Limited Secondary Transmission of the Novel Coronavirus (SARS-CoV-2) by Asymptomatic and Mild COVID-19 Patients in Bhutan

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Abstract. As the COVID-19 pandemic continues, there is growing concordance and persisting conflicts on the virus and the disease process. We discuss limited transmissibility of the virus by asymptomatic and mild cases of COVID-19 patients in Bhutan. We followed up the secondary transmission of SARS-CoV-2 in the contacts of asymptomatic and mild COVID-19 patients in Bhutan. Bhutan had 33 confirmed COVID-19 cases in the country as of May 29, 2020. Of these, 22 (67%) were females. Except the first two cases (American tourists), the rest were Bhutanese living outside the country. The mean age of the Bhutanese patients was 26.3 (range 16–33) years. Close contacts of 27 of the 33 cases were followed up for signs and symptoms and COVID-19 positivity. The first two cases had 73 and 97 primary contacts, respectively, and equal number of secondary contacts (224). From the third case, a mandatory 21-day facility quarantine was instituted, all primary contacts were facility quarantined, and there were no secondary contacts. In total, the 27 cases had 1,095 primary contacts and 448 secondary contacts. Of these, 75 individuals were categorized as definite high-risk contacts. Secondary transmission occurred in seven high-risk contacts. Therefore, the overall secondary transmission was 9.0% (7/75) and 0.6% (7/1,095) among the high-risk and primary contacts, respectively. No transmission occurred in the secondary contacts. In contrast to several reports indicating high transmissibility of SARS-CoV-2 in contacts of confirmed cases, the mostly young, asymptomatic, and mild cases of COVID-19 in Bhutan showed limited secondary transmission.

INTRODUCTION

The COVID-19 caused by the SARS-CoV-2 started as a cluster of unexplained pneumonia in late December 2019 in Wuhan, China.1 The outbreak spread quickly, and the WHO declared it as a public health emergency of international concern on January 30, 2020 and as a pandemic on March 11, 2020.2 As of May 29, 2020, the pandemic has infected 5,657,529 people and caused 356,254 deaths globally.3 As of this day, Bhutan had 33 confirmed COVID-19 cases in the country as of May 29, 2020. Of these, 22 (67%) were females. Except the first two cases (American tourists), the rest were Bhutanese living outside the country. The mean age of the Bhutanese patients was 26.3 (range 16–33) years. Close contacts of 27 of the 33 cases were followed up for signs and symptoms and COVID-19 positivity. The first two cases had 73 and 97 primary contacts, respectively, and equal number of secondary contacts (224). From the third case, a mandatory 21-day facility quarantine was instituted, all primary contacts were facility quarantined, and there were no secondary contacts. In total, the 27 cases had 1,095 primary contacts and 448 secondary contacts. Of these, 75 individuals were categorized as definite high-risk contacts. Secondary transmission occurred in seven high-risk contacts. Therefore, the overall secondary transmission was 9.0% (7/75) and 0.6% (7/1,095) among the high-risk and primary contacts, respectively. No transmission occurred in the secondary contacts. In contrast to several reports indicating high transmissibility of SARS-CoV-2 in contacts of confirmed cases, the mostly young, asymptomatic, and mild cases of COVID-19 in Bhutan showed limited secondary transmission.

METHODS

This is a descriptive study related to the first 27 COVID-19–confirmed cases in Bhutan. Ethical approval was not required for descriptive and noninterventional studies related to the COVID-19 pandemic. At the time of detecting these cases, viral RNA was extracted from 140 μL of nasopharyngeal swab collected in universal transport medium using a QIAamp viral RNA mini kit (QIAGEN, Hilden, Germany). SARS-CoV-2 viral genome was detected with the WHO-supplied MolBiol RT-PCR kit (TIBMolBio, Berlin, Germany) that targets E and RdRp gene of SARS-CoV-2. The kit claimed a sensitivity of 3.8 and 5.5 RNA copies/μL for E and RdRp genes, respectively. The E and RdRp genes were amplified under the following PCR conditions: 50°C for 30 minutes, 95°C for 2 minutes, followed by 45 cycles of 95°C for 15

