

# SERUM IGM AND IGG TITERS 2 WEEKS AND 8 WEEKS FROM BEGINNING OF SYMPTOMS AND THEIR RELATION TO SEVERITY IN COVID-19

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Submitted: 27/7/2022; Accepted: 5/2/2023; Published: 21/9/2023

## ABSTRACT

### *Background*

COVID-19 pandemic, which started in late December 2019, has resulted in a significant number of morbidity and mortality worldwide. Estimating serum antibody titers of both IgM & IgG against the coronavirus in patients plays a crucial role in diagnosis and assessing the severity of the infection.

### *Objectives*

Our objective is to assess IgM and IgG levels at 2 and 8 weeks from the onset of COVID-19 symptoms and examine their relationship with disease severity and mortality. Additionally, we aim to determine how these antibody levels relate to patient age, BMI, gender, and any chronic illnesses they may have.

### *Patients and Methods*

This prospective study was conducted at Dr. Hemn Teaching Hospital in Sulaymaniyah, from December 4th, 2021 to March 5th, 2022. It included 33 males and 28 females, aged between 17 and 92 years, all of whom were confirmed to have COVID-19 by Reverse Transcription Polymerase Chain Reaction and/or High-resolution computed tomography. Blood samples were taken 2 and 8 weeks from starting symptoms and processed by ELISA to detect IgM and IgG titers.

### *Results*

Male patients accounted for 54.1%, and 63.93% were between 30-70 years of age, with 90.16% residing in the city center. The majority were non-smokers (68.85%), and 86.89% did not consume alcohol. In terms of infection severity, 22.95% had mild cases, 40.98% were moderate and 36.07% were severe-critical infections. We observed that higher antibody titers in the early phase were associated with increasing severity and mortality. A higher body mass index was identified as a risk factor for elevated antibody production while hypertension and diabetes were not.

### *Conclusion*

Our findings suggest that higher levels of IgM and IgG antibodies during the early phase of COVID-19 are associated with increased disease severity and, consequently, higher mortality rates. Furthermore, a higher BMI was found to be a risk factor for elevated antibody production. After 8 weeks from symptoms, IgG levels remained elevated, while IgM levels declined sharply.

**Keywords:** COVID-19: coronavirus disease of 2019, ELISA, RT-PCR.

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## INTRODUCTION

COVID-19 is caused by a virus called SARS-Cov-2, which was the origin of the last pandemic originating from China, resulting in significant global morbidity and mortality.

Rapid and accurate detection of COVID-19 is crucial for an effective response to prevent further transmission within large populations. Since the initial identification of SARS-CoV-2, the Centers for Disease Control and Prevention (CDC) had employed molecular assays, primarily utilizing Real-Time Polymerase Chain Reaction (RT-PCR) methods, for its detection <sup>(1)</sup>. It's important to note that PCR tests for coronavirus can only determine whether a person is currently infected with the specific coronavirus, but cannot diagnose individuals who have cleared the virus and recovered from the disease <sup>(2)</sup>. Serology tests also play a vital role as they help assess the immune response <sup>(3)</sup>, monitor disease progression, and evaluate the duration of immune protection following COVID-19 recovery <sup>(4)</sup>. The serological test in question is an ELISA-based test designed to detect SARS-CoV-2 antibodies (specifically IgG and IgM) in serum or plasma. The ELISA used by the CDC employs purified SARS-CoV-2 protein (not the live virus) as an antigen. However, it's important to acknowledge that serologic tests may exhibit cross-reactivity with antibodies generated by other coronaviruses, which cannot be entirely ruled out <sup>(5)</sup>. Diagnostic methods for COVID-19 are predominantly

employed in cases of suspected acute respiratory infection or for screening of asymptomatic cases as part of an outbreak management. Both, RT-PCR and antigen detection methods aim to identify COVID-19 during the early phase of infection. However, in instances where individuals have tested negative for COVID-19 through molecular or antigen tests but remain strongly suspected of infection, serum antibody testing can provide valuable insights into whether these individuals were previously infected with COVID-19.

