Original Article

Epidemiology of Bloodstream Infections and Antimicrobial Susceptibility Pattern in ICU and Non-ICU Wards: A Four-Year Retrospective Study in Isfahan, Iran

Nazila Kassaian[1], Shadnosh Nematbakhsh[2], Mohammadreza Yazdani[2], Soodabeh Rostami[1], Zary Nokhodian[2], Behrooz Ataei[1]

[1]Nosocomial Infection Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, [2]Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: Bloodstream infections (BSIs) are one of the causes of morbidity and mortality in hospitalised patients. This study evaluated BSI's incidence, trend, antimicrobial susceptibility patterns and mortality in AL Zahra Hospital in Isfahan, Iran.

Materials and Methods: This retrospective study was conducted in AL Zahra Hospital from March 2017 to March 2021. The Iranian nosocomial infection surveillance system was used for data gathering. The data included demographic and hospital data, type of bacteria, and antibiotic susceptibility findings and were analysed in SPSS-18 software.

Results: The incidence of BSIs was 1.67% and 0.47%, and the mortality was 30% and 15.2% in the intensive care unit (ICU) and non-ICU wards, respectively. In the ICU, the mortality was correlated with the use of the catheter, type of organism and year of study, but in non-ICU, correlated with age, gender, use of the catheter, ward, year of study and duration between the incidence of BSIs and discharging/death. *Staphylococcus epidermidis*, *Acinetobacter* spp. and *Klebsiella* spp. were the most frequent germs isolated in all wards. Vancomycin (63.6%) and Gentamycin (37.7%) for ICU and Vancomycin (55.6%) and Meropenem (53.3) for other wards were the most sensitive antibiotics.

Conclusion: Despite the few rate of BSI in the last four years in AL Zahra Hospital, our data showed that its incidence and mortality in the ICU ward are significantly more than in other hospital wards. We recommend prospective multicentre studies to know the total incidence of BSI, local risk factors and patterns of pathogens causing BSI.

Keywords: Drug resistance, incidence, intensive care units, non-intensive care units, sepsis

Address for correspondence: Dr. Zary Nokhodian, Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, 8183676119, Isfahan, Iran.
E-mail: Nokhodian@yahoo.com
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Introduction

Bloodstream infections (BSIs) are defined by the presence of various pathogenic microorganisms in the bloodstream, primarily bacteria and fungi. Bloodstream infections are one of the most causes of morbidity and mortality in hospitalised patients, particularly in higher ages and immunocompromised patients.[1-4] According to the reported data, due to the increasing invasive procedures and the misuse of corticosteroids and antibacterial drugs, the incidence of BSIs has increased in recent years. An estimated 30 million BSIs occur annually in the world, which causes 6 million deaths.[5,6] In developing countries, the proportion of patients with BSIs reported ranges from 11% to 28%.[1,7,8] At the same time, the incidence rate of BSIs in North America ranges between 113 and 204 per 100,000 person-years.[9] Studies performed in European countries

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show a variable trend; sometimes, it shows an increase, and sometimes, it is accompanied by a decrease.[4,10,11] Several factors, such as demographic features, immunodeficiency and the prevalence of multi-drug-resistant pathogens, influence the epidemiology of BSIs. The most prevalent BSIs are related to intravascular and invasive devices.[12,13]

Bloodstream infections are considered by the presence of fungal and bacterial germs in the bloodstream that causes an inflammatory reaction and is often accompanied by alteration of hemodynamic parameters and clinical signs and symptoms, with laboratory findings.[14,15] These germs may include Gram-negative bacteria (such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella* spp, etc.) and/or Gram-positive bacteria (such as *Staphylococcus aureus*, *Streptococcus pneumonia,* etc.).[16]

Continuously monitoring antibiotic susceptibility and resistance patterns the bacterial pathogens and periodically publishing reports is vital to guide empiric antibiotic treatment strategies and prevention plans to decrease mortality and morbidity of BSIs in hospitals. Unfortunately, in Iran, such information is scarce. In a recent study in a hospital in Dezful, Iran, of 186 *Staphylococcus aureus* strains isolated from various specimens, 27.4% were methicillin-resistant *Staphylococcus aureus* (MRSA), with a 26.8% rate in the ICU.[17] Updated data is crucial to physicians and infection control committees for treatment and preventive programmes. In this study, we have retrospectively analysed and reported the epidemiological and antimicrobial susceptibility profiles of BSI patients during the past four years in AL Zahra Hospital, Isfahan, Iran.

Materials and Methods

From March 2017 to March 2021, this study was conducted in different wards of AL Zahra Hospital in Isfahan, Iran. AL Zahra Hospital is a 700-bed university hospital that integrates medical treatment, teaching and scientific research in Isfahan province and the central region of Iran.