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COVID-19 was reported to be greater than that for influenza.8 In Taiwan, an average secondary clinical attack rate of 0.9% (95% CI: 0.7–1.5) was reported, with a higher attack rate in those exposed within 5 days of symptom onset (2.4%) than those exposed later (zero cases in 605 close contacts). The attack rate was also higher in family contacts (13.6%) and non-household contacts (8.5%) than healthcare or other contacts.13 Bhutan’s national preparedness and response plan for COVID-19 is constantly reviewed based on emerging evidence. The most unique feature of Bhutan’s strategy includes a mandatory 21-day facility quarantine for all incoming individuals. During the quarantine period, individuals were tested by RT-PCR on days 3–5 and 13–14 and a rapid antibody test on day 22 (on completion of quarantine). In addition, an individual was tested on arrival at the point of entry (if symptomatic) and anytime during quarantine (if onset of symptoms reported). Secondary transmission of COVID-19 among the close contacts of these asymptomatic or mild cases has been minimal. We describe these limited secondary transmissions by the asymptomatic to mild Bhutanese patients and attempt to explain this from different perspectives.
SECONDARY TRANSMISSION OF SARS-CoV-2 BY BHUTANESE PATIENTS

RESULTS

Bhutan had 33 laboratory-confirmed cases of COVID-19 as of May 29, 2020. Of these, 22 (67%) were females, indicating a definite female predominance of infected people. All cases were imported, and there was no community transmission at the time of this study. Except the first two cases who were American tourists (a 79-year-old man and a 59-year-old woman), the rest were all Bhutanese and of young age-group with a mean age of 26.3 (range 16–33) years. Of the 27 cases followed up and included in this study, 14 (52%) were asymptomatic, 12 (44%) were mild, and one (4%) was moderate (later progressed to severe disease) in clinical presentation. Among those symptomatic, fever, sore throat, loss of smell, and gastrointestinal presentation were the common symptoms. The first and the second cases had 73 and 97 primary contacts, respectively, and equal number of secondary contacts (224) because they traveled together. From the third case, a mandatory 21-day facility quarantine was instituted, and positive cases did not have any secondary contacts because all people traveling together in the same flight were considered primary contacts. In total, the 27 cases had 1,095 primary contacts and 448 secondary contacts. Of the primary contacts, there were 75 definite high-risk contacts among the primary contacts. The details of the confirmed cases are presented in Table 1.

Every individual in description had been tested a minimum of three times with RT-PCR, unless they have turned positive before the next scheduled testing. From all these contacts, transmission occurred only in seven high-risk contacts. Therefore, the overall secondary transmission rate among the high-risk contacts was 9.0% (7/775), and that among the primary contacts was 0.6% (7/1,095), and none (0/448) among the secondary contacts. Of the seven positive cases, six of them tested positive with the normal incubation period (14 days) from last contact with a confirmed case and one tested positive on day 21 of exposure (Figure 1).

