Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Clinical and Imaging features of COVID-19 Patients: Analysis of Data from High-Altitude Areas

Dear Editor

SARS-CoV-2 has spread worldwide. We read Wenjie's[1] report about the characteristics of the COVID-19 outside Hubei. Due to the inclusion of the center, these data are basically from large cities. However, about 100 million residents around the world live above 2,500 meters all year around,[2] and the residents in high altitude areas may have particular pathophysiology changes, especially in cardiopulmonary function.[3] If they are combined with COVID-19, these may cause more uncertainty in diagnosis and treatment. Given the rapid spread of COVID -19, we performed an updated analysis of 68 cases from a high altitude area from Sichuan province, which might help the physicians to learn more about the COVID-19.

The study has been reviewed by the Ethics Committee of Sichuan Provincial People's Hospital and informed consent was obtained from the participants. We enrolled 68 patients from Daofu County People's Hospital in Ganzi Prefecture(Elevation:2979 meters), Sichuan, China, who were diagnosed with COVID-19, including 38 males and 30 females, from February 08 to March 01, 2020. The clinical characteristics were shown in supplementary Table 1.

Images from all cases were collected and analyzed by two radiologists. Each segment of the lung was examined to determine the affected lung segment, range, and location of the lesion, and whether there were Ground Glass Opacities (GGO), Consolidation, Mix GGO and Consolidation, reticular shadows, pleural effusion, and lymphadenopathy. We use semi-quantitative score system to evaluate the area of the lesion.[4] CT imaging features recorded from our cohort were summarized in supplementary Table 2.

The infected people ranged in age from 3 to 77 years old. The patients under the age of 14 account for 7/68 (10%). Most of the patients had no specific COVID-19 symptoms, which is quite different from previous research. Laboratory results suggest that lymphocytes had varying degrees of decrease. CRP was not too high (75% patients were in the normal range) and 79% patients had normal PCT levels. Among all patients, 22 patients had negative initial CT and follow-up of lung CT, 5 patients had negative first CT scan, and positive after follow-up. The infection involved range in lung can be seen in the supplementary as Table 2.

The total lung severity score of 46 CT-positive patients was 161, with an average score of 3.5 (range 1-10). Pulmonary cavity and tree bud signs appeared in 3 patients with tuberculosis, and the other patients did not present similar lesions. There were 3 cases of pleural effusion (3/46) (small-medium amount of left pleural effusion). There were 7 / 46 patients with old tuberculosis signs.

During the study period, 65 patients underwent a CT review. The average time between first chest CT and follow-up rescan was 3.7 days (2-10 days). 3 patients developed pleural effusion, but all of them had a history of tuberculosis. Emphysema was present in 3 people. There were 7 patients with previous tuberculosis.

SARS-CoV-2 is highly contagious and spreads quickly among the population and has spread to 79 countries worldwide in the last 3 months. Some patients can progress to severe or critical condition, which might need oxygen supplementation or ventilation support. It was hypothesized that patients were initially infected with SARS-CoV-2 due to exposure to wildlife. But in our study, none of the patients have been exposed to wildlife, nor have they been to Wuhan since the outbreak. Therefore, the cases mentioned in our study are all infections caused by imported epidemic areas.

The oxygen content is low in high altitude areas. The incidence of SARS-CoV-2 infection in this region is unclear. This is the first report talking about COVID-19 from high altitude areas. In our study, the patients under the age of 14 account for 7/68 (10%), which is higher than previous reports, and we thought that this may be related to family clustering. This differs from previously reported clinical data that 2% of the 72,314 infected patients were younger than 20 years old.[5] It may be because these groups do not have such a large range of social activities and have fewer opportunities to contact the source of infection.

The clinical symptoms of patients in this study group are quite different; most of the patients had no specific COVID-19, they had a significantly lower rate of fever symptoms than other studies present before.[4,6,7] We believe that most of our patients are not from the epidemic area, and the virus may have been passaged several generations. Because of the early prevention measure by the health department, the patients received early diagnosis and treatment and this might change the natural course development of COVID-19. However, among these patients, 6 severe patients still needed oxygen therapy to relieve their dyspnea symptoms. We analyzed that these patients were older and had more comorbidities than mild patients. It is worth mentioning that a 77-year-old female patient had a history of tuberculosis, and although only one lobe was involved with SARS-CoV-2, her condition still progressed to severe illness. Therefore, the severity of COVID-19 is closely related to the underlying lung disease.

