Original Article

Journal of Occupational Health and Epidemiology
Journal homepage: http://johe.rums.ac.ir

Epidemiological Changes in Serum Virus-Specific IgM/IgG Antibody in SARS-CoV-2 Patients in Guilan Province: A Comparative Study

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Citation: Heidarzadeh A, Kazemi S, Amini Moridani M. Epidemiological Changes in Serum Virus-Specific IgM/IgG Antibody in SARS-CoV-2 Patients in Guilan Province: A Comparative Study. J Occup Health Epidemiol. 2023;12(1):12-7.

Article Info

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Article history
Received: Apr 2022
Accepted: Jan 2023

10. 61186/johe.12.1.12

Print ISSN: 2251-8096
Online ISSN: 2252-0902

Peer review under responsibility of Journal of Occupational Health and Epidemiology

Abstract

Background: The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the respiratory disease coronavirus disease 2019 (COVID-19) pandemic. To identify those who have been exposed to the virus and maybe to forecast disease immunity, antibody tests are crucial. We aimed to examine the association between prior COVID-19 infection and antibody levels, including immunoglobulin M (IgM) and immunoglobulin G (IgG) while considering the underlying illnesses in COVID-19 patients in Guilan province.

Materials and Methods: In this descriptive study, 212 individuals with a COVID-19 history participated. Blood samples were taken from people twice. The first time of blood sample collection was in April 2020. The second blood sample collection was around three months after the first time in August 2020. The total immunoglobulins levels specific to SARS-CoV-2 were measured using quantitative enzyme-linked immunosorbent assay (ELISA).

Results: The study included 212 participants, 101 (47.6%) were males, and 111 (52.4%) were women. The age of those who recovered most commonly ranged from 31 to 45 years (31.1%). The most common underlying diseases were Hypertension (31/212), obesity (23/212), cardiovascular disease (17/212), diabetes (17/212), and chronic obstructive pulmonary disease (COPD), respectively. The findings showed that, three months after recovery, the level of IgG remained persistent while the level of IgM had decreased. This revealed that 26/212, or 12.26%, had IgG levels above 1.1.

Conclusion: In individuals who had previously contracted COVID-19, the level of IgG increased over time, whereas the level of IgM decreased.

Keywords: Antibodies, Immunoglobulin M, Immunoglobulin G, SARS-CoV-2, Patients

Introduction

In December 2019, the first case of Coronavirus Disease 2019 (COVID-19), an illness caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was reported from Wuhan, Hubei Province in China [1]. On March 11, 2020, the World Health Organization (WHO) declared the outbreak of the novel coronavirus (COVID-19) a s a global pandemic [2]. COVID-19 was identified as viral-induced pneumonia based on clinical symptoms, blood tests, and chest radiography [3]. The frequency of thrombotic reactions due to the severe SARS-CoV-2 infection is increased [4].

The SARS-CoV-2 virus is extremely contagious and spreads quickly [5]. Therefore, it is crucial to identify COVID-19 quickly and treat it. Real-time quantitative polymerase chain reaction (RT-PCR) is used to measure SARS-CoV-2 RNA load to

diagnose COVID-19 [6]. Some COVID-19 patients will go undiagnosed if the diagnosis is limited to viral RNA load [7]. On March 3, 2020, SARS-CoV-2-specific IgM and IgG antibody levels were added to the diagnostic and treatment guidelines for Chinese coronavirus pneumonia because viral RNA detection has a high rate of false-negative results. Antibody detection is an alternative method for diagnosing suspicious cases, saving time and money compared to viral RNA load monitoring [8]. Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibody levels against nuclear and surface protein receptor-binding domains (RBDs) gradually increased after the onset of symptoms [9]. IgM and IgG antigens are mutually exclusive and frequently used in clinical settings [10]. IgM levels peaked at 3 weeks and then started to decline, whereas IgG levels kept increasing and could last for up to 7 weeks [11]. In this study, we investigated the association between previous COVID-19 infection and antibody levels- IgM and IgG- considering the underlying diseases in COVID-19 patients in Guilan province.

Materials and Methods

In this descriptive and comparative study, 212 patients with a COVID-19 history participated in Guilan province. The first time of blood sample collection was about in April 2020. The second blood sample collection was around three months after the first time in August 2020. This study protocol was approved by the Ethics Committee of the Iran University of Medical Sciences (code: IR . IUMS. REC . 1400. 123).

