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The epidemiology of reverse transmission of COVID-19 in Gansu Province, China

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ABSTRACT

Background: The transmission of COVID-19 is about to come under control within China, however, an emerging challenge to the Chinese authorities is reverse transmission due to COVID-19 patients/carriers evacuating from overseas to China.

Methods: We analysed the epidemiological characteristics of 311 Chinese citizens evacuated from Iran. All confirmed COVID-19 cases amongst the returnees were displayed by the spatial distribution pattern of the extent of COVID-19 infection.

Results: Characteristics that differed significantly amongst these returnees compared to the original infected cohorts in Gansu were mean age, occupation and sex. Differences observed between infected patients and non-patients amongst returnees were age, sex, race, occupation, the use of facemasks, and residential situation in Iran. The clinical features that were significantly related to infection were chill, shortness of breath, chest pain and nausea. Spatial distribution pattern analysis indicated that infected returnees had resided within Iranian provinces that had experienced high levels of COVID-19. The spatial distribution of the original homes of these returnees before departure for Iran demonstrated that returnees will largely return to northwest China, to regions that have only experienced low levels of infection within China.

Conclusion: Blocking the reverse transmission of COVID-19 is critical in preventing a secondary outbreak of COVID-19.
thousand moderately ill, confirmed COVID-19 patients are operational [5]. Importantly, substantial social isolation restrictions have been implemented in an attempt to control the outbreak of COVID19 throughout China, including mandatory wearing of face masks, and extremely strict limitations on outdoor and group activities, particularly mandating almost no public and/or private social gatherings [6]. In addition, there has been an extension of school holidays and the introduction of the use of internet classes only. At April 3, 2020, the total number of COVID-19 patients in Gansu Province has been 92, with two deaths and 90 recoveries. Consequently, the rate of newly identified COVID-19 cases has been reduced substantially in China, probably due to the active approaches outlined above, combined with substantial limitations to interstate/international travel.

We have reported previously that 54 cases of COVID-19 were identified prior to February 3, 2020 in Gansu Province, which was within 2 weeks of the lockdown of Wuhan city [7]. Gansu Province is a long, handle-shaped province, with a total land area of 454,000 km2 and a population of 26,257,100 in 2019. It is a relatively remote region of north-western China, comprising 12 prefecture-level cities and 2 autonomous prefectures (86 counties and districts), with the lowest GDP, and relatively low population density, within China. Furthermore, Gansu has complex terrain with mountains, plateaus, plains, and the Gobi Desert. On the other hand, Gansu Province is the key transportation hub connecting to five provinces in northwest China due to the special geographic location [8]. Epidemiological data show that COVID-19 is gradually being brought under control in Gansu Province, similar to other provinces in China that have reported a low level of infections. At March 2, 2020, in Gansu Province the total number of COVID-19 patients was 91, with two deaths and 87 recoveries. Consequently, the Gansu government decided at that time to lower the emergency response measures to COVID-19 from level 1 (top) to level III (low), primarily because there had been no new confirmed COVID-19 case for 14 consecutive days [9]. Thus, most students have been able to return to schools now in Gansu, and most factories have also reopened [10]. However, by March 22, 2020, in Iran the morbidity and mortality of COVID-19 had increased to 20,610 and 1,556, respectively [11].

However, a new crisis is emerging, i.e. reverse transmission of COVID-19 from abroad into China, which is becoming a huge challenge to the Chinese authorities, despite stringent measures being enforced in all of the airports within China, monitoring the body temperature of incoming passengers, disinfecting luggage and quarantining suspected COVID-19 passengers. The most updated information from The General Administration of Quality Supervision, Inspection and Quarantine of the People’s Republic of China, now requires that a mandatory 14 days quarantine is to be applied to anyone entering China from abroad from the data being not normally distributed. For categorical variables, if expected cell sizes were < 5, the Fisher exact test was used to compare the frequency between or among groups; otherwise, the χ² test was used. A two-sided α of less than 0.05 was considered statistically significant. Statistical analyses were performed using the SAS software, version 9.4, unless otherwise indicated.

Ethics approval

This study has been approved by the Ethics Committee of the Affiliated Hospital of Gansu University of Chinese Medicine (no. 20200201).

