

The incidence rate, species distribution and dynamic trends of bloodstream infection in China, 2010-2019

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Abstract

Background Recent epidemiological studies on bloodstream infections (BSIs) that include the incidence rate, species distribution and dynamic changes are scarce in China. This study was performed to understand these epidemiological data of BSIs over the past 10 years in China. **Method** Using real-time nosocomial infection surveillance system, this study was retrospectively performed on BSIs in one of the largest hospitals in China, from January 2010 to December 2019. **Results** From 2010 to 2019, there were totally 9381 episodes of BSIs out of 1,437,927 adult hospitalized patients in the hospital, the total incidence rate of BSIs was 6.50‰ (6.50 episodes per 1000 adult-hospitalized patients per year) and the incidence rates had significantly decreased (8.24‰ to 6.00‰, time trend $P < 0.05$). Among the 9381 episodes of BSIs, 93.1% were bacteremia and others (6.9%) were fungemia. As the most common species, the composition ratios of coagulase-negative staphylococcus (25.6% to 32.5%), *Escherichia coli* (9.8% to 13.6%) and *Klebsiella pneumoniae* (5.3% to 10.4%) had been dynamic increased (time trends $P < 0.05$) and the proportion of *Pseudomonas aeruginosa* had dynamic decreased (4.0% to 2.4%, time trend $P = 0.007$). However, *Staphylococcus aureus* (3.3% to 3.1%) and *Acinetobacter baumannii* (4.4% to 4.2%) had not changed significantly (time trend $P > 0.05$). These common species were consistent with China Antimicrobial Surveillance Network reported in 2018 (2018 CHINET report), but their composition ratios were different. Additionally, among bacteremia, the proportion of the multidrug-resistant bacteria gradually increased from 52.9% to 68.4% (time trend $P < 0.001$). **Conclusion** The incidence rate and the species distribution had been dynamic changing and this study could be supplements to the 2018 CHINET report.

Introduction

Bloodstream infections (BSIs) refer to various pathogenic microorganisms that have invaded the blood, primarily bacteria and fungi^[1]. With the increasing number of invasive procedures and the unreasonable use of broad-spectrum antibacterial drugs and corticosteroids, the incidence and mortality of BSIs increase annually, as has been reported in many studies^[2, 3]. For example, the incidence of BSIs increased by 64% from 945 to 1,546 per 100,000 hospitalized patients per year from 2000 to 2013 in a Swedish county, and the 30-day mortality of BSIs was up to 12.8%^[4].

The administration of early empirical antimicrobial therapy based on the epidemiology of the species distribution and its antimicrobial susceptibility is crucial. A previous study revealed that gram-positive bacteria were more prevalent than gram-negative bacteria in BSIs in the United States and Europe^[5], and the gram-negative bacilli accounted for the majority of BSIs (54%) in Colombia^[6]. However, the clinical microbiological data of BSIs has constantly changed in recent years^[6, 7]. For example, the proportion of gram-negative bacteria increased from 44–53% over 9 years and that of gram-positive bacteria decreased from 49–45% in an Australian tertiary hospital^[8].

There were many studies on bloodstream infections in China, but most of these studies were separate cases studies involving the clinical characteristics, the risk factors of these BSI cases and (or) the species

distributions and drug resistance of BSIs. For example, Liu J et al. found that the 30-day mortality of carbapenem-resistant *Klebsiella pneumoniae* bacteremia was 24.7% and that the only risk factor was carbapenem exposure within 30 days before the onset of bacteremia in 89 oncohematological patients (HR 25.122)^[9]. Bai Y et al. collected 174 patients with BSIs after interventional therapy from 2013 to 2018 and found that gram-positive bacteria accounted for 56.05% of BSIs in these patients and that coagulase-negative Staphylococcus was the main infectious bacteria. They also found that days of prophylactic antibiotic use (OR = 1.586, P < 0.05) and replacement of antibiotics (OR = 13.349, P < 0.05) were the main risk factors associated with the development of BSIs using multivariate analysis^[10].

Nonetheless, due to the complexity and huge financial expense of bloodstream infection surveillance, recent epidemiological studies on bloodstream infections in China that include the incidence rate, species distribution and dynamic changes are scarce. To understand the changing trends in the epidemiology of BSIs, the present study retrospectively analyzed the incidence rate, species distribution and drug resistance of BSIs and their dynamic changes over 10 years in one of the largest tertiary hospitals in China.

Methods

Hospital setting

This retrospective study was performed at a 3500-bed tertiary medical center with more than 140,000 hospitalized patients per year, Chinese People's Liberation Army General Hospital (CPLAGH). This hospital is one of the largest general hospitals and integrates medical treatment, teaching and scientific research. CPLAGH primarily provides medical services for patients in northern China. Therefore, the dynamic trends of the microbiology and incidence rate of BSIs in this hospital basically reflect the prevalence of BSIs in northern China.

All data were collected by reviewing the real-time nosocomial infection surveillance system (RT-NISS) medical electronic database in the hospital. The system is capable of daily, automatic, and real-time screening of all suspicious infections of hospitalized patients, such as BSIs, respiratory tract infection, urinary tract infection, surgical site infection, gastrointestinal tract infection, skin and soft tissue infection and other infections. Simultaneously, the system also can eliminate contamination and colonization infections. A previous study showed that the sensitivity and specificity of the RT-NISS system were 98.8% and 93.0%, respectively, for nosocomial infections^[11].

