Iranian Journal of Microbiology
Volume 16 Number 3 (June 2024) 285-292

ORIGINAL ARTICLE

Predictors of thirty-day mortality among patients with blood stream infection with WHO priority pathogens: single centre exploratory study from a referral teaching hospital in central India

Akshit Budhiraja[1], Tadepalli Karuna[2], Farhan Khan[3], Shweta Kumar[1], Namitha Shaji[1], Ehsaas Bajaj[4], Shashank Purwar[2], Abhijit Pakhare[3], Rajnish Joshi[1], Saurabh Saigal[5], Sagar Khadanga[1*]

[1]Department of General Medicine, AIIMS Bhopal, Saket Nagar, Bhopal, India
[2]Department of Microbiology, AIIMS Bhopal, Saket Nagar, Bhopal, India
[3]Department of Community and Family Medicine, AIIMS Bhopal, Saket Nagar, Bhopal, India
[4]Department of General Medicine, Undergraduate Student, AIIMS Bhopal, Saket Nagar, Bhopal, India
[5]Department of Critical Care, AIIMS Bhopal, Saket Nagar, Bhopal, India

Received: April 2023**, Accepted:** April 2024

ABSTRACT

Background and Objectives: Bloodstream infection (BSI) is defined by the presence of viable microorganisms in the bloodstream. BSI is one of the major causes of sepsis and subsequent adverse clinical outcomes all across the globe. The present study was undertaken to identify clinico-epidemio-microbiological variables associated with 30-day mortality in patients having BSI with WHO priority pathogens.

Materials and Methods: The study was conducted at a public sector tertiary care institute in central India from April 2019 to March 2021. Blood samples collected from patients with clinical suspicion of sepsis, were processed by automated bacterial culture system and interpreted as per CLSI guidelines. Calculated sample size was 150. Data was analyzed by R software.

Results: Respiratory tract infection was the most common source (43.3%) of BSI, followed by the gastrointestinal (20%) and urinary tract (18.7%). Among the patients, 33% required invasive mechanical ventilation, and 31% required inotropes. Diabetes mellitus (DM) was the most common co-morbidity (34%). The incidence of multi-drug resistant organisms (MDRO) was 59.3%. *Escherichia coli* was the most commonly (24%) isolated organism, followed by *Klebsiella pneumoniae* (17.3%) and *Acinetobacter baumannii* (16%).

Conclusion: Higher age, higher qSOFA score / SIRS score / mean SOFA score at presentation had higher mortality. Use of mechanical ventilation and inotropes during treatment and isolation of critical category organisms of WPP and multi drug resistant organisms were independent 30-day mortality predictors.

Keywords: Antimicrobial stewardship; Bacteremia; Drug resistance; Mortality; Sepsis

INTRODUCTION

Sepsis is defined as a life-threatening organ dysfunction due to a dysregulated immune response of the host in response to an infection by the International Consensus Definitions for sepsis and septic shock (1). Sepsis is a major global burden and accounts for nearly 48.9 million cases and 11 million

*Corresponding author: Sagar Khadanga, MD, Department of General Medicine, AIIMS Bhopal, Saket Nagar, Bhopal, India. Tel: +91-7771001557 Email: drsagarkhadanga@gmail.com

deaths annually (2). Bloodstream infection (BSI) is defined as the presence of viable bacteria or fungi in the bloodstream and is identifiable by microbiological culture among patients with suspected sepsis (3). Bloodstream infections (BSI) may be due to community acquired infections or hospital acquired (4). BSI cause a huge economic burden on the patient and healthcare system (5-8).

The World Health Organisation priority pathogen (WPP) list was identified for multi-drug resistant (MDR) and extensively drug-resistant (XDR) bacteria to prioritize the research and development of newer antibiotics (9, 10). Patients having co-morbidities and infection with MDR organisms are known to have adverse clinical outcomes in sepsis (11).

