", "septicaemia", "septicemia", "bloodstream infection", "blood-stream infection" in combination with "Bahrain", "Kuwait", "Oman", "Qatar", "Saudi Arabia", "KSA", "United Arab Emirates", "UAE", "Gulf Cooperation Council" and "GCC". No patient age restrictions were applied to the searches. Article types included in the searches were full articles, reviews, randomized clinical trials, brief communication, regional and national reports as well as case series. Letters, editorials, notes and conference abstracts were excluded.

Literature from the search results was collated into an Excel database, which catalogued, by country, publication title, authors, journal title and volume, publication year and abstract. The publication titles and abstracts in the database were then screened to identify suitable literature for inclusion. From the identified publications, the full text was collected and reviewed to assess eligibility for inclusion in the review, and a final list of publications was drawn up. Articles were excluded if they reported on sepsis (defined as organ dysfunction caused by a dysregulated host response to infection)[18] without reporting BSIs, or were from neighboring regions or countries without specifically focusing on the GCC countries. Articles were similarly excluded if they were a case series reporting less than 10 cases.

Outcomes

Outcomes of interest included the prevalence, diagnosis and epidemiology of BSI in the region, risk factors associated with BSIs, clinical outcomes and mortality, causal pathogens, antimicrobial susceptibility and treatment. Antimicrobial susceptibility data were only included if data were presented on at least 10 isolates.

A summary of the literature captured for this review, by country and outcome, is presented in Supplemental Table 1.

Prevalence of BSI in the GCC Region

Literature from the region shows that BSIs are prominent HCAIs particularly in intensive care settings such as ICUs[19–21] and are often device-associated.[19–23] In Kuwait, between 2018 and 2019 the most frequently occurring HCAI reported in the ICU were BSI (42.3%), followed by pneumonia (28.8%), UTI (15.3%) and skin and soft tissue infections (SSTI) (9.6%).[19] Abulhasan et al[24] reported a rate of HCAI of 11.9/100 patients (22.1/1000 ICU days) among neurocritical care patients in a study from a tertiary care hospital in Kuwait between 2015 and 2017. Among these HCAIs, the most common infection type was UTI (36.7% [40/109]), followed by BSI (27.5% [30/109]) and pneumonia (14.7% [16/109]); of the 30 patients with BSI in the study, 66.7% (20/30) were CLABSIs. Similarly, in a point prevalence survey in Saudi Arabia (from September to December 2016), among 184 HCAIs, surgical site infections were the most common (32.6%), followed by BSI (19.5%).[25] In a second point prevalence study, from 2017, the most common infection types among 114 HCAIs were identified as pneumonia (27.2%), UTIs (20.2%) and BSI (10.5%);[21] the same study also identified that 19.2% of HCAI were device-associated. Gupta et al[23] reported the most frequent HCAIs in critical care as device-associated. Furthermore, Saleem et al[26] have reported that, among culture positive HCAI, CLABSIs were the third most common infection in the ICU, after ventilator-associated pneumonia and catheter-associated urinary tract infections.

Two studies focused on infections caused by *A. baumannii*. Saleem et al[27] found CLABSI was the third most common *A. baumannii* infection in 2019 (11.4%, 4/35) but accounted for 4.3% (2/47) of *A. baumannii* infections in 2020. In the second study, of 321 patients, the most common infection types were respiratory (58.6%) and SSTI (29.3%), followed by BSI (8.6%) and UTI (2.1%).[28] In the case of carbapenem-resistant Enterobacterales infections, BSI was more prevalent with 40.7% (77/189) reported as BSI, followed by pneumonia (23.8%, 45/189) and complicated UTI (23.8%, 45/189).[29] Conversely, in a retrospective matched case-controlled study among children (≤17 years old) with carbapenem-resistant Enterobacterales infections in Saudi Arabia in 2016–2017, only 10.5% (2/19) of patients had BSI; the majority of infections were related to bodily fluids (eg, pleural, pericardial, cerebrospinal, etc) and wound discharge (9/19, 47.4%) or urinary tract (8/19, 42.1%).[30] Among patients in a children's hospital with infections due to *Stenotrophomonas maltophilia,* the main infection types were pneumonia (45.8%, 22/48) and BSI (29.2%, 14/48).[31]

Two studies from Saudi Arabia reported SSTI as the most common infection associated with Gram-positive organisms. In a study of MRSA, the majority of infections were SSTIs, followed by BSIs and lower respiratory tract infections,[32] and among patients with infections caused by *Streptococcus anginosus* group organisms, the most common infection types were SSTIs (55.2%, 58/105) followed by IAIs (23.8%, 25/105) and BSIs (14.3%, 15/105).[33] In their retrospective cohort study of adult patients with BSIs caused by enterococci between 2009 and 2018 from Qatar, Ali et al[20] determined that the most common sources of BSIs were central-line infections (18.3% 48/263); however, in 119 cases (45.2%) there was no identified source of infection.

A number of studies looked at immunocompromised patients. Among adult febrile neutropenic cancer patients in Saudi Arabia, the most common infection was BSI (33.3%, 46/138) followed by UTIs (29.7%, 41/138) and wounds (19.6%, 27/138).[34] Al-Mulla et al[35] reported on the rates of bacteremia among pediatric oncology patients between 2004 and 2011 in Qatar and found that the rates among patients with acute lymphoblastic and acute myelocytic leukemia (33/66, 50.0% and 5/9, 55.6%, respectively) were significantly higher than among patients with lymphoma, solid and brain tumors (12/39, 30.8%; 14/56, 25.0%; 6/15, 40.0%, respectively) ($P = 0.038$).

Similarly, among febrile patients from Saudi Arabia aged <12 years with sickle cell disease who had up-to-date vaccination and were in receipt of penicillin prophylaxis, the overall rate of serious bacterial infection was reported as 3.6% (30/833) with 11 (1.3%) cases of bacteremia.[36]

Central Line–Associated Bloodstream Infections (CLABSI)

Rates of CLABSIs reported in the region are shown in Table 1. In their study of CLABSIs across Saudi Arabia, Bahrain and Oman, Balkhy et al[37] reported a rate of 3.1 per 1000 central-line days (95% CI, 2.8–3.3) across age groups and ward types (Table 1).

Use of Care Bundles

A number of studies in the region have reported on efforts made to reduce CLABSIs through the use of care bundles.[60] A care bundle is a set of evidence-based interventions performed collectively to improve patient outcomes and, in the case of CLABSIs, includes hand hygiene, skin antisepsis, barrier precautions (eg, sterile gloves and gowns) and timely removal of the central line.[48] A number of studies across the region have reported a successful reduction in rates of CLABSIs through the use of care bundles (Table 1),[39,41–45,47–49,54,56,57] with Khalid et al[56] reporting a 15-month period with no CLABSIs following the introduction of care bundles. Alrebish et al[59] attributed their low rate of CLABSI (2.6/1000 central-line days) to the 100% compliance with the CLABSI bundle, and Yaseen et al[42] reported a change from 2.0/1000 central-line days with 37% bundle compliance in 2008 to 0.0/1000 central-line days with 98.0–100% bundle compliance in 2014–2015. In a study in ICUs across the United Arab Emirates (UAE), the introduction of a number of interventions resulted in a reduction in CLABSIs from 2.56/1000 catheter-days to 1.79/1000 (Table 1).[39] Interventions in the study by Latif et al[39] included a focus on collaboration, training, a checklist of evidence-based practices, safety program and performance feedback as described in the Keystone ICU Project.[61] Hand hygiene interventions have also been shown to be effective in reducing the incidence of CLABSI (Table 1).[38,58]

The importance of infection control procedures was shown in a study of an outbreak of bacteremia in Saudi Arabia caused by *Burkholderia cepacia*-contaminated ultrasound probe gel.[62] Also, rates of CLABSI were reported to have increased in Saudi Arabia during the COVID-19 pandemic (from 2.16/1000 central-line days in 2019 [pre-pandemic] to 2.50/1000 central-line days in 2020–2021 [during the pandemic], P = 0.01), which the authors suggested was due to the impact of the pandemic on infection control practices and surveillance.[52]

Pediatric Patients

Al-Tawfiq et al[50] reported a higher rate of CLABSI in pediatric and neonatal ICUs than seen in adult ICUs (3.38/1000 central-line days, 2.28/1000 central-line days and 1.21–2.13/1000 central-line days, respectively, Table 1). A retrospective, observational study from Qatar (January 2019 – June 2020) looked at the impact of introducing closed intravenous administration sets in the neonatal ICU on the incidence of CLABSIs.[55] The study reported the rate of CLABSIs dropped from 2.87/1000 central-line days pre-intervention to a post-intervention rate of 0.22/1000 central-line days and concluded that compliance with infection control bundles and the use of pre-assembled closed intravenous administration sets may have a positive impact on CLABSI rates. Among children receiving parenteral nutrition, Al Lawati et al[53] reported a CLABSI rate of 14/1000 central-line days (Table 1) and a mortality rate of 25% among patients with a CLABSI. They concluded that the introduction of care bundles, which were not widely utilized at their hospital, would be a useful tool to reduce the rates of CLABSIs.

