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# Seroprevalence of antibodies to SARS-CoV-2 among blood donors in the early months of the pandemic in Saudi Arabia

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ABSTRACT

*Background:* Serologic testing provides better understanding of SARS-CoV-2 prevalence and its transmission. This study was an investigation of the prevalence of antibodies to SARS-CoV-2 among blood donors in Saudi Arabia.
*Objective:* To estimate the seroprevalence of anti-SARS-CoV-2 antibodies among blood donors in Saudi Arabia during the early phase of the COVID-19 pandemic.
*Methods:* Serology results and epidemiological data were analyzed for 837 adult blood donors, with no confirmed SARS-CoV-2 infection, in Saudi Arabia from 20th to 25th May 2020. Seroprevalence was determined using electrochemical immunoassay to detect anti-SARS-CoV-2 antibodies.
*Results:* The overall seroprevalence of anti-SARS-CoV-2 antibodies was 1.4% (12/837). Non-citizens had higher seroprevalence compared with citizens (OR 13.6, $p = 0.001$). Secondary education was significantly associated with higher seroprevalence compared with higher education (OR 6.8, $p = 0.005$). The data showed that the highest seroprevalence was in Makkah (8.1%). Uisng Makkah seroprevalence as the reference, the seroprevalence in other areas was: Madinah 4.1% (OR 0.48, 95% CI 0.12–1.94), Jeddah 2.3% (OR 0.27, 95% CI 0.31–2.25), and Qassim 2.9 % (OR 0.34, 95% CI 0.04–2.89) and these were not statistically different from seroprevalence in the Makkah region.
*Conclusions:* At the early months of the COVID-19 pandemic in Saudi Arabia, the seroprevalence of antibodies to SARS-CoV-2 among blood donors was low, but was higher among non-citizens. These findings may indicate that non-citizens and less educated individuals may be less attentive to preventive measures. Monitoring seroprevalence trends over time require repeated sampling.


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## Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a novel coronavirus causing Coronavirus Disease-19 (COVID-19) infection at a pandemic scale. It was first detected in Wuhan city, China, in December 2019 and has since rapidly spread worldwide including the Kingdom of Saudi Arabia (AlJishi and Al-Tawfiq, 2021; AlJishi et al., 2021; Al-Tawfiq and Memish, 2020b). Patients with COVID-19 have a wide clinical spectrum from an asymptomatic or mild infection in most cases to a severe acute respiratory syndrome (SARS) in others (Al-Tawfiq, 2020).

The first confirmed COVID-19 case in Saudi Arabia was reported on 02 March 2020 (Al-Tawfiq and Memish, 2020a; AlJishi et al., 2021); the reported cases reached 62,545 nationally and >4.8 million globally by 20 May 2020 (World Health Organization, 2020). The main diagnostic tests for detecting SARS-CoV-2 infection relies on molecular diagnostic tests, namely reverse transcription polymerase chain reaction (RT-PCR) (Al-Tawfiq and Memish, 2020b; Gronvall et al., 2020). Serologic tests are important to understand the extent and prevalence of COVID-19 infections (Al-Tawfiq and Memish, 2020b). In addition, such tests are needed to determine the proportion of the population that has an immune response to SARS-CoV-2.

The clinical presentation and epidemiology of COVID-19 infection in Saudi Arabia are parallel to those from around the globe (Al-Omari et al., 2020; Al Mutair et al., 2020). To understand the extent of the disease in Saudi Arabia, the Ministry of Health (MoH) and the Saudi Center for Disease Prevention and Control (SCDC) conducted nationwide serologic testing early in May 2020 to estimate the prevalence of antibodies to SARS-CoV-2 in multiple settings and populations, including social care homes, rehabilitation centers, healthcare workers (Alserehi et al., 2020), and blood donors. The advantage of using blood banks for seroprevalence studies is that they usually have multiple blood donors, which facilitate serial cross-sectional studies at multiple times.