Regardless of age, all persons living in a household were invited through multistage cluster random sampling. We selected clusters from the list of Comprehensive Healthcare Centers (CHCs) and used a simple random sampling method to select households from those covered by CHCs.

Antibody Detection: Two blood samples were obtained from each subject. 2.5 ml of blood was taken from each person and 2 ml of serum was obtained from this amount. Then 10 µL of serum was used to perform the VivaDiag Rapid test kit. Once on the day, the participants arrived at the CHC and once roughly three months later. The demographics, medical history, COVID-19 symptoms in the previous three months, and history of SARS-CoV-2 exposure were all collected. A VivaDiag Rapid test kit examined samples using an enzyme-linked immunosorbent (ELISA) assay (https://www.vivachek.com/en/index.html).

To determine serum IgM and IgG antibodies against SARS-CoV2, an ELISA test was created and used to coat with SARS-CoV2 recombinant spike protein. Every participant provided their informed permission.

The data were analyzed using the Kolmogorov-Smirnov, Chi-square, and Wilcoxon tests. Based on the Kolmogorov-Smirnov test, quantitative variables (IgM/IgG) did not follow the normal distribution.

(P-value <0.005). Chi-square tests are used to the difference between qualitative-qualitative variables. Using the Wilcoxon test, changes in IgM/IgG were measured in two separate times. Data is analyzed using SPSS-22.

Results

The demographic characteristics of individuals are shown in (Table 1). About one-third of people were between the ages of 31-45 (31 %). The most common underlying diseases were Hypertension (31/212), obesity (23/212), cardiovascular disease (17/212), diabetes (17/212), and chronic obstructive pulmonary disease (COPD), respectively (Table 2). As shown in Table 3, the most common symptoms included fatigue 16.5% (35/212), pain 16% (34/212), cough 15.6% (33/212), and sore throat 15.7% (32/212), respectively.

Table 1. Demographic and clinical characteristics of individuals

Characteristics		COVID-19 patients (n=212)	Asymptomatic cases (n=137)	Symptomatic cases (n=75)
Age	0-15	29(13.7)	25(11.8)	4(1.9)
	16-30	31(14.6)	17(8)	14(6.6)
	31-45	66(31.1)	41(19.3)	25(11.8)
	46-60	51(24.1)	31(14.6)	20(9.4)
	61-75	29(13.7)	18(8.5)	11(5.2)
	>76	6(2.8)	5(2.4)	1(0.5)
Sex	Male	101(47.6)	62(29.2)	39(18.4)
	Female	111(52.4)	75(35.4)	36(17)

Table 2. Frequency of underlying diseases of individuals

Characteristics		COVID-19 patients (n=212)	Asymptomatic cases (n=137)	Symptomatic cases (n=75)
Smoking	Yes	12(5.66)	7(3.3)	5(2.4)
	No	200(94.34)	130(61.3)	70(33)
Diabetes	Yes	17(8.02)	13(6.1)	4(1.9)
	No	195(91.98)	124(58.5)	71(33.5)
Immunodeficiency	Yes	3(1.41)	1(0.5)	2(0.9)
	No	209(98.59)	136(64.2)	73(34.4)
Obesity	Yes	23(10.85)	12(5.7)	11(5.2)
	No	189(89.15)	125(59)	64(30.2)
Flu	Yes	9(4.24)	5(2.4)	4(1.9)
	No	203(95.76)	132(62.3)	71(33.5)
Hemodialysis	Yes	3(1.41)	1(0.5)	2(0.9)
	No	209(98.59)	136(64.2)	73(34.4)
Liver disease	Yes	3(1.41)	0(0)	3(1.4)
	No	209(98.59)	137(64.6)	72(34)
Hypertension	Yes	31(14.62)	17(8)	14(6.6)
	No	181(85.38)	120(56.6)	61(28.8)
Cardiovascular disease	Yes	17(8.01)	4(1.9)	13(6.1)
	No	195(91.9)	133(62.7)	62(29.2)
COPD	Yes	13(6.1)	4(1.9)	9(4.2)
	No	199(93.9)	133(61.7)	66(31.1)

