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Evaluation of measles immunity in patients with COVID-19 infection in Isfahan

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Abstract

Introduction: COVID-19 has become a widespread epidemic worldwide. The different vaccines may play a protective effect on illness intensity. Therefore, in this study, we aimed to evaluate measles IgG titer in COVID-19 patients and correlate it with disease severity.
Objectives: We evaluated the measles IgG titer and intensity of illness with measles-specific immunoglobulin G (IgG) in COVID-19 patients.
Patients and Methods: This cross-sectional study was conducted on 72 patients infected with COVID-19 with high and low severity. An enzyme-linked immunosorbent assay (ELISA) was used to detect the measles-mumps-rubella (MMR) vaccine's serum IgG antibody in COVID-19 patients. Then, the correlation of disease intensity and IgG level was evaluated using one-way analysis variance (ANOVA) in SPSS 26.
Results: In this study, there was a significant difference between illness intensity and IgG serum level of MMR in experimental groups ($P<0.05$).
Conclusion: There is a significant relationship between the severity of COVID-19 and measles IgG titer.

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Introduction

The coronavirus is a virus that originated in Wuhan, China (1). COVID-19, caused by the SARS-CoV-2, quickly spread worldwide (2). This single-stranded RNA virus encodes proteins such as spike, membrane, nucleocapsid, and envelope proteins (3). The viruses are called "Corona," which means "crown" in Latin because they have a spike protein on their surfaces. This glycoprotein binds the virus to the host cell membrane (4).

The severity of SARS-CoV-2 is categorized into mild, moderate, and severe. During the COVID-19 pandemic, children typically experience mild symptoms, and the mortality rate for this disease is much lower in children than in older age groups (5). This is probably due to the immunization children receive from birth to six years of age through various viral vaccines such as varicella, hepatitis B, measles-mumps-rubella (MMR), poliomyelitis, and rotavirus (6). These vaccines activate memory B and T cells that lead to protective immunity in the body. They also produce interferons and natural killer cells that can limit disease severity by increasing body immunity and protecting lung cells against SARS-CoV-2 (7).

Key point

Vaccination against similar viruses and prior infection with other coronaviruses has reduced the risk of severe COVID-19.

The MMR vaccine is used routinely to prevent three viral diseases: mumps, measles, and rubella. It is typically administered at 12 months, and a booster dose is given at 6-8 years of age (8). This vaccine is safe and has very few side effects. Several studies have hypothesized that the MMR vaccine may result in mild COVID-19 in children (9,10) due to the structural similarities of the spike

protein with the measles virus, as confirmed by molecular evaluations (11).

Objectives

This study aims to investigate the measles IgG titer in COVID-19 patients and correlate it with disease severity.

Patients and Methods

Study design

This study was conducted on patients with SARS-CoV-2 who were visited as outpatients in Alzahra and Amin Infectious Diseases Clinics (mild group) or were hospitalized in Alzahra and Amin Hospitals (severe group), which is affiliated with Isfahan University of Medical Sciences. Seventy-two patients were analyzed and divided into two groups based on the severity of their illness according to the WHO disease severity criteria. The two groups were low severity (31 patients) and high severity (41 patients).

1. For patients with mild disease, the following criteria apply: symptomatic patients with a diagnosis of pneumonia in chest X-ray, a respiration rate of less than or equal to 30 breaths per minute, or blood oxygen saturation of 93% or more on room air.
2. For patients with severe disease, the following criteria apply: symptomatic patients with a respiration rate of 30 breaths per minute or higher or blood oxygen saturation of less than or equal to 93%, and this condition worsens over 24 to 48 hours.

Quantitative evaluation of measles IgG

After recording the patient's demographics and medical history, 5 mL of blood samples were collected from patients infected with SARS-CoV-2 and stored at -20°C. The enzyme-linked immunosorbent assay (ELISA) determined the measles-specific IgG titer. The standards' obtained optical density (OD) was plotted against their concentration on semi-logarithmic graph paper. For the calculation of the standard curve, each signal of the standards was used. The concentration of the samples was then read from the standard curve. Finally, the patients were categorized into two groups based on the severity of their condition, either low or high.

