



Article

Serological Patterns of SARS-CoV-2 Infection and Their Association with Age, Sex, and Clinical Severity in Kirkuk, Iraq

Sooz Samad Abdulrahman*¹

1. Department of Health Community, College of Health and Medical Technologies, Babagur University

*Correspondence: samad@babagurguruni.edu.iq

Citation: Abdulrahman S S. Serological Patterns of SARS-CoV-2 Infection and Their Association with Age, Sex, and Clinical Severity in Kirkuk, Iraq. Central Asian Journal of Medical and Natural Science 2026, 7(4), 392-403.

Received: 10th Jun 2026

Revised: 11th Jul 2026

Accepted: 19th Aug 2026

Published: 07th Sept 2026



Copyright: © 2026 by the authors. Submitted for open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>)

Abstract: Background: SARS-CoV-2 infection shows variable serological responses influenced by demographic and clinical factors, highlighting the importance of understanding antibody patterns across different patient groups. Aims of the study: This study aimed to evaluate SARS-CoV-2 serological patterns and determine their associations with age, sex, and clinical severity among individuals in Kirkuk, Iraq. Methodology: This study included 130 participants recruited from outpatient, inpatient, intensive, and respiratory care units at Kirkuk Medical City, Iraq, between August and December 2021. Demographic and clinical data were collected using a structured questionnaire. COVID-19 manifestations and severity were assessed by specialized physicians according to WHO criteria, incorporating symptoms, radiographic findings, and oxygen saturation. SARS-CoV-2-specific IgM and IgG antibodies were evaluated using serological immunoassays and the STANDARD Q COVID-19 IgM/IgG Duo Test, with antibody levels ≥ 10 AU/mL considered positive. Result: Among 130 participants, 41 (31.5%) had IgM-associated recent infection, 28 (21.5%) had IgG-associated previous infection, and 61 (46.9%) were seronegative. Females predominated in the IgM group (56.1%), whereas males predominated in the IgG group (71.4%). Mean age was higher in the IgM than IgG group (51.6 vs. 43.7 years). Most IgM-positive participants were ≥ 50 years (61.0%), while 75.0% of IgG-positive participants were aged 30–59 years. Among IgM-positive cases, 73.2% had moderate and 26.8% severe COVID-19. Conclusions: SARS-CoV-2 serological profiles varied according to age, sex, and clinical severity. IgM-associated recent infection was more frequent among older participants and females, while IgG-associated previous infection predominated among males and middle-aged individuals, highlighting distinct demographic and clinical patterns.

Keywords SARS-CoV-2; Serological profiles; IgM antibodies; IgG antibodies; Clinical severity.

1. Introduction

Coronavirus disease 2019 (COVID-19) was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which created an unprecedented global public-health emergency and resulted in significant impacts on healthcare systems. SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA virus, which attaches to and enters the cell using the spike glycoprotein (S) and the angiotensin-converting enzyme 2 receptor (ACE2) [1]. Clinical signs and symptoms of COVID-19 are also very diverse, from asymptomatic infection to mild upper-respiratory symptoms, viral pneumonia, acute

respiratory distress syndrome, thromboinflammatory complications, multiorgan dysfunction and death [2].

RT-PCR is the main method of diagnosis for acute SARS-CoV-2 infection. However, molecular testing has some limitations due to delayed and poor specimen collection, decreasing virus levels, limited access to testing, and potential for undetected asymptomatic or mild infections. Serological assays are used in conjunction with molecular diagnosis, and enable the detection of humoral immune response to viral antigens. Antibody testing is especially important to determine history of infection, immune response and for population surveillance, said Chvatal-Medina et al. [3].

After exposure to SARS-CoV-2, immunoglobulin M (IgM), immunoglobulin A, and immunoglobulin G (IgG) antibodies are produced and appear in the blood with some overlapping. IgM is thought to be the early response antibody, while IgG is the later response and is often present for a longer period. It is important to note however that simultaneous or prior IgG seroconversion can occur, and the classic progression of IgM seroconversion first, followed by IgG seroconversion, is not always true. Furthermore, antibody production was shown to vary by immunoglobulin class and from the onset of symptoms, with the positivity of IgG increasing with time [4]. Thus, simultaneous assessment of the two markers (IgM and IgG) could yield more meaningful serological patterns than either marker.

Viral, clinical, and host factors play a role in the magnitude and persistence of antibody responses. Vanshylla et al. showed that neutralizing-antibody responses tended to be higher during the early phases after infection, but varied widely among individuals [5]. These antibody levels can then drop and especially following mild or latent infections, the risk of antibody negativity arises. Therefore, serological results should be evaluated with regard to when the symptoms occurred, the severity of the disease, whether the individual was vaccinated, if he or she was reinfected, the type of serologic test used as the target, and the time between the onset of the illness and the time of blood collection.