This study investigates seroprevalence of antibodies to SARS-CoV-2 among blood donors in Saudi Arabia. The objectives were to help determine seroprevalence and to support the understanding of the epidemiological characteristics, including factors associated with infection.

## Methods

This study was a cross-sectional study of SARS-CoV-2 antibodies in blood donors. All blood donors, irrespective of their sociodemographic characteristics, who presented for blood donation at one of the 24 main blood banks in Saudi Arabia were included in the study. Blood donors with a contraindication for blood donation, those with a past or currently confirmed SARS-CoV-2 infection, and those who declined to give informed consent to participate in the study were excluded. Participants were included in the study from 20 to 25 May 2020. The study was conducted at the time when the Kingdom of Saudi Arabia had 62,000–80,000 cases and just before the peak of cases in the country (Alserehi et al., 2020). All participants signed informed consent and completed the study questionnaire.

### *Study questionnaire*

Each participant was instructed to complete a written questionnaire, which covered demographics (age, sex, citizenship status, education level), clinical data (current symptoms, date of onset, health conditions, smoking behavior), and exposure characteristics (contacted a confirmed or suspected SARS-CoV-2 case, attended a gathering, and/or visited a healthcare setting during the last 14 days; and SARS-CoV-2 RT-PCR testing). Location information of the blood bank site and the province were also collected.

### *Serum sample collection*

Before beginning blood donation, 4 ml of blood were collected in a serum collection tube from each participant by trained blood bank staff. All collected serum samples were transported and stored for antibody testing at one of the designated MoH regional laboratories in the cities of Jeddah or Dammam, as per the study protocol and manufacturer's instructions.

### *Serological testing*

To detect anti-SARS-CoV-2 antibodies, an electrochemiluminescent immunoassay (ECLIA) was performed using the Elecsys® Anti-SARS-CoV-2 test from Roche Diagnostics International Ltd. (Rotkreuz, Switzerland) for the qualitative detection of antibodies (including IgG) to SARS-CoV-2. The test is based on in-solution double-antigen sandwich format that can detect antibodies using a recombinant protein representing the nucleocapsid (N) protein of SARS-CoV-2 (Lau et al., 2020; Migchelsen and Duggan, 2020; Muench et al., 2020). The test has 99.8% sensitivity (14 days after a PCR-confirmed infection) and 99.5% specificity (with limited cross-reactivity of 4/792 (0.5%) to the four human coronaviruses causing the common cold) (Muench et al., 2020). The result of a sample is given either as reactive (i.e. positive for anti-SARS-CoV-2 antibodies if the result's cut-off index is $\geq$1.0) or non-reactive (i.e. negative for anti-SARS-CoV-2 antibodies if the result's cut-off index is <1.0) (Migchelsen and Duggan, 2020).

### *Statistical analysis*

Descriptive analysis was used to summarise the data using range and mean $\pm$ standard deviation (SD), as appropriate, for continuous variables and proportion (%) for categorical variables. Inferential analysis was performed using *t*-test and Chi-squared test, as appropriate, to compare demographic, clinical and exposure characteristics between seropositive and seronegative participants. Logistic regression was then performed to establish the correlates of seroprevalence using odds ratio (OR) for the statistically significant characteristics. STATA® (Stata/IC software version 15.1) from StataCorp LLC (College Station, Texas, USA) was used to perform statistical analysis. A two-tailed $p$-value <0.05 was considered statistically significant and 95% confidence interval (CI) was used, as appropriate, to report the estimates.

### *Ethical considerations*

This study was approved by the MoH's Central Institutional Review Board (log number: 20-107M) according to the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)'s Good Clinical Practice (GCP) guidelines. The study's national registration number at the National Committee of BioEthics, King Abdulaziz City for Science and Technology, Saudi Arabia is H-01-R-009.