The Sequential Organ Failure Assessment (SOFA) score and the quick SOFA (qSOFA) score serve as a quantitative indicators of the patient's clinical condition and outcome (12, 13). Systemic inflammatory response syndrome (SIRS) is an exaggerated defence response of the body to a noxious stressor to localize and then eliminate the source of the insult (14). SIRS is defined by the satisfaction of any two of the criteria below: a) Body temperature over 38 or under 36 degrees Celsius b) Heart rate greater than 90 beats/minute. c) Respiratory rate greater than 20 breaths/minute or partial pressure of CO2 less than 32 mmHg d) Leukocyte count greater than 12000 or less than 4000 /microliters or over 10% immature forms or bands. Among the patients with BSI, elderly age group, MDR infection and presence of co-morbidity is associated with increased 30-day mortality (6, 15-17). The present study was conceived to identify clinico-epidemio-microbiological factors associated with 30-day mortality among patients of BSI with critical and high categories of WPP as in Table 1.

MATERIALS AND METHODS

Study design. This study was planned as a longitudinal chart review, conducted at the All India Institute of Medical Sciences (AIIMS), Bhopal a public sector tertiary care institute of national importance in central India from April 2019 to March 2021. As a referral tertiary care centre, AIIMS Bhopal caters to adjacent 4-5 states and more than 100 districts in central India. The primary aim was to identify and compare demographic (age, sex), clinical (source of infection, SOFA score, need for respiratory and inotrope support), and microbiological variables (causative bacteria, presence of MDR isolate) associated with 30-day all-cause mortality among the patients having BSI with WPP.

Ethics statement. The study was approved by the Institutional Human Ethics Committee (IHEC) of AIIMS, Bhopal vide reference number: IHEC-PGR/MD/003. The study was designed as per the guidelines of Good Clinical Practice and the Helsinki guidelines for informed patient consent.

Study population. Inclusion criteria: Participants aged 18 years or older with microbiologically proven BSI with critical and high categories of WPP were considered for further evaluation after informed written consent; Exclusion criteria: Cases whose records could not be traced by Medical Records Department (MRD) or who could not be contacted by telephone were excluded.

Sample size. The sample size was calculated by the software OpenEpi, with a presumed population size of 1,00,000 with cumulative mortality of 25% with a design effect of 1 to be 139. However, with a possible attrition rate of 7.5%, a total sample size of 150 was calculated (18).

Study procedure. Blood samples of patients from in-patient departments (IPD) of various clinical departments of AIIMS Bhopal with clinical suspicion of sepsis were sent to the Clinical Microbiology De-

Table 1. WHO priority pathogens List for R&D of new antibiotics

Priority 1: Critical	Priority 2: High	Priority 3: Medium
Acinetobacter baumannii	*Enterococcus faecium*	*Streptococcus pneumoniae*
Pseudomonas aeruginosa	*Staphylococcus aureus*	*Haemophilus influenzae*
Enterobacteriaceae	*Helicobacter pylori*	*Shigella* spp.
(Escherichia coli, Klebsiella pneumoniae)	*Campylobacter*	
	Salmonella spp.	
	Neisseria gonorrhoeae	

partment. Blood samples were processed by automated bacterial culture system (BacTAlert and Vitek-II BioMérieux, France) and interpreted as per CLSI guidelines. All the patients having blood stream infections with critical and high-category WPP were identified by consecutive sampling and were taken into the sampling frame. The patients were then screened as per the inclusion and exclusion criteria as mentioned above for recruitment. The flow of work has been shown in Fig. 1.

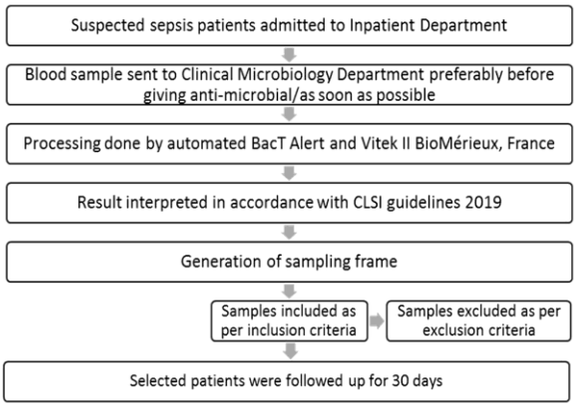

Fig. 1. Flow of work

The demographic variables, the SOFA score, qSOFA score and the SIRS score, the source of infection, the causative organism, and its sensitivity pattern were identified and recorded at admission. The need for respiratory and ventilatory support anytime during the course of the treatment was taken as a dichotomous variable. Those patients, who were discharged, before 30 days, were contacted by telephone and encouraged to visit our institute with their case records. Patients, who were not able to visit physically, were interviewed by telephone. Any WPP that was resistant to at least 3 groups of antibiotics were identified as Multi Drug Resistant (MDR) pathogen.