Case definition

Positive-blood culture and the definition of BSIs

All suspicious BSIs were screened and under surveillance by the RT-NISS system. The following screening strategies for BSIs were used. (1) At least one positive blood culture: Each set of blood cultures in our hospital included an aerobic blood culture bottle and an anaerobic blood culture bottle. A positive blood

culture was defined as at least one isolation of microorganisms for a set of blood cultures, including bacterial, fungal and other rare pathogens. (2) At least one BSI-related clinical symptom, such as chills, fever ($> 37.3^{\circ}\text{C}$), and hypotension (systolic pressure < 100 mmHg). (3) Elevated levels of at least one BSI-related molecular marker, such as procalcitonin (PCT), C-reactive protein (CRP), and white blood cell count (WBC).

All hospitalized patients with positive blood cultures were considered as being suspicious for BSI, but only patients who had at least one BSI-related clinical symptom and (or) elevated levels of at least one BSI-related molecular marker were diagnosed with BSI by the RT-NISS system. Otherwise, the positive blood culture was considered a contaminant or colonization.

Inclusion and exclusion of BSIs

The RT-NISS system identified repeated and identical BSIs in the same patient. If the patient who was diagnosed with BSI had two or more positive blood cultures caused by an identical specie within 14 consecutive days, only the first blood culture was used to diagnose an episode of BSI, and the other cultures were excluded. However, if the identical BSI recurred after 14 days, the recurrent BSI was considered a new episode of BSI by the RT-NISS system. Additionally, if the patient had one or more positive blood cultures caused by two or more different species and each of the species in the blood culture could be diagnosed as BSI, then each species that caused the BSI was considered as a separate episode of BSI.

Community-acquired BSI and hospital-acquired BSI

BSIs were divided into community-acquired BSIs (CA-BSIs) and hospital-acquired BSIs (HA-BSIs) based on the onset date and the date when the positive blood culture was drawn. The BSI was defined as a CA-BSI when its onset was within 48 hours after admission, and HA-BSI was defined when BSI onset occurred longer than 48 hours after admission.

Study variables

From January 1, 2010, to December 31, 2019, the total number of adult hospitalized patients diagnosed with BSIs each year and the total number of adult hospitalized patients were collected for each year. The incidence rate in each year and the dynamic trend were calculated.

The following microbiological data were collected: the species of the microorganism isolated in the blood culture; the gram stain type of the species that led to bacteremia (defined as gram-positive cocci, gram-negative bacilli and others); the species that led to fungemia (defined as *Candida* or non-*Candida*); the antibiotic resistance of bacteria (defined as multidrug resistance or sensitive according to the Clinical and Laboratory Standards Institute (CLSI) standards); and the corresponding numbers. The composition ratios were separately calculated annually; then, their dynamic time trend could be evaluated from 2010 to 2019. Multidrug resistance was defined as a species of bacteria that was resistant to three or more types of antibiotics (such as aminoglycosides, erythromycins, penicillins, cephalosporins, β -lactams,

carbapenem, tetracyclines, glycopeptides, linezolid, sulfa antibiotics), but not three of the same type of antibiotics.

The dynamic time trends of the incidence rates and species distribution in these 10 years were the focus of the present study. To reduce the coefficient of variation of all the variables in one year, the average value of each variable over two consecutive years was used to assess dynamic changes. Therefore, the 10-year data were divided into five groups: 2010–2011, 2012–2013, 2014–2015, 2016–2017 and 2018–2019.

Statistical analysis

All statistical analyses were performed using SPSS version 22.0 software (SPSS, Inc., Chicago, IL, USA). The number of adult hospitalized patients and the episodes of BSIs were described as N, and the incidence rates of BSIs in all adult hospitalized patients were described as N ‰ (N episodes per 1000 adult-hospitalized patients per year). The number of species and the composition ratios were described as N and a percentage (%), respectively. The dynamic time trends of the incidence rate and the composition ratios of the various species were statistically analyzed using the Mantel-Haenszel chi-square test, which is equivalent to the Cochran-Armitage trend test, and the p-value of linear-by-linear association and Pearson correlation coefficient (R) were exhibited to evaluate the dynamic time trends and the directions of these trends (increase or decrease), respectively. All results with a 2-tailed p-value < 0.05 were significant. $R > 0$ represented that the dynamic time trend increased, and $R < 0$ represented that the dynamic time trend decreased.

Results

Incidence rate of BSIs and dynamic time trend

From January 1, 2010, to December 31, 2019, there were 1,437,927 adult hospitalized patients in the hospital and 9381 episodes of BSIs. The total average incidence rate of BSIs over these 10 years was 6.50‰ (6.50 episodes per 1000 adult hospitalized patients per year). As shown in Table 1 and Fig. 1a, although the number of adult hospitalized patients and the number of BSIs over the two consecutive years increased from 2010 to 2019, the time trend of the average incidence rates of BSIs decreased gradually from 8.24‰ to 6.00‰. The linear-by-linear association was statistically significant ($P < 0.05$). The incidence rates of community-acquired BSIs (CA-BSIs) and hospital-acquired BSIs (HA-BSIs) showed similar trends. The CA-BSIs decreased from 2.10‰ to 1.43‰, and the HA-BSIs decreased from 6.05‰ to 4.57‰. However, as showed in Fig. 1b, among the 9381 episodes of BSIs, the composition ratio of the HA-BSIs increased significantly from 73.4% (1279/1743) to 76.2% (1664/2184). In contrast, the composition ratio of the CA-BSIs decreased significantly from 26.6% (464/1743) to 23.8% (520/2184). These time trends were statistically significantly (time trend $P = 0.003$).