As part of efforts to reduce CLABSI, Bayoumi et al[63] carried out a retrospective observational study to look at the impact of antimicrobial-impregnated peripherally inserted central catheters (PICCs) versus conventional PICCs in a neonatal ICU in Qatar between 2017 and 2020. When comparing the two PICCs, they found no difference in the rates of CLABSI; however, they did observe a higher rate of elective removal after completion of therapy when the antimicrobial-impregnated PICC was used.

Central Line Location

There is debate on whether the access location of a central venous catheter (CVC) impacts the chance of developing a BSI. Alhazmi et al[64] reported on adult hemodialysis patients in Saudi Arabia, among whom 90 had arteriovenous fistulas for vascular access and 69 had a CVC. In the arteriovenous fistula group, three (3/90, 3.3%) patients developed a BSI and in the CVC group 18 (18/69, 26.1%) patients developed a BSI, and the authors concluded that the type of vascular access was a risk factor for developing BSIs in hemodialysis patients.[64] In an analysis comparing femoral lines with internal jugular in pediatric patients, Al-

Table 1 Rates of Central-Line Associated Bloodstream Infections (CLABSI) Reported in the GCC Region, by Age Group

Reference	Study type and Date/Period	Country	Age Group	Ward	Intervention	Most Common Bacterial Species	Rate of CLABSI
All ages combined							
Balkhy et al[37]	Retrospective 2008–2013	Saudi Arabia, Bahrain and Oman	All	Critical care, oncology, adult step down	N/A	N/A	3.1/1000 CL days
Al-Tawfiq et al[38]	Interventional Oct 2006 – Dec 2011	Saudi Arabia	All	Across hospital	Hand hygiene	N/A	Baseline: 8.23/1000 CL days Post intervention: 4.8/1000 CL days
Latif et al[39]	Prospective 2011–2014	UAE	All	ICU	Infection prevention education, safety teams, infection rate reporting	N/A	Baseline: 2.56/1000 CL days Post intervention: 1.79/1000 CL days
Al-Mousa et al[40]	Prospective, cohort Nov 2013– March 2015	Kuwait	Adult, Pediatric	ICU	N/A	N/A	3.5/1000 CL days
Al-Abdely et al[41]	Prospective Oct 2013 – Sept 2015	Saudi Arabia	Adult, Pediatric	ICU	SHEA/IDSA/IHI/CDC/JCI recommendations. Care bundle	*Acinetobacter* spp. and *K. pneumoniae* at baseline and post intervention. *P. aeruginosa* increased after intervention	Baseline: 6.9/1000 CL days Post intervention: 3.1/1000 CL days
Adults							
Yaseen et al[42]	Prospective 2008–2015	Saudi Arabia	Adults	ICU	Care bundle	N/A	2008: 2.0/1000 CL days 2010: 0.7/1000 CL days 2015: 0.0/1000 CL days
Salama et al[43]	Prospective, cohort Jan 2010 – Feb 2012	Kuwait	Adult	ICU	Care bundle	*K. pneumoniae, A. baumannii*, and *P. aeruginosa* at baseline and after intervention	Baseline: 14.9/1000 CL days Post intervention: 11.08/ 1000 CL days
Bukhari et al[44]	Prospective, cohort 2012	Saudi Arabia	Adult	ICU	Care bundle	MRSA, *A. baumannii* and *E. faecalis*	Baseline: 10.1/1000 CL days Post intervention: 6.5/1000 CL days
Al-Khawaja et al[45]	Prospective, Jan 2013 – Dec 2016	Bahrain	Adult	ICU	Care bundle, education, surveillance, feedback	N/A	Baseline: 10.4/1000 CL days Post intervention: 1.2/1000 CL days
Gaid et al[46]	Retrospective, cohort 2013–2016	Saudi Arabia	Adult	ICU	N/A	N/A	0–22.8/1000 CL days

(*Continued*)

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Table 1 (Continued).

Reference	Study type and Date/Period	Country	Age Group	Ward	Intervention	Most Common Bacterial Species	Rate of CLABSI
Al-Khawaja et al[47]	Prospective Jan 2015 – Dec 2018	Bahrain	Adult	ICU	Care bundle, education, surveillance, feedback	*Acinetobacter, E. coli, Pseudomonas, Enterococcus*, coag-neg *Staphylococcus*	2015: 4.7/1000 CL days 2018: 1.4/1000 CL days
Abulhasan et al[24]	Retrospective, cohort 2015–2017	Kuwait	97.0% ≥18 y	Neurological ICU	N/A	*Klebsiella* spp.	2015 5.8/1000 CL days 2016 5.7/1000 CL days 2017 6.8/1000 CL days
Gupta et al[48]	Prospective 2015–2018	Qatar	Adults	Coronary ICU	Care bundle, training and education	N/A	2015: 2.82/1000 CL days 2016: 3.11/1000 CL days After intervention: 0.4/1000 CL days
Mazi et al[49]	Prospective 2016–2019	Saudi Arabia	13–83 y (Mean 51)	ICU	SHEA/IDSA recommendations. Care bundle	Included MDR *K. pneumoniae*	Baseline: 1.12/1000 CL days Post intervention: 0.46/1000 CL days
Al-Tawfiq et al[50]	Retrospective 2017–2020	Saudi Arabia	Adults	Cardiac care unit	N/A	N/A	1.21/1000 CL days
Al-Tawfiq et al[50]	Retrospective 2017–2020	Saudi Arabia	Adults	Surgical ICU	NA	N/A	1.26/1000 CL days
Al-Tawfiq et al[50]	Retrospective 2017–2020	Saudi Arabia	Adults	Medical ICU	NA	N/A	2.13/1000 CL days
Alfouzan et al[19]	Retrospective, surveillance 2018–2019	Kuwait	Adult	ICU	N/A	*A. baumannii, K. pneumoniae*	6.27/1000 CL days
Al-Shukri et al[51]	Retrospective, case control 2018–2019	Oman	Adult	ICU	N/A	*S. epidermidis, S. aureus, E coli*	8.6/1000 CL days
Alsaffar et al[52]	Retrospective 2019–2021	Saudi Arabia	Adult	ICU	N/A	N/A	2019 (pre-pandemic): 2.16/1000 CL days 2020–2021 (during pandemic): 2.50/1000 CL days
Pediatric patients							
Al Lawati et al[53]	Retrospective, cohort 2011–2014	Oman	Pediatric	Receiving parenteral nutrition outside ICU	N/A	*S. epidermidis*	14/1000 CL days
Al-Mousa et al[40]	Prospective Nov 2013–March 2015	Kuwait	Pediatric	ICU	N/A	N/A	1.0/1000 CL days

Hamza et al[54]	Pre-, Post-intervention 1 Jan 2015–31 Mar 2017	Kuwait	1–60 months	ICU	Care bundle, education and training	*E. cloacae, K. pneumoniae, P. aeruginosa*	Baseline: 7.5/1000 CL days After intervention: 3.0/1000 CL days
Al-Tawfiq et al[50]	Retrospective 2017–2020	Saudi Arabia	Pediatric	ICU	N/A	N/A	3.38/1000 CL days
Van Rens et al[55]	Retrospective, observational Jan 2019 – Jun 2020	Qatar	23 – ≥ 37 weeks	ICU	Closed intravenous system	N/A	Baseline: 2.87/1000 CL days Post intervention: 0.22/1000 CL days
Neonatal							
Al-Mousa et al[40]	Prospective, cohort Nov 2013–March 2015	Kuwait	Neonatal	ICU	N/A	N/A	3.9/1000 CL days
Al-Tawfiq et al[50]	Retrospective 2017–2020	Saudi Arabia	Neonates	ICU	N/A	N/A	2.28/1000 CL days
Not specified							
Khalid et al[56]	Prospective Feb 2009 – Jul 2012	Saudi Arabia	Not defined	ICU	Care bundle, education	Gram-negatives	Baseline: 6.9/1000 CL days Post intervention (1 y): 1.06/1000 CL days Post intervention (2 y): 0.35/1000 CL days
Mazi et al[57]	Prospective 2011–2012	Saudi Arabia	Not given	ICU	Care bundle, education, CLABSI prevention team	*K. pneumoniae, E. faecalis, A. baumannii*	Baseline: 3.87/1000 CL days Post intervention: 1.5/1000 CL days
Al-Tawfiq et al[58]	Prospective May 2014–Sept 2015	Saudi Arabia	Not given	Oncology, hematology	Hand hygiene	N/A	May-Aug 2014: 5.9/1000 CL days Sept 2014—Sept 2015: 2.9/1000 CL days
Alrebish et al[59]	Retrospective 2021	Saudi Arabia	Not given	All	N/A	N/A	2.6/1000 CL days

Abbreviations: N/A, not relevant to, or not presented in, the study; CL, central-line; y, years.

