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Coronavirus Pandemic

A study of anti-SARS-CoV-2 antibody positivity in Duhok City, Iraq

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Abstract

Introduction: The study aimed to investigate the positivity rate of anti-SARS-CoV-2 antibodies and associated factors.
Methodology: Data and blood samples were collected between January 10th and December 30th, 2021 based on COVID-19 infection by using a designated questionnaire. The blood samples were used for the detection of total SARS-CoV-2 antibodies.
Results: 743 participants were recruited and 62.58% of them were positive for SARS-CoV-2 antibodies. Among these, 56.34% denied any symptoms of COVID-19. A higher positivity rate was found among females than men (OR = 1.5, CI = 1.1-2.0, $p = 0.0073$). Participants that had been diagnosed with COVID-19 in the past had a significantly higher prevalence of antibodies, and were nearly four times more likely to develop antibodies (OR = 4.0, CI = 2.4-6.8, $p < 0.0001$). Interestingly, only 3% of the participants with previous COVID-19 were seronegative while 46.54% were positive for antibodies without having a history of COVID-19 infection. Participants that reported symptoms were 2.6 times more likely to develop antibodies (OR = 2.6, CI = 1.9-3.6, $p < 0.0001$). Lastly, we found age to be significantly associated with the production of antibodies (CI = 13.3-14.7, $p < 0.0001$).
Conclusions: The information from this study can be used to mitigate and develop tailored vaccination efforts and plan evidence-based strategies to better mitigate the ongoing COVID-19 pandemic in Kurdistan-Iraq.

Key words: SARS-CoV-2; COVID-19; Antibody; IgG; Seropositivity; Duhok; Iraq.

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Introduction

The novel coronavirus disease (COVID-19) pandemic has been impacting the global community since December 2019. Infection is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was first discovered in Wuhan City, China but has rapidly spread worldwide [1]. The first case of COVID-19 infection was confirmed in the Kurdistan Region of Iraq on March 1st, 2020, and just 10 days later, on March 11th 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic [2]. The number of patients with COVID-19 in Iraqi Kurdistan has been on the rise [3]. A recent report showed that from January to July 2022, the COVID-19 positivity rate increased from 2.0% to 40.0% as of July 20th, 2022. One contributing factor may be weak vaccination efforts across the region.

Vaccinations are considered the best method to mitigate the spread of disease and mortality due to COVID-19. Despite this, various studies have found that COVID-19 vaccine hesitancy is prevalent in Iraqi Kurdistan, with one study reporting that more than half of the study participants refused the vaccine or were vaccine hesitant [3-5]. The Ministry of Health in the Kurdistan Region, Iraq started an online registration system for the COVID-19 vaccines early in March 2021. COVID-19 vaccines manufactured by BNT162b2 (BioNTech, Fosun Pharma, Pfizer, USA),

AZD1222 (AstraZeneca, University of Oxford, UK), and BBIBP-CorV (Beijing Institute of Biological Products, Sinopharm, China) are available in our locality. The general practitioners, frontline health professionals and the elderly people were prioritized for vaccination against COVID-19 and the campaign started on 04 March 2021.

The WHO defines vaccine hesitancy as "a delay in acceptance or refusal of vaccination despite the availability of vaccination services" and states that it is "complex and context specific influenced by factors such as complacency, convenience, and confidence" [6]. Previous studies have found that increased vaccine hesitancy in Iraqi Kurdistan is correlated with lower levels of education, concern over side effects, trauma over losing family members to COVID-19, and having a history of chronic disease [3-5]. In addition, the breakdown of trust between the community and local authorities due to devastating socioeconomic impacts of the lockdown and disruption to social cohesion may contribute to lower vaccination rates in the region [7]. Therefore, it is imperative to better understand the immunity levels of the population of the Iraqi Kurdistan region.

To address the lack of regional data, this study aimed to investigate the positivity rate of anti-SARS-CoV-2 antibodies among non-vaccinated participants from different districts in Duhok City in Iraqi Kurdistan. In order to better understand the effectiveness of immunity mediated through vaccinations, we examined factors associated with acquiring natural immunity after COVID-19 infection in Duhok City.

