

Anti-Infection Experience Analysis of a Patient with *Bacillus cereus* Lung Empyema Diagnosed by Targeted Next-Generation Sequencing (tNGS)

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Abstract: *Bacillus cereus* is an aerobic, Gram-positive bacterium widely present in soil and food, causing human infections primarily through foodborne diseases, manifesting as abdominal pain, vomiting, and diarrhea. There are rare reports of it causing pulmonary infections domestically and internationally. This paper reports a case of lung empyema caused by *Bacillus cereus* diagnosed with the aid of targeted Next-Generation Sequencing (tNGS) technology. We retrospectively analyzed the diagnosis and treatment process of the patient and reviewed literature to enhance our understanding and treatment level of such diseases. Currently, there is no standard anti-infection treatment plan for lung empyema caused by *Bacillus cereus*. Clinical physicians, by understanding the epidemiological characteristics of this bacterium, consulting relevant literature, and combining the patient's clinical condition, tests, and related etiological results, adjusted the antimicrobial treatment to effectively control and treat the infection focus.

Keywords: *Bacillus Cereus*; tNGS Technology; Lung Empyema; Anti-infection; Clinical Physicians.

1. Case Material

1.1. Case Introduction

The patient, a 37-year-old male, was admitted on August 30, 2023, for chemotherapy after being diagnosed with acute lymphocytic leukemia for over a year. He had a history of gastric antral wall ulcer perforation repair surgery, as well as erosive gastritis and hiatal hernia. Physical examination upon admission showed no significant abnormalities, and routine blood laboratory tests, chest X-rays (Figure 1A), and chest CT scans (Figure 2A) were unremarkable.

1.2. Diagnosis and Treatment Course

From the 1st to the 17th day of admission, the patient underwent bone marrow puncture, lumbar puncture with intrathecal injection, and other examinations, and began induction chemotherapy. During chemotherapy, the patient did not experience fever, cough, or other discomfort symptoms. On the 18th day of admission, after chemotherapy-induced bone marrow suppression and neutropenia (Figure 3), on the 20th day, the patient developed fever and chest pain, marking the first clinical turning point. The initial empirical anti-infection treatment used cefoperazone-sulbactam but failed to control the condition, with the patient's symptoms worsening, blood pressure dropping, indicating a more severe infection. On the 21st day of admission, the patient's condition deteriorated rapidly with chest pain, chest tightness, fever, chills, and low blood pressure. Chest CT suggested infection or exudative lesions in the lower lobes of both lungs, with a small amount of pleural effusion on the right side (Figure 2B). The treatment plan was quickly upgraded to meropenem and amphotericin B cholesterol sulfate complex (Figure 4). On the 23rd day of admission, the patient continued to have a fever, with significant increases in inflammatory markers CRP and PCT

(Figure 3), suggesting sepsis, and the treatment plan was adjusted again, adding vancomycin and voriconazole. On the 25th day of admission, sputum culture and tNGS test results indicated new pathogens, including *Staphylococcus haemolyticus*, *Aspergillus fumigatus*, *Stenotrophomonas maltophilia*, and *Serratia marcescens*, and the treatment strategy was adjusted accordingly. On the 31st day of admission, chest CT showed a large amount of pleural effusion on the right side (Figure 2C), and the patient underwent thoracentesis and catheter drainage. On the 32nd day of admission, pleural fluid tNGS testing first detected *Bacillus cereus*, with a sequence number as high as 181334, confirming the pathogen of lung empyema. On the 37th day of admission, the patient's temperature rose again, and blood tNGS testing found cytomegalovirus, indicating a possible mixed infection. The treatment plan included the addition of ganciclovir tablets and tigacycline. On the 41st day of admission, the patient's temperature peak decreased, and the second pleural fluid tNGS test showed a decrease in the sequence number of *Bacillus cereus*, indicating effective anti-infection treatment. On the 44th day of admission, chest X-ray (Figure 1B) showed right lower lung inflammation, right-sided hydropneumothorax, possible partial fluid encapsulation, and about 40% lung compression. The patient's temperature was basically normal, inflammatory indicators decreased, and the infection was controlled, and the antibiotic treatment plan was adjusted (Figure 4). On the 46th day of hospitalization, a repeat chest X-ray (Figure 1C) revealed approximately 35% atelectasis of the right lung, along with an increase in the right-sided pleural effusion as compared to previous assessments. Consequently, continuous thoracentesis with closed drainage was maintained to facilitate the evacuation of air. On the 47th day of admission, chest CT (Figure 2D) showed that the right lung inflammation had absorbed compared to before, the right lung was not fully

