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Original Article

Retrospective analysis of the impact of pathogen spectrum and antibiotic resistance on the treatment efficacy of respiratory tract infections from 2012 to 2022

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Abstract: Objectives: To examine the impact of pathogen spectrum and antibiotic resistance on the treatment efficacy of clinical microbial infections from 2012 to 2022. Methods: Retrospective analysis of clinical data from 1200 patients with microbial infections admitted to The Fifth Hospital of Xiamen. Bacterial cultures and drug sensitivity tests were conducted, and the efficacy of first-line antibiotics was evaluated. Results: A total of 1258 pathogens were identified, with 57.23% Gram-positive and 37.84% Gram-negative bacteria. Staphylococcus aureus and Staphylococcus epidermidis showed high resistance to penicillin and cephalosporins. Klebsiella pneumoniae and Escherichia coli exhibited elevated resistance to imipenem and cephalosporins. From 2018 to 2022, there was an increase in resistance to cephalosporins and a decrease in treatment efficacy ($P<0.05$). Conclusions: Rising resistance rates to cephalosporins among Gram-positive and Gram-negative bacteria have led to diminished antibiotic efficacy. Adjustments in antibiotic selection, such as using glycopeptide antibiotics, are needed to combat resistance.

Keywords: Microbial infection, pathogen spectrum, antibiotics, resistance

Introduction

Microbial infection encompasses the invasion of pathogenic microorganisms into the human body through diverse routes, eliciting bodily reaction symptoms [1]. Upon entry, most pathogens are eradicated by the body's immune system, often resulting in either asymptomatic presence or mild tissue damage as latent infection symptoms [2]. However, under conditions of heightened toxicity, substantial quantity, or compromised immune response, pathogenic microorganisms can induce tissue damage, leading to pathological alterations and clinical manifestations such as fever, rash, and diarrhea [3]. While acute symptoms in the human immune system can facilitate the clearance of some microbial infections, in other instances, the body's immune response is inadequate, culminating in chronic infection [4]. Although antibiotics are primary in microbial infection treatment, prolonged and excessive utilization can foster resistance development [5]. Antibiotic resistance ensues when formerly susceptible pathogens undergo changes, rendering them tolerant to specific antibiotics due to a variety of influencing factors, thereby adversely affecting patient outcomes [6].

In the context of clinical microbial infections, Gram-positive and Gram-negative bacteria represent the predominant pathogenic categories. Gram-positive bacteria, characterized by their thick peptidoglycan cell walls, are known for their ability to form biofilms and exhibit resistance to certain antibiotics [7]. Common Gram-positive pathogens include Staphylococcus aureus and Staphylococcus epidermidis, which frequently develop resistance to penicillin and cephalosporins [8]. On the other hand, Gram-negative bacteria, distinguished by their outer membrane containing lipopolysaccharides, tend to show higher resistance to many antibiotics due to the presence of efflux pumps and the production of extended-spectrum beta-lactamases (ESBLs). Notable examples include Klebsiella pneumoniae and Escherichia coli, which exhibit high resistance to imipenem and

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cephalosporins [9]. Understanding the resistance patterns of these bacteria is essential for developing effective treatment strategies and preventing the spread of multidrug-resistant organisms.

Currently, the treatment of bacterial infections relies heavily on the use of broad-spectrum antibiotics such as cephalosporins [10]. However, the increasing prevalence of antibiotic resistance has led to a decline in the efficacy of these drugs, necessitating the exploration of alternative treatments. The overuse and misuse of antibiotics contribute significantly to the development of resistance, prompting healthcare providers to seek more targeted and personalized therapeutic approaches [11]. Strategies such as the use of glycopeptide antibiotics like vancomycin, enhanced infection control measures, and the development of novel antimicrobial agents are being considered to combat the growing problem of antibiotic resistance [12, 13].