Methodology

Data collection

This study was carried out in the Duhok Governorate of the Kurdistan Region of Iraq, an autonomous region recognized by Iraq's Constitution. Iraqi Kurdistan is made up of four majority-Kurdish Governorates: Duhok, Erbil, Halabja, and Sulaymaniyah. The target population for this study was the Governorate of Duhok, with an estimated population of 1.6 million. The study population included participants from six different districts within Duhok that include Amedye, Akre, Bardarash, Zakho, Semel, and Duhok City. The sample size was calculated and since there were no recorded data regarding the prevalence of COVID-19 in this region, a prevalence of 50% was estimated and used in the calculation of sample size. The sample size was calculated to be 662 with confidence interval of 95%, margin of error of 0.05, design effect of 1.5 and expected participation rate of 0.85. In the end, we were able to interview 743 participants.

Study population and study design

This cross-sectional study was conducted by recruiting volunteers from the aforementioned districts. The study was conducted between January 10th and December 30th of 2021. We asked the people who visited healthcare centers in different districts to participate in the project voluntarily. In our society, patients with hypertension and diabetes have a chronic disease card. When asked about chronic diseases, the patients show their cards. Patients with immunodeficiency and those who received immunosuppressive and corticosteroid therapy were excluded from the study. People who were vaccinated or did not give their consent were excluded from the study.

Anti-SARS-CoV-2

Seropositivity was determined by in vitro detection of total SARS-CoV-2 antibodies performed by Elecsys anti-SARS-CoV-2 (Roche Diagnostics International Ltd, Rotkreuz, Switzerland), an enzyme immunoassay. The Elecsys anti-SARS-CoV-2 S serology test identifies the presence of antibodies (including IgG) in human serum and plasma that are directed against the spike (S) protein receptor binding domain (RBD) of SARS-CoV-2. The assay was performed on stored sera samples collected to measure the SARS-CoV-2 antibody level according to the manufacturer's protocols. Antibody positivity was determined by the numerical value of the semi-quantitative test being greater than the threshold of ≥ 1.0 IgG.

We developed different teams to be allocated to each district within Duhok Governorate to conduct the study and data collection. Akre and Berdaresh were visited by one team due to small population sizes. All teams were trained on using personal protective equipment. Participants completed a questionnaire that included personal information such as, marital status, history of chronic disease, gender, history of COVID-19 infection, and history of COVID-19 symptoms. We obtained 5-10 mL of venous blood from each study participant and transported the samples to a lab in Duhok City where the sera were separated by centrifuging them at 1500 rpm for 3 minutes. The sera samples were then stored in a –20 °C environment for laboratory investigations.

Statistical Analysis

The primary aim of this study was to examine factors that may influence the production of SARS-CoV-19 antibodies among the majority-Kurdish population of Duhok Governorate in Iraqi Kurdistan. We estimated the antibody positivity rates while standardizing these rates to age, gender, and time of study testing. We conducted Chi-square tests to investigate the associations between gender, history of COVID-19, time since COVID-19 diagnosis, history of chronic disease, marital status, and the development of COVID-19 antibodies. The Chi-square test was used to find the association and significance between our model variables and the likelihood of developing sero-positivity among those with a history of COVID-19 diagnosis. Unpaired t-test was conducted to investigate the relationship between antibody positivity and continuous data. A p value of < 0.05 was considered statistically significant. All analyses were conducted using SAS Studio version 3.81.

Ethical statement

Research protocols and methods for obtaining consent were approved by the College of Medicine, Zakho University's Ethics and Science Committee. Informed consent was obtained from all participants. Prior to data collection, personal consent was obtained from all study subjects for using their samples and demographic data for research objectives.