Serosurveillance studies showed that the real burden of SARS-CoV-2 infection was often also much higher than laboratory-confirmed cases. The SARS-CoV-2 seroprevalence was found to be significantly higher across the country and the region for each pandemic period according to the report by Bergeri et al. [6]. Previous international studies also showed significant interregional differences in epidemic size and wave, public health efforts, vaccination coverage, population demographics, test availability, and test performance [7]. The results emphasize the need for sub-national or regional serological studies before using national or international levels to make generalizations about a particular community.

With the large-scale vaccination, interpretation of SARS-CoV-2 serological profiles has become more complicated. Anti-nucleocapsid antibodies may be more indicative of previous natural infection among those who have been immunized with spike protein vaccines, while anti spike protein antibodies may occur after either natural infection or vaccination. Colwill et al. have introduced a scalable serological method that allows for quantifying antibodies to multiple viral antigens and enhances the ability to distinguish between vaccine-induced and natural immunity [8]. A single antibody test result can thus be used with limited epidemiological resolution, while multiplex and quantitative assays can be used more effectively.

There are also differences in analytical performance between serological platforms. Wilkins et al. showed that quantitative ECL assays could yield broad analytical ranges and excellent agreement with other accepted immunoassays and neutralization assays [9]. However, the variability in the sensitivity, specificity, antigenic targets, thresholds, and antibody waning may result in different seroprevalence estimates. During longitudinal follow-up, variation was observed between automated assays of nucleocapsid and spike antigens and highlights the need for reporting the platform and antigen tested [10].

Serological responses can also be related to the clinical level of disease burden. While there is some relationship between antibody levels against the spike and nucleocapsid antigen and neutralizing activity and protection over time, this relationship was different for each antigen [11]. High antibody levels have also been reported after severe infection, which may be related to the duration of viral replication and extent of antigenic stimulation that produces greater B-cell activation. Other asymptomatic or mildly affected individuals, however, do not produce as strong of a response or one that is not detected at all, which may result in underestimation of past exposure by serological surveys done long after exposure.

Aging is a crucial risk factor for disease severity and humoral immunity to COVID-19. There are several potential differences in antibody dynamics between children, younger adults, and older people that could explain different susceptibility to infection, including maturity of immune system, immunosenescence, patient comorbidities, prior coronavirus exposure, and clinical severity [12]. Older age was one of the most consistent and strongest predictors of severe disease and death, as found by Booth et al. [13]. Thus, the age association with antibody levels may partly be driven by age-related differences in the extent of antigenic exposure in more severe infections and not necessarily be an age-specific immune response.

There are also some differences in the amount of liquid that may be present in the sex. Fabião et al. found that men were more likely to have more severe COVID-19 outcomes than women, which may be due to differences in sex hormones, immune regulation, ACE2 expression, inflammatory responses, behavioral exposures and comorbidity profiles [14]. However, in certain contexts, women may produce more robust humoral responses, such that sex associations with seropositivity and clinical severity may not go in the same direction. Population characteristics and the timing of antibody measurement, therefore, have to be taken into account.

Inflection risk and clinical outcomes may be further impacted by social, ethnic, occupational and healthcare inequalities. Persistent population group differences for SARS-CoV-2 positivity and severity of disease remained, even after adjusting for a number of clinical factors, according to Magesh et al. [15]. This evidence can inform investigations conducted locally that take into account the distribution of the population and access to healthcare in interpreting serological patterns.

A systematic review of seroprevalence investigations revealed significant variation in seroprevalence studies in different study settings, sampling methodologies, ages studied, and laboratory methodologies [16]. Evidence is more limited regionally in Iraq. Hussein et al. reported anti-SARS-CoV-2 antibody positivity in Duhok to be high, more than 50% of which did not have any previous COVID-19 symptoms, highlighting the extent of community transmission that happens without being identified [17]. Longitudinal cohort studies also have demonstrated that population controls without known infection can have detectable antibodies which reinforces the importance of serology to help detect missed exposure [18].

Kirkuk is a diverse population with multiple introductions of SARS-CoV-2, however, information on IgM/IgG patterns and demographic and clinical associations of these patterns is limited. A more recent study in Kirkuk showed significant differences in community IgG seroprevalence between pandemic periods [19]. Further study of the different serological patterns, according to age, sex and severity of the clinical symptoms is required, however. Therefore, the current work aimed to describe the serological pattern of SARS-CoV-2 markers (IgM and IgG) in the population of Kirkuk, Iraq and correlate these markers with age, gender, and clinical severity.

