

The prevalence of asymptomatic and symptomatic COVID19 disease in a cohort of quarantined subjects

Manaf Al-Qahtani, Salman AlAli, Abdul Karim Abdul Rahman, Adel Salman Alsayyad, Sameer Otoom, Stephen L. Atkin

PII:	S1201-9712(20)32294-3
DOI:	https://doi.org/10.1016/j.ijid.2020.10.091
Reference:	IJID 4812
To appear in:	International Journal of Infectious Diseases
Received Date:	21 September 2020
Revised Date:	27 October 2020
Accepted Date:	27 October 2020

Please cite this article as: { doi: https://doi.org/

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier.

### Tracked changes in red

The prevalence of asymptomatic and symptomatic COVID19 disease in a cohort of quarantined subjects

Manaf Al-Qahtani#, Salman AlAli, Abdul Karim, Abdul Rahman, Adel Salman Alsayyad,

Sameer Otoom, Stephen L Atkin\*#,

Manaf Al-Qahtani#, Bahrain Defense Force Hospital, Bahrain, mqahtani@rcsi-mub.com, tel

+97339766000

Salman AlAli, Bahrain Defense Force Hospital, Bahrain, salmanyalali@gmail.com, tel +97339788500

AbdulKarim AbdulRahman, Mohammed bin Khalifa Cardiac Centre, Bahrain, abdulkarim.md@live.com, tel +97333008525

Adel Salman Alsayyad, Ministry of Health, <u>ASayyad@health.gov.bh</u>, tel +97333499599

Sameer Otoom, Royal College of Surgeons, Bahrain. <u>sotoom@rcsi.com</u>, tel +97339587030

Stephen L Atkin<sup>\*#</sup>, Royal College of Surgeons, Bahrain, <u>satkin@rcsi.com</u>, tel +97332360392

\*Corresponding author: Stephen L Atkin, Royal College of Surgeons in Ireland-Bahrain, PO

Box 15503, Bahrain

#Joint senior authors

Highlights

- 2714 individuals underwent mandatory quarantine
- 136 individuals were SARS-CoV-2 positive on arrival of whom the majority (92) were asymptomatic
- A further 52 individuals became SARS-CoV-2 positive over a 14 day period

- 24 subjects found to be SARS-CoV-2 positive at day 14 remained asymptomatic until viral clearance
- Asymptomatic patients with COVID-19 were more prevalent than those exhibiting symptoms and are an infection reservoir

2

#### Abstract

**Background.** The frequency of asymptomatic SARS-CoV-2 infection with viral spread is unclear. Here, we investigated asymptomatic SARS-CoV-2 infection development and progression in subjects undergoing mandatory quarantine on airport arrival.

**Methods.** 2714 subjects were tested for SARS-CoV-2 and all were quarantined for 2 weeks. Viral retesting was undertaken on symptom development and routinely at 14 days if asymptomatic. Asymptomatic positive patients underwent viral testing every 2 days to determine viral clearance.

**Results.** 188/2714(6.9%) patients became SARS-CoV-2 positive. On arrival, 44/188(23.4%) testing positive were symptomatic and 92/188(48.9%) were asymptomatic (136/188 positive on arrival); all 92 patients remained asymptomatic and were retested every 2-days until viral clearance. 2526 quarantined subjects remained virus free at 14-days. Viral clearance did not differ between these symptomatic and asymptomatic patients ( $12.6\pm1.0$ days and  $12.1\pm0.4$ days, respectively). Of the 52/188(27.7%) testing negative on arrival, 27/52 became positive and developed symptoms from day 2 to day 13 following arrival. 25/188(13.3%) subjects remained asymptomatic and tested positive at day 14; viral testing was undertaken every 2 days in these subjects, 24/188(12.8%) remained asymptomatic with viral clearance (9.4 $\pm$ 0.7days) less than those asymptomatic on arrival(p<0.002).

**Conclusion.** Asymptomatic patients with COVID-19 were more prevalent than those exhibiting symptoms and are an infection reservoir.