3. Results

3.1. The relationship between epidemiology and reverse transmission incidence

There was a total of 311 overseas Chinese evacuated from Iran to Gansu Province, China, arriving on 3–4 March (Fig. 1). Most of these provide critical and objective information to help control the spread of COVID-19 to other provinces and countries.
returnees were students (82%, 255/311). Their demographics were: male vs female 209 vs 102, age range 3 months – 77 years, median age was 23 years (IQR: 20, 26). The ethnicity of the majority of these returnees (78%, 242/311) is from the Hui race whose religious background is Islamic. There were 37 COVID-19 laboratory confirmed cases (12%, 37/311) among the returnees until March 14, 2020 (first 10–11 days after arrival in Gansu) and no more new cases up to date. Most of the cohort were between 20 and 35 years old, because most are students studying in Iran, with the exception of 18 children, who were 3 months to 3 years old, and 6 people who were > 50 years old. Of the positive 37 cases, there were only 17 or 23 persons who believed that they had no close contact with either COVID-19 symptomatic persons or COVID-19 patients, respectively. Among a total of 311 returnees, there was a significant positive correlation between the incidence of COVID-19 infection and male sex ($\chi^2 = 11.615, p = 0.001$), younger age (16–30 y) ($p = 0.014$), Hui/other races ($p = 0.026$), or residing in a dormitory ($\chi^2 = 4.088, p = 0.043$) (Table 1). Paradoxically, we also observed that wearing a facemask while in Iran increased the risk for COVID-19 infection ($\chi^2 = 7.902, p = 0.005$) (Table 1).

3.2. The epidemiology of the confirmed COVID-19 cases

Among the 37 confirmed COVID-19 patients, the age ranged from 18 to 29 years, median 23 years (IQR: 22, 25). There were 2 cases that developed into a critical condition (5%, 2/37 COVID-19 cases) in the period till March 21, 2020.

We further analysed differences in clinical symptoms and pre-existing illnesses as a function of COVID-19 status between the infected patients and non-infected returnees. The clinical presentations included fever, chill, cough, stuffy nose, running nose, sore throat, headache, fatigue, dizziness, muscle pain, joint pain, shortness of breath, dyspnoea, chest stress, chest pain, conjunctivitis, nausea, vomiting, diarrhoea, and stomach ache. Significant differences were observed for the following symptoms: chill ($p = 0.038$), shortness of breath ($p = 0.038$), chest pain ($p = 0.038$) and nausea ($p = 0.038$), comparing the infected patients and non-infected returnees (Table 2). Pre-existing diseases amongst all the returnees included hypertension, diabetes mellitus, cardiovascular diseases, asthma, chronic obstructive pulmonary disease, lung cancer, chronic renal and liver diseases, and immunodeficiency diseases. However, there was no difference in the presence of pre-existing disease between the infected patients and non-infected returnees.

3.3. The spatial analysis of the returnees and the confirmed COVID-19 cases

The original places of residence of these 311 returnees were from 25

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### Table 1

| Characteristics | Nucleic acid detection | $\chi^2$ | p |
|-----------------|------------------------|---------|---|
|                 | Positive (%) | Negative (%) |       |   |
| Sex             | Male   | 34 (36) | 175 (64) | 11.615 | 0.001 |
|                 | Female  | 3 (8)  | 99 (92)  |         |       |
| Age             | < 16    | 0 (0)  | 24 (100) | NA      | 0.014 |
|                 | 16–30   | 37 (14) | 225 (86) |         |       |
|                 | > 30    | 0 (0)  | 25 (100) |         |       |
| Race            | Hui     | 27 (11) | 215 (89) | NA      | 0.026 |
|                 | Han     | 2 (5)  | 37 (95)  |         |       |
|                 | Other   | 8 (27) | 22 (73)  |         |       |
| Occupation      | Student | 37 (15) | 218 (85) | 9.223   | 0.002 |
|                 | Other   | 0 (0)  | 56 (100) |         |       |
| Attend to mosque within 14 d | Yes | 2 (22) | 7 (78) | NA | 0.291 |
|                 | No      | 35 (12) | 267 (88) |         |       |
| Worn facemask   | Yes     | 11 (24) | 34 (76)  | 7.902   | 0.005 |
|                 | No      | 26 (10) | 240 (90) |         |       |
| Had close contact with COVID-19 symptomatic person | Yes | 3 (18) | 14 (82) | NA | 0.329 |
|                 | No      | 34 (12) | 269 (88) |         |       |
| Had close contact with COVID-19 patients | Yes | 5 (22) | 18 (78) | 3.280 | 0.204 |
|                 | No      | 22 (13) | 152 (87) |         |       |
|                 | Not clear | 10 (9) | 104 (91) |         |       |
| Residential situation | Apartment | 29 (15) | 168 (85) | 4.088 | 0.043 |
|                 | With family or alone | 8 (7) | 106 (93) |         |       |