Sofyani et al[65] found that femoral lines were 4.67 times more likely to be associated with a CLABSI, although the difference was not statistically significant. Al-Khawaja et al[47] reported that the most common site among adult patients who developed a CLABSI was the femoral vein, followed by the jugular vein.

Secondary BSIs

Although central lines are a common source of BSI, other infection sites can also lead to a BSI, including genitourinary, SSTI, gastrointestinal tract, bone and joint, reproductive tract and the central nervous system.[20] While endovascular infections were the most common source of infection among adults with MRSA bacteremia in a tertiary care center in Saudi Arabia (30.4% of cases), 19.6% of patients had pneumonia and 19.0% had SSTIs.[66] Arabi et al[67] reported that among renal transplant patients who developed a first UTI within the first 6 months after transplant, the UTIs were complicated with bacteremia in 6.2% (6/97) of cases. In a study assessing the impact of the timing of ureteric stent removal in renal transplant recipients on UTI rates, UTI recurrence and hospitalization, the occurrence of UTIs while stents were still in place was associated with bacteremia and hospitalization.[68]

Diagnosis of BSIs

Signs and Symptoms

Fever is the symptom most commonly reported for patients with BSIs although a great deal of the reported evidence in the region is for BSI caused by Gram-positive bacteria.[69–71] In a retrospective study of pediatric and adult patients with Group A streptococcal bacteremia in Saudi Arabia between 2007 and 2015, common symptoms of bacteremia among the 33 patients included fever (69.7%), cough (48.5%), vomiting (33.3%) and tachycardia (30.3%).[69] El-Kady et al[70] assessed symptoms of BSIs according to the causative organism among hemodialysis patients, concluding that fever was more common with *S. aureus* (20.9%) but rigors were more common with coagulase-negative staphylococci (19.4%). They also found that, for BSIs caused by Gram-negative bacilli, the percentage of patients who presented with fever, rigors, vomiting or hypotension was similar (6.5%, 7.2%, 8.6%, and 7.9%, respectively).[70]

For bacteremia due to the Gram-negative *S. maltophilia* among pediatric patients in Saudi Arabia, the most common signs and symptoms were fever (67.6% of patients) and respiratory symptoms (38.2%).[72] Of note, the study included polymicrobial infections with the other organisms identified as *Enterobacter* spp., *Acinetobacter* spp., *Pseudomonas* spp., *Klebsiella* spp., *Enterococcus* spp., coagulase-negative staphylococci and streptococci.

Microbiology Laboratory methods

Accurate microbiological identification is essential as sample contamination can complicate the diagnosis of bacteremia. Skin commensals, in particular coagulase-negative staphylococci, can be identified in blood culture samples but occur because of the contamination during sample collection, not because they are true pathogens.[8] The US National Healthcare Safety Network has defined false-positive blood infections as the culture of commensal skin bacteria such as coagulase-negative staphylococci, *Aerococcus* spp, *Micrococcus* spp., *Propionibacterium* spp., some species of *Bacillus* spp. (excluding *Bacillus anthracis), Corynebacterium* spp. or viridans group streptococci from a single blood culture (only one bottle in a series).[4] Studies in the GCC region have described steps taken to identify true BSIs. Al-Otaibi et al[73] defined bacteremia as isolates of the same bacterial species from at least one set of blood cultures (ie, from two bottles taken at the same time). Nasef et al[74] described a contaminant as a single positive coagulase-negative staphylococci culture from two simultaneous blood samples. The same study also concluded that the use of multiplex PCR-based blood culture identification reduced the amount of time to organism identification and time to appropriate antimicrobial therapy; however, there was no significant change in mortality rate, recurrence of bacteremia, length of stay, ICU admission or cost when compared with conventional culture methods.[74]

The Clinical and Laboratory Standards Institute (CLSI) guidance states that healthcare facilities should aim for ≤1% blood culture contamination rate.[75]

Risk Factors for Acquiring a BSI

Adults

Significant risk factors for the development of a CLABSI in the adult ICU include heart failure, infection (eg, respiratory or urinary tract), pressure ulcers and tracheostomy.[51] In a retrospective study of adult patients (defined in the study as >14 years) in a single tertiary center in Saudi Arabia, the predictors of bacteremia were determined as length of hospitalization (OR, 1.30; 95% CI, 1.14–1.48), presence of a central line (OR, 1.37; 95% CI 1.21–1.55) and a lactic acid concentration of ≥2 mmol/L (OR, 1.31; 95% CI 1.13–1.52).[76] Risk factors for acquiring an MDR *Pseudomonas aeruginosa* infection include the presence of an invasive device, healthcare contact, antimicrobial exposure within 90 days of developing the infection and previous isolation of *P. aeruginosa*.[77] In the case of MDR *A. baumannii* BSIs, risk factors among patients in the ICU were the presence of an intravascular device or a higher Sequential Organ Failure Assessment (SOFA) score.[78] Al-Dorzi et al[79] reported that most patients in their ICU study of BSIs due to *Acinetobacter* spp. had a CVC (98.3%) and received mechanical ventilation (59.3%). Among cancer patients with bacteremia caused by Gram-negative bacteria in Saudi Arabia, Al-Otaibi et al[73] reported that 54% were hematological and 46% were solid tumors, and the risk factors for developing bacteremia included admission to the ICU and the presence of a central line. Most patients in the study were >18 years (49/56).

Regarding Gram-positive organisms, factors that were independently associated with bacteremia due to coagulase-negative staphylococci in Saudi Arabia included the presence of a CVC ($P \leq 0.0001$), prior antibiotic therapy ($P \leq 0.0001$), more than one positive blood culture ($P \leq 0.0001$) and admission to the ICU ($P = 0.007$).[8]

Age has also been shown to be a factor, with Bandy et al[80] reporting that the majority of BSIs in their study were in patients ≥60 years of age (132/222, 59.5%), with 47/222 (21.2%) coming from patients 41–59 years, 29/222 (13.1%) from patients 21–40 years of age and 14/222 (6.3%) from patients ≤20 years.

Neonates and Pediatric Patients

Using a multivariate logistic regression analysis, Bayoumi et al[63] found that gestational age at birth, insertion technique and number of insertion attempts were associated with more CLABSIs among neonates.

Comorbid Conditions

Diabetes mellitus has been reported as a common underlying condition for both Gram-positive and Gram-negative BSIs,[66,69,71,77,81,82] as well as CLABSI among dialysis patients,[83] and hemodialysis-related bacteremia.[84] Hypertension has also been reported to be common.[66,81,82,84] Immunosuppression was reported as an underlying condition for patients in Saudi Arabia with Group A streptococcal bacteremia (18.2% of 33 patients);[69] other conditions included cardiac disease (33.3%), malignancy (27.3%), recent trauma (18.2%) and recent influenza infection (18.2%). In a case series with *Elizabethkingia meningoseptica* bacteremia, all 12 patients had at least one underlying condition or intervention, and these included chronic illness and surgery.[85]

Similar underlying conditions are reported for patients with bacteremia due to MDR organisms. Studies of bacteremia due to MDR *P. aeruginosa* and carbapenem-resistant Enterobacterales in Saudi Arabia reported diabetes mellitus, hypertension and chronic kidney failure as common underlying conditions,[81,82] in addition to the presence of malignancy.

Clinical Outcomes and Mortality Associated with BSI

Across the studies there was a large range of mortality rates associated with BSI. Crude mortality among adult and pediatric ICU patients from Kuwait with CLABSI was reported as 27.3% by Al-Mousa et al[40] which increased to 38.9% for patients from neonatal ICUs (Table 2). Among adults, rates ranged from 10% to ≥67%,[86,87] with the highest rates attributed to infections caused by antimicrobial-resistant pathogens (Table 2). In their retrospective analysis of carbapenem-resistant bacteremia between 2007 and 2016, Balkhair et al[88] found that patients with *A. baumannii* infections were significantly younger (41.2 years) than patients with infections due to *P. aeruginosa* or *K. pneumoniae* (51.3 and 52.1 years, respectively) ($P = 0.049$). Also, of the 775 patients with bacteremia in the study, 252 (32.5%) died within 30 days of bacteremia onset.[88] Rates of 30-day all-cause mortality were 40.2% for *A. baumannii*, 31.5% for *K. pneumoniae* and

Table 2 Rates of Mortality From Bloodstream Infections (BSIs) in the GCC Region, by Age Group