## Results

A total of 837 participating blood donors, aged 17–70 years, were included in the study. Anti-SARS-CoV-2 antibodies were detected in 12 (1.4%) participants (Table 1). Males constituted 96% of the study participants and all seropositive participants. National citizens formed 72% of the study participants and 17% of the seropositive participants. There was no significant difference for mean age or prevalence in the different age groups of seropositive

**Table 1**
Characteristics of participating blood donors and seroprevalence of anti-SARS-CoV-2 antibodies according to characteristics, Saudi Arabia, 20–25 May 2020.

| Characteristic | Number of participants | Seronegative participants | Seropositive participants | Prevalence of seropositivity (%) | $p^*$ |
|---|---|---|---|---|---|
| Anti-SARS-CoV-2 test result | 837 | 825 | 12 | 1.4 | – |
| Age[a] range (years) | 17–70 | 17–70 | 25–50 | – | – |
| Age[a], mean (SD) (years) | 33.3 (8.3) | 33.2 (8.3) | 37.4 (8.4) | – | 0.081 |
| Age[a] group (years) | – | – | – | – | 0.723 |
| 17–19 | 23 | 23 | 0 | 0.0 | – |
| 20–29 | 256 | 253 | 3 | 1.2 | – |
| 30–39 | 381 | 377 | 4 | 1.0 | – |
| 40–49 | 135 | 131 | 4 | 3.0 | – |
| 50–59 | 34 | 33 | 1 | 2.9 | – |
| 60–69 | 2 | 2 | 0 | 0.0 | – |
| 70+ | 1 | 1 | 0 | 0.0 | – |
| Sex[b] | – | – | – | – | 0.484 |
| Male | 796 | 784 | 12 | 1.5 | – |
| Female | 32 | 32 | 0 | 0.0 | – |
| Citizenship status[c] | – | – | – | – | <0.001 |
| Citizen | 605 | 603 | 2 | 0.3 | – |
| Non-citizen | 231 | 221 | 10 | 4.3 | – |
| Education level[d] | – | – | – | – | 0.005 |
| Higher education | 540 | 537 | 3 | 0.6 | – |
| Secondary education | 218 | 210 | 8 | 3.7 | – |
| Lower education | 75 | 74 | 1 | 1.3 | – |
| Directorate of health affairs[e] | – | – | – | – | 0.002 |
| Aseer | 51 | 51 | 0 | 0.0 | – |
| Baha | 31 | 31 | 0 | 0.0 | – |
| Bisha | 31 | 31 | 0 | 0.0 | – |
| Eastern Region | 53 | 53 | 0 | 0.0 | – |
| Hafr Al Batin | 31 | 31 | 0 | 0.0 | – |
| Hail | 2 | 2 | 0 | 0.0 | – |
| Hasa | 43 | 43 | 0 | 0.0 | – |
| Jazan | 42 | 42 | 0 | 0.0 | – |
| Jeddah | 43 | 42 | 1 | 2.3 | – |
| Madinah | 73 | 70 | 3 | 4.1 | – |
| Makkah | 86 | 79 | 7 | 8.1 | – |
| Najran | 43 | 43 | 0 | 0.0 | – |
| Northern Borders | 23 | 23 | 0 | 0.0 | – |
| Qassim | 34 | 33 | 1 | 2.9 | – |
| Qunfudhah | 23 | 23 | 0 | 0.0 | – |
| Qurayyat | 22 | 22 | 0 | 0.0 | – |
| Riyadh | 116 | 116 | 0 | 0.0 | – |
| Tabouk | 29 | 29 | 0 | 0.0 | – |
| Taif | 61 | 61 | 0 | 0.0 | – |
| Current symptoms[f] | – | – | – | – | 0.574 |
| No | 808 | 796 | 12 | 1.5 | – |
| Yes | 21 | 21 | 0 | 0.0 | – |
| Health conditions[g] | – | – | – | – | 0.673 |
| No | 819 | 807 | 12 | 1.5 | – |
| Yes | 12 | 12 | 0 | 0.0 | – |
| Smoker[h] | – | – | – | – | 0.067 |
| No | 547 | 536 | 11 | 2.0 | – |
| Yes | 269 | 268 | 1 | 0.4 | – |
| Exposure history (contacted confirmed or suspected COVID-19 case, attended gathering, and/or visited healthcare setting during last 14 days) | – | – | – | – | 0.943 |
| No | 691 | 681 | 10 | 1.5 | – |
| Yes | 146 | 144 | 2 | 1.4 | – |
| SARS-CoV-2 RT-PCR testing[i] | – | – | – | – | 0.231 |
| No | 747 | 735 | 12 | 1.6 | – |
| Yes | 88 | 88 | 0 | 0.0 | – |