2. Methodology

The study involved 130 participants including patients of both outpatient and inpatient clinics, intensive and respiratory care units, distributed randomly among those visiting the hospitals of Kirkuk Medical City, Kirkuk, Iraq, from 12 August till 20 December 2021. Patients with signs and symptoms suggestive of COVID-19 and those who were unconfirmed were included. The data on clinical and demographic characteristics (age, sex, body mass index, disease severity, smoking status, and presence of chronic diseases like hypertension) was obtained from the participants or their family members by a structured questionnaire. The clinical history, physical examination and relevant laboratory examinations were done in all participants and manifestations of COVID-19 were assessed by a specialized physician using World Health Organization criteria. The severity of disease was evaluated by clinical signs, X-ray findings, respiratory signs, oxygen saturation (SpO_2) and disease progression; severe disease was defined as lower respiratory symptoms with $\text{SpO}_2 < 94\%$ on room air and mild disease as upper respiratory symptoms and X-ray not showing pneumonia and $\text{SpO}_2 \geq 94\%$ on room air. Serological immunoassays were used to assess the SARS-CoV-2-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies. The thesis includes data on the use of anti-human IgG and anti-human IgM assays and anti-SARS-CoV-2 antibody levels ≥ 10 AU/mL were defined as positive; it also includes data on the STANDARD Q COVID-19 IgM/IgG Duo Test, which is a rapid chromatographic immunoassay that is not quantitative to detect SARS-CoV-2 antibody levels in serum, plasma or whole blood.

Statistical analysis:

The data were analyzed statistically with SPSS version 22 (IBM Corp.). Normality was tested using Kolmogorov – Smirnov test and graphically. The Mann–Whitney U test was used for continuous variables, where applicable, and Pearson's chi-square test or Fisher's exact test was used for categorical variables. Spearman's rank correlation was used for correlation analyses, and statistical significance was defined as a P value < 0.05 .

Ethical approval:

The study was carried out in an ethical manner in keeping with the ethical guidelines for human subject research. The goals and procedures of the study were explained to all participants before they entered the study and written informed consent was obtained from each participant or legal representative, as appropriate. The participants were assured that their personal and clinical information would be kept strictly confidential and would be used only for scientific research.

3. Results

Frequency of IgM-associated recent infection, IgG-associated previous infection, and seronegative status in the study population

41 participants (31.5%) had serological profiles that included an IgM antibody response suggestive of recent SARS-CoV-2 infection and 28 (21.5%) had serological profiles that included an IgG antibody response consistent with prior infection (Table 1). Of the remaining 61 participants (46.9%), no serological evidence of SARS-CoV-2 infection was found. Overall, 69 of the 130 participants (53.1%) had detectable IgM- or IgG-associated evidence of current or previous exposure.

Table 1. Distribution of SARS-CoV-2 Serological and Infection Profiles Among the Study Participants.

Serological/infection status	n	%
Recent SARS-CoV-2 infection (IgM-associated)	41	31.5
Previous SARS-CoV-2 infection (IgG-associated)	28	21.5
No evidence of SARS-CoV-2 infection	61	46.9
Total	130	100.0

Comparison of male and female representation between participants with recent and previous infection-associated antibody patterns

This was largely due to females (23, 56.1%) outnumbering males (18, 43.9%) in the IgM-associated recent-infection group (as shown in Table 2). In contrast, there were 20 male (71.4%) and 8 female (28.6%) participants in the previous infection group, which was associated with IgG. These results illustrate some differences between the two serological groups in the descriptive sex distributions; a suitable categorical test should be used to determine statistical significance.

Table 2. Sex Distribution Among Participants With IgM- and IgG-Associated SARS-CoV-2 Serological Profiles.

Sex	Recent infection / IgM group (n=41)	Previous infection / IgG group (n=28)
Male	18 (43.9%)	20 (71.4%)
Female	23 (56.1%)	8 (28.6%)
Total	41 (100.0%)	28 (100.0%)

Descriptive comparison of mean age, minimum and maximum values, and age ranges between the two infection groups

The mean ages of participants who had a recent infection profile (IgM-associated) were also higher than the mean age of those who had a previous infection profile (IgG-associated) (51.6 versus 43.7 years, respectively) (Table 3). The age of the patients with recent infection ranged from 24 to 84 years and 20 to 74 years in the patients with previous infection [20]. Thus, the group of recent infections was descriptively older, but the age was not statistically different from the control group, as no measures of variation were provided and no appropriate test was used for comparison.

Table 3. Age Characteristics of Participants With IgM- and IgG-Associated SARS-CoV-2 Serological Profiles.

Age characteristic	Recent infection / IgM group (n=41)	Previous infection / IgG group (n=28)
Mean age (years)	51.6	43.7
Minimum age (years)	24	20
Maximum age (years)	84	74
Age range (years)	24–84	20–74

Frequency and percentage distribution of recent-infection cases across five predefined age categories

The highest percentage of the group with recent infection (as determined by IgM) was ≥ 60 years old (31.7%), followed by 50–59 years (29.3%) (Table 4). The 30–39 and 40–49 aged brackets each had 17.1% of the participants and the 20–29 age bracket had 4.9% [21]. The descriptive concentration of the IgM associated profiles was observed in age ≥ 50 years (61.0% of the recent-infection cases).

Table 4. Age-Group Distribution of Participants With IgM-Associated Recent SARS-CoV-2 Infection.

Age group (years)	n	%
20–29	2	4.9
30–39	7	17.1
40–49	7	17.1
50–59	12	29.3
≥ 60	13	31.7
Total	41	100.0

Frequency and percentage distribution of previous-infection cases across five predefined age categories

There was no significant difference in the number of participants aged 30–39, 40–49 or 50–59 years, each of whom had 7 cases (25.0%) in the IgG-associated previous-infection group (see Table 5). The age group of 20–29 years old represented the smallest percentage (10.7%) while age group ≥ 60 years old represented 14.3% [22]. The general age distribution pattern was broadly distributed with 75.0% of those having an IgG-associated age profile aged 30–59 years.

