Original Research Article

Association of Anti-SARS-CoV-2 Virus IgG antibody levels in COVID-19 recovered individuals with age, gender, blood group and computerized tomography severity index

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Abstract

Introduction: The continued spread of corona virus disease 2019 (COVID-19) has prompted widespread concern around the world. Currently, the antibody responses against SARS-CoV-2 remain poorly understood and the clinical utility of serological testing is unclear.**Aim:** To study association of anti-SARS-CoV-2 IgG antibody levels in COVID-19 recovered individuals with age, gender, blood group and computerized tomography (CT) severity index.**Material and methods:** This cross sectional observational study was done in the department of Transfusion Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati from April 2020 to June 2020. CT severity index was classified into mild, moderate and severe depending on the CT score. Anti-SARS-CoV-2 IgG antibodies were measured by enhanced chemiluminescence immunoassay technology and signal to cutoff ratio was measured. The collected data was analyzed using SPSS 21.0, continuous data by Mann Whitney U test and categorical data by Fisher's exact test.**Results:** The mean age of study population was 45.4 years with majority of the study population between 41-50 years (36.8%). Males constituted 57.9% and remaining 42.1% were females. The most common blood group was B positive (42.1%) followed by O (36.8%) and 'A' positive (21.1%). Majority of study population (57.9%) had severe CT severity index. Anti-SARS-CoV-2 IgG antibody levels with S/C ratio of <9.5 belongs to 42.1%, remaining 57.9% had >9.5 (S/C).**Conclusion:** The significant association between CT severity index and SARS CoV-2 IgG antibodies may be helpful to select convalescent plasma donors for the centres where the facilities for SARS CoV-2 IgG antibodies testing are not available.

Keywords: Chemiluminescence assay, Corona virus, Convalescent plasma, Immunoglobulin.

Introduction

COVID-19 is the disease caused by a new coronavirus called SARS-CoV-2. WHO first learned of this new virus on 31 December 2019, following a report of a cluster of cases of 'viral pneumonia' in Wuhan, People's Republic of China[1].People aged 60 years and over, and those with underlying medical problems like high blood pressure, heart and lung problems, diabetes, obesity or cancer, are at higher risk of developing serious illness. Among those who develop symptoms, most (about 80%) recover from the disease without needing hospital treatment, 15% become seriously ill and require oxygen and remaining 5% become critically ill and need intensive care.Till date, no definitive treatment against SARS-CoV-2 has been established. A similar picture of lack of definitive treatment can be traced back to the Ebola outbreak when the use of convalescent plasma(CP) was considered to control the infection by the WHO[2].The history of CP as therapeutic therapy for SARS-CoV-1 had shown promising results in 20th century, which renders the consideration of CP in the management of COVID-19. The principle of CP is the ability of neutralizing antibodies (NAbs) from recovered patients to neutralize the pathogen and eventually causing eradication from the blood circulation.Serologic assays for SARS-CoV-2,now broadly available,can play an important role in understanding the virus's epidemiology in the general population.

Unlike direct detection methods such as viral nucleic acid amplification or antigen detection tests that can detect acutely infected persons,antibody tests help determine whether the individual being tested was previously infected or not. Serologic tests detect resolving or past SARS-CoV-2 virus infection indirectly by measuring the person's humoral immune response to the virus.

The majority of patients who recover from COVID-19 illness develop circulating antibodies to various SARS-CoV-2 proteins 2-3 weeks following infection, which are detectable by ELISA or other quantitative assays and often correlate with the presence of neutralizing antibodies. This antibody test detects antibodies to S1 protein, a primary target for NAbs against SARS-CoV-2.

In India, Drug Controller General of India permitted to conduct clinical trial of CP for COVID-19 patients in early April

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2020. The Indian Council for Medical Research (ICMR) has initiated a multi-center clinical trial by inviting letters of interest from sites which had the facilities to undertake the study. During the course of enrolling, many discussions were carried out by experts to look into the criteria for donor selection. At that time ICMR permitted to collect the CP from COVID-19 recovered patients by testing for SARS-CoV-2 IgG antibody levels only, where the facilities to check for Nabs were not available. In this study we tried to correlate the relationship between various parameters of COVID-19 recovered patients and their SARS-CoV-2 IgG antibody levels. Further we tried to establish feasibility of collecting CP from COVID-19 recovered patients with the availability of limited resources.

Aim: To study association of Anti-SARS-CoV-2 Virus IgG antibody levels in COVID-19 recovered individuals with various parameters like age, gender, blood group and CT severity index.