Species distribution and dynamic trends

The species distribution and dynamic trends are presented in Table 2 and Fig. 2. Among the 9381 episodes of BSIs, 93.1% (8737/9381) were bacteremia and 6.9% (644/9381) were fungemia. As shown in Fig. 2a, the proportion of fungemia decreased significantly from 10.8–5.0% for all species over the 10 years of the study (time trend $P < 0.001$, $R = -0.070$). All species in fungemia decreased, regardless of whether they were *Candida* (6.1%, 573/9381) or non-*Candida* (0.8%, 71/9381). Both time trends were statistically significantly ($P < 0.001$).

Among the species in the BSIs, 45.9% (4310/9381) were gram-positive cocci (GPC), and 42.8% (4015/9381) were gram-negative bacilli (GNB). coagulase-negative staphylococcus (CoNS) accounted for the majority of GPC (26.2%, 2459/9381), and the four most common species were *Staphylococcus hominis* (8.8%), *Staphylococcus epidermidis* (7.2%), *Enterococcus faecium* (5.6%) and *Staphylococcus aureus* (3.5%). The four most common species of GNB were *Escherichia coli* (14.3%), *Klebsiella pneumonia* (8.9%), *Acinetobacter baumannii* (4.9%) and *Pseudomonas aeruginosa* (3.4%).

From 2010 to 2019, the composition ratios of these species in BSIs exhibited some dynamic changes over time. As shown in Table 2 and Fig. 2, the proportion of GNB increased from 35.8–40.2% (time trend $P < 0.001$). Although GPC exhibited no significant change (time trend $P = 0.615$), as the most common species group in GPC, the proportion of CoNS had increased from 25.6–32.5% (time trend $P < 0.001$, $R = 0.037$). The proportions of *Escherichia coli* (9.8–13.6%) and *Klebsiella pneumonia* (5.3–10.4%) in the GNB group increased significantly over the 10 years of the study. However, the proportion of *Pseudomonas aeruginosa* decreased significantly from 4.0–2.4% (time trend $P = 0.007$, $R = -0.028$). Some species did not significantly change, such as *Staphylococcus aureus* (3.3–3.1%, time trend $P = 0.754$) and *Acinetobacter baumannii* (4.4–4.2%, time trend $P = 0.879$), which are two important pathogenic bacteria in the clinic.

Antimicrobial susceptibility of bacteria and dynamic trends

Although the RT-NISS system screened the antimicrobial susceptibility of 8737 species in bacteremia, only 6224 species (71.2%, 6224/8737) had complete data related to antimicrobial susceptibility to evaluate multidrug resistance, and 2513 species (28.8%, 2513/8737) lacked all or part of the data related to antimicrobial susceptibility. As shown in Table 2, 68.4% (4257/6224) of the 6224 species were resistant to at least three types of antibiotics and were considered multidrug resistant and 31.6% (1967/6224) were still sensitive to common antibiotics. However, as showed in Fig. 3, the proportion of drug-sensitive bacteria gradually decreased from 47.1–31.6% from 2010 to 2019, and the proportion of multidrug-resistant bacteria gradually increased from 52.9–68.4%. Both of these time trends were statistically significantly (time trend $P < 0.001$).

Discussion

Bloodstream infections (BSIs) are characterized by high mortality and multidrug resistance worldwide^[12, 13]. The dynamic changes in species distribution and antimicrobial susceptibility are important clinical

evidence for early empirical antimicrobial therapy of BSIs, and these factors were the emphasis of the present study.

With the assistance of the highly sensitive and specific real-time nosocomial infection surveillance system (RT-NISS) in our hospital, we identified 9381 episodes of BSI out of 1,437,927 adult hospitalized patients over 10 years in CPLAGH, and we found that the total number of adult hospitalized patients over two consecutive years increased from 2010–2011 to 2018–2019 (211,546 to 359,547 patients every two years) and that the corresponding number of the episodes of BSI increased from 1743 to 2184 episodes every two years. However, it was encouraging that the corresponding average incidence rates of BSI decreased significantly from 8.24 to 6.00 episodes per 1000 adult hospitalized patients per year. The incidence rate was less than that in a Swedish county, which was from 9.45 to 15.46 per 1000 hospitalized patients per year from 2000 to 2013^[4]. This result might be due to the increased awareness of nosocomial infections and national action on infection control in China^[14]. This decrease might be similar to that in the United States, in which the central line-associated BSI rate decreased by 46% between 2008 and 2013 as a result of national medical control^[15].

