Wide spread and diversity of mutation in the gyrA gene of quinolone-resistant Corynebacterium striatum strains isolated from three tertiary hospitals in China

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Abstract

Background: Corynebacterium striatum was confirmed to be an important opportunistic pathogen, which could lead to multiple-site infections and presented high prevalence of multidrug resistance, particularly to quinolone antibiotics. This study aimed to investigate the mechanism underlying resistance to quinolones and the epidemiological features of 410 quinolone-resistant C. striatum clinical strains isolated from three tertiary hospitals in China.

Methods: A total of 410 C. striatum clinical strains were isolated from different clinical samples of patients admitted to three tertiary teaching hospitals in China. Antibiotic susceptibility testing was performed using the microdilution broth method and pulsed-field gel electrophoresis (PFGE) was used for genotyping. Gene sequencing was used to identify possible mutations in the quinolone resistance-determining regions (QRDRs) of gyrA.

Results: In total, 410 C. striatum isolates were sensitive to vancomycin, linezolid, and daptomycin but resistant to ciprofloxacin. Depending on the antibiotic susceptibility testing results of 12 antimicrobial agents, the 410 C. striatum strains were classified into 12 resistant biotypes; of these, the three biotypes R1, R2, and R3 were dominant and accounted for 47.3% (194/410), 21.0% (86/410), and 23.2% (95/410) of the resistant biotypes, respectively. Mutations in the QRDRs of gyrA were detected in all quinolone-resistant C. striatum isolates, and 97.3% of the isolates (399/410) showed double mutations in codons 87 and 91 of the QRDRs of gyrA. Ser-87 to Phe-87 and Asp-91 to Ala-91 double mutation in C. striatum was the most prevalent and accounted for 72.2% (296/410) of all mutations. Four new mutations in gyrA were identified in this study; these included Ser-87 to Tyr-87 and Asp-91 to Ala-91 (double mutation, 101 isolates); Ser-87 to Val-87 and Asp-91 to Gly-91 (double mutation, one isolate); Ser-87 to Val-87 and Asp-91 to Ala-91 (double mutation, one isolate); and Ser-87 to Ile-87 (single mutation, one isolate). The minimum inhibitory concentration of ciprofloxacin for isolates with double (96.5%; 385/399) and single (72.7%; 8/11) mutations was high (≥32 µg/mL). Based on the PFGE typing results, 101 randomly selected C. striatum strains were classified into 50 genotypes (T01-T50), including the three multidrug-resistant epidemic clones T02, T06, and T28; these accounted for...
Background
Recently, several reports have revealed that Corynebacterium striatum leads to multiple invasive infections [1, 2], and most C. striatum isolates are multidrug resistant, particularly to quinolones [3]. Point mutations in codons 87 and 91 in the quinolone resistance-determining regions (QRDRs) of gyrA were believed to be majorly responsible for the resistance of C. striatum to quinolones [4]. Quinolones tend to accumulate in the organs, and the resistant subpopulations of some common genus of bacteria may be selected upon exposure to quinolones, including multiple kinds of bacteria that colonize the skin and mucous membranes (such as corynebacteria) [5].

Although a high frequency of C. striatum was recently reported in China, the mechanism underlying the resistance of C. striatum to quinolones has been rarely reported in China [6, 7]. In addition, quinolone consumption was observed to be high in many hospitals in the last decade [8]. Furthermore, the previous use of fluoroquinolones or beta-lactam antibiotics was believed to be an essential risk factor for promoting the colonization or infection of C. striatum [9]. C. striatum is known to colonize multiple environmental and bodily surfaces [10] and spread among susceptible patients or even lead to outbreaks, which were observed in previous studies [3, 11].

This study investigated the actual resistance mechanism of C. striatum to quinolones with a larger number of isolates collected from three tertiary hospitals in China and explored its genotypic characterization and prevalence potential.