Material and methods

This cross sectional observational study was done in the department of Transfusion Medicine,Sri Venkateswara Institute of Medical Sciences,Tirupati from April 2020 to June 2020. Reverse transcription polymerase chain reaction **(**RT PCR) confirmed COVID-19 recovered individuals and who underwent CT chest during their disease period were included in the study. Individuals with CT chest suggestive of COVID-19 changes but RT-PCR negative and individuals with RT PCR positive didn't undergo any CT scan were excluded.

CT severity index was classified into mild(1-10), moderate(10-15) and severe(15-25) depending on the CT score. Anti-SARS-CoV-2 IgG antibodies were measured after 28 days of recovery from active disease of COVID-19 individuals, by enhanced chemiluminiscence immunoassay technology (VITROS, Ortho-Clinical Diagnostics UK). The sample result was considered as negative if the signal/cutoff (S/C) is <1 and as positive if S/C ≥ 1. The collected data and the demographic details were entered in Microsoft excel and analyzed using SPSS 21.0. Continuous data was analyzed by Mann Whitney U test. Categorical data was expressed as percentages and was analyzed by Fisher's exact test. A 'P' value of less than 0.05 was considered statistically significant.

Results

The current cross sectional study was carried out during the period from April 2020 to June 2020. During this period a total of 46 donors were screened for SARS-Co-19 IgG antibodies. After considering inclusion and exclusion criteria, a total of 19 donors were included in the study. The mean age was 45.4 years (range 25-69 years); majority of the study population were in between 41-50 years (36.8%) [Table/Fig-1]. Males constituted to 57.9% and remaining 42.1% were females.The most common blood group among all COVID-19 recovered patients were B positive 8 (42.1%), followed by 'O' positive 7 (36.8%) and 'A' positive 4 (21.1%). Majority of study population (57.9%) had severe CT severity index followed by mild (26.3%) and moderate (15.8%).The positive test result of SARS-Co-19 IgG antibody levels ranges from 3 to 12 (S/C) with mean of 7.84 (S/C). Among 19 COVID-19 recovered patients the antibody levels <9.5 (S/C) belongs to 8 (42.1%), remaining 11 (57.9%) had >9.5 (S/C).There was no significant association between the age, gender and blood group of study population with SARS-Co-19 IgG antibody levels [Table/Fig-2,3,4].There was a significant association between CT severity index and SARS-Co-19 IgG antibody levels [Table/Fig-5].

Discussion

With few treatment options available to manage COVID-19, the disease presents a unique set of challenges for healthcare providers globally. In addition to using non-drug interventions, convalescent plasma is a source of antiviral neutralizing antibodies and becomes an option for the treatment of COVID-19. The United States Food and Drug Administration (US FDA) granted emergency use authorization on August 23, 2020 for use of convalescent plasma in hospitalized patients with COVID-19[3].In India ICMR launched a multicentre, randomized controlled trial (PLACID trail) on May 4, 2020 to study the effectiveness of CP in COVID-19 patients[4].

In the present study the male population were high (57.9%) compared to the female population (42.1%), this is similar to the study done by Hou H et al, where they observed 50.6% of males and 49.4% of females[5].

In our study we observed a statistically insignificant difference between age, sex and blood group with the level of SARS-CoV-2 antibodies. In a study by Chen W et al, observed a statistically higher level of neutralizing antibodies with increasing age (p=0.020) and the male patients had similar level of NAbs compare to the females (p=0.316)[6].

We observed a statistically significant difference between CT severity index and SARS-CoV-2 antibody levels, which correlates to high level of NAbs.Chen W et al,observed a statistically significant trend of higher median NAbs titers with higher levels of pulmonary abnormalities, as reflected by larger CT scores ($p < 0.001$) [6].

In another study, using receptor-binding domain-angiotensin converting enzyme2 (RBD–ACE2 blockade), pseudo-virus neutralization, and authentic virus neutralization, observed that disease severity positively correlates to NAb responses. The patients recovered from severe illness mounted the most robust NAb responses.

Strikingly,asymptomatic patients fail to generate competent Nabs[7].The US FDA accepted the test result of the cutoff of Ortho VITROS Anti-SARS-CoV-2 IgG from S/C≥12.0 to S/C≥9.5 for qualification of COVID-19 convalescent plasma as high titer, in the manufacture of COVID-19 convalescent plasma[8]. In our study 57.9% of study population had >9.5 S/C levels of Anti-SARS-CoV-2 IgG antibodies. David G Grenache et al,[9] detected neutralizing antibodies in only 66% of SARS-CoV-2 IgG antibody positive patient samples.

