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***Retrospective Study***

**Distribution and drug resistance of pathogenic bacteria in emergency patients**

Huai W *et al*. Pathogenic bacteria in emergency patients

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**Abstract**

***BACKGROUND***

Antibiotic resistance has become a global threat for human health, calling for rational use of antibiotics.

***AIM***

To analyse the distribution and drug resistance of the bacteria, providing the prerequisite for use of antibiotics in emergency patients.

***METHODS***

A total of 2048 emergency patients from 2013 to 2017 were enrolled. Their clinical examination specimens were collected, followed by isolation of bacteria. Bacterial identification and drug susceptibility testing were conducted.

***RESULTS***

A total of 3387 pathogens were isolated. The top six pathogens were *Acinetobacter baumannii* (660 strains), *Staphylococcus aureus* (436 strains), *Klebsiella pneumoniae* (347 strains), *Pseudomonas aeruginosa* (338 strains), *Escherichia coli* (237 strains), and *Candida albicans* (207 strains). The isolation rates of these pathogens decreased each year except *K. pneumoniae*, which increased from 7.1% to 12.1%. *A. baumannii* is a widely resistant strain with multiple resistance to imipenem, ciprofloxacin, minocycline, and tigecycline. *S. aureus* had high resistance rates to levofloxacin, penicillin G, and tetracycline, but its susceptibility to vancomycin and tigecycline was 100%. *K. pneumoniae* had high resistance rates to imipenem, cefoperazone/sulbactam, amikacin, and ciprofloxacin, with the lowest resistance rate to tigecycline.The resistance rates of *P. aeruginosa* to cefoperazone/sulbactam and imipenem were higher, with the resistance rate to amikacin below 10%. *E. coli* had high resistance rates to ciprofloxacin and cefoperazone/sulbactam and low resistance rates to imipenem, amikacin, and tigecycline.

***CONCLUSION***

The pathogenic bacteria isolated from the emergency patients were mainly *A. baumannii*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*, and *C. albicans*. The detection rates of drug-resistant bacteria were high, with different bacteria having multiple drug resistance to commonly used antimicrobial agents, guiding the rational use of drugs and reducing the production of multidrug-resistant bacteria.

**Key words:** Distribution; Drug resistance; Bacteria; Emergency department

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**Core tip:** The purpose of this study was to analyse the distribution and drug resistance of bacteria isolated from emergency department specimens, providing a prerequisite for the rational use of antibiotics in emergency patients. The top six pathogens were *Acinetobacter baumannii* (660 strains), *Staphylococcus aureus* (436 strains), *Klebsiella pneumoniae* (347 strains), *Pseudomonas aeruginosa* (338 strains), *Escherichia coli* (237 strains), and *Candida albicans* (207 strains). The detection rates of drug-resistant bacteria were high, with different bacteria having multiple drug resistance to commonly used antimicrobial agents, guiding the rational use of drugs and reducing the production of multidrug-resistant bacteria.

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**INTRODUCTION**

With the wide application of antibacterial drugs, the sensitivity of common bacteria to antibiotics is decreasing. In particular, resistance to β-lactams, aminoglycosides, fluoroquinolones, and sulphonamides severely compromises effective anti-infective treatment and seriously threatens the lives of patients. At the same time, the emergence of new antibacterial drugs has made the problem of drug abuse become increasingly serious, making it one of the most important medical problems worldwide. The recent discovery of superbacteria in India and other countries is a serious consequence of the abuse of antimicrobial drugs, but currently there is still no effective treatment that can replace the antibiotics to inhibit and exterminate the pathogens. Therefore, the rational use of antibiotics has become an important topic for clinical use[1]. However, the premise of rational drug use is to understand the distribution of pathogens and the trends and characteristics of drug resistance.