*Abbreviations*: COVID-19, coronavirus disease 2019; ND, no data; *p*, *p*-value; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

[*] 5% significance level. Difference in mean age of seropositive and seronegative participants was tested using *t*-test. Differences in proportion of all other characteristics were tested using chi-squared test, especially Pearson's chi-squared test.

[a] Age was unknown for five seronegative participants who were excluded from the analysis.

[b] Sex was unknown for nine seronegative participants who were excluded from the analysis.

[c] Citizenship status was unknown for one seronegative participant who was excluded from the analysis.

[d] Education level was unknown for four seronegative participants who were excluded from the analysis.

[e] Serology samples were missing for Jouf's Directorate of Health Affairs, so they were excluded from the study.

[f] Current symptoms were unknown for eight seronegative participants who were excluded from the analysis. The list of symptoms in the study questionnaire included cough, fever (> 38.0 °C) or feeling feverish, having headache, joint pain, nasal drip, nausea and/or vomiting, and sore throat. Bone pain was reported by one participant as other symptoms.

[g] Health conditions were unknown for six seronegative participants who were excluded from the analysis. The list of health conditions in the study questionnaire included cardiac disease, chronic lung disease, diabetes, high blood pressure, and obesity. Asthma was reported by one participant as other health conditions.

[h] Smoking behavior was unknown for 21 seronegative participants who were excluded from the analysis.

[i] Blood donors with confirmed SARS-CoV-2 infection were excluded from participation in the study. History of SARS-CoV-2 RT-PCR testing was unknown for two seronegative participants who were excluded from the analysis.

and seronegative participants (Table 1). Other characteristics that had no significant difference for seroprevalence included sex, having current symptoms, having a health condition, being a smoker, having previous exposure to SARS-CoV-2 and/or a high-risk event in the last 14 days, or having had SARS-CoV-2 RT-PCR testing. By contrast, citizenship status, education level and directorate of health affairs (a proxy measure for the home address of the blood donor) had significant differences for the prevalence of anti-SARS-CoV-2 antibodies between the seropositive and seronegative participants with $p < 0.001$, $p < 0.005$ and $p < 0.002$, respectively.

In a logistic regression analysis, non-citizen participants had higher odds ratio of being seropositive than citizens (OR 13.6, 95% CI 2.96–62.75, $p = 0.001$) (Table 2). Education level was also significantly associated with seroprevalence, with participants reporting secondary education as the highest level of education having increased odds than those reporting higher education (OR 6.8, 95% CI 1.79–25.95, $p = 0.005$). The data showed that the highest seroprevalence was in Makkah (8.1%). Having Makkah seroprevalence as the reference, the seroprevalence in other areas was as follow: Madinah 4.1% (OR 0.48, 95% CI 0.12–1.94), Jeddah 2.3% (OR 0.27, 95% CI 0.31–2.25), and Qassim 2.9% (OR 0.34, 95% CI 0.04–2.89); these were not statistically different from seroprevalence in the Makkah Region (Table 2).

## Discussion

This study was conducted as part of Saudi Arabia's nationwide serosurvey estimating the prevalence of antibodies to SARS-CoV-2 in multiple population groups and was started around 20 May 2020. The study investigated the seroprevalence among blood donors with no previously confirmed infection and explored their epidemiological characteristics.