Results

Characteristics of the study population

A total of 903 individuals participated in this study across six health centers in Duhok Governorate from January 10th to December 30th of 2021. We excluded 160 interviewed individuals (including 45 individuals who were already vaccinated) that refused to participate in the study. Consequently, 743 individuals were included in the study and they were distributed in the center of Duhok city and the other five districts belonging to Duhok Governorate in Iraq. The number of females enrolled in the study was 392 (52.8%) and the average age of the participants was 34.6 ± 13.9 years. Among the participants, 519 (69.9%) were married and 164 (22.1%) had a history of chronic diseases (Table 1). In this study, 465/743 (62.58%) participants were positive for SARS-CoV-2 antibodies (Table 2). Among the participants who tested positive for antibodies, fever (166, 81.77%) and myalgia (165, 81.28%) were the most common symptoms.

Association between the presence of symptoms and different variables in antibody positive participants

Among those who tested positive for SARS-CoV-2 antibody, 262/465 (56.34%) did not have any symptoms for COVID-19. We studied the association between the presence of symptoms and different variables for participants who tested positive for antibodies (Table 3). A significant association was found between the history of chronic disease and the presence of symptoms (p = 0.001; CI = 0.2-0.4; OR = 0.3). A significant association was found between marital status and antibody positivity (p =0.046; CI = 0.5-1; OR = 0.7). A t-test was then utilized to investigate the relationship between age and the presence of symptoms. A significant association was found between age and the presence of symptoms (p = 0.0015; CI = 1.01-1.05; OR = 1.022). We also found a

Table 1. Characteristics of all participants including negative participants.

Characteristics	n (%)
Gender: Female	392 (52.8)
Marital status: Married	519 (69.9)
COVID-19 AB positivity	465 (62.6)
Chronic diseases (Yes)	164 (22.1)
Locality	
Duhok	192 (25.8)
Zakho	370 (49.8)
Aqre and Bardarash	80 (10.77)
Amedi	51 (6.9)
Summail	50 (6.7)
Age	34.6 ± 13.9

Table 2. Characteristics of positive participants. Positive only (Total number = 465).

Characteristics	n (%)
Gender: Female	264 (56.77)
Marital status: married	335 (72.04)
Chronic diseases (yes)	113 (24.3)
Symptoms	203 (43.87)
Symptoms	
Fever	166 (81.77)
Myalgia	165 (81.28)
Loss of smell	114 (56.79)
Loss of taste	95 (46.79)
Shortness of breath	89 (43.84)
Cough	41 (20.19)
Diarrhea	44 (21.67)
Headache	40 (19.7)
Duration of symptoms in symptomatic patients (Days + SD)	11.81 ± 10.80
Locality	
Duhok	111 (23.87)
Zakho	241 (51.83)
Aqre and Bardarash	55 (11.83)
Amedi	27 (5.81)
Semeel	31 (6.67)
Age	34.40 ± 13.73

SD: Standard deviation.

Table 3. Association between the presence of symptoms and variables in antibody positive samples.

Characteristics	Asymptomatic positive (n = 262)		Symptomatic positive (n = 203)		*p* value	95% CI	OR
	No	%	No	%			
Gender							
Female	152	58.01	111	54.68	0.266	0.8-2	1.02
Male	110	41.98	92	45.32			
Chronic disease							
Yes	37	14.1	76	37.4	0.001	0.2-0.4	0.3
No	225	85.9	127	62.6			
Marital status							
Married	179	68.3	154	75.86	0.046	0.5-1	0.7
Single	83	31.7	49	24.14			
Age (Year ± SD)	32.6 ± 13.5		36.8 ± 13.8		0.0015	1.01-1.05	

CI: Confidence interval; OR: Odd ratio; SD: Standard deviation.

small significant impact of marital status on antibody production (75.9%, CI = 0.5-1, OR = 0.7, $p = 0.046$).