Like clinical symptoms, the imaging of this group of patients is also diverse. Among the patients in this group, 41 CT tests were positive at the initial scan. In terms of lesion distribution, most of the patients' lung CT lesions were distributed at subpleural site and the right lower lung involvement was the most common (33/46). 32/46 patients involved more than 2-lobe segments. Among them, 16 patients had lung lesions (all the 5-lobe lesions) (Fig. 1g-i.) Although the patients in this group were original local residents, their lung performance was basically the same as that in other regions. However, there were 18 patients with underlying disease, especially those with pulmonary tuberculosis. We found that in the mentioned 77-year old female patient, although the

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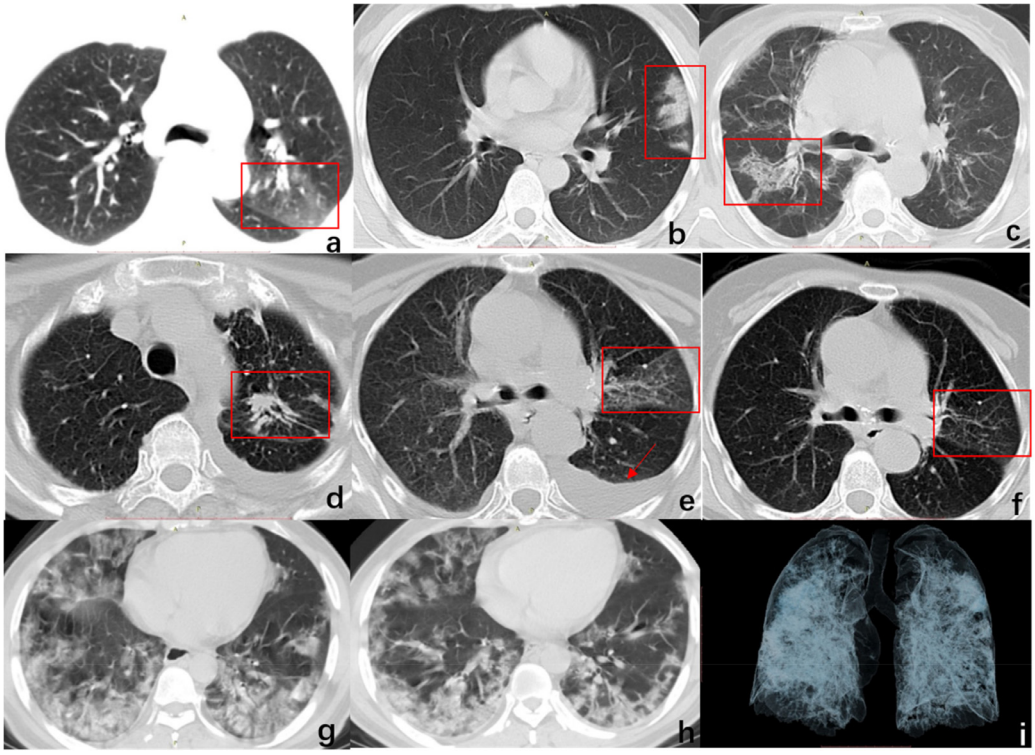

Fig. 1. a-c Typical CT features of COVID-19. (**a**) GGO (**b**) Mix GGO and consolidation (**c**) Crazy paving. d-f A 77-year-old female with tuberculosis and epidemiological histroy, presenting with dry cough in fever clinic (**d**) Initial CT present tuberculosis in upper lobe of left lung. (**e**) Initial CT present GGO and small to moderate amount of pleural effusion in the left lung. (**f**) Nine days follow-up CT image present improvement at the same level. g-i A 55-year-old man with epidemiological history, presenting with dyspnea, dry cough and fatigue in fever clinic (**g**) Initial CT present bilateral diffuse GGO lesions. (**h**) Two days follow-up CT image present a little improvement at the same lavel. (**i**) 3D Volume rendering present the distribution of lesions.

typical COVID-19 CT score was not high, her condition still progressed to severe, which is related to the patient's underlying lung tuberculosis (Fig. 1d-f).

Follow-up CT scans in 5 exacerbated patients indicated lung disease progression. There were 5 patients who had a negative initial CT scan but positive follow-up CT, which means that negative CT images cannot completely rule out COVID-19. We also found pleural effusion in COVID-19 patients, which was in accordancewith previous research,[8] and the pleural effusion was completely absorbed after treatment. In terms of treatment, most patients have a negative nucleic acid review after 1-2 weeks. After the treatment, most patients' respiratory symptoms were relieved, but the severe patients are still being followed up.

In conclusion, this is the first report of COVID-19 in a high altitude area in the world. In a high altitude area, the population is generally susceptible, including children, so everyone should be well protected. Residents in a high altitude area may face more complicated medical and social conditions (such as hypoxia, tuberculosis, and relative lack of medical resources), which may increase the complexity and severity of the disease. Our research shows that early screening and intervention could significantly reduce the severity of the disease in patients, and that pulmonary tuberculosis could significantly increase the severity of the disease.

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