



Seroprevalence of the General Lebanese Population to COVID-19 Between 2023 and 2024

Hilal Abdessamad¹, Elsy Jabbour², Danielle Abou Khater², Mariana Helou²

ABSTRACT

BACKGROUND

Understanding population immunity to SARS-CoV-2 is crucial for public health planning, especially Lebanon where unique healthcare challenges exist. This study aimed to assess the seroprevalence of SARS-CoV-2 antibodies and identify predictors of serostatus in a sample of the Lebanese population in 2023.

METHODS

We conducted an observational study of 350 adult patients presenting to two emergency departments in Lebanon. Participants were tested using a ZEKMED COVID-19 IgG/IgM rapid test, a qualitative rapid SARS-CoV-2 anti-E antibody kit. A comprehensive statistical analysis including logistic regression, Bayesian modeling, and a Random Forest classifier was performed to identify predictors of IgG seropositivity.

RESULTS

Our results showed high IgG seroprevalence of 95.1% (n=333), suggesting prevalent natural infection. While vaccination status and self-reported prior infection were not significant predictors of serostatus in standard analyses, both Bayesian and Random Forest models identified increased age as a potential predictor associated with a negative IgG antibody response (94% HDI: [-1.531, -0.000]; importance score: 0.61).

CONCLUSION

Our findings indicate high exposure to natural SARS-CoV-2 infection in this Lebanese cohort. However, the association of advanced age with a negative antibody response suggests that older populations may remain more vulnerable. This highlights the need for continued targeted public health surveillance and strategies despite high overall seroprevalence from past infections.

CORRESPONDING AUTHOR

Hilal Abdessamad

(University of Missouri - Columbia,
Columbia, United States)

hilal.abdessamad@gmail.com

A COMPLETE LIST OF THE AUTHORS' AFFILIATIONS
IS AVAILABLE AT THE END OF THE ARTICLE.

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INTRODUCTION

Covid-19 infection is a recent pandemic, known to cause severe respiratory illness. Since the Coronavirus Infectious Disease 19 (COVID-19) pandemic hit, vaccination, infection control and immunity became a major interest for healthcare [1]. People were infected in groups, sometimes whole communities, which while overwhelming, contributed to population-level seroprevalence after resolution [2]. However, not everyone had the same COVID-19 presentation, as a large number of individuals had asymptomatic infection, detected by contact tracing or random antibody testing. Others acquired passive immunity through vaccination [3]. Historically speaking, as was the case with poliomyelitis and measles, a detectable immunity in up to 80 to 95% of the population is needed for effective herd immunity [3].

In the case of COVID-19, the data shows a similar story. In the United States of America (USA), 60% adult vaccination rates did not provide enough population immunity to impede the virus spread [4, 5]. A similar trend was seen in Wales [6]. However, the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a ribonucleic acid (RNA) virus that mutates and creates new variants and strains [7]. In addition, the gained immunity wanes over time, which is why we sometimes over-estimate the immunity we have, ending up with a more vulnerable population with the coming variant waves, as in the case of New England in August 2021 [8].

Population level antibody responses for COVID-19 shows consistent international trends. However, they can be influenced by a variety of local factors unique to each region. For instance, the attitude of people in the Middle East towards lockdowns and vaccination would create unique conditions that influence seroprevalence in the region.

In Lebanon, several studies emerged assessing the population immunity to COVID-19. A nationwide study published in January 2022 by Hoballah et al assessing over 2000 participants showed that despite all efforts to vaccinate the public, the population remained vulnerable to a new COVID-19 outbreak [9]. According to the World Health Organization (WHO), a total of 5,814,699 vaccine doses have been administered in Lebanon as of December 2022 [10]. Nevertheless, according to the Lebanese Ministry of Public Health (MoPH), we still have new infections and deaths related to COVID-19 as of May 2023 [11]. The vaccination rates are not likely to increase further, especially that a lot of the Lebanese people have concerns regarding vaccine safety and efficacy, rendering them unlikely to get vaccinated [12]. This is alarming in the setting of a country that suffers a suffering healthcare system due to massive challenges and a major economic collapse, making the country less likely to be able to deal adequately with a new wave [13].

There is no new update regarding the Lebanese population preparedness and immune status regarding COVID-19. It is of importance to assess the population-level immunity in Lebanon against COVID-19, as it would provide updated insight on the magnitude of a possible new wave in the country, especially as social distancing and mask wearing measure have stopped. In addition, it would provide an idea of the how the Lebanese population reacts to new outbreaks.

METHODS

STUDY DESIGN AND POPULATION

Our study is an observational study conducted on a sample of patients presenting to the Emergency Departments (ED) at the Lebanese American University Medical Center – Rizk Hospital (LAUMC-RH) and Kesrwan Medical Center (KMC) between July 2023 and January 2024. All adult patients above 18 years of age presenting to the ED were offered to perform a rapid fingerstick antibody test for COVID-19. This was done for any visit at any time in the ED, offered to all adult patients. People who cannot give an informed consent with waiver of documentation, and patients on chemotherapy and immunomodulators were excluded. Data collection included the number of COVID-19 vaccination doses and whether they had a prior COVID-19 infection in the past.

