Research Article

Efficacy Of Covid-19 Vaccination Among Health Care Workers From Amritsar District Of Punjab

Dr. Amandeep Kaur (Ph.D), Dr. Kanwardeep Singh (MD Microbiology), Dr. Sarabjot Singh (Ph.D), Dr. Mohan Jairath (Ph.D), *Dr. Shailpreet Kaur Sidhu (MD Microbiology)

1Research Scientist, Department of Virology, Government Medical College, Amritsar-143001, India
2Professor and PI, Department of Virology, Government Medical College, Amritsar-143001, India
3Research Scientist, Department of Virology, Government Medical College, Amritsar-143001, India
4Research Scientist, Department of Virology, Government Medical College, Amritsar-143001, India
5Associate Professor and Co-PI, Department of Virology, Government Medical College, Amritsar-143001, India.

ARTICLE INFO

ABSTRACT

Various studies on antibody mediated immune response against SARS-CoV-2 infection has revealed that Abs plays crucial role in COVID-19 disease. Waning of Abs post vaccination (2 doses) prompt the consideration for booster dose. Therefore, measuring the antibody titres (Total Abs- IgG+IgM+IgA and Neutralizing Abs) at different phases of vaccination, will aids in updating vaccines effective against each and every strain. Hence, the present study was conducted to measure Ab titres at different phases of vaccination.

Materials and methods: The present study was conducted on 67 healthcare workers (38 males and 29 females within the age group of 22-64 years) as cases who got vaccinated for COVID-19 vaccine at Government Medical College and Hospital, Amritsar. The first blood samples were taken at day 0 before vaccination followed by 4th week, 8th week, 12th week, 24th week, 1 year post vaccination and 12 weeks post booster dose. The semi-quantitative detection of anti-SARS-CoV-2 total Abs (IgG+IgM+IgA) and Neutralizing Abs in the samples were detected using ErbaLisa COVID-19 IgG indirect ELISA kit.

Results: Abs were detected in all the samples taken at different intervals (4th week, 8th week, 12th week, 24th week, 1 year after complete vaccination and at 2 weeks post booster dose of vaccine). A consistent rise of Ab index was seen from 4th week till 24th week post vaccination and after that a decline was noticed until 1 year. Ab index again showed an increase post booster doses No statistically significant difference was found between antibody index, age and gender.

Conclusion: Though, Ab index was seen post COVID-19 vaccination, however, its durability needs to be investigated to determine further requirement of vaccine doses.

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Corresponding Author: Dr. Shailpreet Kaur Sidhu, Associate Professor and Co-PI, Department of Virology, Government Medical College, Amritsar-143001, India.
INTRODUCTION:
The coronavirus disease (COVID-19) is caused by SARS-CoV-2 has rife worldwide that has detrimentally impacted the globe and posed grave challenges to public health. Globally, over 300 million people are infected with COVID-19 which resulted in 5 million deaths as on 15 January 2022. To curb this, various novel vaccines received Emergency Authorization Use (EAU) by numerous agencies, which are then administered to health-care workers, front-line workers, elderly individuals including those with comorbidities. India initiated Covid-19 vaccination on 16 January 2021, with strategy expanded in phased manner to cover individuals aged 60 years and above and those between 45 and 59 years with specified comorbidities (phase 2, 1 March 2021), all individuals aged 45 years and above (phase 3, 1 April 2021), and all individuals aged 18 years and above (phase 4, 1 May 2021).[1] Till today, antibody mediated immune response against SARS-CoV-2 infection has been studied that revealed antibodies play a crucial role in COVID-19 disease development, however, no such studies are there for adaptive immune response.[2] Waning antibody levels against SARS-CoV-2 has been correlated with infection after vaccination, prompting consideration for booster dose.[3,4] Numerous studies on vaccine potency that focus on patients with COVID-19 infection [5] and protective effects of various vaccines against differential strains of SARS-CoV-2, may leads to overestimation of level of priming immunity which is not generalized for entire population.[6] Therefore, measuring the antibody percentage inhibition (Neutralizing Abs) at different phases of vaccination, will aids in updating vaccines effective against each and every strain.[7] Hence, the present study was conducted to measure Ab percentage inhibition at different phases of vaccination.

