

**Editor:**

Korakot Nganvongpanit,
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Article history:

Received: August 20 2021;
Revised: October 25, 2021;
Accepted: October 26, 2021;
<https://doi.org/10.12982/CMUJNS.2022.014>

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Review article**Suggested Quarantine Decision for International Travelers in COVID-19 Situation in Thailand: A Case Report**

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Abstract During the COVID-19 pandemic, international travelling has been altered. Thailand requires a 14-day travel quarantine for travelers entering the country. However, extra self-quarantine might be ordered by the local authorities, so the healthy travelers could be kept isolated and excluded from work or other responsibilities. We reported a male traveler who was unnecessarily quarantined for 30 days since he arrived Thailand. Based on a symptom and an antibody result, we also proposed the promising quarantine decision for international travelers in Thailand. Reducing the length of quarantine may make it easier for people to quarantine by reducing the time they cannot work. A shorter quarantine period also can lessen stress on the public health system, especially when new infections are rapidly rising.

Keywords: COVID-19, International travelers, Quarantine decision, Thailand



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Citation: Kewcharoenwong, C., Khamduang, W., Jiranosornkul, S., Nazir, Y., and Pornprasert, S. 2022. Suggested quarantine decision for international travelers in COVID-19 situation in Thailand: A case report CMU J. Nat. Sci. 21(1): e2022014.

INTRODUCTION

Since March 2020, the World Health Organization declared the coronavirus disease 2019 (COVID-19) outbreak, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (WHO 2021). During the COVID-19 pandemic, international travelling has been changed. The Centre for COVID-19 Situation Administration (CCSA), Thailand announced that people who received permission to enter Thailand have to undergo a mandatory 14-day quarantine in a government-designated quarantine facility (state-quarantine facility) or a pre-booked designated hotel. A negative COVID-19 test performed up to 72 hours before entering Thailand is necessary (CCSA 2021). At least three tests will be carried out on day 0-1, 6-7 and 12-13 of the quarantine period, according to the Royal Thai Government Gazette on March 31, 2021. If all tests present negative, travelers will receive a free travel pass that will allow them to be around in Thailand. However, some particular measures and extra self-quarantine might be ordered by the local authorities, so the healthy travelers could be kept unnecessarily isolated and excluded from work or other responsibilities.

Up to date, COVID-19 vaccination was provided around the world. Centers for Disease Control and Prevention (CDC) reported the considerations for international travelers who received full-dose COVID-19 vaccination without any symptoms have to receive RT-PCR test 3-5 days after travel and self-monitor for COVID-19 symptoms. Only if the travelers develop symptoms, they need self-isolation (CDC 2021). However, the best COVID-19 vaccine, nowadays, is unable to protect people completely from the variant infection (Zhou et al. 2021) and some cases present as asymptomatic infection (Kewcharoenwong et al. 2021). Full vaccination without symptoms may not be the only factor for consideration of quarantine procedures.

From recent studies, most of fully-vaccinated people develop antibodies, especially IgG to SARS-CoV-2 proteins (Walsh et al. 2020, Zhou et al. 2021). These raised antibodies from COVID-19 vaccination in theory should be reduced viral infection (Ahluwalia et al. 2021). Moreover, the commercial antibody detection kits, especially IgG to SARS-CoV-2 are now available in most countries and the cost is reducing recently. Hence, antibody detection should be another promising factor for a quarantine decision. According to CDC and Thailand procedures, the practical quarantine decision for international travelers who visit Thailand was suggested.

CASE REPORT

A healthy 35-year-old male traveler from a country in South Asia. Via questionnairing, the case reported that he had no underlying diseases. He did not be diagnosed with COVID-19, nor did he receive any pre-travel COVID-19 vaccine immunization. He arrived Suvarnabhumi Airport, Bangkok, Thailand on 8 January 2021 with undetectable COVID-19 tested by RT-PCR up to 72 hours prior to traveling. He was accommodated in a pre-booked designated hotel to wait out the required at least 14-day quarantine (Figure 1). On day 5 (13 January 2021) and day 12 (20 January 2021) of his visit, he had been tested COVID-19 by RT-PCR and the results were negative.