Statistical analysis. The variables about demographic, clinical, and microbiological data as mentioned above were collected on a pre-structured data sheet either as dichotomous or continuous variables, as appropriate. After data cleaning, data were analyzed by R software (v4.1.2; R Core Team 2021). The chi-square test was used for dichotomous variables and the student's t-test or Wilcoxon rank-sum test for continuous variables was used to compare proportions. Confounding co-morbidities were analyzed by appropriate univariate / multivariate analysis as mentioned in detail in the results section. Statistical significance was considered as all p values were less than 5% ($p<0.05$).

RESULTS

The study involved 150 participants who presented with BSI with WPP. The studied population had a mean age of 48.2 ± 18.4 years (Mean ± Standard Deviation), with slight male predominance (62.7%). The mean age among males was 49.4 ± 18.6 years and among females was 46.2 ± 18.1 years (Table 2). Out of the 150 number of participants 84 patients (56%) had at least one or more comorbidity. Diabetes mellitus was the most common co morbidity in 34% cases followed by chronic renal failure (18%), chronic lung diseases (8.7%), cirrhosis of liver (6%), heart failure (4%), cancer (4%) and immunosuppression in 1.3% cases.

The prevalence of BSI attributed to WPP did not show any significant variation across ages. Around 27% of all patients were recruited from low-priority areas (LPA) such as general wards, and 73% of patients were recruited from high-priority areas (HPA) like intensive care units (ICU) or high dependency units (HDU) as mentioned in Table 2. The most common source of BSI was respiratory tract infection in 43.3% of patients, followed by gastrointestinal infections (20%) and urinary tract infection (18.7%) as mentioned in Table 2.

Among the total patients, 63.3% required respiratory support (30% required non-invasive ventilation and 33.3% required invasive mechanical ventilation) and 31% required support of inotropes. Among the BSI cases, 38% had one co-morbidity and 18% had more than one co-morbidity. Diabetes mellitus was the most common co-morbidity seen in 34% of patients, followed by chronic kidney disease (18%) and chronic obstructive pulmonary disease: COPD (8.7%). The details of co-morbidities are presented in Table 2.

SIRS score of ≥2 was seen in 91.3% of patients. The mean SIRS score was 2.55 ± 0.9. Quick sequential organ failure assessment SOFA (qSOFA) score of ≥2 was seen in 49.3% of individuals. The mean qSOFA score was 1.5 ± 1.1. The median sequential organ failure assessment (SOFA) score was 5 with an IQR of 3 to 9. Thirty-six percent of patients had a SOFA score

Table 2. Baseline Demographic and Clinical variables of the patients (n=150)

Variable	N (%)
Age in years	
Age in years (Mean ± SD1)	48.2 ± 18.4
Gender	
Male	94 (62.7)
Male age in year (Mean ± SD)	49.4 ± 18.6
Female	56 (37.3)
Female age in year (Mean ± SD)	46.2 ± 18.1
Source of infection	
Respiratory tract infection	65 (43.3)
Gastrointestinal infection	30 (20)
Urinary tract infection	28 (18.7)
Skin and soft tissue infection	18 (12)
Others	9 (6)
Type of care	
Low-priority area (Ward)	41 (27.3)
High-priority area (HPA)	
High-dependency unit (HDU)	51 (34.0)
Intensive care unit (ICU)	58 (38.7)
Respiratory Support	
No support	55 (36.7)
Oxygen support/Non-invasive ventilation	45 (30)
Invasive ventilation	50 (33.3)
Inotrope Support	47 (31.3)
Co-morbidities	
Presence of co-morbidities	84 (56)
Diabetes mellitus	51 (34)
Chronic renal failure	27 (18)
COPD2	13 (8.7)
Cirrhosis	9 (6)
Heart failure	6 (4)
Cancer	6 (4)
Immunosuppression	2 (1.3)
HIV infection	0 (0)
No co-morbidities	66 (44)
1 co-morbidity	57 (38)
≥2 co-morbidities	27 (18)
Received antibiotics in previous 30 days	17 (11.3)