Methods
Isolation and identification of C. striatum
The hospitals enrolled in this study included The Affiliated Hospital of Inner Mongolian Medical University (hospital A, 3,000 beds), Shandong Provincial QianFushan Hospital (hospital B, 2,813 beds), and Bayannaoer People’s Hospital (hospital C, 1,700 beds), China, from March 2013 to May 2019. All C. striatum strains isolated from aseptic sites were identified. The quality of the sputum samples was evaluated for qualification based on the number of leukocytes and epithelium via microscopy [3], and the isolates collected from the qualified samples were enrolled in this study. All cultures suspected to be positive for C. striatum were routinely identified using VITEK-2 ANC card (BioMérieux, France) and stored at −80 °C. The isolates were further validated by MALDI-TOF microTyper (Tianrui, China) as well as 16S rRNA and rpoB sequencing technique [12]. Only one C. striatum strain from the same patient was selected in this study, whereas the repeated ones were excluded.

Antibiotic susceptibility test
The antibiotic susceptibility test was performed using the broth microdilution method, and the antibiotics tested include penicillin (1–64 μg/mL), cefepime (1–64 μg/mL), imipenem (1–64 μg/mL), linezolid (0.5–4 μg/mL), erithromycin (0.5–64 μg/mL), clindamycin (1–32 μg/mL), gentamycin (1–32 μg/mL), tetracycline (1–64 μg/mL), vancomycin (0.5–4 μg/mL), sulfamethoxazole (0.5/9.5–8/152 μg/mL), daptomycin (0.06–1 μg/mL), ciprofloxacin (1–256 μg/mL), and moxifloxacin (0.06–32 μg/mL). The susceptibility test and result analysis were performed according to the 30th edition of the Clinical and Laboratory Standards Institute guidelines [13] and the recommendation of the European Committee on Antimicrobial Susceptibility Testing [14]. Streptococcus pneumoniae ATCC 49619 was used as the control.

Pulsed-field gel electrophoresis (PFGE)
The bacterial density of the tested C. striatum isolates was adjusted to 3.5–4.0 Mcf and digested with lysostaphin (1 mg/mL) (Merck, USA) at 37 °C for 30 min. The bacterial chromosomal DNA of the isolates was extracted and cleaved using 40 U Swal (Takara, China). The DNA of the S. Braenderup H9812 standard strain was extracted and cleaved using 40 U XbaI (Takara, China) and utilized as the molecular mass standard. Electrophoresis was performed on the CHEF-Mapper XA PFGE system (BioRad, Hercules, CA, USA), and PFGE profiles were analyzed using the Bionumerics v.7.6 software. The isolates...
with 100% similarity were considered indistinguishable [15, 16], and each clone was named using a single capital letter.

**Detection of mutation in the QRDR region of gyrA**
The bacterial chromosomal DNA of the tested *S. aureus* isolates was extracted as per the instructions of the TIANamp Bacterial DNA kit (Tiangen Biotech, China). The pair of primers used for polymerase chain reaction (PCR) amplification and sequencing were Coryn-1 (GCG GCT ACG TAA AGT CC) and Coryn-2 (CCG CCG GAGCCG TTC AT). For PCR amplification, the protocol detailed by Sierra et al. was followed [5]. The PCR products were sequenced with the same primers as those used in PCR amplification on ABI 3730XL DNA Analyzer (Applied Biosystems, USA). Additionally, the sequence of *C. striatum* ATCC6940 was used as the control for sequence comparison among different clinical *C. striatum* isolates.

**Results**

**Characterization of the isolates**

From the 410 isolates analyzed in this study, 77.8% (319/410) were collected from hospital A, 10.0% (41/410) from hospital B, and 12.2% (50/410) from hospital C. Most of the *C. striatum* strains (88.3%; 362/410) were isolated from sputum (Table 1). The average age of the patients was 63 years, and male and female patients accounted for 71.2% (292/410) and 28.8% (118/410), respectively.