Generally, patients in the emergency department have relatively rapid disease progression. Without a clear aetiology and bacteriological basis, the early and empirical use of antibiotics is required. In China, the emergency department of the central hospitals is an important department for the treatment and rescue of critically ill patients. It is difficult to avoid the body injury of patients caused by invasive treatment while rescuing patients, so it is also inevitably complicated with various hospital infectious diseases[2]. In addition, most emergency departments are open management, with more patients’ family members, more hospital staff flow, and more severe ward environmental pollution, further increasing the probability of hospital-acquired infection in critically ill patients in the emergency department[3]. For patients with severe infections, a combination of multiple antibiotics is often required, which may lead to bacterial resistance. Due to the great difference in the resistance of different pathogenic bacteria to antibacterial drugs, it causes great drawback to clinical medication and poor therapeutic effects[4,5]. In this study, we analysed the distribution characteristics and drug resistance to different antibiotics of the bacteria isolated from the emergency department specimens in our hospital from 2013 to 2017. This study is of great significance for the selection of drugs for initial empirical treatment in the emergency department and the careful selection of antibiotics to reduce the generation of drug-resistant strains.

**MATERIALS AND METHODS**

***Source of strain***

This study was approved by the Ethics Committee of Peking University Third Hospital (Beijing, China), and all patients provided written informed consent.

A total of 2048 critically ill patients hospitalised in the emergency department of Peking University Third Hospital from January 2013 to December 2017 were enrolled. The clinical examination specimens of these patients were collected, including deep sputum retained after adequate gargling (secretions from deep respiratory tract in patients with tracheotomy or intubation), urine, localised secretions, and blood from the apical segment of the catheter in patients with central venous catheterisation1. Finally, the respiratory specimens accounted for 51.6% of all samples, blood specimens accounted for 23.3%, urine specimens accounted for 18.7%, sterile body fluid specimens accounted for 4.0%, and other specimens accounted for 2.4%. Then the bacteria were isolated from these specimens. Only the first isolated strains were used for patients with replicate strains isolated. *Staphylococcus aureus* ATCC25923, *Enterococcus faecalis* ATCC29212, *Escherichia coli* ATCC25922, and *Pseudomonas aeruginosa* ATCC27853 were used as control strains.

***Methods***

Bacterial identification and drug susceptibility testing were carried out according to the routine methods of the National Clinical Laboratory Procedures for bacteria culture, isolation, and identification.

The isolation media including China-blue plate and blood agar plate were purchased from Oxoid (Basingstoke, United Kingdom). Then bacterial identification was performed using the VITEK 2 Compact automatic microorganism analysis system (bioMerieux, Marcy-l'Étoile, France) and BD-Bruker MALDI Biotyper microorganism mass spectrometry rapid identification system (BD, Wokingham, United Kingdom).

Machine-based and paper-based susceptibility tests were used for evaluating drug sensitivity. Among them, the machine-based susceptibility test applied VITEK 2 Compact automatic microbiological analysis system to determine the minimum inhibitory concentration (MIC) of commonly used antibacterial drugs; the paper-based susceptibility test used Mueller Hinton Agar plates (Oxoid). Cefoperazone-sulbactam, imipenem, tigecycline, amikacin, ciprofloxacin, and minocycline were purchased from Oxoid. According to the Clinical and Laboratory Standards Institute M100-S27 document, 2017 edition, the sensitivity of both tests was determined as sensitive (S), intermediate resistant (I), and resistant (R). The determination of susceptibility to cefoperazone-sulbactam referred to cefoperazone. The susceptibility to tigecycline of *Enterobacteriaceae* and *Acinetobacter* was determined based on the United States Food and Drug Administration standard: S (MIC ≤ 2 μg/mL), I (MIC ≤ 4 μg/mL), and R (MIC ≥ 8 μg/mL).

***Statistical analysis***

Data were analysedusing the R 3.5.1 software.The rate was expressed as a percentage. The Cochran-Armitage trend test (referred to as CATT) was used to analyse the changing trend of drug resistance rates with time. *P <* 0.05 was considered statistically significant.

**RESULTS**
***Bacterial distribution***

A total of 3387 pathogens were isolated from various clinical specimens of 2048 critically ill patients, including 1805 strains of Gram-negative bacteria (53.29%), 1141 Gram-positive bacteria (33.69%), and 441 fungi (13.02%). The Gram-negative bacteria were mainly *A. baumannii* (660 strains), *Klebsiella pneumoniae* (347 strains), *P. aeruginosa* (338 strains), and *E. coli* (237 strains). The Gram-positive bacteria mainly included *S. aureus* (436 strains), *S. epidermidis* (181 strains), *S. haemolyticus* (161 strains), and *E. faecalis* (140 strains). The fungi were mainly *Candida albicans* (207 strains), followed by *C. tropicalis* (95 strains). As a result, the top six bacteria isolated from emergency patients were *A. baumannii*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*, and *C. albicans*.

