

The Impact of Measles IgG Titer on COVID-19 Symptom Severity

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Abstract— Background: While the global efforts are now targeting the discovery of a new vaccine for the recently emerged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), investigating already existing vaccines in regard to their effect on the Coronavirus disease 2019 (COVID-19) is also of paramount importance. In this study, we aim to assess the relation between measles immunoglobulin titer in COVID-19 patients and its relation to symptoms and severity of disease. **Methods:** This was a cross sectional study conducted on confirmed COVID-19 patients admitted to the Royal Medical Services (RMS) hospitals. All patients confirmed to have COVID-19 via nasal swap for polymerase chain reaction (PCR) at royal medical services were referred to queen Alia military hospital and were included in this study. Data regarding demographic, clinical, and radiological characteristics were reviewed, followed by a laboratory test for measles immunoglobulin G antibodies. **Results:** Thirty four patients were enrolled in the study with a mean age of 30.55 (± 16.31) years. They were 24 (70.6%) men and 10 (29.4%) women. The measles IgG results were significant ($p = 0.017$), negative predictor of having symptoms related to the presence of COVID-19 infection, with an odds ratio of 0.046 (95% confidence interval of 0.004 to 0.581). Measles IgG titer didn't show a statistically significant relation with CT abnormalities ($p = 0.536$). We conclude that the presence of high measles IgG titer may ameliorate the severity of COVID-19 symptoms.

Keywords— COVID-19; Coronavirus; SARS-CoV-2; Measles; Immunity.

I. INTRODUCTION

In December 2019, a new Corona virus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged as a cause of highly contagious human disease, known as Coronavirus disease 2019 (COVID-19). The new virus caused a rapid exponential growth in number of cases that hindered tracking of many people who had close contact with symptomatic patients and raised the possibility of asymptomatic carriers being also a major cause of this spread (1). While a treatment would be beneficial, the development of a vaccine that can prevent further spread is the main goal in the battle against COVID-19 (2). Previous studies pointed to the immunity against SARS-CoV-1 conferred by a live measles vaccine (3), others also described the potential benefits of developing a vaccine for the corona virus from the measles vaccine (4). We propose that COVID-19 patients with higher measles immunoglobulin G titer would have fewer symptoms compared to those with lower titers. In this study, we aim to assess the relation between measles immunoglobulin titer in COVID-19 patients and severity of disease symptoms.

II. MATERIALS AND METHODS

Design and Settings

This was a cross sectional study conducted on confirmed COVID-19 patients admitted to the Royal Medical Services (RMS) hospitals. Institutional review board (IRB) approval

was obtained from RMS directory (-2- 29/7/2020) and written informed consent was obtained from each participant or its guardian before data collection. To assure anonymity, included participants were coded and only data collectors (a research assistant) had access to participants' codes. Participants were allowed to withdraw from the study at any time. Blood samples for measles immunoglobulins were prospectively collected from participants after being checked for eligibility.

Participants

Patients recruitment and data collection for the current study were carried out at queen Alia military hospital, Amman, Jordan, between 15th of April to 25th of May, 2020. All patients confirmed to have COVID-19 via nasal swap for polymerase chain reaction (PCR) at royal medical services were referred to queen Alia military hospital and were included in this study. We excluded patients who didn't provide an informed consent (i.e. refused to participate). We also excluded patients below the age of one year (i.e. two patients provided in supplementary material table). One patient died before being able to provide a sample for laboratory analysis.

Majority of our patients were in direct contact with covid-19 infected patients, and they were tested as part of the screening process for people in contact with confirmed COVID-19 cases. This is why plenty of the included patients had mild or no symptoms at time of presentation. All patients

were started on hydroxychloroquine treatment from first day of admission till discharge, except for pediatric age group patients (i.e. <18 years). No patients had a contraindication for hydroxychloroquine. Patients who developed pneumonia were started on broad spectrum antibiotics (i.e. Levofloxacin). Patients were considered cured if two nasopharyngeal swab cultures done 48 hours apart showed negative results on PCR.

Variables

A research assistant interviewed all patients and patients' characteristics including demographics, co-morbidities (e.g. hypertension diabetes), clinical presentation, and history of contact with COVID patients were all documented. We classified patients in regard to symptoms into either asymptomatic carriers or symptomatic, the symptoms severity may range from mild cough to severe shortness of breath.

A venous blood sample then was obtained from each patient to be analyzed for Measles IgG titer using enzyme linked immunosorbent assay (ELISA), Novatec. IgG titer was categorized further into negative if it was below 9 and positive if it was above 9.

As all patients had a high resolution computed tomography scan, we reviewed all images and classified involvement into either normal, unilateral, or bilateral. We also reviewed vital signs upon admission and at each day and we recorded the maximum temperature reached, then we classified patients as having fever if they had an orally measured temperature above 37.6 Celsius degrees.