**Antibiotic susceptibility testing**
The antibiotic susceptibility testing results showed that all strains were sensitive to vancomycin, linezolid, and daptomycin and resistant to penicillin, cefepime, ciprofloxacin, and moxifloxacin. The total resistance rates of 410 *C. striatum* isolates to imipenem, erythromycin, clindamycin, tetracycline, gentamycin, sulfamethoxazole, and trimethoprim were 90.7% (372/410), 98.8 (405/410), 98.5 (404/410), 70.5 (289/410), 53.2 (218/410), and 98.0 (402/410), respectively (Table 2).

Based on the susceptibility testing results, 410 *C. striatum* strains can be classified into 12 resistance biotypes, designated as patterns R1–R12. Among the isolates, those with resistance to erythromycin, clindamycin, imipenem, tetracycline, and gentamycin were classified to be nonsusceptible as they were resistant or intermediate to the five types of antibiotics tested in this study. Among these, three dominant biotypes (R1, R2, and R3) were identified, which were resistant or intermediate to most antibiotics tested in this study, except for vancomycin, linezolid, and daptomycin. The resistance features of the 12 resistant biotypes diversely changed (Table 3). In total, 319 isolates collected from hospital A belonged to 12 resistance biotypes, and most of the isolates belonged to R1 (46.1%; 147/319), R2 (24.5%; 78/319), and R3 (23.5%; 75/319). In addition, 41 isolates collected from hospital B were divided into eight resistance biotypes, and 56.1% (23/41) and 17.1% of the isolates (7/41) belonged to R1 and R2, respectively. Finally, 50 isolates collected from hospital C were classified into four resistance biotypes, and 48.0% (24/50) and 36.0% of the isolates (18/50) belonged to R1 and R3, respectively.

**Gene sequencing**

Single-site and double-site mutations within the QRDRs of gyrA were observed among all 410 *C. striatum* strains, and eight mutations were observed in this study (Table 4). All isolates showed mutations in codon 87; 97.3% of the isolates (399/410) had double mutations in codons 87 and 91, whereas only 2.7% isolates (11/410) had a single mutation in codon 87. Ser-87 to Phe-87 and Asp-91 to Ala-91 double mutations in *C. striatum* accounted for 72.2% (296/410) of the isolates. Meanwhile, four new mutations in gyrA were found in this study, including Ser-87 to Tyr-87 and Asp-91 to Ala-91 (double mutation, 101 isolates), Ser-87 to Val-87 and Asp-91 to Gly-91 (double mutation, one isolate), Ser-87 to Val-87 and Asp-91 to Ala-91 (double mutation, one isolate), and Ser-87 to Ile-87 (single mutation, one isolate). Isolates with

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**Table 1** Demographic and clinical features of patients (n=410)

| Variable                  | Number (%) |
|---------------------------|------------|
| Age (years)               |            |
| <40                       | 6.6 (27/410) |
| 40–59                     | 33.4 (137/410) |
| 60–79                     | 44.1 (181/410) |
| ≥ 80                      | 15.9 (65/410) |
| Gender                    |            |
| Female                    | 28.8 (118/410) |
| Male                      | 71.2 (292/410) |
| Specimens                 |            |
| Sputum                    | 88.3 (362/410) |
| Wound discharge           | 4.1 (17/410) |
| BALF                      | 1.5 (6/410) |
| Whole blood               | 1.2 (5/410) |
| Pus                       | 1.0 (4/410) |
| Urine                     | 0.7 (3/410) |
| Central venous catheters  | 0.7 (3/410) |
| Nasopharyngeal swab       | 0.7 (3/410) |
| Drainage                  | 0.7 (3/410) |
| Hydrothorax and ascites   | 0.5 (2/410) |
| Cerebrospinal fluid       | 0.5 (2/410) |

*BALF* Bronchoalveolar lavage fluid
double mutations (96.5%; 385/399) in gyrA showed high minimum inhibitory concentration (MIC) of ≥ 32 μg/mL to ciprofloxacin, whereas 72.7% (8/11) of the C. striatum strains with a single mutation in gyrA presented with high MIC of ≥ 32 µg/mL to ciprofloxacin. For five quinolone-sensitive C. striatum clinical isolates collected in this study, no mutation in gyrA was identified.

