

Clinical characteristics and bloodstream infection pathogens by gram-negative bacteria in different aged adults

A retrospective study

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Abstract

This study aims to determine the characteristics and distribution of pathogenic bacteria in bloodstream infections (BSIs) by gram-negative bacteria in adults. One hundred seventy-one adult patients with BSIs who were treated at the Affiliated Hospital of Chengde Medical College between January 2018 and January 2020 were included in this study. The patients were assigned to the young- and middle-aged group and elderly group based on age. General patient data were analyzed. More elderly patients had BSIs and gram-negative bacteria than young- and middle-aged patients. The incidence of underlying diseases in elderly patients was significantly higher than the young- and middle-aged patients ($P < .01$). The composition of *Brucella* spp. was significantly different between the elderly group and young- and middle-aged group ($P < .05$). There were significantly more gallbladder infections in the elderly group than the young- and middle-aged group, and significantly fewer elderly patients had no definite infection sites than the young- and middle-aged group ($P < .05$). The incidence of complications and in-hospital mortality in the elderly group was higher than the young- and middle-aged group ($P < .05$). BSIs caused by gram-negative bacteria mainly involved elderly patients. BSIs were characterized by complications and a poor prognosis, as well as pathogenic bacteria and primary infection sites.

Abbreviations: BSIs = bloodstream infections, *E coli* = *Escherichia coli*.

Keywords: age, bacteremia, bloodstream infection, gram-negative bacteria, prognosis, underlying disease

1. Introduction

A bloodstream infection (BSI) is a severe infectious disease with high morbidity and mortality rates.^[1] Data from the National Center for Health Statistics (NCHS) showed that bacteremia ranks 10th as a cause of mortality in the United States, thus exerting a great impact on human health and leading to significant economic loss. Gram-negative bacteria are the most common pathogens in BSIs. Data from the National Bacterial Resistance Monitoring Network showed that the proportion of gram-negative bacteria was 51.8% among common pathogens in national clinical blood samples between 2014 and 2019. Currently, several studies have shown that the incidence of BSIs,^[2,3] and risk of hospitalization^[4] and mortality^[5,6] increase with age. Relevant studies also analyzed risk factors of death in elderly patients with BSIs; however, few studies have analyzed the clinical characteristics and distribution of pathogenic bacteria in BSIs by gram-negative bacteria in different aged adults. The present study determined the

clinical characteristics and distribution of pathogenic bacteria in 171 patients with BSIs by gram-negative bacteria compared the difference between young- and middle-aged patients and elderly patients, and provided a reference for diagnosis, treatment, and management of patients with BSIs caused by gram-negative bacteria.

2. Methods

2.1. Subjects

The present study included 171 patients ≥ 18 years of age who were cared for at the Affiliated Hospital of Chengde Medical College between January 2018 and January 2020. All patients had complete information and medical records (sample from the same patient was counted once only). Blood cultures were positive for gram-negative bacteria. The study was approved by the Medical Ethics Committee. The inclusion criteria were as follows: (1) age ≥ 18 years; (2) diagnostic criteria for bloodstream

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

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infection complied with the 2001 Diagnostic Criteria for Nosocomial Infection issued by the Ministry of Health, People's Republic of China^[7]; (3) blood cultures positive for gram-negative bacteria; and (4) signed informed consent. The exclusion criteria were as follows: (1) age < 18 years; (2) false-positive blood cultures; (3) incomplete information or medical records; and (4) complicated by inflammatory diseases.

2.2. Data collection

Clinical information was analyzed retrospectively. The clinical characteristics were collected, including gender, age, department, underlying diseases, primary infection sites, complications, prognosis, and blood culture results.

According to the recommendations of the World Health Organization, people ≥ 60 years of age in the Asia Pacific region and developing countries are defined as the elderly.^[8] All included subjects were assigned into the young- and middle-aged group or the elderly group by age.

2.3. Definition

Subjects were from the Intensive Care Unit in the Departments of Internal Medicine and Surgery (including Gynecology). The underlying diseases included diabetes, hypertension, coronary heart disease, solid tumors, gallstones, kidney stones, cerebrovascular diseases (including acute or chronic ischemic or hemorrhagic cerebrovascular disease), chronic kidney diseases (kidney diseases persisting > 3 months, including glomerulonephritis, nephrotic syndrome, chronic renal insufficiency, and end-stage renal disease), hematologic diseases (including hematologic malignancies, aplastic anemia, and hemolytic anemia). Primary infection sites included the respiratory tract, urinary tract, gallbladder, venous catheters, skin and soft tissues, liver, and abdominal cavity. Failure to identify the primary infection site was defined as no primary infection site. Complications included lower extremity deep venous thrombosis, respiratory failure, septic shock, and multiple organ failure. Prognosis referred to survival or death in the hospital. Those who were

discharged with ineffective rescue and without declaration of clinical death were classified as deceased.