expanded, and a small amount of pleural effusion on the left side was basically absorbed. On the 51st day of admission, the patient's temperature was normal, but the chest X-ray showed right-sided hydropneumothorax, with lung tissue compression of about 75%, requiring further thoracic drainage treatment (Figure 1D). On the 54th day of admission, the chest X-ray showed right-sided hydropneumothorax, slightly reduced compared to before, with lung tissue compression of about 55% (Figure 1E). The patient was discharged on the 56th day of admission, with no fever for a week, and continued oral anti-infection drug treatment and

regular gas and fluid aspiration. Follow-up for more than half a year, pleural fluid tNGS found pathogenic microorganisms: *Bacillus cereus*, with a sequence number of 350 and a pathogen concentration of 10^1 . Pneumothorax was absorbed, with a small amount of pleural effusion. Timely and appropriate anti-infection and pleural effusion management ensured the smooth progression of the primary disease. The patient is currently undergoing regular chemotherapy for leukemia maintenance treatment, indicating the success of the treatment process and the patient's recovery (Figure 1F, Figure 2E).

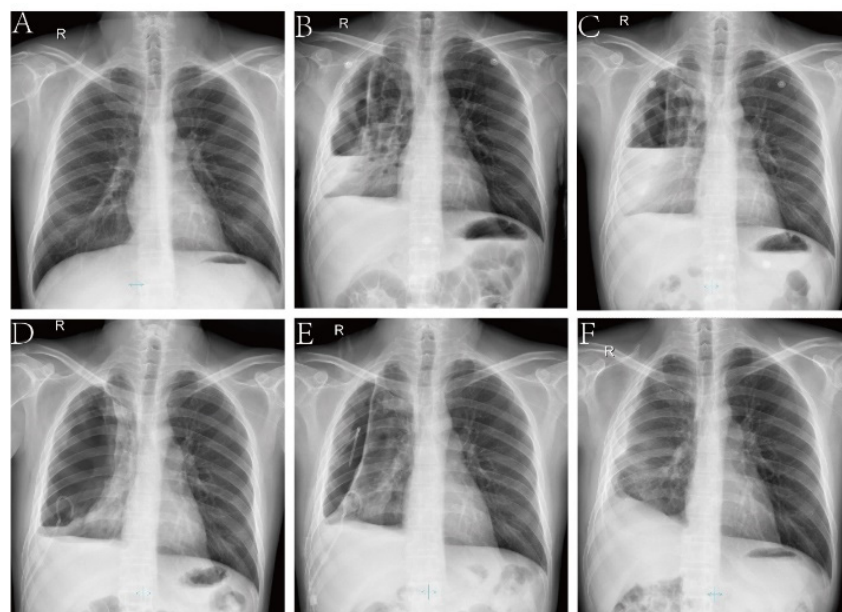


Figure 1. Series of the patient's chest X-rays A: Admission chest X-ray: No significant abnormalities were observed. B: Chest X-ray on the 44th day of admission: Right lower lung inflammation, right-sided hydropneumothorax, possible partial fluid encapsulation, and about 40% lung compression. C: Re-examination chest X-ray on the 46th day of admission: About 35% lung compression on the right side, an increase in right-sided pleural effusion compared to before. D: Chest X-ray on the 51st day of admission: Right-sided hydropneumothorax, with lung tissue compression of about 75%. E: Chest X-ray on the 54th day of admission: Right-sided hydropneumothorax, slightly reduced compared to before, with lung tissue compression of about 55%. F: Follow-up chest X-ray after more than half a year: Pneumothorax has been completely absorbed, with a small amount of pleural effusion on the right side, and partial expansion of the right lower lung.