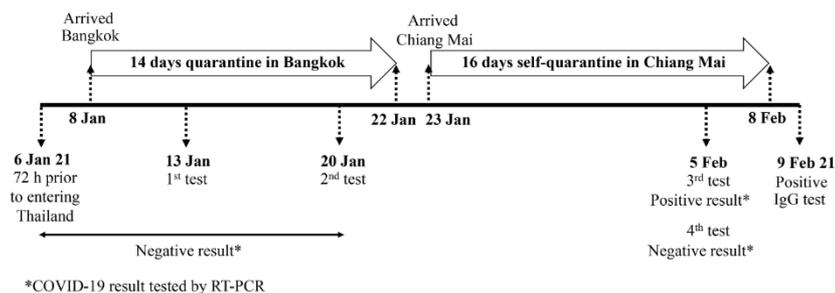


Figure 1. Timeline of the traveler's activity.

On day 14 (22 January), he was released from the hotel and travel to Chiang Mai by bus. He arrived Chiang Mai on 23 January 2021 and stayed at his accommodation for self-quarantine due to the regulation of Chiang Mai province at that time for people who come from the high-risk area with COVID-19 outbreak which included Bangkok. On 5 February 2021, he was tested COVID-19 by RT-PCR in the morning for his third time. The nasopharyngeal and throat swab specimens were tested for the presence of SARS-CoV-2 RNA by two real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assays (Da An Gene 2019-nCoV-2 RT-PCR, Guangdong, P. R. China for detection of the N and ORF1ab genes and DMSc COVID-19 Real-Time RT-PCR Kit, Bangkok, Thailand for detection of the RdRp and E genes) at the Associated Medical Sciences-Clinical Service Center (AMS-CSC), Chiang Mai University, Chiang Mai, Thailand. An RT-PCR cutoff value is 40 cycles, according to the manufacturer's protocols. The result was positive (Table 1) so he was asked for testing again as the fourth time in the evening at the same day by the hospital in Chiang Mai but the RT-PCR result for the last time was negative (Da An Gene 2019-nCoV-2 RT-PCR, Guangdong, P. R. China for detection of the N and ORF1ab genes and LyteStar™ 2019-nCoV RT-PCR Kit (Malaysia, targeting RdRp and E genes) (Table 1).

Until day 16 (8 February 2021) after arriving Chiang Mai, he had been no sign of illness and his last RT-PCR result was negative so the healthcare provider agreed to let him freely move around the city. Due to his inconsistent RT-PCR results, he was tested for antibody screening on 9 February 2021. His antibody results showed that only IgG were positive (Table 1). Total IgM/IgG COVID-19 antibody was determined by the WANTAI SARs-CoV-2 Ab Rapid Test kit, Beijing, China (100% sensitivity and 98.8% specificity). With this kit, anti-SAR-CoV-2 IgM and IgG antibodies can be detected within the same reaction line. If the result is positive, the kit cannot distinguish between IgM and IgG. Another rapid test kit (Acro Biotech COVID-19 Rapid POC CE-IVD Test, CA, USA) was used for confirmation. Based on this method, IgM and IgG antibodies were detected on separated lines with 85% sensitivity and 96% specificity for IgM, while there was 100% sensitivity and 98% specificity for IgG. According to the manufacturer's protocols, both rapid tests were considered positive in cases when the test zone IgM and/or IgG showed colored lines or weakly positive if the lines were faint. The results from these tests may be interpreted as the patient having been exposed to SAR-CoV-2, even weakly positive results were shown.

Table 1. The test results of the case in Chiang Mai.

Test	Date	5 Feb 21	5 Feb 21	9 Feb 21
		(3 rd test) In the morning	(4 rd test) In the evening	
Real-time RT-PCR	N	36.59 ^{a,b}	Undetectable ^{a,b}	ND
	ORF1ab	37.60 ^{a,b}	Undetectable ^{a,b}	ND
	RdRp	35.05 ^{a,c}	Undetectable ^{a,d}	ND
	E	ND	Undetectable ^{a,d}	ND
Antibody	IgM/IgG	ND	ND	Weakly positive ^e
	IgM	ND	ND	Negative ^f
	IgG	ND	ND	Positive ^f

Note: ^aCycle thresholds, Ct > 40 was considered as undetectable.