Inclusion and exclusion criteria

The study included patients aged 18 or older diagnosed with COVID-19 by polymerase chain reaction (PCR) or CT scan and with satisfactory blood samples. Exclusion criteria needed more adequate blood samples for immunoassay or uninterpretable laboratory response. Patients with severe comorbidity were excluded.

Statistical analysis

Data analysis was done using IBM SPSS version 28. After using the Kolmogorov-Smirnov test, the mean and standard deviation were used to describe continuous variables, and the number (%) was conducted to describe categorical variables. Man-Whitney U, independent t-student, chi-square tests, multivariate logistic regression, and ROC curve were employed to compare. Adjusted odds ratio (OR), as well as their 95% confidence intervals, were calculated. A p-value less than 0.05 was considered statistically significant (two-sided).

Results

Characterization of patients

Seventy-two patients with COVID-19 (45 males, 27 females) were divided into two groups based on illness severity. The mean ± standard deviation age of patients was 60.7±14.57 years. The age distribution for all patients is shown in Figure 1.

The relationship of level of IgG and illness intensity

After performing ROC analysis to evaluate measles-specific IgG in patients with different intensities, a serum level of measles antibody above 1572 mIU/mL was introduced as a risk factor for the severity of COVID-19 disease. The obtained cut-off has a sensitivity of 66% and a specificity of 55%, resulting in good accuracy (Figure 2). In the next step, a multivariate logistic regression analysis was conducted, which revealed that individuals with an antibody level above 1572 are 3.4 times more likely to contract a severe form of COVID-19. This difference was statistically significant at 0.021, as shown in Table 1.

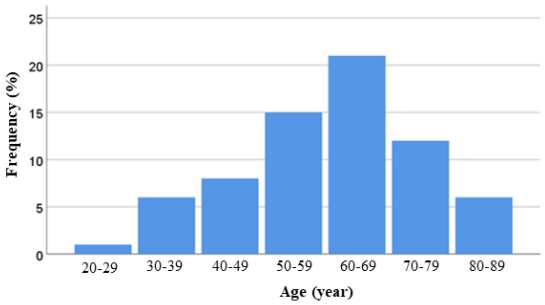

Figure 1. Age distribution of COVID-19 patients in Isfahan.

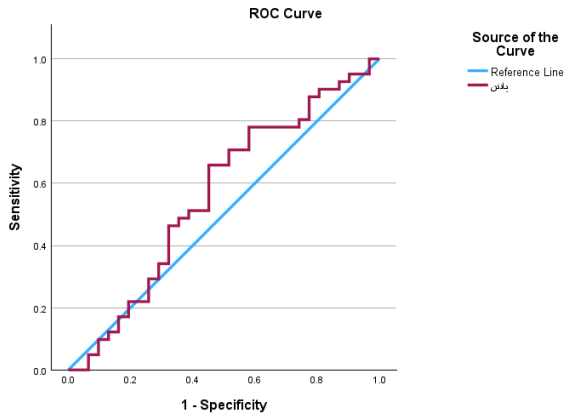

Figure 2. Relationship of level of IgG and illness intensity.

Table 1. The relationship of level of IgG and illness intensity in patients with different age and sex

Variables	Wald	*P* value	OR	95% CI	
				Lower	Upper
Serum level of measles Ig (> 1572 mIU/mL)	5.35	0.021	3.39	1.20	9.57
Sex (men)	0.05	0.817	1.13	0.40	3.16
Age (y)	1.76	0.184	0.98	0.94	1.01

Discussion

In this study, researchers evaluated the measles IgG titer and intensity of illness with measles-specific IgG in COVID-19 patients. The results of the multivariate analysis showed that individuals with an antibody level above 1572 are 3.4 times more likely to develop a severe form of COVID-19.