Given the evolving landscape of antibiotic resistance and its impact on treatment outcomes, this study retrospectively reviewed the clinical records of 198 patients with clinical microbial infections admitted to our hospital from January 2012 to December 2022, with the objective of examining the influence of pathogen spectrum and antibiotic resistance on the treatment efficacy of clinical microbial infections. The aim is to furnish a basis for judicious antibiotic use in clinical practice and augment the effectiveness of clinical microbial infection treatment.

Patients and methods

Study population

A retrospective analysis was conducted on the clinical data of a total of 1200 patients with clinical microbial infections admitted to the Department of Gastroenterology, the Fifth Hospital of Xiamen from January 2012 to December 2022, comprising 600 patients from January 2012 to December 2017 and 600 patients from January 2018 to December 2022. Inclusion criteria: (1) Clinical microbial infection patients admitted to our hospital with positive microbiological culture results; (2) Aged ≥18 years; (3) Clear consciousness and coherent responses; (4) Complete and comprehensive medical records. Exclusion criteria: (1) Severe malnutrition, coagulation disorders, and anemia; (2) Breastfeeding and pregnant women; (3) Patients with malignant tumors; (4) Patients with Parkinson's disease or schizophrenia; (5) Recent history of significant trauma or surgery; (6) Patients with concomitant diseases such as pulmonary tuberculosis. This study was approved by the Ethics Committee of The Fifth Hospital of Xiamen (Approval no. 19-FX-EC-023). Signed written informed consents were obtained from the patients and/or guardians.

Test methods

(1) Bacterial culture: All specimens were inoculated on blood agar plates and cultured for 24 hours at 35°C in a constant temperature incubator, and positive specimens were subcultured on blood agar plates for continued cultivation and bacterial isolation. Bacterial identification was performed strictly following the "National Clinical Laboratory Operating Procedures" standards and analyzed using the VITEK2 compact bacterial identification analyzer (manufacturer: bioMérieux, France) and matching reagents; (2) Drug susceptibility test: The K-B (paper disk diffusion method) was used for drug susceptibility testing, with quality control strains including Staphylococcus aureus ATCC25923, Escherichia coli ATCC25922, Pseudomonas aeruginosa ATCC27853, and Klebsiella pneumoniae ATCC700603. The tested antibacterial drugs included imipenem, cefoxitin, cefepime, gentamicin, ciprofloxacin, levofloxacin, amoxicillin, tetracycline, chloramphenicol, clindamycin, erythromycin, ceftriaxone, ampicillin, penicillin, vancomycin, and teicoplanin; (3) Assessment of efficacy: Cephalosporin antibiotics were used as the first-choice treatment, and patients with clinical symptoms disappeared and microbiological culture results turned negative after treatment were classified as effective, while those who did not meet the aforementioned criteria were deemed ineffective [14]. For the assessment of efficacy, a subset of 120 cases (60 cases from January 2012 to December 2017 and another 60 from January 2018 to December 2022) was selected based on the completeness of medical records, adherence to the inclusion criteria, and random sampling methods to ensure a representative sample size for statistical analysis.

Table 1. Baseline data of 1200 cases of clinical microbiological infections patients from 2012 to 2022

Category	Cases	Percentage (%)
Gender		
Male	649	54.08
Female	551	45.92
Age		
20-40 years old	398	33.17
41-60 years old	562	46.83
Over 60 years old	240	20.00
Disease type		
Acute bronchitis	208	17.33
Chronic bronchitis	296	24.68
Pneumonia	238	19.83
Lung abscess	86	7.17
Acute tonsillitis	306	25.50
Others	66	5.50

Table 2. Distribution of pathogenic microorganisms among 1200 clinical microbiological infection cases from 2012 to 2022

Pathogenic Microorganism	Number of Strains	Percentage (%)
Gram-positive bacteria	720	57.23
Staphylococcus aureus	430	34.18
Hemolytic Staphylococcus	22	1.75
Streptococcus pneumoniae	26	2.07
Staphylococcus epidermidis	230	18.28
Enterococcus	12	0.95
Gram-negative bacteria	538	42.77
Klebsiella pneumoniae	246	19.55
Escherichia coli	154	12.24
Acinetobacter baumannii	52	4.13
Pseudomonas aeruginosa	48	3.82
Citrobacter freundii	38	3.02
Total	1258	100.00