Reference	Study Type	Country	Age Group, n of pts/Cases	Ward	Infection Type Mortality
All ages					
Al-Mousa et al[40]	Prospective, cohort	Kuwait	Pediatric and adult 44	ICU	CLABSI Crude: 27.3%
Al-Khadidi et al[69]	Retrospective	Saudi Arabia	Pediatric and adult 33	All	*Streptococcus pyogenes* BSI Crude: 12.1%
Al-Otaibi et al[73]	Retrospective	Saudi Arabia	Pediatric and adult 56	Oncology, ICU	Gram-negative BSI 30—day: 32.1%
Adults					
Ali et al[20]	Retrospective, cohort	Qatar	Adult 263	Acute/secondary care	Enterococcal BSI 30-day: 66.5%
Balkhair et al[88]	Retrospective	Oman	Adult *P. aeruginosa*: 231 *A. baumannii*: 169 *K. pneumoniae*: 375	All	BSI 30-day, all-cause *P. aeruginosa*: 28.6% *A. baumannii*: 40.2% *K. pneumoniae*: 31.5%
Balkhair et al[87]	Retrospective	Oman	Adult *P. aeruginosa*: 107 *A. baumannii*: 46 *K. pneumoniae*: 181 *E. coli* 244	All	BSI 30-day all-cause *P. aeruginosa*: 32.7% *A. baumannii*: 58.6% *K. pneumoniae*: 48.0% *E. coli*: 20.1%
Balkhair et al[87]	Retrospective	Oman	Adult *P. aeruginosa*: 32 *A. baumannii*: 37 *K. pneumoniae*: 84 *E. coli*: 7	All	BSI 30-day all-cause Carb-R *P. aeruginosa*: 68.8% Carb-R *A. baumannii*: 67.6% Carb-R *K. pneumoniae*: 67.8% Carb-R *E. coli*: 71.4%*
Gaid et al[46]	Retrospective, cohort	Saudi Arabia	Adult >1000	Cardiac, medical, surgical ICU	CLABSI Crude: 41.9%
Alhunaif et al[66]	Retrospective, cohort	Saudi Arabia	Adult 174	All	MRSA bacteremia 30-day: 20.1%
Alotaibi et al[90]	Retrospective, cohort	Saudi Arabia	Adult 283	All	CLABSI 30 day: 18.8%
Mahrous et al[86]	Retrospective phase, prospective phase	Saudi Arabia	Adult Baseline pts: 164 Post-intervention: 148	All	BSI Baseline: 18% Post-intervention: 10%
Pediatric patients					
Al Battashi et al[91]	Prospective, cohort	Oman	≤13 y 38	Oncology	BSI Crude: 15.8%
Al Lawati et al[53]	Retrospective, cohort	Oman	Pediatrics	Receiving parenteral nutrition outside ICU	CLABSI 25.0%
Neonates					
Al-Mousa et al[40]	Prospective, cohort	Kuwait	Neonatal 18	ICU	CLABSI Crude: 38.9%

Notes: * Percentage calculated from less than 10 isolates (71.4%, 5/7).
Abbreviations: Carb-R, carbapenem-resistant; y, years.

28.6% for *P. aeruginosa* bacteremia (Table 2). In a later study by Balkhair et al[87] reporting results from 2017 to 2020, mortality was higher among patients with BSIs caused by carbapenem-resistant isolates than those with carbapenem-susceptible infections, and 30-day all-cause mortality was similar for infections caused by all four carbapenem-resistant species studied (68.8%, *P. aeruginosa*; 67.8%, *K. pneumoniae*; 67.6%, *A. baumannii*; 71.4%, *E. coli*, Table 2). In patients >14 years of age, carbapenem-resistant bacteremia has also been shown to be an independent predictor for mortality in a study from Saudi Arabia and in Oman, the use of broad-spectrum antibiotics (eg, carbapenems and piperacillin-tazobactam), and mechanical ventilation were associated with mortality among patients with carbapenem-resistant Enterobacterales bacteremia.[29,89]

In a study of infections caused by *A. baumannii* carried out in Oman, all-cause mortality rates were higher among adult patients with pneumonia when compared with other infections (P = 0.000, OR 2.85); however, patients with bacteremia died earlier (28-day mortality) (P = 0.042, OR 2.83).[28] Among patients with neutropenia in Saudi Arabia, mortality was associated with the presence of bacteremia (P = 0.016).[92] For *S. maltophilia* bacteremia among pediatric patients, the mortality rate was reported as 33.8% within 7 days of diagnosis.[72]

Al-Otaibi et al[73] reported a high mortality rate (32.1%) among cancer patients with bacteremia at a hospital in Saudi Arabia (Table 2); they also reported a high rate of MDR isolates (43.5%). Comparing outcomes for patients inside and outside the ICU, Alotaibi et al[90] reported that adult patients with CLABSI in the ICU and those admitted to the ICU after infection had higher mortality than those outside the ICU (P < 0.0001), although CLABSI-related sequelae were not associated with increased mortality (P < 0.595).

Length of Stay and Hospital Costs

The time taken to diagnose a BSI and prescribe an appropriate antimicrobial is critical for effective treatment. Mahrous et al[86] analyzed the impact of rapid diagnostic testing coupled with a pharmacist-guided antimicrobial stewardship program on clinical outcomes in the treatment of adults with BSIs. The intervention reduced the time to culture identification from 96 hours to 22 hours (P < 0.0001) and the median time to targeted antimicrobials from 22 hours to 2 hours (P < 0.0001). They concluded that the length of stay was significantly shorter after the practice was introduced (6.5 vs 8 days, P = 0.03).[86] In addition, the intervention reduced mortality (from 18% to 10%, Table 2) and 30-day re-admission.

Retrospective studies of adults and pediatric patients have shown that the presence of a CLABSI is associated with a longer length of stay.[93,94] Alotaibi et al[93] reported that the presence of CLABSI in adults increased the length of stay by 13.13 ± 9.53 days. The length of stay was also significantly longer when central-line removal was delayed (P < 0.001). In a pediatric study, the rate of CLABSI was 16.6% among patients admitted for more than 30 days and 0.6% among patients admitted for ≤30 days.[94]

In Bahrain, adult patients with a CLABSI had a longer median length of stay in the ICU before insertion of the central line (7.6 days compared with 2.8 days for the control group, P < 0.05).[47] Al-Khawaja et al[45] calculated, following the care bundle-related reduction in CLABSI (from 2.3 patients per month to 1 patient per month), that 367 hospital days were saved, which corresponded with a reduction in hospital costs of 1,100,553 USD.

Complications

Al-Khadidi et al[69] reported the most frequent complications of Group A beta-hemolytic bacteremia as shock (10/33, 30.3%), acute respiratory distress syndrome (7/33, 21.2%), renal impairment (7/33, 21.2%) and pneumonia (5/33, 15.2%). Abazid et al[95] reported that septicemia among patients in a critical care unit was a predictor of developing delirium. Among 139 adult hemodialysis patients with CLABSI, El-Kady et al[70] reported that 43.2% developed complications with hospital admission and endocarditis being the most common (15.8% and 11.5%, respectively). Also, 10.1% required ICU admission and 5.8% developed septic embolism.[70]

Causal Pathogens of BSIs

Adults

Gram-negative organisms predominate as the causative pathogens of BSI among adults in the region. In the UAE, among adults with a confirmed BSI, Gram-negative isolates were reported to be more common that Gram-positive isolates [71.8% (148/206) and 24.3% (50/206), respectively], with the most common organism reported to be *E. coli* (31.1%, 64/206).[74] In their study of HCAI among ICU patients in Kuwait, Alfouzan et al[19] reported Gram-negative species as more commonly occurring than Gram-positives among BSI, with *A. baumannii* and *K. pneumoniae* the most frequent (both 21.5% of isolates); 9.2% of isolates were *S. aureus*. In Saudi Arabia, Gram-negative species and MDR isolates have also been more frequently identified than Gram-positive species among adult patients with bacteremia in a number of studies.[64,80,96] Al-Khawaja et al[47] determined that, among patients with a confirmed CLABSI, Gram-negative bacteria were more common (56%) than Gram-positive (41%) pathogens; however, at a species level, the most frequently isolated species were coagulase-negative staphylococci (18%) followed by *Acinetobacter* spp. (15%) and *Enterococcus* spp. (15%). In a 1-year (2019) prospective study, Saleem et al[26] reported that *K. pneumoniae* was the most common pathogen among CLABSI cases in an ICU in Saudi Arabia. Using direct DNA sequencing-based analysis, Alzahrani et al[97] found Gram-negative species to be more common among adults with leukemia and lymphoma. In a study of Gram-negative BSI among cancer patients in Saudi Arabia, the most common organisms were *E. coli* (29.5%, 18/61), *A. baumannii* (18.0%, 11/61), *Pseudomonas* spp. (16.4%, 10/61) and *K. pneumoniae* (13.1%, 8/61).[73] Among hemodialysis patients in Saudi Arabia with CLABSI, Gram-negative organisms have also been reported to be more common than Gram-positive organisms (61.4%, 129/210; 38.6%, 81/210, respectively), with *E. cloacae* being the most common Gram-negative species.[83]

Conversely, a retrospective analysis by a microbiology laboratory in Oman between 2016 and 2017 reported that, among isolates from blood samples, 59.2% (837/1415) were Gram-positive and 40.1% (568/1415) were Gram-negative.[98] Among adult patients with febrile neutropenia in Saudi Arabia, an equal number of Gram-positive and Gram-negative isolates were isolates from blood cultures (n = 23).[34] Among adult hemodialysis patients in Saudi Arabia, CLABSIs were more commonly due to Gram-positive bacteria (97/139, 69.8%) than Gram-negative (42/139, 30.2%).[70] Abdelfattah et al[99] also reported that Gram-positive bacteria were a more common cause of BSI among dialysis patients, with 52% of all BSI caused by *S. aureus*.