However, we also found that the composition ratio of hospital acquired BSIs increased significantly annually (from 73.4–76.2%). This result was consistent with the increase in various hospital-acquired infections in recent years^[16, 17], and the risk factors may be related to the risk factors for BSIs and (or) hospital-acquired infections reported in many previous studies, such as ICU admission, the older age of hospitalized patients (aging population), prolonged hospital stay, leukocytopenia, acute myeloid leukemia and (or) increased use of invasive procedures including central venous catheters (CVCs)^[18–20]. However, more details of the risk factors require further statistical analysis of the decrease in hospital-acquired BSIs in our hospital.

We found that the majority species in the 9381 episodes of BSIs were bacteremia (93.1%) and that the average composition ratio over the two consecutive years gradually increased from 89.2% (2010–2011) to 95.0% (2018–2019) (time trend $P < 0.001$). Conversely, fungemia accounted for the minority of BSIs (6.9%), and the average composition ratio decreased significantly from 10.8–5.0%. This result may be partially related to the increasing proportion of multidrug-resistant bacteria. Our data showed that the proportion of multidrug resistance of 6,224 bacteria increased significantly from 52.9–68.4% during the 10-year study period (time trend $P < 0.001$). This increase may have made bacteria more difficult to control and may have led to a relative increase in the proportion of bacterial BSIs (bacteremia).

Although the composition ratio of bacteremia in the 9381 BSIs increased over the 10-years study period, it did not mean that the composition ratio of all the species in bacteremia did not increase. Our data revealed that gram-positive cocci (45.9%) and gram-negative bacilli (42.8%) had a similar prevalence, and this result was different from the species distribution reported by the China Antimicrobial Surveillance Network (CHINET) in 2018 for all bacterial infections, including BSIs and other bacterial infections (2018 CHINET report)^[21]. The results of the CHINET report suggested that more gram-negative bacilli (70%)

were isolated than gram-positive cocci (30%) and that the composition did not change obviously from 2005 to 2017 in China.

Notably, although the composition ratios of the gram-positive cocci and gram-negative bacilli were similar in BSIs in our study, the most common species of bacteria was consistent with the 2018 CHINET report. The top four most common gram-negative species were *Escherichia coli* (14.3%), *Klebsiella pneumoniae* (8.9%), *Acinetobacter baumannii* (4.9%) and *Pseudomonas aeruginosa* (3.4%), which are identical to the CHINET report. Coincidentally, our data also revealed that the proportions of *Escherichia coli* (9.8–13.6%, time trend $P=0.004$) and *Klebsiella pneumoniae* (5.3–10.4%, time trend $P<0.001$) increased significantly and the proportions of *Acinetobacter baumannii* (4.4–4.2%, time trend $P=0.879$) and *Pseudomonas aeruginosa* (4.1–2.4%, time trend $P=0.007$) both had decreased, similar to the CHINET report. In addition, because the composition ratio of gram-negative bacteria (42.8%) in our study was lower than that in the CHINET report (70%) and fungi were not included in the CHINET report, the composition ratios of various species of gram-negative bacteria were also different. However, the most common species were similar.

However, among gram-positive cocci, the most common species were coagulase-negative staphylococci (26.2%), and their proportion increased (25.6–32.5%, time trend $P<0.001$) over the 10-year study period. *Staphylococcus aureus* accounted for only 3.5% in our study, but were the most common gram-positive cocci in the CHINET report (9.0%). However, our result is not in conflict with the CHINET report because the CHINET report included various infections, not only bloodstream infections. Conversely, CoNS accounted for the minority of bacteria in the CHINET report (4.4%) because CoNS only originated from bloodstream infections. Therefore, the proportion of CoNS might be much higher only among BSIs in CHINET report, and it was up to 26.2% in the present study.

In conclusion, we performed statistical analyses of the incidence rate, species distribution, and drug resistance of BSIs as well as their dynamic changes over the past 10 years in one of the largest hospitals in China. We found that the incidence rate of BSIs decreased dynamically over time and that the species distribution in BSIs changed. The proportion of bacteria and multidrug resistance increased, and some species, such as *Klebsiella pneumoniae*, were obviously increased in bloodstream infections. Many of the increasing data presented above exhibited significant time trends and deserve clinical attention regarding infection control. We compared the species distribution of bacteria-causing BSIs with those reported in CHINET for all infections (2018 CHINET report above) and found that the species distributions of BSIs were partially consistent with the 2018 CHINET report, but there were also many differences. Therefore, our study on BSIs could be supplements to the 2018 CHINET report on BSIs.

Limitations

This study also had several limitations. First, the incidence of BSIs might be underestimated in this study. A few pathogens, such as mycoplasma and chlamydia, are difficult to detect in conventional blood cultures, and some BSIs were missed in false-negative blood cultures. In addition, some BSIs were

mistakenly excluded by the RT-NISS system used in our study because of the lack of typical clinical symptoms related to BSIs (such as fever and increased inflammation makers). However, a previous study used the RT-NISS system to screen BSIs and showed high sensitivity and specificity^[11], and missing data might have had little effect on the results of this study. Second, the CLS standards and the detection technology for blood cultures had been continuously updated and improved each year, which increased the positive detection rate of blood cultures and might have increased the incidence rate of BSIs in recent years. Thus, this improvement in technology might have led to bias in the statistics of the dynamic time trend of the incidence rate over the 10 years. However, our data showed that the dynamic time trend of the incidence rate of BSIs in adult hospitalized patients decreased significantly. Therefore, the results of the statistical analysis of the time trend of the incidence rate could not be affected in this study.