Table 3. Symptoms of individuals

Characteristics		COVID-19 patients (n=212)	Asymptomatic cases (n=137)	Symptomatic cases (n=75)
Fever	Yes	28(13.2)	0(0)	28(13.2)
	No	184(86.8)	137(64.6)	47(22.2)
Chill	Yes	29(13.7)	0(0)	29(13.7)
	No	183(86.3)	137(64.6)	46(21.7)
Fatigue	Yes	35(16.5)	0(0)	35(16.5)
	No	177(83.5)	137(64.6)	40(18.9)
Pain	Yes	34(16)	0(0)	34(16)
	No	178(84)	137(64.6)	41(19.3)
Sore throat	Yes	32(15.1)	0(0)	32(15.1)
	No	180(84.9)	137(64.6)	43(20.3)
Cough	Yes	33(15.6)	0(0)	33(15.6)
	No	179(84.4)	137(64.6)	42(19.8)
Runny nose	Yes	23(10.8)	0(0)	23(10.8)
	No	189(89.2)	137(64.6)	52(24.5)
Dyspnea	Yes	17(8)	0(0)	17(8)
	No	195(92)	137(64.6)	58(27.4)
Wising	Yes	11(5.2)	0(0)	11(5.2)
	No	201(94.8)	137(64.6)	64(30.2)
Chest pain	Yes	9(4.2)	0(0)	9(4.2)
	No	203(95.8)	137(64.6)	66(31.1)
Headache	Yes	26(12.3)	0(0)	26(12.3)
	No	186(87.7)	137(64.6)	49(23.1)
Vomiting	Yes	8(3.8)	0(0)	8(3.8)
	No	204(96.2)	137(64.6)	87(31.6)
Abdomen pain	Yes	10(4.7)	0(0)	10(4.7)
	No	202(95.3)	137(64.6)	65(30.7)
Diarrhea	Yes	14(6.6)	0(0)	14(6.6)
	No	198(93.4)	137(64.6)	61(28.8)

According to our findings, 12.26% (26/212) of individuals had IgG above1.1 after three months of recovery. Most common underlying disease among them was HTN and then COPD, and the IgM of people was negative (Table 4).

Table 4. Characteristics of individuals had IgG above 1 and IgM was negative

Case no.	Sex	Age	IgM (mg/dL)	IgG (mg/dL)	Underlying diseases
1	M	4	0.03	3.4	-
2	F	6	0.02	2.1	-
3	M	7	0.03	2.1	-
4	F	10	0.03	2.9	-
5	M	14	0.02	3	-
6	F	15	0.3	5.2	Obesity
7	F	30	0.4	4.9	COPD
8	F	32	0.01	1.5	-
9	F	32	0.2	1.5	-
10	M	35	0. 1	2.6	-
11	M	36	0.01	1.2	-
12	M	36	0.02	3.2	-
13	F	36	0.09	1.3	-
14	M	38	0.03	2.5	-
15	F	40	10.3	13.6	-
16	M	47	0.01	1.2	Liver disease
17	F	48	0.01	7.2	-
18	F	49	0.01	5.6	COPD
19	M	53	0.02	2	CVD/COPD
20	F	59	0.3	11.6	HTN
21	F	60	0.05	1.8	Hemodialysis
22	M	66	0.1	6.4	HTN/Diabetes
23	M	66	0.04	6.2	-
24	F	69	0.02	3.9	HTN/Obesity
25	M	77	0.03	4.5	HTN
26	M	78	0.02	12.8	HTN

Conc: Concentration; **M:** Male; **F:** Female; **COPD:** Chronic obstructive pulmonary disease; **CVD:** Cardiovascular disease; **HTN:** Hypertension

In addition, changes in IgM/IgG between April and August had a statistically significant difference. (P-value<0.05). We presented the sensitivity and specificity for IgM/IgG at two different times separately (Figures 1 and 2). The test accuracy was 56% with (%0.95 CI: 0.465-0.671) for IgM (p = 0.187). The test accuracy is 82.5% with (%0.95 CI: 0.747-0.903) for IgG (P-value <0.05). Our results showed that IgG remains in most people about three months after exposure to the virus.