In this retrospective study, patient demographic data and other information, including hospital admission date, inpatient ward, type and date of catheter insertion, date of development of BSIs, mortality rate, the type of microorganism isolated from blood culture and its antibiotic susceptibility pattern were collected from Iranian Nosocomial Infection Surveillance Software. The primary outcome was the incidence of BSIs. Secondary outcomes were the length of hospital stay and hospital mortality. The trends of the proportion in these four years were calculated as well.

Inclusion criteria consisted of all hospitalised patients data in the AL Zahra Hospital who developed a BSI after 48 hours of admission. The BSI's diagnosis included at least two positive blood cultures and one of the following clinical symptoms: fever (body temperature > 38°C), chills or hypotension.

Exclusion criteria comprised patients who died within the early 48 hrs of hospitalisation, the contaminated blood samples and patients with uncompleted data. One blood culture positive of the common skin commensals germs (such as *non-diphtheria Corynebacterium spp., Propionibacterium spp., coagulase-negative staphylococcus, Bacillus spp., Aerococcus spp., viridans group streptococci* and *Micrococcus spp*.) was considered as contaminated.[18]

Statistical data analysis was performed using SPSS version 18 software (SPSS Inc., Chicago, IL, USA). The BSI episodes number were described as N, and the BSI proportions among all adult-hospitalised patients were described as *N* (%). The number of microbial isolated and the composition ratios were described as *N* (%). The normal distribution of all studied parameters was checked with the Kolmogorov–Smirnov test. To compare qualitative variables between groups Chi-square test was performed. Student *t*-test was used for quantitative variables that were distributed normally, and Mann-Whitney was performed for variables that did not have a normal distribution. The two-tailed P value < 0.05 was considered significant.

This study was approved by the ethical committee of Isfahan University of Medical Sciences (Ethical code; IR.MUI.MED.REC.1399.886). The names and details of the patients remained confidential.

Results

The results were presented in two sections: ICU and non-ICU wards.

Twenty-three thousand eight hundred and seventy patients were admitted to four ICU wards, 398 (1.67%) of whom were 232 males and 166 females, with a mean age of 55.92 ± 18.24, showed BSIs. The total mean hospitalisation length was 47.16 ± 51.12 days, and the mean time between hospital admissions to the beginning of BSIs was 37.33 ± 60.89 days. The average length of catheter insertion and incidence of BSIs was 38.24 ± 53.93 days.

One hundred and two (30%) and 238 (70%) cases died and were discharged, respectively. There is no information on the death or discharge of 58 patients. The lowest number of deaths from BSIs was in 2019 ($P < 0.001$). Central venous catheter use was significantly higher in dead patients than in discharged individuals ($P < 0.001$). The type of microorganism showed a significant difference between the two groups [Table 1].

As Table 1 shows, 174 (43.72%) subjects used catheters. The length of hospitalisation and duration between admission to the hospital and BSIs incidence was significantly higher in patients who used the catheter than in the other group. The type of organism showed a significant difference between the group that used the catheter and those that did not. The type of catheter and the type of microorganisms did not show significant differences ($P = 0.275$).

As Figure 1 shows, *Klebsiella* spp. (27.1%), *S. epidermidis* (25.9%) and *Acinetobacter* spp. (25.3%) were the most

frequent germ responsible for BSIs. Antibiotic susceptibility pattern of isolated bacteria showed that the most sensitive antibiotics were Vancomycin (63.6%), Gentamycin (37.7%), Co-trimoxazole (33.6%), Amikacin (20.7%), Clindamycin (14.1%), piperacillin-tazobactam (9%), Oxacillin (7.3), Meropenem (6.5%), Penicillin and ceftazidime (5.7%).

Of 133928 cases hospitalised in different wards of AL Zahra Hospital (except ICU), 626 patients had BSIs (0.47%). In other words, the incidence rate of BSIs was 470 per 100,000 person-years.

The mean age of patients with BSIs was 55.43 ± 21.87–year olds, and 345 individuals (55.1%) were male. The total mean hospitalisation length was 26.72 ± 22.91 days, and the duration between hospitalisation and incidence of BSIs was 13.53 ± 18.91 days. The time between catheter insertion and incidence of BSIs was 24.74 ± 55.62 days, and finally, the duration between the incidence of BSIs and discharging/death was 13.24 ± 12.19 days.