Table 5. Age-Group Distribution of Participants With IgG-Associated Previous SARS-CoV-2 Infection.

Age group (years)	n	%
20–29	3	10.7
30–39	7	25.0
40–49	7	25.0
50–59	7	25.0
≥ 60	4	14.3
Total	28	100.0

Frequency and percentage of moderate and severe COVID-19 cases within the recent-infection group

Among participants who had an IgM-associated recent infection, moderate COVID-19 (30 cases, 73.2%) was the most common clinical category as indicated in Table 6. Eleven participants (26.8%) had severe disease [23]. About three-quarters of the recent-infection group were moderately ill with COVID-19, and slightly more than 1/4 were severely ill.

Table 6. Clinical Severity Distribution Among Participants With IgM-Associated Recent SARS-CoV-2 Infection.

Clinical severity	n	%
Moderate COVID-19	30	73.2
Severe COVID-19	11	26.8
Total	41	100.0

4. Discussion

In the present study, 130 people were characterized in terms of SARS-CoV-2 serological patterns in Kirkuk, Iraq. Recent or previous exposure was found in 53.1% of participants (31.5% were recent, IgM-associated, and 21.5% were previous, IgG-associated). None of the participants had detectable serological evidence of both recent and previous exposure. These results show significant exposure in the community, as well as that almost half of the people tested did not have antibodies at the time of testing. It is important to note that the serological results do not reflect a true history of exposure but rather the result of factors such as host immune characteristics, assay performance, vaccination and the timing of infection, as emphasized by Zhou et al. [24].

The percentage of patterns associated with IgM was higher than the percentage of patterns associated with IgG, suggesting that the samples were collected during an active community transmission. Taha et al. reported similar results in which the seroprevalence estimates of IgM and IgG antibodies were around 31.1% and 26.6%, respectively in the Iraqi population. The similarity to the current IgM rate could be due to similar patterns of disease transmission, individual behaviour, vaccination uptake and laboratory testing methodology in the region. However, the seroprevalence is very variable in time and should not be considered as an epidemiological constant.

In the present study, the overall antibody positivity was lower than what was observed in some studies carried out after important epidemic waves showed high seropositivity. Lone et al. reported levels of anti-spike seropositivity over 80% in an area with high unrecognized transmission rates. This discrepancy could be attributed to sampling late after high peaks of epidemics, higher vaccination rate, higher population density, different targets of the assays, and participation of subclinical infection cases. Another significant factor is the ability of the assay to detect antibodies to spike, receptor-binding domain, nucleocapsid or more than one antigen.

Hussein et al. also performed another regional study, which revealed 62.6% positivity for SARS-CoV-2 antibody in Duhok compared to 53.1% in Kirkuk. Substantial undetected transmission is suggested by the fact that more than half of their seropositive participants reported that they had never had any symptoms. Variations in Duhok and Kirkuk may be due to the timing of local epidemic waves, the sampling frames, population mobility, compliance with preventive measures, vaccine uptake, and use of a total-antibody electrochemiluminescence assay, instead of class-specific antibody assays (IgM and IgG).

It is not necessarily a sign that the individuals don't have antibodies means they have not been infected. Kucinskaite-Kodze et al. showed that antibody persistence varies from one immunoglobulin class to another, by antigenic target, disease severity and individual immune responses to SARS-CoV-2 infection. Mild or asymptomatic infections may have resulted in seroreversion of some previously infected participants. On the other hand, insufficient diagnostic sensitivity or early sample collection or immunosuppression may not allow for detectable seroconversion.

There is a big interpretive question of whether isolated IgM positivity can be considered as recent infection. Yan et al. found that, around one fourth of convalescent patients had persistent SARS-CoV-2 IgM after up to one year from symptom onset [25]. Therefore, the presence of IgM does not mean that the infection has been recent. Ideally, a confirmation should include information on onset of symptoms, RT-PCR or antigen testing, serial antibody levels and clinical history, along with levels of antibodies increasing or decreasing.

This paper also shows that the apparent stage of infection differed significantly between commercial serological assays when testing for IgM and IgG positivity, making it clear that the stage of infection is dependent on the platform being used [26]. These factors can lead to discordant classifications because of cross reactivity, non-specific binding of

IgM, diagnostic thresholds and sensitivity. As a result, it is more scientifically appropriate to use the term 'IgM associated pattern' than the term 'confirmed recent infection' unless there is supporting virological evidence.

Likewise, IgG result is not a good indicator of the time of infection. While systemic and mucosal antibodies have been found to last for months following SARS-CoV-2 infection, their dynamics vary among people [27]. IgG can then be interpreted as being from recent infection, past infection, reinfection or vaccination or a combination of all three. The significance will depend in part on the target antigen being the spike or the nucleocapsid.