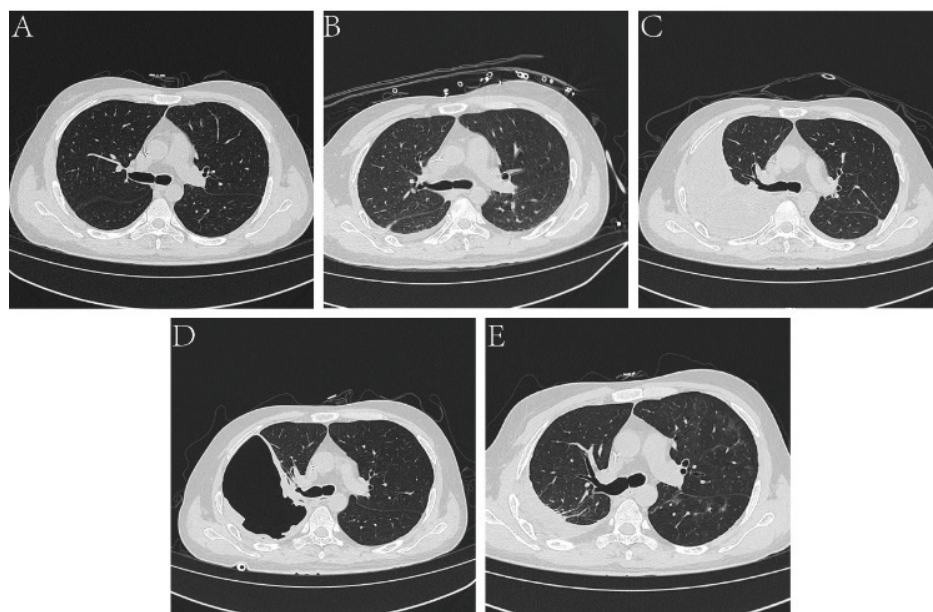


Figure 2. Series of the patient's chest CT scans: A: Chest CT at admission: No significant abnormalities were observed. B: Chest CT on the 21st day of admission: Infection or exudative lesions in the lower lobes of both lungs, with a small amount of pleural effusion on the right side. C: Chest CT on the 31st day of admission: A large amount of pleural effusion on the right side. D: Chest CT on the 47th day of admission: Right lung inflammation has absorbed compared to before, the right lung is not fully expanded, and a small amount of pleural effusion on the left side has been basically absorbed. E: Follow-up chest CT after more than half a year: Pneumothorax has been completely absorbed, with a small amount of pleural effusion on the right side and partial expansion of the right lower lung.