Abbreviations

BSI: bloodstream infection; RT-NISS: real-time nosocomial infection surveillance system; PCT: procalcitonin, CRP: C-reactive protein, WBC: white blood cell count; R: Pearson correlation coefficient; CA-BSIs: community-acquired BSIs; HA-BSIs: hospital-acquired BSIs; GPC: gram-positive cocci, GNB: gram-negative bacilli; CoNS: coagulase-negative staphylococcus; CVC: central venous catheter; CHINET: China Antimicrobial Surveillance Network; CLSI: Clinical and Laboratory Standards Institute; PLAGH: Chinese People's Liberation Army General Hospital.

Declarations

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Ethics

This study had approved by Clinical Trial Ethics Review Committee of the PLAGH Hospital, but the formal consent was waived in our hospital since this study was a retrospective study and private information was not involved in the study, such as patient name and address.

Authors' contributions

JC and ML collected the clinical data and wrote the manuscript. XQ collected and analysed the results. JW and QZ participated in data collection and the critical revision of the manuscript. ZL designed this study and was responsible for the manuscript.

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Availability of data and materials

In order to avoid violating the privacy rules of the medical database in our hospital, all data involved in this study were not publicly available, but all data are available from the corresponding author for any reader if necessary.

Conflict of interest

All authors declared that they had no conflict of interest.

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Tables

Table 1 The incidence rate and the dynamic trend of BSIs in all adult hospitalized patients.

	Total	2010-2011	2012-2013	2014-2015	2016-2017	2018-2019	χ^2	P-value	R
Number of hospitalized patients	1437927 (1000‰)	211564 (1000‰)	257621 (1000‰)	287033 (1000‰)	322162 (1000‰)	359547 (1000‰)			
Number of episodes of BSIs	9381	1743	1694	1707	2053	2184			
Incidence rate of BSI (%)	6.52‰	8.24‰	6.58‰	5.95‰	6.37‰	6.07‰	64.77	<0.001*	-0.007
Hospital acquired BSIs	6901 (4.80‰)	1279 (6.05‰)	1202 (4.67‰)	1228 (4.28‰)	1528 (4.74‰)	1664 (4.63‰)	30.36	<0.001*	-0.005
Community acquired BSIs	2480 (1.72‰)	464 (2.19‰)	492 (1.91‰)	479 (1.67‰)	525 (1.63‰)	520 (1.44‰)	47.6	<0.001*	-0.006
Composition ratio	9381 (100%)	1743 (100%)	1694 (100%)	1707 (100%)	2053 (100%)	2184 (100%)			
Hospital acquired BSIs	6901 (73.6‰)	1279 (73.4‰)	1202 (71.0%)	1228 (71.9%)	1528 (74.4%)	1664 (76.2‰)	8.933	0.003*	0.031
Community acquired BSIs	2480 (26.4‰)	464 (26.6%)	492 (29.0%)	479 (28.1%)	525 (25.6%)	520 (23.8%)	8.933	0.003*	-0.031

BSI bloodstream infection, χ^2 Chi-Square Tests Value, R pearson correlation coefficient. ‰, episodes per 1000 adult-hospitalized patients per year.

***Bold font** means that the linear-by-linear association was statistically $P < 0.05$ and the dynamic time trend was significant.

Table 2 The species distribution, antimicrobial resistance and their dynamic trends in BSIs.