^bDa An Gene 2019-nCoV-2 RT-PCR

^cDMSc COVID-19 Real-Time RT-PCR Kit

^dLyteStar™ 2019-nCoV RT-PCR Kit

^eWANTAI SARs-CoV-2 Ab Rapid Test

^fAcro Biotech COVID-19 Rapid POC CE-IVD Test

ND, Not done

Totally, he was quarantined for 30 days since he arrived Thailand on 8 January 2021. After stopping quarantine, he lives and works in Chiang Mai and no close contact of him has been diagnosed with COVID-19 for months. He consented to share his story under ethic approval from Research Ethics Committee, Faculty of Associated Medical Sciences, Chiang Mai University (AMSEC-63EX-030). These quarantine procedures led us to a question whether this long-term quarantine procedure was necessary for the international travelers.

DISCUSSION

The COVID-19 results by RT-PCR of the male traveler in this study showed positive for the third time but negative for the fourth time in the same day. It was possible that the virus amount was scanty and it depended on swab positions. A population-based observational study in China found that non-stable excretion of low-level viral RNA may result in recurrent-positive occurrence, rather than re-infection. Moreover, virus collected from asymptomatic patients with recurrent SARS-CoV-2 RNA could not be cultured (Yang et al. 2020). From a clinical viewpoint, fully recovered individuals with persistent viral RNA shedding are unlikely to be a significant source of SARS-CoV-2 transmission and seem to have a more durable immunity, strongly reducing the risk of re-infection (Park et al. 2020). In addition, persistent viral RNA shedding at a low level of viral replication ($<1 \times 10^6$ copies/mL or Ct value by RT-PCR >24) did not increase the risk of transmission (Cento et al. 2020, Kewcharoenwong et al. 2021, Plebani 2021).

Furthermore, the chance of SARS-CoV-2 infection during a gap when this traveler was released from hotel in Bangkok or traveled to Chiang Mai is still questionable. However, the possibility of the infection was extremely low because the incidence of new COVID-19 cases throughout the country, at the time when the patient was released, was around 100-300 a day (WHO 2021). Unfortunately, we cannot prove that this case was infected during releasing from Bangkok because the amount of virus was too low to perform sequencing analysis.

In this study, commercial rapid lateral flow immunoassay (LFIA) kits were used to provide a quick, point-of-care approach to antibody testing. Nevertheless, currently available commercial LFIA kits do not perform sufficiently well for individual patient applications (Adams et al. 2020). Enzyme-linked immunosorbent assay (ELISA)-based test can be calibrated to be specific for detecting and quantifying SARS-CoV-2 IgM and IgG in the future. Current published data support that SARS-CoV-2 induces a classic viral response pattern, where IgM is the first isotype to appear, followed closely by IgA which peaks at 2-3 weeks post symptom onset (PSO) before declining, and finally with IgG antibodies that remain detectable for several months PSO (Seow et al. 2020). The presence of IgG antibodies indicates that the person had been exposed to the SARS-CoV-2 or vaccination.

In present case, both IgM and/or IgG detected by WANTAI SARS-CoV-2 Ab Rapid Test was detected while Acro Biotech COVID-19 Rapid POC CE-IVD Test obviously demonstrated that IgG was positive and IgM was negative. It thus implied that weakly positive for both IgM and IgG detected by WANTAI Test should be linked with a presence of IgG solely, replying that he had possibly been exposed several weeks ago. Moreover, if person had no symptom, vaccinated, and IgG antibodies positive, the virus may be eliminated or is not anymore contagious and poses a low-risk of transmission even he has been infected. These findings strengthen the justification for relying on a symptom and an antibody test rather than RT-PCR test-based strategy for ending isolation, so that adults who were no signs of infection with or without fully-vaccinated and only IgG positive should not be kept unnecessarily quarantined.

Reducing the length of quarantine may make it easier for people to quarantine by reducing the time they cannot work. A shorter quarantine period also can lessen stress on the public health system, especially when new infections are rapidly rising. Recently, CDC continues to endorse quarantine for 14 days and recognizes that any quarantine shorter than 14 days balances reduced burden against a small possibility of spreading the virus (CDC 2021). CDC also evaluates new information for the options to reduce quarantine, for instance, at least 10 days without testing, or at least 7 days after receiving a negative test

result (a test must occur on day 5 or later) (Quilty et al. 2021). However, if stopping quarantine, self-monitoring until 14 days after exposure must be done.

