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Research Article* | *Open Access

Cases of 193 Inpatients and Caregivers with COVID-19 Negative Conversion Positive— A Single-Center Analysis

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Key words: Coronavirus disease 2019, Severe acute respiratory syndrome coronavirus 2, Tibet, Inpatients, Caregivers

1. Abstract

Background: A sudden outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the Tibetan Autonomous Region in August 2022 disrupted the coronavirus disease 2019 (COVID-19)-free status of the Tibetan over the past 3 years and poses severe risks to public health.

Methods: A total of 2966 patients and caregivers were admitted to our hospital from August 01, 2022 to October 10, 2022 and cases of negative-to-positive conversion were analyzed during hospitalization.

Results: In total, 193 cases of negative-to-positive conversion were identified. The rates of hospitalization for adults (age, ≥15 years), children (age, 0–14 years), and caregivers were 4.04%, 3.07%, and 5.94%, respectively. For the majority of COVID-19 cases, negative-to-positive conversion occurred within 1–4 days. The rates of cases with mild, moderate, and severe symptoms were 41.45%, 46.63%, and 11.92%, respectively. The Tibetan population accounted for 86.01% of all positive cases.

Conclusion: Mutant variants of SARS-CoV-2 can adapt to harsh conditions at high altitudes and spread among local populations, suggesting that infection prevention and control efforts should be continued in some regions to protect public health.

2. Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in millions of deaths worldwide since December 2019 [1,2]. Due to constant evolution and spread through asymptomatic carriers, there have been more than 50 variants of SARS-CoV-2 to date [3]. Hence, SARS-CoV-2 continues to pose a serious threat to human health globally [3-5].

COVID-19 spread to almost all provinces of China after first detected in the city of Wuhan [6,7]. Before August 2022, there were relatively few cases of COVID-19 in the mountainous Tibetan Autonomous Region, which may be

associated with high-altitude hypoxia, exposure to ultraviolet light (UV), and low atmospheric pressure [8-11]. However, the sudden outbreak of COVID-19 throughout the Tibetan Plateau after July 2022 contradicts the notion that Tibet has been exempt from COVID-19 for the past 3 years. Hence, COVID-19 also poses a surmountable threat to the health of the Tibetan population, as prevention and control in Tibet have been especially challenging.

The COVID-19 pandemic has overwhelmed healthcare systems worldwide due to the large number of infected patients and asymptomatic carriers, as a secondary source of SARS-CoV-2 transmission [12-14]. Since there is a certain incubation period for SARS-CoV-2, nucleic acid test results of some patients were negative before admission, but positive after admission, demonstrating transmission from SARS-CoV-2-positive patients to caregivers. Meanwhile, nucleic acid test results of some caregivers were negative before admission, but positive after admission, demonstrating transmission from SARS-CoV-2-positive caregivers to patients. Therefore, the aim of this study was to assess the negative-to-positive conversion rate among hospitalized patients and caregivers admitted to our center to help prevent and control the current epidemic.

3. Materials and Methods

3.1 Diagnosis and treatment

All diagnoses and treatment of symptoms were performed in accordance with the clinical guidelines for COVID-19 Diagnosis and Treatment published by the National Health Commission of China (9th edition). Nucleic acid tests were conducted by trained personnel in the Outpatient and Emergency Medicine Departments.

3.2 General data collection

In total, 2966 individuals (1435 patients and 1531 caregivers) were admitted to our hospital from August 1, 2022 to October 10, 2022. Among the 1435 patients, 1294 (90.2%) were adults aged ≥15 years (320 males [median age, 47.5 years] and 974 females [median age, 34.5 years]), while 46 (3.2%) were children aged 1–14 years (31 males [median age, 5.7 years] and 15 females [median age, 6.9 years]) and 95 (6.6%) were infants aged<1 year (55 males [median age, 59 days] and 40 females [median age, 53 days]). In the patient cohort, 89% (1277/1435) were Tibetan and 11% (158/1435) were Han. Patient management was conducted in accordance with current quality of care standards.