[1]SD - Standard Deviation

[2]COPD - Chronic Obstructive Pulmonary Disease

of ≥7 with a mean SOFA score of 6.0 ± 4.6.

Among the organisms under study, 69.9% of patients had BSI with WPP from the critical category. *Escherichia coli* was identified as the most common cause of BSI (24%) followed by *Klebsiella pneumoniae* (17.3%), *Acinetobacter baumannii* (16%), *Staphylococcus aureus* (12.7%), *Pseudomonas aeruginosa* (12%), *Enterococcus faecium* (9.3%) and *Salmonella* spp. (8.7%) among patients. The incidence of MDR organisms amongst BSI was 59.3%. *K. pneumoniae* had the highest incidence of MDR (73%), followed by *Enterococcus* (71.4%), followed by *E. coli* (66.7%) and *Acinetobacter baumannii* (62.5%) the details of which is mentioned in Table 3.

The thirty-day mortality in patients with BSI with WPP was 36%. Advanced age was associated with significantly higher mortality (p=0.016). The mean age of patients in the mortality group was 53.3 ± 16.1 as compared to 45.4 ± 19.1 in patients who survived on day 30. Among cases with various sources of BSI, the highest incidence of mortality was found in respiratory tract infections (46%), followed by skin-soft tissue infections (38.9%), abdominal infections (36.7%), and cardiovascular infections (33.3%). Respiratory tract infection was also responsible for the highest absolute mortality and was responsible for 55.6% of all mortalities. This was followed by gastrointestinal infection (20.4%), skin and soft tissue infection (13%) and urinary tract infection (5.6%) as in Fig. 2.

Among the patients who were on mechanical ventilation, 70% ultimately succumbed by day 30. Among the patients who required inotropes, 76.5% of them died by day 30. A higher qSOFA score was associated with higher mortality. The mean qSOFA score in patients who died by day 30, was 2.35 ± 0.80 as compared to 1.02 ± 0.94 in survivors. This difference was statistically significant (p-value: <0.001). The SIRS score in the mortality group; 2.85 ± 0.74, was significantly higher as compared to the score in those who survived; 2.38 ± 0.94 (p-value: 0.046). The mean SOFA score was 10.1 ± 4.2 in patients who died by day 30, as compared to a SOFA score of 3.7 ± 2.9 in the survivors. A higher SOFA score was significantly associated with higher mortality (p-value: <0.001). Higher values of all the components of SOFA score were associated with significantly increased mortality except for the renal component (Table 4).

The descending order of association of predictors for mortality was the presence of MDR organism (OR-4.25; CI:2.01-9.57), isolation of critical category of WPP (OR-3.77; CI:1.67-9.41), higher SOFA score (OR-1.52; CI:1.33-1.78). The descending order of association of predictors for prolonged hospital stay was a critical category of WPP (OR-2.80; CI:1.36-5.74),

Table 3. Causative organism and incidence of sepsis

Organism	Total N (%)	MDR[1] N(%)	Characteristics: N (%)
Priority pathogen	150 (100)	89 (59.3)	_
Acinetobacter baumannii	24 (16)	15 (62.5)	Carbapenem-resistant: 17 (70.8)
Pseudomonas aeruginosa	18 (12)	9 (50)	Carbapenem-resistant: 8 (44.4)
Escherichia coli	36 (24)	24 (66.7)	Carbapenem-resistant: 9 (25)
Klebsiella pneumoniae	26 (17.3)	19 (73)	Carbapenem-resistant: 15 (57.6)
Enterococcus faecium	14 (9.3)	10 (71.4)	Vancomycin-resistant: 2 (14.3)
Staphylococcus aureus	19 (12.7)	12 (63.2)	Methicillin-resistant: 5 (26.3)
Salmonella spp.	13 (8.7)	0 (0)	Ceftriaxone-resistant: 0 (0)