 From 2013 to 2017, the isolation rates of common pathogens in the emergency department decreased including *A. baumannii* (25.5% to 17.4%), *S. aureus* (21.0% to 7.1%), *P. aeruginosa* (12.3% to 10.3%), and *E. coli* (7.6% to 6.5%). However, the isolation rate of *K. pneumoniae* increased from 7.1% to 12.1% (Figure 1).

***Drug resistance of Gram-negative bacteria***

Although the isolation rate of *A. baumannii* has been decreasing over the years, it was still ranked first for many years and is a widely resistant strain, whose resistance rates to imipenem and ciprofloxacin are above 90%. The drug with the lowest resistance rate of *A. baumannii* to common clinical antibiotics was tigecycline, followed by minocycline, but sensitivity to the two drugs has also been decreasing each year (*P* < 0.01).

The resistance rates of *P. aeruginosa* to cefoperazone/sulbactam and imipenem were higher, with the resistance to cefoperazone/sulbactam increasing year over the years (*P* < 0.01), but its resistance rate to amikacin was below 10%.

*K. pneumoniae* had higher resistance rates to imipenem, cefoperazone/sulbactam, amikacin, and ciprofloxacin, with the lowest resistance rate to tigecycline. The resistance rate to minocycline was also high but it decreased year over year (*P* < 0.01).

For *E. coli*, the resistance to ciprofloxacin was high, and the resistance rate to cefoperazone/sulbactam showed an upward trend year after year (*P <* 0.01). In addition, the resistance rates to imipenem, amikacin, and tigecycline were low, with the resistance rate to tigecycline being zero for the last 3 years (Table 1).

***Drug resistance of Gram-positive bacteria***

*S. aureus* is the one of the top Gram-positive bacteria isolated from clinical examination specimens of emergency department patients. As shown in Table 2, the resistance rates of *S. aureus* to levofloxacin, penicillin G, and tetracycline were high, but the resistance rates to penicillin G and tetracycline showed a downward trend (*P <* 0.01). Moreover, the resistance rates to vancomycin and tigecycline were always zero.

***Analysis of patients infected with K. pneumoniae***

As mentioned above, the isolation rates of common pathogens decreased each year, with the exception of *K. pneumoniae*. We further analysed the clinical data of all patients infected with *K. pneumoniae* (Table 3). There were 347 patients with *K. pneumoniae* infection aged between 18 years and 96 years, with an average age of 73.35 ± 14.60 years. Notably, we found that the percentage of patients with deep venous catheterisation or retention catheterisation was much higher than that of patients without both operations.

**DISCUSSION**

This study showed that the top six pathogens isolated from emergency patients in our hospital from 2013 to 2017 were *A. baumannii*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*, and *C. albicans,* consistent with other reports in the emergency department of the top three hospitals in the same area. The detection rates of drug-resistant bacteria were high, showing the severe situation of antibiotic resistance. Therefore, these findings provide a good basis for the early delivery of empirical medication for critically ill patients.

With the emergence of antibacterial drugs, the rate of bacterial resistance remains high[6]. In this study, we found that *S. aureus* had high resistance rates to levofloxacin, penicillin G, and tetracycline, but the resistance rates to vancomycin and tigecycline were always zero. In addition, five linezolid-insensitive strains of *S. aureus* were discovered, consistent with a previous report[7]. Therefore, vancomycin should be given priority in the clinical treatment of severe patients with *S. aureus* infection. However, in case of adverse reactions, such as hyperpyrexia and hypersensitivity after vancomycin administration, tigecycline may be selected and targeted drugs may be given after drug sensitivity testing[8,9]. Hussein *et al* indicated that high methicillin-resistant *Staphylococcus aureus* (MRSA) prevalence was found among healthcare workers (HCWs) in Kurdistan Region, Iraq. A total of 22.5% of HCWs were *S. aureus* carriers compared with 18.7% of non-HCWs; 61.0% of *S. aureus* strains isolated from HCWs were MRSA compared with 21.6% from non-HCWs. The mean working years of MRSA carriers was significantly higher than that of MRSA non-carriers. Basic infection control measures, a screening programme, and treatment of MRSA-positive HCWs can help as an effective measure to control MRSA infections[10]. In addition, it was shown that among 13 patients infected with vancomycin-resistant *Enterococcus*, most patients had lower limb wound infection[11]. Therefore, for patients with lower limb infection of vancomycin-resistant enterococcus, strict observation and active treatment are required to prevent multiple infections.