Our data showed that 92 patients died, and 513 patients were discharged (no information was available on the death or discharge of 21 patients). The mean age of dead patients was significantly higher than discharged individuals ($P = 0.001$). In contrast, the duration between BSIs incidence and discharging/death was significantly lower in dead cases than in the discharged group ($P = 0.003$). Sex, use of the instruments, ward and year of study showed a significant difference between the two groups [Table 2].

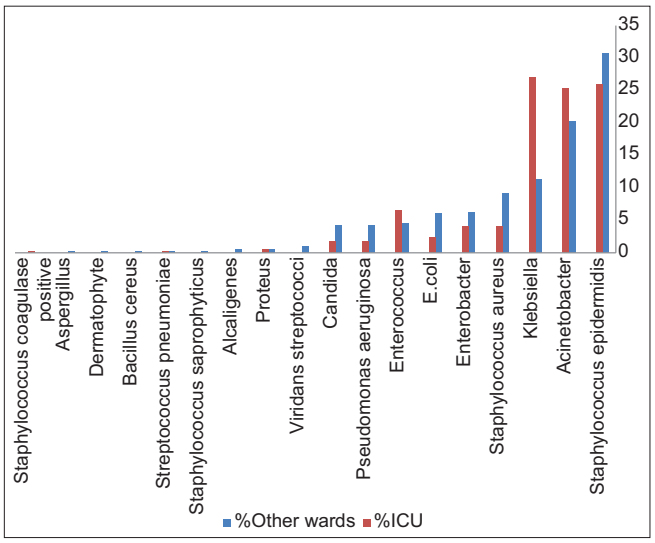

Figure 1: Organism responsible for BSI

Table 1: Studied variables in BSIs cases based on outcomes and use of the catheter in ICU wards

Variables	Outcome			Catheter		
	Discharge 238	Dead 102	*P**	Yes 174	No 224	*P*
Age (year)	55.83±18.78	57.21±16.15	0.495	55.23±18.40	56.46±18.14	0.504
Hospitalisation length (day)	47.07±44.15	47.38±64.79	0.959	63.57±65.75	38.67±39.13	<0.001
Duration between hospitalisation and incidence of BSIs (day)	29.44±39.55	37.21±62.41	0.248	53.27±79.39	24.95±36.85	<0.001
Duration between inserting catheter and incidence of BSIs (day)	28.90±31.59	33.98±39.16	0.441	-	-	-
Sex						
Male	138 (58.0%)	59 (57.8%)	0.981	95 (54.6%)	137 (61.2%)	0.188
Female	100 (42.0%)	43 (42.2%)		79 (45.4%)	87 (38.8%)	
Year						
2017	30 (56.6%)	23 (43.4%)	<0.001	70 (40.2%)	2 (0.9%)	<0.001
2018	32 (47.8%)	35 (52.2%)		100 (57.5%)	6 (2.7%)	
2019	76 (93.8%)	5 (6.2%)		3 (1.7%)	78 (34.8%)	
2020	100 (71.9%)	39 (28.1%)		1 (0.6%)	138 (61.6%)	
Catheter						
Central venous catheter	38 (44.2%)	48 (55.8%)		-	-	-
Peripheral venous catheter	24 (80.00%)	6 (20.00%)	<0.001			
Without catheter	176 (78.6%)	48 (21.4%)				
Organism						
Acinetobacter	50 (21.0%)	36 (35.3%)	0.004	33 (19.0%)	63 (28.1%)	0.002
Staphylococcus epidermidis**	75 (31.5%)	13 (12.7%)		29 (16.7%)	70 (31.3%)	
Enterobacter	12 (5.0%)	2 (2.0%)		10 (5.7%)	7 (3.1%)	
Pseudomonas aeruginosa	5 (2.1%)	1 (1.0%)		3 (1.7%)	4 (1.8%)	
Candida	4 (1.7%)	2 (2%)		5 (2.9%)	2 (0.9%)	
Enterococcus	18 (7.6%)	4 (3.9%)		20 (11.5%)	11 (4.9%)	
Klebsiella	58 (24.4%)	34 (33.3%)		60 (34.5%)	54 (24.1%)	
Staphylococcus aureus	8 (3.4%)	6 (5.9%)		6 (3.4%)	8 (3.6%)	
E. coli	6 (2.5%)	2 (2%)		5 (2.9%)	3 (1.3%)	
Other	2 (0.8%)	2 (2.0%)		3 (1.7%)	2 (0.9%)	

*$P<0.05$ was considered significant. **Confirmed with two sample

One hundred and eleven (17.7%) patients used catheters. The duration between BSIs incidence and discharging/death was significantly higher in patients who used the catheter than in the other group. Table 2 shows that the type of organism and the hospital ward significantly differed between the two groups. We did not find a significant difference between the type of catheter and the type of microorganisms ($P = 0.131$).