Observation indicators

The distribution of pathogen spectrum during bacterial culture and the resistance of major Gram-positive and Gram-negative bacteria to antibiotics during drug susceptibility testing were observed for all patients. The resistance of major Gram-positive and Gram-negative bacteria from January 2012 to December 2017 and January 2018 to December 2022 was compared, along with the efficacy of first-line antibiotics.

Statistical analysis

Data were analyzed using Statistic Package for Social Science (SPSS) 25.0 statistical software (IBM, Armonk, NY, USA), with frequency data presented as n (%). When the sample size was ≥40 and the theoretical frequency was $1 \leq T < 5$, the chi-square test correction formula was used; for sample sizes <40 or theoretical frequency $T < 1$, the Fisher exact probability method was employed for statistical analysis, with $P < 0.05$ indicating statistical significance.

Results

Baseline characteristics of 1200 patients with clinical microbial infections from 2012 to 2022

During the period of 2012 - 2022, baseline data of 1200 clinical microbiological infection patients were collected. As shown in **Table 1**, of the 1200 patients, 54.08% were male and 45.92% were female. The distribution of age groups was as follows: 33.17% were 20-40 years, 46.83% were 41-60 years, and 20.00% were over 60 years old. The distribution of specific infections was: acute bronchitis accounted for 24.00%, chronic bronchitis accounted for 33.00%, pneumonia accounted for 19.83%, lung abscess accounted for 7.17%, acute tonsillitis accounted for 25.50%, and 4.83% were classified as other.

Distribution of pathogen spectrum in 1200 patients with clinical microbial infections from 2012 to 2022

Similarly, during the period of 2012 - 2022, the distribution of pathogenic bacteria in 1200 cases of clinical microbiological infections is presented in **Table 2**. A total of 1258 strains of pathogenic bacteria were detected, including 720 strains of Gram-positive bacteria, accounting for 57.23%, and 538 strains of Gram-negative bacteria, accounting for 42.77%. This suggests that Gram-positive and Gram-negative bacteria are the main infecting pathogens, with some patients experiencing mixed infections.

Table 3. Antimicrobial resistance of major Gram-positive bacteria

Category	Staphylococcus aureus (n=430)		Staphylococcus epidermidis (n=230)	
	Resistant Strains (strains)	Percentage (%)	Resistant Strains (strains)	Percentage (%)
Imipenem	120	27.91	112	48.70
Cefepime	224	52.09	120	52.17
Ceftazidime	172	40.00	110	47.83
Erythromycin	121	28.14	58	25.22
Ciprofloxacin	175	40.70	102	44.35
Levofloxacin	182	42.33	105	45.65
Amoxicillin	241	56.05	129	56.09
Tetracycline	182	42.33	100	43.48
Chloramphenicol	122	28.37	56	24.35
Clindamycin	65	15.12	36	15.65
Erythromycin	121	28.14	65	28.26
Ceftriaxone	223	51.86	120	52.17
Ampicillin	181	42.09	98	42.61
Penicillin	344	80.00	162	70.43
Vancomycin	1	0.23	0	0.00
Teicoplanin	0	0.00	0	0.00

Table 4. Antimicrobial resistance of major Gram-negative bacteria

Category	Klebsiella Pneumoniae (n=246)		Escherichia Coli (n=154)	
	Resistant Strains (strains)	Percentage (%)	Resistant Strains (strains)	Percentage (%)
Imipenem	123	50.00	50	32.47
Cefepime	144	14.52	52	33.77
Ceftazidime	125	50.81	54	35.06
Erythromycin	120	48.78	48	31.17
Ciprofloxacin	62	25.20	52	33.77
Levofloxacin	62	25.20	55	35.71
Amoxicillin	65	26.42	51	33.12
Tetracycline	120	48.78	49	31.82
Chloramphenicol	62	25.20	50	32.47
Clindamycin	64	26.02	52	33.77
Erythromycin	82	33.33	49	31.82
Ceftriaxone	158	64.23	102	66.23
Ampicillin	82	33.33	53	34.42
Penicillin	62	25.20	52	33.77
Vancomycin	2	0.81	0	0
Teicoplanin	0	0	0	0

