Nationwide study of rates of reinfection with SARS-CoV-2 among adults in Kuwait

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Abstract

Background: Data are scarce on differences in the rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reinfection after the first infection.

Aims: We examined nationwide data on SARS-CoV-2 reinfection in Kuwait according to four-time windows to reinfection: 29–45 days, 46–60 days, 61–90 days, and ≥ 91 days.

Methods: This was a population-level retrospective cohort study conducted between 31 March 2020 and 31 March 2021. We reviewed evidence of second positive RT-PCR test results for those who had previously recovered from COVID-19 and tested negative.

Results: Reinfection rates were: 0.52% for reinfection window 29–45 days, 0.36% for 45–60 days, 0.29% for 61–90 days, and 0.20% for ≥ 91 days. The mean age (standard deviation [SD]) of individuals with the shortest reinfection time interval (29–45 days) was significantly older than the mean age of all other groups – 43.3 years (SD 17.5) compared with: 39.0 years (SD 16.5), $P = 0.037$ for 46–60-day interval; 38.3 years (SD 16.5), $P = 0.002$ for 61–90-day interval; and 39.2 years (SD 14.4), $P = 0.001$ for ≥ 91-days interval.

Conclusion: SARS-CoV-2 reinfection was uncommon among this adult population. Older age was associated with a shorter time to reinfection.

Keywords: SARS-CoV-2; COVID-19; reinfection, adults, Kuwait.

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Introduction

Since the emergence of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in central China in December 2019 *(1)*, studies have examined different time windows to define reinfection, namely < 45 days, ≥ 45 days or ≥ 90 days after the first infection. In August 2020, the United States Centers for Disease Control and Prevention (US CDC) defined two time windows for investigation of reinfection after initial infection: ≥ 90 days for persons with or without COVID-19-like symptoms and 45–89 days for persons with COVID-19-like symptoms *(2)*. Many studies indicate that accessing data on the actual clinical symptoms is a challenge and hence a recognized limitation for such studies. Comparative data on the differences between the three aforementioned time windows are scarce.

We systematically reviewed evidence of a second positive COVID-19 test (reverse transcription polymerase chain reaction [RT-PCR]) for those who had been declared free of COVID-19 in 4 time windows for a comparative analysis. This was a nationwide study in Kuwait with a full-year follow-up from March 2020 to March 2021 and included an analysis of clinical symptoms.

Methods

This was a population-level retrospective cohort study between 31 March 2020 and 31 March 2021 which included adults 18 years and older. Patients were identified through multiple national-level electronic COVID-19 databases. SARS-CoV-2 reinfection was defined as having two or more positive SARS-CoV-2 PCR tests done on a respiratory sample, at least 29 days apart and in 4 time periods: 29–45 days, 46–60 days, ≥ 61–90 days and ≥ 91 days. Clinical data were obtained from the COVID-19 registry for adults in Kuwait. A total of 232 103 PCR patients were positive on the first testing. Of those who tested positive, a second PCR was performed for 1198 patients.

We used descriptive statistics to analyse the data.

We used a registry database and had no direct contact with the patients, except patients with COVID-19

who attended our regular clinical practice. They were informed about the risk and outcomes of the procedure and provided informed consent.

Results

Reinfection rates (all patients who had a reinfection after 29 days of the first PCR divided by the total number of patients [232103]) were: 0.52% for a reinfection window 29–45 days; 0.36% for 46–60 days; 0.29% for 61–90 days; and 0.20% for ≥ 91 days. Individually, the reinfection rate (number of patients who had positive PCR within 29–45 days of first positive PCR divided by total number of patients) was 0.16% for 29–45 days, 0.06% for 46–60 days, 0.09% for 61–90 days and 0.20% for ≥ 91 days.

Characteristics of the reinfected patients are shown in Table 1. No significant differences were seen in reinfection symptoms, fever, sex, nationality (all chi-square tests, $P > 0.05$) when compared by reinfection time interval (29–45 days, 46–60 days, 61–90 days and ≥ 91 days).