	Total (n=9381, 100%)	2010-2011 (n=1743)	2012-2013 (n=1694)	2014-2015 (n=1707)	2016-2017 (n=2053)	2018-2019 (n=2184)	χ^2	P-value	R
Bacteremia	8737 (93.1%)	1555 (89.2%)	1574 (92.9%)	1606 (94.1%)	1927 (93.9%)	2075 (95.0%)	45.610	<0.001*	0.070
All Gram-positive cocci	4310 (45.9%)	843 (48.4%)	802 (47.3%)	678 (39.7%)	881 (42.9%)	1106 (50.6%)	0.253	0.615	0.009
<i>Enterococcus faecium</i>	524 (5.6%)	66 (3.8%)	97 (5.7%)	109 (6.4%)	113 (5.5%)	139 (6.4%)	8.442	0.004*	0.030
<i>Staphylococcus aureus</i>	333 (3.5%)	58 (3.3%)	63 (3.7%)	65 (3.8%)	79 (3.8%)	68 (3.1%)	0.098	0.754	-0.003
<i>Enterococcus faecalis</i>	176 (1.9%)	25 (1.4%)	28 (1.7%)	40 (2.3%)	48 (2.3%)	35 (1.6%)	0.787	0.375	0.009
All CoNS	2459 (26.2%)	447 (25.6%)	463 (27.3%)	357 (20.9%)	483 (23.5%)	709 (32.5%)	12.818	<0.001*	0.037
<i>Staphylococcus hominis</i>	821 (8.8%)	37 (2.1%)	122 (7.2%)	155 (9.1%)	192 (9.4%)	315 (14.4%)	#####	<0.001*	0.136
<i>Staphylococcus epidermidis</i>	678 (7.2%)	40 (2.3%)	73 (4.3%)	123 (7.2%)	184 (9.0%)	258 (11.8%)	#####	<0.001*	0.131
<i>Staphylococcus haemolyticus</i>	204 (2.2%)	18 (1.0%)	31 (1.8%)	41 (2.4%)	47 (2.3%)	67 (3.1%)	18.448	<0.001*	-0.044
<i>Staphylococcus capitis</i>	131 (1.4%)	2 (0.1%)	20 (1.2%)	21 (1.2%)	37 (1.8%)	51 (2.3%)	35.910	<0.001*	0.062
All Gram-negative bacilli	4015 (42.8%)	624 (35.8%)	694 (41.0%)	856 (50.1%)	963 (46.9%)	878 (40.2%)	12.798	<0.001*	0.037
<i>Escherichia coli</i>	1339 (14.3%)	170 (9.8%)	242 (14.3%)	324 (19.0%)	305 (14.9%)	298 (13.6%)	8.525	0.004*	0.030
<i>Klebsiella pneumoniae</i>	839 (8.9%)	93 (5.3%)	129 (7.6%)	153 (9.0%)	236 (11.5%)	228 (10.4%)	45.038	<0.001*	0.069
<i>Acinetobacter baumannii</i>	457 (4.9%)	76 (4.4%)	89 (5.3%)	77 (4.5%)	124 (6.0%)	91 (4.2%)	0.023	0.879	0.002
<i>Pseudomonas aeruginosa</i>	323 (3.4%)	70 (4.0%)	55 (3.2%)	81 (4.7%)	65 (3.2%)	52 (2.4%)	7.365	0.007*	-0.028
Fungemia	644 (6.9%)	188 (10.8%)	120 (7.1%)	101 (5.9%)	126 (6.1%)	109 (5.0%)	45.610	<0.001*	-0.070
Candida	573 (6.1%)	146 (8.4%)	107 (6.3%)	95 (5.6%)	119 (5.8%)	106 (4.9%)	18.689	<0.001*	-0.045
Non-Candida	71 (0.8%)	42 (2.4%)	13 (0.8%)	6 (0.4%)	7 (0.3%)	3 (0.1%)	60.189	<0.001*	-0.080
Antimicrobial resistance of Bacterial #	6224 (100%)	816 (100%)	941 (100%)	1298 (100%)	1470 (100%)	1699 (100%)			
Multidrug resistance	4257 (68.4%)	432 (52.9%)	472 (50.2%)	1085 (83.6%)	1106 (75.2%)	1162 (68.4%)	#####	<0.001*	0.133
Sensitive	1967 (31.6%)	384 (47.1%)	469 (49.8%)	213 (16.4%)	364 (24.8%)	537 (31.6%)	#####	<0.001*	-0.133

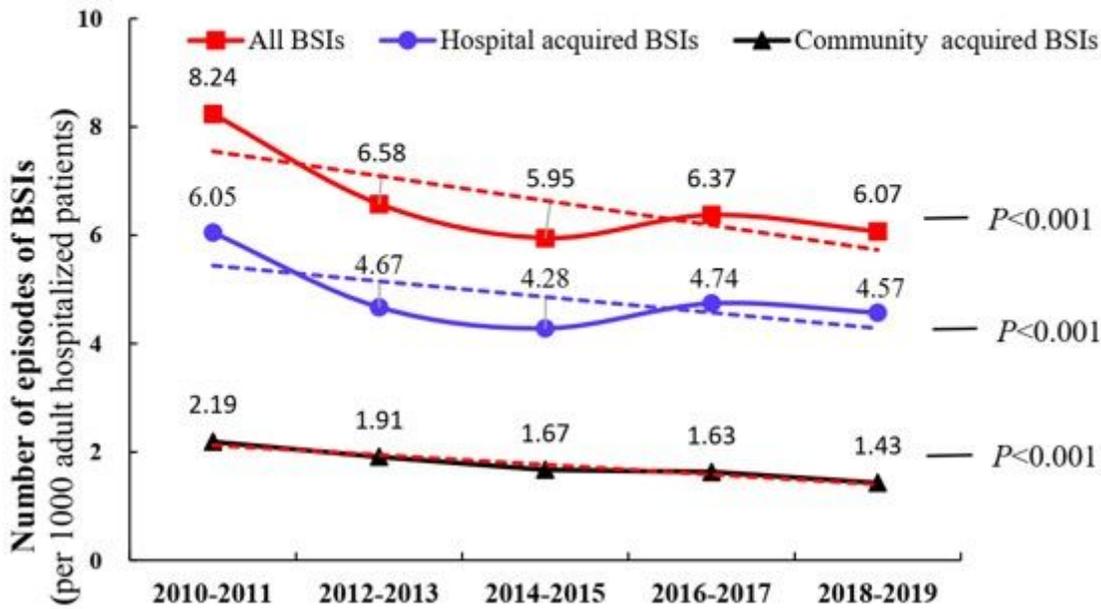
BSI bloodstream infection, CoNS coagulase-negative staphylococci, χ^2 Chi-Square Tests Value, R pearson correlation coefficient.

#Because the antimicrobial resistance test results of 2513 (28.8%, 2513/8737) bacteria were lacked in the database, only 6224 bacteria were described in the table.