**PFGE**

A total of 101 C. striatum strains with different resistance biotypes were randomly selected for PFGE typing, and 50 PFGE types were identified, among which types T02 (15 isolates), T06 (6 isolates), and T28 (12 isolates) were dominant clones that accounted for 14.9% (15/101), 5.9% (6/101), and 11.9% (12/101), respectively. The isolates belonged to the clones with similar antibiotic resistance features and were multidrug resistant. These three clones were mainly isolated from patients admitted to the neurosurgery unit and intensive care unit (ICU) (Fig. 1). The T02 clone prevailed in hospital A (40.00%; 6/15) and hospital C (60.00%; 9/15), whereas the T06 and T28 clones were only isolated from the patients admitted to hospital C (18/18; 100.0%). The T02 clone showed a long-term persistence in hospital A from 2016 to 2018, and

### Table 2 Antibiotics susceptibility profiles of 410 C. striatum strains

| Antibiotics       | MIC (μg/ml) | MIC<sub>50</sub> | MIC<sub>90</sub> | Range          | Percentage of resistant isolates, % (n/410) |
|-------------------|-------------|------------------|------------------|----------------|---------------------------------------------|
| Penicillin        | ≥ 8         | > 64             | ≤ 1, ≥ 4         | 100 (410/410)  |
| Cefepime          | ≥ 8         | > 64             | ≤ 1, ≥ 4         | 100 (410/410)  |
| Imipenem          | ≥ 32        | > 64             | ≤ 4, ≥ 16        | 90.7 (372/410) |
| Ciprofloxacin     | ≥ 32        | 64               | ≤ 1, ≥ 4         | 100.0 (410/410) |
| Moxifloxacin      | 8           | 16               | ≤ 0.5, > 0.5     | 100.0 (410/410)<sup>a</sup> |
| Erythromycin      | 32          | 64               | ≤ 0.5, > 0.5     | 98.8 (405/410) |
| Clindamycin       | 16          | > 32             | ≤ 0.5, ≥ 4       | 98.5 (404/410) |
| Tetracycline      | ≥ 32        | > 64             | ≤ 4, ≥ 16        | 70.5 (289/410) |
| Gentamycin        | 8           | ≥ 32             | ≤ 4, ≥ 16        | 53.2 (218/410) |
| Sulfamethoxazole and trimethoprim | ≥ 8/152 | ≥ 8/152 | ≤ 2/38, ≥ 4/76 | 98.0 (402/410) |
| Linezolid         | <0.5        | <0.5             | ≤ 2              | 0 (0.0)        |
| Daptomycin        | <0.5        | <0.5             | ≤ 1              | 0 (0.0)        |
| Vancomycin        | <0.5        | <0.5             | ≤ 2              | 0 (0.0)        |

<sup>a</sup> Based on EUCAST breakpoint for Corynebacterium spp

### Table 3 Resistance biotypes of 410 C. striatum strains

| Resistance biotypes | No. of isolates (n) | Antibiotics |
|---------------------|---------------------|-------------|
|                     | VAN DAP LNZ P FEP CIP SXT E CLI IPM TE GEN |
| R1                  | 194                 | S S S R R R R R I/R I/R I/R I/R |
| R2                  | 86                  | S S S R R R R R I/R R I/R S |
| R3                  | 95                  | S S S R R R R R R R I/R S I/R |
| R4                  | 17                  | S S S R R R R R R S R R |
| R5                  | 6                   | S S S R R R R R I/R R R S S |
| R6                  | 2                   | S S S R R R S R I/R R S S |
| R7                  | 2                   | S S S R R R S R R R R I |
| R8                  | 2                   | S S S R R R S R R R S |
| R9                  | 2                   | S S S S S R R R R R S S R |
| R10                 | 2                   | S S S R R R S R R R S I |
| R11                 | 1                   | S S S R R R S R R R R R |
| R12                 | 1                   | S S S R R R R R R R R S |

