Short Communication
The Difference in Immunoglobulin G Levels Between Outpatients and Inpatients With COVID-19

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) has rapidly become a pandemic since it was first reported in late December 2019. Serological reports are of great value to medical specialists in developing health policies. The detection of Immunoglobulin G (IgG) level in COVID-19 patients can specify a preclinical infection or previous exposure to the virus.

Objective: This study aims to assess the IgG rate in patients with COVID-19.

Methods: This is a cross-sectional study on 172 patients with confirmed COVID-19 (having positive PCR test) in Qazvin, Iran in 2020, including 86 inpatients and 86 outpatients. In order to measure the IgG levels, the serum samples were collected 3-5 weeks after onset of their clinical symptoms. Data were statistically analyzed in SPSS software v. 20, considering the significance level of P<0.05.

Results: Of 172 patients, 81(94.2%) inpatients and 74(86%) outpatients tested positive for IgG, while 5(5.8%) inpatients and 10(11.6%) outpatients tested negative for IgG. The mean IgG level in inpatients was significantly higher than in outpatients (P<0.001) 3-5 weeks after a positive PCR test.

Conclusion: The amounts of IgG in the sera of COVID-19 patients 3-5 weeks after the onset of symptoms can help health care authorities develop policies and control strategies by determining the burden of disease, monitoring the spread of disease, and estimating the epidemiological factors.

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1. Introduction

The Coronavirus disease 2019 (COVID-19) which was initiated in 2020, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has affected more than 43 million people in 215 countries [1, 2]. Immunoglobulin M (IgM) and Immunoglobulin G (IgG) responses against SARS-CoV-2 are detectable in serum of patients within the first week (4 days) after symptom onset. Approximately, all patients become seropositive in the first three weeks after infection [3]. There are several antigens or antibody-based techniques for detection of COVID-19 which have different sensitivity and specificity. The most important methods are enzyme-linked immunosorbent assays (ELISA), immunofluorescence method, indirect fluorescent antibody technique, and rapid immunochromatographic test [4, 5].

Serological tests are rapidly evolving and are effective in verifying the COVID-19 retrospectively. These tests had a key role in assessing the epidemiology of SARS and other coronavirus epidemics in the past, and have been demonstrated to be beneficial for detection of symptomatic or asymptomatic infected cases [6]. The value of these tests becomes even more obvious when it is found out that the polymerase chain reaction (PCR) method and other rapid diagnostic tests show positive results only when the virus is present in the body. In this regard, 25% or more patients are asymptomatic [7, 8]. It is assumed that some of people who have recovered from the SARS-COV-2 have immunity to the virus. Serological tests are useful for determining the disease's prevalence [9]. However, it is yet unknown at what level of IgG the immunity exists, or for how long this immunity will continue.

Regarding the negative impact of COVID-19 on health care sectors and economy in the world, especially in Iran, the current study aims to estimate the prevalence of IgG seropositivity rate in COVID-19 patients three weeks after PCR test become positive, and assess the association of the disease severity and IgG levels.

2. Material and Methods

This is a cross-sectional study on hospitalized and non-hospitalized patients with confirmed COVID-19 (having positive PCR test) in Velayat and BouAli hospitals of Qazvin, Iran from June 21 to September 21, 2020. A total of 172 samples were included (86 inpatients and 86 outpatients). In order to measure the IgG levels, the serum samples were collected 3-5 weeks after the PCR

test was positive. The demographic information, clinical symptoms, Oxygen saturation, and chest images of hospitalized patients were obtained from their medical records; for outpatients, the data was gathered using a questionnaire. The examinations for serum antibody against SARS-COV-2 (IgG) were conducted using ELISA kits (Pishtaz Teb, Iran).

The criteria for hospitalized patients were O_2 saturation <93%, having underlying diseases such as diabetes melitus, and moderate or severe involvement of the lungs detected by Computed Tomography (CT scan). The severity of lung involvement was classified into three categories of mild, moderate, and severe (0=No involvement, 1=25% involvement, 2=26-50% involvement, 3=50-75% involvement, 4=75-100% involvement). With regard to CT scan findings, outpatients were those with mild lung involvement. In inpatients, the involvement score up to 8 indicated moderate involvement and a score >8 indicated severe involvement.