2.4. Reagents and equipment

The Bact/Alert3D blood culture system (Biomérieux, France) and the VITEK-2compact Automated Microbiology System (Biomérieux, France) were used. *Escherichia coli* (*E. coli*) (ATCC25922) and *Pseudomonas aeruginosa* (ATCC27853) were used for quality control.

2.5. Statistical analysis

SPSS 23.0 software was used for statistical analysis. Enumeration data are represented by percentages and were analyzed using a chi-square or Fisher exact test. Measurement data are represented by the mean \pm SD. A $P < .05$ indicated a significant difference.

3. Results

3.1. General information

As shown in Table 1, 171 patients (110 elderly patients [64.33%] and 61 young- and middle-aged patients [35.67%]) with BSIs caused by gram-negative bacteria were included in the study. The mean age was 73.55 ± 9.20 and 47.51 ± 10.67 years in the elderly group and young- and middle-aged group, respectively. The gender distribution was not significantly different between the elderly group (59 males [53.64%]) and young- and middle-aged group (33 males [54.10%]; $P > .05$). The distribution of departments was also not significantly different between the elderly group and young- and middle-aged group ($P > .05$), including the Departments of Internal Medicine and Surgery, and the Intensive Care Unit.

3.2. Underlying diseases

As shown in Table 2, the distribution of underlying diseases was significantly different between the elderly group and the young- and middle-aged group. The underlying diseases in

Table 1

General information of patients with BSIs caused by gram-negative bacteria (mean \pm SD), n (%).

Group	n (%)	Age (years)	Male	Department		
				ICU	Internal medicine	Surgery
Elderly	110 (64.33)	73.55 \pm 9.20	59 (53.64)	11 (10.00)	68 (61.82)	31 (28.18)
Young- and middle-aged	61 (35.67)	47.51 \pm 10.67	33 (54.10)	3 (4.92)	42 (68.85)	16 (26.23)
Total	171 (100)	64.26 \pm 15.84	92 (53.80)	14 (8.19)	110 (64.33)	47 (27.49)
χ^2/t			0.003		1.594	
P			.954		.451	

BSIs = bloodstream infections; ICU = Intensive Care Unit.

Table 2

Underlying diseases of patients with BSIs caused by gram-negative bacteria, n (%).

Group	N	Diabetes	Hypertension	Coronary heart disease	Cerebrovascular diseases	Chronic kidney diseases	Hematologic diseases	Solid tumors	Gallstone	Kidney stone
Elderly	110 (64.33)	27 (24.55)	49 (44.55)	24 (21.82)	31 (28.18)	6 (5.45)	17 (15.45)	24 (21.82)	26 (23.64)	6 (5.45)
Young- and middle-aged	61 (35.67)	3 (4.92)	10 (16.39)	2 (3.28)	2 (3.28)	3 (4.92)	16 (26.23)	9 (14.75)	4 (6.56)	3 (4.92)
Total	171 (100)	30 (17.54)	59 (34.50)	26 (15.20)	33 (19.30)	9 (5.26)	33 (19.30)	33 (19.30)	30 (17.54)	9 (5.26)
χ^2/F		10.450	14.208	10.461	15.927	0.023	2.925	1.257	7.912	0.023
P		.001*	.000*	.001*	.000*	.880	.087	.262	.006*	1.000

BSIs = bloodstream infections.

*Indicates that the differences in baseline conditions among different age groups are statistically significant.

the elderly group were, in descending order of incidence, hypertension (44.55%), cerebrovascular diseases (28.18%), diabetes (24.55%), gallstones (23.64%), coronary heart disease (21.82%), solid tumors (21.82%), hematologic diseases (15.45%), chronic kidney diseases (5.45%), and kidney stones (5.45%). The underlying diseases in the young- and middle-aged group were, in descending order of incidence, hematologic diseases (26.23%), hypertension (16.39%), solid tumors (14.75%), gallstones (6.56%), diabetes (4.92%), chronic kidney diseases (4.92%), kidney stones (4.92%), coronary heart disease (3.28%), and cerebrovascular diseases (3.28%). The incidence of diabetes, hypertension, coronary heart disease, cerebrovascular diseases, and gallstones was significantly different ($P < .01$).

3.3. Bacterial composition

As shown in Table 3, *E. coli* accounted for the majority of BSIs caused by gram-negative bacteria (47.95%), followed by *Klebsiella pneumoniae*, *Brucella* spp., *P. aeruginosa*, and *Enterobacter cloacae*. Bacterial composition was significantly different between the elderly group and the young- and middle-aged group ($P < .05$). A pairwise comparison indicated that *Brucella* spp. in blood cultures were significantly less frequent in the elderly group than the young- and middle-aged group ($P < .05$).