Serum IgM antibodies typically appear earlier but have a shorter half-life, while IgG antibodies are the most abundant antibodies that provide longer-lasting immunity. The presence of neutralizing antibodies against SARS-CoV-2 after natural infection indicates protection against reinfection <sup>(6)</sup>.

Point-of-care serological tests offer a convenient and timely means of antibody testing. They are particularly advantageous when rapid results are required or

when access to central laboratories involves logistical challenges, such as in community-based screening, non-referral hospitals, outpatient settings, or home-based environments. Most importantly, serological tests for SARS-CoV-2 are indispensable for population-based epidemiological surveillance. These tests play a crucial role in public health policy-making by helping gauge the extent of SARS-CoV-2 spread within communities and evaluating the effectiveness of infection control strategies <sup>(7)</sup>.

The aim of this study is to assess dynamics of the COVID-19 antibodies (IgM and IgG) at 2 and 8 weeks from the onset of symptoms and their correlation with disease severity. Additionally, we aim to evaluate the level of these antibodies in relation to sociodemographic features of patients such as age, BMI, gender, and underlying chronic illnesses. Finally, we seek to determine if the pattern of antibody response holds any prognostic value.

## PATIENTS AND METHODS

This descriptive prospective study was conducted at a single center in Sulaimaniyah City, specifically Shahid Dr. Hemn Teaching Hospital, from December 4th, 2021 to March 5th, 2022. We enrolled a total of sixty-one patients, consisting of 33 males and 28 females. The diagnosis of COVID-19 was confirmed either by RT-PCR or HRCT of the chest depending on availability at the time of hospital presentation. Inclusion criteria encompassed patients aged over 16 years who exhibited symptoms for more than 2 weeks (but less than 3 weeks), were unvaccinated, and were not immunosuppressed.

We collected and evaluated sociodemographic data, including age, gender, occupation, residency, marital status, level of education, past medical history, immunosuppressant drug use, history of allergy, income (categorized as low, moderate, high), smoking (shisha or cigarette) and alcohol use for all patients.

A comprehensive physical examination was conducted for each patient, covering BMI, SpO<sub>2</sub>, vital signs, level of consciousness, chest examination and other systemic examinations. The severity of condition was classified according to WHO classification: mild, one who has respiratory symptoms without evidence of pneumonia or hypoxia, moderate; one who has pneumonia but SpO<sub>2</sub> ⇒ 90% on room air, and severe cases as pneumonia with either SpO<sub>2</sub> < 90% on room air or respiratory rate > 30 / min. Serum samples were

## *Serum IgM and IgG Titers 2 Weeks and 8 Weeks from Beginning...*

obtained at two time points: 2 weeks and 8 weeks after the onset of symptoms to determine the levels of IgM and IgG. Out of 61 patients, 39 completed the full 8-week duration of the study. Unfortunately, 16 of the remaining 22 patients passed away, and 6 did not attend follow up, despite the tests being provided free of charge.

Data were collected and analyzed using SPSS 25 software, and the relationships between different factors were assessed using one-way ANOVA, Chi-square test and t-test with a significance level of set at <0.05.

### RESULTS

We enrolled 61 patients ranging in age from 16 to 75 years; with a mean age of  $59.83 \pm 16.36$ , and 54.1% of them were males. Most of patients fell within the age

group of 30-70 (63.93%) while 32.79% of them were above 70 years, and the remaining 3.28% were under 30 years of age. In terms of residency, 90.16% of patients lived in the city center, with the remainder residing in nearby towns and villages.

Severity of cases is shown in Figure 1, Table 2 shows serum antibody levels, Table 3 shows distribution of antibodies in relation to severity, The antibody productions in relation to age and gender were not significant.

There were no significant relations with diabetes and hypertension as well. The following Table shows relation of antibody production with mortality from COVID-19 in which high levels found in those who passed away.