NA: Fisher’s exact test.
Table 2

| Clinical symptoms | Nucleic acid detection | \( \rho \) |
|-------------------|------------------------|---------|
| Fever             | Yes 2 (11)             | 17 (89) | 1.000  |
|                   | No 35 (12)             | 255 (88)|         |
| Chill             | Yes 2 (67)             | 1 (33)  | 0.038  |
|                   | No 35 (11)             | 273 (89)|         |
| Cough             | Yes 0 (0)              | 7 (100) | 1.000  |
|                   | No 37 (12)             | 267 (88)|         |
| Stuffy nose       | Yes 0 (0)              | 2 (100) | 1.000  |
|                   | No 37 (12)             | 267 (88)|         |
| Running nose      | Yes 2 (33)             | 4 (67)  | 0.152  |
|                   | No 35 (12)             | 270 (88)|         |
| Sore throat       | Yes 0 (0)              | 10 (100)| 0.614  |
|                   | No 37 (12)             | 264 (88)|         |
| Headache          | Yes 1 (17)             | 5 (83)  | 0.535  |
|                   | No 36 (12)             | 269 (88)|         |
| Fatigue           | Yes 0 (0)              | 2 (100) | 1.000  |
|                   | No 37 (12)             | 272 (88)|         |
| Dizziness         | Yes 1 (33)             | 2 (67)  | 0.317  |
|                   | No 36 (12)             | 272 (88)|         |
| Muscle pain       | Yes 0 (0)              | 3 (100) | 1.000  |
|                   | No 37 (12)             | 271 (88)|         |
| Joint pain        | Yes 1 (33)             | 2 (67)  | 0.317  |
|                   | No 36 (12)             | 272 (88)|         |
| Shortness of breath| Yes 2 (67)           | 1 (33)  | 0.038  |
|                   | No 35 (11)             | 273 (89)|         |
| Dyspnoea          | Yes 0 (0)              | 0 (0)   | NA      |
|                   | No 37 (12)             | 274 (88)|         |
| Chest stress      | Yes 0 (0)              | 0 (0)   | NA      |
|                   | No 37 (12)             | 274 (88)|         |
| Chest pain        | Yes 2 (67)             | 1 (33)  | 0.038  |
|                   | No 35 (11)             | 273 (89)|         |
| Conjunctivitis    | Yes 0 (0)              | 0 (0)   | NA      |
|                   | No 37 (12)             | 274 (88)|         |
| Nausea            | Yes 2 (100)            | 0 (0)   | 0.038  |
|                   | No 35 (11)             | 273 (89)|         |
| Vomiting          | Yes 0 (0)              | 1 (0)   | 1.000  |
|                   | No 37 (12)             | 273 (88)|         |
| Diarrhoea         | Yes 0 (0)              | 2 (1)   | 1.000  |
|                   | No 37 (12)             | 272 (88)|         |
| Stomach ache      | Yes 1 (25)             | 3 (75)  | 0.399  |
|                   | No 36 (12)             | 271 (88)|         |

NA: Not application.

provinces or municipalities in China, mainly within the north west of China, e.g. Ningxia Hui Autonomous Region (87, 28%), Gansu Province (60, 19%) and Henan Province (48, 15%) (Fig. 2). Prior to their evacuation from Iran, the majority of these returnees had been living in Qom Province (108, 35%), Tehran Province (77, 25%), and Golestan Province (49, 16%) in Iran (Fig. 3).