KITS

Detection of SARS-CoV-2 antibodies was performed using the ZEKMED COVID-19 IgG/IgM Rapid Test Cassette (ZENUM Sarl, Marly, Switzerland), which is a qualitative lateral flow immunoassay that was used with whole blood.¹⁴ It uses a colloidal gold-conjugated recombinant Coronavirus envelope antigen to detect IgG and IgM antibodies against the COVID-19 envelope protein (anti-E), with results interpreted at 15 minutes per the manufacturer's instructions.¹⁵ The kit's performance has been independently validated, demonstrating a sensitivity of 97% and specificity approaching 100% in clinical trials [14].

SAMPLE SIZE CALCULATION

Based on the standard for prevalence studies, a 95% confidence level ($Z=1.96$) and a 5% margin of error ($d=0.05$) were selected for reliability and precision. The expected prevalence (P) of IgG seropositivity was estimated at 85% (0.85). This estimation was informed by the high reported rates of prior SARS-CoV-2 infection and widespread vaccination coverage in the Lebanese population,^{16,17} while also accounting for antibody waning over time and detection capabilities of rapid IgG kits, which can miss very low titers. Using the formula for estimating a population proportion, $n=(Z^2 \cdot P(1-P))/d^2$, the initial calculation yielded approximately 196 participants. To increase the study

power and account for non-response rates, incomplete data, or invalid test, a target sample size of 230 participants as a buffer was used. The study successfully recruited 350 participants, exceeding the calculated sample size, which increased the statistical power of the derived estimates of COVID-19 IgG immunity within this patient population.

STATISTICS

Descriptive statistics were used to summarize the demographic, clinical, and serological characteristics of the 350 participants. Bivariate analyses were performed to check associations with IgG antibody status. Chi-Square (χ^2) test was used to test associations between categorical variables, and the Mann-Whitney U test was used for continuous variables.

To assess the combined and independent effects of all factors, two multivariate approaches were used. A multivariate logistic regression was performed first, but due to perfect separation in the data, it was adjusted by combining the vaccination status into a yes/no variable. Then, a Bayesian logistic regression was employed as an alternative to handle these challenges. It used weakly informative priors (Normal (0, sigma=5)) to estimate the full posterior probability distribution for the effect of each predictor, with results assessed via the 94% Highest Density Interval (HDI).

To explore non-linear relationships and predictive power, a Random Forest Classifier was used. Random Forests are a powerful machine learning method that creates many simple decision-making flowcharts and then combines all their outcomes to a single comprehensive prediction. This model identified the most important features for predicting the rare IgG-negative outcome. To address the class imbalance in the data, the SMOTE (Synthetic Minority Over-sampling Technique) was applied to the training dataset, which is a method that creates new, synthetic data points for the minority class to create a more balanced dataset for model training.

ETHICAL CONSIDERATIONS

This study was approved by the LAU Institutional Review Board. Patient names and personal identifiers were not stored.

RESULTS

A total of 350 patients visiting the emergency department consented to participate in the study. The cohort had a mean age of 48.5 (+/- 15.2) years, with participants distributed across multiple age groups. The 31-40 age group was the largest, comprising 18% (n=63) of the sample. Regarding vaccination status, 77.4% (n=271) of participants reported receiving two doses of a COVID-19 vaccine, 20.6% (n=72) reported receiving three doses, and 2.0% (n=7) reported being

unvaccinated. A history of prior SARS-CoV-2 infection was reported by 15.7% (n=55) of participants, while 84.3% (n=295) reported no known prior infection.

Rapid antibody testing using the mentioned kits revealed that 95.1% (n=333) of participants were positive for SARS-CoV-2 IgG antibodies, while only 1.1% (n=4) were positive for IgM antibodies.

STATISTICAL ASSOCIATIONS

The bivariate and multivariate analyses did not find any statistically significant predictors of IgG status. No significant association was found between IgG status and prior infection ($p=0.21$), the number of vaccine doses ($p=0.46$), or participant age ($p=0.051$). The adjusted logistic regression model confirmed that none of these factors were significant independent predictors. After that, the Bayesian logistic regression showed a credible small, negative association between age and the likelihood of IgG positivity (94% HDI: [-1.531, -0.000]), which was not seen with prior infection and vaccination. As for predictive power, the Random Forest model identified age as the most important predictive feature for IgG positivity (importance score: 0.61), followed by the number of vaccine Doses (0.30) and prior infection (0.09).

DISCUSSION

Our study findings show that the majority of the people presenting to the emergency department in our sample had a previous exposure to COVID-19, demonstrated by the 95% IgG seroprevalence. This antibody response mirrors what is seen in other countries such as the United States, but is higher than what is observed in the United Kingdom [19]. However, the COVID-19 antibody response comes from infection and vaccination. Since all mRNA based vaccines target the S protein, they will induce an anti-S response not detected by our kits. Thus, anti-E antibodies are detected in prior infection or by vaccination using the conventional inactivated, non-mRNA based vaccines [20]. Since most COVID-19 vaccines used in Lebanon were mRNA based, our detected seropositivity most likely comes from natural immunity [21].