### Table 1

Details of the first 27 COVID-19–confirmed cases in Bhutan

| Cases | Age (years) | Gender | Case origin | Disease category | Main symptoms | Primary contacts | Secondary contacts | High-risk contacts |
|-------|-------------|--------|-------------|------------------|---------------|-----------------|-------------------|--------------------|
| C0001 | 76          | M      | Tourist (USA) | Moderate/severe | Gastrointestinal | 73              | 224               | 5                  |
| C0002 | 59          | F      | Tourist (USA) (partner of C0001) | Asymptomatic | – | 97 | 224 | 3 |
| C0003 | 20          | F      | Bhutanese (London) | Mild | Fever and chills | 31 | 0 | 2 |
| C0004 | 19          | F      | Bhutanese (London) | Mild | Anosmia | 28 | 0 | 1 |
| C0005 | 16          | F      | Bhutanese (New York) | Asymptomatic | – | 16 | 0 | 2 |
| C0006 | 24          | F      | Bhutanese (Dubai) | Mild | Sore throat | 24 | 0 | 3 |
| C0007 | 24          | M      | Bhutanese (Doha) | Mild | Anosmia | 14 | 0 | 2 |
| C0008 | 27          | M      | Bhutanese (Dubai) | Asymptomatic | – | 24 | 0 | 2 |
| C0009 | 27          | F      | Bhutanese (Dubai) | Asymptomatic | – | 24 | 0 | 2 |
| C0010 | 25          | M      | Bhutanese (Kuwait) | Asymptomatic | – | 37 | 0 | 3 |
| C0011 | 27          | F      | Bhutanese (Dubai) | Mild | Fever and sore throat | 39 | 0 | 3 |
| C0012 | 33          | M      | Bhutanese (Dubai) | Asymptomatic | – | 36 | 0 | 4 |
| C0013 | 23          | F      | Bhutanese (Abu Dhabi) | Mild | Fever and headache | 36 | 0 | 2 |
| C0014 | 32          | M      | Bhutanese (Doha) | Mild | Fever, sore throat, and body ache | 36 | 0 | 7 |
| C0015 | 26          | F      | Bhutanese (Abu Dhabi) | Mild | Sore throat and diarrhea | 19 | 0 | 2 |
| C0016 | 31          | F      | Bhutanese (Dubai) | Asymptomatic | – | 65 | 0 | 2 |
| C0017 | 29          | F      | Bhutanese (Abu Dhabi) | Asymptomatic | – | 65 | 0 | 3 |
| C0018 | 24          | F      | Bhutanese (Dubai) | Asymptomatic | – | 65 | 0 | 2 |
| C0019 | 27          | F      | Bhutanese (Dubai) | Asymptomatic | – | 65 | 0 | 3 |
| C0020 | 30          | M      | Bhutanese (Doha) | Mild | Fever and diarrhea | 37 | 0 | 3 |
| C0021 | 29          | F      | Bhutanese (Doha) | Asymptomatic | – | 36 | 0 | 5 |
| C0022 | 30          | F      | Bhutanese (Abu Dhabi) | Asymptomatic | – | 45 | 0 | 3 |
| C0023 | 28          | F      | Bhutanese (Abu Dhabi) | Asymptomatic | – | 45 | 0 | 2 |
| C0024 | 34          | F      | Bhutanese (Dubai) | Asymptomatic | – | 36 | 0 | 2 |
| C0025 | 23          | M      | Bhutanese (Kuwait) | Mild | Nose block and anosmia | 30 | 0 | 2 |
| C0026 | 29          | M      | Bhutanese (Doha) | Mild | Fever and sore throat | 36 | 0 | 3 |
| C0027 | 29          | M      | Bhutanese (Doha) | Mild | Nasal irritation | 36 | 0 | 2 |

**Total**

1,085 448 75

F = Female; M = Male.
Definite close contacts with high risk for transmission of the virus from confirmed cases, their contact details, and transmission status are individually detailed in Table 2. Secondary transmission occurred commonly in partners/spouse (4/7), close friends (2/7), and flight seat partner (1/7). The observed Ct value of the sample and the presence of symptoms did not seem to affect the occurrence of secondary transmission.

DISCUSSION

Rapidly increasing cases of COVID-19 worldwide with shortening durations between doubling numbers of confirmed cases in many countries seem to indicate high transmissibility of COVID-19. Presymptomatic transmissions with cluster transmissions also suggested easy transmissibility even through vocal activities such as singing and choir groups.\(^{14,15}\) By contrast, our study argues that asymptomatic or mild cases may not transmit the virus easily. The limited secondary transmission of SARS-CoV-2 presented in our study has been deduced from observing and testing the close contacts of laboratory-confirmed COVID-19 patients up to 21 days or more in strict facility quarantine. All contacts have undergone constant monitoring for the onset of symptoms and scheduled testing (at least three RT-PCR tests) including the antibody testing at the end of the 21-day facility quarantine. Therefore, for an accepted mean incubation period of 5.2 (range 2–14) days\(^{26}\) for COVID-19 disease, a quarantine period of 21 days or more followed by testing would have not missed any cases, and the findings of this study hold much value.