*VAN* vancomycin, *DAP* daptomycin, *LNZ* linezolid, *P* penicillin, *FEP* cefepime, *CIP* ciprofloxacin, *SXT* sulfamethoxazole and trimethoprim, *E* erythromycin, *CLI* clindamycin, *IPM* imipenem, *TE* tetracycline, *GEN* gentamicin
an outbreak was observed in the ICU of hospital C from May 12 to May 19, 2019. The other two outbreaks of the T06 and T28 clones also emerged in the ICU of hospital C from April to May 2019 (Fig. 2). Furthermore, three dominant clones showed high levels of ciprofloxacin or moxifloxacin resistance, and the MICs of moxifloxacin of dominant clones showed high levels of ciprofloxacin or erythromycin. The moxifloxacin MIC of the strains belonged to the T06 and T28 clones. Double mutations in codons 87 (S → F/Y) and 91 (D → A) of gyrA were identified in these three dominant clones (Table 5).

In the three nosocomial outbreaks caused by the three clones of *C. striatum*, 33 patients were involved and 12.1% (4/33) of the patients died. The average age of patients and length of hospital stay were 58 years and 30 d, respectively. Moreover, 97% (32/33) of the patients were exposed to different antibiotics 2 weeks before *C. striatum* isolation, and most of these patients had different comorbidities, including cerebrovascular events (39.4%; 13/33), chronic obstructive pulmonary disease (36.4%; 12/33), and malignant diseases (21.1%; 7/33) (Table 6).

### Discussion

**Resistance features of *C. striatum* isolates**

In this study, most of the 410 *C. Striatum* strains were isolated from lower respiratory tract samples (93.2%; 382/410). Meanwhile, five *C. Striatum* strains were isolated from whole blood samples and one strain was repeatedly isolated from an immunosuppressed patient with infective endocarditis. Consistent with the results of previous investigations [6, 16], the *C. Striatum* strains detected in this study were sensitive to vancomycin and linezolid. By contrast, all isolates were ciprofloxacin-resistant, and most had high MICs ($\geq 32 \mu g/mL$) to ciprofloxacin. Three dominant resistance biotypes were identified in this study, which accounted for 91.5% (375/410), and the strains were resistant to penicillin, cefepime, ciprofloxacin, and erythromycin. Although the isolates from the three hospitals were categorized into 12 resistant biotypes, no significant difference in geographical distribution was observed. Daptomycin resistance in *C. Striatum* has been reported in previous studies [17, 18]; however, no daptomycin-resistant isolate was identified in this present study.