[1] MDR – Multi-Drug Resistant

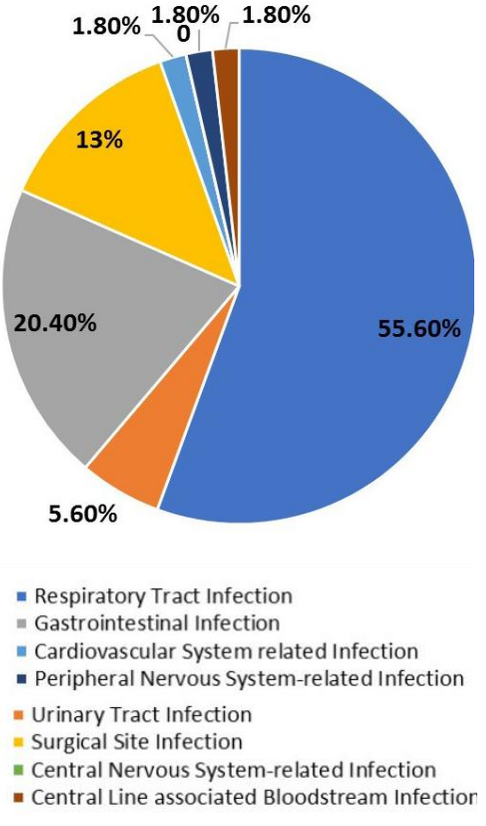

Fig. 2. Distribution of mortality by the source of infection

MDR organisms (OR-2.21; CI:1.18-4.12), higher SOFA score (OR-1.25; CI:1.08-1.47).

DISCUSSION

Of the 150 participants, the mean age was observed to be 48.2 ± 18.4 years with a male predominance (62.7%). Similarly in a Japanese cohort, Hattori et al. (2018, Japan) stated male predominance of 63.6% (15). However, it was in contrast to the study of Rudd et al. (2020) which had near equal distribution with 46.5% males (2). In our study, the most common source of infection was respiratory tract infection (43.3%), followed by gastrointestinal infection (20%), urinary tract infection (18.6%), and skin and soft tissue infection (12%). This was similar to the study of Chatterjee et al. (2017, India) who reported the majority of sepsis cases were due to respiratory infection (53.3%) followed by gastrointestinal infections (14.9%), and skin-soft tissue infection (12.9%) (19). Similarly in the study by Cao et al. (2021, Chi-

Table 4. Association of SOFA components with mortality

SOFA components	No mortality at day 30	Mortality on day 30	p-value
PaO2[1]/FiO2[2]	373.4 ± 85.8	258.7 ± 104.5	<0.001
PaO2/FiO2 SOFA[3]	0.71 ± 0.94	2 ± 1.16	
Platelet count	199.6 ± 126.6	151.4 ± 131.0	0.008
Platelet SOFA	0.68 ± 1.13	1.39 ± 1.35	
S. Bilirubin	1.2 ± 1.5	3.4 ± 6.7	0.020
Bilirubin SOFA	0.35 ± 0.74	0.96 ± 1.35	
MAP[4]	81.8 ± 13.3	73.0 ± 7.0	<0.001
MAP SOFA	0.47 ± 1.18	2.5 ± 1.92	
CNS	13.4 ± 3.1	9.4 ± 4.2	<0.001
CNS SOFA	0.67 ± 1.18	2.33 ± 1.39	
Creatinine	1.9 ± 2.3	2.3 ± 2.6	0.142
Creatinine SOFA	0.92 ± 1.33	1.18 ± 1.33	
Total SOFA	3.7 ± 2.9	10.1 ± 4.2	<0.001

[1] PaO2 – Partial Pressure of Oxygen
[2] FiO2 – Fraction of Inspired Oxygen
[3] SOFA – Sequential Organ Failure Assessment
[4] MAP – Mean Arterial Pressure

na), respiratory infection was the most common cause of sepsis (65%), followed by abdominal infection (35.4%) and urinary tract infection (8.8%) (20).