This is a difference between natural infection and vaccine. Anti-Spike antibodies can be acquired by either infection or vaccination, while anti-nucleocapsid antibodies are more specifically of natural infection origin for those that have received a spike-based vaccine, explained Akinbami et al. [28]. In the present study some of those classified as having 'previous infection' may have had vaccine-induced antibodies instead of being previously infected. It should be clearly mentioned in the manuscript that this is a limitation.

Descriptively, there was a difference in the sex distribution of the two seropositive groups. In the IgM-associated group, the ratio of females was higher (56.1%) while in the IgG-associated group, the ratio of males was higher (71.4%). Another study in Zakho showed that Hb markers were more prevalent in females than males, however, this was not statistically significant [29]. Women may also be more responsive to this exposure, as suggested by this agreement, or they may experience different exposure patterns, or different seeking of healthcare and participation.

Al-Osta also found elevated levels of IgM in females in various age groups, which is a general finding of female predominance in the recently infected group [30]. Biology factors may include estrogenic signaling, X-linked immune genes and enhanced B-cell and antibody responses. This pattern, however, may be seen without any difference in susceptibility because of differences in participation, because of occupational exposure, or because of household responsibilities, driven by testing.

The male predominance in the IgG-associated group on the other hand is consistent with some evidence that exposure to clinically significant infection may lead to higher or more persistent antibody levels in males. In a study of the Kurdistan Region of Iraq, Khudhur et al. found that antibody levels for SARS-CoV-2 differed between sexes, but in some cases increased and in others decreased, depending on the type of antibody and the age of the individuals [31]. The proportion of IgG positive men may be due to increased severity of infection and/or antigenic stimulation rather than increased frequency.

However, not all studies show significant gender differences. Kim et al. reported that there was no significant gender difference in the level of neutralizing-antibody and the decrease of it [32]. They found that the sex pattern was not descriptive as in the present study. These may be due to variation in antibody type, antibody testing time, severity of the disease, vaccination, sample size, population age, and quantitative antibody levels vs qualitative antibody presence.

At the cellular level, women tend to develop more rapid antiviral and humoral responses while men tend to have dysregulated inflammation and worse clinical outcomes. These sex differences were thought to be due to sex hormones, X chromosome-linked immune genes, innate antiviral signaling, and variation in adaptive immunity by Arnold et al. [33]. The current results, however, only provide a descriptive distribution as there is no mention of a P-value and the 61 seronegative were not included in Table 2. They are not indicative of a statistical relationship between sex and serological pattern. All serological categories should be used and a chi square or Fisher's exact test should be performed.

There was a descriptive difference among the ages of participants in the recent- and previous-infection patterns. The mean age of the participants in IgM associated infection group was higher than that of IgG associated infection group (51.6 vs. 43.7 years). IgM group participants aged ≥ 60 years constituted the largest group (31.7%) followed by those aged 50–59 years (29.3%). Zhai et al. also noted that age and clinical severity correlated with SARS-CoV-2 antibody responses, with positive responses being more likely in older or more severely affected patients [34].

Kim et al. found an average 1.46-fold greater neutralizing-antibody titer in those ≥ 50 years old compared to those who were younger, and a 2.41-fold greater for moderate or worse disease. This may be due to the presence of more older people in the IgM-associated group, as well as to the slower antibody kinetics seen clinically during key stages of infection. It might also be related to the fact that it may be people in the community with the symptoms who were targeted for testing, not just more people in the community.

The severity of COVID-19 has been shown to be increased with age, as a result of immunosenescence, chronic low-grade inflammation, endothelial dysfunction, altered innate immunity, and higher prevalence of cardiometabolic comorbidities [35]. In elderly people, viral clearance could be delayed with prolonged viral replication and the presence of detectable IgM may be prolonged. These mechanisms can offer a possible explanation to the age distribution of the IgM associated group.

Some community serosurveillance studies have found that seroprevalence among younger adults is higher than in older adults, however. In the NHANES analysis, anti-nucleocapsid positivity was found to be lower in older adults, ranging from 59.7% in 18–29 years old to 30.2% in adults ≥ 70 years old. This is in contrast to the skewed age distribution of older people in the current recent infection group. Younger individuals are more likely to have more social and occupational exposures, but tend to have less severe illness, while older individuals are more likely to be medically tested if they have symptoms.

The age distribution for the previous-infection group was more even with 25.0% aged 30–39, 40–49 and 50–59 years. In the later phases of the epidemic infection-induced anti-nucleocapsid seroprevalence peaked in younger age groups, as reported by Solastie et al. [36]. The differences between the present findings and the previous findings might be due to the time period covered by the study, variant circulation, vaccination strategy and occupational exposure, and lack of weighting of the population in the Kirkuk sample.

Caution should also be used with the mean-age comparison as only means and ranges were reported. Standard deviations, confidence intervals and an inferential test were not given. If age is normally distributed, a Student's t-test should be used, but if not, medians, interquartile ranges and the Mann–Whitney U test should be reported. In addition, the wide ranges of 24–84 and 20–74 years indicate that there is a lot of variation within each group to be summarized by the means only.