3.3 Post-hospital processing

After admission, nucleic acid testing was conducted daily for 3–7 days by trained personnel. Patients and caregivers with negative-to-positive conversion of the nucleic acid test results were transferred to mobile field hospitals. A flow chart of the patient and caregiver transfer process is presented in Figure 1.

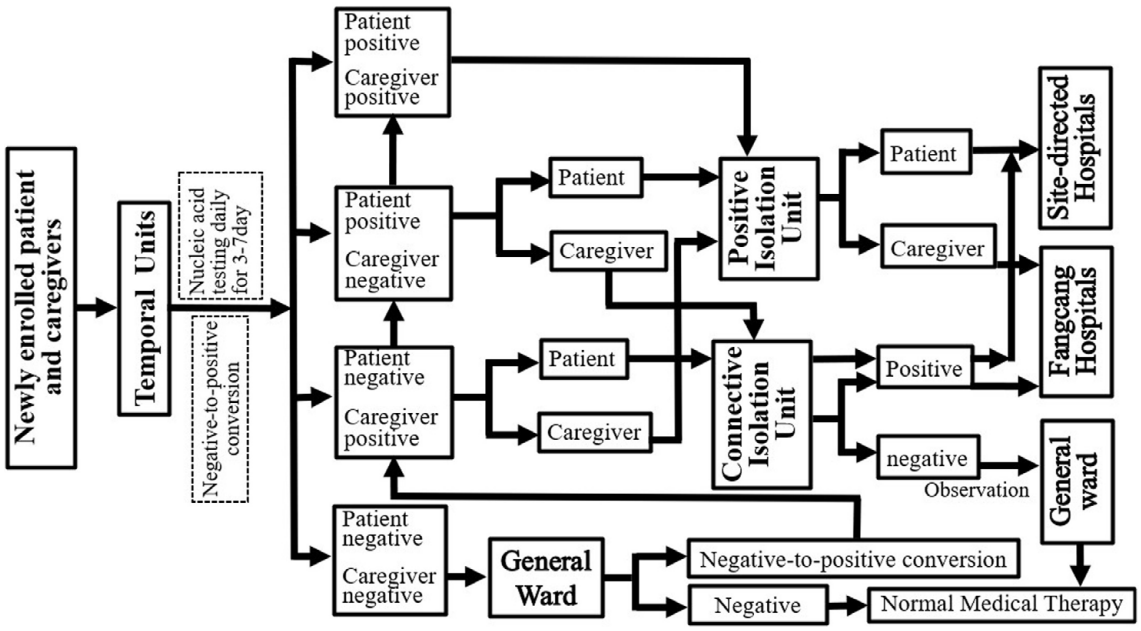

Figure 1: Time trends for conversion of negative to positive

The time to negative-to-positive conversion of the nucleic acid test results for patients and caregivers, which was mostly concentrated on 1–4 days. After 5 days, it was decreased significantly, but in a few cases more than 7 days.

4. Results

4.1 Negative-to-positive conversion rates of patients

In total, 1435 patients were admitted from August 1 to October 10, 2022. Overall, negative-to-positive conversion of the nucleic acid test results was observed in 58 (4.04%) adults (age, ≥15 years), which included 11 (18.97%) males (median age, 50.6 years) and 47 (81.03%) females (median age, 35.4 years), and 44 (3.07%) children (age, 0–14 years), which included 26 (59.09%) males (median age, 5 years) and 18 (40.91%) females (median age, 3.7 years).

4.2 Negative-to-positive conversion rates of caregivers

Among the 1531 caregivers who were admitted, negative-to-positive conversion of the nucleic acid test results was observed in 91 (5.94%), which included 34 (37.36%) males (median age, 40.9 years) and 57 (62.64%) females (median age, 33.4 years).

4.3 Time for conversion of negative to positive

After admission, the time to negative-to-positive conversion of the nucleic acid test results differed between the patients and caregivers. However, in most cases, the time to conversion was 1–4 days and up to 10 days for a small proportion (Figure 2).