Table 3
Distribution of pathogenic bacteria, n (%).

Pathogenic bacteria	Elderly	Young- and middle-aged	Total
<i>Escherichia coli</i>	56 (50.91)	26 (42.62)	82 (47.95)
<i>Klebsiella pneumoniae</i>	20 (18.18)	7 (11.48)	27 (15.79)
<i>Brucella</i> spp.	6 (5.45)*	13 (21.31)*	19 (11.11)
<i>Pseudomonas aeruginosa</i>	5 (4.55)	5 (8.20)	10 (5.85)
<i>Enterobacter cloacae</i>	3 (2.73)	1 (1.64)	4 (2.34)
Other gram-negative bacteria	20 (18.18)	9 (14.75)	26 (16.96)

BSIs = bloodstream infections.

The distribution of pathogens differs significantly among different age groups, F value = 11.342, $P = 0.037$.

*Indicates pairwise comparisons where the differences are statistically significant ($P < 0.05$).

Table 4
Distribution of primary lesions in patients with BSIs caused by gram-negative bacteria, n (%).

Group	n	Respiratory tract	Urinary tract	Gallbladder	Venous catheter	Skin and soft tissues	Liver	Abdominal cavity	No
Elderly	110 (64.33)	17 (15.45)	24 (21.82)	34 (30.91)*	4 (3.64)	3 (2.73)	4 (3.64)	5 (4.55)	19 (17.27)*
Young- and middle-aged	61 (35.67)	12 (19.67)	11 (18.03)	7 (11.48)*	2 (3.28)	4 (6.56)	0 (0.00)	6 (9.84)	19 (31.15)*
Total	171 (100)	29 (16.96)	35 (20.47)	41 (23.98)	6 (3.51)	7 (4.09)	4 (2.34)	11 (6.43)	38 (22.22)
χ^2/F					15.631				
P					.021*				

BSIs = bloodstream infections.

There is an overall statistical difference in the distribution of primary infection sites among different age groups ($P < 0.05$).

*Indicates pairwise comparisons where the differences are statistically significant ($P < 0.05$).

Table 5
Complications and prognosis in patients with BSIs caused by gram-negative bacteria, n (%).

Group	n	Lower extremity deep venous thrombosis	Respiratory failure	Septic shock	Multiple organ failure	In-hospital deaths
Elderly	110 (64.33)	9 (8.18)	15 (13.64)	26 (23.64)	16 (14.55)	13 (11.82)
Young- and middle-aged	61 (35.67)	0 (0.00)	1 (1.64)	5 (8.20)	0 (0.00)	1 (1.64)
Total	171 (100)	9 (5.26)	16 (9.36)	31 (18.13)	16 (9.36)	14 (8.19)
χ^2/F		5.268	6.659	6.302	9.789	5.409
P		.027*	.010*	.012*	.002*	.020*

BSIs = bloodstream infections.

*Indicates that there are statistically significant differences in complications and outcomes among different age groups ($P < 0.05$).

3.4. Distribution of primary infection sites

As shown in Table 4, the distribution of primary infection sites was significantly different between the elderly group and the young- and middle-aged group ($P < .05$). A pairwise comparison indicated that a primary infection site in the gallbladder was significantly more frequent in the elderly group (30.91%) than the young- and middle-aged group (11.48%; $P < .05$). Patients who had no definite infection site were significantly less frequent in the elderly group (17.27%) than the young- and middle-aged group (31.15%; $P < .05$).

3.5. Complications and prognosis

As shown in Table 5, the proportion of BSIs caused by gram-negative bacteria with septic shock was highest (18.13%), with an 8.19% in-hospital mortality rate. The incidence of complicated septic shock, multiple organ failure, respiratory failure, and lower extremity deep venous thrombosis, like in-hospital mortality, was significantly higher in the elderly group than the young- and middle-aged group.

4. Discussion

A BSI occurs when pathogenic bacteria invade the bloodstream, proliferate, and release toxins, leading to systemic inflammation, septic shock, and multiple organ dysfunction, posing a severe threat to human health.^[9] Current studies suggest that gram-negative bacteria are the major pathogenic bacteria that cause BSIs.^[10] BSIs caused by multi-drug resistant gram-negative bacteria are on the rise, thus posing a challenge to treatment.^[11] The elderly, due to factors like malnutrition, decreased immune function, and underlying diseases, are more susceptible to BSIs than younger individuals, which influences the clinical characteristics and pathogen distribution.^[12,13] A recent study reported that gram-negative bacteria are the most common pathogens in elderly patients, accounting for 40% to 60% of BSIs.^[14] In this study, 171 patients with gram-negative BSIs had an average age of 64.26 ± 15.84 years, with elderly patients comprising 64.33% of the cohort. The distribution of gender and hospital departments did not significantly differ between age groups ($P > .05$).