The severity of COVID-19 in individuals depends on their body's response to the infection. The immune response to the virus, which varies from person to person, is responsible for the severity of the illness. Some individuals' immune response is strong enough to fight off the virus, while others are too weak to do so. In some cases, the immune response can be too strong, leading to an overreaction of the immune system, which can harm the body's tissues and organs. In some individuals, the inflammatory response can also be too strong, causing a cytokine storm, which is an overproduction of cytokines, proteins that regulate the immune response. A higher IgG titer may indicate a more robust immune response to vaccination or infection (12-14). This, however, can cause damage to the body's tissues and organs and be life-threatening. Our findings suggest that a higher measles IgG titer may indicate a more robust immune response, which could result in a more severe inflammatory response to COVID-19.

Antiphospholipid antibodies were frequently found in COVID-19-infected patients, and COVID-19 infection might trigger the development of a condition of autoimmunity resembling the antiphospholipid syndrome (APS), forming what is called a "COVID-19-induced APS-like syndrome" (15). Moreover, COVID-19 patients with severe disease had higher levels of RF, an antibody that can attack healthy tissue in the body (16). A study found that people previously infected with other coronaviruses (such as those that cause the common cold) had lower antibodies against SARS-CoV-2. The study suggested that pre-existing immunity to other coronaviruses may affect the severity of COVID-19 disease (17). These findings may suggest the potential relationship between COVID-19 and other antibodies.

Various theories were discussed about the effect of different vaccinations against COVID-19 disease. Moreover, the evaluations showed that the mortality rate of COVID-19 cases is lower in countries with higher vaccination against measles (18). The mechanism of SARS-CoV2, similar to other viruses, may stop interferon production and evade natural killer cells (19); a suitable and innate immune response can help to the low intensity of COVID-19 or it may relieve the symptoms of illness (20). Vaccines play an important role in protecting against infectious diseases by producing specific IgG antibodies and memory cells (21). Due to the structural similarity with SARS-CoV-2, some viruses like measles may provide an innate immune against COVID-19. So, measles vaccine may induce immunity for SARS-CoV-2 disease (22). Also, some researchers have suggested that the MMR vaccine can improve the severe lung inflammation and sepsis resulting from COVID-19 (23,24),

A study showed a significant reverse relationship between mumps IgG titers and COVID-19 severity in individuals who had injected MMR vaccine in childhood (25). Another study found that individuals vaccinated with MMR have a lower mortality rate for COVID-19 infection (9). Despite this, a study showed that the severity of COVID-19 and its outcome are unrelated to measles IgG titer (22). However, the current study could prove the hypothesis of the protective role of measles vaccine. Also, a study evaluated the effect of age on mortality and showed that individuals with higher age have more mortality compared with the younger age group. So, older adult patients need to take preventive measures (26,27).

The limitations of the current study are the small number of exceptionally mild COVID-19 cases because patients with mild intensity are usually not hospitalized and receive medical care at home. Moreover, three antibodies are in the body after MMR vaccine administration, but only anti-measles antibodies have been measured in this study. Therefore, the results could not necessarily be attributable to anti-measles antibodies. Therefore, suggestions for further research include utilizing a larger sample size, investigating anti-mumps and other titers antibodies to assess potential effects against SARS-CoV-2, and evaluating an equal number of patients with different intensities.

Conclusion

This study observed that individuals with higher levels of measles antibodies had an increased likelihood of experiencing a more severe course of COVID-19. However, this finding should not be misconstrued to suggest that measles vaccination increases susceptibility to COVID-19. Vaccination against similar viruses and prior infection with other coronaviruses has reduced the risk of severe COVID-19. Serum measles antibody levels may predict the likelihood of developing severe COVID-19.

Limitations of the study

The study is limited by the small sample size.

Authors' contribution

Conceptualization: Morteza Pourahmad.
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Supervision: Morteza Pourahmad.
Validation: Morteza Pourahmad.
Visualization: Morteza Pourahmad.
Writing–original draft: Sara Nasirharandi.
Writing–review & editing: Mahnaz Momenzadeh.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Isfahan University of Medical Sciences (Ethical code #IR.MUI.MED.REC.1399.587). Prior to any intervention, all participants provided written informed consent. The authors have fully complied with ethical issues, such as plagiarism, data fabrication, and double publication.

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