*A. baumannii* is a common colonised pathogen in hospital, and is also a relatively common pathogen of nosocomial acquired pneumonia[12]. In this study, its isolation rate ranked first for many years, and it was an extensively drug-resistant strain. *A. baumannii* in the emergency department is mostly due to nosocomial infection during hospitalisation[13,14], and there are few reports that *A. baumannii* causes community infection.

*K. pneumoniae* ranked second in the number of Gram-negative strains isolated in the emergency department. Recently, it has been reported that the drug resistance rate of *carbapenem-resistant enterobacteriaceae* shows a steady increasing trend, among which *Klebsiella* bacteria account for the largest proportion[15]. In this study, *K. pneumoniae* showed higher resistance to imipenem, cefoperazone/sulbactam, amikacin, and ciprofloxacin. The resistance of *K. pneumoniae* to carbapenem is mainly due to the production of carbapenemases, and few antibacterial drugs are available for the strains resistant to carbapenem, making clinical treatment difficult. A study in southern Europe showed a higher incidence of inappropriate empirical treatment for the multidrug-resistant *K. pneumoniae* bloodstream infection, resulting in a more than two-fold increase in patient mortality[16]. However, it has also been demonstrated that patients who receive carbapenem monotherapy or combination therapy within the first 5 d after blood culture positive for β-lactamase-producing *K. pneumoniae* infection have a significantly lower mortality than those who receive non-carbapenem antibiotics[17]. Therefore, carbapenems are still recommended as the treatment of choice for patients with severe infections, and compound agents containing β-lactamase inhibitors can be considered for patients with mild to moderate infections. Moreover, due to the increasing reports of carbapenem-resistant *K. pneumoniae* in recent years, high doses of carbapenem can be given for treatment[18], and tigecycline can also be selected due to its good *in vitro* antibacterial activity[19].

The positive rate of β-lactamase-producing *E. coli* from emergency sources should be low, but our study revealed that *E. coli* had high resistance to ciprofloxacin and cefoperazone/sulbactam, indicating that its resistance to quinolones and cephalosporins is still very prominent. In addition, the resistance rate of *E. coli* to imipenem was low, consistent with a previous study[20].

As mentioned above, *K. pneumoniae* has been the only bacteria with increasing detection rate among the most common bacteria at the emergency department for the past 5 years, and the resistance to antibiotics such as meropenem and imipenem is also gradually increasing. These findings were in agreement with previous study[21], bringing great difficulties for clinical anti-infective treatment. Therefore, we further analysed the clinical data of all patients infected with *K. pneumoniae* and found that the proportion of patients with deep venous catheterisation or retention catheterisation was much higher than that of patients without both operations, indicating that indwelling deep venous catheter or urinary catheter is an independent risk factor for bloodstream infection with *K. pneumoniae*[22]. Long-term indwelling urethral catheter causes bloodstream infection likely due to the colonisation of *K. pneumoniae* in damaged urethral mucosa during intubation and its regular release into the blood[23]. Whereas the central venous catheter provides a direct way for bacteria to invade into the bloodstream, inducing catheter-related bloodstream infection. Furthermore, because the catheter is left in the blood vessel, pathogenic bacteria in the blood can easily attach to the front end of the catheter to gradually form a biofilm that is difficult to remove, which becomes a secondary infection source and aggravates the severity of infection. Therefore, in patients with clinically diagnosed bloodstream infections, when anti-infective drug therapy fails, the possibility of catheter-associated bacteraemia should be considered. The ureter or central venous catheter should be removed timely. Other reports show that the use of antibiotics, especially cephalosporins and quinolones, is a risk factor for *K. pneumoniae* bloodstream infection[23,24]. In addition, the total amount and days of antibiotic use were also found to be significantly associated with the development of *K. pneumoniae* infection[25]. Hence, short-course antibiotics may be useful in reducing drug-resistant bacteria[26].