The overall prevalence of antibodies to SARS-CoV-2 among the participants was 1.4%, with substantial variation in the different cities. The low prevalence of antibodies might not indicate a true low prevalence of past infection. In a review article (Tirupathi et al., 2020b), it was noted that antibody response can decrease in 1–3 months after acute infection (Long et al., 2020; Robbiani et al., 2020) and that the level of antibodies, persistence and duration of antibodies may differ among different patients (Lee et al., 2020; To et al., 2020; Xu et al., 2020). This overall seroprevalence rate was lower than the 2.36% rate among healthcare workers in Saudi Arabia (Alserehi et al., 2020). For non-citizens, the probability of testing positive for anti-SARS-CoV-2 antibodies was 13.6 times higher than for citizens. The difference in seroprevalence among citizens and non-citizens was likely related to the fact that there was a difference in the initial number of cases in Saudi Arabia. The initial cases were reported more among non-citizens, due to sociodemographic characteristics. A similar disparity in the positivity rate of acute COVID-19 infection was noted among different races and ethnicities (Tirupathi et al., 2020a). Racial and ethnic minority families may live in congested and overcrowded households and this may lead to increased likelihood of contracting SARS-CoV-2 (Tirupathi et al., 2020a). The difference in serology among different regions and non-citizens compared with citizens may shed light on priorities for vaccine. However, there are multiple factors that are being considered for prioritizing the vaccine based on risk of exposure and risk of disease and its associated morbidity and mortality. Also, the seroprevalence probability was 6.8 times higher for participants having secondary education than those having higher education. The study found no significant difference in seropositivity for age group and gender.

The seroprevalence in this study, albeit conducted among blood donors who had no confirmed SARS-CoV-2 infection, was consistent with most findings from other studies of the prevalence of anti-SARS-CoV-2 antibodies among blood or plasma donors, or of stored samples, from January to June 2020. Notwithstanding the differences in study methods and SARS-CoV-2 transmission patterns between different areas, most of these studies found low levels of seroprevalence of 0–23% (Erikstrup et al., 2021; Filho et al., 2020; Gallian et al., 2020; Grzelak et al., 2020; Ng et al., 2020; Percivalle et al., 2020; Sughayer et al., 2020; Thompson et al., 2020; Valenti et al., 2020). For example, 0% seroprevalence was reported in Amman city, Jordan (Sughayer et al., 2020); 0.1% in the San Francisco Bay Area, California, USA (Ng et al., 2020); 0.9% (IgG) in three federal states (North Rhine-Westphalia, Hesse and Lower Saxony) in Germany (Fischer et al., 2020); 1.9% in Denmark (Erikstrup et al., 2021); 2.7% in blood donors in the Netherlands (Slot et al., 2020b); 2.7% in four departmental areas in France (Gallian et al., 2020); 3.0% in two blood banks in Clermont and Noyon cities, Oise, France (Fontanet et al., 2020); 3.2% in Scotland (Thompson et al., 2020); 4.0% in the State of Rio de Janeiro, Brazil (Filho et al., 2020); 7.1% in Milan metropolitan area, Lombardy, Italy (Percivalle et al., 2020; Valenti et al., 2020); and 8.5% (overall weighted adjusted) in England (Erikstrup et al., 2021; Filho et al., 2020; Gallian et al., 2020; Grzelak et al., 2020; Ng et al., 2020; Percivalle et al., 2020; Sughayer et al., 2020; Thompson et al., 2020; Valenti et al., 2020).

One study reported 23.0% seroprevalence in the Lodi Red Zone (in Lombardy region) in Italy, which was highly affected by the pandemic and under complete lockdown (Percivalle et al., 2020). In the current study, Makkah's directorate of health affairs, the health authority for the city of Makkah and its surrounding areas, had the highest proportion of seropositivity with 8.1% prevalence compared with the other participating directorates. The city of Makkah itself was also highly affected and under complete lockdown and had curfew for a longer time than the other cities in the country (Algaissi et al., 2020; Alserehi et al., 2020; Obeid et al., 2020). In addition, Madinah had 14.6% of the cases and a 4.1% positivity rate. On the other hand, the Eastern Province had about 19% of the cases and Riyadh had 20.2% of the cases, with no positivity among blood

