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Seroprevalence of SARS-CoV-2 IgG Antibodies among Post-Infection COVID-19 Patients and Post Vaccination at a Tertiary Care Hospital

Sidra Sadiq[1]*, Maria Khan[2], Tayyaba Sadiq[3], Mirza Muhammad Dawood Ramin[1], and Najeeb Ul Haq[3]

Abstract

Background: The SARS-CoV-2 pandemic has generated a global health crisis, which needs more comprehensive analysis into immunological reactions to improve treatment and vaccine options.

Objective: The aim of this study was to evaluate SARS COV2 spike protein antibodies against COV19 in post infection and post vaccinated individuals.

Methods: 256 patients were included in this cross sectional study conducted at Rehman Medical Institute (RMI), Peshawar. We described the immunogenicity 35 days after vaccination and 90 days after infection in 70 patients and established its correlation with age and gender, specimens were collected and investigated for SARS-CoV-2 spike protein antibodies by consuming Electro-chemiluminescence immunoassay (ECLIA) (Abbot Advice Dx SARS-CoV-2 IgG II assay (USA).

Results: 97% of patients revealed robust positive findings to SARS COV2 spike proteins antibodies i.e. >50 IU/mL. Our study shows that post infected and post vaccinated individuals can mount robust immune reactions against SARS-CoV-2.

Conclusion: Majority of the patients had significant higher antibody titers against SARS COV2 after infection and vaccination. Males and younger individuals developed a significant humoral immunity compared to females. Those vaccinated had antibody titers one scale higher than infected patients. Constant monitoring of antibodies titers in infected or vaccinated population is estimated to attain humoral immunity grade against SARS-CoV-2 infection.

Keywords

SARS-CoV-2; COVID 19; Vaccination; Antibodies

List of Abbreviations

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; WHO: World Health Organization; ASCs: Antibody secreting cells; ECLIA: Electro-chemiluminescence immunoassay; APC: Antigen-Presenting Cell; ACE2: Angiotensin-Converting Enzyme 2; AT2: Alveolar type 2 progenitor; RT PCR: Reverse Transcriptase Polymerase Chain Reaction; CT: Cycle Threshold

*Corresponding author: Sidra Sadiq, Department Clinical Chemistry & Endocrinology, Rehman Medical Institute, Peshawar, Khyber Pakhtunkhwa, Pakistan, Tel: +923209395802; E-mail: sidrasadiq920@gmail.com

Introduction

The coronavirus a novel positive-strand RNA coronavirus of Coronaviridae family declared as pandemic by WHO on March 11, 2020 [1], continues to spread despite after repeated lockdowns and long-term control measures in most countries. The envelope (E), membrane (M), nucleocapsid (N), and spike proteins(S) in the SARS-CoV-2 genome are non-structural and structural proteins, respectively. The S glycoproteins interact with angiotensin converting enzyme 2 (ACE2) via epithelial Alveolar type 2 progenitor (AT2) cells during SARS-CoV-2 infection and regulate several intracellular biochemical mechanisms and pathways to enhance viral pathogenesis [2]. As a conclusion, the anti-SARS-CoV-2 antibody response was assessed using an assay based on the spike protein's trimerized, stabilized ectodomains [3].

The humoral immune response to infection or vaccination has two basic outcomes: antibody production by antibody secreting cells (ASCs), which can provide rapid serological immunity, and the development of long-lived memory B cells, which can mount recall responses [4,5]. Memory B cells drive the recall response by producing new antibodies by establishing new ASCs or re-entering germinal centers for subsequent rounds of somatic hyper mutation if circulating antibodies fail to protect against a future exposure[6,7]. COVID-19 infected persons are expected to have to have antibodies and memory B cells for at least 6 to 8 months [8-12]. In SARS-CoV-2 exposed persons, no memory responses or effective vaccine dose protocols have been investigated [13].

Control techniques such as mask wearing, physical separation, and the use of contact tracing were beneficial to decrease virus spread but no significant advantages were observed, and it grew into the fact that vaccinations were the only realistic way out of the pandemic. The most of COVID-19 vaccination approaches to date have aimed to generate neutralizing antibodies against S, hence preventing SARS-CoV-2 infection in its early stages. Several vaccine candidates have been demonstrated to be safe and effective in clinical studies [14] and vaccination in huge numbers (when used in combination with other existing control measures) is recognized as one of the most important aspects of pandemic management. Although the results of clinical trials are encouraging, real-world evidence on vaccines is still lacking.