The only difference was observed in patients' age. When compared using the *t*-test, the mean age of patients with the shortest reinfection time interval (29–45 days) was significantly older than the mean age of all other groups of patients: $P = 0.037$ compared with 46–60-day interval; $P = 0.002$ compared with 61–90-day interval; and $P = 0.001$ compared with ≥ 91-day interval.

Discussion

Our study is comparable with previous studies for reinfection rates at different time windows. Our results on sex and age differences are in line with some studies *(3–5)*, partly in line with others *(6)* and contrary to other studies *(7,8)*. Our data are consistent with another nationwide study in Mexico that used a 28-day window for reinfection with 100 000 PCR-confirmed cases *(7)*. The authors reported a 0.21% reinfection rate which was higher among healthcare workers and immunosuppressed or renal patients, and lower among those with mild primary disease. However, unlike our findings, higher rates of reinfection were found among younger people with no sex differences.

Another nationwide study in Denmark, which included 4 million individuals (69% of the population), compared the first and second waves of SARS-CoV-2 infection – before June 2020 versus September–December 2020 *(3)*. The authors reported that the reinfection rate was 0.65% during the second wave with an estimated protection of 80.5%. However, this protection rate fell to 47.1% in persons aged ≥ 65 years with no sex differences.

A study in Qatar using a 45-day window and 133 266 PCR-positive patients aged 15–57 years found a reinfection rate of 0.18%, with higher rates in males *(9)*. A United States study using a 45-day window and 13 603 PCR-positive patients detected a 0.2% reinfection rate with significantly higher rates in females but not in persons aged ≥ 65 years *(6)*.

Two Italian studies that used a 90-day window for reinfection detected a reinfection rate of 0.31% *(4)* and 0.33% *(5)*, with older age being a risk factor for reinfection. A study in Pakistan using a similar 90-day window for reinfection and 142 787 PCR-positive patients detected a 0.22% reinfection rate, with higher rates in males and people younger than 45 years *(8)*.

This nationwide study included the largest number of previously positive COVID-19 patients in Middle East countries. At the time of our study, vaccination, which started in December 2020, had not yet had a substantial effect on SARS-CoV-2 infection. To the best of our knowledge, this is the first study on a large population comparing rates of reinfection at different time windows for reinfection.

Our study has certain limitations: data on clinical severity of the disease in relation to PCR positivity were not available and we did not consider the effect of vaccination on reinfection. However, our study showed that SARS-CoV-2 reinfection is generally uncommon in an adult population. Further studies are needed, using genomic sequencing surveillance.

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Competing interests: None declared.

Table 1 Characteristics of adults with SARS-CoV-2 reinfections, by time to reinfection, Kuwait