**Table 1. Demographic characteristics of the patients.**

Variables		Frequency	Percent
<b>Gender</b>	Male	33	54.10
	Female	28	45.90
<b>Age (years)</b>	<30	2	3.28
	30-50	15	24.59
	50-70	24	39.34
	>70	20	32.79
<b>Residency</b>	Urban	55	90.16
	Rural	6	9.84
	Employed	20	32.79
	Un-employed	5	8.20
<b>Occupation</b>	Retired	14	22.95
	Housewife	21	34.43
	Student	1	1.64
	Normal 18.5-24.9 kg/m <sup>2</sup>	26	42.62
<b>BMI</b>	Overweight 25-29.9 kg/m <sup>2</sup>	20	32.79
	Obese class 1 30-34.9 kg/m <sup>2</sup>	11	18.03
	Obese class 2 35-39.9 kg/m <sup>2</sup>	4	6.56
<b>Smoking</b>	Non-smoker	42	68.85
	Current smoker	5	8.20
	Ex-smoker	14	22.95
<b>Alcoholic</b>	Non-alcoholic	53	86.89
	Daily drinker	1	1.64
	Social drinker	1	1.64
	Ex-alcoholic	6	9.84

**Table 2. Frequency of antibody response in two different times.**

Antibody	Status	Frequency	Percent
<b>IgM (week 2)</b>	Negative	31	50.8
	Positive	30	49.2
	Negative	33	54.1
<b>IgM (week 8)</b>	Positive	6	9.8
	No data	22	36.1
<b>IgG (week 2)</b>	Negative	14	23.0
	Positive	47	77.0
	Negative	3	4.9
<b>IgG (week 8)</b>	Positive	36	59.0
	No data	22	36.1

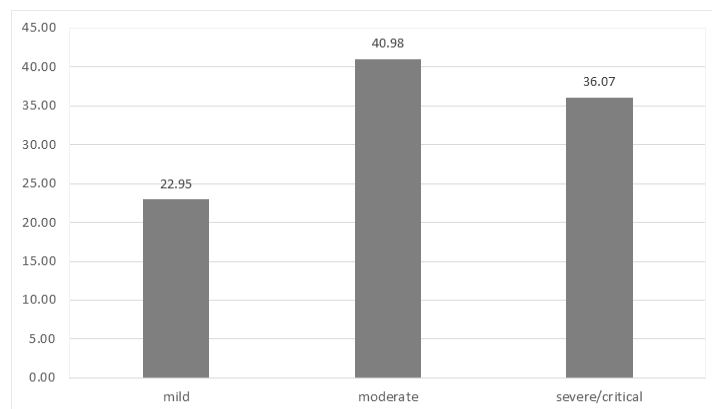
**Table 3. Correlation of the Antibody titer with the severity of the disease.**

Antibody	Severity	No. of patients	Mean	Std. Deviation	p value *
<b>IgM (week 2)</b>	Mild	14	9.6	12.4	
	Moderate	25	15.8	12.2	<b>0.012</b>
	Severe/critical	22	26.1	21.7	
<b>IgM (week 8)</b>	Mild	13	6.1	1.5	
	Moderate	20	10.4	6.4	<b>0.031</b>
	Severe/critical	6	6.2	2.0	
<b>IgG (week 2)</b>	Mild	14	25.4	16.1	
	Moderate	25	24.8	14.6	<b>0.050</b>
	Severe/critical	22	35.2	15.9	
<b>IgG (week 8)</b>	Mild	13	22.5	10.9	
	Moderate	20	39.0	11.6	<b>0.001</b>
	Severe/critical	6	29.3	11.9	

**Table 4. Antibody levels in relation to mortality.**

Antibody	Outcome	No. of patients	Mean	Std. Deviation	P- value #
<b>IgM (week 2)</b>	Dead	16	26.44	21.47	<b>0.23</b>
	Alive	45	15.13	14.71	
<b>IgM (week 8)</b>	Dead	0	0	0	
	Alive	39	8.31	5.10	
<b>IgG (week 2)</b>	Dead	16	37.30	13.37	<b>0.11</b>
	Alive	45	25.59	15.80	
<b>IgG (week 8)</b>	Dead				
	Alive	39	31.99	13.46	

