

# Characteristics of pathogens detected in adults with hematological malignancies and nosocomial infections in the tropics

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*To the Editor:* Human pathogens have evolved over a long time to become mesophiles to adapt to the typical 37°C temperature of the human body. Yeast and yeast-like fungi also grow very well at this temperature, while the optimal temperature for the growth of filamentous fungi is 25 to 28°C. Hainan Island in China has a tropical oceanic monsoon climate with indistinct seasons. The mean temperature at this place for many years has been 24.4°C, and the annual temperature variation is small; the precipitation is approximately 1718.6 mm, and the relative humidity is 82%. These unique weather characteristics provide a favorable growth environment for pathogens. Patients with hematologic malignancies have poor immunity and are susceptible to pathogens. This results in high nosocomial infection rates in patients with hematologic malignancies and frequent antibiotic use. Epidemiological surveys of different regions and hospitals can provide more guidance for clinical drug administration by hematologists in treating infections in patients with hematologic malignancies.

The Hainan Branch of the People's Liberation Army (PLA) General Hospital is located in a tropical region. This study aimed to carry out a retrospective analysis of 1817 patients with hematologic malignancies in this hospital from June 2014 to March 2018 to understand the distribution characteristics of pathogens detected in adults with hematological malignancies and nosocomial infections in this tropical region and their drug resistance characteristics to provide a reference for the treatment of infections by clinicians.

The retrospective analysis of the 2471 hospitalized admissions included 1817 patients with hematologic malignancies, including acute leukemia (AL,  $n = 421$ ), chronic leukemia ( $n = 133$ ), non-Hodgkin lymphoma (NHL,  $n = 587$ ), multiple myeloma (MM,  $n = 471$ ), Hodgkin lymphoma (HL,  $n = 121$ ), and myelodysplastic syndrome (MDS,  $n = 84$ ). The

patients were admitted to the Hainan Branch of PLA General Hospital for more than 48 h. A variety of 269 strains were detected from 198 patients diagnosed with nosocomial infection. Of these, 94 strains were from patients with AL ( $n = 74$ ; 37.4%), 71 from patients with NHL ( $n = 48$ ; 24.2%), 58 from patients with MM ( $n = 43$ ; 21.7%), 17 from patients with CL ( $n = 15$ ; 7.5%), 9 from patients with HL ( $n = 6$ ; 3.0%), and 20 from patients with MDS ( $n = 14$ ; 6.5%). Of the included patients, which the median age was 56 years (13–87 years). Informed consent was obtained from all patients before treatment, in accordance with the *Declaration of Helsinki*.

The diagnostic criteria for AL, HL, NHL, MM, and MDS were based on the World Health Organization (2008) Classification of Tumors of Hematopoietic and Lymphoid Tissues.<sup>[1]</sup> The diagnostic criteria for nosocomial infections were based on the unified infection diagnosis standards adopted in the national nosocomial infection surveillance network. Nosocomial infections were determined based on fever and other clinical presentations, laboratory, and imaging tests. The infections occurred >48 h after admission, and no evidence regarding the presence of the infection or incubation was found at the time of admission.

Samples were collected in strict compliance with the "Sample collection manual" formulated by the hospital. Samples sent for testing included sputum, intravenous blood samples, midstream urine, peripherally inserted central catheter tubing, and wound secretions. Repeat pathogens from multiple tests from the same site in the same patient within a short period were not included in the analysis. The BioMérieux BacTAlert 3D 240 blood culture system (Biomérieux, Inc., l'Etoile, France) and fully automated microbiological VITEK 2 COMPACT analysis system (Biomérieux, Inc.) were used to carry out the culture, identification, and drug-sensitivity testing of

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pathogens. Pathogen isolation and culture were carried out according to the National Operating Procedures for Clinical Tests implemented in 2006.

Continuous variables were reported as a median and interquartile range, or mean and standard deviation; descriptive statistics were evaluated, and categorical variables were reported as percentages and frequencies. SPSS 17.0 (SPSS Inc. Chicago, IL, USA) was used for statistical analysis of the relevant data.

A total of 198 patients from 1817 admissions with hematologic malignancies and 269 strains from 214 samples tested positive for the pathogens. Of these, 94 strains were from patients with AL, 71 were from patients with NHL, 58 were from patients with MM, 17 were from patients with CL, nine were from patients with HL, and 20 were from patients with MDS. Of the various strains, 79 were fungal strains (29.4%; 76 *Candida* strains and three filamentous fungi); 109 were Gram-negative bacterial strains (40.5%); and 80 were Gram-positive bacterial strains (29.7%) [Supplementary Table 1, <http://links.lww.com/CM9/A269>].