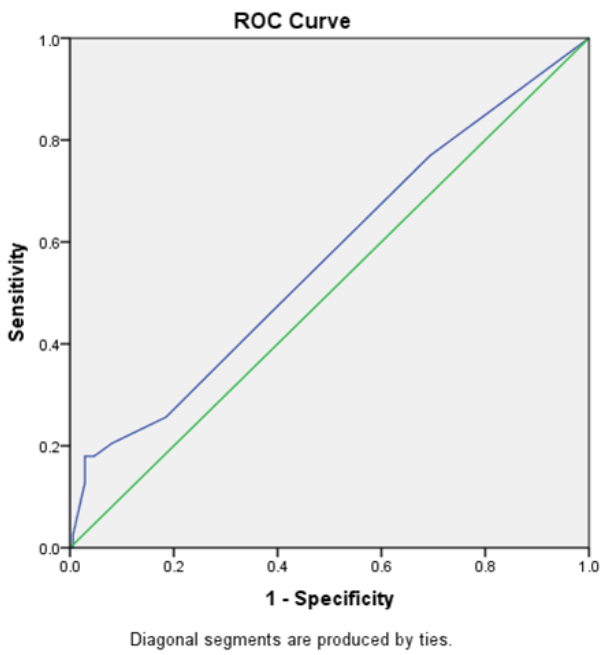

Fig.1. ROC curve for IgM in two periods of different times

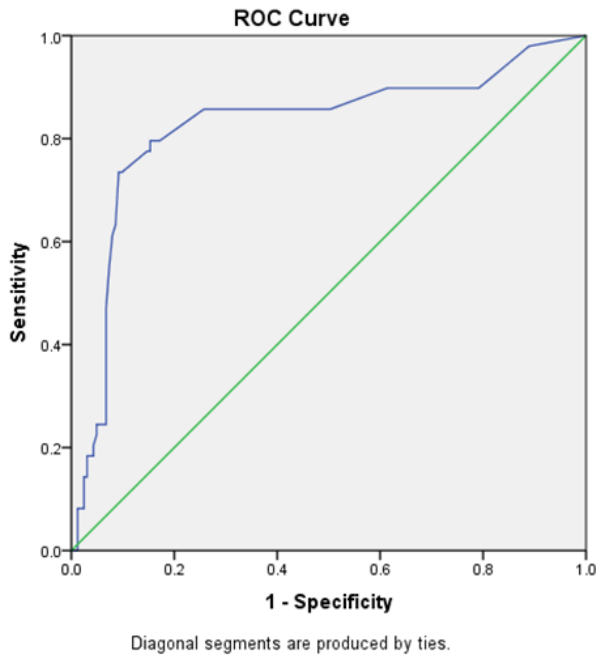

Fig.2. ROC curve for IgG in two periods of different times

Discussion

Identifying SARS-CoV-2-specific antibodies may be useful for both the profiling of COVID-19 illness and the assessment of whether the host mounted a successful humoral immune response. Our study indicated that the changes of IgM/IgG at two separate times had statistically significant differences and remained in recovered patients for more than 3 months. Xiaoyong et al. (2020) showed IgM was diagnosed earlier than IgG and vanished in most cases 4–6 weeks after symptoms, while IgG may last up to 194 days after the start of symptoms. In contrast to our study, they showed that antibodies remained in recovered patients for more than 6 months [12].

In agreement with our study, Alsayb et al. (2021) revealed an Anti-S IgG antibody in participants 90 days after infection [13]. Similar to our findings, Liu et al. (2020) estimated the lifetime of specific antibodies against SARS-CoV-2 and confirmed that the antibodies disappeared within three months after the onset of symptoms [14]. Chirathaworn et al. (2020) found similar results, which shown 4–12 weeks after disease onset, IgM, IgG, and IgA antibodies to SARS-CoV-2 remained in 13.8 %(30/217), 88.5%(192/217), and 83.4% (181/217) of recovered cases, respectively [15].

Several studies have shown an apparent decrease in antibody response over time, with variable decreasing neutralizing antibody titers [16,17]. Cheng et al. (2021) indicated for the first 5–7 weeks, the proportion of patients with positive IgM antibodies was 100%, then steadily decreased to 50 % during the next 34–42 weeks. In comparison, 34–42 weeks after symptom initiation, the positive proportion of IgG and neutralizing antibodies were 100%. Generally, those results represented that the IgM antibody in the recovered patients faded over time [18]. A similar study conducted by Jiang et al. (2021) demonstrated that 3 – 4 months after infection, most patients had virus-specific T cell responses. All COVID-19 patients had durable IgG responses. However, the IgM antibody decreased quickly [19].

Conclusion

In conclusion, our findings revealed that over time, the level of IgG increased in subjects with previous COVID-19 infections, and the level of antibody IgM decreased.

Acknowledgement

All authors appreciate the support of the Vice Chancellorship of Health of Guilan University of Medical Sciences (GUMS).

Conflict of interest: None declared.

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