We aimed to evaluate SARS-CoV-2 spike antibody levels among post infected and post vaccinated group of individuals in a tertiary hospital.

Materials and Methods

After ethical approval from institutional ethical approval board, a cross sectional study was conducted on 256 participants to assess SARS-CoV-2 spike antibody response in post-infected and post-vaccinated individuals in Peshawar populations, among which 70 patients had a positive history of post infection or post vaccination. Post infection status was validated by PCR report. Post vaccination status was validated by vaccination certificate. Samples for IgG quantitative antibodies were obtained by trained personnel at Rehman Medical Institute, Peshawar at an average day 90 and day 35 in post infection and post vaccinated individuals, respectively. A written and informed consent was taken from all subjects prior to sample collection and

written consent was obtained. Patients receiving immunosuppressive therapy or suffering from an immunosuppression-related disease, no history of infection or vaccination as well as pregnant women were excluded.

SARS-CoV-2 in Nasopharyngeal swab RT-PCR

Standard protocols were used to collect a nasopharyngeal swab, and the presence of SARS-CoV-2 was identified by reverse transcriptase polymerase chain reaction (RT-PCR) (Light Mix Modular SARS-COV2 COVID 19 RdRP by Roche Switzerland) testing as directed by the manufacturer. According to manufacturer recommendations, a cycle threshold (CT) result of 15 to 30 was considered positive.

Serological screening

An Electro-chemiluminescence immunoassay (ECLIA) (Abbot Architect USA) based on double-antigen sandwich assay principle was tested using Abbot Advice Dx SARS-CoV-2 IgG II assay (USA) kit, for quantitatively determining antibody levels to the SARS-CoV-2 spike protein. Blood samples were collected using acid citrate dextrose, sodium citrate, potassium EDTA, tri potassium EDTA or lithium heparin tubes. The serum samples were incubated with biotinylated and ruthenylated RBD antigen, following which streptavidin coated micro particles were added, and relocated to the measuring cell, where micro particles were magnetically caught onto the exterior of the electrode. The manufacturers recommended antibodies cutoff level of 50.0 AU/mL, above which is considered positive and vice versa. The diagnostic measuring interval of 22.0 to 25 000.0 AU/mL was found to be linearity.

Results

Of the total 256 enrolled patients, 70 individuals took part in the study. In 30 individuals with positive PCR result, the time between PCR and antibody screening ranged between 30 to 150 days (mean 90 days). Similarly, in 40 vaccinated individuals the time between vaccination and antibody screening ranged between 21 to 60 days (Mean 35 Days). Male subjects were 69 % while 29.6 % were females. The mean age was 44 years (range 8 -79).The test findings revealed positive SARS-COV-2 spike antibody titers among 70 of the enrolled patients. Antibody levels were reported using units of AU/mL. 97% patients had positive antibody titers of >50 AU/mL. In males, the antibody titers were 3589 AU/mL. Females had an antibody titer of 1968 AU/mL (Table 1). Males had significant immunogenic responses compared to females; this difference (3589 vs. 1968) was statistically significant (p=0.001). Immunogenicity decreased with advancing age (p <0.001) (Table 2). Post infection peak antibody titers were 1305 AU/mL. Post vaccination peak antibody titers were 1773 AU/mL (Table 3).

Table 1: Demographic Characteristics of the patients: n=70.

Variables	Frequency (%)
Gender	
Male	49 (69%)
Female	21 (29.6%)
Average Age (years)	44
Range (years)	8-79
Antibody titers AU/mL in Positive cases 68 (97 %)	
Males	3589
Females	1968

Table 2: Correlation of age and gender with immunogenicity.

Variables	rs	P value
Gender (Male)	0.141	0.001
Gender (Female)	0.82	0.236
Age group (years)		
<30	0.72	0.215
30-40	.221	.003
40-49	0.35	0.001
50-59	.076	.272
>60	.0.72	.028

Table 3: Post Infection and post vaccination IgG spike antibodies titers.

Post infected patients	30	Post Vaccinated patients	40
Antibody titers	1305 AU/mL	Antibody titers	1773 AU/mL

Discussion

The immune responses to SARS CoV-2 spike antibodies must be determined in order to comprehend the potential protective implications. We initiated and established serological screening on 70 patients to determine IgG quantitative antibodies against S protein in a tertiary care hospital.