Badawy et al[100] in their study of dialysis patients in Kuwait in 2012 determined that common skin commensals (including coagulase-negative staphylococci and diphtheroids) were the most frequently isolated species followed by Gram-negative rods (40.2% and 31.8%, respectively); 12.1% of all blood culture isolates were *S. aureus*. The study authors stated that they could not determine if the skin commensals were causative pathogens or specimen contamination.[100] Similarly, in Oman, *Staphylococcus epidermidis* has been reported as the most frequent microorganism in CLABSI.[51] Care must be taken when attributing BSIs to common skin commensals. Asaad et al[8] reported that of the coagulase-negative staphylococci that grew from 208 positive blood cultures, 75 (36.1%) were causative pathogens and 133 (63.9%) were contaminants. Further to this, the emergency department was identified as the most common area for contamination (81.3%, 26/32 culture-positive samples) while the ICU was the least common (11.8%, 2/17 of samples).[8] Al-Tawfiq reported that, of 67 patients with blood cultures positive for coagulase-negative *Staphylococcus*, antimicrobial therapy was stopped in 65% of cases because there was no evidence of infection.[101]

Neonates and Pediatric Patients

In contrast to many of the adult studies, those presenting data on neonates and pediatric patients reported that Gram-positive organisms were more common than Gram-negatives as a cause of BSIs. In their study of pediatric oncology patients in Qatar, Al-Mulla et al[35] found that Gram-positive pathogens were more common than Gram-negative pathogens (64/116, 55.2% and 52/116, 44.8%, respectively); however, the percentages changed over time, with a higher percentage of Gram-positive isolates in 2004–2005 (17/29, 58.6%) than in 2010–2011 (15/28, 53.6%). *K. pneumoniae* was the most common Gram-negative species and *S. epidermidis* the most common Gram-positive. Gram-positive organisms were also the most common pathogen among neonates in an ICU in Oman.[102] In Saudi Arabia, between May 2016 and December 2017, among non-neutropenic children with cancer and a CLABSI, Gram-positive

isolates were more common than Gram-negatives (8/13, 61.5% and 5/13, 38.5%, respectively), although it should be noted that the number of isolates was small.[103] A similar result was reported among pediatric patients in receipt of stem cell transplants who developed bacteremia (55.6%, 10/18 Gram-positive; 44.4%, 8/18 Gram-negative).[104] Also, among neonates, Gram-positive BSIs have been shown to be more common than Gram-negative BSIs (64.2% and 32.5%, respectively), with *S. aureus* and *K. pneumoniae* being the most common species from the two groups, respectively.[105] Group B streptococci have also been reported to be a common cause of BSIs among neonates.[106]

As seen among the studies of adults, not all studies reported the same pattern. In pediatric (≤13 years) oncology patients in Oman, *Staphylococcus* was the most common Gram-positive organism (68.8%, 22/32) and *Klebsiella* the most common Gram-negative (21.4%, 9/42); however, Gram-negative organisms were more common overall with 42 isolates (56.8%) compared with 32 Gram-positive isolates (43.3%).[91] In a study of neonates at a COVID-19 segregation center in Saudi Arabia in 2020, Gram-negative organisms were reported to be more common than Gram-positives (68.2% and 31.8%, respectively), and among patients with sickle cell disease between 2005 and 2015 in Saudi Arabia, 7.8% (25/320) reported a bacterial infection, three of which were from the bloodstream and all caused by *Salmonella* spp.[107,108]

Rarely Reported Pathogens

Rarely reported causes of bacteremia include *Sphingomonas paucimobilis* (Bahrain, hemodialysis patients);[84] non-typhoidal *Salmonella* (Kuwait);[109] *Actinomyces odontolyticus* (Qatar);[110] *Streptococcus gallolyticus subsp gallolyticus* (Qatar);[111] *Bacteroides fragilis* (Kuwait);[112] and *Chryseobacterium/Elizabethkingia* spp (Saudi Arabia).[85,113]

Antimicrobial Susceptibility Among Gram-Positive Pathogens

Antimicrobial susceptibility (or resistance) among Gram-positive pathogens causing BSIs, as reported across the GCC countries, is presented in Table 3. Antimicrobials for which results were frequently reported included oxacillin, gentamicin, tetracycline, trimethoprim-sulfamethoxazole, ciprofloxacin, clindamycin and vancomycin. Among *S. epidermidis* and *Staphylococcus haemolyticus* isolates, susceptibility was high to daptomycin and vancomycin. There was little data available on *S. aureus*; however, Alhunaif et al[66] reported on 184 MRSA isolates from adults with BSIs in Saudi Arabia between January 2013 and June 2017 and ≥98% were susceptible to vancomycin, linezolid and tigecycline. All 196 isolates of Group B streptococci from BSIs isolated in Qatar between January 2015 and March 2019 were susceptible to penicillin, ceftriaxone and vancomycin and 71.4% were susceptible to clindamycin (Table 3);[71] however, the study also reported an increasing trend in infections, from 1.48 per 100,000 people to 2.09 per 100,000. In an analysis of 263 enterococci from BSI by Ali et al[20] in Qatar 2009–2018, the majority of isolates were susceptible to vancomycin, ampicillin, linezolid, daptomycin and gentamicin (Table 3); however, the study did not distinguish between enterococcal infections and polymicrobial infections that included enterococci.[20]

Multidrug Resistance

Among pediatric oncology patients in Oman (January 2015 – October 2017), 38% (n = 12) of Gram-positive organisms were resistant to ≥4 antimicrobials; however, no isolates were resistant to vancomycin and among neonates in Saudi Arabia, 54.5% of *S. aureus* isolates were resistant to ≥3 antimicrobials.[91,105]

Antimicrobial Susceptibility Among Gram-Negative Pathogens

Rates of antimicrobial susceptibility (or resistance) among Gram-negative pathogens causing BSIs, as reported across the GCC countries, are presented in Table 4. Studies reported variable rates of susceptibility or resistance; however, high rates of susceptibility (≥80%) were reported by a number of studies among *P. aeruginosa* to cefepime, gentamicin, amikacin and meropenem (Table 4). Low rates of susceptibility among *A. baumannii* isolates were reported to a range of antimicrobials; however, Bandy et al[80] reported 100% colistin susceptibility. Among *K. pneumoniae*, susceptibility to meropenem and ciprofloxacin was >80% and to cephalosporins ≥70% across a number of studies (Table 4).

Table 3 Antimicrobial Susceptibility and/or Resistance Among Gram-Positive Pathogens Causing Bloodstream Infections (BSIs) in GCC Countries

					Antimicrobial, %								
Organism/ Reference	**Country**	**Years**	**Number isolates**	**S or R**	**PEN, AMP, OXA**	**Cephalosporins (CAZ, CEF, CFZ, CRO, CTX, FEP or FOX)**	**MEM, IMP, MOX**	**AMK, GEN or TET**	**CIP**	**SXT**	**CLI, ERY**	**LZD, DAP**	**VAN, TEC, TGC**
S. epidermidis													
Al-Mulla et al[35]	Qatar	2004–2011	26	S	OXA, 8.0	CFZ, 0.0		GEN: 73.0		SXT, 16.0	CLI, 53.0; ERY: 100	LZD, 100	VAN, 96.0; TEC, 95.0
Asaad et al[8]	Saudi Arabia	Oct 2014 – July 2015	26	R	PEN, 96.2; OXA, 92.3			GEN, 42.3; TET, 19.2	CIP, 69.2	SXT, 50.0	CLI, 53.8; ERY, 88.5	DAP, 0.0	VAN, 0.0; TEC, 19.2
S. hominis													
Asaad et al[8]	Saudi Arabia	Oct 2014 – July 2015	16	R	PEN, 100; OXA, 87.5			GEN, 25.0; TET, 25.0	CIP, 18.8	SXT, 62.5	CLI, 18.8; ERY, 87.5	DAP, 0.0	VAN, 0.0; TEC, 0.0
S. haemolyticus													
Asaad et al[8]	Saudi Arabia	Oct 2014 – July 2015	12	R	PEN, 100; OXA, 100			GEN, 58.3; TET, 41.7	CIP, 58.3	SXT, 33.3	CLI, 83.3; ERY, 91.7	DAP, 0.0	VAN, 0.0; TEC, 0.0
S. aureus													
Alarjani et al[105]	Saudi Arabia	N/A	33	R	PEN, 54.5; AMP, 42.4; OXA, 15.1	FOX, 39.3; CRO, 33.3		TET, 42.4; GEN, 39.3	CIP, 31.0		CLI, 12.1; ERY, 54.5		VAN, 54.5;
MRSA													
Alhunaif et al[66]	Saudi Arabia	Jan 2013 – June 2017	184	S			MOX, 75.5	GEN, 73.9		SXT, 75.0	ERY, 55.4; CLI, 58.2	LZD, 98.4	TGC, 98.4; VAN, 100
***Staphylococcus* spp.**													
Al-Matary et al[114]	Saudi Arabia	2011–2015	111	S						SXT, 53.0			VAN, 100
Group B Streptococci													
Ali et al[71]	Qatar	Jan 2015-Mar 2019	196	S	PEN, 100	CRO, 100					CLI, 71.4; ERY, 51.0		VAN, 100