Antibiotic resistance of major Gram-positive bacteria

As illustrated in **Table 3**, both Staphylococcus aureus and Staphylococcus epidermidis, major Gram-positive bacteria, exhibited higher resistance rates to penicillin, amoxicillin, cefoxitin, and ceftriaxone, suggesting the need to avoid using these antibiotics when treating Gram-positive bacterial infections.

Antibiotic resistance of major Gram-negative bacteria

As indicated in **Table 4**, the major Gram-negative bacteria, Klebsiella pneumoniae and Escherichia coli, showed higher resistance rates to imipenem, cefepime, and ceftriaxone, underscoring the necessity to avoid these antibiotics in the clinical management of Gram-negative bacterial infections.

Table 5. Comparison of antimicrobial resistance of major Gram-positive bacteria between January 2012 to December 2017 and January 2018 to December 2022 (%)

Category	Klebsiella Pneumoniae (n=246)		Escherichia Coli (n=154)	
	Jan 2012 to Dec 2017	Jan 2018 to Dec 2022	Jan 2012 to Dec 2017	Jan 2018 to Dec 2022
Imipenem	62 (28.18)	58 (27.62)	62 (49.60)	50 (47.62)
Cefepime	100 (45.45)	124 (59.05)*	50 (40.00)	70 (66.67)*
Ceftazidime	72 (32.73)	100 (47.62)*	52 (41.60)	58 (55.24)*
Erythromycin	62 (28.18)	59 (28.10)	31 (24.80)	27 (25.71)
Ciprofloxacin	89 (40.45)	86 (40.95)	56 (44.80)	46 (43.81)
Levofloxacin	92 (41.82)	90 (42.86)	58 (46.40)	47 (44.76)
Amoxicillin	125 (56.82)	116 (55.24)	69 (55.20)	60 (57.14)
Tetracycline	90 (40.91)	92 (43.81)	55 (44.00)	45 (42.86)
Chloramphenicol	62 (28.18)	60 (28.57)	31 (24.80)	25 (23.81)
Clindamycin	34 (15.45)	31 (14.76)	22 (17.60)	14 (13.33)
Erythromycin	60 (27.27)	61 (29.05)	38 (30.40)	27 (25.71)
Ceftriaxone	113 (51.36)	110 (52.38)	61 (48.80)	59 (56.19)
Ampicillin	91 (41.36)	90 (42.86)	54 (43.20)	44 (41.90)
Penicillin	174 (79.09)	170 (80.95)	82 (65.60)	80 (76.19)
Vancomycin	1 (0.45)	0 (0.00)	0 (0.00)	0 (0.00)
Teicoplanin	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

*$P<0.05$.

Comparison of antibiotic resistance of major Gram-positive bacteria between January 2012 to December 2017 and January 2018 to December 2022

As shown in **Table 5**, a comparison between January 2012 to December 2017 and January 2018 to December 2022 revealed an increasing trend in the resistance of major Gram-positive bacteria to cefoxitin and cefepime ($P<0.05$), indicating a continual rise in resistance to cephalosporin antibiotics among patients with Gram-positive bacterial infections from 2012 to 2022.

Comparison of antibiotic resistance of major Gram-negative bacteria between January 2012 to December 2017 and January 2018 to December 2022

As depicted in **Table 6**, a comparison between January 2012 to December 2017 and January 2018 to December 2022 indicated an increasing trend in the resistance of major Gram-negative bacteria to cefepime and ceftriaxone ($P<0.05$), suggesting a continual rise in resistance to cephalosporin antibiotics among patients with Gram-negative bacterial infections from 2012 to 2022.