Association between antibody positivity and different variables

We identified 465 individuals that had antibodies against SARS-CoV-2. In this study, 46.26% were positive for antibodies without having a history of COVID-19 infection while only 3% of the participants with a history of confirmed COVID-19 were seronegative. Interestingly, we found a significantly higher prevalence of antibody positivity in females (OR = 1.5, CI = 1.1-2.0, $p = 0.0073$) vs. males (Table 4). Participants that had been diagnosed with COVID-19 in the past, had a significantly higher prevalence of antibody positivity and those without, were nearly four times more likely to develop antibodies (OR = 4.0, CI = 2.4-6.8, $p < 0.0001$) (Table 4). Similarly, participants who reported symptoms were 2.6 times more likely to develop antibodies (OR = 2.6, CI = 1.9-3.6, $p < 0.0001$). We found that the age of patients with positive antibody test (36.8 ± 13.6 years) was almost similar to the age of patients with negative antibody test (36.9 ± 14.6 years) ($p = 0.94$). Regarding symptomatic patients, the duration of symptoms in patients with negative antibody tests (7.08 ± 5.5 SD days) was significantly shorter than the duration of symptoms (11.8 ± 10.8 SD days) in patients with antibody positive tests (OR = 112, CI = 1.0569-1.1905, $p < 0.0001$).

Discussion

This study aimed to study the prevalence of natural anti-SARS-CoV-2 antibodies positivity to better understand the burden of COVID-19 on the Duhok Governorate in the Kurdistan region of Iraq.

After the first confirmed case of COVID-19 in the Kurdistan Region of Iraq on March 1st 2020, the Kurdistan Regional Government took strict measures to control the infection. These measures included cancellation of gatherings and religious rituals and closing airports, borders, schools, and other institutions [2]. In addition, the region further adopted strict containment measures which included government mandated quarantine periods [8]. Despite these precautionary actions, Duhok city, one of the largest cities in the region, experienced disproportionately high COVID-19 infection case fatality rates in Kurdistan and Iraq at large [9]. Nearly 20% of individuals in our study sample had a previous COVID-19 diagnosis and 35.9% reported symptoms such as fever, myalgia, headache, diarrhea, loss of appetite, loss of taste, sore throat, and cough. These containment efforts were lifted on May 21st, 2020, due to mounting socioeconomic pressure and demands to immediately start the reopening process. The lockdown was lifted out of political necessity but it did not include a plan to protect high-risk groups such as the elderly and immunocompromised. Upon reopening, the region experienced a sharp increase in the number of COVID-19 cases, an increase in the

Table 4. Association of characteristics to the seroprevalence of SARS-CoV-2 antibodies.

Variables		Seropositive people (No.)	Prevalence of antibodies %	*p value	95% CI	OR
Gender	Female	263	35.4	0.0073*	1.1-2.0	1.5
Marital status	Married	334	26.1	0.2117	0.9-1.8	1.3
History of chronic disease	Yes	112	15.1	0.0870	0.9-2.0	1.4
History of confirmed COVID-19	Yes	139	16.0	< 0.0001*	2.4-6.8	4.0
Symptoms	Yes	203	27.3	< 0.0001*	1.9-3.6	2.6

CI: Confidence interval; OR: Odd ratio. 743 unvaccinated individuals; **p*-value for test of seroprevalence within categorical groups and indicate a significant difference.

number of symptomatic patients and a doubling of the case-fatality rate [7].

Despite increases in COVID-19 infections and fatalities after lifting COVID-19 restrictions, Duhok still reported lower COVID-19 burden than its neighboring countries Iran or Turkey with a cure rate of 86.4% and a fatality rate of 1.99% compared to Iran and Turkey's higher fatality rates of 6.35% and 2.6%, respectively [9, 10]. Previous studies have found that Duhok's COVID-19 low reinfection rate of 0.031% possibly indicates that a large majority of unvaccinated patients developed immunity against the infection that may last for months, substantially reducing the risk of COVID-19 reinfection [9]. In our study sample we found 62.6% of individuals had developed antibodies against COVID-19 which is substantially higher than seroprevalence in neighboring countries [11].