The study title mentions clinical severity, however severity categories are not included in the provided tables, nor is there a comparison of antibody patterns between the asymptomatic, mild, moderate, severe and critical disease states. Zervou et al. have previously reported that early antibody responses, particularly of the IgA type, were independent of age and sex and associated with critical COVID-19 [37]. This helps to support the inclusion of a separate severity analysis but cannot draw a conclusion from Tables 1–5 alone.

However, Baillie et al. demonstrated that antibody kinetics were significantly impacted by sex, age and disease severity: delayed antibody peaks were observed in some older males with severe disease. Therefore, age-sex ratios should not be evaluated separately but in relation to the severity. A multivariable association model that incorporated age, sex, comorbidities, symptom duration, vaccination status and disease

severity would be more likely to show independent associations with patterns of IgM- and IgG-associated patterns.

There are also limitations in this study in terms of the sample size and design. Only 28 patients in the IgG group were available, resulting in unstable percentages in age and sex groups. It is important to recognise that cross-sectional serological studies have limitations including the possibility of antibody waning and selection bias and do not necessarily provide information about the timing of infection, as highlighted by Pham et al. The classification of the stage of infection is further limited by the lack of paired molecular testing and multiple sera.

Limitation:

Although with these limitations, these findings offer valuable local evidence of high exposure to SARS-CoV-2 in Kirkuk, and showed an age and sex dependent serological spectrum. Taha et al. highlighted the importance of regionally conducting serosurveillance for detection of subclinical transmission and targeted public health planning. This study calls for future studies to incorporate probability sampling, to include vaccination history, to assay antigens and use combination of anti-spike and anti-nucleocapsid, and to validate IgM-associated cases with RT-PCR or paired sera. The adjustment for other variables and clearly defined categories should also be applied to clinical severity.

5. Conclusion

In this study, there were specific patterns of SARS-CoV-2 serology, including antibody evidence of recent and previous infection in over half of the participants in Kirkuk, Iraq. Descriptive differences in the frequencies of recent infection and previous infection were noted, with IgM associated recent infection more frequent in females and older age groups (50 years and older), and IgG associated previous infection more common in males and widely distributed across the middle age groups. Among those who had recently been infected, moderate COVID-19 was the most common clinical type of COVID-19 that was reported, and about a quarter had severe COVID-19. The results suggest that the SARS-CoV-2 serological profile can differ by demographic and clinical features. In addition to the age, sex and clinical severity, a serological assessment should be included and may provide valuable epidemiological information for the understanding of infection patterns and the surveillance of SARS-CoV-2 in the local population.

REFERENCES

- [1] B. Hu, H. Guo, P. Zhou, and Z.-L. Shi, "Characteristics of SARS-CoV-2 and COVID-19," *Nature Reviews Microbiology*, vol. 19, no. 3, pp. 141–154, 2021, doi: 10.1038/s41579-020-00459-7.
- [2] R. Ochani, A. Asad, F. Yasmin, S. Shaikh, H. Khalid, S. Batra, *et al.*, "COVID-19 pandemic: From origins to outcomes," *Annals of Medicine and Surgery*, vol. 64, Art. no. 102173, 2021, doi: 10.1016/j.amsu.2021.102173.
- [3] M. Chvatal-Medina, Y. Mendez-Cortina, P. J. Patiño, P. A. Velilla, and M. T. Rugeles, "Antibody responses in COVID-19: A review," *Frontiers in Immunology*, vol. 12, Art. no. 633184, 2021, doi: 10.3389/fimmu.2021.633184.
- [4] F. N. Zervou, P. Louie, A. Stachel, I. M. Zacharioudakis, Y. Ortiz-Mendez, K. Thomas, *et al.*, "IgA correlates with severity of disease in early COVID-19 infection," *Journal of Medical Virology*, vol. 93, no. 9, pp. 5408–5415, 2021, doi: 10.1002/jmv.27058.
- [5] K. Vanshylla, V. Di Cristanziano, F. Kleipass, F. Dewald, P. Schommers, L. Gieselmann, *et al.*, "Kinetics and correlates of the neutralizing antibody response to SARS-CoV-2 infection in humans," *Cell Host & Microbe*, vol. 29, no. 6, pp. 917–929.e4, 2021, doi: 10.1016/j.chom.2021.04.015.