Key words: COVID-19; SARS-CoV-2; symptoms, screening

#### Introduction

Coronavirus disease 2019 (COVID-19) is caused by the newly identified strain of the Coronavirus family Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (1). Whilst some patients may have mild symptoms, others develop a severe respiratory distress syndrome with features of a blood coagulopathy requiring intensive support (2), resulting in a severe healthcare burden (3). Mass testing helps to identify cases, isolate them and allows tracing of their contacts, which are all vital to limit the spread of coronavirus (4). The median COVID-19 incubation period is estimated at between 5.1 to 6.4 days (5, 6) and it has been estimated that 30-40% of all COVID-19 infections may be asymptomatic within a 14 day period(7), with higher estimates being suggested (8), whilst others estimated that 81% of COVID-19 may be asymptomatic in a study of a cruise ship outbreak (9). The Center for Disease Control and Prevention estimates that 35% of COVID-19 cases are asymptomatic, and 40% of transmission occurs before symptom onset (10). Following the SARS-CoV-2 infection of a healthcare worker, contact screening identified that 56% of those testing positive for SARS-CoV-2 were asymptomatic (11). Clearly, these asymptomatic cases may act as a reservoir and are critical to community spread of the virus.

All travelers arriving through Bahrain International Airport from highly endemic areas were tested on arrival by by quantitative real-time reverse transcription polymerase chain reaction (RT-PCR) technique of the extracted RNA, and those negative underwent mandatory quarantine for a 14 day period, allowing a prospective analysis of those who were initially asymptomatic and negative becoming subsequently positive and their outcome, within a regulated environment.

#### Methods

The Kingdom of Bahrain implemented a policy that all travelers arriving through Bahrain International Airport undergo nasopharyngeal RT-PCR testing in the airport clinic. Those that were positive were transferred to hospital facilities, whilst those who were negative were quarantined for a 14-day period with further testing on development of any symptoms of cough, fever, sore throat, or at the end of the 14-day period. At the end of the 14-day period each subject was tested again by RT-PCR, and if negative were discharged from quarantine. A total of 2714 travellers entered Bahrain between the defined period of 18 days from 25th February to 14<sup>th</sup> March 2020. All were tested and all were quarantined if RT-PCR negative. For those subjects that were found to be asymptomatic and tested positive at 14 days on routine testing, they were transferred to a dedicated isolation facility and viral testing was undertaken every 2 days until viral clearance occurred, defined as 2 RT-PCR negative tests 24 hours apart.

The diagnostic test used for SARS-CoV-2 was real time RT-PCR using a Protocol from Charité Virology, Berlin, Germany. PCR was performed on Nasopharyngeal samples. All samples were tested for E gene and positive samples were confirmed after being tested for N Gene and RdRp gene (from Tib Molbiol) (12).

The study was approved by the National Covid-19 Taskforce Ethics Committee number CRT-COVID2020-064.

### The Quarantine policy and the facility

All travellers who arrived during the study period and tested negative on arrival were quarantined. Those who arrived from high risk countries based on the risk assessment (which included China, Iran, Iraq, and South Korea) were quarantined at a dedicated quarantine facility due to the high prevalence of COVID19 noted within these groups. The Quarantine facility is made up of 8 large multistorey buildings, a large outdoor area, and a medical clinic.