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Al-Matary et al[114]	Saudi Arabia	2011–2015	15	S	PEN, 100								VAN, 100
Enterococci													
Ali et al[20]*	Qatar	2009–2018	263	S	AMP, 82.5			GEN, 63.1	CIP, 24.7			DAP, 72.2%; LZD, 80.2	VAN, 89.4
S. pyogenes													
Alarjani et al[105]	Saudi Arabia	N/A	28	R	PEN, 25.0; AMP, 64.2; OXA, 46.4	FOX, 42.8; CRO, 42.8		TET, 64.2; GEN, 25.0	CIP, 35.7		CLI, 14.3; ERY, 39.0		VAN, 17.8

Notes: %S or %R are calculated to 1 decimal place, or as presented in the article where numerators are not given. %S or %R not presented when N <10. When denominator is different to the total isolates (N), numerator, denominator and % are presented. * Includes polymicrobial infections.

Abbreviations: AMK, amikacin; AMP, ampicillin; CAZ, ceftazidime; CEF, cefalotin; CFZ, cefazolin; CIP, ciprofloxacin; CLI, clindamycin; CRO, ceftriaxone; CTX, cefotaxime; DAP, daptomycin; ERY, erythromycin; ESBL, extended-spectrum β-lactamase; FEP, cefepime; FOX, cefoxitin; GEN, gentamicin; IPM, imipenem; LZD, linezolid; MEM, meropenem; MOX, moxifloxacin; MRSA, methicillin-resistant *Staphylococcus aureus*; N/A, not relevant to, or not presented in, the study; OXA, oxacillin; PEN, penicillin; R, resistant; S, susceptible; spp., species; SXT, trimethoprim-sulfamethoxazole (co-trimoxazole); TEC, teicoplanin; TET, tetracycline; TGC, tigecycline; VAN, vancomycin; and y, years.

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Table 4 Antimicrobial Susceptibility and/or Resistance Among Gram-Negative Pathogens Causing Bloodstream Infections (BSIs) in GCC Countries

					Antimicrobial, %								
Organism/ Reference	**Country**	**Years**	**Number Isolates**	**S or R**	**AMP**	**AMC or TZP**	**Cephalosporins (CAZ, CEF, CRO, CTX, CXM, FEP or FOX)**	**MEM, IMP**	**AMK, GEN or TET**	**SXT**	**CIP, LVX, MOX**	**AZT, COL**	**TGC**
P. aeruginosa													
Al-Matary et al[114]	Saudi Arabia	2011–2015	22	S		TZP, 100	FEP, 100; CAZ, 77.0	IMP, 91.0; MEM 91.0	GEN, 100; AMK, 100				
Al-Otaibi et al[73]	Saudi Arabia	Jan 2013 – Oct 2015	10	S		TZP, 70.0	FEP, 90.0; CAZ, 80.0	IMP, 70.0; MEM, 80.0	GEN, 90.0; AMK, 100		CIP, 100	AZT, 90.0	
El-Kady et al[70]	Saudi Arabia	2019–2020	12	S		TZP, 66.7	FEP, 33.3	MEM, 83.3; IMP, 66.7	AMK, 66.7		CIP, 50.0		
Aloraifi et al[115]	Saudi Arabia	2016–2020	MEM: 283; IPM: 275	R				MEM, 71.0; IMP, 88.4					
A. baumannii													
Al-Otaibi et al[73]	Saudi Arabia	Jan 2013 – Oct 2015	11	S		TZP, 18.2	FEP, 18.2; CAZ, 18.2	IMP, 27.3; MEM, 18.2	GEN, 45.5; AMK, 27.3		CIP, 9.1	AZT, 9.1	
Bandy et al[80]	Saudi Arabia	2019	17	S	AMP, 0.0	AMC, 0.0; TZP, 0.0	CEF, 0.0; CXM, 0.0; FOX, 0.0; CRO, 0.0, CAZ, 0.0; FEP, 0.0	MEM, 0.0; IMP, 0.0	AMK, 5.9; GEN, 0.0	SXT, 29.4	CIP, 0.0; LVX, 0.0	AZT, 0.0; COL, 100	
Aloraifi et al[115]	Saudi Arabia	2016–2020	MEM: 365; IPM: 381	R				MEM, 97.3; IMP, 92.1					
K. pneumoniae													
Al-Mulla et al[35]	Qatar	2004–2011	10–14	S			FEP, 83.0; CRO, 80.0; CAZ, 77.0	MEM, 100; IMP, 100	GEN, 75.0; AMK, 100	SXT, 42.0	CIP, 82.0		
Al-Otaibi et al[73]	Saudi Arabia	Jan 2013 – Oct 2015	10	S	AMP, 0.0	TZP, 50.0	FEP, 70.0; CTX, 70.0; FOX, 80.0; CAZ, 70.0; CRO, 70.0; CXM, 70.0	MEM, 80.0; IMP, 80.0	GEN, 80.0; AMK, 80.0		CIP, 80.0	AZT, 70.0	

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Bandy et al[80]	Saudi Arabia	2019	63	S	AMP, 0.0	AMC, 13.1; TZP, 31.7	CEF, 9.5; CXM, 12.7; FOX, 36.5; CAZ, 15.9; CRO, 14.3; FEP, 19.4	IMP, 34.9; MEM, 36.5	AMK, 77.4; GEN, 59.7	SXT, 30.6	CIP, 30.6; LVX, 33.9	AZT, 15.9; COL, 82.4	TCG, 78.0
El-Kady et al[70]	Saudi Arabia	2019–2020	15	S		TZP, 100	FEP, 60.0; CRO, 46.7	MEM, 93.3; IPM, 93.3	AMK, 93.3	SXT, 60.0	CIP, 80.0		TGC, 100
Aloraifi et al[115]	Saudi Arabia	2016–2020	MEM: 774; IPM: 865	R				MEM, 50.8; IMP, 36.5					
Alarjani et al[105]	Saudi Arabia	N/A	20	R	AMP, 90.0	AMC, 31.6	CRO, 75.0; CAZ, 10.5		TET, 36.8; GEN, 15.0; AMK, 10.5	SXT, 40.0	CIP, 15.0		
Klebsiella spp.													
Al-Matary et al[114]	Saudi Arabia	2011–2015	40	S	AMP, 0.0	TZP, 95.0	FEP, 83.0; CAZ, 85.0; CTX, 83.0	IMP, 100; MEM, 100	GEN, 83.0; AMK, 98.0	SXT, 83.0			
E. coli													
Al-Matary et al[114]	Saudi Arabia	2011–2015	29	S	AMP, 14.0	TZP, 86.0	FEP, 62.0; CAZ, 59.0; CTX, 62.0	IMI, 100; MEM, 100	GEN, 62.0; AMK, 100	SXT, 48.0			
Al-Otaibi et al[73]	Saudi Arabia	Jan 2013 – Oct 2015	21	S	AMP, 14.3	TZP, 57.1	FEP, 47.6; CTX, 57.1; FOX, 71.4; CAZ, 57.1; CRO, 52.4; CXM, 42.9	IMP, 85.7; MEM, 85.7	GEN, 71.4; AMK, 81.0		CIP, 42.9	AZT, 57.1	
Bandy et al[80]	Saudi Arabia	2019	23	S	AMP, 4.3	AMC, 19.0; TZP, 82.6	CEF, 8.7; CXM, 13.0; FOX, 87.0; CAZ, 26.1; CRO, 26.1; FEP, 26.1	IMP, 95.7; MEM, 100	AMK, 95.7; GEN, 78.3	SXT, 30.4	CIP, 34.8; LVX, 39.1	AZT, 26.1; COL, 100	TGC, 100 (n=11)
Aloraifi et al[115]	Saudi Arabia	2016–2020	MEM: 682; IPM: 875	R				MEM, 3.5; IMP, 2.2					
Alarjani et al[105]	Saudi Arabia	N/A	19	R	AMP, 42.1	AMC, 25.0	CRO, 25.0; CAZ, 5.2		TET, 16.7; GEN, 8.3; AMK, 0.0	SXT, 33.3	CIP, 0.0		
Non-typhoidal *Salmonella* spp.													
Albert et al[109]	Kuwait	April 2013 – May 2016	61	R	AMP, 36.1	TZP, 0.0	CAZ, 8.2; CTX, 9.8; CRO, 8.2	IMP, 0.0; MEM, 0.0	GEN, 3.3; TET, 50.8	SXT, 14.8	CIP, 39.3		

(*Continued*)

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Table 4 (Continued).