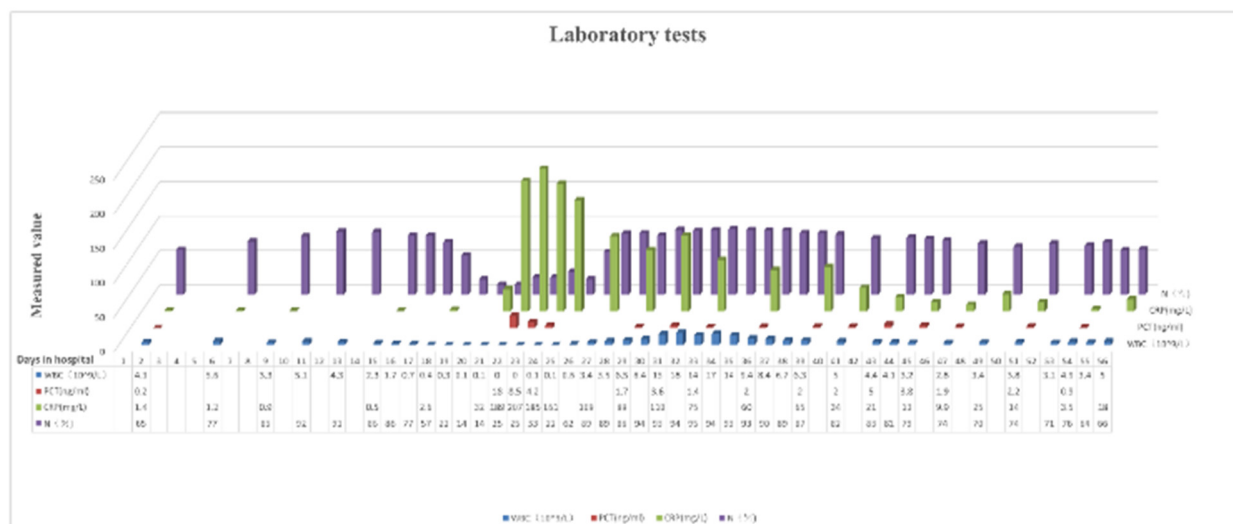


Figure 3. Patient's inflammatory marker change curve: X-axis: Hospitalization days, representing the timeline of the patient's hospital stay. Y-axis: Values of various indicators, white blood cell count ($\times 10^9/L$), neutrophil percentage (%), C-reactive protein (CRP, mg/L), procalcitonin (PCT, ng/mL). (Blue bar chart: Changes in white blood cell count, reflecting the dynamic changes in white blood cell count during the patient's hospital stay. Purple bar chart: Changes in neutrophil percentage, showing the fluctuations in the percentage of neutrophils during the patient's hospital stay. Green bar chart: Changes in C-reactive protein (CRP) levels, depicting the rise and fall of CRP levels during the patient's hospital stay. Red bar chart: Changes in procalcitonin (PCT) levels, indicating the fluctuations in PCT levels during the patient's hospital stay. Color coding: Each bar chart uses different colors to distinguish different indicators.)