The facility can occupy up to 492 people with adequate distancing. Building were assigned for males, females and for families. The facility has separate single occupancy rooms with dedicated washing and toilet facilities and was under the operation of a licenced well-trained medical team who were aware about principal precautionary measures with suspected COVID-19 cases. The medical team included physicians and nursing staff, all who were available 24/7 through 8 hours shifts. Basic necessary medical equipment was provided at the facilities that included blood pressure monitors, thermometers, swabs, medication and a cardiopulmonary resuscitation cart. The facility had security staff for the supervision of subjects who ensured quarantined patients could not leave the facility and to ensure that they followed the facility's visiting policies. Staff entered a dedicated cubicle to change and wear PPE. Staff used a different cubicle on removing the contaminated personal protective equipment. All staff had access to all necessary resources such as personal protective equipment and regular active monitoring was undertaken of the medical team for the absence/presence of symptoms. A dedicated clean area and cubicle were provided for the staff. On arrival, all quarantined individuals were instructed and informed about the aim and duration of quarantine. The medical team explained the necessity of compliance to the infection control measures. All admission to the facilities were documented through the electronic medical records and medical rounds were conducted on daily basis to check for symptoms. If a person developed symptoms, following a medical assessment the patient was swabbed, isolated, and transferred out to a COVID-19 treatment facility. The quarantined individuals were given the option to cohort as families within a building (using different rooms) or be segregated by gender. Children could stay with their mothers and beds separated by 2 meters. Food, snacks, face masks and gloves were provided on a daily basis. Subjects were given colour coded bracelets for identification. Frequent cleaning of the area was undertaken. All room were disinfected following the discharge of any person as per national

6

public health department instructions using disposable equipment. Visiting by families was allowed with strict protective measures being implemented in a dedicated outdoor area.

#### Statistical analysis

Data trends were visually and statistically evaluated for normality. Non-parametric tests (Mann-Whitney U and Kruskall-Wallis tests) were applied on data that violated the assumptions of normality when tested using the Kolmogorov-Smirnov Test. Statistical analysis was performed using STATA statistical computer package (StataCorp. 2013. Stata Statistical Software).

#### Results

Progression of patients developing SAR-CoV-2 positivity are shown in Figure 1. No subject had contact with a known positive COVID-19 case. Overall, a total of 188 (6.9%) patients eventually became SARS-CoV-2 positive either on immediate testing in the airport or on subsequent testing in the quarantine facility from the 2714 subjects returning to Bahrain by air from Iran or Egypt, of whom 90 were male and 98 were female. Of the other 2526 subjects quarantined, all showed a RT-PCR negative test at 14 days indicating that they were not infected.

44 of 188 (23,4%) were symptomatic on arrival (16 male and 28 female) and RT PCR positive, of whom 3 patients (2 females and 1 male) subsequently deteriorated and died on ventilatory support.

144/188 (76.6%) were asymptomatic on arrival (41 male and 103 females) and of those patients 92/188 (48.9%) tested positive on arrival and were transferred to hospital care: all 92 patients remained asymptomatic until viral clearance. All subjects who tested positive were retested every 2 days until viral clearance was achieved.

52/188 (27.7%) of those testing negative were transferred to quarantine as detailed, 27/52 developed symptoms and were confirmed positive by RT PCR (subjects and days to symptoms; 6 at 2 days, 4 at 3 days, 2 at 4 days, 1 at day 5, 5 at 6 days, 1 at day 7, 5 at day 12, and 3 at day 13). 25/188 (13.3%) subjects remained asymptomatic and tested positive at day 14; viral testing was undertaken every 2 days in these subjects, 1/25 became symptomatic at 5 days, whilst 24/25 (24/188 (12.8%), 11 male and 13 female remained asymptomatic with viral clearance (2 negative tests 24 hours apart) between 6-14 days after initial positive testing (subjects and days to viral clearance; 9 at 6 days, 1 at day 7, 2 at day 8, 3 at day 9, 1 at day 11, 5 at day 12, and 3 at day 14). When divided into deciles, of the 24 asymptomatic patients 8 were 60 years and above, 8 were aged 50-59 years, 3 aged 40-49 years and 5 aged 20-29 years.

Time to viral clearance for those detected as positive on arrival for symptomatic was  $12.6\pm1.0$  days and for asymptomatic was  $12.1\pm0.4$  days (p=ns). Those who tested positive at 14 days had a shorter time to viral clearance (9.4±0.7 days) compared to those who were asymptomatic on arrival (p<0.002).