Conclusion

As the CT severity index increases, there is a significant rise in anti-SARS-CoV-2 IgG antibodies and those recovered patients with increased CT severity index can be tested for anti-SARS-CoV-2 IgG antibodies for them to become as convalescent plasma donors instead of testing all COVID-19 recovered patients. This may be helpful for the centres where the facilities for NAb/SARS CoV-2 IgG antibodies testing are not available. This also helps to decrease the screening time and to have a better component quality.

Limitations: Relatively very small sample size.

Neutralizing antibodies were not done for conformation in SARS CoV-2 IgG antibodies.

Table 1: Distribution of study population in relation to age group.

Sr.No.	Age group in years	No. (%)
1.	<30	5 (10.9)
2.	31-40	12 (26.1)
3.	41-50	17 (36.9)
4.	51-60	7 (15.2)
5.	>60	5 (10.9)
	Total	46 (100)

Table 2: Association between age groups of study population and SARS-Co-19 IgG antibody levels.

Sr.No.	Age group of population	SARS-Co-19 IgG antibody levels (n =19)		p value
		<9.5 S/C (%)	>9.5 S/C	
1.	<30	2 (25)	-	0.503
2.	31-40	1 (12.5)	4 (36.3)	
3.	41-50	4 (50)	3 (27.3)	
4.	51-60	1 (12.5)	2 (18.2)	
5.	>60	-	2 (18.2)	
Total		8 (42.1)	11 (57.9)	

Table 3: Association between gender and SARS-Co-19 IgG antibody levels.

Sr.No.	Age group of population	SARS-Co-19 IgG antibody levels (n =19)		p value
		<9.5 S/C (%)	>9.5 S/C	
1.	Male	3 (37.5)	8 (72.7)	0.447
2.	Female	5 (62.5)	3 (27.3)	
Total		8 (42.1)	11 (57.9)	

Table 4: Association between blood groups and SARS-Co-19 IgG antibody levels.

Sr.No.	Blood group	SARS-Co-19 IgG antibody levels (n =19)		p value
		<9.5 S/C (%)	>9.5 S/C	
1.	A positive	3 (37.5)	1 (9.1)	0.117
2.	B positive	2 (25)	6 (54.5)	
3.	O positive	3 (37.5)	4 (36.7)	
Total		8 (42.1)	11 (57.9)	

Table 5: Association CT severity index and SARS-Co-19 IgG antibody levels.

Sr.No.	CT severity index	SARS-Co-19 IgG antibody levels (n =19)		p value
		<9.5 S/C (%)	>9.5 S/C	
1.	Mild	5 (62.5)	0	0.010
2.	Moderate	2 (25)	1 (9.1)	
3.	Severe	1 (12.5)	10 (90.9)	
Total		8 (42.1)	11 (57.9)	

References

1. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease-covid-19. Accessed on 12/03/2021.
2. Casadevall A,Pirofski LA.The convalescent sera option for containing COVID-19. J Clin Invest 2020;130:1545-8.
3. US Food and Drug Administration. Recommendations for Investigational COVID-19 Convalescent Plasma. FDA. 2020. Available from:https:// www.covidplasma.org.Accessed on 12/ 03/2021.
4. Agrwal A, Mukherjee A, Kumar G, Chatterjee P, Bhatnagar T, Malhotra P et al. Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentre ranadomised controlled trial (PLACID Trial). Br Med J 2020;371:m3939.
5. Hou H,Wang T,Zhang B,Luo Y,Mao L,Wang F et al. Detection of IgM and IgG antibodies in patients with corona-virus disease 2019. Clin Transl Immunology 2020;9:1-8.
6. Chen W, Zhang J, Qin X, Wang W, Wang LF, et al. SARS-CoV-2 neutralizing antibody levels are correlated with severity of COVID-19 pneumonia. Biomed Pharmacother 2020;130:1-7.
7. Chen X, Pan Z, Yue S, YU Fie, Zhang J, Yang Y, et al. Disease severity dictates SARS-CoV-2-specific neutralizing antibody responses in COVID-19. Sig Transduct Target Ther.2020; 180:1-6.
8. https://www.fdanews.com/ext/resources/files/2021/02-05-21-COVID 19.pdf. Accessed on 12/03/2021.
9. David G Grenache,Chunyan Ye,Steven B Bradfute. Correlation of SARS-CoV-2 Neutralizing Antibodies to an Automated Chemiluminescent Serological Immunoassay.The Journal of Applied Laboratory Medicine 2021;6:491-5.

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