This observation may be attributed to many factors such as clinical severity, race, younger patients, and living in high altitude which were opined to be protective against transmission and severity of COVID-19 clinical manifestations. In addition, the preventive measures such as using face masks, cough etiquette, and hand hygiene, which were already being widely promoted, could have had positive impact on preventing the transmission of the virus. Clinically, patients who are asymptomatic or mild with none or minimal cough, sneezing, or respiratory distress (with no labored breathing) probably do not transmit the virus easily because of the limited respiratory secretions or droplets expelled into the air. Racial differences in COVID-19 susceptibility and disease severity have been described in the Americas with African American individuals and, to a lesser extent, Latino individuals bearing a disproportionate burden of COVID-19–related outcomes.\(^{16}\)

Such racial and ethnic effects may be relevant to the Bhutanese ethnicity who are uniquely adapted to the Himalayas. Epidemiological data from Tibet and high-altitude regions of Bolivia and Ecuador compared with lowland suggested that high-altitude inhabitants (+2,500 m above sea level) are less susceptible to develop severe adverse effect in acute SARS-CoV-2 virus infection. This was likely because of physiological adaptations counterbalancing the hypoxic environment of high altitude that protect from severe impact of acute SARS-CoV-2 virus infection.\(^{17}\) Bhutan has human settlement at altitudes of up to 3,700 m above mean sea level,\(^{18}\) and this relation to high altitude may provide an explanation for almost all asymptomatic to mild cases among all the 33 cases. In another Tibetan study, 36 of the 67 (54%) COVID-19 patients were asymptomatic, with only seven (10%) progressing to severe disease and recovered with no death. In addition, imported cases of COVID-19 in Tibetan patients were reported to be generally mild with absence of fever or radiologic abnormalities.\(^{19}\) This observation is also in concurrence with imported cases of COVID-19 in Bhutan, with all the 33 Bhutanese cases being asymptomatic to mild. Plausible explanations for asymptomatic to mild cases in the Bhutanese patients are age (all young patients, the oldest being 33 years) and universal childhood vaccinations with Bacillus Calmette-Guerin (BCG) and oral polio vaccine (OPV) vaccinations as part of the Expanded Program on Immunization, with high vaccine coverage. This conclusion is in line with the finding that countries with BCG and OPV vaccination had lesser cases and low mortality from COVID-19.\(^{20}\) Analysis on BCG concluded that countries without universal policies of BCG vaccination (Italy, the Netherlands, the United States) had been severely affected compared with countries with universal and long-standing BCG policies. BCG vaccination was also found to be associated with the number of reported COVID-19 cases in a country.\(^{21,22}\)

A modeling in Singapore has shown that implementing a combined intervention of quarantining infected individuals and their family members, workplace distancing, and school
Table 2