Comparison of treatment efficacy of first-line antibiotics between January 2012 to December 2017 and January 2018 to December 2022

As shown in **Table 7**, a comparison between January 2012 to December 2017 and January 2018 to December 2022 revealed a trend of decreased efficacy and increased inefficacy of antibiotic treatment ($P<0.05$), indicating a decreasing trend in the effectiveness of antibiotic treatment for clinical microbial infections from 2012 to 2022.

Discussion

In recent years, with the increasing variety and widespread use of antimicrobial drugs in China, antimicrobial resistance has been on the rise, significantly affecting the efficacy of patient treatment [15, 16]. Hospitals themselves harbor a large number of pathogenic bacteria, and patients with clinical microbiological infections often have weakened immune systems, making them vulnerable to pathogen invasion and subsequent infections during diagnosis and treatment [17-20]. Timely identification of the pathogenic spectrum and changes in antimicrobial resistance among patients with clinical microbiological infections holds crucial signifi-

Table 6. Comparison of antimicrobial resistance of major Gram-negative bacteria between January 2012 to December 2017 and January 2018 to December 2022 (%)

Category	Staphylococcus aureus (n=430)		Staphylococcus epidermidis (n=230)	
	Jan 2012 to Dec 2017	Jan 2018 to Dec 2022	Jan 2012 to Dec 2017	Jan 2018 to Dec 2022
Imipenem	63 (28.64)	60 (28.57)	38 (30.40)	24 (22.86)
Cefepime	60 (27.27)	84 (40.00)*	20 (16.00)	30 (28.57)*
Ceftazidime	50 (22.73)	75 (35.71)*	21 (16.80)	31 (29.52)*
Erythromycin	60 (27.27)	60 (28.57)	17 (13.60)	14 (13.33)
Ciprofloxacin	32 (14.55)	30 (14.29)	30 (24.00)	26 (24.76)
Levofloxacin	33 (15.00)	29 (13.81)	31 (24.80)	27 (25.71)
Amoxicillin	35 (15.91)	30 (14.29)	37 (29.60)	32 (30.48)
Tetracycline	63 (28.64)	57 (27.14)	30 (24.00)	25 (23.81)
Chloramphenicol	32 (14.55)	30 (14.29)	18 (14.40)	13 (12.38)
Clindamycin	38 (17.27)	24 (11.43)	13 (10.40)	9 (8.57)
Erythromycin	43 (19.55)	39 (18.57)	22 (17.60)	16 (15.24)
Ceftriaxone	78 (35.45)	80 (38.10)	30 (24.00)	29 (27.62)
Ampicillin	42 (19.09)	40 (19.05)	28 (22.40)	26 (24.76)
Penicillin	32 (14.55)	30 (14.29)	42 (33.60)	40 (38.10)
Vancomycin	2 (0.91)	0 (0.00)	0 (0.00)	0 (0.00)
Teicoplanin	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

*$P<0.05$.

Table 7. Comparison of the efficacy of first-line antibiotic therapy in patients between January 2012 to December 2017 and January 2018 to December 2022 (%)

Time Period	Effective	Ineffective
Jan 2012 to Dec 2017 (n=60)	48 (80.00)	12 (20.00)
Jan 2018 to Dec 2022 (n=60)	37 (61.67)	23 (38.33)
χ^2	4.881	
P	0.027	

cance in guiding the development and adjustment of clinical treatment regimens [21, 22].

Research by Mehri et al. [23] found that in the spectrum of pathogens among infectious disease patients, Gram-positive bacteria accounted for 57.14%, Gram-negative bacteria for 35.71%, and fungi for 7.14%. In this study encompassing 1200 clinical microbiological infection cases from 2012 to 2022, a total of 1258 pathogenic strains were identified, with 720 (57.23%) being Gram-positive bacteria, 538 (42.77%) Gram-negative bacteria, and 52 (4.13%) fungi. These findings are consistent with the aforementioned research, indicating that clinical microbiological infection patients are predominantly affected by Gram-positive bacteria, followed by Gram-negative bacteria and fungi.