Of the 37 confirmed COVID-19 cases, all were international Chinese students who had mainly been attending Al-Mustafa International University at the Qom campus (16, 43%), in Qom Province and the Gorgan campus (15, 41%), located in Golestan Province. There was an exceptionally higher rate of infection amongst these returnees; 16 of the 108 returnees (15%) who resided in Qom province and 15 of the 49 returnees (30%) who resided in Golestan Province tested positive for COVID-19. On the other hand, only 2 of the 71 returnees (3%) who resided in Tehran tested positive (Fig. 3). Notably, both Qom and Tehran were reported to have experienced a large number of infections amongst the local population (> 400 persons) at the time of evacuation, while Golestan Province had experienced a much lower number of local infection (100–199) (Fig. 3).

Furthermore, among these 37 identified COVID-19 infected returnees, there were 13 (35%) from Ningxia Hui Autonomous Region (13, 35%), 9 (24%), from Gansu Province and 7 (19%) from Qinghai Province (Fig. 2). These infected patients had lived in Qom Province (18, 49%), and Golestan Province (15, 41%) in Iran (Fig. 3).

For easy identification of the provinces in China and Iran, the map with all of the provinces of China and Iran is provided in Supplementary Fig. 1 and Supplementary Fig. 2, respectively.

4. Discussion

We reported here on the government organised evacuation of Chinese nationals from Iran to Gansu Province, north-western China in response to the COVID-19 international pandemic. The selection of the designated area to return to within China was mainly based on geographic location, cultural background and religious distribution [16] of the returnees. There were 37 confirmed cases of COVID-19 infection detected upon arrival in China, amongst the 311 returnees from Iran. The highest levels of infection amongst the returnees corresponded well with the location of residence within Iran and the levels of infection within the local Iranian population [17]. Conversely, the likely final destination province within China (mainly within the north west of China), corresponds to areas with relatively low rates of infection amongst the local Chinese population, highlighting the large potential risk of reverse transmission of COVID-19 within China from returnees from high risk international locations.

The outbreak of COVID-19 is coming under controlled in China at this stage, evidenced by the gradual reduction in new cases, particularly that there have been no more new confirmed local cases all over the country. The clearance of COVID-19 infection has been mainly due to the enforcement of stringent restriction orders, banning public activities, minimising outdoor activities, and enforcing mandatory face-masks. Of course, there is a substantial financial cost in terms of restriction of travel and social gathering, shopping and working. In addition, there is very high psychological stress accumulated over the nearly 6 weeks of lockdown amongst the general population in China, which should be taken into consideration [18]. Thus, with the improving situation of COVID-19 cases, the authorities from a number of major cities and/or provinces in China have been able to lift the restrictions-orders, with the expectation that this will ease the people's anxiety and there will be a recovery from the business loss, commencing during April 2020 [19]. However, new COVID-19 cases have been identified amongst the overseas returnees from Italy, Iran and the United States [17], leading to reverse transmission cases of SARS-CoV-2 virus exceeding local cases from March 14, 2020 [20]. This phenomenon has been aggravated by the large numbers of overseas Chinese who have hastily returned to China in order to shelter from the risk of exposure to the SARS-CoV2 virus, based on the recognition that COVID-19 infection is almost under control in China [21]. Inevitably, such activities cause much concern about reverse transmission of COVID-19 to China.

Our data are consistent with the reports above, demonstrating that most of these returnees from Iran were young adult international students, who would be expected to have strong immune systems and few co-morbidities. However, in the current study, the infection rate was extraordinarily high among the 311 returnees, being 12% (37/311), compared to the rates in the general population in Gansu of 0.35 per 100,000 or < 0.001% (92/26,257,100). The 12% infection rate amongst the returnees was also much higher than that of a symptomatic secondary attack rate of 0.45% (95% CI = 0.12%–1.6%) among all close contacts [22], but similar to the symptomatic secondary attack rate of 10.5% (95% CI = 2.9%–31.4%) among household members in USA [22]. The authors acknowledge that the explanation for the higher infection rate among these 311 returnees may be mainly due to two possible reasons: firstly, the relative lack of self-protection or, secondly, lack of knowledge about COVID-19 concerning other procedures to limit spread, such as social distancing, sanitisation during the early stages of spread during their stay in Iran.