### Mechanism of quinolone resistance in *C. Striatum* isolates

The level of quinolone resistance depended on the type of amino substitution; isolates with double mutations on codons 87 and 91 showed a higher level of quinolone resistance than those with a single mutation on codon 87 [5, 16]. In this study, most of the quinolone-resistant *C. Striatum* isolates were confirmed to have double mutations in gyrA (codons 87 and 91). However, not all isolates presented with MIC of $\geq 32 \mu g/mL$ to ciprofloxacin. By contrast, a single mutation in gyrA (codon 87) was detected in 11 *C. Striatum* isolates, and the MICs of 72.7% (8/11) isolates to ciprofloxacin were $\geq 32 \mu g/mL$. The significant relationship between amino mutation patterns and resistance levels to quinolones was not observed in this study. Furthermore, four new mutation patterns in *C. Striatum* were found in this study, including three double mutations in codons 87 and 91 of gyrA and a single mutation in codon 87 of gyrA. Two kinds of new mutations, the double mutation pattern (87-S → F/Y, 91-D → A) and the single mutation pattern (87-S → I), were previously found in *C. urealyticum* and *C. jeikeium* [4]. To the best of our knowledge, the remaining two types of newly detected mutation patterns in *C. Striatum* have not been reported previously, which had double mutations in codon 87 and 91. In particular, isolates with the double mutation pattern (87-S → Y, 91-D → A) accounted for 24.6% (101/410). Further, Sierra et al. [5] found that some *C. Striatum* strains with a single mutation in codon 87 were ciprofloxacin-resistant but sensitive to moxifloxacin, suggesting that other resistance mechanisms contribute to moxifloxacin resistance in *C. Striatum*. However, no moxifloxacin-sensitive strain was detected in this study, and a higher level of resistance of *C. Striatum* to moxifloxacin was observed. The MIC$_{90}$ of the 410 *C. Striatum* isolates to moxifloxacin was high, i.e., up to 8 $\mu g/mL$, indicating severe quinolone resistance in *C. Striatum* in these hospitals. Unfortunately, quinolones appear to exert double effects on *C. Striatum*, which could both induce its resistance to quinolones and promote *C. Striatum* acquisition among susceptible patients [3, 9]. Cumulatively, preventing quinolone exposure appears to be the most efficient way to control *C.
Fig. 1 Molecular characterization of 101 C. striatum strains with different resistance biotypes. For each types of T02, T06, T20 and T27, only the PFGE gel of one representative isolate were presented here. T02 clone, T06 clone, T20 clone, and T27 clone were composed by 12, 6, 4 and 15 isolates, respectively.
in the several wards of hospital A from 2016 to 2018. This suggests a strong fitness ability of *C. striatum* among susceptible patients within the hospital environment. Unfortunately, based on the current data, it was difficult to confirm whether the dominant clones belonged to the same origin in these three hospitals as they are located at long distances. Further, three outbreaks were observed among patients admitted to the ICU of hospital C in 2019, resulting from the T02, T06, and T28 clones, respectively. Of note, the three clones coexisted among different patients in the ICU of hospital C from April to June 2019, indicating a multisource feature and rapid spread of *C. striatum*. Therefore, more efficient measures for infection control should be implemented to better controlling the transmission of *C. striatum*. Moreover, 33 patients were confirmed to be involved in these three nosocomial outbreaks; most of these patients had at least one comorbidity and 97% (32/33) were exposed to at least one broad-spectrum antibiotic 2 weeks before *C. striatum* isolation. This finding implies that for special hospital units with critically ill patients, more attention should be paid when *C. striatum* strains are isolated.

A recent report revealed that some dominant *C. striatum* clones showed resistance to some widely used biocides at different levels, including high-level disinfectants (such as glutaraldehyde) [23]. Therefore, the sensitivity of dominant *C. striatum* isolates from different hospitals to commonly used biocides should be further evaluated, and the selective use of effective biocides should be considered. In this study, 50 PFGE genotypes were identified among 101 *C. striatum* isolates, and high genotyping diversity was observed in the strains isolated from the same hospital, particularly those isolated from hospitals A and B. This suggests that multidrug *C. striatum* isolates originate from diverse origins and more dominant clones are selected under suitable circumstances, such as an increasing number of susceptible patients and nonrational application of broad-spectrum antibiotics.

**Limitations**

The limitations of this study are indicated as follows. Only 101 *C. striatum* isolates were genotyped using the PFGE method owing to the limitation of the expenditure.

### Table 5 Characterization of quinolone resistance of three dominant *C. striatum* clones

| Clones | Ciprofloxacin (µg/mL) | Moxifloxacin (µg/mL) | Sequence of gyrA gene (aa) |
|-------|-----------------------|-----------------------|---------------------------|
|       | MICs | Sensitivity (≤1, ≥4) | MICs | Sensitivity (≤0.5, >0.5) | 87-S | 91-D |
| T28   | ≥ 32 | R                     | ≥ 4  | R                     | F    | A    |
| T06   | ≥ 32 | R                     | ≥ 4  | R                     | Y    | A    |
| T02   | ≥ 32 | R                     | ≥ 8  | R                     | Y    | A    |
The actual classification and distribution of different clones among different wards or patients may lack accuracy owing to selection bias. Therefore, dominant clones and nosocomial outbreaks may have been underestimated based on these data. Furthermore, a limited number of isolates were obtained from hospitals B and C, and only the isolates from 2019 were eventually analyzed in this study. Therefore, the actual resistant phenotypes of C. striatum isolates and prevalence potential of dominant clones within these two hospitals need to be further explored.