**Table 2**
Association of participating blood donors' characteristics with seroprevalence of anti-SARS-CoV-2 antibodies, Saudi Arabia, 20–25 May 2020.

| Characteristic | Category | Number of participants | Seroprevalence (%) | OR | 95% CI | $p^*$ |
|---|---|---|---|---|---|---|
| Citizenship status | Citizen | 605 | 0.3 | 1.00 | Ref. | – |
| | Non-citizen | 231 | 4.3 | 13.64 | 2.96–62.75 | 0.001 |
| Education level | Higher education | 540 | 0.3 | 1.00 | Ref. | – |
| | Secondary education | 218 | 4.3 | 6.81 | 1.79–25.95 | 0.005 |
| | Lower education | 75 | 1.3 | 2.41 | 0.24–23.55 | 0.447 |
| Directorate of health affairs | Makkah | 86 | 8.1 | 1.00 | Ref. | – |
| | Madinah | 73 | 4.1 | 0.48 | 0.12–1.94 | 0.306 |
| | Jeddah | 43 | 2.3 | 0.27 | 0.31–2.25 | 0.226 |
| | Qassim | 34 | 2.9 | 0.34 | 0.04–2.89 | 0.324 |

*Abbreviations*: CI = confidence interval; OR = odds ratio; $p$ = $p$-value; Ref. = reference; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
* 5% significance level. Differences are relative to the variable listed first as a reference in each characteristic.

donors at the same time. The current study found a prevalence of 4.1% in Madinah. A recent study showed a prevalence of 19.3% and that study was conducted from mid-May to mid-July 2020. Thus, the difference could be related to the difference in the timing of these two studies (Mahallawi and Al-Zalabani, 2020). Other factors may have contributed to the differences in the serology among blood donors.

The current study found that seroprevalence among those with secondary education was higher than with higher education (OR 6.8, 95% CI 1.79−25.95, $p = 0.005$). Similarly, in a study from Rio de Janeiro in Brazil, there was a significant association between lower educational level among blood donors and higher prevalence of antibodies to SARS-CoV-2 (Filho et al., 2020). No significant difference for mean age or prevalence was found in the different age groups of seropositive and seronegative participants. In a study from the Netherlands, a significant positivity rate was found among younger donors aged 18–30 years, with a prevalence of 4.2% compared with about 2.7% in other age groups (Slot et al., 2020a). In addition, a significant association was found across geographical areas (Erikstrup et al., 2021). Samples collected at later time periods during studies were significantly associated with an increase in seroprevalence in the studies from Brazil and Milan metropolitan area in Italy (Filho et al., 2020; Valenti et al., 2020).

Therefore, to monitor the SARS-CoV-2 spread and seroprevalence trend over time, a nationwide repeated cross-sectional study is needed to better determine how the prevalence is changing in different areas of the country, especially if the reported cases do not reflect the true scale of the pandemic, and to ascertain the cumulative population immunity. Such epidemiologic studies have been performed in different countries. For example, the seroprevalence was 4.8% in the first week, 8.5% in the second week, 10.9% in the third week, 6.6% in the fourth week, and 10.8% in the fifth week in Switzerland (Fontanet et al., 2020). However, the interpretation of serology tests so far is problematic, especially with the fact that antibodies may not last for a long time. One study showed that the antibody response remains stable for two months (Fontanet et al., 2020).

In conclusion, in the early stages of the COVID-19 pandemic in Saudi Arabia, the seroprevalence of antibodies to SARS-CoV-2 among blood donors was low but was higher among non-citizens and in high-prevalence areas. Monitoring seroprevalence trends over time requires repeated sampling and testing to characterize the prevalence of COVID-19. With the introduction of vaccination, such serologic testing would need to be looked at carefully.

## Conflict of interest

The authors declare no conflict of interest.

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None.

## Ethical approval

The study was approved by the Ministry of health Central Institutional Review Board (20-107M). The study's national registration number at the National Committee of BioEthics, King Abdulaziz City for Science and Technology, Saudi Arabia was H-01-R-009.

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