#### Discussion

This data shows that in a large cohort of at-risk subjects for COVID-19 disease, all of whom were monitored closely, that the majority of those who were or subsequently became positive were asymptomatic and remained asymptomatic until viral clearance. Only a minority of subjects (23%) with SARS-CoV-2 infection were symptomatic and would have likely been picked up by temperature scanning at the airport. Of those that were asymptomatic and infected, on site RT-PCR screening picked up an additional 49% of the infections; however, 28% would not have been picked up even if tested at 48 hours. Of particular concern are the 13% who remained asymptomatic and were only picked up with routine 14 day viral testing at the end of quarantine and who remained asymptomatic until viral clearance up to 14 days later, a full 28 days post-arrival. There are few reports on how transmission may occur with these silent transmitters, there is evidence that asymptomatic patients are infectious (13) and therefore these subjects would be a reservoir of infectivity.

It remains possible, though unlikely, that some subjects have picked up the infection from being at the facility itself, as it is difficult to expect complete compliance with self-isolation for 14 days. Even if so, it is still clear that the infection was transmitted from an asymptomatic subject, as all symptomatic patients were isolated and transferred. The number of asymptomatic COVID-19 patients reported here is greater than those estimated by others from 17.9% and 35% in the population (8-10) and not dissimilar to that reported in the cruise ship outbreak(9); however, this population was under direct observation throughout the quarantine period in isolation facilities and is therefore likely to be a more accurate determination than previous estimates.

The limitations of the study are that those who are asymptomatic for COVID-19 disease and were identified as positive for SARS-COV-2 at day 14 may have become positive anytime within that time frame as regular testing was not done unless the individual became

9

symptomatic. There is also the concern that individuals may have been infected whilst they were in quarantine, but this is unlikely in this closely monitored facility as detailed above. While this study was carried out early in the pandemic and test-based strategies (sequential PCR testing) were used to determine when infection control precautions can be lifted it is important to acknowledge that practice has now switched predominantly to non-test based strategies.

In conclusion, asymptomatic patients with SARS-CoV-2 infection were found to be positive 14 days after initial testing and remained symptomatic until viral clearance. Asymptomatic patients with COVID-19 were more prevalent than those exhibiting symptoms and are an infection risk requiring multiple testing for detection.

#### **Author contributions**

AA and SLA analyzed the data and wrote the manuscript. AA and SAA performed data collection, ASA and SO interpreted data and edited the manuscript. MA supervised data collection, data analysis and edited the manuscript. All authors reviewed and approved the final version of the manuscript.

Manaf Alqahtani is the guarantor of this work.

#### DECLARATIONS

**Ethics approval and consent to participate:** The study was approved by the National Covid-19 Ethics Committee.

Consent for publication: All authors gave their consent for publication.

**Availability of data and materials:** All the data for this study will be made available upon reasonable request to the corresponding author.

Funding: No funding was received to perform this study.

Conflict of interest. The authors have declared that no conflict of interest exists.

### References

1. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal of autoimmunity. 2020;109:102433.

2. Fogarty H, Townsend L, Ni Cheallaigh C, Bergin C, Martin-Loeches I, Browne P, et al. COVID-19 Coagulopathy in Caucasian patients. British journal of haematology. 2020.

3. Carenzo L, Costantini E, Greco M, Barra FL, Rendiniello V, Mainetti M, et al. Hospital surge capacity in a tertiary emergency referral centre during the COVID-19 outbreak in Italy. Anaesthesia. 2020.

4. Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. The Lancet Global health. 2020;8(4):e488-e96.

5. Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. Euro Surveill. 2020;25(5).

Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The Incubation
Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases:
Estimation and Application. Ann Intern Med. 2020;172(9):577-82.

 Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review. Ann Intern Med. 2020.

 Nishiura H, Kobayashi T, Miyama T, Suzuki A, Jung SM, Hayashi K, et al.
 Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19).
 International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020;94:154-5. 9. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020;25(10).

 CDC. Pandemic Planning Scenarios 2020 [23 June 2020]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html.

Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al.
 Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. N
 Engl J Med. 2020;382(22):2081-90.

12. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25(3).

 Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. The New England journal of medicine. 2020;382(12):1177-9.



**Legend to Figure 1.** SARS-CoV-2 detection and subsequent quarantine of 2714 travellers arriving in Bahrain airport over an 18-day period showing those that were initially and those that were subsequently disease positive, with viral clearance for each group.