There is a certain course of treatment with antibiotics, which should be administered on time once adopted to maintain sufficient concentration of drugs in patients to reduce the generation of drug-resistant strains[27,28]. Some recent studies offer some hope for tackling bacterial resistance[29]. Bacteriophages have many advantages over antibiotics in their use to treat and prevent infection by drug-resistant bacteria. Their therapeutic effects are significantly different from those of antibiotics, making them still sensitive to multidrug-resistant bacteria[30]. Therefore, phages are currently seen as a potential effective treatment for many multidrug-resistant bacteria[31]. However, at the present stage, it is still of great significance to strengthen the pathogenic examination and monitoring in the emergency department and understand the distribution and drug resistance trends of the prevalent strains, so as to guide the rational use of drugs, reduce the production of multidrug-resistant bacteria, reduce the hospital infection rate and improve the success rate of patient treatment.

In summary, the pathogenic bacteria isolated from the emergency department were mainly *A. baumannii*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*, and *C. albicans*, with high detection rates of drug-resistant bacteria. When critically ill patients are admitted to the emergency department, initial antibiotic treatment should be selected empirically according to the distribution characteristics of bacteria in this area while bacteriological examination should be conducted on the clinical samples as soon as possible, and the later drug regimen should be adjusted timely according to the results of pathogen culture and drug sensitivity. For patients with extremely serious infections and life risk at any time, multi-drug regimens can be considered to achieve early control of the disease.

**Article Highlights**

***Research background***

Antibiotic resistance has become a global threat for human health, calling for rational use of antibiotics.

***Research motivation***

The premise of rational drug use is to understand the distribution of pathogens and the trends and characteristics of drug resistance.

***Research objectives***

In this study, we analysed the distribution characteristics and drug resistance to different antibiotics of the bacteria isolated from the emergency department specimens in our hospital from 2013 to 2017. This study is of great significance for the selection of drugs for initial empirical treatment in the emergency department and the careful selection of antibiotics to reduce the generation of drug-resistant strains.

***Research methods***

The isolation media including China-blue plate and blood agar plate were purchased from Oxoid. The bacterial identification was then performed using the VITEK 2 Compact automatic microorganism analysis system and BD-Bruker MALDI Biotyper microorganism mass spectrometry rapid identification system. Data were analysedusing R 3.5.1 software.The rate was expressed as a percentage. The Cochran-Armitage trend test was used to analyse the change trend of drug resistance rates with time. *P <* 0.05 was considered statistically significant.

***Research results***

The top six bacteria isolated from emergency patients were *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Candida albicans*. From 2013 to 2017, the isolation rates of common pathogens in the emergency department decreased, including *A. baumannii* (25.5% to 17.4%), *S. aureus* (21.0% to 7.1%), *P. aeruginosa* (12.3% to 10.3.%), and *E. coli* (7.6% to 6.5%). However, the isolation rate of *K. pneumoniae* increased from 7.1% to 12.1%. The drug with the lowest resistance rate of *A. baumannii* to common clinical antibiotics was tigecycline, followed by minocycline, but the sensitivity to the two drugs has been also decreasing each year (*P* < 0.01). The resistance rates of *P. aeruginosa* to cefoperazone/sulbactam and imipenem were higher, with the resistance to cefoperazone/sulbactam increasing each year (*P* < 0.01), but its resistance rate to amikacin was below 10%. *K. pneumoniae* had higher resistance rates to imipenem, cefoperazone/sulbactam, amikacin, and ciprofloxacin, with the lowest resistance rate to tigecycline. The resistance rate to minocycline was also high but it decreased year over year (*P* < 0.01). For *E. coli*, the resistance to ciprofloxacin was high, and the resistance rate to cefoperazone/sulbactam showed an upward trend year after year (*P <* 0.01). the resistance rates of *S. aureus* to levofloxacin, penicillin G, and tetracycline were high, but the resistance rates to penicillin G and tetracycline showed a downward trend (*P <* 0.01).