Blood culture results showed that the most frequent germ responsible for BSIs were *S. epidermidis* (30.7%), *Acinetobacter* spp. (20.3%) and *Klebsiella* spp. (11.3%) [Figure 1].

Antibiotic susceptibility pattern of isolated bacteria showed that the most sensitive antibiotics were Vancomycin (55.6%) and Meropenem (53.3%), which was followed by Cefepime (38.8%), Ciprofloxacin (31.3), Ceftazidime (30.6%), Oxacillin and Clindamycin (18.4%), Erythromycin (12.1%) and Penicillin (6.7%).

Discussion

According to our results, the incidence of BSIs in the ICU and non-ICU wards were 1.67% and 0.47%, respectively. Other studies in Iran reported different results. In a similar study in Shiraz, southern Iran, the total prevalence of BSI was 1.3% (4.1% for ICU and 0.4–6.4% for other wards).[19] In another study in Iran, the frequency of the BSIs in ICU was 14%, and in total was 16.3%.[20] In other countries, the BSI rate was 6 per 10000 patients per day in Queensland.[21]

Table 2: Studied variables in BSIs cases based on outcomes and use of the catheter in Non- ICU wards

Variables	Outcome			Catheter		
	Discharge ($n=513$)	Dead ($n=92$)	*P**	Yes (111)	No (515)	*P*
Age (year)	54.27±21.95	62.55±21.06	0.001	56.45±21.47	55.22±21.97	0.605
Hospitalisation length (day)	26.94±23.65	25.47±18.32	0.573	30.22±27.26	26.07±21.97	0.164
Duration between hospitalisation and incidence of BSIs (day)	13.07±19.19	15.74±15.81	0.209	14.03±18.97	13.44±18.92	0.765
Duration between inserting catheter and incidence of BSIs (day)	27.22±62.00	21.00±40.68	0.728	-	-	-
Duration between incidence of BSIs and discharging/death (day)	13.87±12.19	9.73±11.61	0.003	17.13±18.16	12.52±10.59	0.018
Sex						
Male	239 (46.6%)	32 (34.8%)	0.036	54 (19.2%)	227 (80.8%)	0.38
Female	274 (53.4%)	60 (65.2%)		57 (16.5%)	288 (83.5%)	
Year						
2017	60 (84.5%)	11 (15.5%)	<0.001	73	12	<0.001
2018	191 (82%)	42 (18%)		33	205	
2019	150 (95.5%)	7 (4.5%)		5	153	
2020	112 (77.8%)	32 (22.2%)		0	145	
Catheter						
Central venous catheter	49 (80.3%)	12 (19.7%)	0.019	-	-	-
Peripheral venous catheter	25 (100%)	0				
Arterial catheter	2 (66.7%)	1 (33.3%)				
Other	6 (100%)	0				
Without catheter	431 (84.5%)	79 (15.5%)				
Organism						
Acinetobacter	98 (19.1%)	27 (29.3%)	0.13	14 (12.6%)	113 (21.9%)	<0.001
Staphylococcus epidermidis**	168 (32.7%)	20 (21.7%)		40 (36.0%)	152 (29.5%)	
Enterobacter	36 (7%)	3 (3.3%)		1 (0.9%)	38 (7.4%)	
Pseudomonas aeruginosa	19 (3.7%)	7 (7.6%)		11 (9.9%)	16 (3.1%)	
Candida	20 (3.9%)	5 (5.4%)		5 (4.5%)	21 (4.1%)	
Enterococcus	21 (4.1%)	6 (6.5%)		7 (6.3%)	22 (4.3%)	
Klebsiella	59 (11.5%)	9 (9.8%)		6 (5.4%)	65 (12.6%)	
Staphylococcus aureus	45 (8.8%)	8 (8.7%)		12 (10.8%)	45 (8.7%)	
E. coli	33 (6.4%)	4 (4.3%)		8 (7.2%)	30 (5.8%)	
Other	14 (2.7%)	3 (3.3%)		7 (6.3%)	13 (2.5%)	
Ward						
Neurology	47 (9.2%)	13 (14.1%)	0.032	10 (9%)	52 (10.1%)	0.002
Pediatrics	13 (2.5%)	0		8 (7.2%)	5 (1.0%)	
Surgery	160 (31.2%)	29 (31.5%)		30 (27.0%)	166 (32.2%)	
Internal medicine	269 (52.4%)	44 (47.8%)		58 (52.3%)	266 (51.7%)	
Obstetrics and Gynecology	13 (2.5%)	0		1 (0.9%)	12 (2.3%)	
Infectious	11 (2.1%)	6 (6.5%)		4 (3.6%)	2.7%)	