MATERIALS AND METHODS:
The present study was conducted on 67 healthcare workers (38 males and 29 females within the age group of 22-64 years) as cases who got completely vaccinated for 2 doses of COVID-19 vaccine at Government Medical College and Hospital, Amritsar. Before commencement of the study, ethical permission and approval was obtained from the Ethics Commission at Viral Research and Diagnostic Laboratory (VRDL), Government Medical College (GMC), Amritsar, India (GMC/IEC/21/KD/14; DATED 20/4/2021). Individuals vaccinated with COVID-19 vaccine were enrolled as cases while individuals with previous SARS-CoV-2 history and/or were symptomatic at the time of sample collection were excluded. About 5ml of blood sample was withdrawn to detect COVID-19 specific IgG Ab base line titre. The first blood samples were taken at 4th week, 8th week, 12th week, 24th week, 1 year post vaccination and 2 weeks post booster dose. The detection of anti-SARS-CoV-2 Neutralizing Abs percentage inhibition in the samples were detected using ErbaLisa COVID-19 IgG indirect ELISA kit using standard protocol as described by manufacture. Antibody percentage inhibition was evaluated on the basis of cut off values following comparison between negative control and sample. The sample was evaluated negative if its value was less than 30% inhibition whereas if the value obtained was more than cut more than equals to 30% it was considered as positive.
FINDINGS:
Antibody titre was measured in 67 HCWs at 4th week, 8th week, 12th week, 24th week and 1 year after complete vaccination. Another sample was taken at 2 weeks post booster dose of vaccine. Abs were detected in all the samples taken at different intervals and a consistent rise of Ab index was seen from 4th week till 24th week post vaccination. However, a decline was noticed thereafter until 1 year which can be attributed to reduced immune potency. Ab index again showed an increase post booster dose which is due to an active involvement of the immune system functions in building up defense against the future encounters of the pathogen (Table 1). The age grouping (Group 1= 20-50 years; Group 2= 51-70 years) for the data was done based on a similar study carried out by Davies et al. [8]

The Chi-square test was performed to evaluate the difference between the expected and the observed frequencies between the age group and the gender which was found to be non-significant (p-value <= 0.05).

Analysis of Variance (Anova) was performed to study the difference in the means of Antibody index, Age group and Gender. The p-value for all the observations across the time periods was found to be non-significant (p<=0.05). The correlation between the antibody index of different time points in the study was studied using a correlation matrix or correlogram. All the time points in the study only show a positive correlation among each other with varying intensities implying that between two variables if one increases by proportion the other also increases simultaneously. The p-values for the correlation between antibody index of the post vaccination time points were calculated which showed significance between 56 days P.V and booster dose at p<=0.05. The correlation study also showed little significance between 56 days P.V and 1 year P.V at p<=0.01 (Figure 1).

Table 1: Antibody percentage inhibition at different intervals (4th week to booster dose)

<table>
<thead>
<tr>
<th>Antibody %age inhibition</th>
<th>Male</th>
<th>Female</th>
</tr>
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<tbody>
<tr>
<td>4th week</td>
<td></td>
<td></td>
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<tr>
<td>Age Group 1</td>
<td>43.50 ± 4.6</td>
<td>36.35 ± 3.4</td>
</tr>
<tr>
<td>Age Group 2</td>
<td>46.05 ± 5.3</td>
<td>48.14 ± 12.6</td>
</tr>
<tr>
<td>8th week</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Group 1</td>
<td>68.50 ± 2.8</td>
<td>67.96 ± 3.7</td>
</tr>
<tr>
<td>Age Group 2</td>
<td>67.94 ± 4.4</td>
<td>75.03 ± 7.5</td>
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</table>
Antibody %age inhibition 12\textsuperscript{th} week Post vaccination

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
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<tbody>
<tr>
<td>Age Group 1</td>
<td>91.28 ± 2.2</td>
<td>89.11 ± 3.9</td>
</tr>
<tr>
<td>Age Group 2</td>
<td>89.50 ± 3.4</td>
<td>92.65 ± 5.3</td>
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Antibody %age inhibition 24\textsuperscript{th} week Post vaccination

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<tr>
<td>Age Group 1</td>
<td>114.32 ± 2.4</td>
<td>109.57 ± 5.1</td>
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<tr>
<td>Age Group 2</td>
<td>116.11 ± 3.9</td>
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Antibody %age inhibition 1 Year Post vaccination

<table>
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<tr>
<td>Age Group 1</td>
<td>91.44 ± 3.3</td>
<td>86.54 ± 4.1</td>
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<td>Age Group 2</td>
<td>87.11 ± 4.0</td>
<td>97.07 ± 7.7</td>
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Antibody %age inhibition Booster Dose

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<th>Female</th>
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<tbody>
<tr>
<td>Age Group 1</td>
<td>124.02 ± 2.5</td>
<td>117.97 ± 5.1</td>
</tr>
<tr>
<td>Age Group 2</td>
<td>124.48 ± 4.8</td>
<td>125.05 ± 8.9</td>
</tr>
</tbody>
</table>