Additionally, it is likely that the Iran government has experienced difficulties scaling up its response to combating the epidemic due to the economic loss and supply issues caused by the ever-higher politically-
induced sanctions imposed by the USA and other members of the international community [23]. The source of COVID-19 infection amongst these returnees may be from the study places at the University and/or the Mosques where they worshiped. During studies and/or worship, SARS-CoV-2 can easily be transmitted via close contact on the prayer mats or shaking hands, or even through breathing [24]. Thus, in attempts to stop the spread of the virus, Iranian authorities decided to limit inter-state travel between major cities by placing checkpoints and have halted the Friday prayers in all major cities till further notice [25]. Using the same approach has proven effective in controlling virus transmission in China over the last 6 weeks in combating the COVID-19 outbreak [21]. It has been reported that it may be possible for COVID-19 to be transmitted during flights, which has prompted the mandatory wearing of N95 facemasks for crew and passengers on any incoming flights to China, and when known positive COVID-19 cases are onboard, isolation in a screened-off section of the aircraft and the wearing of fully protective gowns, face masks and goggles [26]. Thus, during the repatriation flight and during the short interval in China prior to swab testing, stringent quarantine precautions were used, making infection during the repatriation flight and upon return to China unlikely. Nevertheless, this caveat needs to be acknowledged when trying to clearly identify and quantitate the infection source and spread range.

On 19 February 2020, the first two confirmed COVID-19 cases were reported at Qom, Iran, starting the outbreak of COVID-19 in Iran. In the current study, the confirmed COVID-19 patients among the returnees from Iran were all students from Al-Mustafa International University at the Qom and Gelstan campuses, which together enrol 9000 students [27]. The outbreak of COVID-19 at these university campuses, and the subsequent repatriation of international students’ to their home countries, has created an enormous challenge for the authorities to control the viral transmission [28]. The most immediate concern facing the Authorities of Disease Control around the world is working on blocking the viral transmission to ameliorate a COVID-19 pandemic.

The number of new COVID-19 cases from the returnees were more than Gansu local existing cases on March 17, 2020 [29]. Importantly the routine quarantine period of 14 days for COVID-19 may not be suitable for the returnees, because it has been reported that the longest incubation period of COVID-19 in China can be up to 19 days [30] and infectivity may persist for up to 21 days even after an apparently asymptomatic infection [31]. Thus, a substantial threat could occur in the community if such COVID-19 case(s) are misdiagnosed and these returnees are allowed to eventually proceed to their final destination(s) after 14 days quarantine. Although the infection rate was high (12%), there was a relatively low severe/critical attack rate among these returnees from Iran with only 2 (5%), which was far below the results from Jiangxi Province (18%) [32] and Gansu Province (17.1%) within China [7]. However, this rate is close to the age-based rate published recently by Imperial College London of approximately 1.2% of patients requiring hospitalisation in the age range 20–29 years [33]. Our explanation for such a difference might be due to most of the returnees being young adults with relatively competent host defence. The majority of these returnees were male students, which may be mainly due to the Universities preference for religious study in Iran [34]. Interestingly, the attack rate of COVID-19 amongst females was rather less.
than male (1:4.5) in our current study, which is very different from the reports in the general population (1:1.1) in China [35]. A possible explanation for this difference may relate to the likely social roles undertaken by returnee women while in Iran, where female returnees may have predominantly undertaken domestic household and childcare duties, minimising their exposure to SARS-CoV-2.

There was a 15% rate of COVID-19 cases amongst international students, which is substantially higher compared to the rate of infection amongst local Chinese students (9%) [7]. This discrepancy may be due to multiple factors, including the timing of the start of the spread of the infection and the earlier intervention and more rigorous measures taken by local Chinese students. For example, Chinese students had just started their winter vacation when the COVID-19 outbreak occurred in December 2019. Additionally, the enforcement of a restriction order in Gansu: mandatory to wear facemasks in public places, no public gathering and lockdown of Gansu from 28 January until further notice [36] is expected to have mitigated spread. Furthermore, the Ministry of Education enforced the subsequent suspension of the opening of schools and all classes have been conducted online to allow the students to stay at home, facilitating the battle against COVID-19 [37]. Such measures have effectively controlled the epidemic in schools. On the other hand, most of the international students in Iran lived in the school dormitories with several roommates and shared facilities. Another reason for the higher attack rate may be almost complete absence of precautions taken by the returnees prior to their returning back to Gansu Province, for example, only a small number of the students (12%) wore facemasks amongst those already identified or suspected of being sick students [38].