Statistical Analysis

We used SPSS version 21.0 (Chicago, USA) in our analysis. We used mean (\pm standard deviation) to describe continuous variables (e.g. age). We used count (frequency) to describe other nominal variables (e.g. gender).

We performed binary logistic regression to analyze the effect of measles IgG titer on the presence or absence of symptoms, controlling the effect of age, gender, and co-morbidities as confounders. We also performed a binary logistic regression to analyze the effect of measles IgG titer on the presence or absence of CT scan abnormalities, controlling for age as a confounder. We presented the results as regression coefficient, odds ratio and its 95% confidence interval. All underlying assumptions were met. We adopted a p value of

0.05 as a significant threshold. We calculated the power of the current analysis using the mean IgG titer difference between both symptomatic and asymptomatic groups and using normal approximation method. We adopted a two-sided confidence interval of 80%.

III. RESULTS

Thirty two patients were enrolled in the study with a mean age of 32.43(\pm 14.87) years, the age was ranged from 2 to 66 years. Out of the total sample, 23(71.9%) were men with a mean age of 32.14 (\pm 16.98) years, and 9(28.1%) were women with a mean age of 26.74 (\pm 14.69) years (p= 0.388). Only three (9.4%) patients had comorbidities. According to our power analysis, the power at 80% confidence interval was 59.52%. Table 1 details the characteristics of included patients.

TABLE 1: Characteristics of included sample.

		Mean (standard deviation)	Count (%)
Age (Years)		32.43 (\pm 14.87)	
Gender	Male		23 (71.9%)
	Female		9 (28.1%)
Comorbidity	No		29 (90.6%)
	Yes		3 (9.4%)
Symptoms	Asymptomatic		19 (59.4%)
	Symptomatic		13 (40.6%)
Lung involvement on computer tomography	None		20 (62.5%)
	Unilateral		6 (18.8%)
	Bilateral		6 (18.8%)
Presence of fever	no fever		24 (75.0%)
	yes fever		8 (25.0%)
Measles IgG titer		19.31 (\pm 11.24)	
Measles immunity	Negative		6 (18.8%)
	Positive		26 (81.3%)

The described regression model showed a good prediction with Omnibus test of model with a p= 0.011, and a model accuracy of 59.4%. The measles IgG results were found to be a significant (p= 0.039) negative predictor of having symptoms related to the presence of COVID-19 infection, with a regression coefficient of -0.095 and an odds ratio of 0.910 (95% confidence interval of 0.831to 0.995). Other included factors didn't show any statistical significant. Figure 1 shows the percentage of symptomatic patients in the Measles immune and non-immune groups.

TABLE 2: A comparison between symptomatic and asymptomatic COVID-19 patients.

		Symptoms					
		Asymptomatic			Symptomatic		
		Mean (standard deviation)	Count	%	Mean (standard deviation)	Count	%
Age (Years)		29.52 (\pm 14.33)			36.69 (\pm 15.17)		
Gender	Male		15	78.9%		8	61.5%
	Female		4	21.1%		5	38.5%
Comorbidity	No		18	94.7%		11	84.6%
	Yes		1	5.3%		2	15.4%
Lung involvement on computer tomography	None		15	78.9%		5	38.5%
	Unilateral		3	15.8%		3	23.1%
	Bilateral		1	5.3%		5	38.5%
Presence of fever	no fever		17	89.5%		7	53.8%
	yes fever		2	10.5%		6	46.2%
Measles IgG titer		21.92 (\pm 9.12)			15.49 (\pm 13.23)		
Measles immunity	Negative		1	5.3%		5	38.5%
	Positive		18	94.7%		8	61.5%

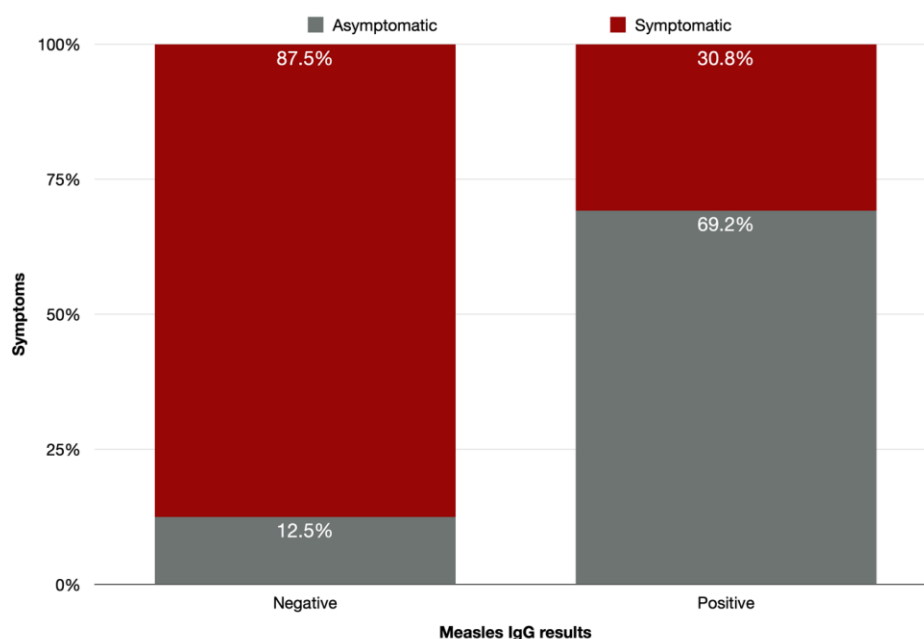


Figure 1: the percentage of symptomatic patients in the Measles immune and non-immune groups