Similar to previous studies, we found that seroprevalence rates were higher among women than men [11-13]. These results can partly be explained by findings that women produce more antibodies, specifically IgG, in the early stages of COVID-19 which may prevent the disease from getting worse and are therefore protected for longer [14]. In addition to a lower risk of immune dysregulation in women, gender differences in antibody positivity can be explained by differences in lung size and capacity, with men having larger lungs and therefore elevated virus replication and subsequently higher viral load [14,15].

Furthermore, in alignment with previously published studies we found individuals with a previous COVID-19 diagnosis, presence of symptoms, and age significantly contribute to the production of SARS CoV-19 antibodies [11,16,17]. It is important to note that 46.5% of individuals that never underwent COVID-19 real time reverse transcriptase polymerase chain reaction (RT-PCR) testing or received a negative test result produced protective antibodies. These individuals are likely not included in official regional statistics. It was previously noted that asymptomatic spread indeed carries a risk, including the potentially long-term burden of long COVID [18]. It's noteworthy that patients with both symptomatic and asymptomatic infections have comparable viral load, indicating that they have a similar capacity for transmission. However, it's also worth noting that the virus may clear faster in asymptomatic infections, indicating a reduced period of transmission [19]. Also, it is important to note that 3.0% of individuals that reported a previous COVID-19 diagnosis were seronegative. It is possible that a person who was infected with COVID-19 may no longer have detectable levels of antibodies as antibody levels decline over time. Besides, antibody levels depend on the level of exposure to the virus. Individuals who had a mild case of COVID-19 and produced a lower level of antibodies can result in a negative test result. As suggested by previous studies, these individuals may have been exposed but did not have a systemic immune response and instead were able to rid the virus using mucosa-associated lymphoid tissues [20]. Furthermore, we found that time since COVID-19 diagnosis is significantly associated with the presence of antibodies. Previously published studies found that local immunity, and seroconversion of IgG, can last for up to 6 months post infection and decreases with each month post infection [13,21,22]. This suggests positive anti-SARS-CoV-2 antibodies results can be used to predict future dynamics of the ongoing COVID-19 pandemic.

Lastly, we found individuals who exhibited symptoms of COVID-19 were significantly more likely to develop antibodies. These findings suggest self-reported symptoms may be used to identify COVID-19 cases without RT-PCR testing which is crucial for areas with limited testing availability such as Iraqi Kurdistan. When isolating these individuals, we found that symptomatic patients with a history of chronic disease and confirmed previous COVID-19 diagnosis were more likely to develop positive SARS-CoV-2 antibodies. Previously published studies found comorbidities connected to chronic disease may lead to a more prevalent antibody response [23,24].

Study strengths and limitations

To the best of our knowledge, this study is the first to examine SARS-CoV-19 antibodies positivity in the Iraqi Kurdistan region during the COVID-19 pandemic. The major strengths of our study are that we conducted population-based sampling in the Duhok Governorate and standardized the in vitro detection of total SARS-CoV-2 antibodies including class IgG using Elecsys. Additionally, we sent all blood samples to the same lab in Duhok City and as a result we obtained strong agreement on seroprevalence results.

There are important limitations worth noting. The first major limitation is that individuals self-selected to be a part of our study which may have led to an oversampling of sicker individuals. Another important limitation is that we did not take into consideration patients that may have been infected with COVID-19 more than once as COVID-19 infection was self-reported. We were also limited in our knowledge of the duration and severity of COVID-19 infection among those that reported a history of COVID-19 diagnosis.

Lastly, we were limited in our knowledge of the types and severity of chronic disease among those that reported a history of chronic conditions.

Conclusions

The high presence of positive SARS-CoV-2 antibodies in our study sample demonstrates the extensive exposure of the Duhok Governorate population to the COVID-19 virus. Our findings highlight the importance of serological population-based studies in mitigating the spread of the SARS-CoV-2 virus in the coming years and months. The situation in Iraqi Kurdistan calls for urgency in public health decision to better mitigate this ongoing pandemic.

Authors' Contributions

All authors have contributed, reviewed and approved this manuscript. The order of the authors listed in the manuscript has been approved by all authors.

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