*P<0.05 was considered significant. **Confirmed with two sample

Chmielarczyk *et al*.[22] reported 279 (76.9%) from 363 patients admitted to ICU, 382 (68.6%) from 557 patients in surgical units, and 3557 (44.6%) from 7979 patients in other units had BSIs. Also, the prevalence of BSI was 17.2% in Rome, Italy.[23] Different factors, such as various research methods (for example, teaching or non-teaching hospital), different programmes for the prevention and control of diseases and the level of health services in different countries could explain different results. The incidence of BSIs in our study was lower than in other studies, even compared to similar studies conducted in Iran. Iranian Nosocomial Infection Surveillance Software was designed based on a guideline set by the health ministry in 2007, and BSIs are a fundamental and vital infection recorded in it. Our data show that more research needs to assess if the incidence of infection is low or if there is a problem in detecting and recording the infection. Of course, it should be noted that the programme does not have a research base and is for routine surveillance for record data.

Our data showed that the incidence of BSIs in the ICU is higher than in non-ICU wards, as in other studies.[19,20,22] It can be because hospitalised patients in ICU are more susceptible than other patients and are hospitalised for a more extended period.

Respectively, 30% and 15.2% of ICU and non-ICU patients died during the study. A study by Hattori *et al*.[24] showed that out of 2,105 patients with BSIs, 319 died, and the 30-day mortality rate was 15.2%. The 7, 30, and 90-day mortality rates in BSIs patients were 12.11%, 25.17%, and 36.13%, respectively, in a hospital in Italy.[25] The total mortality rate of BSI was 15.3% in Ireland.[26] Although mortality rates show different results in various studies, all reports presented BSIs as a severe disease that can be life-threatening. In our study, a decrease was seen in the death percentage in 2019; the reason is unknown to us.

Over 78% of patients who did not use catheters survived. A meta-analysis study with 18 articles and 1976 cases documented that using catheters in patients with BSIs increases the risk of death.[27] It is expected because using the catheter increases the infection risk.

Unlike ICU, in non-ICU wards, a significant relationship was seen between mortality and age. Other research showed that the mortality rate of BSIs was higher in older people.[12] Many studies described age as a risk factor for nosocomial infections, especially aged extremities. Very old patients are considered the most vulnerable and susceptible to immune system dysfunction.[28]

In the present study, the mortality was more in women than men in non-ICU wards. In a study conducted in Minnesota, USA, no differences were observed between sex and mortality rate[23,29]. In two other researches, the mortality rate was more in men than in women.[12,30] Some studies believe the association between sex and mortality rate is probably multifactorial; physiological and behavioural factors play an essential role in the difference.[31]

The present study revealed a significant relationship between mortality and the type of microorganism in ICU. The most frequent pathogens were isolated *Acinetobacter* spp., *Klebsiella* spp. and *S. epidermidis*. Coagulase-negative *staphylococci*, *S. aureus* and *Klebsiella* spp. were the commonly isolated BSIs pathogens in ICU and non-ICU wards in S˘uljagic's study.[32] In a study in Italy, coagulase-negative *staphylococci*, *K. pneumonia* and *A. baumannii* were the most frequent bacteria. Their results revealed a significant association between *K. pneumonia* and death.[33] *E. coli, S. aureus*, and *Streptococcus* species were the common microorganisms in research in Japan.[24] In a study on hospitalised patients in Isfahan, out of 72 confirmed *P. aeruginosa* isolates, 50% were from ICU.[34] In studies conducted in different hospitals and health centres, the types of bacteria isolated from nosocomial infections are different, which can be caused by the different microbial ecosystems in each hospital. In our study, hospitalisation length, duration between hospitalisation and incidence of infection in ICU, and duration between the incidence of BSIs and discharging/death in non-ICU patients were dominant risk factors.

Due to the study's retrospective design, we had some limitations. The quality of recorded data might have been affected. For example, we could not determine whether the infection was caused by the catheter or another factor in the patients who used a catheter.

Conclusions

The main results of this study showed that the reported BSI in the last four years in AL Zahra Hospital is severely lower than the actual rate. On the other hand, our data demonstrated that the incidence of BSIs and mortality in the ICU wards are significantly higher than in other hospital wards. We recommend a validation study to get the exact number of infections in the hospital. The prospective multicentre studies also help us to know the total incidence of BSI and local risk factors and patterns of pathogens causing BSI. Without a doubt, infection control programmes are only possible by knowing the exact number of cases.

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Conflicts of interest

There are no conflicts of interest.

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