Risk factors for gram-negative BSIs include diabetes, hypertension, coronary heart disease, and cerebrovascular diseases.^[15,16] This study also identified hematologic diseases, solid tumors, and kidney stones as major comorbidities, with hypertension, diabetes, coronary heart disease, cerebrovascular diseases, and gallstones more prevalent in the elderly group. These findings suggest that managing these conditions in elderly patients could reduce the incidence of gram-negative BSIs.^[13]

E. coli accounted for the majority of gram-negative bacteria (47.95%), followed by *K. pneumoniae*. This finding is consistent with the detection results of pathogenic bacteria in blood samples from the 2014 to 2019 National Bacterial Resistance Monitoring Network.^[17] The present study compared the distribution of BSIs caused by gram-negative bacteria and found that the distribution of pathogenic bacteria was statistically significant between the elderly group and the young- and middle-aged group ($P < .05$). A pairwise comparison showed a different distribution of *Brucella* spp. in patients of different ages. Of patients with a BSI caused by *Brucella* spp. fewer were in the elderly group than the young- and middle-aged group, indicating that young- and middle-aged people are at high risk for infections caused by *Brucella* spp. This finding was consistent with Lian et al.^[18]

The gallbladder, urinary tract, and respiratory tract were the main routes of BSIs caused by gram-negative bacteria. Patients with gallbladder infections in the elderly group (30.91%) were significantly more than the young- and middle-aged group (11.48%; $P < .05$); this was different from a study of BSIs by mixed pathogenic bacteria. It was reported that urinary and respiratory tract infections in elderly patients with BSIs are more frequent than young- and middle-aged patients.^[19–22] Thus, in addition to the urinary and respiratory tract, the gallbladder should be considered as a main route of BSI infections caused by gram-negative bacteria. We analyzed patients with gallbladder infections and found that most gallbladder infections were secondary to gallstones. Current studies have shown that elderly patients are more susceptible to gallstone and gallbladder infections than young patients, and are also more susceptible to septic shock and death.^[7,23] Thus, timely management of gallstones in elderly patients can reduce the risk of BSIs caused by gram-negative bacteria via the biliary tract. We noted that 22.22% of patients had no definite route of infection, and elderly patients who had no definite route of infection were significantly fewer in number than young- and middle-aged patients ($P < .05$). Nineteen patients (11.11%) with *Brucella* spp. BSIs had no definite route of infection, with a greater number of patients in the elderly group than the young- and middle-aged group.

The incidence of in-hospital deaths for 171 patients with BSIs caused by gram-negative bacteria was 8.19%, with a higher incidence in the elderly group (11.82%) than the young- and middle-aged group (1.64%; $P = .02$); this was consistent with relevant studies of BSIs caused by mixed pathogenic bacteria.^[24,25] This study compared 4 complications (septic shock [18.13%], respiratory failure [9.36%], multiple organ failure [9.36%], and lower extremity deep venous thrombosis [5.26%]). The incidences of these 4 complications in elderly patients were significantly higher than the young- and middle-aged patients ($P < .05$). This finding indicated the possibility of complications and in-hospital deaths were significantly higher for elderly patients with BSIs caused by gram-negative bacteria. In addition, blood pressure, oxygen saturation of blood, organ function, D-dimer, and color Doppler ultrasound of deep veins of both lower limbs should be closely monitored to prevent complications. A previous prospective study investigating bacteremia episodes in patients over 80 years old in comparison with episodes in patients aged 18 to 64 and 65 to 79 years showed that the main infectious foci included primary (25.3%) and urinary tract (20.5%) infection, and the most frequent isolates were *E. coli* (28.2%), coagulase-negative *Staphylococcus* (14.7%) and *S. aureus* (13.6%).^[26] Meanwhile, very elderly bacteremic patients showed a lower frequency of immunodeficiency,

a higher percentage of community-acquired and gram-negative infections. The results of this previous study were similar with our results.

In conclusion, the elderly patients were primarily affected by BSIs caused by gram-negative bacteria. The clinical characteristics and distribution of pathogenic bacteria in patients with BSIs were significantly different. In comparison with young- and middle-aged patients, elderly patients had underlying diseases, complications, and poor prognosis as well as various pathogenic bacteria and primary infection sites. Clinicians should note these differences in patients of different ages, and provide categorical diagnosis, treatment, and management.

Author contributions

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