***Bold font** means that the linear-by-linear association was statistically $P < 0.05$ and the dynamic time trend was significant.

Figures

(1a) **Incidence rates of BSIs and time trends**
(1,437,927 adult hospitalized patients in 10 years)



(1b) **Composition ratios of BSIs and time trends** (n=9381)

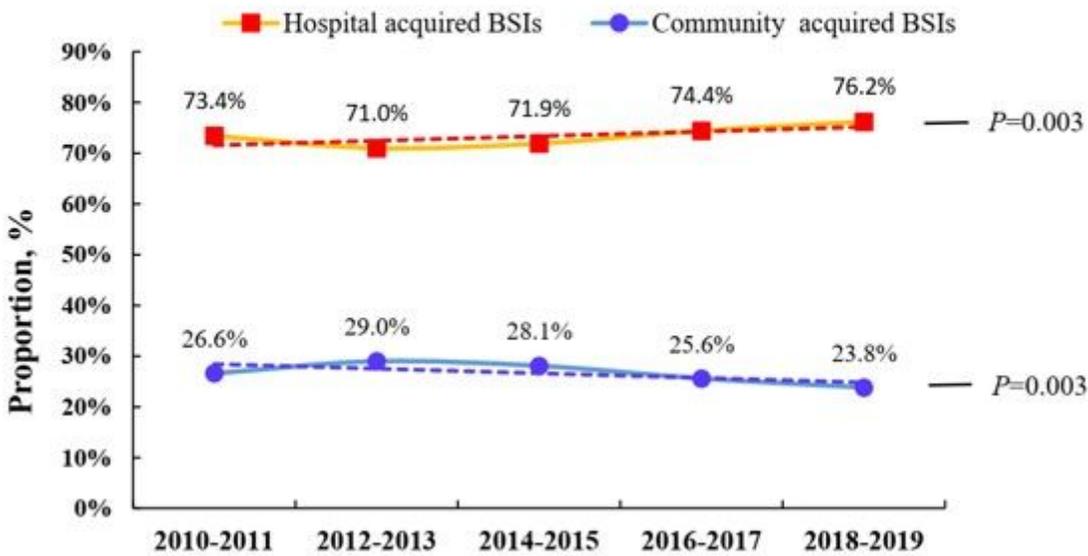
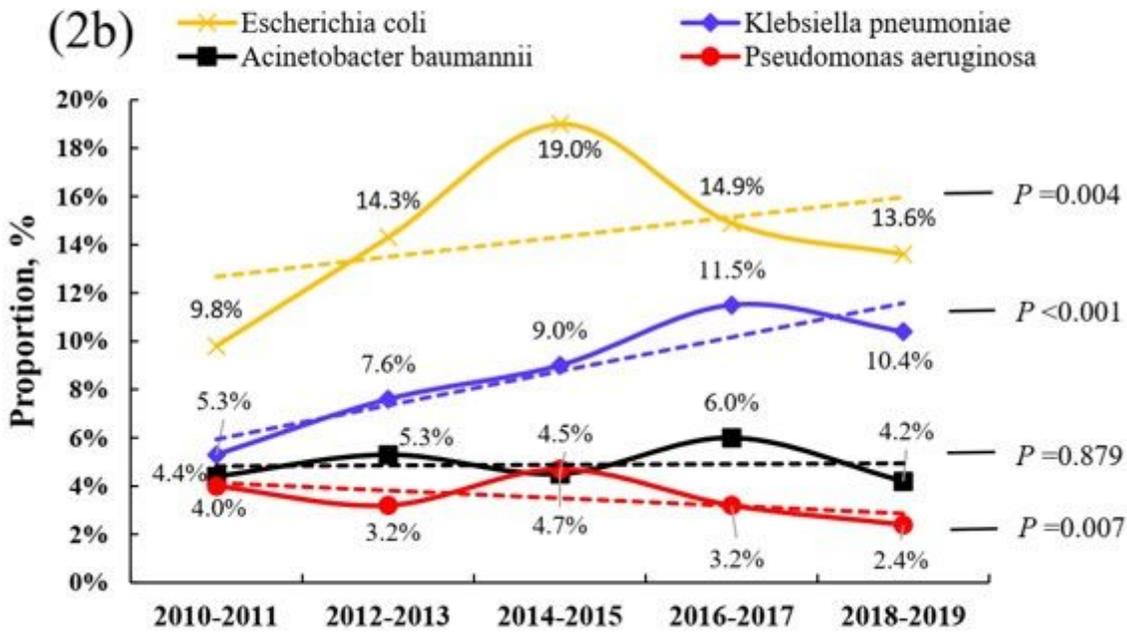
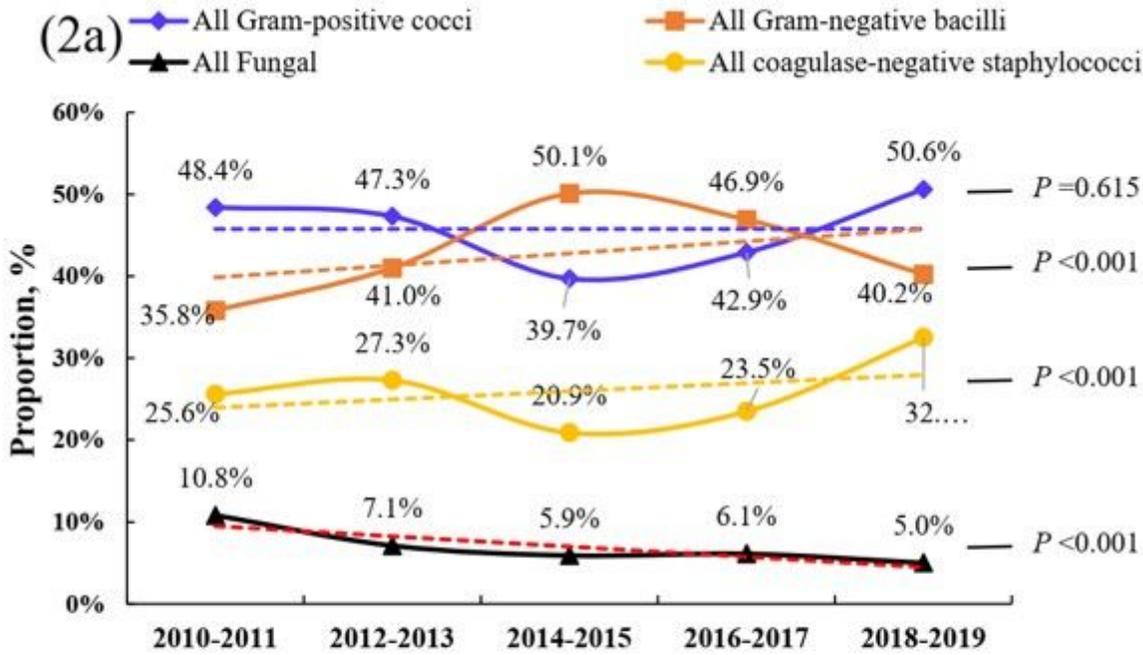