In regard to relation of measles IgG titer and CT scan abnormalities, the model showed a good prediction with Omnibus test of model with a $p= 0.030$, with a model accuracy of 62.5%. While measles IgG titer didn't show a statistically significant relation with CT abnormalities ($p= 0.763$), age was a significant ($p= 0.041$) positive predictor for CT abnormalities, with a regression coefficient of 0.078 and an odds ratio of 1.081(95% confidence interval of 1.003 to 1.166).

IV. DISCUSSION

Previous studies showed that children under the age of 20 have generally lower susceptibility to infection and lower propensity to show clinical symptoms (5). This finding was also supported by the lower incidence of COVID-19 in communities with younger age groups (5). Despite these findings, the reason behind this age-based discrepancy is still not well understood. One of the theories to explain this finding was the presence of vaccine-induced immunity against other viruses(6).

Previous studies pointed to the potential efficacy of measles vaccine in protecting against SARS-CoV-2 virus, mainly due to similarity in structure(7). The use of MMR vaccine to induce bystander immunity against other virus strains was the hypothesis of a recent publication(8), where structure similarities between measles and the SARS-CoV-2 might be the reason(9). Our results confirmed this hypothesis, we found that patients who had higher measles IgG titer were mostly asymptomatic, unlike patients without measles immunity. The relation between vaccination and immunity against COVID-19 was also previously described for BCG vaccine, where countries with higher BCG vaccine coverage showed better outcomes for COVID-19 infections(10).

The main limitation of our study is its small sample size that included mostly healthy patients without comorbidities. Despite having positive results for our primary hypothesis, we believe larger studies should be done and should consider testing for other components of the measles mumps and rubella titer. Moreover, the majority of our patients didn't have a severe COVID-19 infection. We recommend future studies to include patients who had severe COVID-19 infection and compare their measles IgG titer with either asymptomatic or mildly symptomatic patients.

V. CONCLUSION

We conclude that patients with high level of measles IgG titer had fewer symptoms. Further studies are needed with larger sample size to clearly capture mortality and morbidity rate associated with vaccinated patients compared to non-vaccinated patients.

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Declaration of interest

All authors have no conflicts of interest to disclose.

REFERENCE

- [1] Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *International Journal of Surgery*. 2020 Apr 1;76:71–6.
- [2] Lurie N, Saville M, Hatchett R, Halton J. Developing Covid-19 Vaccines at Pandemic Speed. *New England Journal of Medicine*. 2020 May 21;382(21):1969–73.
- [3] Escriou N, Callendret B, Lorin V, Combredet C, Marianneau P, Février M, et al. Protection from SARS coronavirus conferred by live measles

- vaccine expressing the spike glycoprotein. *Virology*. 2014 Mar 1;452-453:32-41.
- [4] Frantz PN, Teeravechyan S, Tangy F. Measles-derived vaccines to prevent emerging viral diseases. *Microbes and Infection*. 2018 Oct 1;20(9):493-500.
- [5] Davies NG, Klepac P, Liu Y, Prem K, Jit M, Eggo RM. Age-dependent effects in the transmission and control of COVID-19 epidemics. *Nature Medicine*. 2020 Jun 16;1-7.
- [6] Salman S, Salem ML. Routine childhood immunization may protect against COVID-19. *Med Hypotheses*. 2020 Jul;140:109689.
- [7] Wang L, Wang Y, Ye D, Liu Q. Review of the 2019 novel coronavirus (SARS-CoV-2) based on current evidence. *International Journal of Antimicrobial Agents*. 2020 Jun 1;55(6):105948.
- [8] Salman S, Ahmed MS, Ibrahim AM, Mattar OM, El-Shirbiny H, Sarsik S, et al. Intralesional immunotherapy for the treatment of warts: A network meta-analysis. *Journal of the American Academy of Dermatology*. 2019 Apr 1;80(4):922-930.e4.
- [9] Saad ME, Elsalamony RA. Measles vaccines may provide partial protection against COVID-19. *International Journal of Cancer and Biomedical Research*. 2020 Apr 2;5(1):14-9.
- [10] D K, I B, N R, M L. Significantly Improved COVID-19 Outcomes in Countries with Higher BCG Vaccination Coverage: A Multivariable Analysis. 2020 Jun 7 [cited 2020 Aug 5]; Available from: <https://europepmc.org/article/ppr/ppr172887>

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