4.4 Referral and classification

Of the 2966 patients and caregivers, 193 cases (6.51%) had positive nucleic acid test results, which included 102 (52.8%) patients and 91 (47.2%) caregivers. 140 cases (72.54%, including 38 positive caregivers) who were referred to hospitals designated by the Tibet Autonomous Regional Health Committee. Among the 140 individuals referred to hospitals in Tibet, 51 (36.43%) were classified as mild, 72 (51.43%) as moderate, and 17 (12.14%) as severe in accordance with the clinical guidelines for COVID-19 Diagnosis and Treatment published by the National Health Commission of China (9th edition). Among the 53 individuals referred to "Fangcang" hospitals, 29 (54.72%) were classified as mild, 18 (33.96%) as moderate, and 6 (11.32%) as severe. Among all positive cases, 41.45% were classified as mild, 46.63% as moderate, and 11.92% as severe.

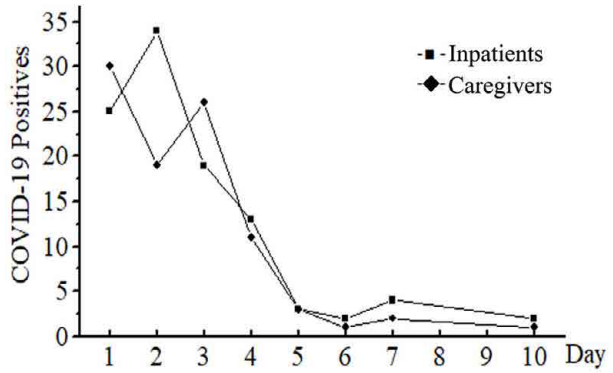

Figure 2: A flow chart of the patient and caregiver transfer process

After enrolled, patient and caregiver were admitted to the temporal units, nucleic acid testing was conducted daily for 3–7 days by trained personnel. According to nucleic acid results, they are divided into four types: Patient and caregiver all positive; Patient and caregiver all negative; Positive for patient, negative for caregiver; Positive for caregiver, negative for patient.

4.5 Racial distribution among all SARS-CoV-2-positive cases

Among the 102 patients with active SARS-CoV-2 infection, 87 (85.3%) were Tibetan and 15 (14.7%) were Han. Meanwhile, among the 91 caregivers with active SARS-CoV-2 infection, 79 (86.8%) were Tibetan and 12 (13.2%) were Han. Overall, the Tibetan population accounted for 86.01% (166/193) of all active SARS-CoV-2 infections.

5. Discussion

The COVID-19 pandemic that began in December 2019 remains a serious threat to public health. Previous studies have reported that SARS-CoV-2 infection and COVID-19-related mortality rates are lower in populations residing in high-altitude, as compared to low-altitude regions [10,15,16], which may be related to the physiological capacity to tolerate hypoxia, high UV exposure, and lower atmospheric pressure [8,17-19]. Tolerance to long-term hypoxia of populations residing in high-altitude environments leads to increased molecular levels of hypoxia-inducible factor 1α and 2α, which trigger adaptive responses to hypoxic conditions and attenuation of acute respiratory illnesses [20-22]. COVID-19 in conjunction with underlying disorders (e.g., diabetes mellitus, hypertension, and chronic renal insufficiency) is reportedly associated with a lower mortality rate in the Intensive Care Unit (ICU) than in low-lying regions (median survival, 39 vs. 21 days, respectively) [15, 23].

Several studies have shown that SARS-CoV-2 infection at high altitudes is rarely associated with severe symptoms [24,25], although it remains unclear whether this is phenomenon is related to the mutant strains of SARS-CoV-2 with attenuated virulence. However, interleukin-1, 2, 6, 7, and 10, as well as ferritin receptor and hepcidin expression, affect oxygen transport and uptake in ICU patients with severe symptoms [26,27], as the respiratory, circulatory, and

hematologic systems of individuals residing in high-altitude regions (≥2,500 m) are adapted to hypotensive and hypoxic conditions [17, 28].

However, an outbreak of the SARS-CoV-2 omicron sub-variant BA.2.76 throughout the Tibetan Plateau in August 2022 demonstrated that the virus is also highly infectious in high-altitude regions with strong UV and low atmospheric pressure, in contrast to previous reports [17,29], suggesting transmission related to viral mutation, thereby presenting new challenges to control efforts.