In situations where a quarantine period is required for international travelers who show negative COVID-19 testing by RT-PCR conducted up to 72 hours before arrival at Thailand; the current procedures (update on 17 June 2021) are announced that all international travelers must be quarantined at least 14 days and tested for COVID-19 by RT-PCR for 3 times (Figure 2A). In the following, the practical procedures are recommended (Figure 2B): (i) Upon arrival, travelers must be checked for infectious symptoms. If they present any symptoms including fever, cough, tiredness, loss of taste or smell, they must be quarantined at least 14 days and tested for COVID-19 by RT-PCR for 2 times, day 0-1 and 12-13 and no need to test on day 6-7 to reduce an extra cost (ii) No symptoms without fully-vaccinated travelers should be quarantined at least 10 days and tested by RT-PCR 2 times, day 0-1 and 8-9. (iii) No symptoms with fully-vaccinated travelers who are tested for COVID-19 antibody and found only IgG positive should be only self-monitored at least 7 days and no RT-PCR test required. However, if the travelers show other results of antibody testing, they should be quarantined at least 10 days and follow (ii). Based on the MoPH guideline, person with SARS-CoV-2 RT-PCR positive result has to be quarantined at the place provided by the local department of disease control. The purpose of all these 3 steps is to ensure that the virus had been eliminated and the persons are being at a low-risk of transmission even they had been infected.

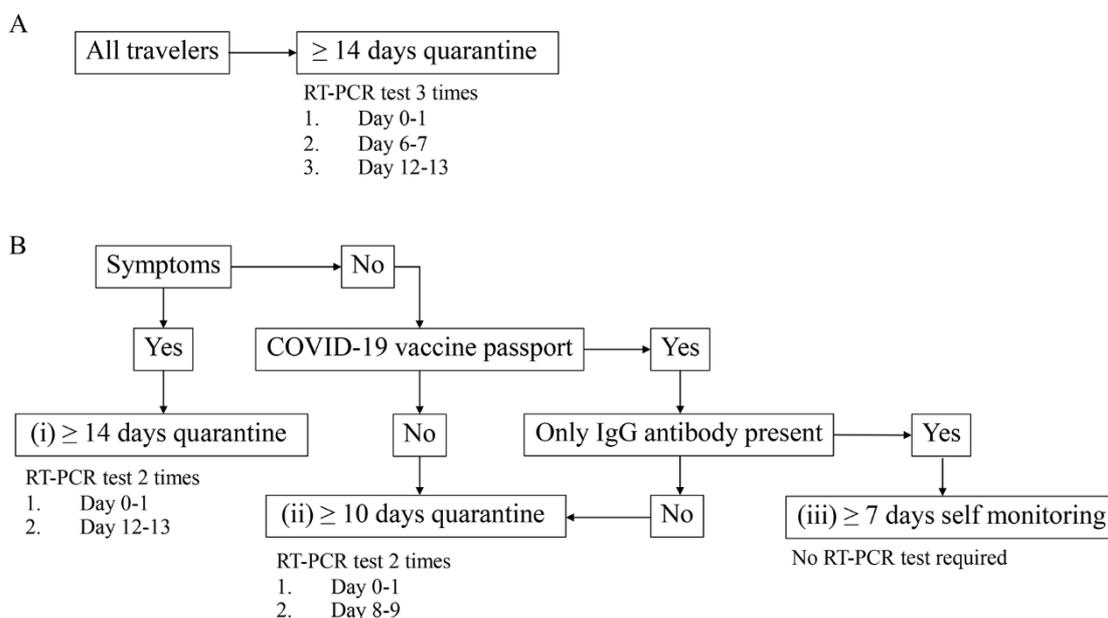


Figure 2. (A) The current procedure for international travelers and (B) Suggested quarantine decision flowchart.

According to this suggested decision, the further cases similar to the male traveler in this report should be quarantined only 14 days in Bangkok and if they are fully-vaccinated with IgG positive alone, they should be only self-monitored. Nevertheless, the general health requirements need to be followed, including social distancing and wearing a mask in public places.

AUTHOR CONTRIBUTIONS

Chidchamai Kewcharoenwong wrote the manuscript. Sakorn Pornprasert, Supat Jiranusornkuland, Yasir Nazir, and Wootichai Khamduang reviewed the manuscript. All authors have read and approved of the final manuscript.

CONFLICT OF INTEREST

The authors declare that they hold no competing interests.

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