Supplementary Table 1 (<http://links.lww.com/CM9/A269>) provides the data of 154 strains from 117 positive sputum cultures. The fungal strains had the highest incidence (76 strains, 49.4%), of which *Candida albicans* (26 strains), unclassified *Candida* strains (36 strains), and filamentous fungi (three strains) were the primary pathogens. Of the 59 Gram-negative bacterial strains (38.3%), *Escherichia coli* (six samples), *Pseudomonas aeruginosa* (nine samples), *Klebsiella pneumoniae* (seven strains), *Stenotrophomonas maltophilia* (five strains), and *Acinetobacter baumannii* (two strains) were the primary pathogens. Of the 19 Gram-positive bacterial strains (12.3%), *Enterococcus* bacteria (five strains) and *Staphylococcus aureus* (four strains) were the primary pathogens. In tropical regions, the incidence of fungi from sputum cultures was the highest, particularly *C. albicans*, which was significantly different from that observed in Northern regions. The pathogen distribution was similar in AL, NHL, and MM ( $P = 0.2$ ).

A total of 94 pathogens were identified through culture and isolated from patients with AL. Of these, 26 were fungal strains (27.7%; 25 *Candida* strains and one filamentous fungi); 40 were Gram-negative bacterial strains (42.6%); 27 were Gram-positive bacterial strains (28.7%); and one was non-tuberculous mycobacterial strain (1.0%).

A total of 71 pathogens were identified through culture and isolated from patients with NHL. Of these, 17 were fungal strains (24.0%; all were *Candida* strains, with five *C. albicans* strains); 26 were Gram-negative bacterial strains (36.6%), and 28 were Gram-positive bacterial strains (39.4%).

Totally, 58 pathogens were identified through culture and isolated in patients with MM. Of these, 17 were fungal strains (29.3%; 16 *Candida* strains and one filamentous fungi); 27 were Gram-negative bacterial strains (46.6%), and 14 were Gram-positive bacterial strains (24.1%).

The probability of comorbid appearance with various pathogenic fungi and bacteria was relatively high, and the comorbidity rate exceeded 39%. Of the 79 fungal strains detected in various samples, 48 had only fungal infections and 31 had comorbid fungal and bacterial infections. The comorbidity rate was 39.2%. Of the 190 bacterial strains detected in various samples, 115 had only bacterial infections and 33 had comorbid fungal and bacterial infections. The comorbid infection rate was 28.7%.

Although some studies reported the incidence of nosocomial infections in hematological malignancies,<sup>[2-5]</sup> few studies reported the characteristics of pathogens detected in adults with hematological malignancies and nosocomial infections in tropical regions. In the present study, a retrospective analysis of 1817 admissions with hematologic malignancies in tropical regions was carried out to provide a reference for treating infections. The proportion of fungal infection detected in tropical regions was 29.4% and the proportion of *Candida* species and filamentous fungi was 76:3, which were higher than those reported in previous studies in non-tropical regions.<sup>[2]</sup>

The primary pathogens found in patients with hematologic malignancies in the tropical region admitted to the Hainan Branch of PLA General Hospital were Gram-negative bacteria, followed by Gram-positive bacteria. This was similar to previous reports on pathogens responsible for nosocomial infections in Northern regions of China, including Lianyungang and Zhengzhou.<sup>[2]</sup> However, in the present study, the proportion of fungal infections was higher and the proportion of *Candida* species and filamentous fungi was 76:3. This was not consistent with the results of the two aforementioned studies in non-tropical regions that reported only a smaller percentage of fungal infections and the prevalence of *Aspergillus* species in patients with leukemia.<sup>[2]</sup> The differences between the present and previous studies might be attributed to the higher temperatures in tropical regions throughout the year, which was suitable for the growth of yeast and yeast-like fungi.

In summary, the incidence of fungi from sputum cultures was the highest in tropical regions, particularly *C. albicans*, which was significantly different from that observed in Northern regions. Clinicians in tropical regions should pay attention to the occurrence of fungal infections, particularly *Candida* infections. Colonization and infection of the respiratory tract by *Candida* species increase the risk of infection with other pathogens. Promoting antifungal treatment (especially drugs for the treatment of *Candida*), for hospitalized patients with hematological malignancies, actively carrying out pathogen culture simultaneously, and transitioning from empirical treatment to targeted treatment are important in reducing drug resistance in bacteria and decreasing dysbacteriosis.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s)/ or his/her guardian has/have given his/her/their consent for his/her/their images and other clinical information to be reported

in the journal. The patients or his/her guardian understand that his/her/their name(s) and initials will not be published and due efforts will be made to conceal his/her/their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

None.

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