# p – value was calculated using independent t-test.



**Figure 1. Distribution of clinical status of patients.**

## DISCUSSION

In this study, male patients had higher incidence of infection (54.1%), which is in agreement with other studies conducted in Iran, China and Italy<sup>(8, 9, 10)</sup>. This is likely due to the fact that this disease is community-acquired, and men tend to spend more time outside their homes. Middle aged individuals were more prone to infection in this study (63%), consistent with findings in Iran<sup>(8)</sup>, Canada<sup>(11)</sup> and China<sup>(12)</sup>. Urban residents were more affected (90.2%) than rural ones, aligning with studies in Iran<sup>(13)</sup> and India<sup>(14)</sup>, but in contrast to a study in US<sup>(15)</sup> where rural residents were more affected. The rate of infection was higher in married patients (75.4%)

compared to single patients, while another study in Bangladesh<sup>(16)</sup> confirmed the opposite. Most of the patients (57.4%) were overweight or obese, which was also observed in the USA<sup>(17)</sup> and China<sup>(18)</sup>. In contrast a study in South Africa<sup>19</sup> showed that only 19.5% of patients were overweight or obese. This discrepancy may be due to differences in the prevalence of obesity in different societies.

The incidence of infection among illiterate group was 37.7%, much higher than the rate found in a study in Ethiopia<sup>(20)</sup> which was 4.4%. More than half of the patients (60.7%) had underlying chronic illnesses, in agreement with two studies conducted in the USA<sup>(21)</sup>

and China<sup>(22)</sup>, but contrasting a study in Wuhan City<sup>(23)</sup> which showed that less than half of patients had underlying chronic illnesses.

Regarding the severity of cases, it was as follows: mild (22.95%), moderate (40.98%) and severe (36.07%). In China<sup>(24)</sup>, the percentages were different: 32.8%, 61.5% and 5.7% for mild, moderate and severe cases. The difference may be due to the fact that mild cases did not attend the hospital in this study. Regarding significant antibody production after 2 weeks for both IgM and IgG in all patients, it was 49.2% and 77% respectively, in contrast to a study in China in which the rates of IgM and IgG levels were 75% and 50% respectively<sup>(25)</sup>. After 8 weeks, the rate of antibody production for IgM and IgG were 15.38% and 92.30% respectively, while in China it was 42.9% and 90.5% respectively<sup>(26)</sup>.

The IgM and IgG antibody titers after 2 weeks of symptoms revealed a significant difference ( $P=0.012$ ) and ( $P=0.05$ ), respectively, between patients in different severity statuses. This is in agreement with a study done in China<sup>(27)</sup>. The same was found for both IgM and IgG antibody productions after 8 weeks with p-values (0.031) and (0.001), respectively. Although statistically not significant, this study showed that the higher the antibody productions (IgM and IgG) the worse the outcome would be.

To compare this to a study done in China<sup>(28)</sup>, which showed severe cases to be more frequently occurring in patients with low IgM and high IgG levels. Different age groups were associated with different levels of antibody (IgG) production; those who were younger than 30 years mounted least antibody productions while those who fell between 30-70 years had highest level of antibody productions. However, this was statistically not significant.

In conclusion, this study indicates a positive association between the level of serum antibodies (IgM and IgG) in COVID-19 cases and clinical severity during the initial phase of the disease and after 8 weeks. Notably, the IgG titer remained elevated after 8 weeks of illness, while IgM levels sharply declined. It's worth noting that patients with higher titers in the early phase of the disease exhibited higher mortality rates. Furthermore, obesity and a high BMI were linked higher antibody titers, while a history of diabetes and/or hypertension did not have a significant impact. Overall, these findings provide valuable insights into the clinical implications of antibody levels in COVID-19 cases.

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