The collected data was analysed in IBM SPSS Statistics software, version 20 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to examine the normality of data distribution. The Independent t-test and Chi-square test were used to analyze the data. The significant level was set at 0.05.

3. Results

Among 172 patients, 81 (94.2%) of inpatients and 74 (86%) of outpatients tested positive for IgG. In outpatients, 2 (2.3%) were borderline test results and 10 (11.6%) tested negative for IgG (Table 1). According to the results in Table 2, the mean total age of patients was 49.19±13.51 years, and 106 (61.6%) were males and 66 (38.4%) were females. There was no significant difference between the two groups in terms of gender (P=0.06). The O_2 saturation in inpatients (86.61±66.05 %) was significantly lower than in outpatients (96.42±1.86 %) (P<0.001). The severity of disease in the majority of inpatients was moderate (n=80, 93%) while it was mild in all outpatients (n=86, 100%). The mean IgG level 3 to 5 weeks after a positive PCR test in inpatients was significantly higher than in outpatients (P<0.001) (Table 2).

4. Discussion

Serological data are beneficial for specialists to implement health policies. The estimation of IgG levels in COVID-19 patients can indicate the number of people who have developed an immune response against the virus. Moreover, it is an representative of preclinical infection

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Table 1. The serum IgG test results of 3-5 weeks after positive PCR test

Patient Characteristics		No. (%)	Cumulative %
Inpatients	Negative	5(5.8)	5.8
	Positive	81(94.2)	100
	Total	86(100)	
Outpatients	Negative	10(11.6)	11.6
	Borderline	2(2.3)	14.0
	Positive	74(86.0)	100
	Total	86(100)	

or previous exposure to the virus. These antibodies can stay positive for up to 4-5 weeks [10]. A previous study showed that seroconversion for IgM and IgG occurred on days 10 and 14 after symptoms onset, respectively. Moreover, the highest level of seroconversion for IgG was detectable 3-6 weeks after the onset of symptoms [11]. The current study revealed that 81 (94.2%) of inpatients and 74 (86%) of outpatients were tested positive for IgG, while 2 (2.3%) had borderline IgG and 10 (11.6%) had negative test results.

Similar to the findings of our study, a seroepidemiological survey which assessed the impact of IgG levels on the severity of COVID-19 in India on 200 healthy cases and 185 confirmed COVID-19 patients showed that patients with severe infection had a greater rate of IgG (90.9%) [12].

Our study revealed that the O_2 saturation level in inpatients (86.61 %) was lower than in outpatients (96.42 %). In line with the result of the present study, a systematic review and meta-analysis study showed that O_2 saturation in hospitalized patients with COVID-19 was less than 90% [13].

Epidemiological studies have shown that SARS-CoV-2 IgG antibodies are found in more than 90% of COVID-19 patients two weeks after the onset of symptoms. It's unclear whether the remaining cases that do not acquire antibodies can be re-infected or not [14].

5. Conclusion

This study adds evidence to support the presence of IgG levels in the sera of COVID-19 patients 3-5 weeks

Table 2. Demographic information, disease severity, O_2 saturation, and IgG level in patients

Variables		Mean±SD / No. (%)		P
		Inpatients	Outpatients	
Age (y)		52.06±13.1	46.31±13.3	0.005
Gender	Female	27(31.4)	39(45.3)	0.06
	Male	59(68.6)	47(54.7)	
O_2 saturation (%)		86.61±6.05	96.42±1.86	<0.001
Disease severity	Mild	0(0.0)	86(100.0)	<0.001
	Moderate	80(93.0)	0(0.0)	
	Severe	6(7.0)	0(0.0)	
IgG level (%)		15.2±7.6	8.9±7.93	<0.001

Negative:<0.9; Borderline: 0.9-1.1; Positive:>1.1; please add this info under the table 2.

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after the onset of symptoms which can help health care authorities develop appropriate policies and plans for comprehensive infection control by determining the burden of the disease, monitoring the spread of disease, and estimating its epidemiological factors.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Qazvin University of Medical Sciences (Code: IR.QUMS.REC.1399.481).

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Authors' contributions

All authors equally contributed to the preparation of this article.

Conflict of interest

The authors declared no conflict of interest.

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