**Conclusions**

Most C. striatum clinical strains analyzed in this study showed multidrug resistance, particularly to quinolones. The diversity of mutation in the gyrA of C. striatum is reported for the first time in this study. The strict restriction of quinolone use and prevention of its selective pressure on C. striatum may be the most effective way to minimize C. striatum colonization or infection and suppress the development of its resistance to quinolones. Dominant clones should be paid more attention in future infection control strategies as they can persist in hospitals for a long period and widely spread among susceptible patients.

**Abbreviations**

QRDRs: Quinolone Resistance-Determining Regions; PFGE: Pulsed-field gel electrophoresis; PCR: Polymerase chain reaction; MIC: Minimum inhibitory concentration; ICU: Intensive care unit.

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**Authors’ contributions**

JW and QC are responsible for design of this study, data analysis, manuscript draft and check. YW is responsible for experiment of gene sequencing and data analysis. XS, JZ are responsible for strains isolation and identification. YW is responsible for antibiotics susceptibility testing. XD is responsible for molecular experiments and data analysis. GC is responsible for data analysis, manuscript draft and check. All authors read and approved the final manuscript.

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**Availability of data and materials**

None.

**Declarations**

**Ethics approval and consent to participate**

This work is exempt from formal ethical approval and informed consent according to the local ethical guidelines, and was approved by Ethics committee of Affiliated hospital of Inner Mongolia Medical university (Reference number KY20200029).

**Consent for publication**

No individual person’s data was included in this study, and consent for publication is not required.

**Competing interests**

The authors declare that they have no competing interests.

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**Table 6**

Descriptive characteristics of 33 patients involved in three nosocomial outbreaks

| Variable                                      | Number (%) |
|----------------------------------------------|------------|
| **Length of hospital stay (days)**          |            |
| ≤7                                          | 6.1 (2/33) |
| 8–14                                        | 9.1 (3/33) |
| 15–21                                       | 24.2 (8/33) |
| > 21                                        | 60.6 (20/33) |
| **Age (years)**                              |            |
| < 40                                         | 6.1 (2/33) |
| 40–59                                        | 33.3 (11/33) |
| 60–79                                        | 51.5 (17/33) |
| ≥ 80                                         | 9.1 (3/33) |
| **Outcome of the patients**                  |            |
| Death                                        | 12.1 (4/33) |
| **Antibiotic intake**                        |            |
| Cephalosporins                               | 42.4 (14/33) |
| Carbapenem                                   | 24.2 (8/33) |
| β-lactam/β-lactamase inhibitor combinations  | 36.4 (12/33) |
| Quinolones                                   | 15.2 (5/33) |
| Glycopeptides                                 | 12.1 (4/33) |
| Aminoglycosides                              | 0 (0/33) |
| Macrolides                                   | 0 (0/33) |
| Lincosamides                                 | 0 (0/33) |
| Trimethoprim-Sulfamethoxazole                | 0 (0/33) |
| **Comorbid diseases**                        |            |
| Cerebrovascular event                        | 39.4 (13/33) |
| Chronic obstructive pulmonary disease        | 36.4 (12/33) |
| Malignant diseases                           | 21.1 (7/33) |
| Diabetes mellitus                            | 9.1 (3/33) |
| Chronic renal failure                        | 6.1 (2/33) |
| Heart failure                                | 3.0 (1/33) |

*a The antibiotic intake was calculated within two weeks before C. striatum isolation
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