Figure 1



Species distribution and time trends (n=9381)

Figure 2

(3) Antimicrobial resistance of bacteria (n=6224)

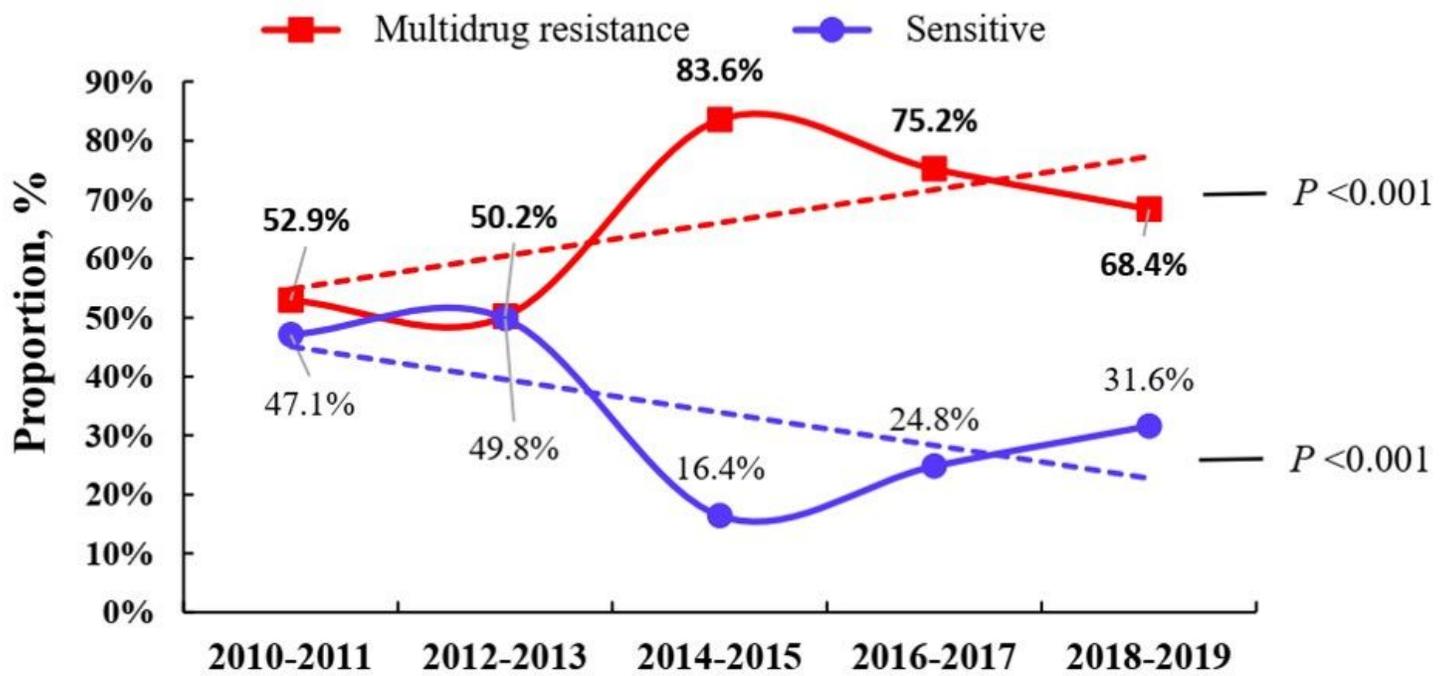


Figure 3