Characteristic	Time interval, in days				
	29–45	46–60	61–90	≥ 91	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Sex					
Female	171 (46.3)	63 (42.3)	88 (41.9)	223 (47.4)	545 (45.5)
Male	198 (53.7)	86 (57.7)	122 (58.1)	247 (52.6)	653 (54.5)
Nationality					
Kuwaiti	222 (60.2)	89 (59.7)	133 (63.3)	262 (55.7)	706 (58.9)
Non-Kuwaiti	126 (34.1)	53 (35.6)	69 (32.9)	191 (40.6)	439 (36.6)
Not recorded	21 (5.7)	7 (4.7)	8 (3.8)	17 (3.6)	53 (4.4)
Fever					
No fever	325 (88.1)	131 (87.9)	185 (88.1)	416 (88.5)	1057 (88.2)
Confirmed fever	2 (0.5)	0 (0.0)	1 (0.5)	4 (0.9)	7 (0.6)
Fever measured but not recorded	2 (0.5)	3 (2.0)	3 (1.4)	9 (1.9)	17 (1.4)
Fever mentioned but not measured	40 (10.8)	15 (10.1)	21 (10.0)	41 (8.7)	117 (9.8)
Risk factors (overall)					
Cardiovascular disease	5 (1.4)	4 (2.7)	4 (1.9)	5 (1.1)	18 (1.5)
Chronic lung disease	4 (1.1)	1 (0.7)	0 (0.0)	3 (0.6)	8 (0.7)
Steroids treatment	2 (0.5)	1 (0.7)	0 (0.0)	0 (0.0)	3 (0.3)
Late pregnancy	2 (0.5)	1 (0.7)	0 (0.0)	0 (0.0)	3 (0.3)
Chronic kidney disease	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)	2 (0.2)
Active cancer	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.1)
Immunodeficiency	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)
Bone marrow transplant recipient	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Poorly controlled HIV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No data	356 (96.5)	142 (95.3)	205 (97.6)	461 (98.1)	1164 (97.2)
Any symptom					
Asymptomatic	252 (68.3)	106 (71.1)	138 (65.7)	353 (75.1)	849 (70.9)
1 symptom	54 (14.6)	18 (12.1)	32 (15.2)	51 (10.9)	155 (12.9)
≥ 2 symptoms	63 (17.1)	25 (16.8)	40 (19.0)	66 (14.0)	194 (16.2)
Combination of symptoms					
Asymptomatic	252 (68.3)	106 (71.1)	138 (65.7)	353 (75.1)	849 (70.9)
Fever only	8 (2.2)	4 (2.7)	3 (1.4)	8 (1.7)	23 (1.9)
Fever + any other symptom	34 (9.2)	11 (7.4)	19 (9.0)	37 (7.9)	101 (8.4)
1 symptom, not fever	46 (12.5)	14 (9.4)	29 (13.8)	43 (9.1)	132 (11.0)
≥ 2 symptoms, but no fever	29 (7.9)	14 (9.4)	21 (10.0)	29 (6.2)	93 (7.8)
Symptoms					
Not recorded	252 (68.3)	106 (71.1)	138 (65.7)	353 (75.1)	849 (70.9)
Cough	58 (15.7)	22 (14.8)	34 (16.2)	51 (10.9)	165 (13.8)
Fever	42 (11.4)	15 (10.1)	22 (10.5)	45 (9.6)	124 (10.4)
Smell/taste changes	19 (5.1)	12 (8.1)	19 (9.0)	32 (6.8)	82 (6.8)
Sore throat	23 (6.2)	7 (4.7)	16 (7.6)	24 (5.1)	70 (5.8)
Headache	16 (4.3)	4 (2.7)	11 (5.2)	27 (5.7)	58 (4.8)
Shortness of breath	23 (6.2)	5 (3.4)	8 (3.8)	13 (2.8)	49 (4.1)
Body ache	13 (3.5)	3 (2.0)	12 (5.7)	20 (4.3)	48 (4.0)
Vomiting	7 (1.9)	7 (4.7)	4 (1.9)	11 (2.3)	29 (2.4)
Rhinorrea	4 (1.1)	2 (1.3)	5 (2.4)	10 (2.1)	21 (1.8)
Diarrhoea	6 (1.6)	3 (2.0)	3 (1.4)	7 (1.5)	19 (1.6)
Bone pain	4 (1.1)	0 (0.0)	2 (1.0)	3 (0.6)	9 (0.8)
Abdominal pain	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)	2 (0.2)
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
PCR test, no.	2.2 (0.6)	2.1 (0.4)	2.1 (0.4)	2.1 (0.5)	2.1 (0.5)
Age, in years	43.3 (17.5)	39.0 (16.5)	38.3 (16.5)	39.2 (14.4)	40.3 (16.1)

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; PCR: polymerase chain reaction; SD: standard deviation.

Étude des taux de réinfection par le SARS-CoV-2 à l'échelle nationale chez les adultes au Koweït

Résumé

Contexte : Les données sur les différences de taux de réinfection par le coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2) après la première infection sont rares.

Objectifs : Nous avons examiné les données nationales concernant la réinfection par le SARS-CoV-2 au Koweït selon quatre intervalles de temps avant la réinfection : 29-45 jours, 46-60 jours, 61-90 jours et 91 jours ou plus.