In the present study, the rate of SARS-CoV-2 infection in hospitalized patients and caregivers was 6.51% (193/2966), resulting in hospitalization rates of 89% (1277/1435) for the Tibetan population and 86.01% (166/193) for the overall SARS-CoV-2-positive population. Furthermore, the rates of mild, moderate, and severe cases were 36.43% (35/102), 51.43% (59/102), and 12.14% (10/102) among the patients, and 50.55% (46/91), 40.66% (37/91), and 8.79% (8/91) among the caregivers, respectively. Overall, the rate of severe cases was 9.33% (18/193). However, there were no deaths, indicating relatively low pathogenicity as a hallmark of the pandemic in Tibet, which is likely related to the genetic background of populations residing in high-altitude regions, such as low expression of angiotensin-converting enzyme 2 receptors, which lowers susceptibility to SARS-Co|V-2 infection [30,31].

Previous studies have been reported that COVID-19 predominantly affects adult, with relatively low childhood infection rates of 2% and 10%, respectively [32,33]. In the present study, the rate of infection in children younger than 14 years was 3.07% (44/1435), which might be related to infection of the infant, mother, or guardian. However, the childhood infection rate was solely based on hospitalizations. Although the overall rate of childhood infection is low, preventive measures are still important in this age group. In addition, the SARS-CoV-2 infection rate of females was 63.21% (122/193), which may be related to predominance of females in the overall population (1988/2966). However, it is unknown whether females are at a greater risk for infection with the SARS-CoV-2 variants.

Negative-to-positive conversion events pose major challenges to the prevention and control of nosocomial infections and might be linked to predisposition to secondary transmission.

The period of negative-to-positive conversion of nucleic acid test results is associated with a very high risk of SARS-CoV-2 infection, which was 1-4 days after admission in the present study, consistent with a mean incubation period of 3–5 days in previous reports [4,14, 34,35]. However, the incubation period was 7 days or more in 4.66% (9/193) of the cohort. The period of negative-to-positive conversion also increase the risk of infection for healthcare workers, which can physical and mental stress. Previous studies have shown that the rate of infection was over 10% among healthcare workers in some countries [36], while the rates of psychological distress and mental health issues were reported as 5.9%–31.2% [12,37,38]. Of the 1600 employees in our center, approximately 95 (5.93%) developed SAR-CoV-2 infections. Hence, timely appropriate measures are particularly important to prevent infection of healthcare workers.

Not all institutions have adequate facilities and resources to care for patients with infectious diseases. So, some regional healthcare administrations stipulate that COVID-19 patents and those with other infectious diseases should receive treatment in designated care facilities. From August 1 to October 10, 2022, 72.54% (140/193) of the SARS-CoV-2-positive cases were transferred to other care facilities, 27.44% (53/193) of positive caregivers who were transferred to “Fangcang” hospitals. These measures ensure timely care for patients, while reducing the risk of secondary infection and transmission by incorporating effective prevention and control measures, such as rapid response, surveillance of suspected cases, and rapid diagnosis [36,39].

There were some limitations to this study that should be addressed. Notably, the data in this study were collected from a single center due to the lack of data from multiple centers. Therefore, future studies of regional data are warranted.

6. Conclusion

Mutant strains of SARS-CoV-2 have adapted to the harsh conditions of high-altitude regions and have spread to local populations. The incubation period of COVID-19 poses a significant risk of infection to caregivers and healthcare workers. Thus, infection-control efforts, such as sequestering of infected individuals, are particularly important to prevent transmission of SARS-CoV-2 variants.

7. Abbreviations

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; COVID-19: Coronavirus Disease 2019; UV: Ultraviolet; ICU: Intensive Care Unit.

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9. Author contributions

Yang C designed, and drafted this paper. Ouzhu LB, Hao CH and Ning EY discussed, revised, and approved the final manuscript. All authors read and approved the final manuscript.

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11. Availability of data and materials

All data used in this paper has been presented.

12. Declarations

Ethics approval and consent to participate

Not applicable.

13. Consent for publication

Not applicable.

14. Competing interests

The authors have no other competing interests to disclose.

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