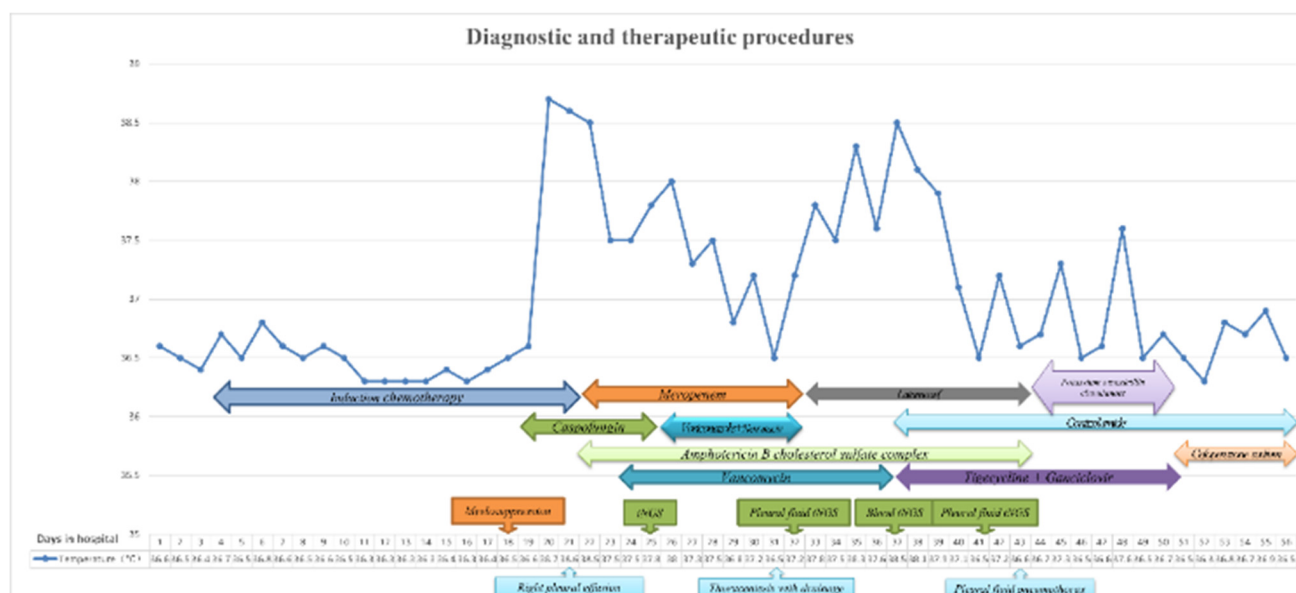


Figure 4. Patient's anti-infection treatment plan adjustment chart: X-axis: Hospitalization days, representing the timeline of the patient's hospital stay. Y-axis: Body temperature ($^{\circ}C$), representing the body temperature values measured daily. Line chart: Body temperature change curve, showing the fluctuations in body temperature during the patient's hospital stay. Left and right arrow annotations: Indicate the medication usage at each stage, with the left arrow indicating the start time of medication and the right arrow indicating the end time.

2. Discussion

2.1. Predisposing Factors for *Bacillus cereus* Lung Empyema

Bacillus cereus is a Gram-positive, aerobic rod bacterium known for its ability to form heat-resistant spores. This bacterium is widely distributed in various foods, such as dairy products, meats, vegetables, desserts, condiments, and cold dishes. Typically, food poisoning can occur due to inadequate food heating [1]. Studies have shown that the host's immune status is a key factor affecting the severity of *Bacillus cereus* infections, with immunocompromised individuals being more susceptible to infections that may progress to severe diseases such as septic shock, respiratory infections, and endocarditis [2]. For instance, leukemia patients undergoing chemotherapy

are more prone to various infections, especially pneumonia, due to neutropenia and decreased immunity [3]. In this case, the patient was diagnosed with acute lymphocytic leukemia and developed leukopenia and neutropenia after regular chemotherapy, impairing systemic immune function. Additionally, having undergone a gastric antral wall perforation repair surgery, the patient's resistance was reduced, making him more susceptible to lung infections and a high-risk group for *Bacillus cereus* infection [4].

2.2. Clinical Diagnosis of *Bacillus cereus* Lung Empyema

Etiological testing is crucial for confirming infectious diseases. In this case, the patient had a history of leukemia and did not exhibit infection symptoms upon admission but developed infections easily due to leukopenia and

neutropenia-induced immunosuppression during chemotherapy [5]. As the condition progressed, the lung infection worsened, eventually leading to lung empyema. The anti-infection treatment plan was adjusted multiple times, and the patient's condition gradually stabilized. Throughout the treatment process, bacterial and fungal cultures of sputum and pleural fluid, combined with tNGS gene detection, detected *Bacillus cereus* multiple times, with one pleural fluid tNGS result showing an extremely high sequence number of *Bacillus cereus* complex, confirming it as the pathogen. This method highlights the importance of molecular diagnostic technology in pathogen detection, especially in infections with microorganisms that are difficult to identify with traditional culture methods. Compared to traditional culture methods, tNGS technology can more quickly and sensitively detect bacteria and fungi in clinical samples, thereby improving the diagnostic efficiency of infectious diseases [6, 7]. In addition, one pleural fluid culture also identified *Bacillus cereus*. Considering the patient's clinical presentation and test results, a diagnosis of *Bacillus cereus* lung empyema was confirmed. The patient experienced a drop in blood pressure and septic shock, and one blood tNGS test detected cytomegalovirus. *Bacillus cereus* is widely present in the hospital environment and can adhere to various medical devices [8]. For immunocompromised patients, early implementation of laminar flow bed protection and strict adherence to aseptic procedures are essential, maintaining cleanliness of hands and medical instruments to prevent infections [9]. Once an infection occurs, antimicrobial treatment should be initiated immediately. For recurrent lung empyema, in addition to strong antimicrobial treatment, closed thoracic continuous flushing and drainage are also crucial for disease recovery [10].