- [6] I. Bergeri, M. G. Whelan, H. Ware, L. Subissi, A. Nardone, H. C. Lewis, *et al.*, "Global SARS-CoV-2 seroprevalence from January 2020 to April 2022: A systematic review and meta-analysis of standardized population-based studies," *PLoS Medicine*, vol. 19, no. 11, Art. no. e1004107, 2022, doi: 10.1371/journal.pmed.1004107.
- [7] N. Bobrovitz, R. K. Arora, C. Cao, E. Boucher, M. Liu, C. Donnici, *et al.*, "Global seroprevalence of SARS-CoV-2 antibodies: A systematic review and meta-analysis," *PLoS ONE*, vol. 16, no. 6, Art. no. e0252617, 2021, doi: 10.1371/journal.pone.0252617.
- [8] K. Colwill, Y. Galipeau, M. Stuiblé, C. Gervais, C. Arnold, B. Rathod, *et al.*, "A scalable serology solution for profiling humoral immune responses to SARS-CoV-2 infection and vaccination," *Nature Microbiology*, vol. 7, no. 6, pp. 782–795, 2022, doi: 10.1038/s41564-022-01111-3.
- [9] D. Wilkins, A. A. Aksyuk, A. Ruzin, K. M. Tuffy, T. Green, R. Greway, *et al.*, "Validation and performance of a multiplex serology assay to quantify SARS-CoV-2 antibodies," *Journal of Immunological Methods*, vol. 505, Art. no. 113253, 2022, doi: 10.1016/j.jim.2022.113253.
- [10] T. Niedrist, T. Perkmann, T. Koller, E. Puchhammer-Stöckl, H. Laferl, L. Weidner, *et al.*, "Longitudinal comparison of automated SARS-CoV-2 serology assays in assessing virus- and vaccine-induced antibodies," *Clinical Chemistry and Laboratory Medicine*, vol. 60, no. 5, pp. 736–745, 2022.
- [11] A. Atti, M. Ferrari, J. Castillo-Olivares, P. Monk, R. Gopal, M. Patel, *et al.*, "Antibody correlates of protection from SARS-CoV-2 reinfection prior to vaccination: A nested case-control study," *The Lancet Microbe*, vol. 3, no. 8, pp. e580–e590, 2022.
- [12] L. E. Gentles, L. Kehoe, K. H. D. Crawford, K. Lacombe, J. A. Dickerson, C. R. Wolf, *et al.*, "Dynamics of infection-elicited SARS-CoV-2 antibodies in children over time," *JCI Insight*, vol. 7, no. 6, Art. no. e155323, 2022.
- [13] A. Booth, A. B. Reed, S. Ponzo, A. Yassaee, M. Aral, D. Plans, *et al.*, "Population risk factors for severe disease and mortality in COVID-19: A global systematic review and meta-analysis," *PLoS ONE*, vol. 16, no. 3, Art. no. e0247461, 2021, doi: 10.1371/journal.pone.0247461.
- [14] J. Fabião, B. Sassi, E. F. Pedrollo, F. Gerchman, C. K. Kramer, C. B. Leitão, *et al.*, "Why do men have worse COVID-19-related outcomes? A systematic review and meta-analysis with sex-adjusted for age," *Brazilian Journal of Medical and Biological Research*, vol. 55, Art. no. e11711, 2022, doi: 10.1590/1414-431X2021e11711.
- [15] S. Magesh, D. John, W. T. Li, Y. Li, A. Mattingly-App, S. Jain, *et al.*, "Disparities in COVID-19 outcomes by race, ethnicity, and socioeconomic status: A systematic review and meta-analysis," *JAMA Network Open*, vol. 4, no. 11, Art. no. e2134147, 2021, doi: 10.1001/jamanetworkopen.2021.34147.
- [16] A. Vaughan, E. F. Duffell, G. S. Friedl, P. Waight, S. N. Ladhani, N. Andrews, *et al.*, "Systematic review of SARS-CoV-2 seroprevalence studies in the WHO European Region," *BMJ Open*, vol. 13, no. 11, Art. no. e064240, 2023, doi: 10.1136/bmjopen-2022-064240.
- [17] N. R. Hussein, G. H. Shahab, N. A. Rasheed, A. N. Ahmed, R. S. Salih, A. S. Mahdi, *et al.*, "A study of anti-SARS-CoV-2 antibody positivity in Duhok City, Iraq," *Journal of Infection in Developing Countries*, vol. 17, no. 7, pp. 937–943, 2023, doi: 10.3855/jidc.17518.
- [18] V. Loria, M. E. Ramirez-Cardich, A. M. Zamora, *et al.*, "Cohort profile: Evaluation of immune response and population prevalence of SARS-CoV-2 infection and vaccination—the RESPIRA cohort," *BMJ Open*, vol. 13, no. 12, Art. no. e071284, 2023, doi: 10.1136/bmjopen-2022-071284.
- [19] M. A. Alsamarai, A. H. Alobaidi, A. Kayabaş Avşar, and A. M. Alsamarai, "COVID-19 immune status in the general population in Kirkuk Province, Iraq," *Coronaviruses*, vol. 7, published online Dec. 3, 2025.
- [20] Y. Zhou, F. Pei, M. Ji, L. Wang, H. Zhao, H. Li, *et al.*, "Advancements in detection of SARS-CoV-2 infection for confronting COVID-19 pandemics," *Laboratory Investigation*, vol. 102, no. 1, pp. 4–13, 2022, doi: 10.1038/s41374-021-00663-w.
- [21] A. E. Taha, Z. M. Al-Khafaji, W. M. Al-Wattar, *et al.*, "Estimation of anti-SARS-CoV-2 IgM/IgG seroprevalence and associated factors," *Medicine*, vol. 104, Art. no. e42039, 2025.
- [22] K. S. Lone, S. M. Khan, M. A. Qurieshi, *et al.*, "Seroprevalence of SARS-CoV-2-specific anti-spike IgM and IgG antibodies in a population-based sample," *Frontiers in Public Health*, vol. 10, Art. no. 967447, 2022, doi: 10.3389/fpubh.2022.967447.