Our study recruited 27% of patients from the low-priority area (LPA), and the rest of the cases were recruited from HPA (34% from HDU and 39% from ICU). This was in contrast to most of the other studies which had patients only from the HPA-like intensive care unit (ICU) (21). Our study was more akin to real-life hospital setting scenario, unlike that of others which were carried out predominantly in HPA (19, 21). We identified the presence of comorbidities in our patients according to the EPIC-II trial (11). In our study, 44% had no comorbidity, 38% had one comorbidity and 18% had more than one comorbidity. In a study by Holmbom et al. (2016, Sweden), 48.9% of individuals had no comorbidities, 28.7% of individuals had one comorbidity, 15.5% had two comorbidities and 6.9% of individuals had more than two comorbidities (6). In our study, Diabetes Mellitus was the most common comorbidity which was anticipated, due to the high prevalence of Diabetes in India unlike the study by Holmbom et al. where malignancy was the most common comorbidity followed by diabetes mellitus (6).

The mean SIRS score in our study was 2.55 ± 0.90 and 137 patients (91.3%) were having SIRS of ≥2. The mean qSOFA score in our study was 1.5 ± 1.1. A total of 74 patients (49.3%) had a qSOFA score of ≥2. In our study, the mean SOFA score was 6.0 ± 4.6. The median SOFA score in our study was 5 with an IQR of 3-9. In study of Baykara et al. (2018, Turkey), the median SOFA score was 7 with an IQR of 5 to 11 (21). A lower median SOFA score was seen in our study as it also included patients from LPA in addition to HPA as compared to the study of Baykara et al. (2018), which included only ICU patients (21).

Escherichia coli was found to be the most common organism (24%) isolated in BSI in our study followed by *Klebsiella pneumoniae* (17.3%), *Acinetobacter baumannii* (16%), *Staphylococcus aureus* (12.7%), *Pseudomonas aeruginosa* (12%), *Enterococcus* spp. (9.3%), *Salmonella* spp. (8.7%). In a similar study by Holmbom et al. (2016, Sweden) the maximum number of patients had BSI due to *Escherichia coli* followed by *Staphylococcus aureus*, *Enterococcus*, and *Klebsiella pneumoniae* (6). In a similar study by Baykara et al. (2018, Turkey), *Acinetobacter baumannii* was the most common isolated organism (33.7%) followed by *Pseudomonas aeruginosa* (16.4%) and *Klebsiella pneumoniae* (16%) (21). However, another study from India by Chatterjee et al. (2017) revealed the maximum prevalence of *Acinetobacter baumannii* (21.2%) followed by *Pseudomonas aeruginosa* (16.9%), *Klebsiella pneumoniae* (15.4%) and *Escherichia coli* (15.4%) in BSI (19).

In our study, 59.3% of organisms were found to be MDR. Among the Gram-negative bacilli (GNB), 69% of Enterobacteriaceae, 62.5% of *Acinetobacter baumannii*, 50% of *Pseudomonas aeruginosa* were MDR. Among the Gram-positive cocci (GPC),71.4% of *Enterococcus* spp. and 63.2% of *Staphylococcus aureus* were MDR. *Acinetobacter baumannii* (71%), *Pseudomonas aeruginosa* (44.4%) and *Enterobacteriaceae* (38.7%) were carbapenem-resistant. Among *Staphylococcus aureus* isolates, 26.3% were methicillin-resistant and 14.3% of *Enterococcus* spp. were vancomycin-resistant. In the study by Baykara et al. from Turkey (2018), about 74.8% of *Acinetobacter* isolates, 39.0% of *Klebsiella* isolates, and 26.5% of *Pseudomonas* isolates were resistant to carbapenems. The same study identified, 2.7% of *Klebsiella* isolates, 2.6% of *Pseudomonas* isolates, and 2.1% of *Acinetobacter* isolates as colistin-resistant and 75.4% of the *Staphylococcus aureus* isolates were identified as methicillin-resistant (MRSA) (21).