For the primary Gram-positive pathogens, *Staphylococcus aureus* and *Staphylococcus epidermidis*, the current treatment guidelines recommend the use of glycopeptides such as vancomycin and teicoplanin when there is confirmed or suspected methicillin-resistance, as these agents are known to have reliable activity against resistant strains [24]. Following initial empirical therapy with cephalosporins, if there is a lack of response or evidence of resistance, clinicians should switch to glycopeptides. Evidence supporting this approach comes from multiple randomized controlled trials showing improved outcomes with glycopeptide use in severe infections caused by methicillin-resistant Staphylococcus species [25, 26].

Regarding Gram-negative pathogens like *Klebsiella* pneumoniae and *Escherichia coli*, carbapenems (such as imipenem) are generally considered the first-line treatment for serious infections caused by extended-spectrum beta-lactamase (ESBL)-producing strains [27]. However, given the elevated resistance to carbapenems noted in our study, alternative options include the use of tigecycline, aminoglycosides (gentamicin), or fluoroquinolones (ciprofloxacin, levofloxacin) [28]. The choice of alternative antibiotics depends on local sus-

ceptibility patterns and the severity of the infection. For instance, tigecycline has been shown to be effective against ESBL-producing Enterobacteriaceae [29], but its use is reserved for multidrug-resistant infections where other options are not available due to potential side effects and its limited efficacy in severe sepsis [30].

Through a retrospective analysis of antimicrobial resistance changes in clinical microbiological infection patients from 2012 to 2022, it was found that from January 2018 to December 2022, there was a rising trend in antimicrobial resistance among the main Gram-positive and Gram-negative bacteria to cefepime and cefpodoxime ($P<0.05$). This potentially resulted from frequent drug switching, empirical drug use, non-standard antimicrobial drug use, changes in drug targets, decreased outer membrane permeability, and biofilm formation. Moreover, compared to January 2012 to December 2017, the efficacy of antibiotic treatment decreased while the inefficacy increased from January 2018 to December 2022 ($P<0.05$). This shift may be associated with the extensive, prolonged, and widespread use of cephalosporin drugs as first-line antibiotics, leading to the emergence of ESBLs, thereby reinforcing the resistance of Gram-positive and Gram-negative bacteria to these drugs and subsequently impacting patient treatment outcomes [31]. Additionally, the variation in patient demographics, underlying health conditions, and adherence to prescribed treatments may also play a role in the observed differences in treatment efficacy.

To further enhance the quality of microbiological testing in our laboratory, the following strategies are proposed: (1) Improving the professional competence and technical skills of laboratory staff, strictly adhering to aseptic principles, standardizing specific operational procedures, and conducting regular disinfection of aseptic laboratories [32]; (2) Strengthening patient education on sample collection, such as informing patients to provide midstream urine for urine samples and to collect sputum from the deepest part of the lungs for sputum samples [33]; (3) Intensifying training for laboratory staff, ensuring proper handling of specimen submission, and rigorously controlling specimen quality [34]; (4) Regularly calibrating the laboratory's testing instruments to avoid errors in test results due to instrument factors [35].

In summary, the spectrum of antibiotic-resistant pathogens in clinical microbiological infection patients at our hospital has evolved over time, with a rising trend in antibiotic resistance rates among main Gram-positive and Gram-negative bacteria to cephalosporin drugs, leading to reduced efficacy of broad-spectrum antibiotics. Therefore, appropriate adjustments to the choice of first-line antibiotics are necessary, such as replacing cephalosporin antibiotics with glycopeptide antibiotics, to mitigate the impact of resistance on antibiotic efficacy.

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Disclosure of conflict of interest

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