To understand this antibody response better, it is important to differentiate between different anti-SARS-CoV-2 antibodies. They are of 3 types, anti-nucleocapsid (N), anti-spike (S) and anti-envelope (E) (Table 1) [20]. In clinical applications, these antibodies have different functional roles. Anti-N antibodies serve as the most reliable diagnostic markers for confirming previous SARS-CoV-2 infection due to their elevation in infected patients [20]. Anti-S antibodies are considered essential for immune protection, as they have the ability to neutralize the. Anti-E increase in levels following infection, but sera with elevated anti-E IgG levels have no virus-neutralizing activity. Therefore,

both N and E antibodies can function as markers of viral exposure, but only S-specific antibodies are associated with immunity [20].

The majority of the Lebanese population was vaccinated using the mRNA vaccines, and most of the detected antibodies would have come from natural exposure to the SARS-CoV-2 virus [21]. In addition, COVID-19 vaccine-induced antibodies wane after several months and are not long-lasting, making them shorter-lived than natural or hybrid immunity [22]. The lack of association between vaccination history and our anti-E test results is an expected finding, as the mRNA vaccines prevalent in Lebanon do not generate an anti-E antibody response. This further supports the conclusion that the detected seropositivity reflects natural immunity.

Since up to 45% of people infected with COVID-19 remain asymptomatic, the number of people reporting a previous infection is an underestimation of the actual estimate of people who got exposed to SARS-CoV-2. This would explain why a reported history of COVID-19 infection did not have a significant association with IgG positivity in our sample.

However, for almost all infections, age is an important predictor of mounting a robust immune response. With increased age, immunity wanes, and so does the antibody response to COVID-19 [23, 24]. This goes with our Bayesian logistic regression findings, that showed advanced age predicting weaker antibody responses and the random forest showing age as a stronger predictor for an IgG response as compared to prior vaccination or reported past infection. However, this might also be explained by the more cautious approach of the older populations towards the pandemic compared to younger populations.

Currently, we are not aware of any on-going surveillance for COVID-19 in Lebanon. The last ministry of public health update was on October 10, 2024 [11]. However, we believe there is a need for more monitoring in the country to assess the population status, number of new cases and the potential of a new impending outbreak and its possible impact.

Our study has its limitations. First, anti-E rapid testing kits were used. These kits only test for exposure to the whole virus, and do not provide information about mRNA vaccination-induced responses or immunity

status. Coupling the results to anti-S or anti-N antibody testing kits would provide a more holistic understanding on the immunologic status of these participants against COVID-19. Besides, data on demographics such as sex as well as other comorbidities was not collected, which might have introduced confounders or other factors to the discussion. Finally, there is the potential selection bias due to having 2 participating hospital emergency departments, which might not be reflective of the actual community numbers. These weaknesses were addressed by using multivariate analysis as well as Bayesian regression and random forest models to suggest associations that would account for known and unknown confounders.

Demographic data such as sex and comorbidities were not collected in this study, to ensure compliance to the approved project by the IRB. Further studies exploring COVID-19 seropositivity would need to aim to collect such data, as these factors are known to influence the COVID 19 immunity status.

CONCLUSION

Our findings show that a large proportion (95.1%) of the Lebanese population presenting to our emergency departments has been exposed to COVID-19, developing anti-E antibodies that indicate of natural infection. While vaccination status and reported infection history were not significant predictors of seropositivity, our results consistently identified increased age as a potential predictor associated with a negative antibody response. This suggests that while anti-E seroprevalence from past infection exists, older populations may remain vulnerable, highlighting the need for continued targeted public health strategies and surveillance. This calls for the need of booster vaccine campaigns, especially for the older populations. In addition, More focused research would be needed to identify the effectiveness of the immunity associated with this anti-E COVID-19 response and its longevity.

KEYWORDS

COVID-19, IgG, ANTIBODIES, ANTI-E, IMMUNITY

TABLE 1 - Different antibodies for COVID-19 and their relevance

Feature	Anti-Nucleocapsid (N)	Anti-Spike (S)	Anti-Envelope (E)
Clinical Role	Marker: Past infection	Immune protection and neutralization	Marker: Past infection
Neutralizing Ability	No	Yes	No
Interpretation	Confirms previous infection	Immunity, post-infection and/or vaccination	Confirms previous infection

AUTHORS' DETAILS

1. Division of Infectious Diseases, Department of Internal Medicine, University of Missouri – Columbia, Columbia, USA
2. Division of Emergency, Department of Internal Medicine, Lebanese American University, School of Medicine, Beirut, Lebanon.

AUTHOR CONTRIBUTIONS

All authors contributed equally and validated the final version of record.

DECLARATIONS

CONFLICTS OF INTERESTS

Zekmed COVID-19 cassettes were provided by Zekmed. However, the study methodology was independently performed, and the results were analyzed exclusively by the authors, without any influence and/or interference from anyone not listed in the author list.

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REGISTRATION

No registration applicable.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

This study was approved by the LAU Institutional Review Board. Patient names and personal identifiers were not stored.

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