In our study, 54 out of 150 patients died, with a mortality percentage of 36%. The mean age of non-survivors was 53.3 ± 16.1 years. According to Holmbom et al. (2016, Sweden), advanced age had a risk ratio of 1.04 for mortality (6). In our study, among the non-survivors, 68.5% were male but this sex difference was not statistically significant. Holmbom et al. (2016, Sweden) had published a risk ratio of 0.95 among the female sex, indicative of a slight protective effect (6).

The major cause of mortality was respiratory tract infections (55.6%), followed by gastrointestinal infections (20.4%) and, skin-soft tissue infections (13.0%). This was similar to the study by Chatterjee et al. (2017, India), with respiratory tract infections leading to 53.3% of BSI, followed by gastrointestinal infections (43%), and urinary tract infections (43%) (19). In the study by Baykara et al. (2018, Turkey), 71.6% of all BSI were due to respiratory infections followed by UTI (7.8%) and gastrointestinal infection (5.6%) (21).

In our study, the presence of only one comorbid-

ity had an odds ratio of 1.64 (CI:0.53-5.16), and two or more comorbidities had an odds ratio of 1.55 (CI:0.35-6.79) for mortality. The presence of diabetes was associated with increased mortality by 16% (p-value: 0.043). However, in the study of Holmbom et al. (2016, Sweden), the presence of one comorbidity was associated with a relative risk of 1.56 of having 30-day mortality (CI:1.48-1.65), and the presence of two or more co-morbidities was associated with a relative risk of 1.89 times of having a 30-day mortality (CI:1.79-2) (6). The association of co-morbidities in our study was not statistically significant, which may be attributable to a comparatively smaller sample size.

On multivariate analysis, for the cases of survivors and non-survivors, isolation of MDRO (OR-4.25, CI:2.01-9.57, p<0.001), isolation of WPP (OR-3.77, CI:1.67-9.41, p=0.002) and higher SOFA score (OR-1.52, CI:1.33-1.78, p<0.001) were associated with higher mortality independently and aggregately. A comparative analysis of various factors and determinants of outcomes of sepsis stratified by the organism, source, sex and the scores has been depicted below in Table 5.

Even after an exhaustive literature search, we could not find any other study akin to that of ours for comparison. The limitations of our study are plenty. The study was conducted in a single centre and the BSI was not differentiated to community acquired or hospital acquired. The study identified 30-day mortality rate and predictors of mortality among BSI patients.

Table 5. A comparative account of factors associated in patients with BSI (30-day mortality): Present study cohorts with other countries

Country	30-day Mortality (%)	Most common organism isolated	Gender predominance	Mean age (years)	Most common source of infection	Most common comorbidity	Mortality trend with age	SOFA	Study group
Japan	15.2	*Staphylococcus aureus*	Male (63.6 %)	82.8	UTI	Malignancy	Increase	8.2 ± 4.4	Haruka et al., 2018
Norway	12.9	NA	Female (53 %)	48.5	Pneumonia	NA	Increase	NA	Liyanarachi et al., 2022
Canada	17	*Escherichia coli*	Male (55%)	NA	NA	NA	Increase	NA	Verway et al., 2022
Sweden	12.8	*Escherichia coli*	Male (54%)	70	NA	Malignancy	Increase	NA	Holmbom et al., 2020
India	36 (with WPP)	*Acinetobacter baumannii*	Male (62.7%)	48.2	RTI	Diabetes mellitus	Increase	10.1 ± 4.2	Current Study