2.3. Anti-Infection Treatment for *Bacillus cereus* Lung Empyema

Currently, there are no specific treatment guidelines for lung empyema caused by *Bacillus cereus*. According to literature reports, *Bacillus cereus* has shown resistance to some antimicrobial drugs, especially β -lactam drugs such as penicillins and cephalosporins, as almost all *Bacillus cereus* can produce β -lactamase [11, 12]. Studies have shown that *Bacillus cereus* exhibits varying degrees of sensitivity to drugs such as vancomycin, clindamycin, imipenem, and fluoroquinolones [13,14]. Therefore, in treating lung empyema caused by *Bacillus cereus*, appropriate antimicrobial drugs should be selected based on drug sensitivity test results, and combination therapy should be considered to improve treatment effectiveness. The initial therapeutic approach should prioritize the use of vancomycin and clindamycin, while fluoroquinolones and imipenem are suggested as alternative treatments. There is evidence to suggest that for *Bacillus cereus* infections, antimicrobial drugs should be used as early as possible, and the course of anti-infection treatment should be appropriately extended according to the condition of empyema to prevent recurrence. Although there are currently no standard guidelines for anti-infection, some studies have reported that *Bacillus cereus* is sensitive to clindamycin [15–17]. In this case, after the first pleural fluid tNGS test detected *Bacillus cereus*, the treatment plan was adjusted to vancomycin combined with lactic acid cephalosporin, supplemented with thoracic flushing and drainage. Considering the patient's history of leukemia and the risk of co-infection with fungi, amphotericin B was also

administered for antifungal treatment. After treatment, the patient's temperature gradually decreased, and chest pain symptoms were relieved. Given that the vancomycin course had reached two weeks to avoid potential side effects, it was decided to discontinue its use. However, after stopping, the patient experienced fever again, leading to intensified anti-infection treatment and regular thoracic flushing and drainage. The patient's temperature gradually decreased, and subsequent sequential treatment with oral fluoroquinolones, cephalosporins, and a new generation of oxazolidinones was administered. After nearly 36 days of anti-infection drug treatment, the patient's empyema gradually absorbed, with no fever symptoms, but pneumothorax occurred, which was absorbed to some extent. The patient chose to be discharged due to personal reasons. Follow-up six month after discharge showed that the lung empyema and pneumothorax had basically absorbed. For patients with complex conditions, a multidisciplinary team approach is recommended, including experts in infectious diseases, pulmonologists, hematologists, and intensive care specialists, to jointly develop personalized treatment plans.

2.4. Summary

In summary, there are rare reports of *Bacillus cereus* causing lung infections. This paper reports a case of lung empyema caused by *Bacillus cereus* diagnosed with the aid of tNGS technology. By retrospectively analyzing the patient's diagnosis and treatment process and reviewing relevant literature to understand the epidemiological characteristics of this bacterium, combined with the patient's clinical condition, tests, and related etiological results, the antimicrobial treatment was adjusted. It is hoped that this will provide reference experience for clinical physicians in the diagnosis and treatment of lung abscesses caused by *Bacillus cereus*, facilitating early detection, early diagnosis, and early treatment of the disease.

Availability of Data and Materials

The original contributions presented in the study are included in the article; further inquiries can be directed to the corresponding author.

Declaration of Competing Interests:

The authors declare no conflict of interest.

Author Contribution Declaration:

All authors listed (Qiuxiang Huang, Yu Zhan, Bin Zuo, Yangyang Xu, Zhencheng Feng) have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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References

- [1] May FJ, Polkinghorne B, Fearnley E. Epidemiology of bacterial toxin-mediated foodborne gastroenteritis outbreaks in australia, 2001 to 2013. *Commun Dis Intell Q Rep*. Published online December 24, 2016.