Paradoxically, our data show that the COVID-19 infection rate was greater amongst those who wore masks while in Iran (24% infection rate) compared to those who did not wear masks (10% infection rate). We speculate that this observation may be related to several factors: firstly, returnees who chose to wear masks may have been involved in activities that placed them at greater risk of exposure, for example, living in dormitories, attending university classes and mosques. All three of these activities were identified in this study as increasing the risk of infection. By comparison, those returnees who chose not to wear masks may have been largely involved in low risk activities, for example, house-bound spouses engaged in domestic duties and childcare. Secondly, those who wore masks may have over-estimated the effectiveness of the masks in preventing infection, and thus may have neglected other measures to avoid infection, such as social distancing and scrupulous hygiene. Thirdly, the masks may not have met P2/N95 standards for use against viral infections and/or the technique for using

Fig. 3. The distribution of returnees and COVID-19 confirmed cases in Iran. The figure above indicates the incidence of COVID-19 infection within the various different regions of Iran, with colour differentiation representing the overall incidence of confirmed COVID-19 cases within the general population within each of these regions within Iran; whereas the round dots represent the number of the Chinese returnees living within each of these regions prior to their return evacuation to China. The difference in the size of the dots corresponds to the number of returnees from each region. The green columns represent the confirmed COVID-19 cases amongst these returnees in each region of Iran. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)
the masks may have been inadequate, for example, touching the outside of the mask after use or multiple uses of the same mask. We note that recommendations concerning the mass wearing of masks remains controversial [39], and we urge caution in the application of our data in relation to this issue.

Apparently, prior to and during the evacuation, many of these returnees were not fully aware who was/were COVID-19 patients, particularly since a number of them (27, 9%) were asymptomatic prior to their return, with their clinical presentations occurring during the current study. Therefore, considerable caution should be exercised in screening for COVID-19 infection based only on clinical presentation.

Our data further confirm that among the reverse transmission COVID-19 returnees, the clinical presentations, including chill, shortness of breath, chest pain and nausea were still the typical manifestations for COVID-19, in comparison with presentations of COVID-19 within the local Chinese population. Furthermore, the transmission routes is/are likely to be similar to the local routes, i.e. the droplet inhalation and faecal-oral routes [40]. Currently, the quarantine approach used at the airport and/or on the airplane is primarily based on the measurement of body temperature only, which is unlikely to be sufficient; alternative more sensitive and specific screening approaches are urgently needed. However, we acknowledge that there does not seem to be another more appropriate screening measurement that is more sensitive and similar in cost available at this stage.

Limitations to this study include that there is scare literature about the demographics and clinical aspects of COVID-19 infection in Iran, which makes it impossible for us to analyse the general population in Iran in comparison with the evacuated Chinese people described in this study. Furthermore, it is difficult to estimate spatial risk factors affecting SARS-CoV-2 infection in Iran and potential risk in China because of the relatively small number of cases and the short study period. However, we expect that COVID-2019 will be under control with the current management in China.

5. Conclusions

In conclusion, our study demonstrates the epidemiological characteristics of Chinese returnees from Iran, who have returned to China for fear of COVID-19 infection and inadequate management overseas. All the identified cases were international students, most from Al-Mustafa International University. Some of COVID-19 infections within these patients were asymptomatic or exhibited minimal symptoms. Such information is useful for other regions and countries to develop effective measures for controlling the spread of SARS-CoV-2 by restricting gatherings and wearing facemasks to ameliorate reverse transmission of COVID-19.

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CRediT authorship contribution statement

Jingchun Fan: Conceptualization, Methodology, Writing - original draft. Xiaodong Liu: Software, Visualization, Data curation, Methodology. Guojun Shao: Data curation, Investigation. Junpin Qi: Data curation, Investigation. Yi Li: Data curation, Investigation. Weimin Pan: Data curation, Investigation. Brett D. Hamby: Writing - review & editing. Shisan Bao: Conceptualization, Methodology, Supervision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2020.107141.

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