Méthodes : Il s'agissait d'une étude de cohorte rétrospective menée au niveau de la population entre le 31 mars 2020 et le 31 mars 2021. Nous avons examiné les données relatives aux deuxièmes résultats positifs au test RT-PCR pour les personnes qui avaient précédemment guéri de la COVID-19 et qui avaient été testées négatives.

Résultats : Les taux de réinfection étaient les suivants : 0,52 % pour l'intervalle de temps avant la réinfection de 29 à 45 jours, 0,36 % pour 45 à 60 jours, 0,29 % pour 61 à 90 jours et 0,20 % pour 91 jours ou plus. L'âge moyen (écart type [ET]) des personnes présentant l'intervalle de temps entre deux infections le plus court (29-45 jours) était significativement plus élevé que celui observé dans tous les autres groupes – 43,3 ans (ET : 17,5) par rapport à 39,0 ans (ET : 16,5), p = 0,037 pour l'intervalle de 46 à 60 jours ; 38,3 ans (ET : 16,5), p = 0,002 pour l'intervalle de 61 à 90 jours ; et 39,2 ans (ET : 14,4), p = 0,001 pour l'intervalle de 91 jours ou plus.

Conclusion : La réinfection par le SARS-CoV-2 était rare dans cette population adulte. Un âge plus avancé était associé à un délai de réinfection plus court.

دراسة وطنية لمعدلات عودة العدوى بفيروس سارس–كوفيد–2 بين البالغين في الكويت

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الخلاصة

الخلفية: يندر وجود بيانات عن الاختلافات في معدلات عودة العدوى بفيروس كورونا 2 المسبِّب للمتلازمة التنفسية الحادة الوخيمة (فيروس سارس–كوفيد–2) بعد العدوى الأولى.

الأهداف: هدفت هذه الدراسة الى مراجعة البيانات الوطنية المتوفرة بشأن عودة العدوى بفيروس سارس–كوفيد–2 في الكويت وفقًا لأربعة أُطر زمنية لعودة العدوى: 29–45 يومًا، و46–60 يومًا، و61–90 يومًا، و91 يومًا أو أكثر.

طرق البحث: أُجريَت هذه الدراسة الأترابية بأثر رجعي على مستوى السكان في المدة من 31 مارس/ آذار 2020 إلى 31 مارس/ آذار 2021. وقد استعرضنا دلائل نتائج اختبارات "التناسخ العكسي لتفاعل البوليميراز المتسلسل" الإيجابية للمرة الثانية لمن تعافَوا سابقًا من كوفيد–19 وكانت نتائج اختباراتهم سلبية.

النتائج: كانت معدلات عودة العدوى كما يلي: 0.52٪ لعودة العدوى خلال الإطار الزمني 45–29 يومًا، و0.36٪ لعودة العدوى خلال 60–45 يومًا، و0.29٪ لعودة العدوى خلال 90–61 يومًا، و0.20٪ لعودة العدوى خلال 91 يومًا أو أكثر. وكان متوسط العمر (مع مراعاة الانحراف المعياري) للأفراد الذين لديهم أقصر مدة زمنية لعودة العدوى (29–45 يومًا) أكبر كثيرًا من متوسط العمر لجميع الفئات الأخرى، حيث بلغ متوسط العمر 43.3 سنة (بانحراف معياري 17.5) مقارنة بـ: 39.0 سنة (بانحراف معياري 16.5)، القيمة الاحتمالية = 0.037 للإطار الزمني 46–60 يومًا؛ و38.3 سنة (بانحراف معياري 16.5)، القيمة الاحتمالية = 0.002 للإطار الزمني 61–90 يومًا؛ و39.2 سنة (بانحراف معياري 14.4)، القيمة الاحتمالية = 0.001 للإطار الزمني 91 يومًا أو أكثر.

الاستنتاجات: كانت عودة العدوى بفيروس سارس–كوفيد–2 غير شائعة بين هؤلاء السكان البالغين. وكان التقدم في العمر مقترنًا بقصر الإطار الزمني لعودة العدوى.

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