

Clinical and etiological characteristics of community-acquired pneumonia at high altitudes in Tibet, China

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To the Editor: Community-acquired pneumonia (CAP) is one of the most common infectious diseases, causing high morbidity and mortality. High altitudes are characterized by a hypoxic environment with low barometric pressure, increased ultraviolet radiation, and low humidity. Hypoxia can disturb normal homeostasis of the immune system, especially impairing the function of the T lymphocytes, leading to an increased susceptibility to bacterial infection. The respiratory symptoms of CAP at high altitudes are similar to that of high-altitude pulmonary edema. However, the occurrence of CAP can exacerbate high-altitude pulmonary edema. Few published data of CAP in adults at high altitudes have been reported worldwide. Tibet is located at an average altitude of over 3000 m above sea level, and the clinical and etiological data of CAP at high altitudes are lacking. Almost all the nationwide epidemiological studies of CAP in China have excluded high-altitude regions (>2500 m). Currently, there is no difference between the management strategies of CAP in Tibet and low-altitude regions, with similar CAP guidelines applied in clinical practice.^[1] The special environmental conditions at high altitudes may influence the etiology of CAP; hence, the optimal strategy for the treatment of CAP needs to be investigated in accordance with the local circumstances. Moreover, tuberculosis is prevalent in Tibet with atypical clinical manifestations and is sometimes difficult to distinguish from CAP exclusively based on clinical features without microbiological evaluation. The high prevalence of prior tuberculosis infection further complicates the diagnosis of CAP. We conducted a pilot study of CAP at a single center in Tibet to understand the clinical profile of CAP at high altitudes and optimize the treatment strategy for the management of CAP at high altitudes.

We retrospectively collected the demographic and clinical data of patients with CAP admitted at our hospital

between March 2017 and December 2018. The diagnostic criteria for CAP included the following: (1) illness onset in the community, (2) chest radiograph or computed tomography (CT) scan showing infiltrates or interstitial changes, and (3) presence of any of the clinical manifestation of pneumonia: new-onset cough, expectoration, chest pain, dyspnea, or hemoptysis; fever or hypothermia; signs of pulmonary consolidation or moist rales; and peripheral white blood cell (WBC) count $>10 \times 10^9/L$ or $<4 \times 10^9/L$ with or without neutrophil predominance.^[1] The exclusion criteria were as follows: age <14 years; definitive active tuberculosis or fungal pulmonary infection on admission; pulmonary infiltrates exclusively induced by non-infectious factors, such as interstitial lung diseases, pulmonary embolism, or pulmonary edema; and immunocompromised hosts, such as patients receiving long-term steroid therapy. The CURB-65 (confusion, uremia, respiratory rate, blood pressure, and age ≥ 65 years) score on admission was utilized to assess the severity of pneumonia. A higher CURB-65 score indicated a higher mortality risk. Qualified sputum samples were collected within 48 h of hospitalization for microbiological evaluation using the conventional methods, including the smear and culture for bacteria and fungi, Ziehl-Neelsen staining, and GeneXpert mycobacterium tuberculosis/rifampicin (MTB/RIF) assay for *Mycobacterium tuberculosis*; serological IgM testing was also performed for *Mycoplasma pneumoniae*. As the positive yield of the conventional methods was extremely low, we introduced a commercial multiplex microchip platform using loop-mediated isothermal amplification (LAMP) assay developed by CapitalBio Co. Ltd (Beijing, China) to identify 12 species of respiratory pathogens from sputum samples, including *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, *Haemophilus influenzae*, *Legionella pneumophila*, *M. pneumoniae*, *Chlamydia pneumoniae*, and

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M. tuberculosis complex. Our study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Ethics Committees of Tibet Autonomous Region People's Hospital (No. G-2016-05).

One hundred and thirty-two patients were initially enrolled, and ten patients were excluded for clinically diagnosed active tuberculosis during follow-up. Finally, 122 patients were eligible for the analysis. The general demographic and clinical characteristics are listed in Table 1. The median pulse oxygen saturation of the patients included in this study when breathing ambient air was 86%. Of the total patients, 86.1% (105/122) showed patchy infiltrates and 13.9% (17/122) showed lobar consolidation on the chest CT scan. Nineteen patients (15.6%) had radiological shreds of evidence of prior tuberculosis infection, such as calcification, cavity, distortion or destruction of pulmonary architecture, and/or pleural thickening. We compared the clinical features between elderly (age >65 years) and younger patients aged <65 years and found that elderly patients presented with a higher percentage of sputum production, dyspnea, bilateral infiltrates, and a higher CURB-65 score, but a lower percentage of fever, lower oxygen saturation, and lower WBC counts ($P < 0.05$). The length of hospital stay was slightly longer in the elderly group, with no significant difference as compared to the younger group ($P = 0.109$). The procalcitonin level showed no significant difference between the elderly and younger patients and between patients with or without positive results of the pathogens.