					Antimicrobial, %								
Organism/ Reference	**Country**	**Years**	**Number Isolates**	**S or R**	**AMP**	**AMC or TZP**	**Cephalosporins (CAZ, CEF, CRO, CTX, CXM, FEP or FOX)**	**MEM, IMP**	**AMK, GEN or TET**	**SXT**	**CIP, LVX, MOX**	**AZT, COL**	**TGC**
***Enterobacter* spp.**													
Al-Matary et al[114]	Saudi Arabia	2011–2015	18	S	AMP, 6.0	TZP, 78.0	FEP, 83.0; CAZ, 67.0; CTX, 61.0	IMP, 100 MEM 100	GEN, 83.0; AMK, 100	SXT, 89.0			
S. maltophilia													
Alsuhaibani et al[72]	Saudi Arabia	2007–2018	See table	S			CAZ, 61.9 (n=42)		GEN, 31.3 (n=16)	SXT 94.1 (n=68)	CIP, 50.0 (n=24); LVX, 85.7 (n=21)		
Elizabethkingia meningoseptica													
Aldoghaim et al[85]	Saudi Arabia	Jun 2013 – May 2019	12	R		TZP, 0.0	CAZ, 91.7; CRO, 100	IMP, 100; MEM, 100	AMK, 100; GEN, 100; TET, 83.3	SXT, 0.0	CIP, 41.7; LVX, 8.3; MOX, 0.0	COL, 91.7	
Gram-negative (species not specified)													
Al Battashi et al[91]	Oman	Jan 2015 – Oct 2017	42	R	AMP, 35.7	PEN, 9.5; TZP, 31.0; AMC, 21.4	CXM, 19.0; CEF, 4.8; FEP, 28.6; CAZ, 26.2; CRO, 35.7	MEM, 7.1	GEN, 26.2; AMK, 16.7		CIP, 11.9		

Notes: %S or %R are calculated to 1 decimal place, or as presented in the article where numerators are not given. %S or %R not presented when N <10. When denominator is different to the total isolates (N), numerator, denominator and % are presented.

Abbreviations: AMC, amoxicillin-clavulanic acid; AMK, amikacin; AMP, ampicillin; AZT, aztreonam; CAZ, ceftazidime; CEF, cephalothin; CIP, ciprofloxacin; CRO, ceftriaxone; CTX, cefotaxime; CXM, cefuroxime; COL, colistin; FEP, cefepime; FOX, cefoxitin; GEN, gentamicin; IPM, imipenem; LVX, levofloxacin; MEM, meropenem; MOX, moxifloxacin; N/A, not relevant to, or not presented in, the study; R, resistant; S, susceptible; spp., species; SXT, trimethoprim-sulfamethoxazole (co-trimoxazole); TET, tetracycline; TGC, tigecycline; and TZP, piperacillin-tazobactam.

Carbapenem Resistance

Carbapenem-resistant pathogens are an increasing problem worldwide, and carbapenemase-positive bacteria have been identified as causative pathogens in BSIs in the GCC region. In Oman, *K. pneumoniae* from BSI were susceptible to carbapenems prior to 2010;[88] however, resistance increased to 40% in 2014. The same study reported that of 66 carbapenem-resistant *K. pneumoniae* isolates tested, 21.2% were also resistant to colistin. In a retrospective study of Gram-negative infections between 2017 and 2020, also in Oman, 46.4% (84/181) of *K. pneumoniae* were carbapenem-resistant.[87] In addition, 29.9% (32/107) of *P. aeruginosa*, 80.4% (37/46) of *A. baumannii* and 2.9% (7/244) of *E. coli* in the same study were carbapenem-resistant and, in total, 13.4% (16/119) of the carbapenem-resistant isolates were resistant to both carbapenems and colistin (15 of 16 were *K. pneumoniae*).[87] In Saudi Arabia, a cross-section retrospective study at a single center identified bacteremia as the most common infection among patients with carbapenem-resistant Enterobacterales.[116]

Multidrug Resistance

MDR Gram-negative infections are increasingly problematic to treat. A study of MDR bacteria in Oman in 2012 reported that BSIs and pneumonia were the infections most frequently associated with multidrug resistance and, although the study did not specify the bacterial species isolated from blood, across the infection sources the most common bacteria were *A. baumannii* and *E. coli*.[117] Among pediatric oncology patients in Oman (January 2015–October 2017), 33.3% (14/42) of Gram-negative bacteria from blood cultures were resistant to ≥4 antimicrobials, and the highest rates of resistance were reported for ampicillin and ceftriaxone (both, n=15/42, 35.7%), piperacillin-tazobactam (n = 13, 31.0%) and cefepime (n = 12, 28.6%).[91]

Among oncology patients in Saudi Arabia, Al-Otaibi et al[73] reported low rates of susceptibility among *A. baumannii* between 2013 and 2015 (Table 4); the same study also found that the MDR rate among *P. aeruginosa* and *A. baumannii* was 43.5% and that the rate of ESBL producers was 34.6% among isolates of *E. coli* and *K. pneumoniae*. For isolates collected in Saudi Arabia in 2019, multidrug resistance among *E. coli* and *K. pneumoniae* was reported to be 78.3% (18/23) and 49.2% (31/63), respectively, and 4.3% (1/23) of *E. coli* and 46.0% (29/63) of *K. pneumoniae* were carbapenemase producers.[80] In addition, a retrospective study of 60 ICU patients (98.3% with central lines) with *Acinetobacter* BSIs in Saudi Arabia between 2005 and 2010 reported that all cases were MDR, 90% were resistant to carbapenems and one isolate was resistant to colistin.[79] The same study concluded that the mortality risk for *Acinetobacter* BSI was lower among patients who received appropriate antimicrobial therapy.

In Qatar, between October 2014 and September 2017, <5% (16/362) of *P. aeruginosa* from BSIs were MDR;[77] against these MDR isolates 12.5% were susceptible to meropenem, 50% were susceptible to ceftazidime-avibactam and ceftolozane-tazobactam, and 100% were susceptible to colistin. MDR *A. baumannii, E. cloacae, K. pneumoniae* and *P. aeruginosa* were identified among the Gram-negative organisms isolated from CLABSI in pediatric/neonatal ICUs in Kuwait in 2015;[54] however, following infection control interventions, along with a decrease in the number of CLABSIs, no MDR isolates were collected in 2016 (January–March). Among neonates in Saudi Arabia 45% (9/20) of *K. pneumoniae* isolates were determined to be resistant to ≥3 antimicrobials.[105]

Among isolates from hemodialysis patients in Saudi Arabia, 46.7% of *K. pneumoniae* were ESBL-producers and 13.3% were MDR;[70] however, only 15 isolates were included in the study.

Resistant Genotypes

Among carbapenem-resistant Enterobacterales, particularly *K. pneumoniae*, isolated from bacteremia patients in Saudi Arabia and Oman, OXA-48 was the most common genotype.[81,87] NDM-positive isolates were also reported.[81,87] In the UAE, four ertapenem-non-susceptible Enterobacterales collected between 2011 and 2012 from patients with healthcare-associated bacteremia were positive for $bla_{\text{OXA-48}}$ and all four isolates were susceptible to tigecycline and colistin and with MICs for meropenem of between 0.25 and 0.5 mg/L.[118] Also, in the UAE, between January 2016 and October 2017, patients with bacteremia caused by Gram-negative pathogens that were positive for AmpC β-lactamases were reported.[74] The carbapenemase VIM-4 has been reported among *K. pneumoniae* and *E. coli* isolates in Kuwait.[119]

A range of resistance genes were identified among MDR *P. aeruginosa* collected between 2014 and 2017, including CTX-M-15, VIM, OXA, PDC and genes encoding aminoglycoside modifying enzymes.[77]

Antimicrobial Management & Clinical Outcomes

The selection of the appropriate antimicrobial treatment for bacteremia should be guided by the most likely source of the infection, microbiological data and knowledge of the local antibiogram. Bacteremia was reported to be the second most common reason for prescribing antimicrobials in a study in Qatar, with teicoplanin being a commonly prescribed antimicrobial for primary bacteremia.[120,121] Also, in Qatar, between October 2014 and September 2017, the most commonly used antimicrobial agents against MDR *P. aeruginosa* BSI were meropenem (75.0%, 12/16 cases) and colistin (62.5%, 10/16 cases), with clinical response achieved in 50% of patients (8/16) and the 30-day all-cause mortality was 31.3% (5/16).[77] A retrospective study by Hakeam et al[82] in Saudi Arabia compared the treatment of MDR *P. aeruginosa* bacteremia with ceftolozane-tazobactam and colistin, concluding that the risk of mortality was similar between the two groups, although clinical success was higher in the ceftolozane-tazobactam group (76.5% and 41.4%, respectively). The study also noted that colistin was always used in combination, most frequently with a carbapenem (22/29 cases, 75.9%), whereas ceftolozane-tazobactam was used in combination with an antipseudomonal antimicrobial in 64.7% of cases (11/17).[82]