- [2] Chou YL, Cheng SN, Hsieh KH, Wang CC, Chen SJ, Lo WT. *Bacillus cereus* septicemia in a patient with acute lymphoblastic leukemia: A case report and review of the literature. *J Microbiol Immunol Infect Wei Mian Yu Gan Ran Za Zhi*. 2016;49(3):448-451. doi:10.1016/j.jmii.2013.06.010.
- [3] Uchino Y, Iriyama N, Matsumoto K, et al. A case series of *Bacillus cereus* septicemia in patients with hematological disease. *Intern Med*. 2012;51(19):2733-2738. doi:10.2169/internalmedicine.51.7258.
- [4] Drobniewski FA. *Bacillus cereus* and related species. *Clin Microbiol Rev*. 1993;6(4):324-338. doi:10.1128/CMR.6.4.324.
- [5] Ba Y, Shi Y, Jiang W, et al. Current management of chemotherapy-induced neutropenia in adults: Key points and new challenges: committee of neoplastic supportive-care (CONS), China anti-cancer association committee of clinical chemotherapy, china anti-cancer association. *Cancer Biol Med*. 2020;17(4):896-909. doi:10.20892/j.issn.2095-941.2020.0069.
- [6] Zhang P, Liu B, Zhang S, et al. Clinical application of targeted next-generation sequencing in severe pneumonia: A retrospective review. *Crit Care Lond Engl*. 2024;28(1):225. doi:10.1186/s13054-024-05009-8.
- [7] Chen P, Sun W, He Y. Comparison of the next-generation sequencing (NGS) technology with culture methods in the diagnosis of bacterial and fungal infections. *J Thorac Dis*. 2020;12(9):4924. doi:10.21037/jtd-20-930.
- [8] Glasset B, Herbin S, Granier SA, et al. *Bacillus cereus*, a serious cause of nosocomial infections: Epidemiologic and genetic survey. *PloS One*. 2018;13(5):e0194346. doi:10.1371/journal.pone.0194346.
- [9] Rutala WA, Weber DJ. Disinfection and sterilization in health care facilities: An overview and current issues. *Infect Dis Clin North Am*. 2016;30(3):609-637. doi:10.1016/j.idc.2016.04.002.
- [10] Elsheikh A, Bhatnagar M, Rahman NM. Diagnosis and management of pleural infection. *Breathe Sheff Engl*. 2023;19(4):230146. doi:10.1183/20734735.0146-2023.
- [11] Torkar KG, Bedenić B. Antimicrobial susceptibility and characterization of metallo- β -lactamases, extended-spectrum β -lactamases, and carbapenemases of *Bacillus cereus* isolates. *Microb Pathog*. 2018;118:140-145. doi:10.1016/j.micpath.2018.03.026.
- [12] Frenzel E, Kranzler M, Stark TD, Hofmann T, Ehling-Schulz M. The endospore-forming pathogen *Bacillus cereus* exploits a small colony variant-based diversification strategy in response to aminoglycoside exposure. *mBio*. 2015;6(6):10.1128/mbio.01172-15. doi:10.1128/mbio.01172-15.
- [13] Liu C, Yu P, Yu S, et al. Assessment and molecular characterization of *Bacillus cereus* isolated from edible fungi in China. *BMC Microbiol*. 2020;20(1):310. doi:10.1186/s12866-020-01996-0.
- [14] Andersson MA, Mikkola R, Helin J, Andersson MC, Salkinoja-Salonen M. A novel sensitive bioassay for detection of *Bacillus cereus* emetic toxin and related depsipeptide ionophores. *Appl Environ Microbiol*. 1998;64(4):1338-1343. doi:10.1128/AEM.64.4.1338-1343.1998.
- [15] Tusgul S, Prod'hom G, Senn L, Meuli R, Bochud PY, Giulieri SG. *Bacillus cereus* bacteraemia: Comparison between haematologic and nonhaematologic patients. *New Microbes New Infect*. 2016;15:65. doi:10.1016/j.nmni.2016.11.011.
- [16] Uchino Y, Iriyama N, Matsumoto K, et al. A case series of *Bacillus cereus* septicemia in patients with hematological disease. *Intern Med*. 2012;51(19):2733-2738. doi:10.2169/internalmedicine.51.7258.
- [17] Chen CY, Huang SY, Tsay W, et al. Clinical characteristics of candidaemia in adults with haematological malignancy, and antimicrobial susceptibilities of the isolates at a medical centre in taiwan, 2001-2010. *Int J Antimicrob Agents*. 2012;40(6):533-538. doi:10.1016/j.ijantimicag.2012.07.022.