Figure 1: Correlogram for Antibody %age inhibition (Neutralizing Abs)
DISCUSSION:
In this longitudinal study, a consistent rise of Ab index was seen from 4th week till 24th week after vaccination; however, a decline was noticed thereafter until 1 year. Again, an increase in Ab index post booster dose was observed indicating that antibody levels could be maintained but not in a significant manner. Various other studies also showed the similar results demonstrated that SARS-CoV-2 specific antibodies were present in the serum up to 18 months.\[9,10,11,12\]

Possible reason is that SARS-CoV-2 shares 79.6% genomic sequence with SARS-CoV, thus, IgG has the potential to exist persistently.\[13\] In a study by Bayram et al.\[14\] and Uysal et al.\[15\] 99.6% seropositivity was observed 4 weeks after vaccination. However, Uysal et al.\[15\] indicated statistically significant reduction in Ab titre post 12 weeks of vaccination and observed that despite decreasing, it still persist in the serum. Another study noticed that RBD antibody response decreases post 6 weeks of vaccine administration which was quite less compared to Ab titres obtained one week after vaccination.\[16\] Tartof et al.\[17\] scrutinize the potency of mRNA vaccine for up to 6 months and found it to be 73% amid individuals fully vaccinated. It has also been reported that vaccine efficacy was 90% during first 5 months in hospital admissions and fell off to 47% after that and to boost up the efficacy, additional dose is required post 6 months of 2 doses of vaccination.\[18\] Tartof et al.\[17\] investigated Ab titres on 27th day post 1st vaccination and 14th day after 2nd dose and levels were seen to be higher on 27th day in previously infected ones than non-infected ones as compared to 14th day.

A clinical trial performed using Moderna vaccine reported higher levels of antibodies six months after the second dose \[20\] while another report on ChAdOx1 showed high level of antibodies 3 months after a single dose. \[21\] The reason behind this disparity is that antibodies that are present in blood for certain period of time emerges as humoral immune response among individuals with prior infection or vaccinated against COVID-19. These Abs give rise to short lived plasma cells in secondary lymphoid organs that escalate expeditiously in the blood and then drops during first 3 months, however, the Abs that are produced by long lived plasma cells in bone marrow decline slowly in the following period.\[22\] A serological analysis performed an average of <3 months confirmed that antibodies last for several months after vaccination.\[23,24\] On the other hand, a rapid linear decline in IgG Abs was observed amid individuals who were not infected as compared to those who were infected.\[25\] This could be explained by assuming additional amount of Abs produced after each infection and after vaccination, which needs to be investigated in follow-up longitudinal studies comparing two groups with little concern about time-invariant confounders, such as age, sex, and BMI.

Age is another important parameter that determines the immune response. As the antibodies derived from T cells decreases and B-lymphocyte generation also reduces with effect to age, the Ab response after infection and vaccination may not be sufficient to combat the disease.\[26\] Various studies investigated impact of vaccination against influenza, hepatitis A, hepatitis B, pneumococcus, tick-borne encephalitis
(TBE), tetanus, and SARS-CoV-2, and observed that Ab response after vaccination was inversely proportional to age. \[23, 27\]

In the present study, no statistically significant difference was found between antibody index, age and gender which was consistent with the report that demonstrated non-significant relationship between age and antibodies, but observed higher antibody titres in the age group 30–39 (38.5%). \[15\]

In a study, Ab response was measured in a pool of vaccinated HCWs and found that 100% participants were seropositive for anti-S and neutralizing Abs; however, both anti-S and neutralizing Ab titres showed tendency to decline with age especially among women who showed higher Ab titres after initial vaccination, however, this difference was eradicated by second dose. \[28\] Another study explored significant difference between variables such as age groups, gender and Ab titre and also suggested that waning of Abs among females were much slower but constant after 3 months of vaccination than males who displayed consistent decrease rate. \[29,30\] This might be because of sex hormones, X-chromosomes and environmental factors. \[31\]

The main findings of the present study was that higher levels of Ab %age inhibition was seen in samples collected at 6 months which decline later and again increases upon administration of booster dose. Also, no significant difference was noticed between Ab index, age and gender. The difference in the levels of Abs could be due to that COVID-19 vaccines are capable of exposing immune system only to certain part of the virus, hence immune system is not able to produce variety of antibodies post vaccination as it would after an actual SARS-CoV-2 infection. Further investigations are eminent to determine the durability of Abs post vaccination by performing serological analysis and monitoring the decrease in Ab index over time. This approach should be used for all individuals in future regardless of vaccination or infection to regulate the requisite for further doses.

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CONFLICT OF INTEREST: None

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Conflict of Interest: None declared

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