A retrospective, multi-center cohort study of adults in Saudi Arabia compared outcomes for patients with carbapenem-resistant Enterobacterales bacteremia who received ceftazidime-avibactam and those who received colistin (32 and 29 patients, respectively).[81] In comparison with the colistin group, the adjusted risk for 14-day mortality was lower in the ceftazidime-avibactam group (hazard ratio 0.32; 95% confidence interval [CI] 0.10–0.99; P = 0.049); however, the crude 14-day mortality, the adjusted 30-day mortality and bacterial eradication were similar between the two groups.[81] Alraddadi et al[29] reported a protective effect when ceftazidime-avibactam was part of the treatment regimen for carbapenem-resistant Enterobacterales bacteremia; however, when age, Charlson comorbidity index and Pitts Bacteremia Score (PBS) were controlled for, the association between 30-day all-cause mortality and treatment with ceftazidime-avibactam was no longer significant (P = 0.06). Colistin is considered a last option in the treatment of BSI, often in cases caused by carbapenem-resistant organisms. However, the use of colistin is complicated by difficulties in determining the appropriate dose and possible toxicity.[122] Colistin-resistant Enterobacterales have been reported in the region (Saudi Arabia).[123]

Another study of infections caused by carbapenem-resistant Enterobacterales in Saudi Arabia compared treatment of adults with ceftazidime-avibactam to other antimicrobials.[124] The study included a range of infections and the rate of bacteremia was 70% (7/10) in the group that received ceftazidime-avibactam and 53.6% (15/28) in the group that received a comparator.[124] In both groups, the time to clearance of bacteremia was similar (median values: 4 days and 5 days, respectively).[124] A retrospective observational study from the UAE looked at the microbiological cure of bacteremia and pneumonia among patients using renal replacement therapy and receiving ceftazidime-avibactam. A total of 22 patients had bacteremia, and microbiological cure was achieved in 20 patients (90.9%) and through the use of multivariate logistic regression, the study determined that Enterobacterales, daily drug dose and bacteremia were associated with microbiological cure.[125]

Among hemodialysis patients in Saudi Arabia, vancomycin was used to treat BSIs in 55.2% of cases, ceftazidime in 48.3% of cases and gentamicin in 13.8%.[64] Alshukairi et al[96] reported the most commonly used antimicrobials in the treatment of bacteremia among febrile neutropenic adults to be carbapenems, vancomycin and aminoglycosides; however, following an imipenem de-escalation study, piperacillin-tazobactam use increased (P = 0.018) and meropenem use decreased significantly (P = 0.009).

Combination Therapy

Combination therapy with piperacillin-tazobactam and amikacin was reported to be a common combination in Oman in the treatment of pediatric oncology patients with BSIs.[91] Other combinations reported in the study included cefepime and amikacin; meropenem, piperacillin-tazobactam or cefepime in combination in vancomycin; and ceftazidime in combination with amikacin.

Antimicrobial Stewardship

Antimicrobial stewardship programs are vital for supporting the appropriate use of antimicrobials. In a study across 6 hospitals in Saudi Arabia, the overall appropriateness of antimicrobial therapy was found to be lowest in BSIs.[126] Al-Omari et al[127] demonstrated that following the introduction of a stewardship program, HCAIs decreased, with the rate of CLABSIs reducing by 94.1%.

Gaps & Recommendations

While a great deal of research has been published on the impact of CLABSI in the region, more information on the clinical impact of other types of BSIs is needed, particularly in the case of secondary infections, as they may benefit from different clinical management. In addition, the majority of available information in the region is related to healthcare-acquired, and in particular ICU-acquired, BSIs. More information is needed on the risk factors and pathogens associated with community-acquired BSIs. There is also a lack of published data on important pathogens such as *Streptococcus pneumoniae, Streptococcus pyogenes, Haemophilus influenzae* and anaerobes.

With the population in the region ageing, more analysis on the impact and appropriate treatment of BSIs among older age groups is also important. More local information on antimicrobial susceptibility profiles and associated resistance mechanisms of organisms causing BSI would also support the appropriate selection of antimicrobial agents, although the region is known to have a high prevalence of OXA-48.[128] Accurate data on colistin susceptibility in the region, using reliable reference methods, would also be beneficial.

There is a lack of national BSI surveillance data, including yearly antibiograms, from most GCC countries, such data would enable the monitoring of epidemiology and resistance trends. One recommendation would be to develop a surveillance network across the GCC region for the BSIs, causative organisms and their antibiograms. Valuable data are also lacking on the costs associated with BSI in the region.

Limitations

This review has comprehensively covered 10 years of data regarding an important aspect of invasive bacterial disease; however, it has some limitations. One of the prime limitations of this review was the fact that not all studies included an undisputed description of their definition of a BSI. As discussed in this review, positive blood cultures may not mean that the patient had a BSI. Also, some of the studies included were from a single center, potentially resulting in giving data undue weight and, as single centers, the reported data may not be reflective of the wider area or country. Additionally, a large number of the studies were from centers in Saudi Arabia resulting in the underrepresentation of other GCC countries. However, these limitations highlight the fact that there is a lack of systematic surveillance of BSI in GCC countries, meaning that data must be aggregated from studies, often from a single center, across the region, with sporadic representation of patients, locations and the use of variable definitions of BSI.

Also, there was a focus on CLABSI in the literature, this is a commonly occurring type of BSI so the focus is not unexpected; however, more studies on other types of BSIs would strengthen the evidence base. In addition, infective endocarditis and osteomyelitis, as hematogenous infections, were perhaps underrepresented in our literature search because they were not included as specific terms.

Finally, because sepsis was excluded from the search terms, no information was collected from the literature about the rates of patients with BSIs who developed sepsis.

Discussion and Conclusions

BSIs are common in the GCC region. However, rates of BSI in the studies included in this review varied by country, setting and population and a number of studies reported that BSI were frequently device-associated.[21,23,26] In Saudi Arabia, Bahrain and Oman, the reported rate of CLABSIs was 146% higher than a study of US hospitals but 33% lower than an international hospital study.[37] These differences might be related to healthcare expenditures in the different countries/regions. Another international study also reported a correlation between infection risk and the socio-economic level of a country.[129] Device associated infections are recognized as an important infection control target and a number of

GCC region studies reported on the effective use of infection control procedures and care bundles to reduce rates of CLABSI.[39,41–45,47–49,54,56,57]

Across the region, a range of Gram-positive and Gram-negative species were reported to cause BSI, with most publications focusing on CLABSI. Species reported included *S. aureus* and MRSA, *S. epidermidis, Enterococcus faecalis, K. pneumoniae, A. baumannii, P. aeruginosa, E. coli, S. maltophilia, Serratia marcescens, Enterobacter aerogenes, Enterobacter cloacae* and *Citrobacter koseri*.[20,26,27,31,32,41,43,44,54,64,66,72,76,79,83,87,99,130] Gram-negative organisms were more commonly reported among adults; however, among neonates and pediatric patients, the majority of studies across the region reported that Gram-positive organisms were more common. The likely causative organisms of an infection will vary due to a number of factors, including patient location (eg, ICU, general ward, and community), comorbidities, and geographic location.

High rates of mortality were associated with antimicrobial-resistant pathogens, particularly carbapenem-resistant Gram-negatives such as carbapenem-resistant Enterobacterales, *P. aeruginosa* and *A. baumannii*.[87,131–133] Patient location was also reported to be associated with mortality, with patients in the ICU with a CLABSI having a higher mortality rate than those outside the ICU.[90]

Carbapenem resistance (imipenem and/or meropenem) was reported to be ≥30% against *P. aeruginosa, A. baumannii* and *K. pneumoniae* in a number of studies included in this review.[70,73,80,115] Among *E. coli*, rates of carbapenem resistance were lower. Antimicrobial resistance is of global concern with many countries reporting increasing rates of resistance, particularly for classes such as the carbapenems.[10] There was a lack of susceptibility data for newer agents such as ceftazidime-avibactam and meropenem-vaborbactam in the region and in vitro and clinical studies involving BSI for these agents would be beneficial.

This review has revealed a number of gaps in the literature from the GCC region. While a great deal of the literature focuses on CLABSI, more information on other BSI, and particularly secondary infections would be beneficial, as would information on pathogens such as *Streptococcus pneumoniae, Haemophilus influenzae* and anaerobes. The interpretation of antimicrobial susceptibility data is limited because of the number of studies that were single centers and included specific patient groups. The GCC region would benefit from surveillance networks to monitor BSIs, causative organisms and antibiograms.

In conclusion, BSIs present significant morbidity and mortality in the GCC region with device associated infections making up an important proportion of such infections. Infection control, and the use of care bundles, has been shown to reduce the burden of device-associated infections. Antimicrobial resistance is a global problem, from which the GCC region is not immune, and it impacts the appropriate selection of antimicrobials and the effective treatment of BSI. The development of national BSI surveillance networks to inform clinicians would aid treatment and decision-making.

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