In current study, the SARS CoV-2 post infected or post vaccinated individuals were pre-determined for investigation. A substantial portion enrolled in study presented remarkably higher anti-SARS-CoV-2 antibody levels of >50 AU/mL, the results are comparable to other clinical trials [15,16]. In our study, 42.8% (30) had past history of CoVID-19 infection while 57.14 % (40) were vaccinated individuals.

It adds to existing research that people who had been previously exposed to COVID-19 had significant humoral immunogenic response compared to non-infected individuals consistent with findings of a study conducted on 3816 individuals in Baltimore [13]. Similar findings are evident from other studies [17,18].

Only a few studies have observed the gender gap in COVID-19 incidence and disease progression and an independent review of the responsible factors is still absent. Based on differences in innate and adaptive immunity, steroid hormone synthesis by the gonads, and sex chromosomal variables it is interesting to know that males showed a greater immunological response than females reported in a study conducted in Italy [19]. In viral infections, sex hormones are known to regulate innate immune responses. Estrogens influence receptor responsiveness and the creation of pro-inflammatory cytokines, which can be life threatening if released in excess. Estrogens that bind to the estrogen receptor alpha (ERa) or beta receptor (ERb) can thereby influence the immune system. All immune cells express ERa, which is essential in their maturation and regulation. It is also immunological protective, since it is involved in the generation of interferon (IFN) type I and the activation of natural killer (NK) cells. ERb is engaged in pro-inflammatory events and has the opposite effects as ERa [20,21]. The decrease of estrogen receptors (ERa) in elderly women is linked to immunosuppression, indicating that estrogen can protect against COV-19.

It was found out that Antibody levels declined with advancing age [15,22]. The immune responses were analyzed in a study conducted in 30,000 population in USA.It is interesting to know that antibody response can last up to months following infection(18). Similarly in another study conducted in 34 individuals in US it was found that peak antibody titers occurs between 30 to 152 days post infection

[23]. Similar findings are evident from a study conducted in Israel involving 1378 Health care workers [15].

Protective correlations have already been established for a range of viral diseases. These associations are typically established on a certain titer of antibody obtained from vaccination or spontaneous infection, which considerably diminishes the chance of (re)infection for example, the Hem agglutination inhibition level for influenza virus, where a 1:40 level minimize the possibility of transmission by 50% [24]. It's uncertain whether human infection with SARS-CoV-2 prevents against reinfection [25] and, if so, for how long. We know that neutralizing antibodies are produced by common human coronaviruses and that these antibodies can last for decades, preventing against reinfection or attenuating symptoms if reinfection occurs [26].

It is perceived that infection with SARS-CoV-2 protects non-human primate models from reinfection for at least some duration [27,28]. Although we cannot give definitive proof that these antibody responses guard against reinfection we have confidence in that is extremely probable to reduce the likelihood of reinfection and in the instance of break through infection, may attenuate infection.

We've perceived a great effort by researchers and the pharmaceutical sector to create a vaccine against SARS-CoV-2 during the last year. When immune reactions to vaccine were studied among 100 participants of a Pakistani population, it was interesting to know that considerably robust immune response after a single vaccine shot were stimulated [16] and similar results were stated by another study [29]. The majority of the patients developed humoral response 35 days post administration of a second dose of COVID19 vaccine [15].

The present study is important not only for strategically planning policy at organization and national level but also reveal necessity for accurately determining SARS-CoV-2 spike antibody levels among the two groups of infected and vaccinated people globally. A small sample size was used in the current study. Establishing Immunogenicity in post-infection and post-vaccination individuals, as well as the impact of age and gender on humoral immune responses requires more research.

Conclusion

These findings imply that maximum number of patients developed immunity post infection and post vaccination. The data suggested that male and younger individuals are more efficient in developing humoral immune responses than females and older population. Although more research is needed, this information could have significant implications for the development of COV-19 vaccination regimens. At the same time our findings are both promising and beneficial to the scientific community.

Conflicts of Interest

There is no conflict of interest claimed by the authors.

Disclosures

None

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Author Affiliations   Top

[1]Department Clinical Chemistry & Endocrinology, Rehman Medical Institute, Peshawar, Khyber Pakhtunkhwa, Pakistan

[2]Department of Consultant Microbiologist, Rehman Medical Institute, Peshawar, Khyber Pakhtunkhwa, Pakistan

[3]BS MLT, Rehman College of Allied Health Sciences, Peshawar, Khyber Pakhutunkhwa, Pakistan