| Case | High-risk contacts | Contact description | Level of contact | COVID-19 transmission status |
|------|-------------------|---------------------|-----------------|-----------------------------|
| C0001 | 5 Partner | Traveled together in flight, cruise, and car | Asymptomatic but positive after 6 days of last contact (C0002) |
| | Tour driver | Chauffeured the patient for 4 days | Asymptomatic and tested negative in between and on 28 days of last contact and discharged from quarantine |
| | Tour guide | Guided the patient for 4 days |  |
| | Physician 1 | Examined and talked with the patient > 2 hours. In close proximity, the patient had no face mask |  |
| | Physician 2 | Common contacts of cases C0001 and C0002 because case C0002 was the partner of case C0001 |  |
| C0002 | 3 Tour driver | Traveled in the same flight from Singapore |  |
| | Tour guide | Roommate in quarantine for 10 days |  |
| C0003 | 2 Roommate | Traveled in the same flight from London and spent three nights together in quarantine |  |
| C0004 | 1 Flight seat partner | Stayed and traveled together from Dubai to Bhutan |  |
| | Flight seat partner and roommate | Roommate in quarantine for three nights |  |
| C0005 | 2 Mother | Lived together in New York, traveled in the same flight to Bhutan, and spent two nights together in quarantine |  |
| | Brother |  |  |
| C0006 | 3 Roommate | Roommate in quarantine for three nights | Asymptomatic but tested positive on day 21 testing (C0008) |
| | Flight seat partner | Traveled together from Dubai to Bhutan | Asymptomatic and tested negative in between and on 21 days of last contact and discharged from quarantine |
| C0007 | 2 Roommate | Traveled together from Doha to Bhutan |  |
| | Flight seat partner | Roommate in quarantine for 21 days |  |
| C0008 | 2 Roommate | Traveled together from Doha to Bhutan |  |
| | Flight seat partner | Roommate in quarantine for 21 days |  |
| C0009 | 2 Roommate | Traveled together from Doha to Bhutan |  |
| | Flight seat partner | Roommate in quarantine for 21 days |  |
| C0010 | 3 Roommate | Traveled together from Doha to Bhutan |  |
| | Flight seat partner | Roommate in quarantine for 21 days |  |
| C0011 | 3 Roommate | Traveled together from Doha to Bhutan |  |
| | Flight seat partner | Roommate in quarantine for 21 days |  |
| C0012 | 4 Spouse | Traveled together and quarantined in the same facility for three nights | Asymptomatic and tested positive on day 11 of quarantine (C0024) |
| | Flight seat partner | Traveled together from Dubai to Bhutan | Asymptomatic and tested negative in between and on 21 days of last contact and discharged from quarantine |
| | Cousin | Stayed and traveled together from Dubai to Bhutan | Asymptomatic and tested positive on day 3 (C0016) |
| | Cousin |  | Asymptomatic and tested negative in between and on 21 days of last contact and discharged from quarantine |
| C0013 | 2 Flight seat partner | Traveled together from Dubai to Bhutan | Asymptomatic and tested negative in between and on 21 days of last contact and discharged from quarantine |
| C0014 | 7 Spouse | Traveled together and quarantined in the same facility for two nights | Asymptomatic and tested positive on day 11 of quarantine (C0027) |
| | Flight seat partner | Traveled together from Doha to Bhutan | Asymptomatic and tested negative in between and on 21 days of last contact and discharged from quarantine |
| | Close friend | Lived together in Doha and traveled together from Doha to Bhutan | Asymptomatic but tested positive on day 4 of quarantine (C0021) |
| | Close friend |  | Asymptomatic but tested positive on day 13 of quarantine (C0026) |
| C0015 | 2 Roommate | Roommate in quarantine for three nights | Asymptomatic and tested negative in between and on 21 days of last contact and discharged from quarantine |
| C0016 | 2 Flight seat partner and roommate | Traveled together from Dubai to Bhutan and quarantined in same room |  |
| | Flight seat partner | Traveled together from Doha to Bhutan |  |
| C0017 | 3 Flight seat partner | Roommate in quarantine for three nights |  |
| | Flight seat partner | Traveled together from Dubai to Bhutan |  |
| | Flight seat partner | Traveled together from Dubai to Bhutan |  |
| | Roommate | Roommate in quarantine for three nights |  |
| C0018 | 2 Spouse | Roommate in quarantine for three nights |  |
| | Flight seat partner | Traveled together and quarantined in the same room for two nights |  |
| C0019 | 3 Flight seat partner | Roommate in quarantine for three nights |  |
| | Flight seat partner | Traveled together from Dubai to Bhutan |  |
| | Flight seat partner | Traveled together from Dubai to Bhutan |  |
| | Roommate | Roommate in quarantine for three nights |  |

(continued)
closures after community transmission ensues could substantially reduce the number of SARS-CoV-2 infections.\textsuperscript{23} Bhutan’s institution of these measures even before the onset of community transmissions has been highly effective in preventing the transmission and spread into the community. Bhutan received its first case of COVID-19 only on March 5, 2020, after a lot of planning and advocacy. By then, people have been educated on preventive measures. Therefore, to a certain extent, it is likely that the contacts of the cases would have been practicing all the preventive measures, which could mitigate the risk of transmission during their contact. In Tianjin (China), cluster outbreaks in families, workplace, transport vehicles, and other public places were reported. These findings emphasized that special attention should be paid to the cases from the same family, same workplace, or other places where clustering is likely to occur, and the epidemiological investigation should be carried out timely to confirm the cluster. It also recommended that the close contacts of the patients should be transferred to an assigned observation place in time for single-room isolation.\textsuperscript{24}

This study is not short of limitations, the main related to the inclusion of primary and secondary contacts. All the cases in description were imported, and all secondary contacts were related to the first two cases. Beginning with the third case, all contacts were invariably included as primary contacts and put under mandatory facility quarantine on arrival at the point of entry into the country. This inclusion potentially biased the cohort and may have impacted the transmission rate. In addition, viral load could not be performed, and transmission dynamics based on Ct values and presence or absence of symptoms may need to be interpreted with caution.

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