***Research conclusions***

The pathogenic bacteria isolated from the emergency department were mainly *A. baumannii*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*, and *C. albicans*, with high detection rates of drug-resistant bacteria

**What are the new findings of this study?** The pathogenic bacteria isolated from the emergency department were mainly *Acinetobacter baumannii*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Candida albicans*, with high detection rates of drug-resistant bacteria. When critically ill patients are admitted to the emergency department, initial antibiotic treatment should be selected empirically according to the distribution characteristics of bacteria in this area while bacteriological examination should be conducted on the clinical samples as soon as possible, and the later drug regimen should be adjusted timely according to the results of pathogen culture and drug sensitivity. For patients with extremely serious infections and life risk at any time, multi-drug regimens can be considered to achieve early control of the disease. These findings provided a good basis for the early delivery of empirical medication for critically ill patients. There is a certain course of treatment with antibiotics, which should be administered on time once adopted to maintain sufficient concentration of drugs in patients to reduce the generation of drug-resistant strains. Some recent studies offer some hope for tackling bacterial resistance. Bacteriophages have many advantages over antibiotics in their use to treat and prevent infection by drug-resistant bacteria. Their therapeutic effects are significantly different from those of antibiotics, making them still sensitive to multidrug-resistant bacteria. A total of 2048 critically ill patients were enrolled. The clinical examination specimens of these patients were collected, including deep sputum retained after adequate gargling (secretions from deep respiratory tract in patients with tracheotomy or intubation), urine, localised secretions, and blood from the apical segment of the catheter in patients with central venous catheterisation. As mentioned above, *K. pneumoniae* has been the only bacteria with the increasing detection rate among the most common bacteria at the emergency department for the past 5 years, and the resistance to antibiotics such as meropenem and imipenem was also gradually increasing. The pathogenic bacteria isolated from the emergency department were mainly *A. baumannii*, *S. aureus*, *Klebsiella pneumoniae*, *P. aeruginosa*, *E. coli*, and *C. albicans*, with high detection rates of drug-resistant bacteria. Phages are currently seen as a potential effective treatment for many multidrug-resistant bacteria. However, at the present stage, it is still of great significance to strengthen the pathogenic examination and monitoring in the emergency department and understand the distribution and drug resistance trends of the prevalent strains, so as to guide the rational use of drugs, reduce the production of multidrug-resistant bacteria, reduce the hospital infection rate and improve the success rate of patient treatment.

***Research perspectives***

There may be bias in data collection of retrospective studies. The future research direction is the rational use of antibiotics.

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**Figure 1 Separation rates of common pathogens in the emergency department from 2013 to 2017.** Aba: *Acinetobacter baumannii*; sau: *Staphylococcus aureus*; pae: *Pseudomonas aeruginosa*; eco: *Escherichia coli*; kpn: *Klebsiella pneumoniae*.

**Table 1 Analysis of resistance rates of Gram-negative bacteria**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gram-negative bacteria** | **Drugs**  | **2013** | **2014** | **2015** | **2016** | **2017** | **CATT** | ***P* value** |
| **R** | **I/S** | **R** | **I/S** | **R** | **I/S** | **R** | **I/S** | **R** | **I/S** |
| *Acinetobacter baumannii* | Cefoperazone/sulbactam | 84  | 97  | 91  | 86  | 79  | 15  | 80  | 23  | 80  | 25  | 47.72  | < 0.01 |
| Imipenem | 174  | 7  | 170  | 7  | 89  | 5  | 97  | 6  | 102  | 3  | 0.05  | 0.82  |
| Tigecycline | 7  | 174  | 6  | 171  | 0  | 94  | 10  | 93  | 12  | 93  | 11.13  | < 0.01 |
| Amikacin | 91  | 90  | 89  | 89  | - | - | - | - | - | - | 0.00  | 1.00  |
| Ciprofloxacin | 171  | 10  | 167  | 10  | 89  | 5  | 98  | 5  | 103  | 2  | 1.46  | 0.23  |
| Minocycline | 116  | 65  | 70  | 107  | 17  | 77  | 29  | 74  | 15  | 90  | 79.13  | < 0.01 |
| *Pseudomonas aeruginosa* | Cefoperazone/sulbactam | 18  | 69  | 17  | 58  | 7  | 49  | 19  | 39  | 27  | 35  | 10.17  | < 0.01 |
| Imipenem | 29  | 58  | 39  | 36  | 28  | 28  | 28  | 30  | 24  | 38  | 0.31  | 0.58  |
| Tigecycline | - | - | - | - | - | - | - | - | - | - | - | - |
| Amikacin | 5  | 82  | 5  | 70  | 2  | 54  | 5  | 53  | 2  | 60  | 0.06  | 0.80  |
| Ciprofloxacin | 19  | 68  | 20  | 55  | 16  | 40  | 15  | 44  | 10  | 52  | 0.47  | 0.50  |
| Minocycline | - | - | - | - | - | - | - | - | - | - | - | - |
| *Klebsiella pneumoniae* | Cefoperazone/sulbactam | 12  | 39  | 58  | 30  | 23  | 41  | 33  | 38  | 40  | 33  | 1.94  | 0.16  |
| Imipenem | 5  | 46  | 54  | 34  | 25  | 39  | 32  | 39  | 34  | 39  | 3.91  | 0.05  |
| Tigecycline | - | - | 6  | 82  | 5  | 59  | 12  | 59  | 7  | 66  | 1.48  | 0.22  |
| Amikacin | 1  | 50  | 36  | 52  | 19  | 45  | 28  | 43  | 25  | 48  | 6.86  | < 0.01 |
| Ciprofloxacin | 20  | 31  | 58  | 30  | 35  | 29  | 35  | 36  | 40  | 33  | 0.04  | 0.85  |
| Minocycline | 23  | 28  | 31  | 57  | 19  | 45  | 13  | 58  | 12  | 61  | 17.53  | < 0.01 |
| *Escherichia coli* | Cefoperazone/sulbactam | 3  | 51  | 2  | 37  | 12  | 45  | 4  | 44  | 13  | 26  | 11.30  | < 0.01 |
| Imipenem | 0  | 54  | 4  | 35  | 3  | 54  | 0  | 48  | 5  | 34  | 3.21  | 0.07  |
| Tigecycline | - | - | 3  | 36  | 0  | 57  | 0  | 48  | 0  | 39  | 　 | 　 |
| Amikacin | 3  | 51  | 1  | 38  | 1  | 56  | 1  | 47  | 7  | 32  | 3.20  | 0.07  |
| Ciprofloxacin | 35  | 19  | 25  | 14  | 34  | 23  | 28  | 20  | 27  | 12  | 0.00  | 0.98  |
| Minocycline | 19  | 35  | 7  | 32  | 4  | 53  | 9  | 39  | 4  | 35  | 8.41  | < 0.01 |