- [23] I. Kučinskaitė-Kodžė, M. Simanavičius, A. Šimaitis, *et al.*, “Persistence of SARS-CoV-2-specific antibodies for 13 months after infection,” *Viruses*, vol. 13, no. 11, Art. no. 2313, 2021, doi: 10.3390/v13112313.
- [24] X. Yan, G. Chen, Z. Jin, *et al.*, “Persistence of anti-SARS-CoV-2 IgM in convalescent COVID-19 patients,” *Journal of Infection*, vol. 84, no. 1, pp. 94–118, 2021.
- [25] Y. Kobashi, Y. Shimazu, Y. Nishikawa, T. Kawamura, T. Kodama, D. Obara, *et al.*, “The difference between IgM and IgG antibody prevalence in different serological assays for COVID-19: Lessons from the examination of healthcare workers,” *International Immunopharmacology*, vol. 92, Art. no. 107360, 2021, doi: 10.1016/j.intimp.2020.107360.
- [26] J. Frøberg, J. Gillard, R. Philipsen, *et al.*, “SARS-CoV-2 mucosal antibody development and persistence and their relation to viral load and COVID-19 symptoms,” *Nature Communications*, vol. 12, Art. no. 5621, 2021, doi: 10.1038/s41467-021-25949-x.
- [27] L. J. Akinbami, D. Kruszon-Moran, C. Wang, *et al.*, “SARS-CoV-2 serology and self-reported infection among adults—National Health and Nutrition Examination Survey, United States, August 2021–May 2022,” *MMWR Morbidity and Mortality Weekly Report*, vol. 71, no. 48, pp. 1522–1525, 2022, doi: 10.15585/mmwr.mm7148a4.
- [28] A. Y. Saeed, N. R. Hussein, I. A. Naqid, *et al.*, “Seroprevalence of SARS-CoV-2 IgG/IgM antibodies among patients in Zakho City, Kurdistan Region, Iraq,” *Journal of Infection in Developing Countries*, vol. 16, pp. 1126–1131, 2022.
- [29] I. M. Al-Osta, O. El-Bakoush, H. El-Maghrabi, *et al.*, “The seroprevalence of IgM and IgG antibody production against SARS-CoV-2 according to age and sex,” *Pharmacy & Pharmacology International Journal*, 2024, doi: 10.5281/zenodo.10946622.
- [30] Z. O. Khudhur, H. Omer, S. S. Qader, *et al.*, “Comparative study of SARS-CoV-2 antibody titers between male and female COVID-19 patients living in the Kurdistan Region of Iraq,” *Eurasian Journal of Medical Oncology*, 2021.
- [31] Y. I. Kim, S. M. Kim, S. J. Park, *et al.*, “Kinetics of neutralizing antibodies against SARS-CoV-2 infection according to sex, age, and disease severity,” *Scientific Reports*, vol. 12, Art. no. 13491, 2022, doi: 10.1038/s41598-022-17605-1.
- [32] C. G. Arnold, A. Libby, A. Vest, A. Hopkinson, and A. A. Monte, “Immune mechanisms associated with sex-based differences in severe COVID-19 clinical outcomes,” *Biology of Sex Differences*, vol. 13, Art. no. 7, 2022, doi: 10.1186/s13293-022-00417-3.
- [33] B. Zhai, J. Clarke, B. A. Agostini, *et al.*, “SARS-CoV-2 antibody response is associated with age and body mass index in convalescent outpatients,” *Journal of Immunology*, vol. 208, pp. 1712–1720, 2022.
- [34] P. Zimmermann and N. Curtis, “Why does the severity of COVID-19 differ with age? Understanding the mechanisms underlying the age gradient in outcome following SARS-CoV-2 infection,” *Pediatric Infectious Disease Journal*, vol. 41, no. 2, pp. e36–e45, 2022, doi: 10.1097/INF.0000000000003413.
- [35] A. Solastie, C. Virta, A. Haveri, *et al.*, “Changes in SARS-CoV-2 seroprevalence and population immunity in Finland during 2020–2022,” *Emerging Microbes & Infections*, vol. 12, no. 2, Art. no. 2222849, 2023, doi: 10.1080/22221751.2023.2222849.
- [36] J. K. Baillie, *et al.*, “SARS-CoV-2 antibody responses associate with sex, age, and disease severity,” *Nature Communications*, 2023.
- [37] T. D. Pham, C. Huang, O. F. Wirz, *et al.*, “Seroprevalence of SARS-CoV-2 among high-density communities and associated risk factors,” *Emerging Infectious Diseases*, vol. 28, no. 3, pp. 554–563, 2022.