CONCLUSION

The study was conducted in a real-life hospital setting with patients from the general wards, high dependence unit (HDU), and intensive care unit (ICU). This study emphasized that patients presenting with higher age and higher qSOFA score / SIRS at presentation had higher mortality among patients with BSI with WPP. Those patients with BSI with WPP, treated with mechanical ventilation and inotropes had poor prognoses and higher 30-day mortality. Isolation of critical category of WPP (*Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*), MDRO and increased SOFA score had increased 30-day mortality independently and aggregately.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016; 315: 801-810.
2. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. *Lancet* 2020; 395: 200-211.
3. Viscoli C. Bloodstream Infections: The peak of the iceberg. *Virulence* 2016; 7: 248-251.
4. Kern WV, Rieg S. Burden of bacterial bloodstream infection-a brief update on epidemiology and significance of multidrug-resistant pathogens. *Clin Microbiol Infect* 2020; 26: 151-157.
5. Prowle JR, Echeverri JE, Ligabo EV, Sherry N, Taori GC, Crozier TM, et al. Acquired bloodstream infection in the intensive care unit: incidence and attributable mortality. *Crit Care* 2011; 15: R100.
6. Holmbom M, Giske CG, Fredrikson M, Östholm Balkhed Å, Claesson C, Nilsson LE, et al. 14-Year Survey in a Swedish County Reveals a Pronounced Increase in Bloodstream Infections (BSI). Comorbidity - An Independent Risk Factor for Both BSI and Mortality. *PLoS One* 2016; 11(11): e0166527.
7. Laupland KB, Davies HD, Church DL, Louie TJ, Dool JS, Zygun DA, et al. Bloodstream infection-associated sepsis and septic shock in critically Ill adults: A population-based study. *Infection* 2004; 32: 59-64.
8. Bharadwaj R, Bal A, Kapila K, Mave V, Gupta A. Blood stream infections. *Biomed Res Int* 2014; 2014: 515273.
9. Asokan GV, Ramadhan T, Ahmed E, Sanad H. WHO Global Priority Pathogens List: A bibliometric analysis of medline-PubMed for knowledge mobilization to Infection prevention and control practices in Bahrain. *Oman Med J* 2019; 34: 184-193.
10. Breijyeh Z, Jubeh B, Karaman R. Resistance of Gram-negative bacteria to current antibacterial agents and approaches to resolve It. *Molecules* 2020; 25: 1340.
11. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA* 2009; 302: 2323-2329.
12. Lambden S, Laterre PF, Levy MM, Francois B. The SOFA score-development, utility and challenges of accurate assessment in clinical trials. *Crit Care* 2019; 23: 374.
13. Barbara P, Graziano C, Caputo W, Litvak I, Battinelli D, Hahn B. The quick sequential organ failure assessment (qSOFA) identifies septic patients in the out-of-hospital setting. *Am J Emerg Med* 2018; 36: 1022-1026.
14. Chakraborty RK, Burns B. Systemic Inflammatory Response Syndrome. In Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Apr 12]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK547669/
15. Hattori H, Maeda M, Nagatomo Y, Takuma T, Niki Y, Naito Y, et al. Epidemiology and risk factors for mortality in bloodstream infections: A single-center retrospective study in Japan. *Am J Infect Control* 2018; 46(12): e75-e79.
16. Verway M, Brown KA, Marchand-Austin A, Diong C, Lee S, Langford B, et al. Prevalence and mortality associated with bloodstream organisms: a population-wide retrospective cohort study. *J Clin Microbiol* 2022; 60(4): e0242921.
17. Liyanarachi KV, Solligård E, Mohus RM, Åsvold BO, Rogne T, Damås JK. Incidence, recurring admissions and mortality of severe bacterial infections and sepsis over a 22-year period in the population-based HUNT study. *PLoS One* 2022; 17(7): e0271263.
18. OpenEpi - Toolkit Shell for Developing New Applications [Internet]. [cited 2023 Mar 15]. Available from: https://www.openepi.com/SampleSize/SSPropor.htm
19. Chatterjee S, Bhattacharya M, Todi SK. Epidemiology of adult-population sepsis in India: A single center 5 year experience. *Indian J Crit Care Med* 2017; 21: 573-577.
20. Cao L, Xiao M, Wan Y, Zhang C, Gao X, Chen X, et al. Epidemiology and mortality of sepsis in intensive care units in prefecture-level cities in Sichuan, China: a prospective multicenter study. *Med Sci Monit* 2021; 27: e932227.
21. Baykara N, Akalın H, Arslantaş MK, Hancı V, Çağlayan Ç, Kahveci F, et al. Epidemiology of sepsis in intensive care units in Turkey: a multicenter, point-prevalence study. *Crit Care* 2018; 22: 93.