CATT: Cochran-Armitage trend test; S: Sensitive; I: Intermediate resistant; R: Resistant.

**Table 2 Analysis of resistance rates of Gram-positive bacteria**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gram-positive bacteria** | **Drugs**  | **2013** | **2014** | **2015** | **2016** | **2017** | **CATT** | ***P* value** |
| **R** | **I/S** | **R** | **I/S** | **R** | **I/S** | **R** | **I/S** | **R** | **I/S** |
| *Staphylococcus aureus* | Vancomycin | 0  | 149  | 0  | 142  | 0  | 58  | 0  | 44  | 0  | 43  | - | - |
| Levofloxacin | 131  | 18  | 130  | 12  | 38  | 20  | 25  | 19  | 21  | 22  | 53.68 | < 0.01 |
| Linezolid  | 1  | 148  | 4  | 138  | 0  | 58  | 0  | 44  | 0  | 43  | 0.75 | 0.39 |
| Tigecycline | 0  | 149  | 0  | 142  | 0  | 58  | 0  | 44  | 0  | 43  | - | - |
| PenicillinG | 146  | 3  | 140  | 2  | 55  | 3  | 41  | 3  | 41  | 2  | 3.45 | 0.06 |
| Tetracycline | 123  | 26  | 131  | 11  | 35  | 23  | 26  | 18  | 25  | 18  | 28.27 | < 0.01 |

CATT: Cochran-Armitage trend test.

**Table 3 Analysis of clinical data of patients with *Klebsiella pneumoniae* infection, *n* = 347**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Influence factors** | **Cases** | **Percentage**  | **Influence factors** | **Cases** | **Percentage**  |
| Gender | Male | 175 | 53.19 | Deep vein catheterisation | Yes | 224 | 68.09 |
|  | Female | 154 | 46.81 |  | No | 105 | 31.91 |
| Age in yr | ≥ 60 | 277 | 84.19 | Mechanical ventilation | Yes | 93 | 28.27 |
|  | < 60 | 52 | 15.81 |  | No | 236 | 71.73 |
| Tracheotomy | Yes | 9 | 2.74 | Retention catheterisation | Yes | 241 | 73.25 |
| 　 | No | 320 | 97.26 | 　 | No | 88 | 26.75 |

CATT: Cochran-Armitage trend test.