Ninety-nine qualified sputum samples were obtained for microbiological evaluation using both the conventional methods and the LAMP assay. Only nine patients were positive by microbiological evaluation using the conventional methods (9.1%). Forty-two patients (42.4%) were positive using the LAMP assay, with 51 strains of pathogens detected, including eight cases of mixed infections. The three most frequently identified pathogens in order of frequency were *S. pneumoniae*, *H. influenzae*, and *M. pneumoniae*. It should be noted that *M. tuberculosis* complex was also detected in three cases by the LAMP assay, and these cases were not diagnosed as active tuberculosis during hospitalization or follow-up. Ninety-four patients (77.0%) received antimicrobial treatment before admission. Monotherapy was administered for empirical treatment in 82.9% of patients, while the other patients received two-drug combination regimens. Beta-lactam monotherapy was the most frequently used regimen. One patient died of multiple organ failure, and all the other patients were discharged after the assessment of being clinically stable.

Since the precise clinical and etiological landscapes of CAP at high altitudes are unknown, the management of patients with CAP at high altitudes is challenging. Although the prevalence of tuberculosis in Tibet has significantly declined in recent years, its prevalence in Tibet is still higher than that of the national rate in China,^[2] because of the socioeconomic factors in Tibet, such as poverty, inadequate sanitation, poor transmission control of tuberculosis, and low Bacille Calmette-Guérin vaccine

Table 1: Demographic and clinical characteristics in CAP patients ($n = 122$) on admission.

Parameters	CAP patients	Parameters	CAP patients
Gender		Laboratory	
Male	69 (56.6)	Leukocytosis	12 (9.8)
Female	53 (43.4)	Leukopenia	18 (14.8)
Age (years)	64.5 (41.5, 72.3)	Increased neutrophils	40 (32.8)
Symptom		Elevated transaminase	32 (26.2)
Fever	66 (54.1)	Elevated creatinine	6 (4.9)
Cough	118 (96.7)	Hypoalbuminemia	16 (13.1)
Sputum production	113 (92.6)	Elevated ESR	60 (49.2)
Chest pain	51 (41.8)	CRP ≥ 10 mg/L	58 (47.5)
Dyspnea	64 (52.5)	PCT ≥ 0.1 ng/mL	83 (68.3)
Hemoptysis	1 (0.8)	PCT ≥ 0.5 ng/mL	18 (14.8)
SpO ₂ when breathing ambient air (%)	86 (83, 89)	Radiology	
Previous or current smoker	44 (36.1)	Bilateral infiltrates	84 (68.9)
Underlying diseases		Unilateral infiltrates	38 (31.1)
Diabetes	3 (2.5)	Pleural effusion	26 (21.3)
Cardiovascular diseases	9 (7.4)	CURB-65 score	
Cerebrovascular diseases	4 (3.3)	0	55 (45.1)
Hypertension	12 (9.8)	1	58 (47.5)
COPD or emphysema	16 (13.1)	2	7 (5.7)
Destruction of pulmonary architecture due to TB	8 (6.6)	3	2 (1.6)
Bronchiectasis	7 (5.7)		
Pulmonary fibrosis	2 (1.6)		

Values are presented as $n(\%)$ or median (P25, P75). CAP: Community-acquired pneumonia; SpO₂: Pulse oxygen saturation; TB: Tuberculosis; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; PCT: Procalcitonin; COPD: Chronic obstructive pulmonary disease; CURB-65: Confusion, urea, respiratory rate, blood pressure, and age ≥ 65 years.

immunization rates in childhood. Since the distribution profile of CAP pathogens revealed heterogeneity in different regions, the identification of pathogens in the local area is critical for guiding empirical antimicrobial decisions. Molecular techniques facilitate the evaluation of causative microorganisms at high altitudes. The LAMP assay used in our study was proved as a rapid and accurate method with a higher sensitivity than the conventional methods. Previous studies of CAP in China showed that *M. pneumoniae*, *S. pneumoniae*, and *H. influenzae* were the three most frequently identified pathogens.^[3-5] Since the microbial spectrum of CAP in our study is similar to the published data, even though no available data at high altitudes were taken into consideration in the establishment of guidelines, we could still follow these guidelines for antimicrobial treatment. Nevertheless, potential alterations in drug susceptibility for the pathogens and a comprehensive profile of pathogens should be explored with a larger sample size in further investigations.

Conflicts of interest

None.

References

1. Cao B, Huang Y, She DY, Cheng QJ, Fan H, Tian XL, *et al.* Diagnosis and treatment of community-acquired pneumonia in adults: 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association. *Clin Respir J* 2018;12:1320–1360. doi: 10.1111/crj.12674.
2. Li B, Zhang X, Guo J, Wang J, Pianduo B, Wei X, *et al.* Prevalence of pulmonary tuberculosis in Tibet autonomous region, China, 2014. *Int J Tuberc Lung Dis* 2019;23:735–740. doi: 10.5588/ijtld.18.0614.
3. Tao LL, Hu BJ, He LX, Wei L, Xie HM, Wang BQ, *et al.* Etiology and antimicrobial resistance of community-acquired pneumonia in adult patients in China. *Chin Med J* 2012;125:2967–2972.
4. Liu Y, Chen M, Zhao T, Wang H, Wang R, Cai B, *et al.* Causative agent distribution and antibiotic therapy assessment among adult patients with community acquired pneumonia in Chinese urban population. *BMC Infect Dis* 2009;9:31. doi: 10.1186/1471-2334-9-31.
5. Bao Z, Yuan X, Wang L, Sun Y, Dong X. The incidence and etiology of community-acquired pneumonia in fever outpatients. *Exp Biol Med (Maywood)* 2012;237:1256–1261. doi: 10.1258/ebm.2012.012014.

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